Anhang 4-G: Ergänzende Unterlagen

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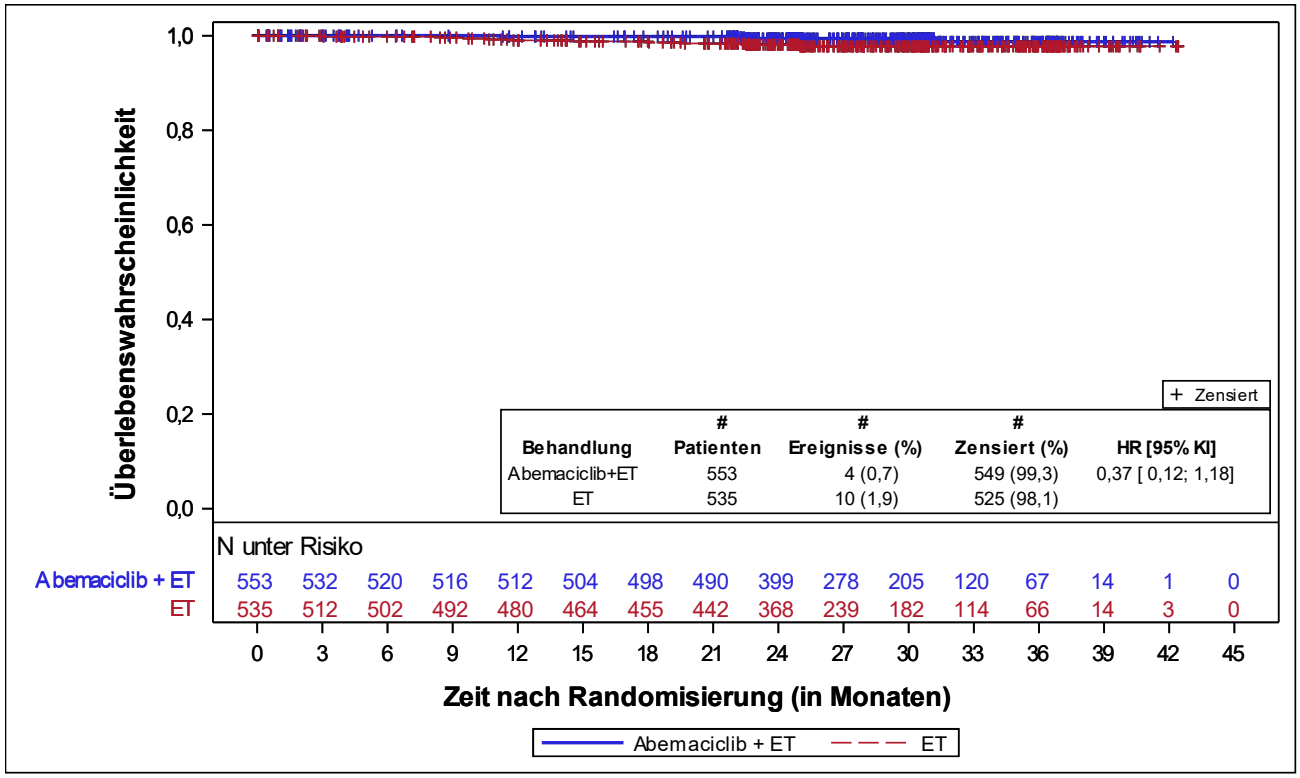
Anhang 4-G1: Ergänzende Darstellung der Hauptanalysen der Studie MONARCH-E

Anhang 4-G1.1: IDFS: Kaplan-Meier-Kurven der Teilendpunkte

Abbildung 22 (Anhang): Kaplan-Meier-Kurven der Teilendpunkte von IDFS

Kaplan-Meier-Kurven - lokales Brustkrebsrezidiv
Kohorte 1 Population - ITT - Prämenopausal



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Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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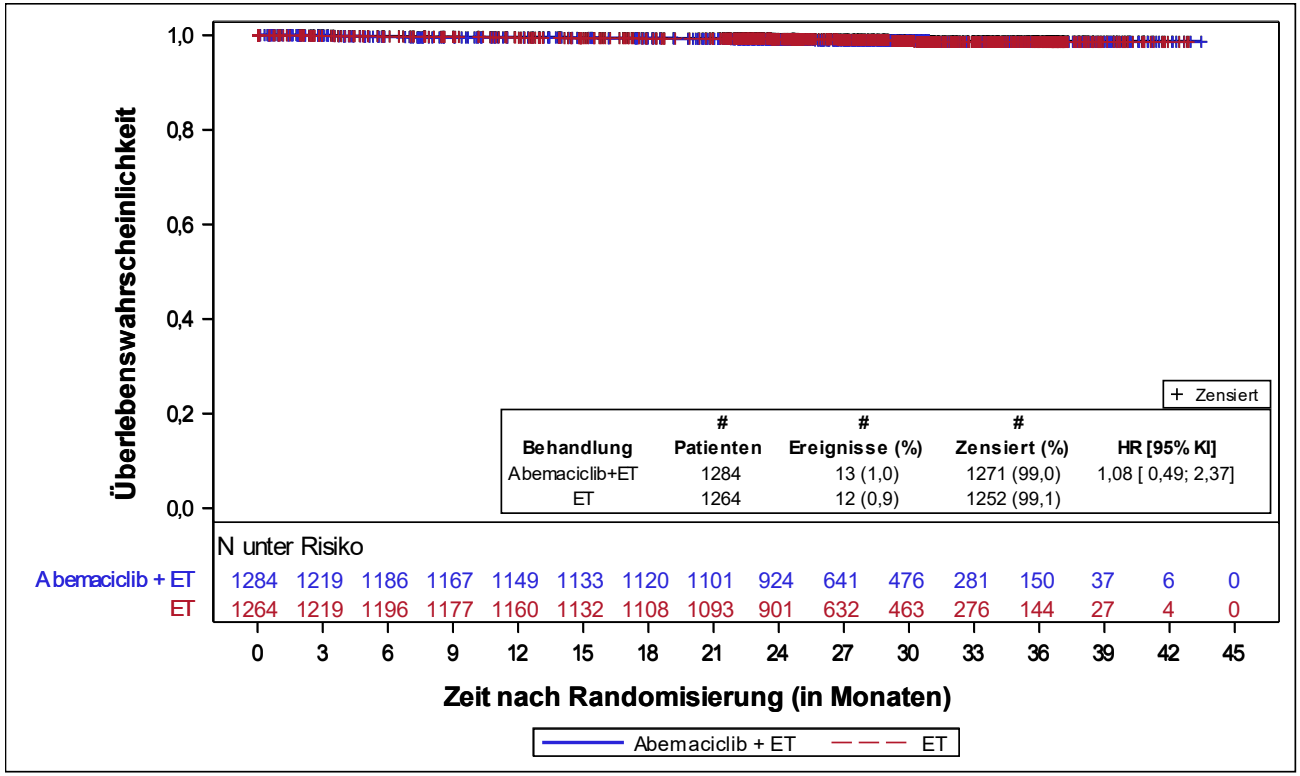
Kaplan-Meier-Kurven - lokales Brustkrebsrezidiv
Kohorte 1 Population - ITT - Postmenopausal



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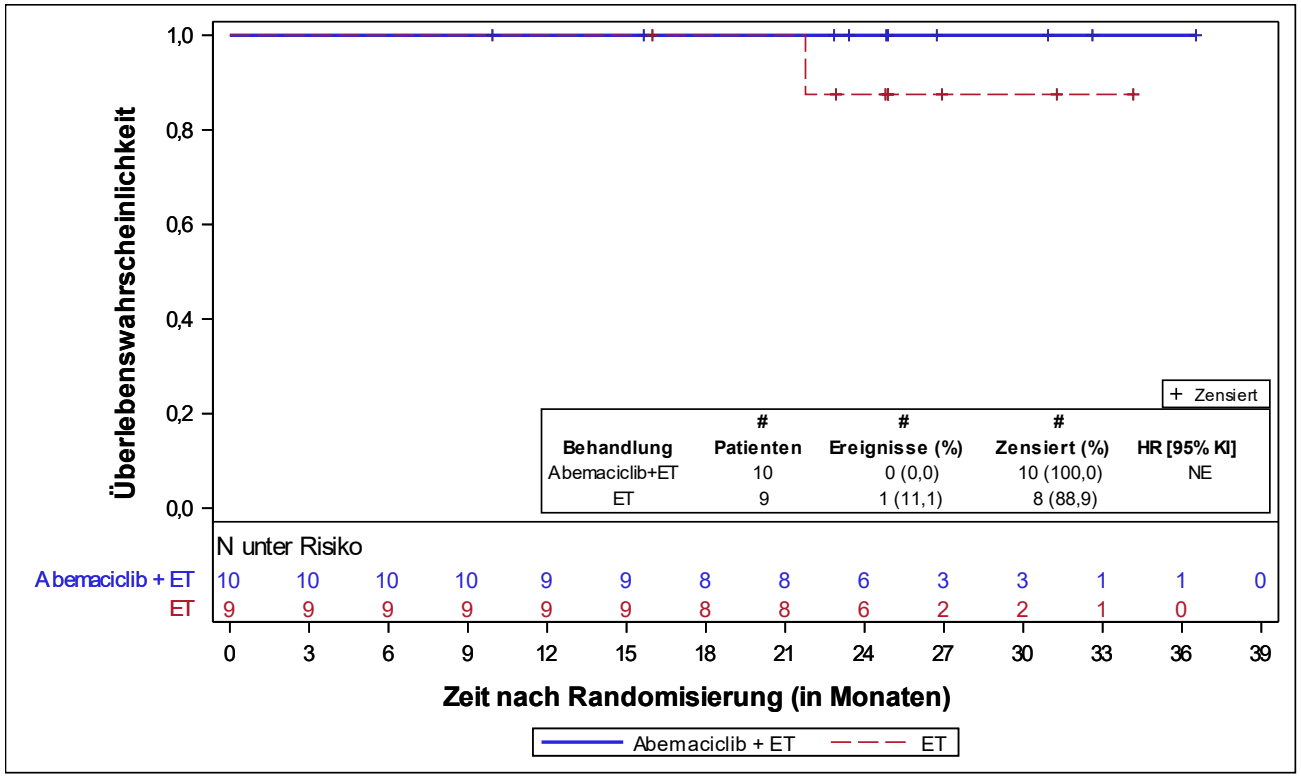
Kaplan-Meier-Kurven - lokales Brustkrebsrezidiv
Kohorte 1 Population - ITT - Männer



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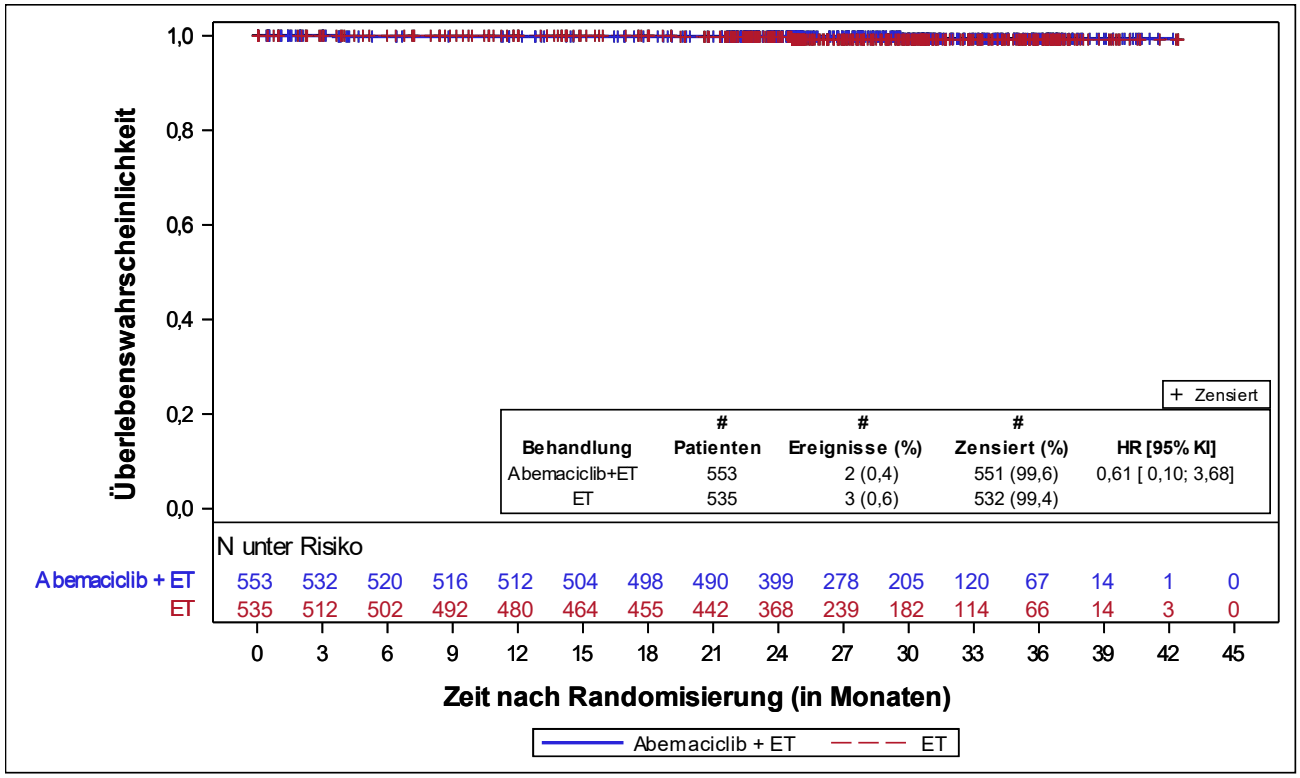
Kaplan-Meier-Kurven - regionäres invasives Brustkrebsrezidiv
Kohorte 1 Population - ITT - Prämenopausal



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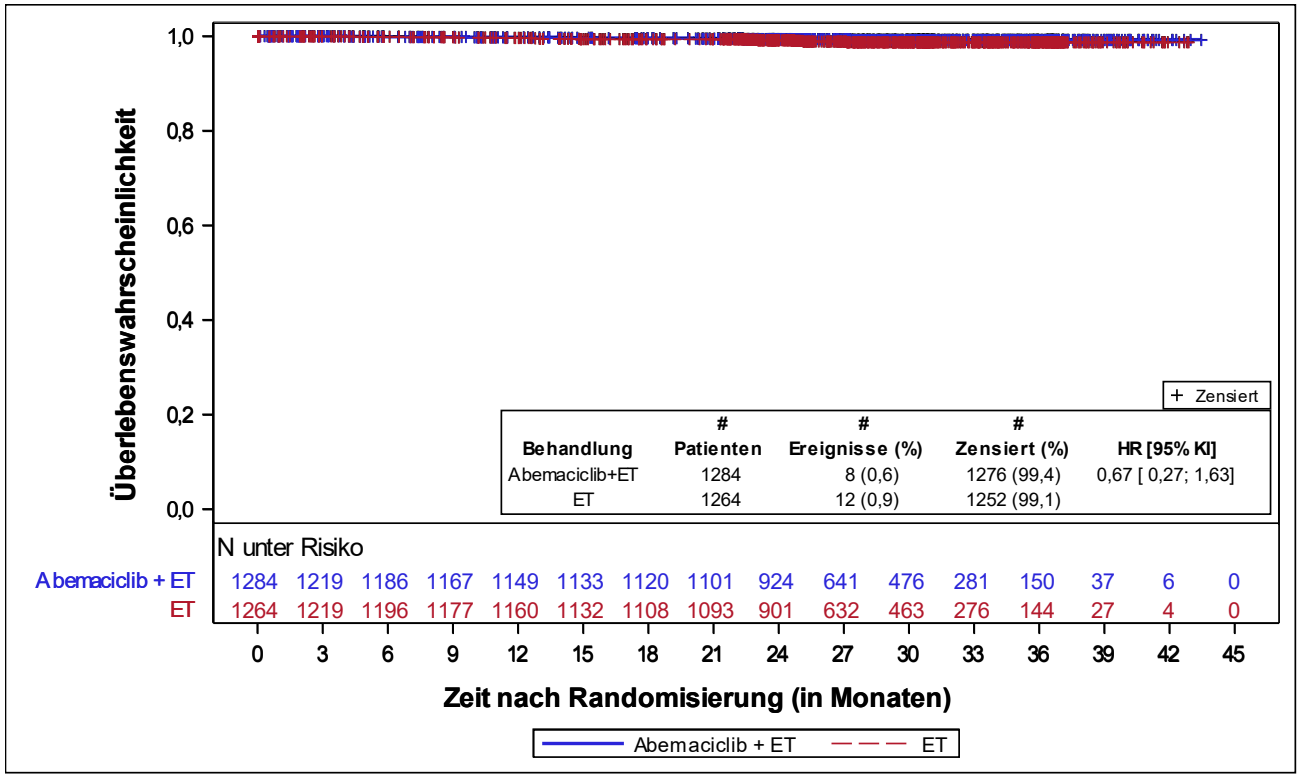
Kaplan-Meier-Kurven - regionäres invasives Brustkrebsrezidiv
Kohorte 1 Population - ITT - Postmenopausal



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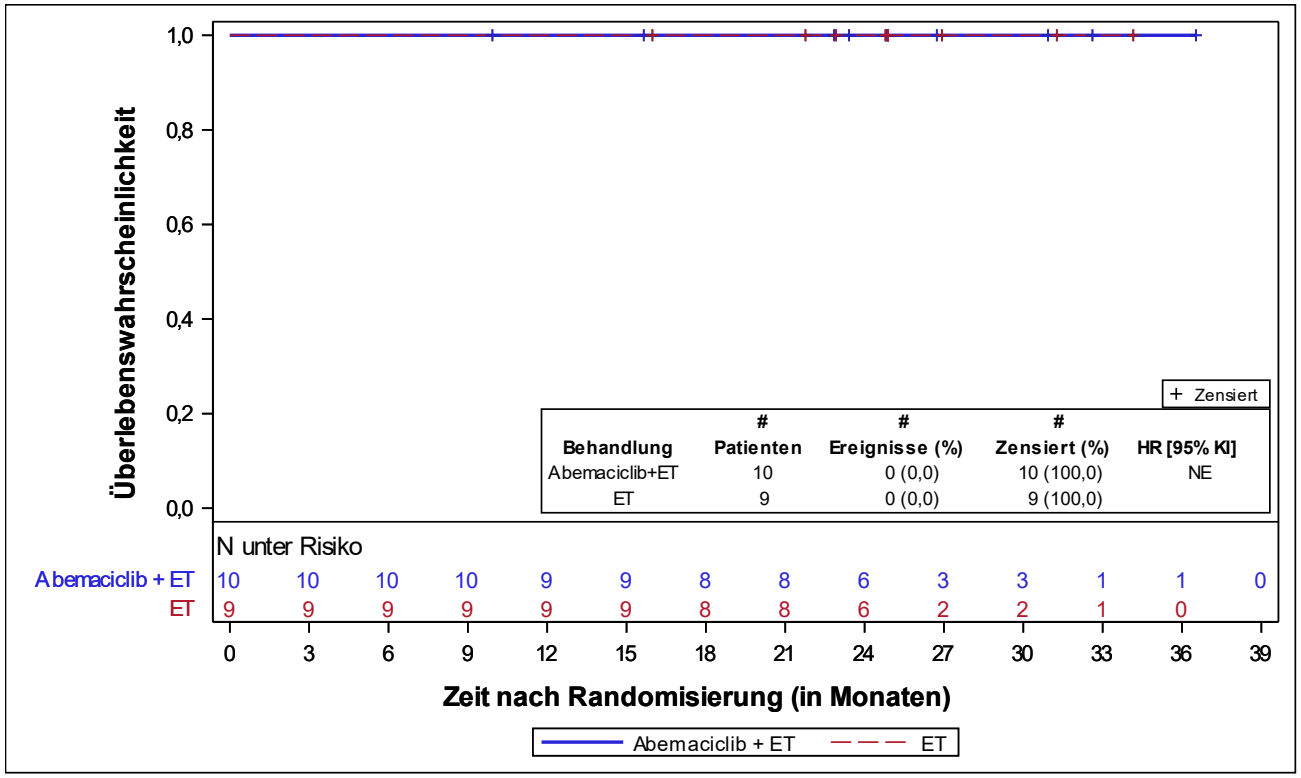
Kaplan-Meier-Kurven - regionäres invasives Brustkrebsrezidiv
Kohorte 1 Population - ITT - Männer



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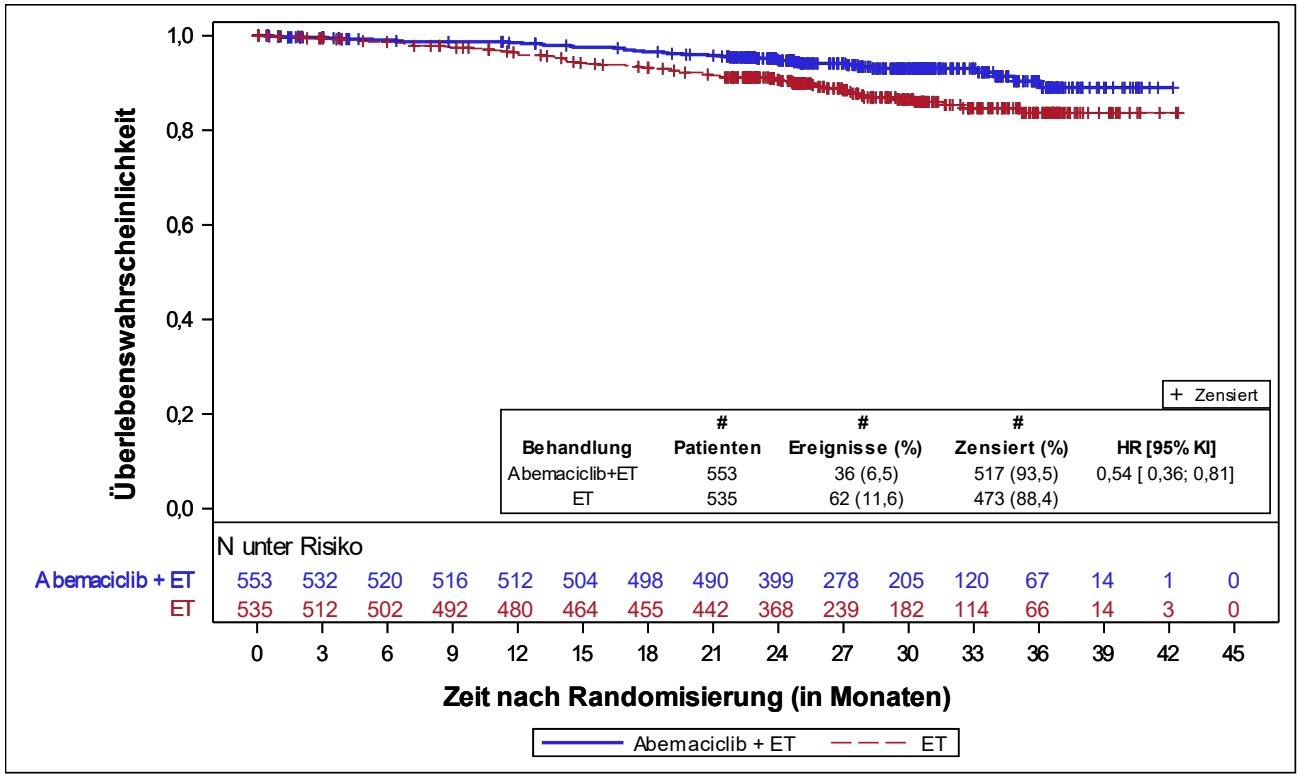
Kaplan-Meier-Kurven - Fernrezidiv
Kohorte 1 Population - ITT - Prämenopausal



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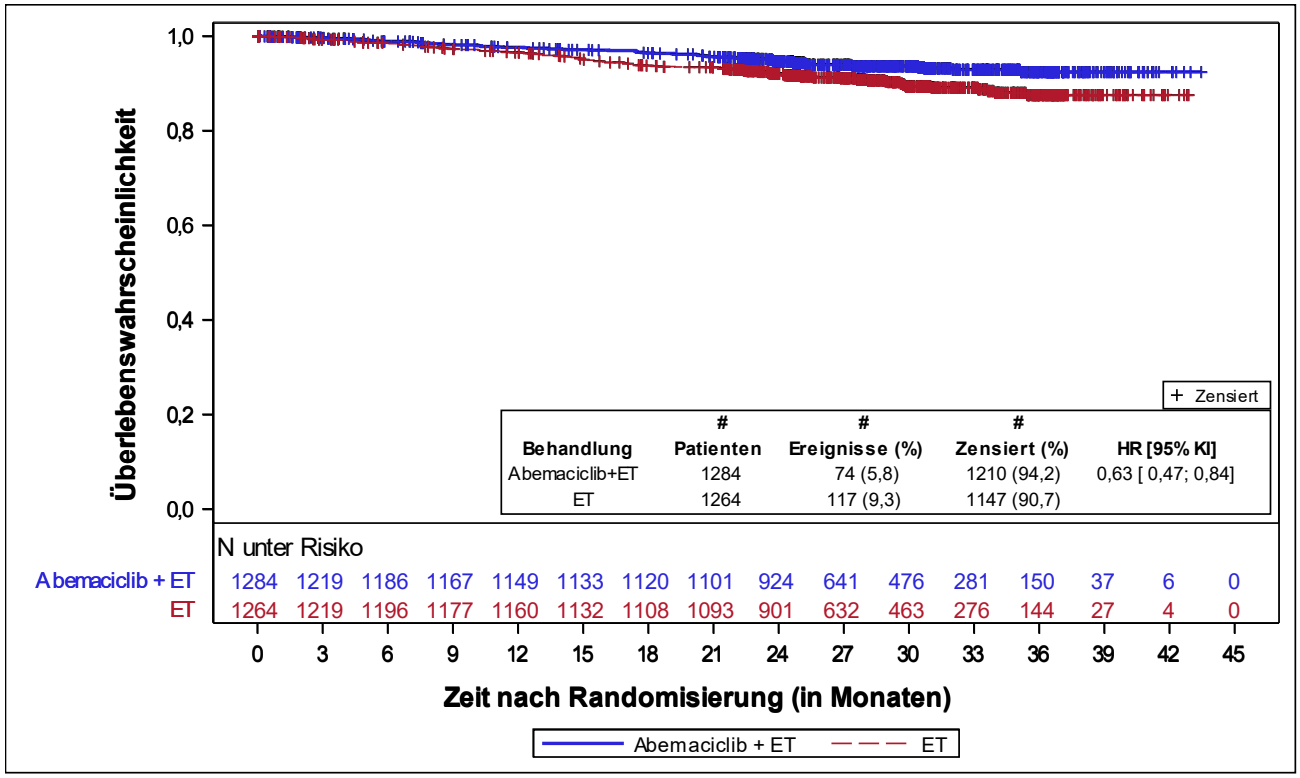
Kaplan-Meier-Kurven - Fernrezidiv
Kohorte 1 Population - ITT - Postmenopausal



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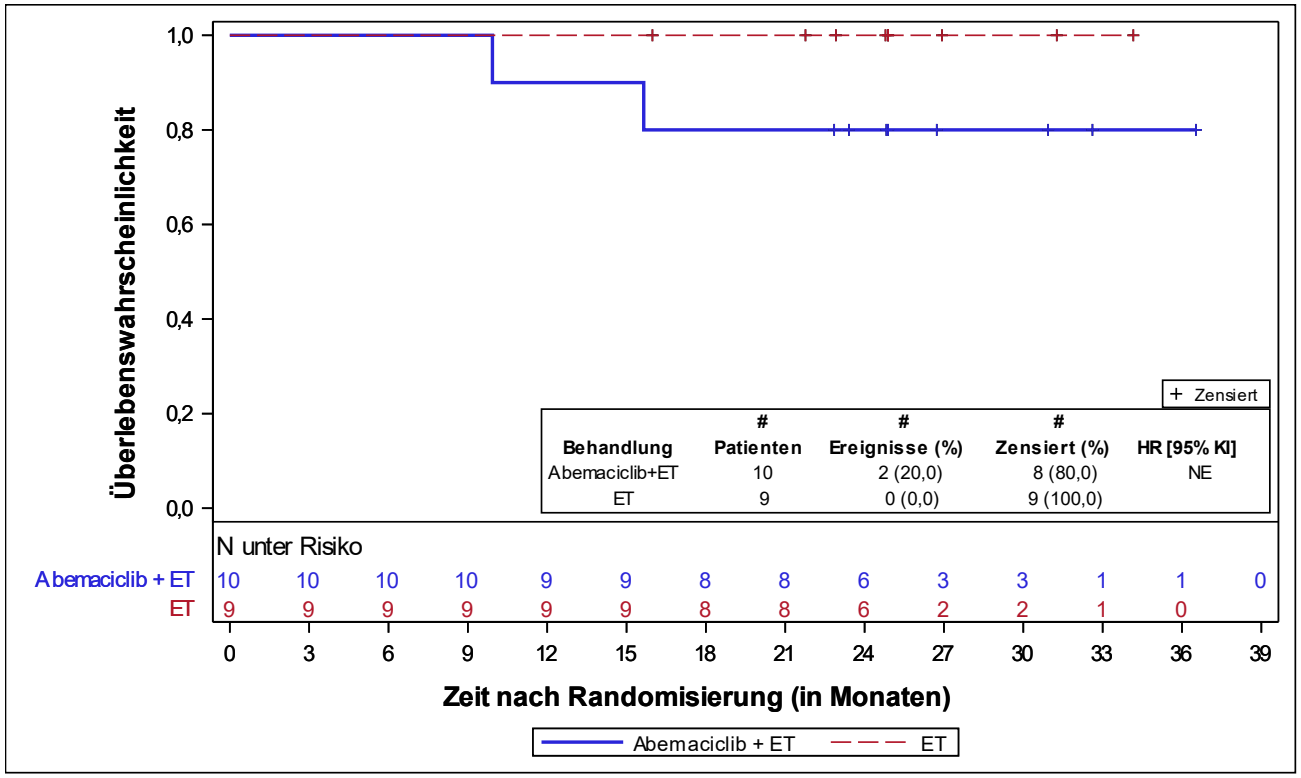
Kaplan-Meier-Kurven - Fernrezidiv
Kohorte 1 Population - ITT - Männer



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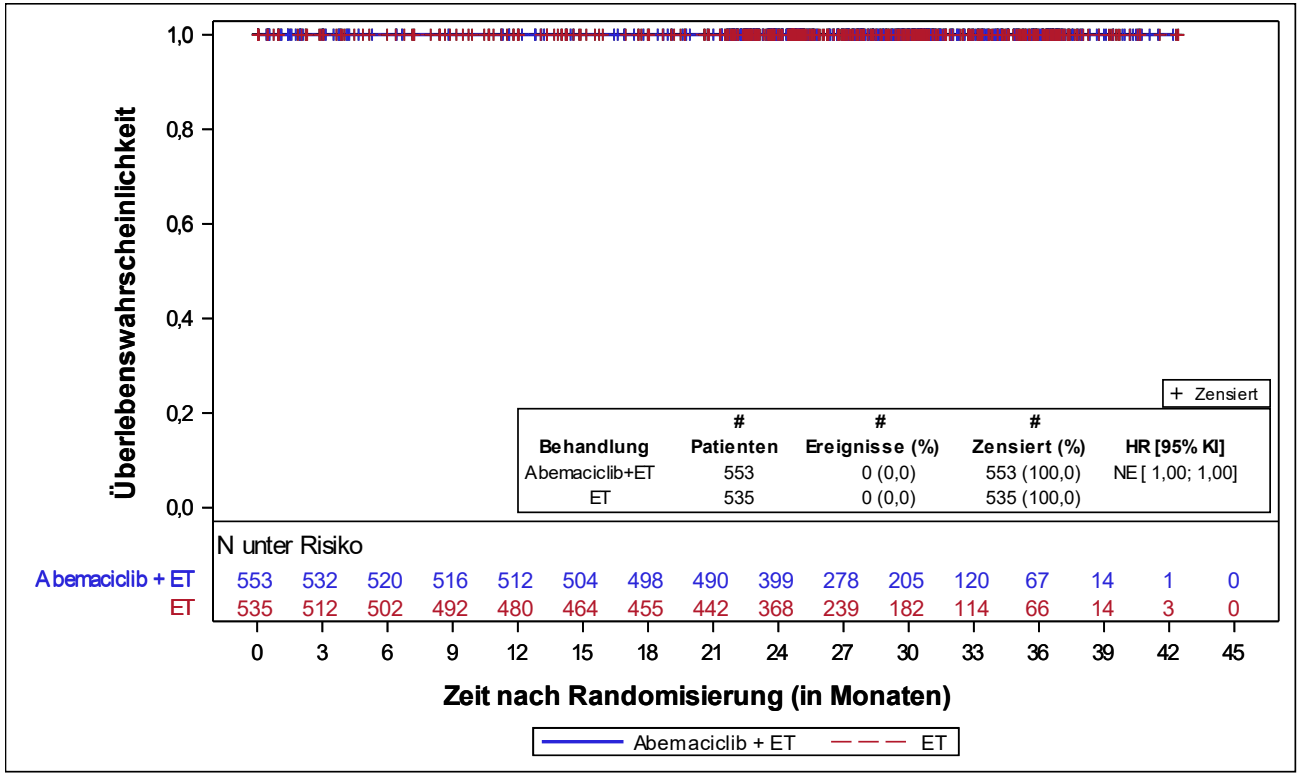
Kaplan-Meier-Kurven - Tod jeglicher Ursache
Kohorte 1 Population - ITT - Prämenopausal



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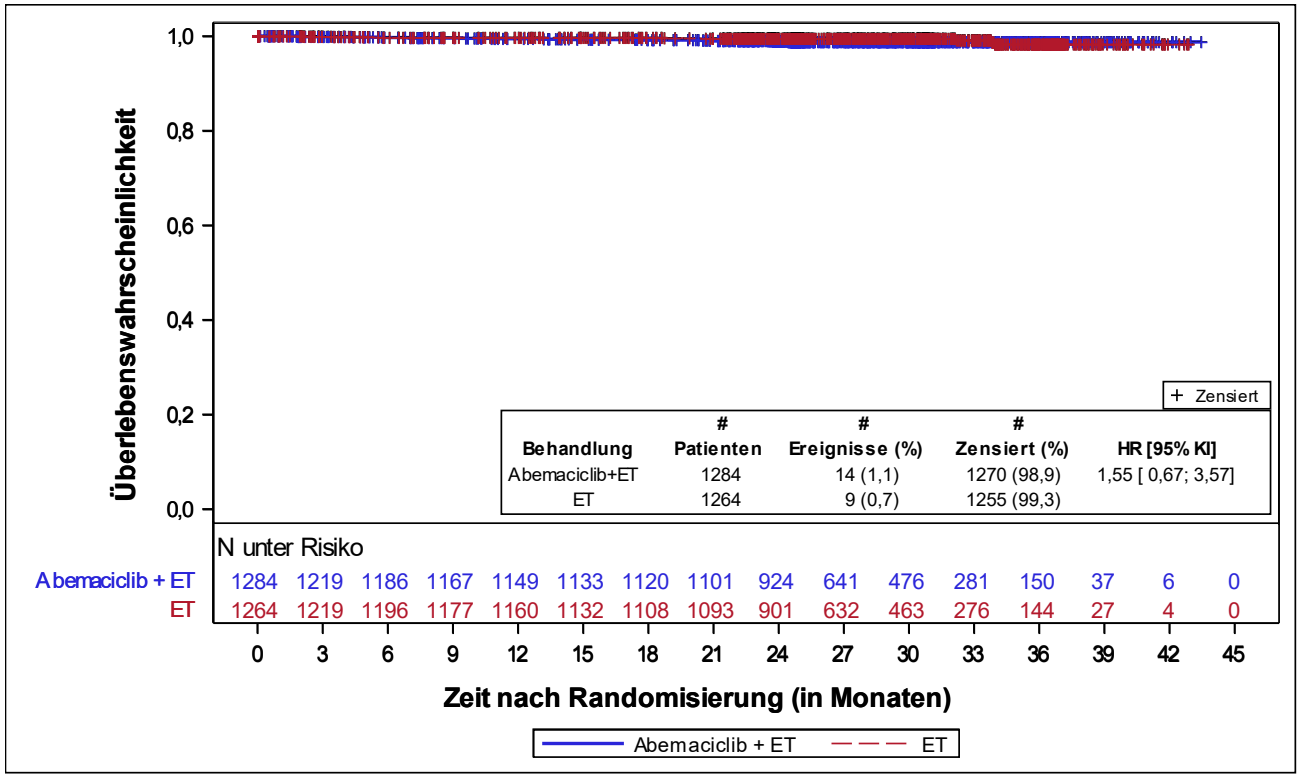
Kaplan-Meier-Kurven - Tod jeglicher Ursache
Kohorte 1 Population - ITT - Postmenopausal



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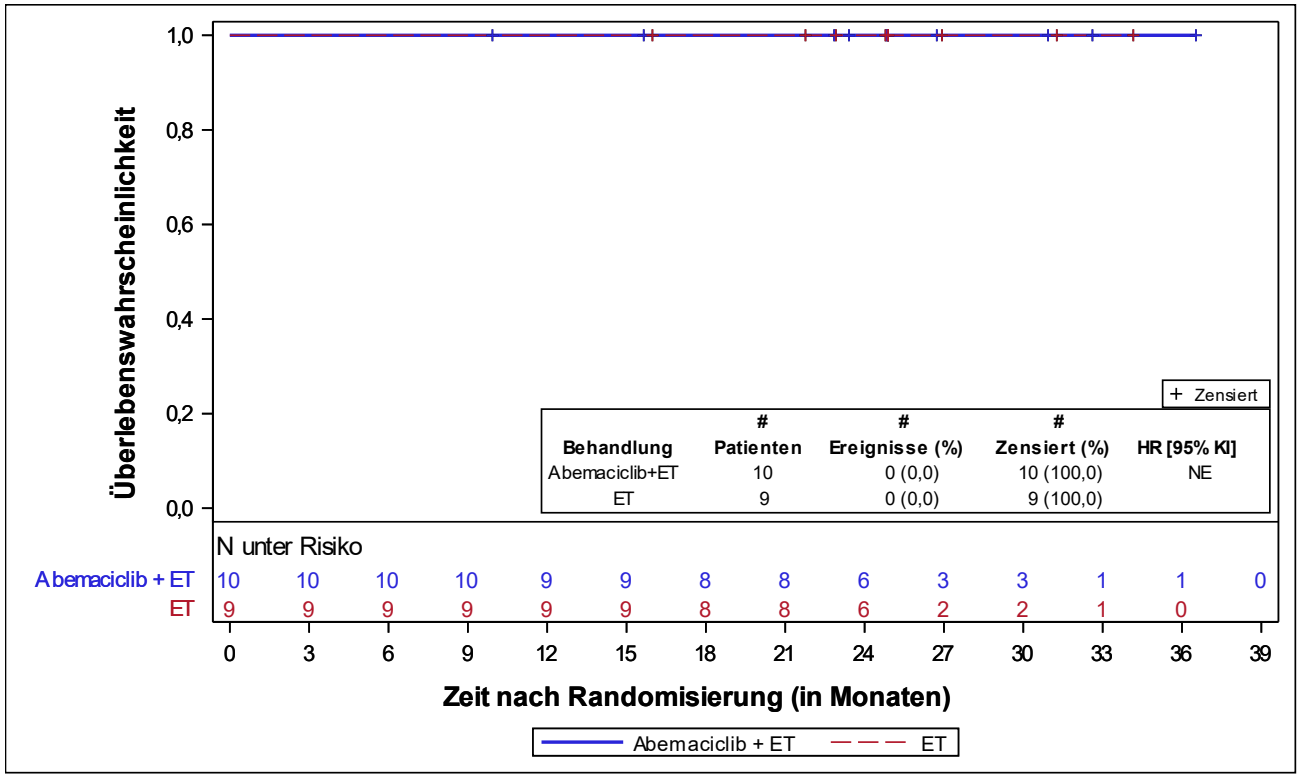
Kaplan-Meier-Kurven - Tod jeglicher Ursache
Kohorte 1 Population - ITT - Männer



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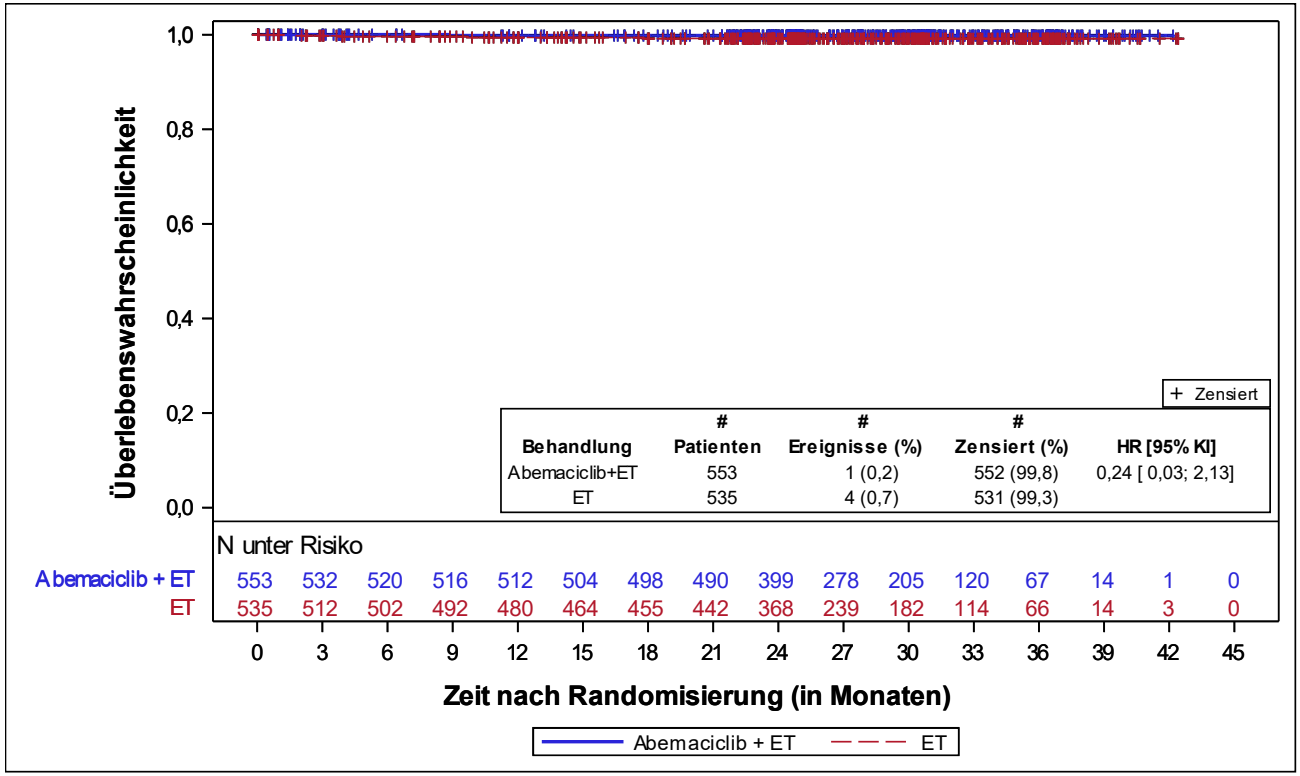
Kaplan-Meier-Kurven - kontralateraler invasiver Brustkrebs
Kohorte 1 Population - ITT - Prämenopausal



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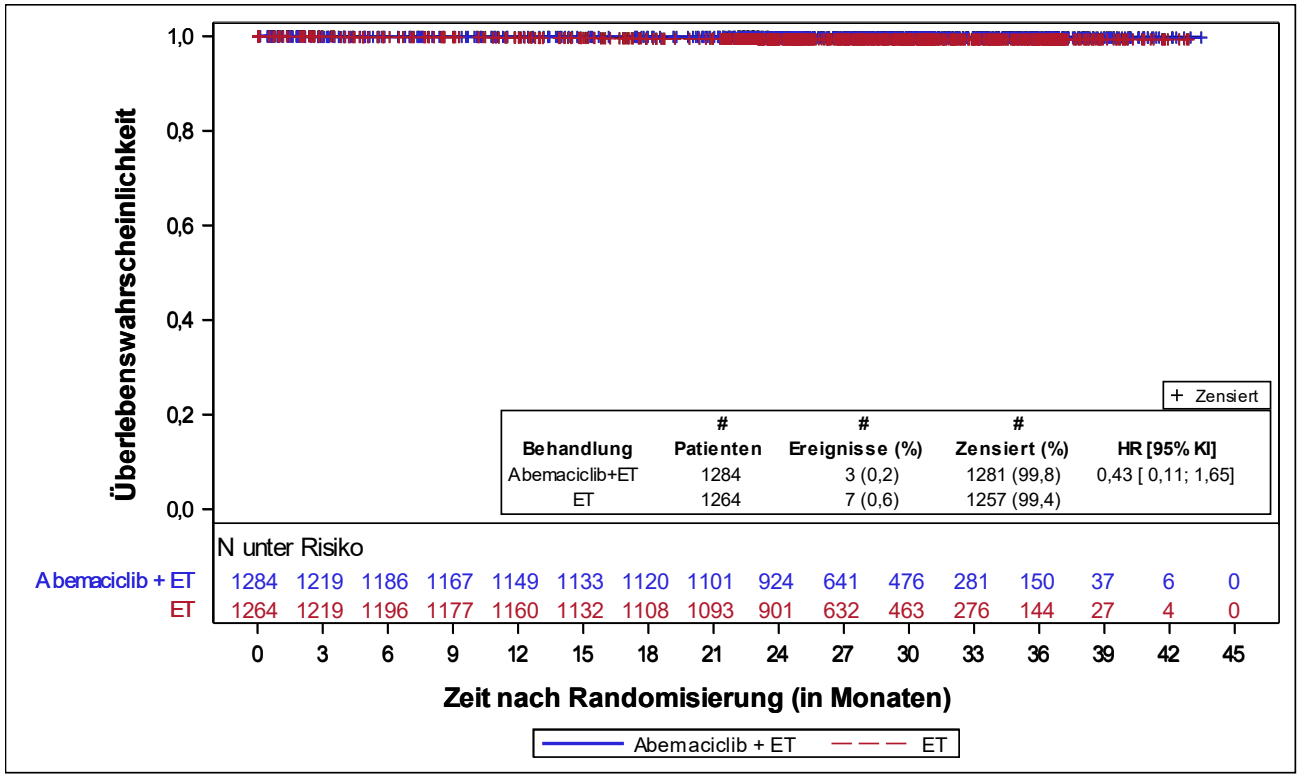
Kaplan-Meier-Kurven - kontralateraler invasiver Brustkrebs
Kohorte 1 Population - ITT - Postmenopausal



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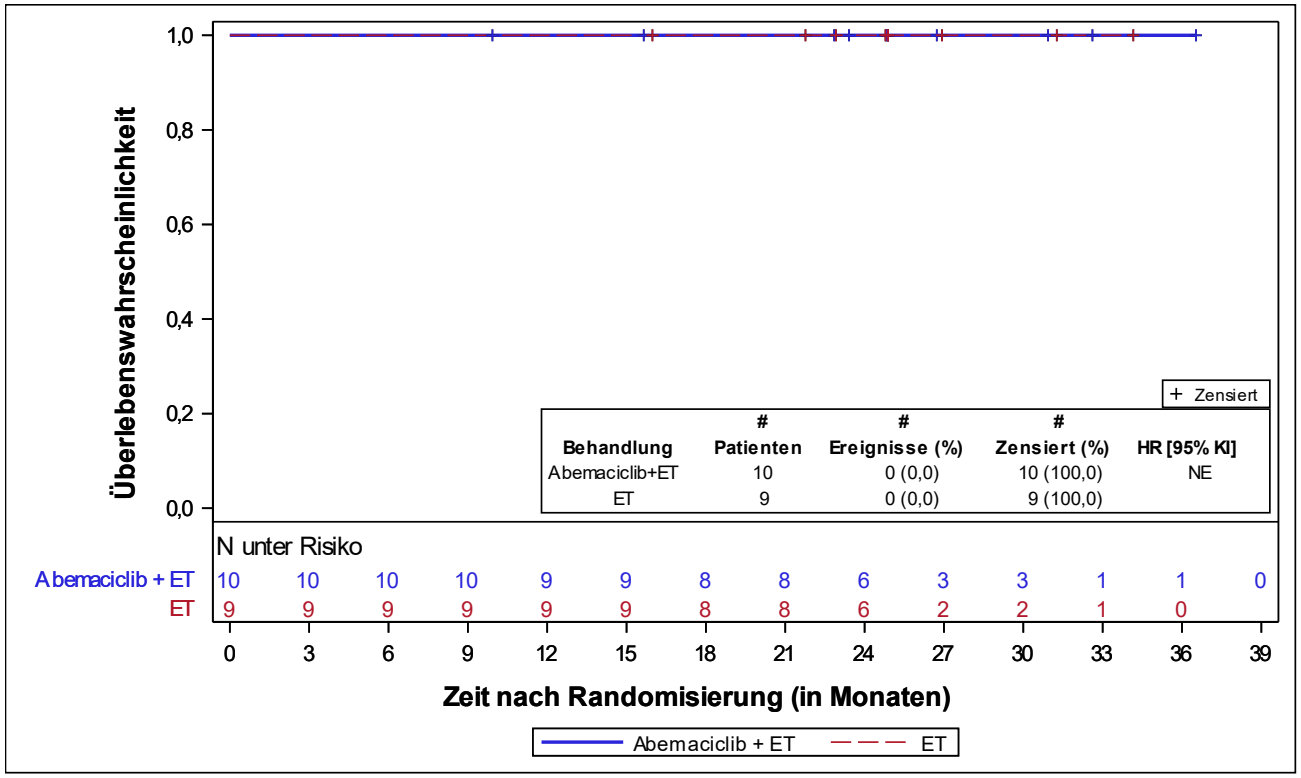
Kaplan-Meier-Kurven - kontralateraler invasiver Brustkrebs
Kohorte 1 Population - ITT - Männer



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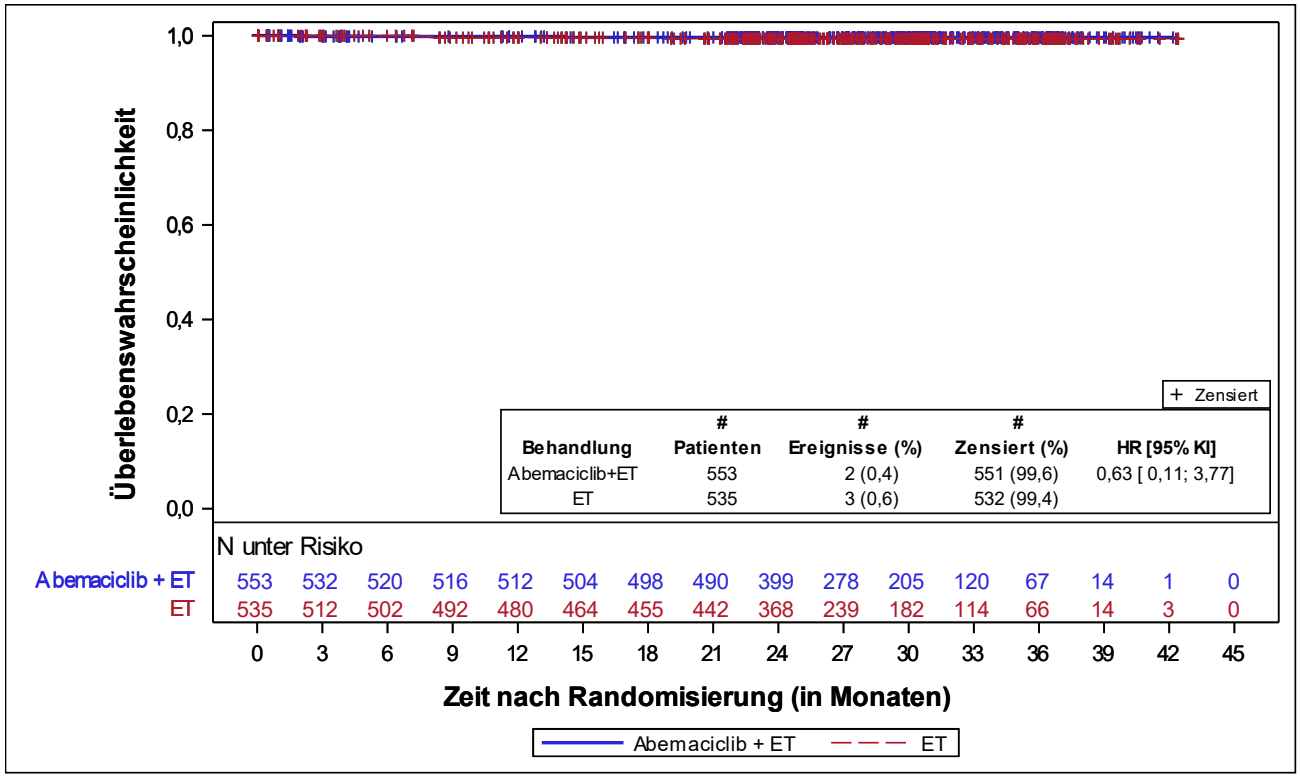
18NOV2021 / 02:02

Kaplan-Meier-Kurven - Sekundäres Primärkarzinom (kein Brustkrebs)
Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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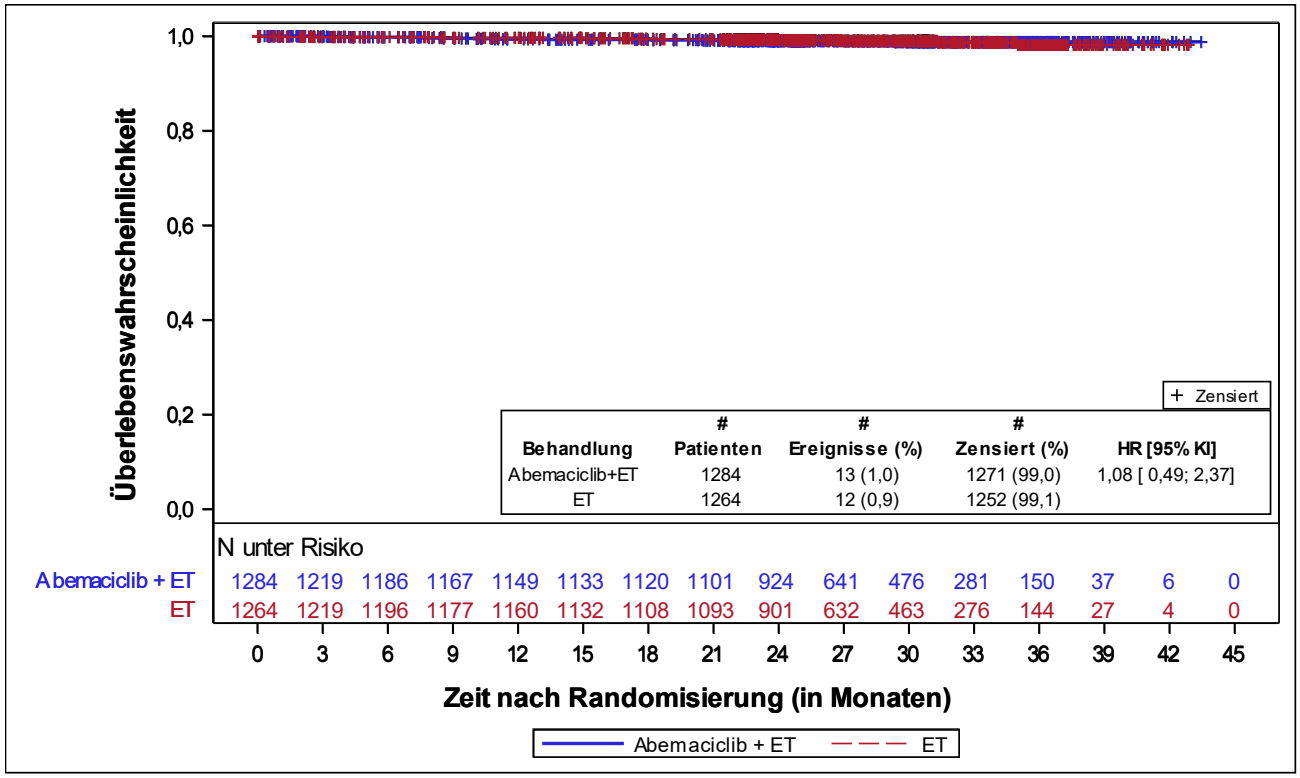
18NOV2021 / 02:02

Kaplan-Meier-Kurven - Sekundäres Primärkarzinom (kein Brustkrebs)
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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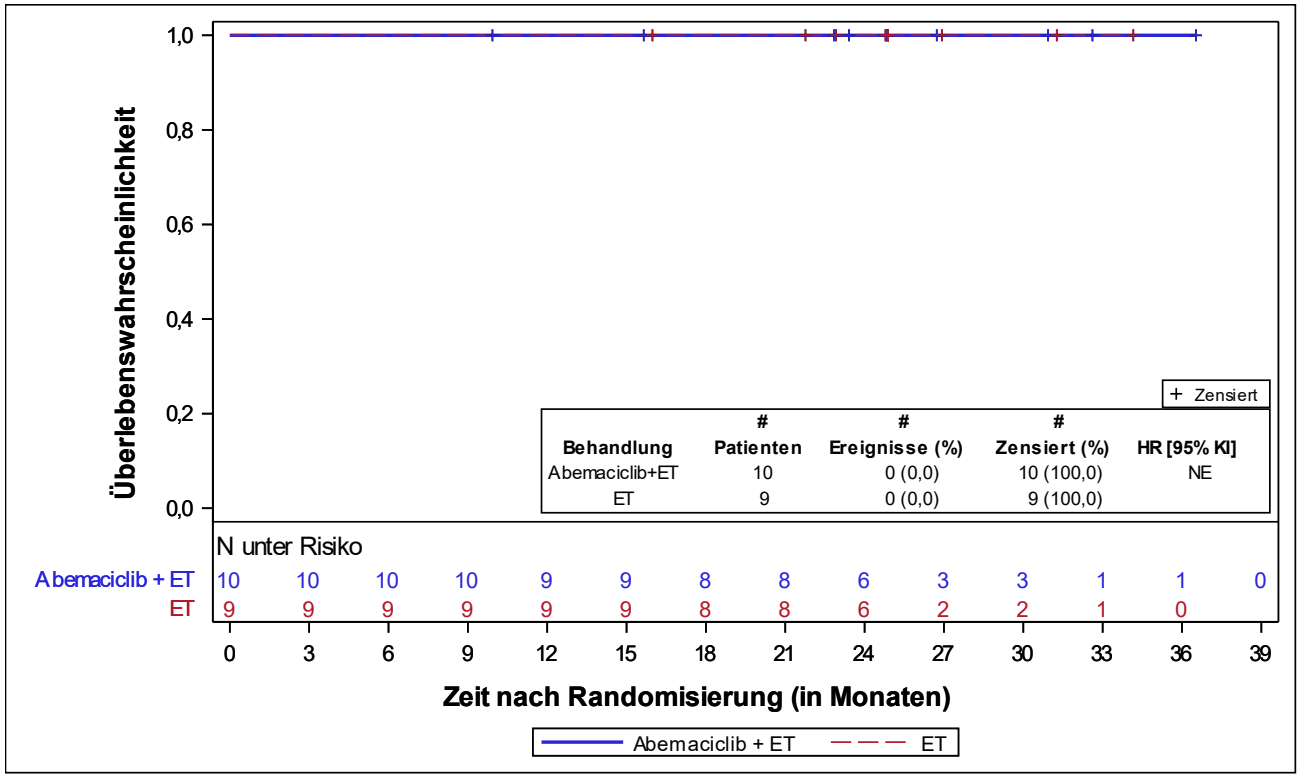
18NOV2021 / 02:02

Kaplan-Meier-Kurven - Sekundäres Primärkarzinom (kein Brustkrebs)
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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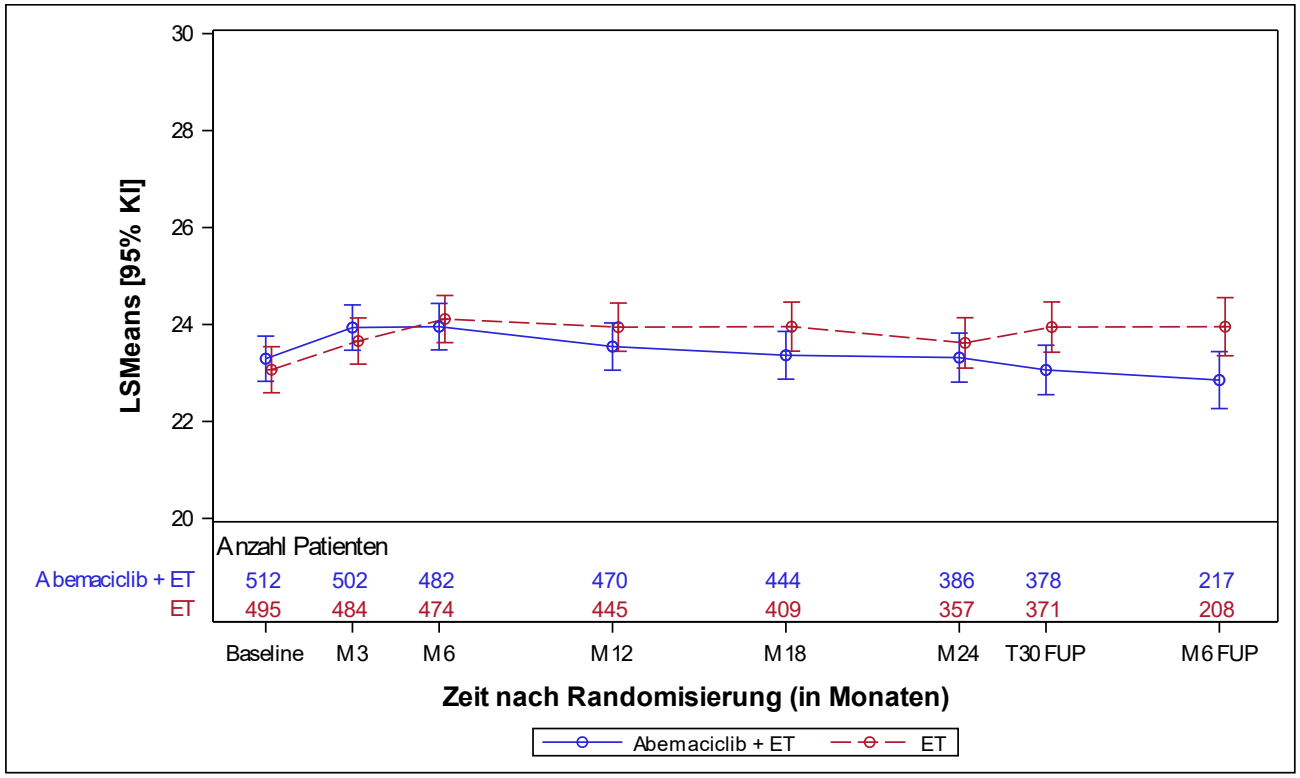
Anhang 4-G1.2: Verlaufskurven von Teilskalen patientenberichteter Endpunkte

Anhang 4-G1.2.1: FACT-B (Teilskalen)

Abbildung 23 (Anhang): FACT-B (Teilskala)

Verlaufskurven - FACT-B-Subskala: BCS

Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021

*LSMeans aus dem MMRM Modell: FACT-B BCS = Behandlung, Visite, Behandlung*Visite.*

Abkürzungen: BCS: Mammakarzinomspezifische Subskala; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gbac1_lineplot_qol.sas

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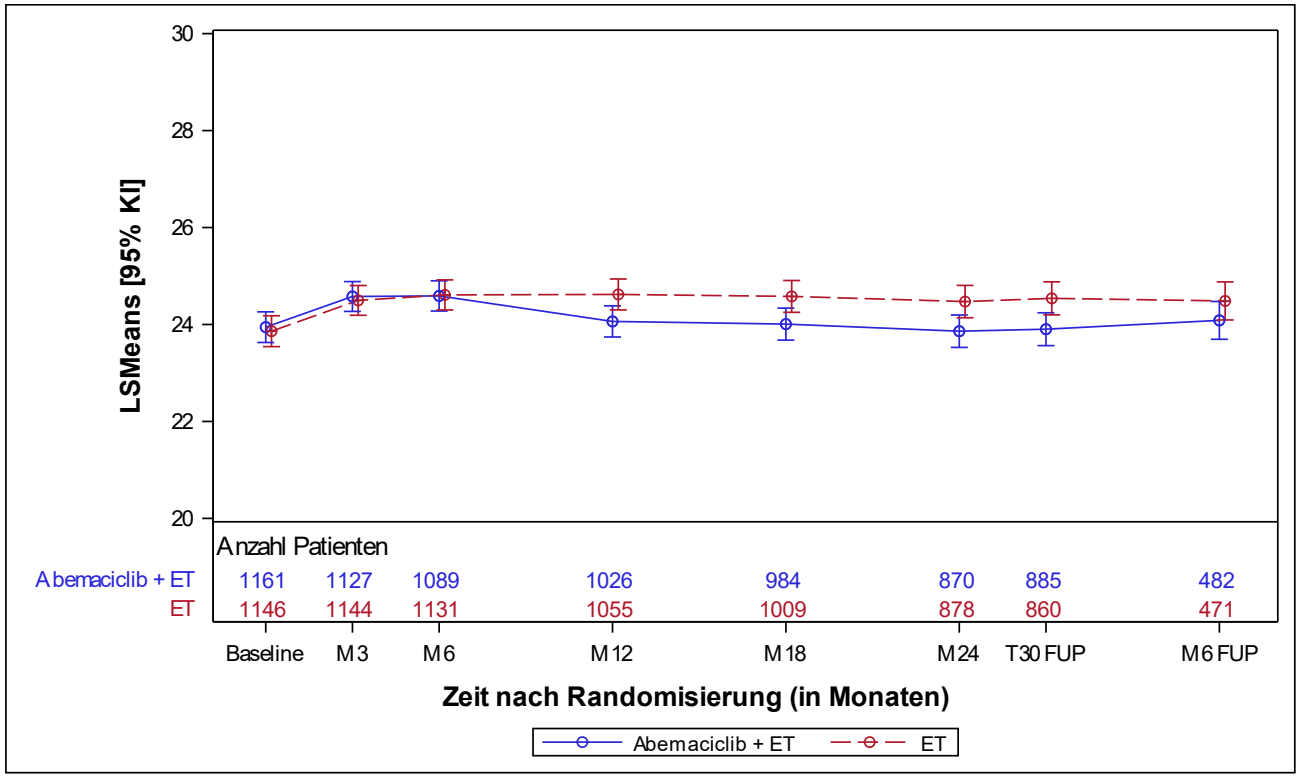
Verlaufskurven - FACT-B-Subskala: BCS
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACT-B BCS = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: BCS: Mammakarzinomspezifische Subskala; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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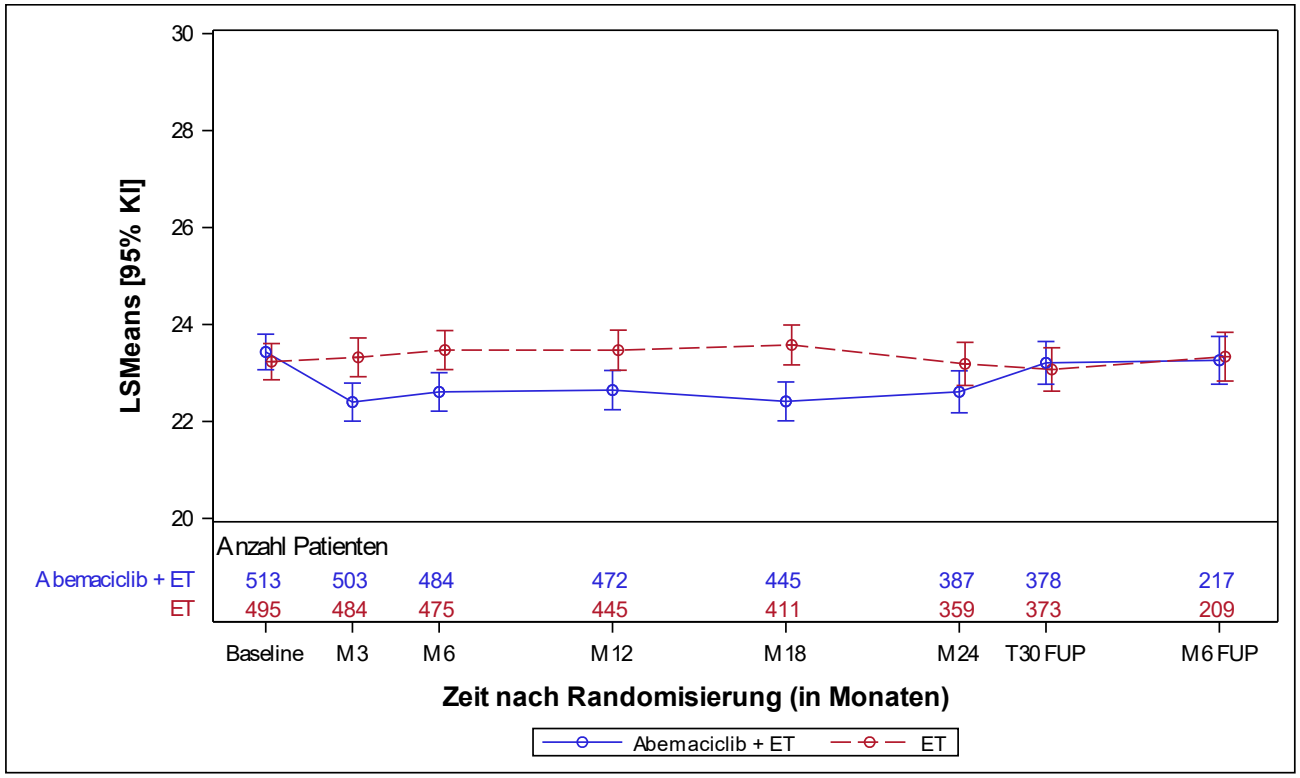
Verlaufskurven - FACT-B-Subskala: PWB
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACT-B PWB = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag; PWB: körperliches Wohlbefinden
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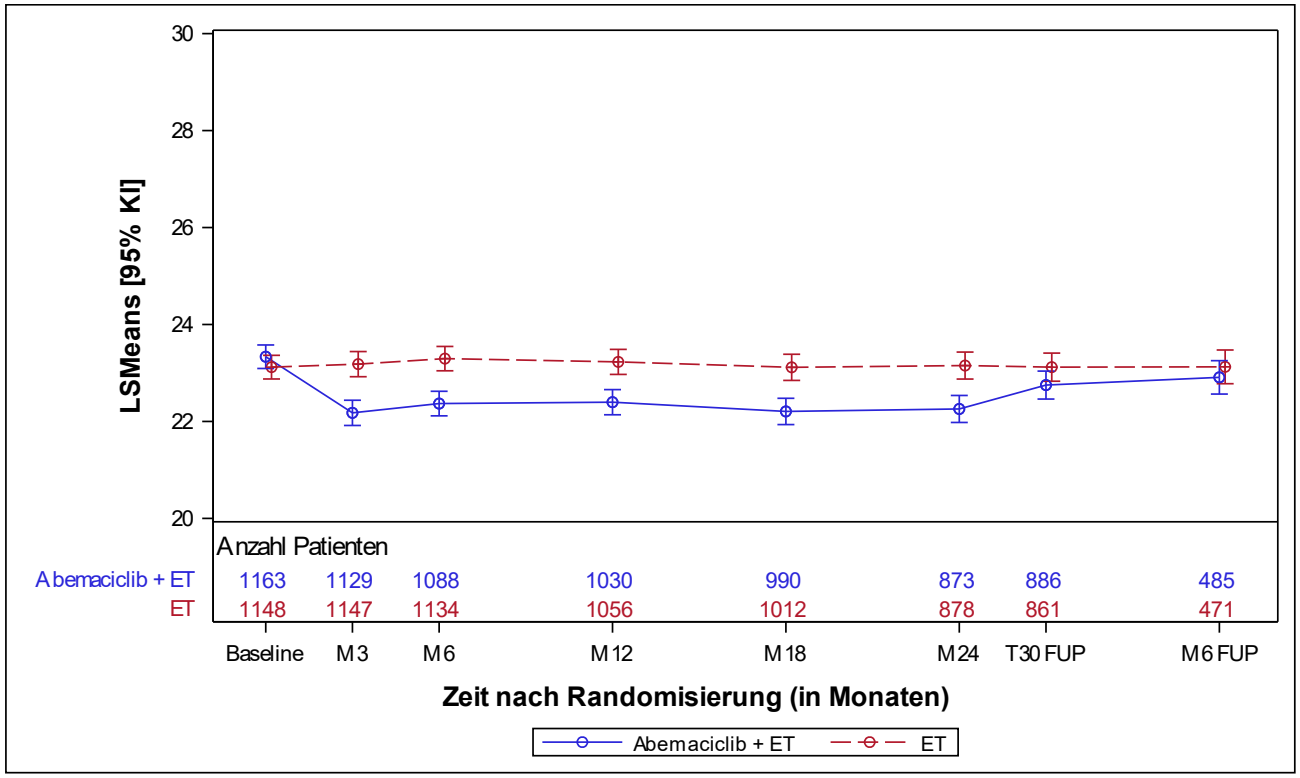
30NOV2021 / 02:40

Verlaufskurven - FACT-B-Subskala: PWB
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACT-B PWB = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag; PWB: körperliches Wohlbefinden
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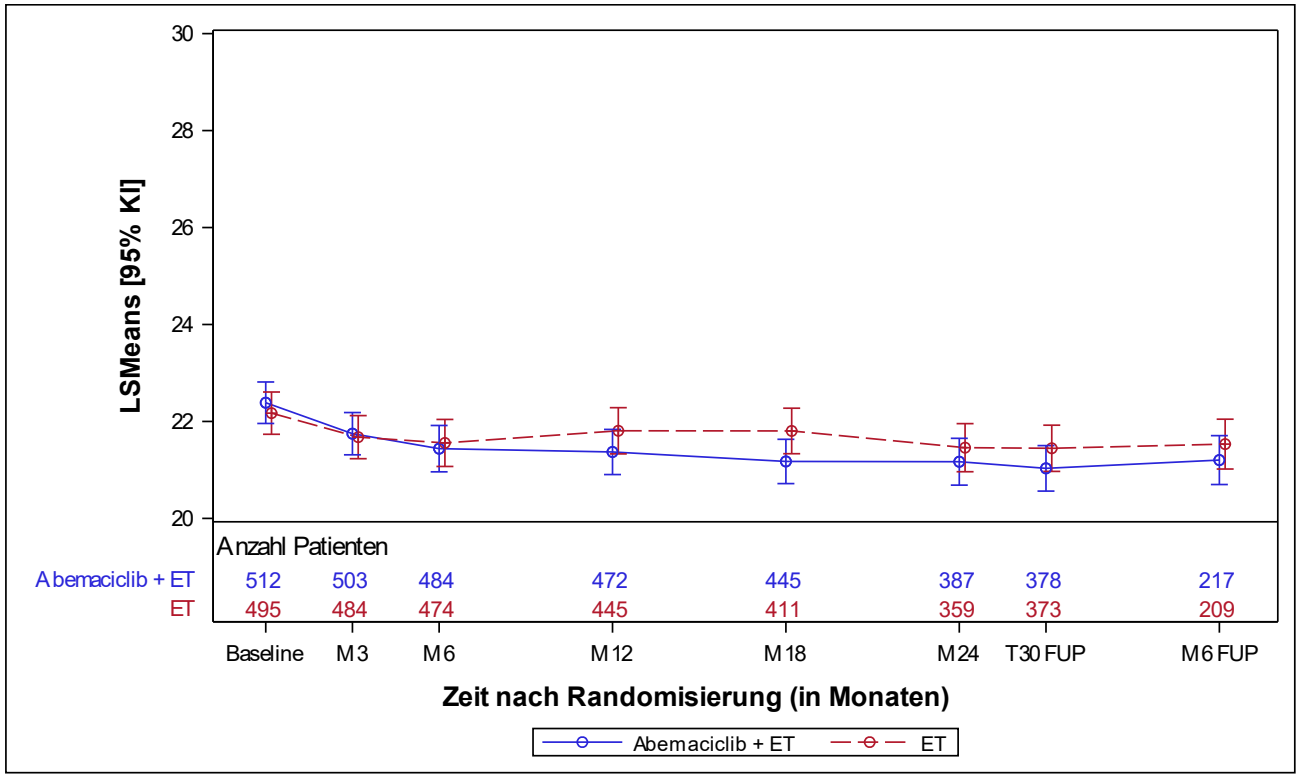
30NOV2021 / 02:40

Verlaufskurven - FACT-B-Subskala: SWB
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACT-B SWB = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; SWB: soziales und familiäres Wohlbefinden; T: Tag
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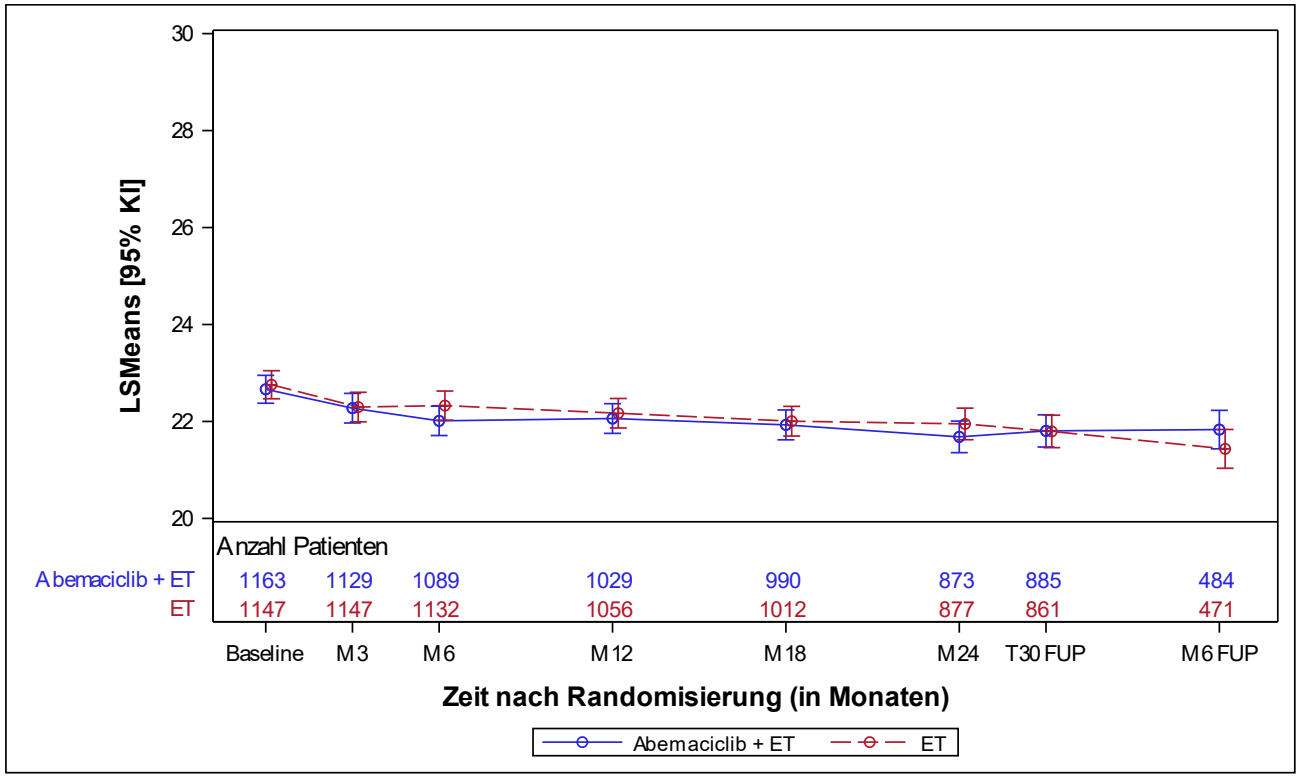
30NOV2021 / 02:40

Verlaufskurven - FACT-B-Subskala: SWB
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACT-B SWB = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; SWB: soziales und familiäres Wohlbefinden; T: Tag
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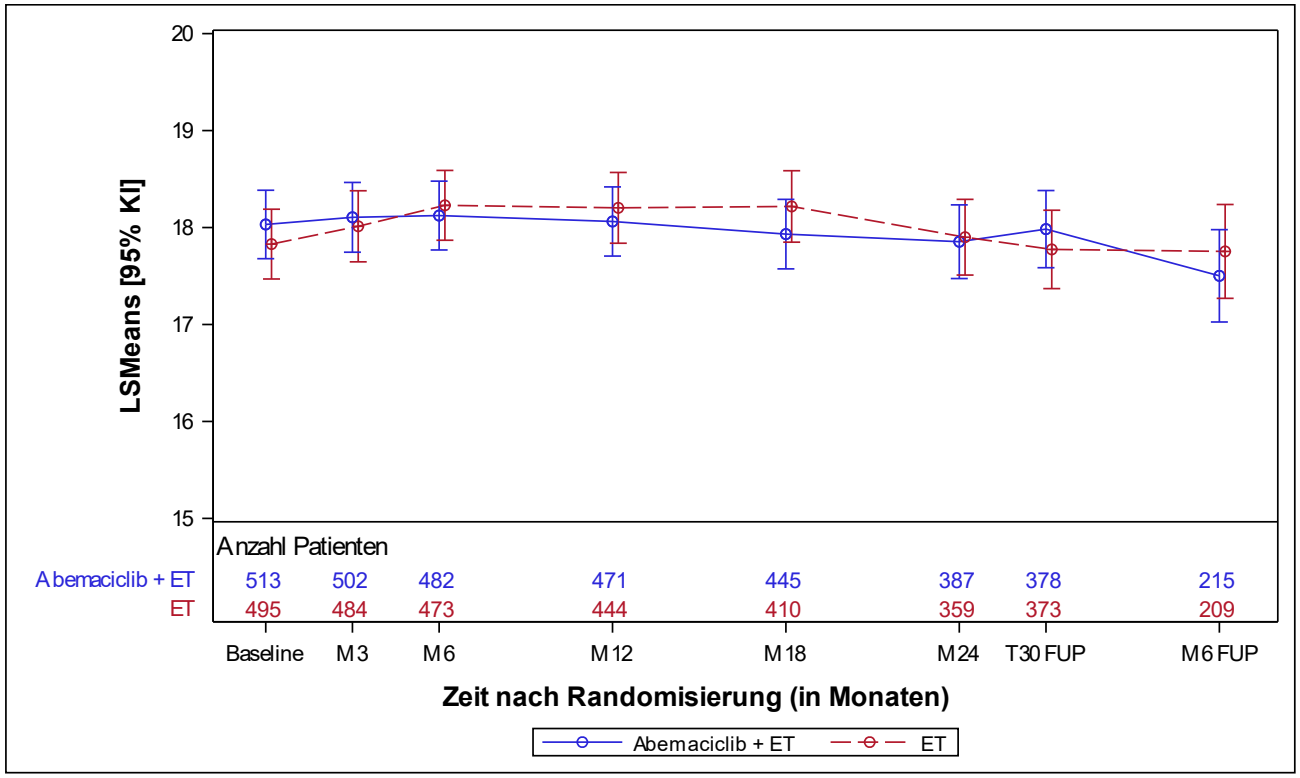
30NOV2021 / 02:40

Verlaufskurven - FACT-B-Subskala: EWB
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACT-B EWB = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; EWB: emotionales Wohlbefinden; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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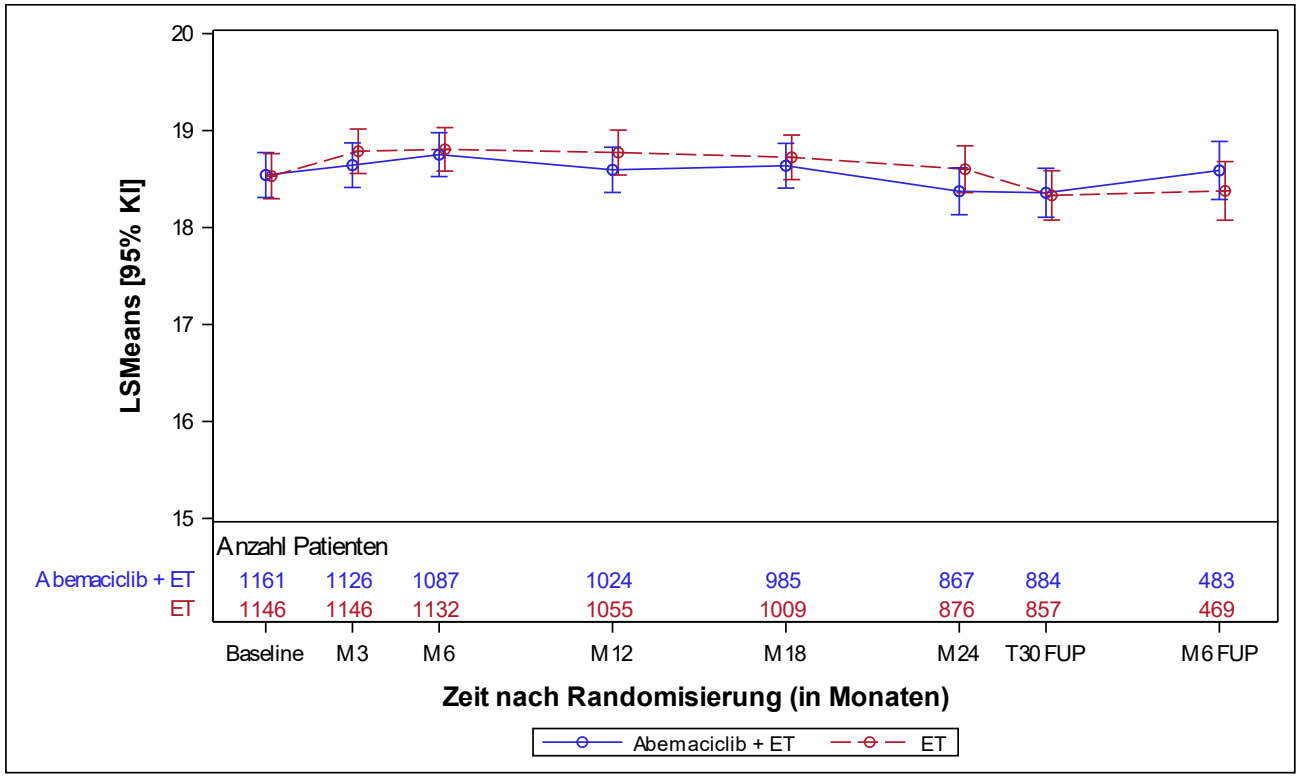
30NOV2021 / 02:40

Verlaufskurven - FACT-B-Subskala: EWB
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACT-B EWB = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; EWB: emotionales Wohlbefinden; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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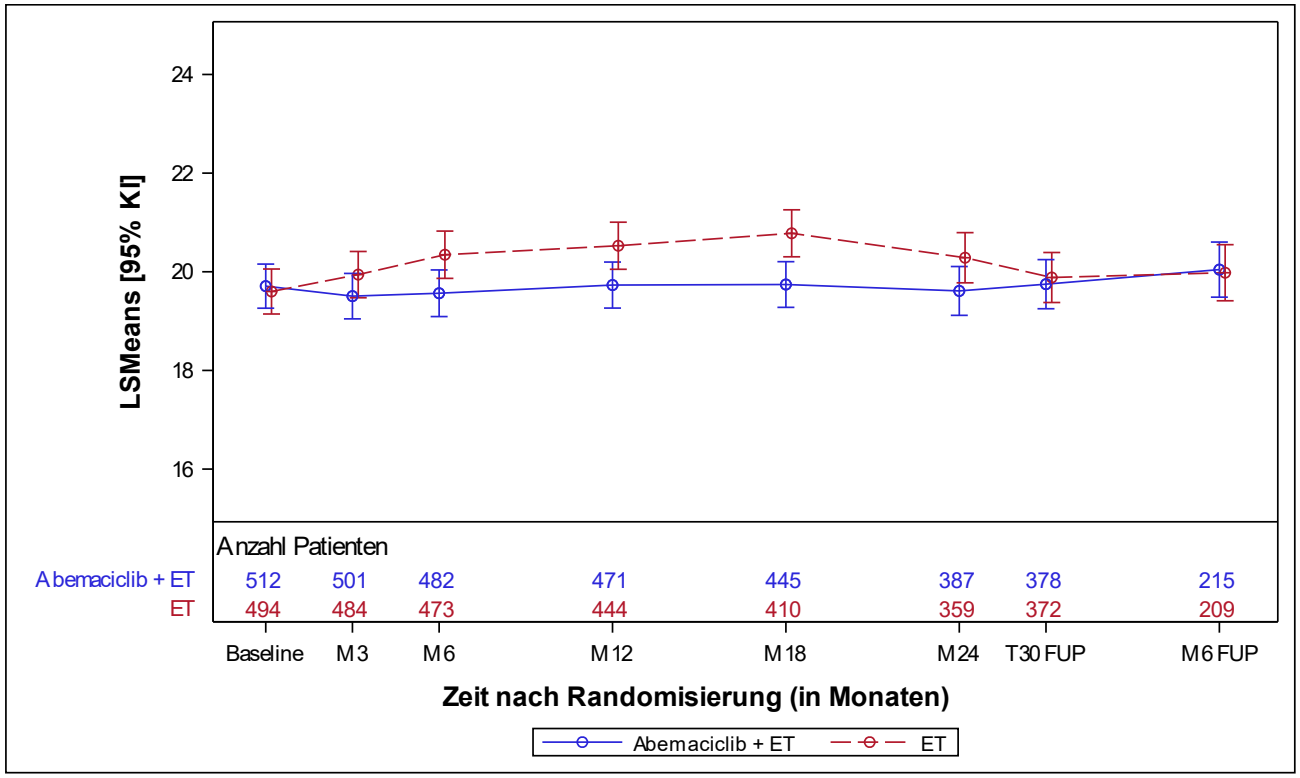
30NOV2021 / 02:40

Verlaufskurven - FACT-B-Subskala: FWB
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACT-B FWB = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FWB: funktionales Wohlbefinden; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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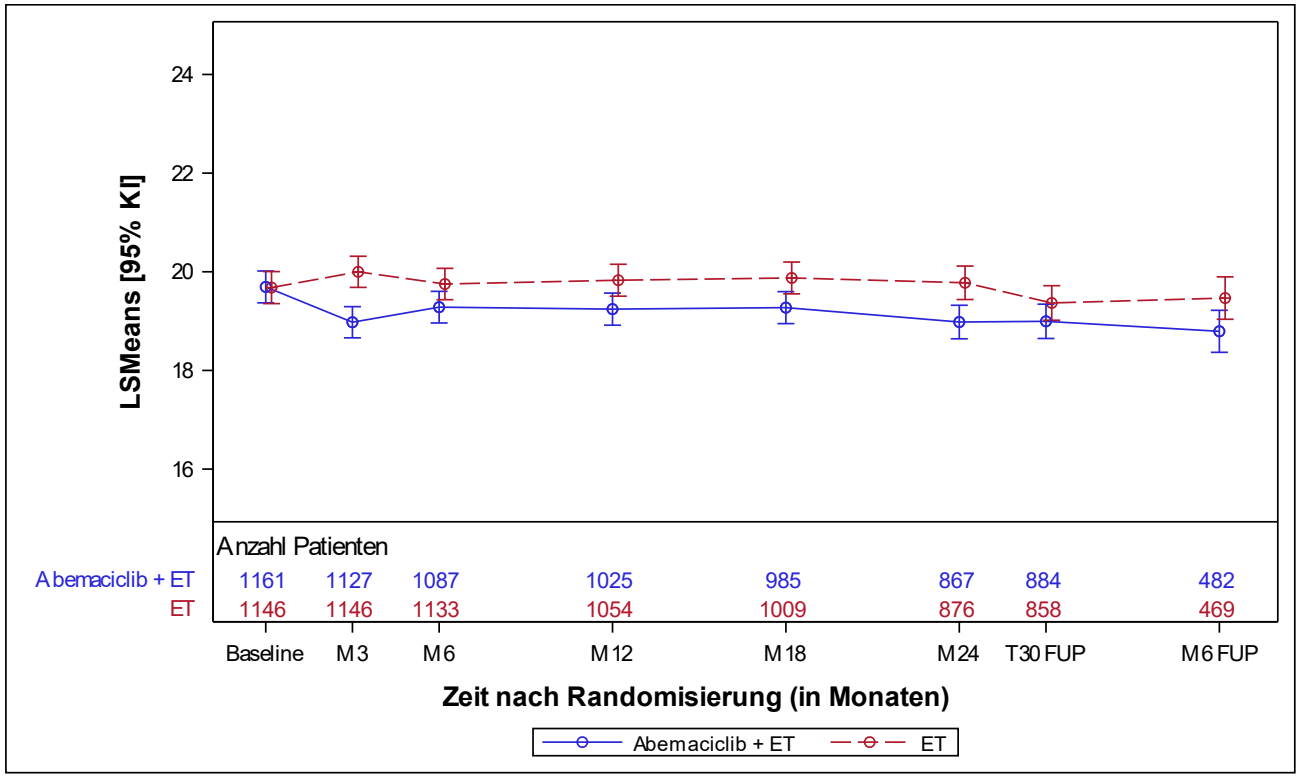
30NOV2021 / 02:40

Verlaufskurven - FACT-B-Subskala: FWB
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACT-B FWB = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FWB: funktionales Wohlbefinden; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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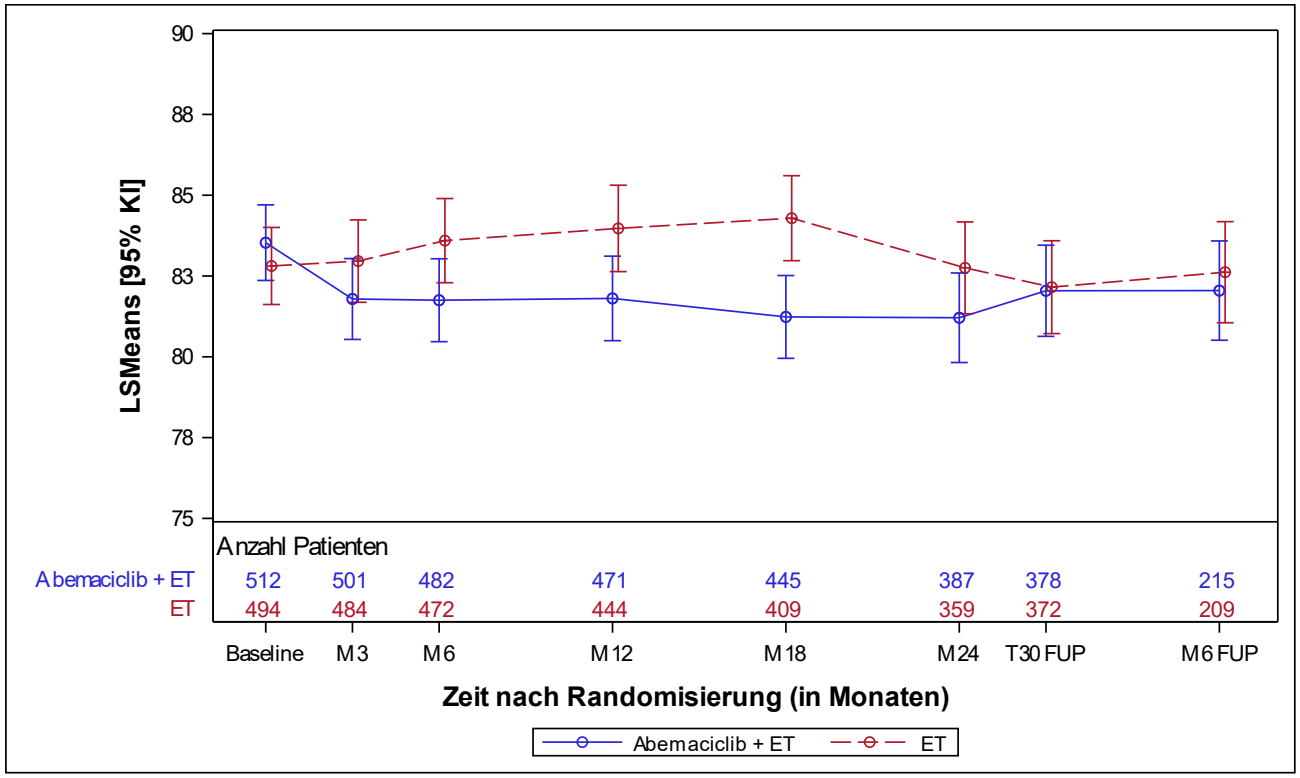
30NOV2021 / 02:40

Verlaufskurven - FACT-G (Gesamtscore)
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACT-G Gesamtscore = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACT-G: Functional Assessment of Cancer Therapy - General; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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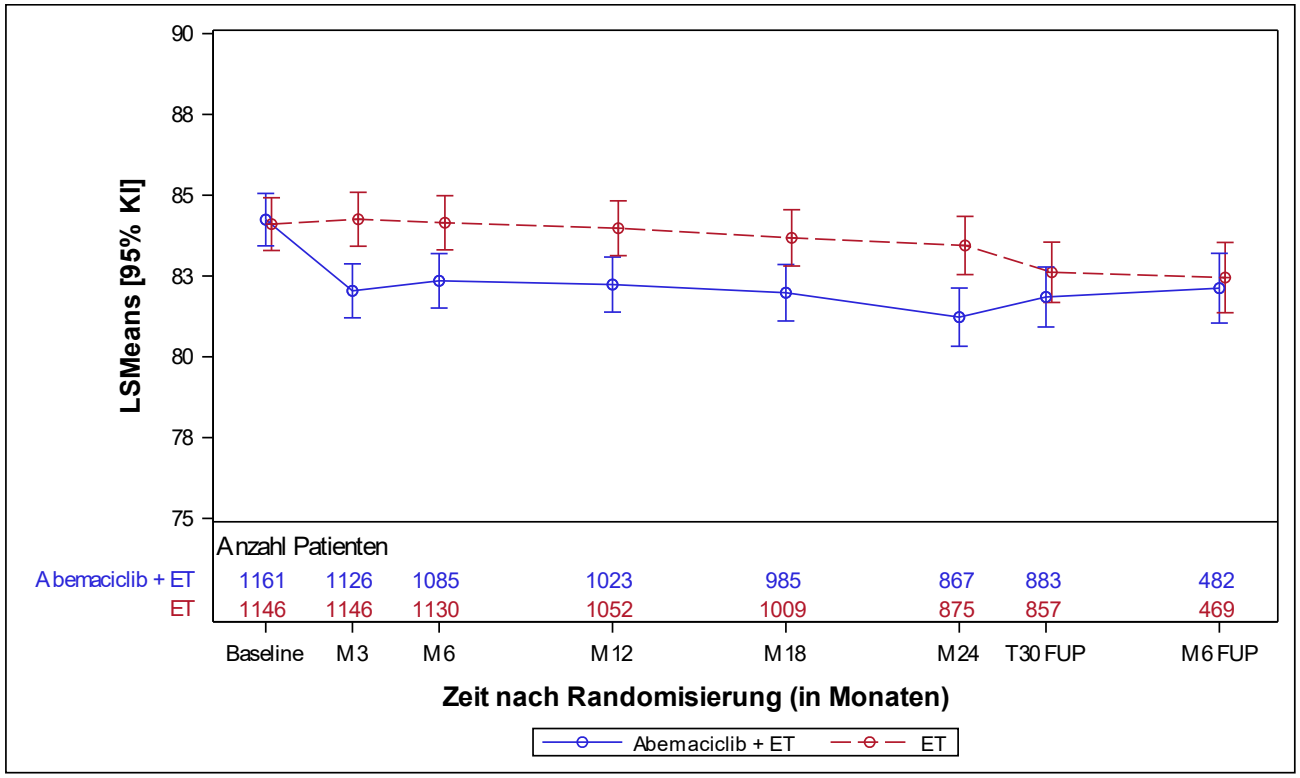
30NOV2021 / 02:40

Verlaufskurven - FACT-G (Gesamtscore)
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
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Abkürzungen: ET: Endokrine Therapie; FACT-G: Functional Assessment of Cancer Therapy - General; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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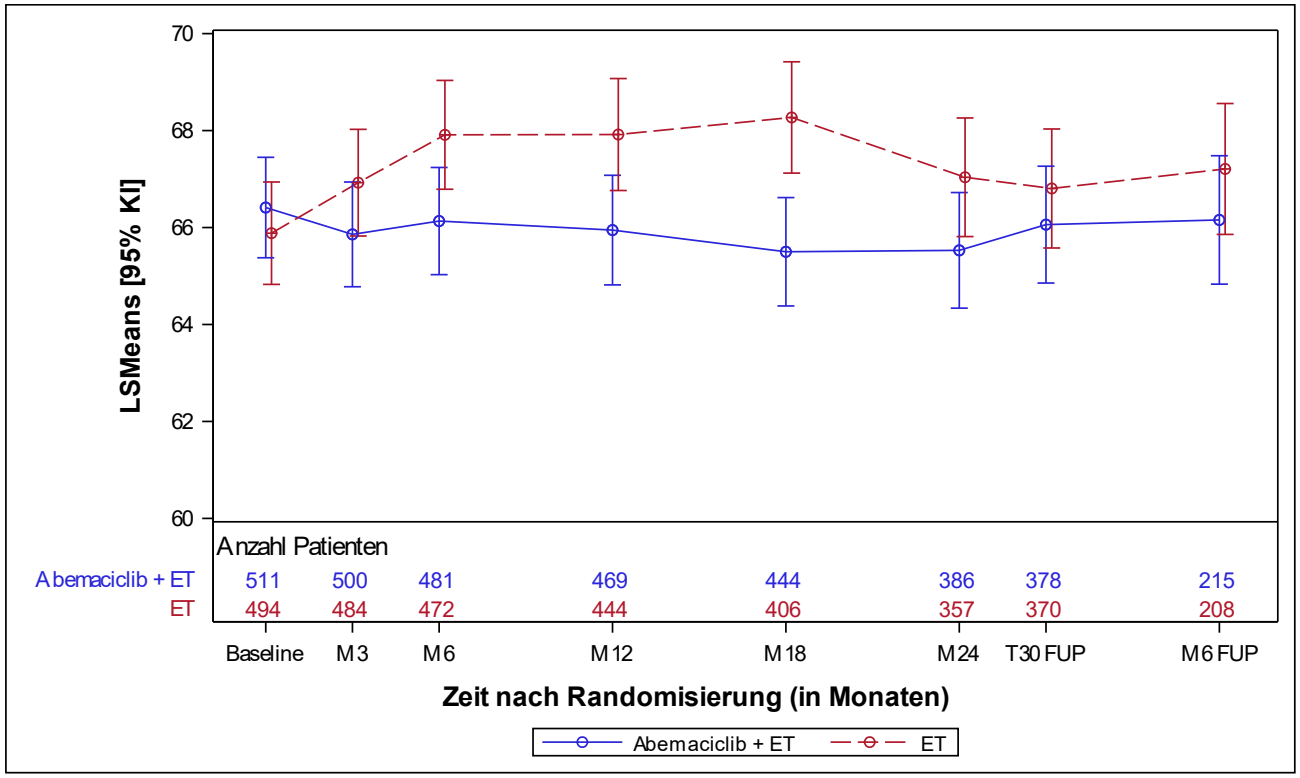
30NOV2021 / 02:40

Verlaufskurven - FACT-B: TOI
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACT-B TOI = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag; TOI: Trial Outcome Index
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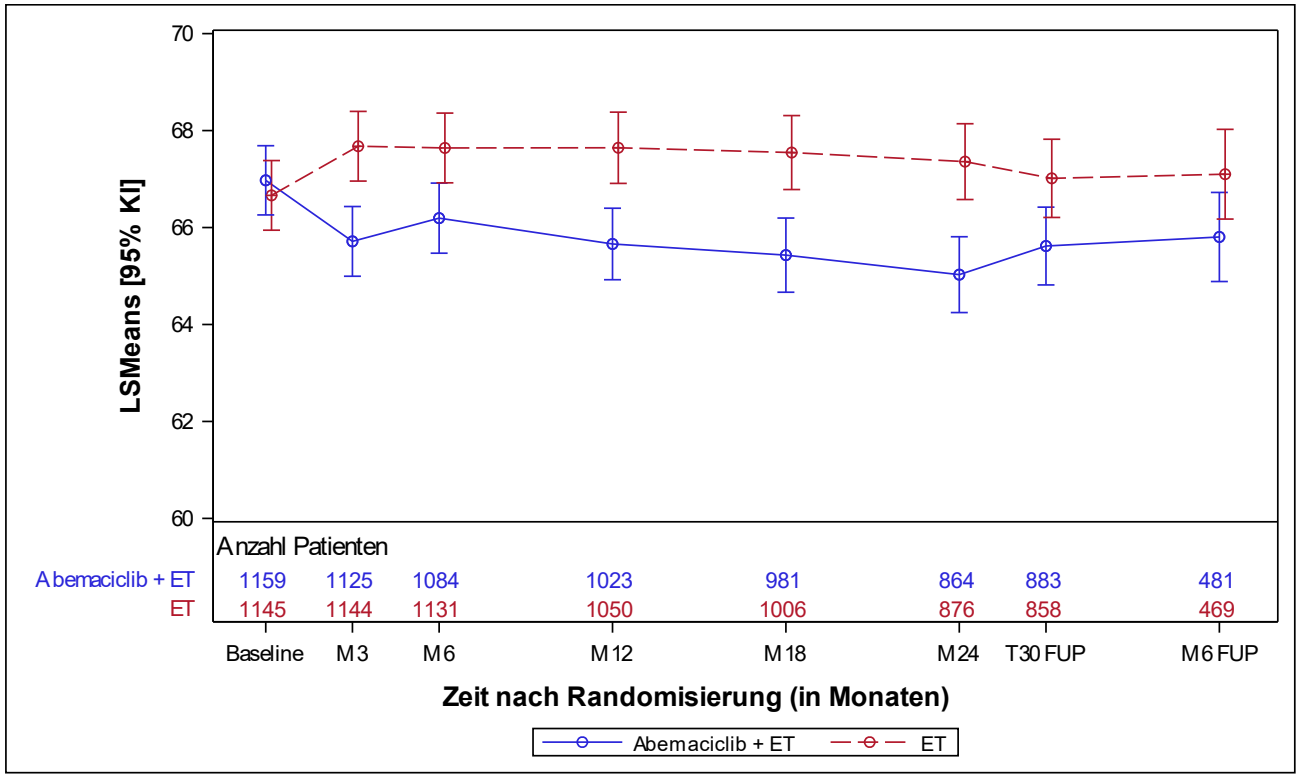
Verlaufskurven - FACT-B: TOI
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACT-B TOI = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag; TOI: Trial Outcome Index
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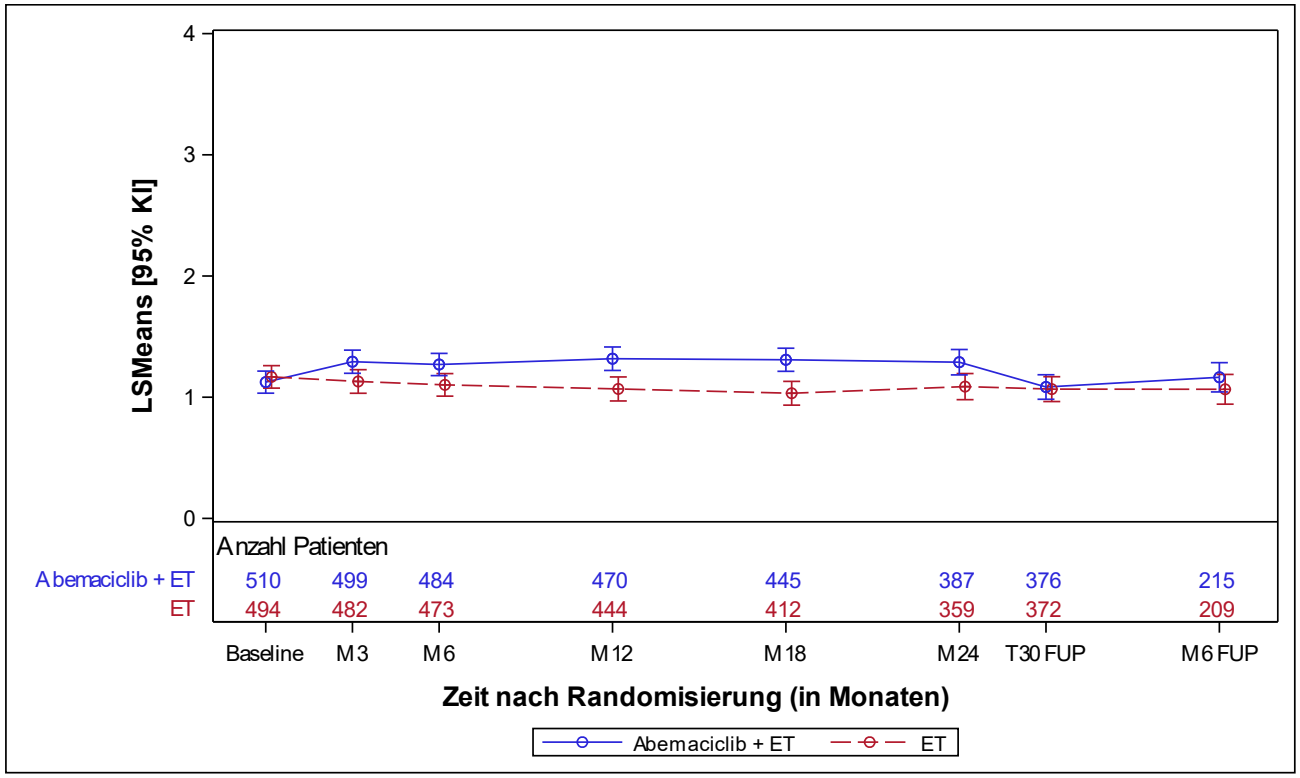
30NOV2021 / 02:40

Anhang 4-G1.2.2: FACIT-Fatigue (Teilskalen)

Abbildung 24 (Anhang): FACIT-Fatigue (Teilskala)

Verlaufskurven - FACIT-Fatigue: I feel fatigued

Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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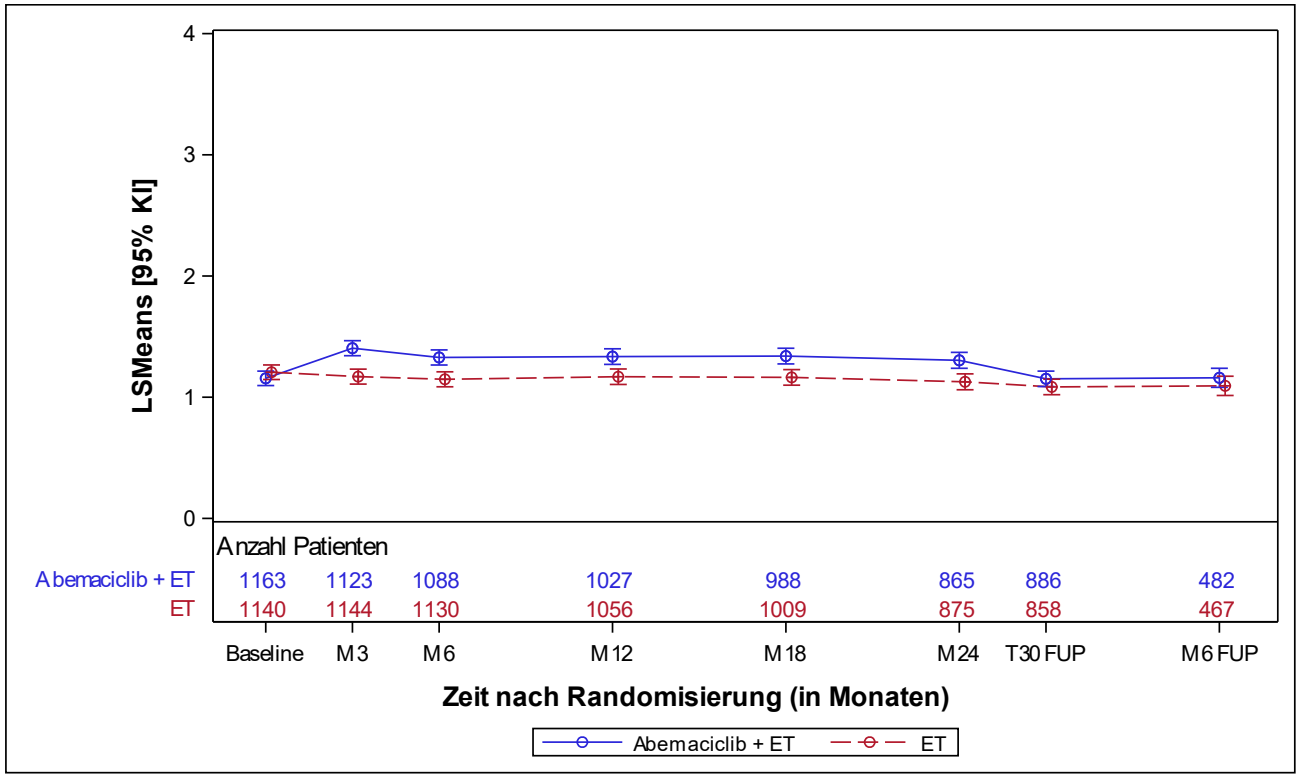
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I feel fatigued
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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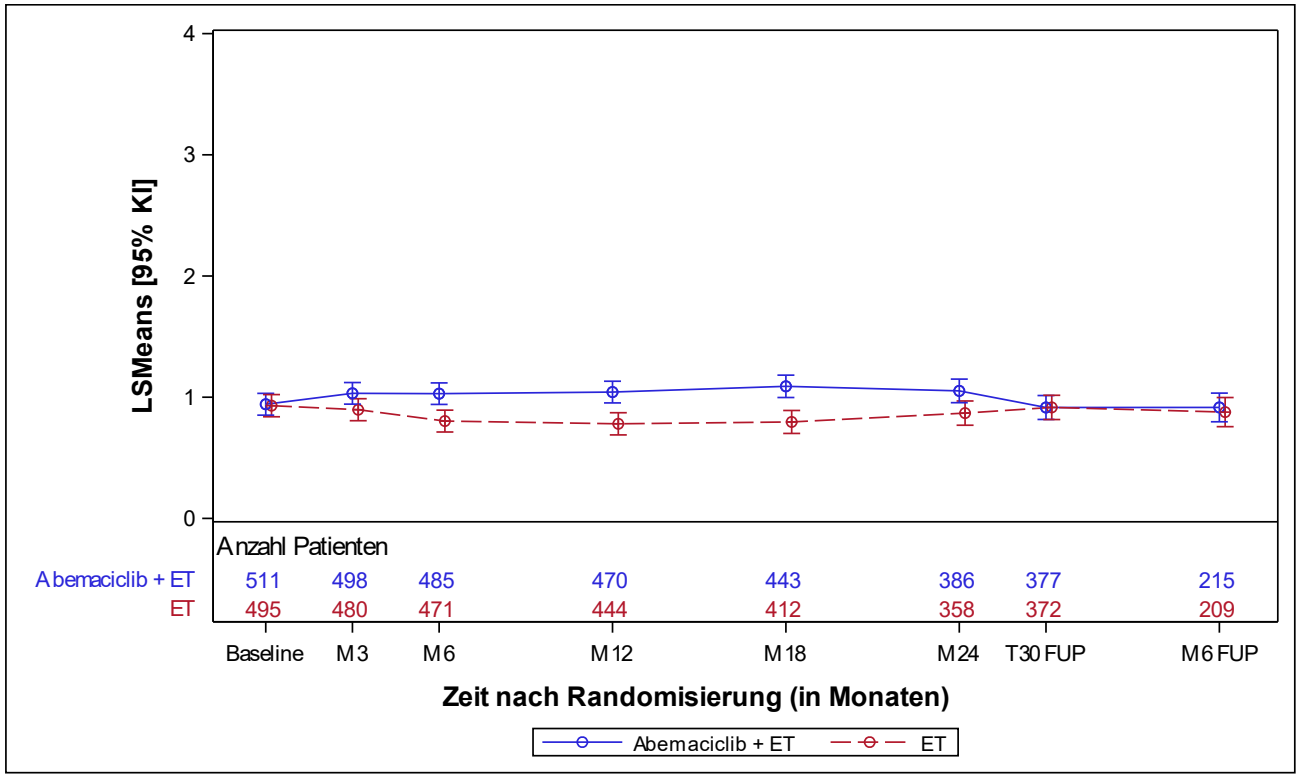
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I feel weak all over
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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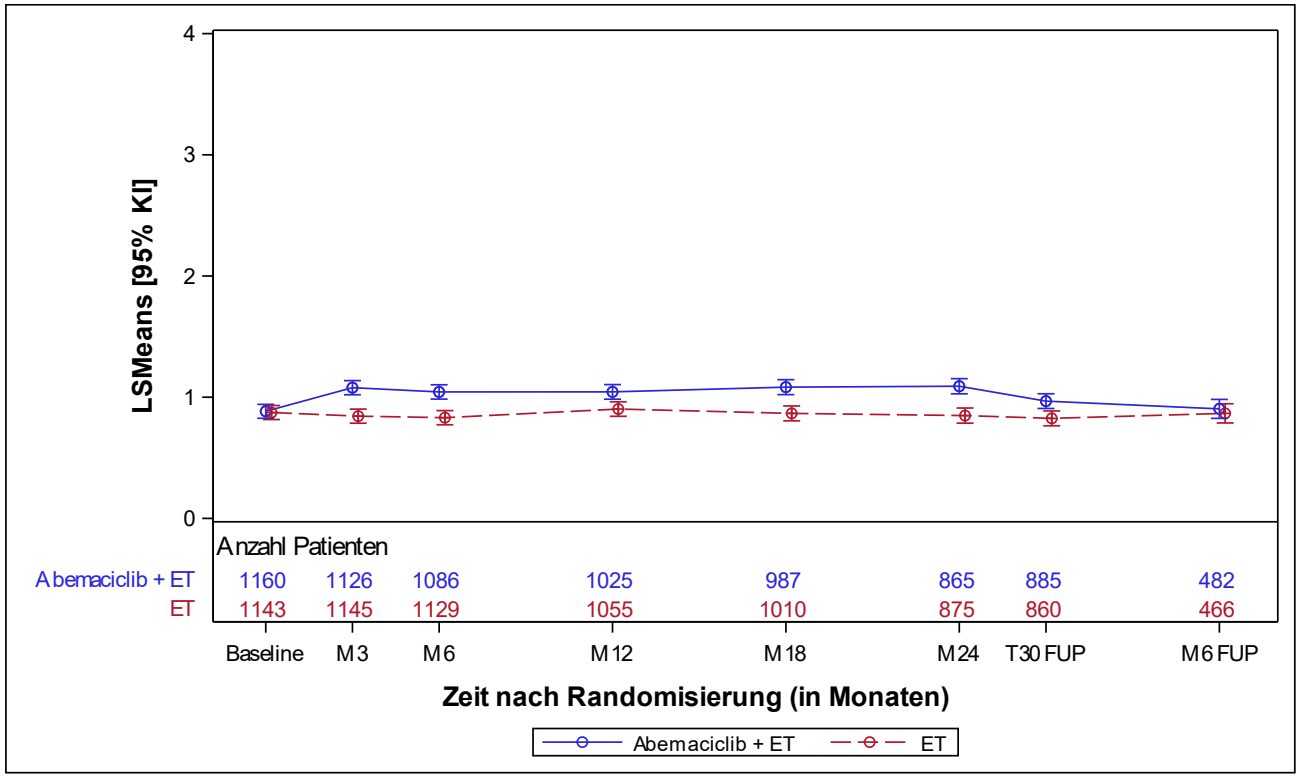
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I feel weak all over
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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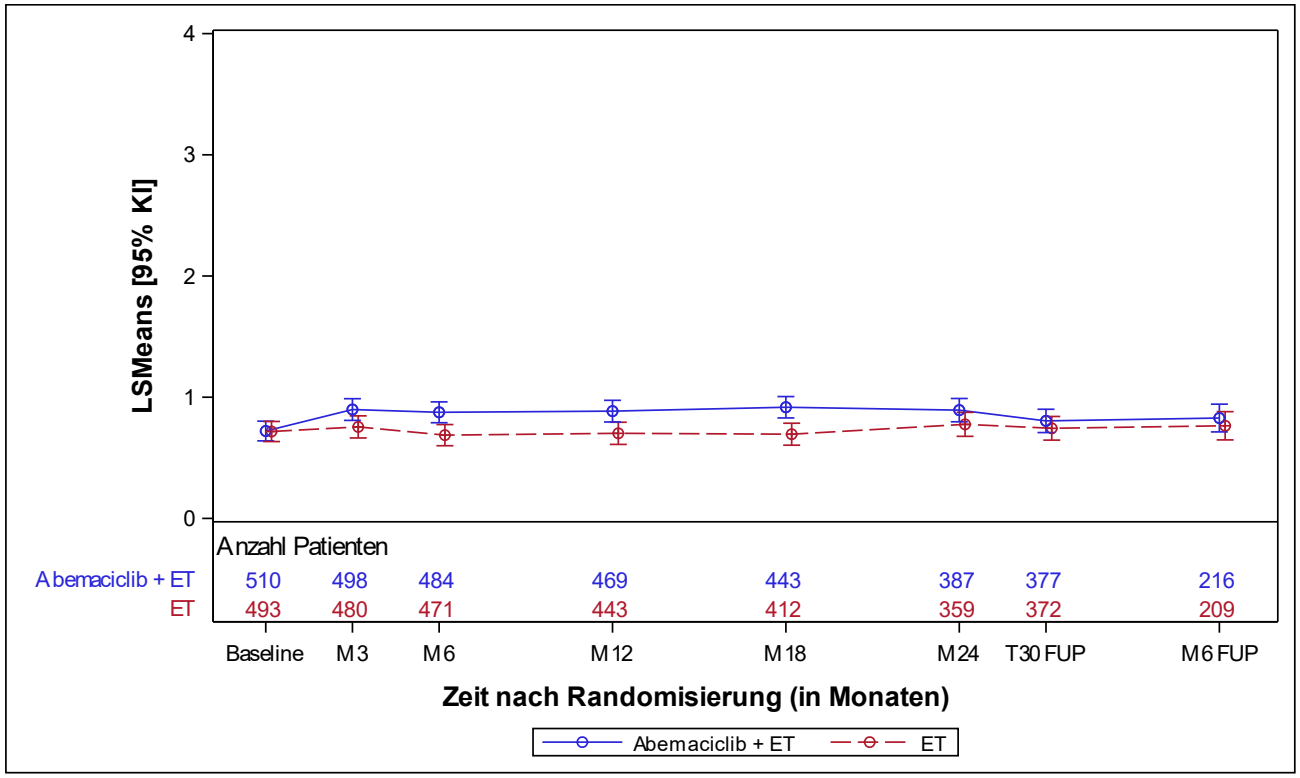
Verlaufskurven - FACIT-Fatigue: I feel listless ('washed out')
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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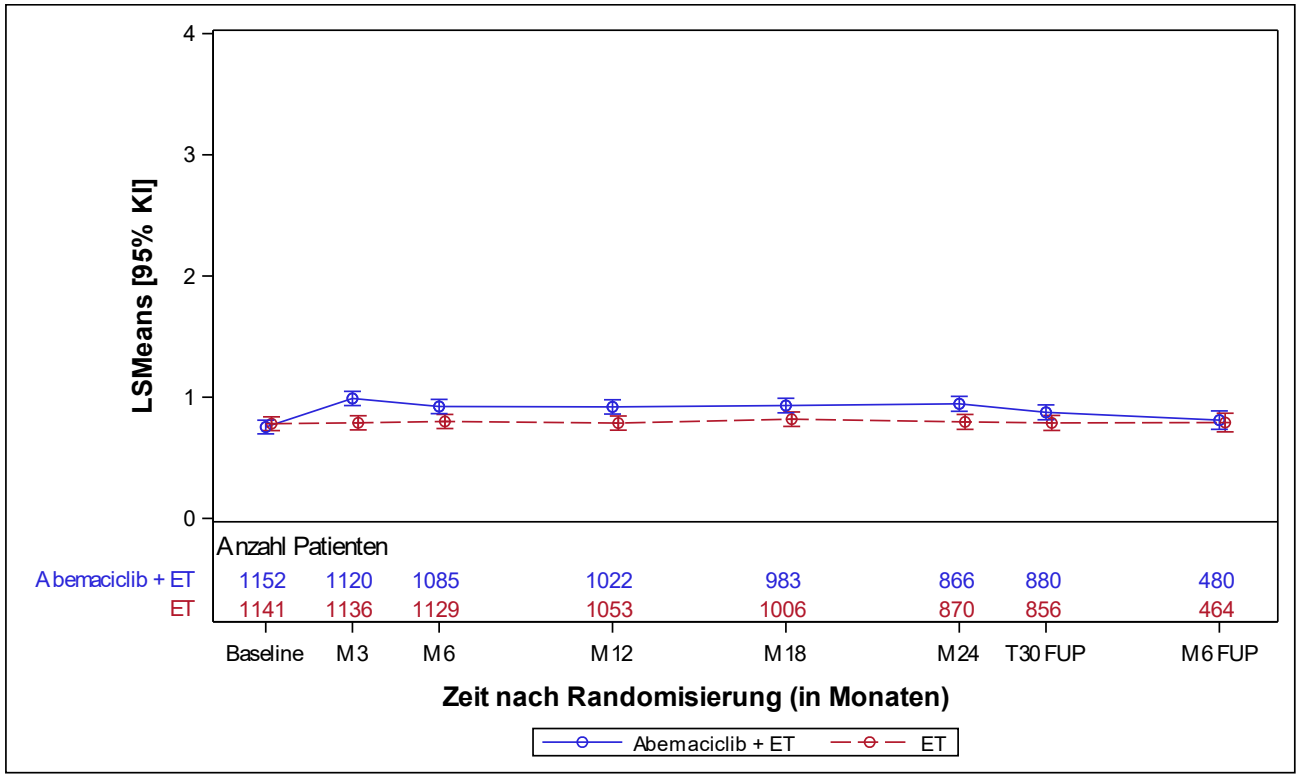
Verlaufskurven - FACIT-Fatigue: I feel listless ('washed out')
Kohorte 1 Population - Safety - Postmenopausal



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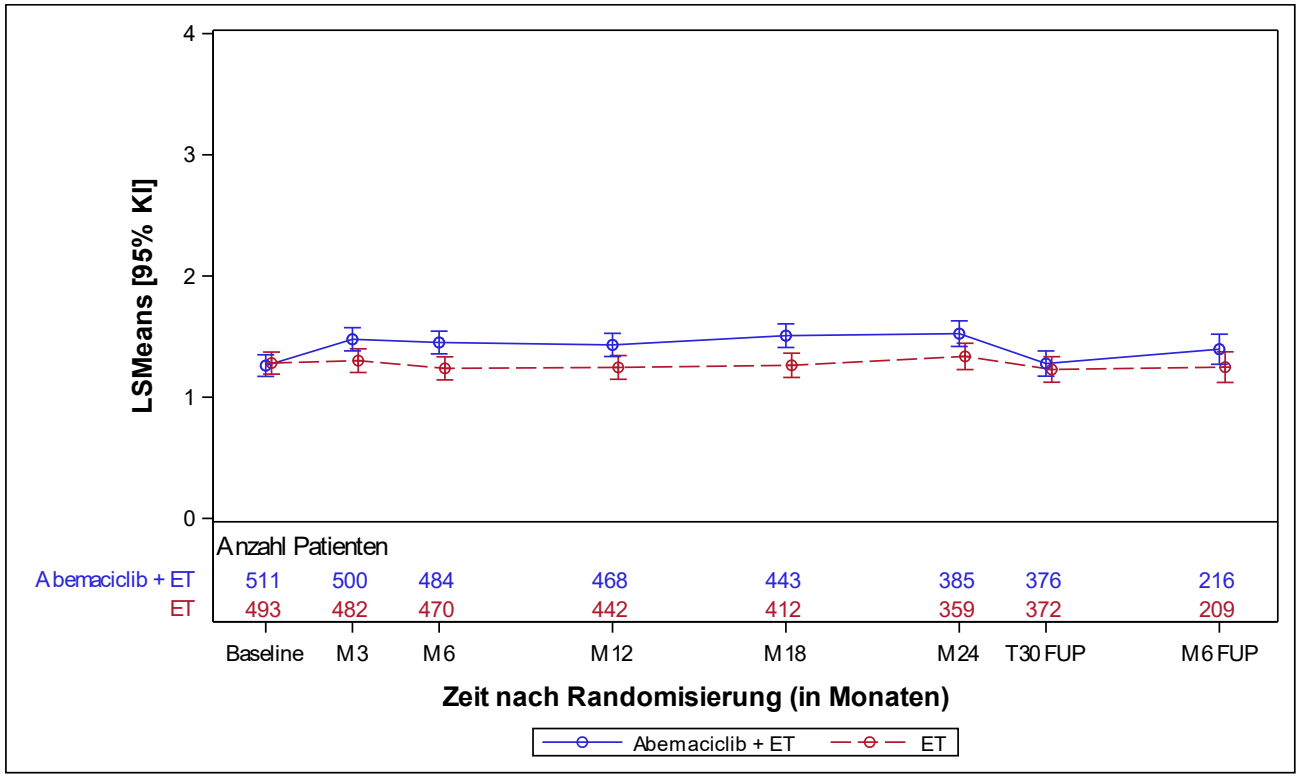
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I feel tired
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
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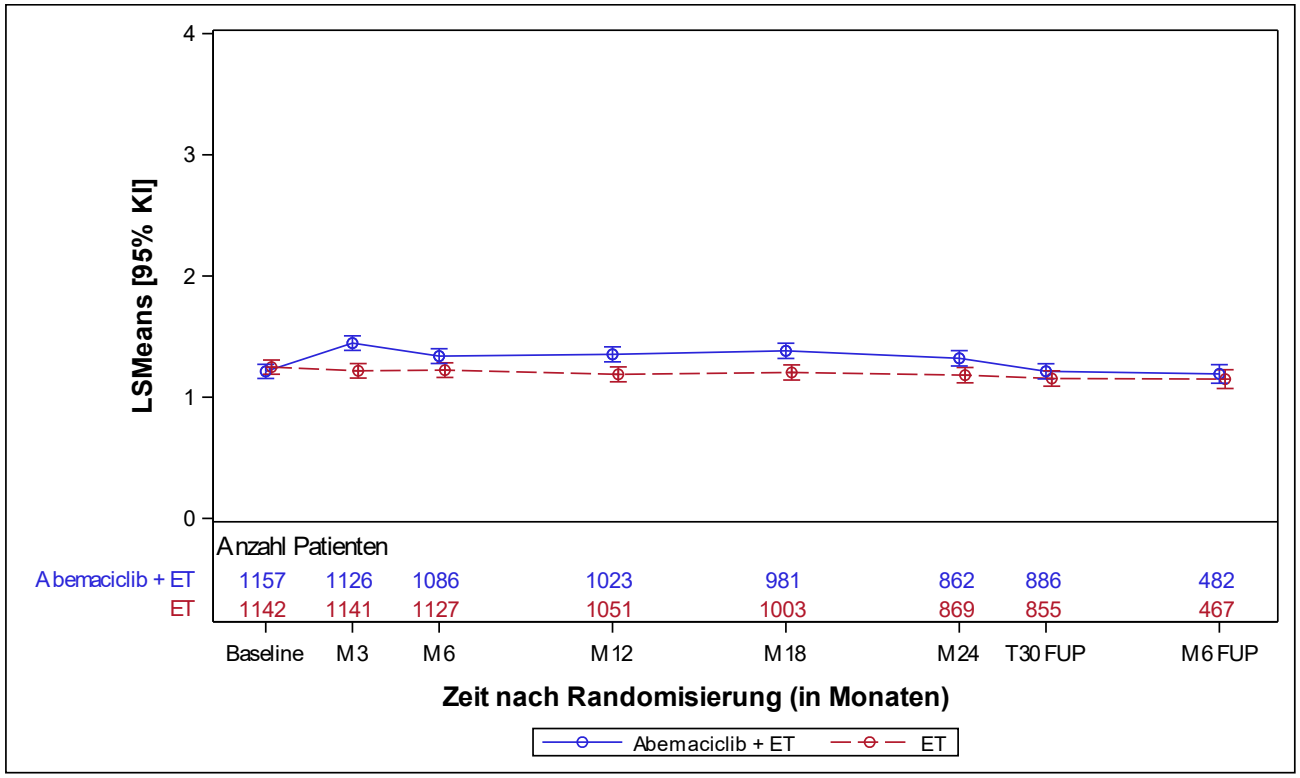
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I feel tired
Kohorte 1 Population - Safety - Postmenopausal



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*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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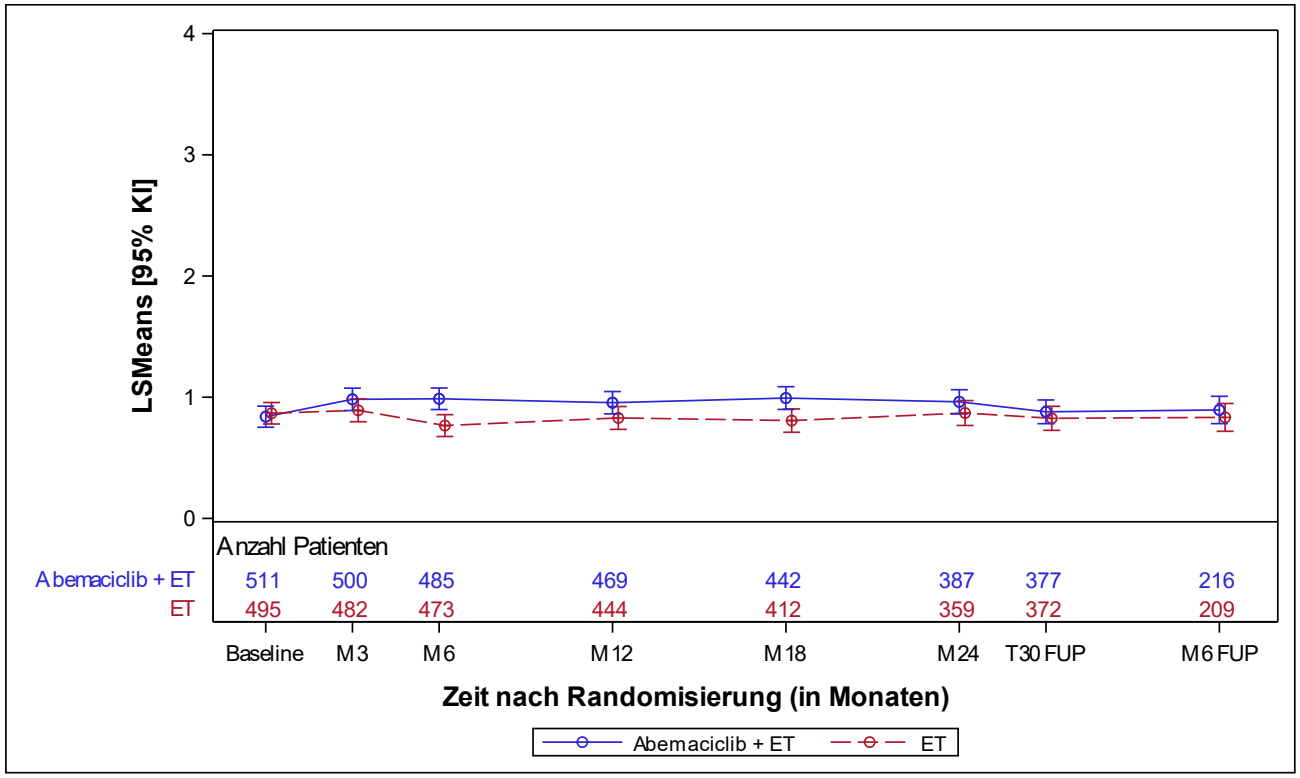
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I have trouble starting things because I am tired
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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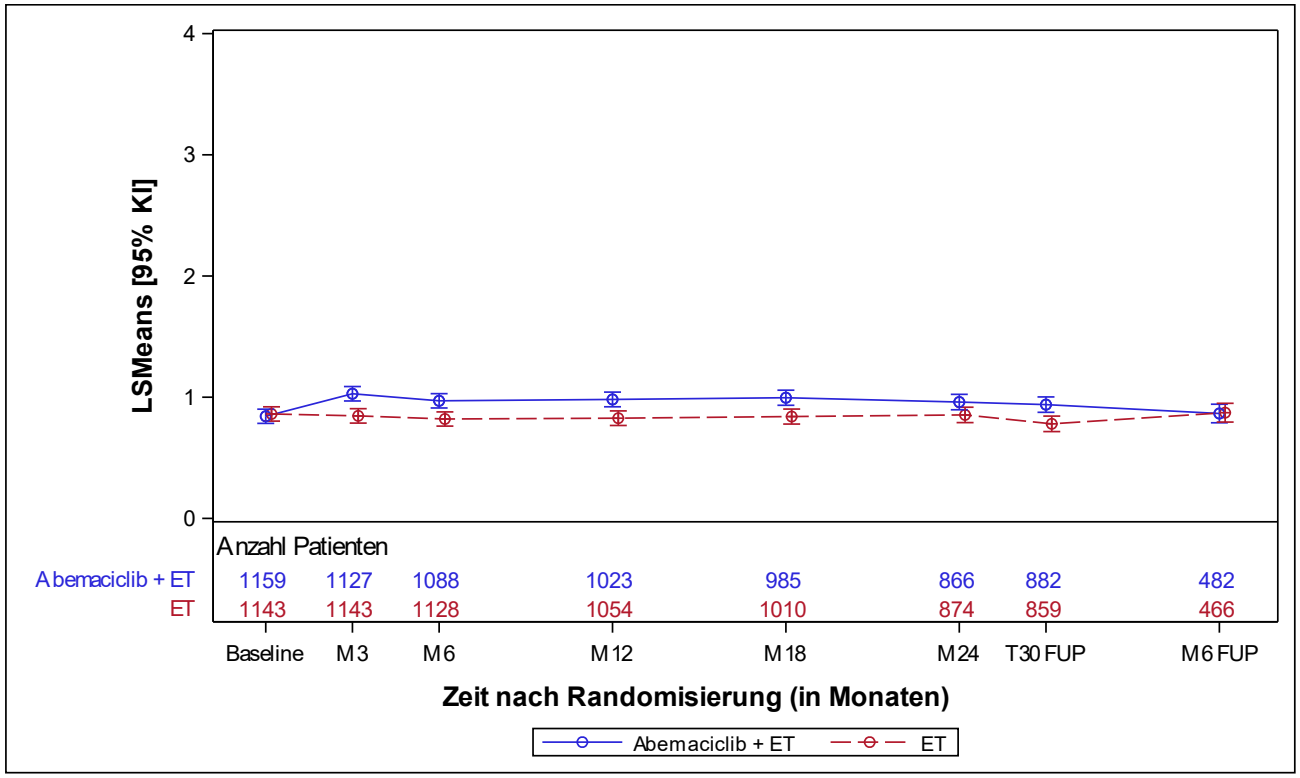
Verlaufskurven - FACIT-Fatigue: I have trouble starting things because I am tired
Kohorte 1 Population - Safety - Postmenopausal



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LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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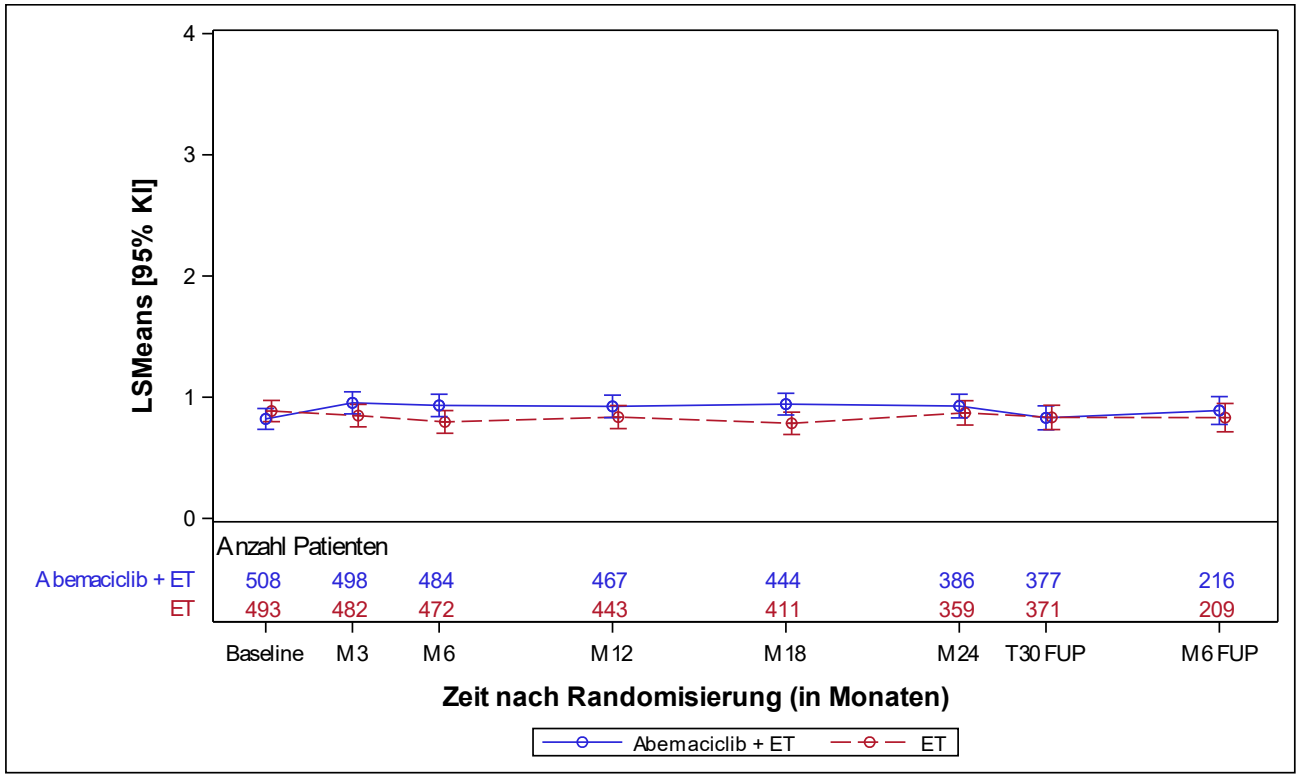
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I have trouble finishing things because I am tired
Kohorte 1 Population - Safety - Prämenopausal



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Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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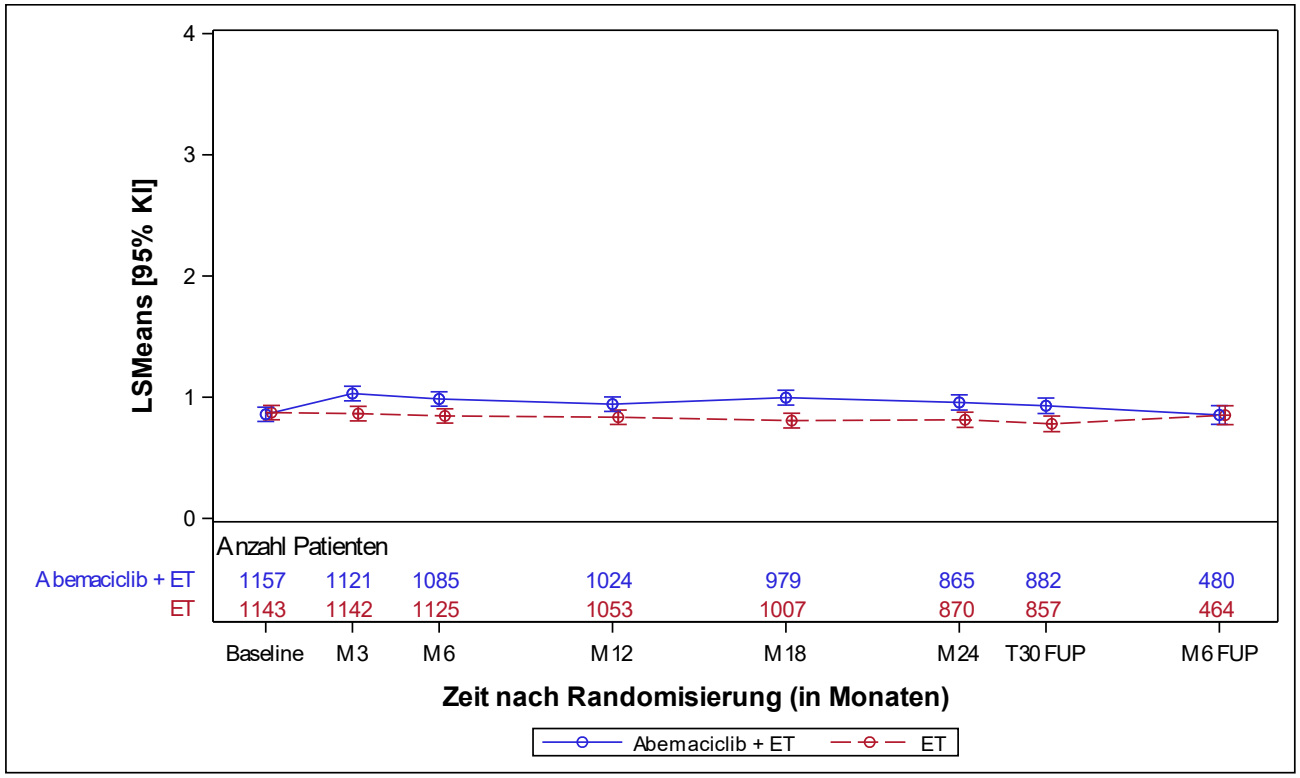
Verlaufskurven - FACIT-Fatigue: I have trouble finishing things because I am tired
Kohorte 1 Population - Safety - Postmenopausal



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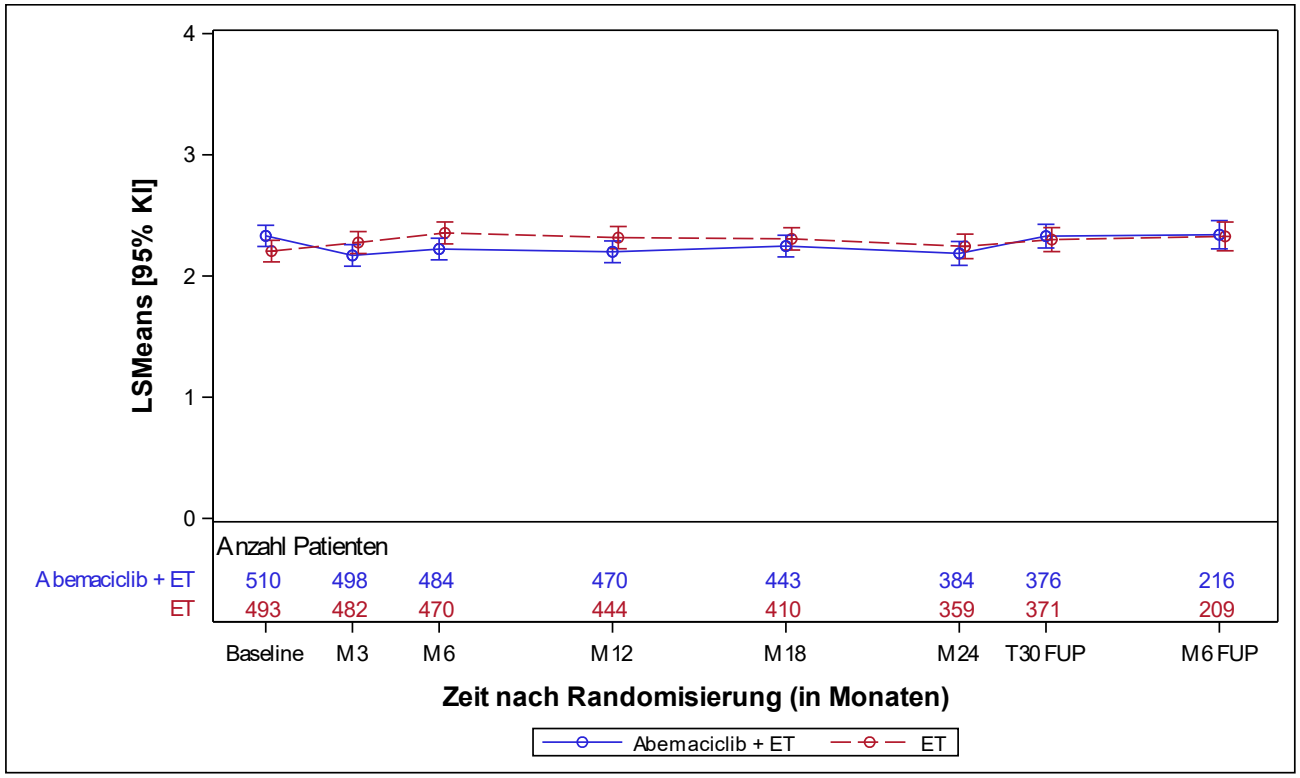
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I have energy
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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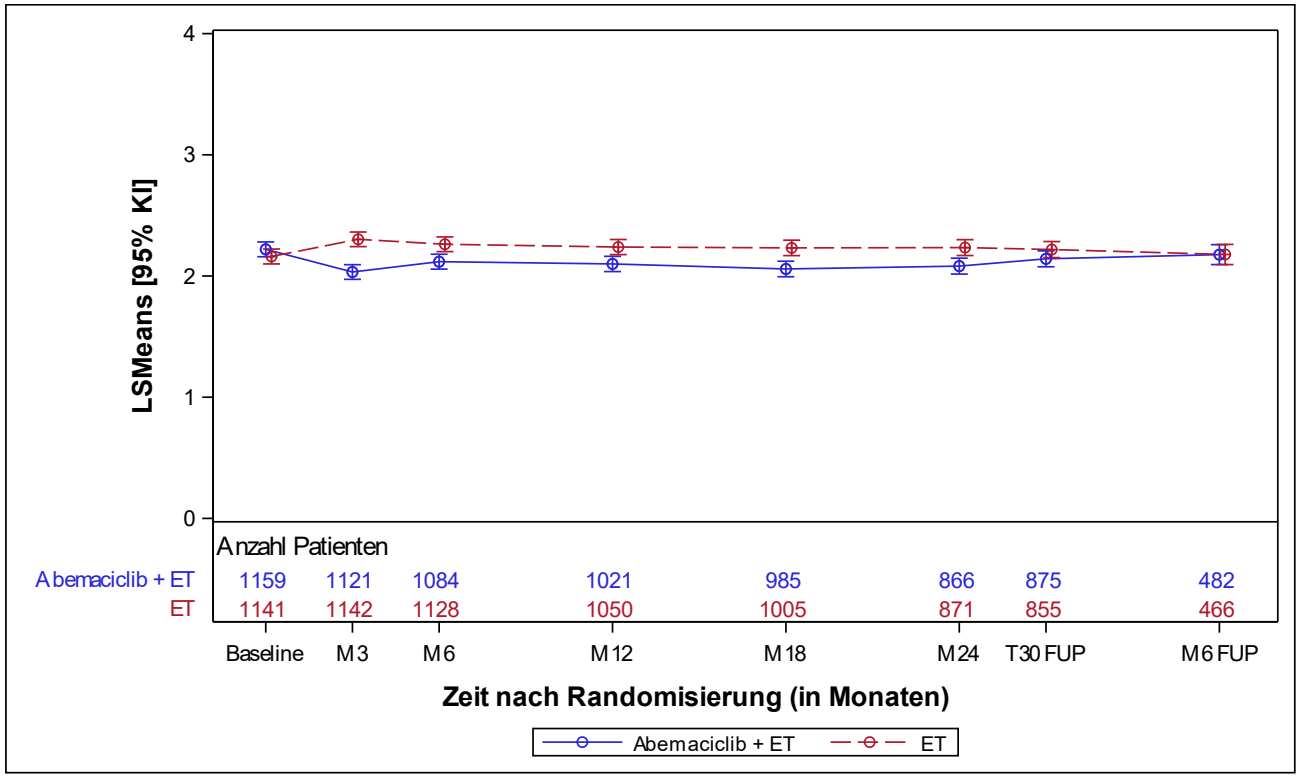
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I have energy
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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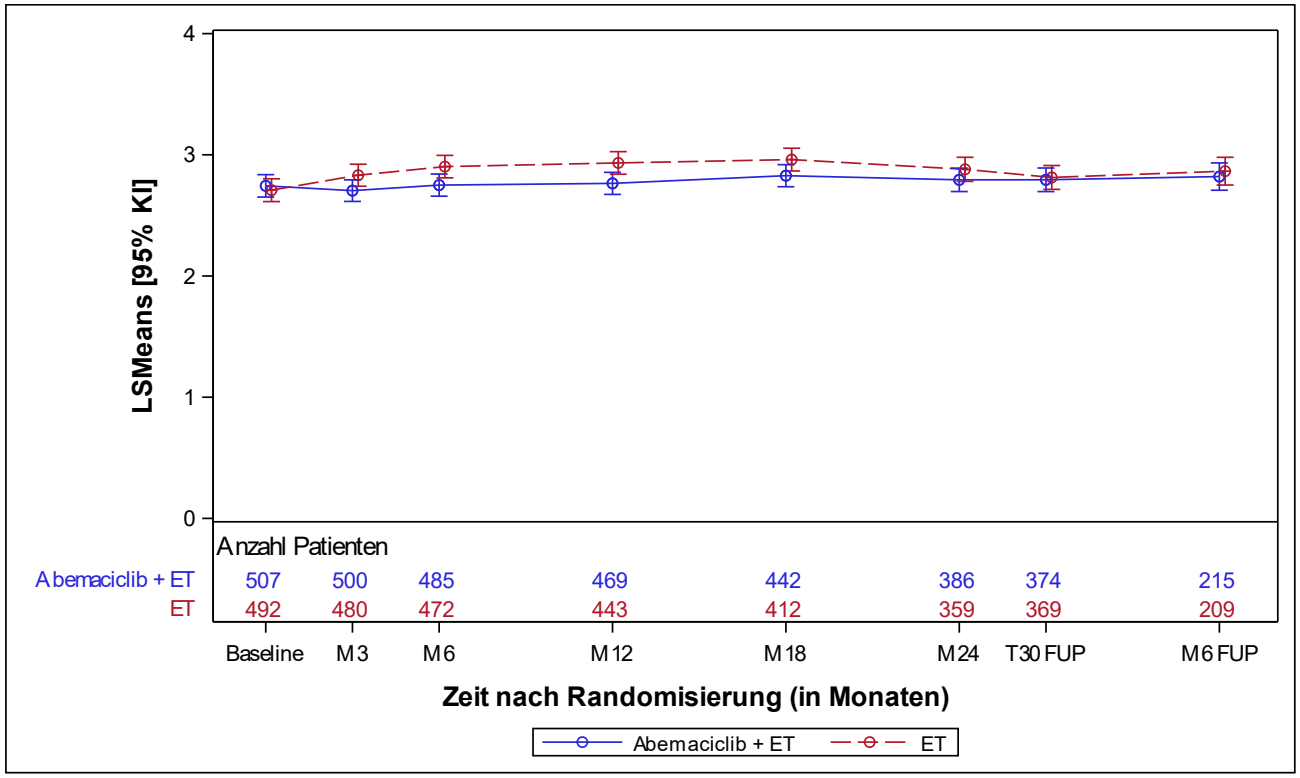
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I am able to do usual activities
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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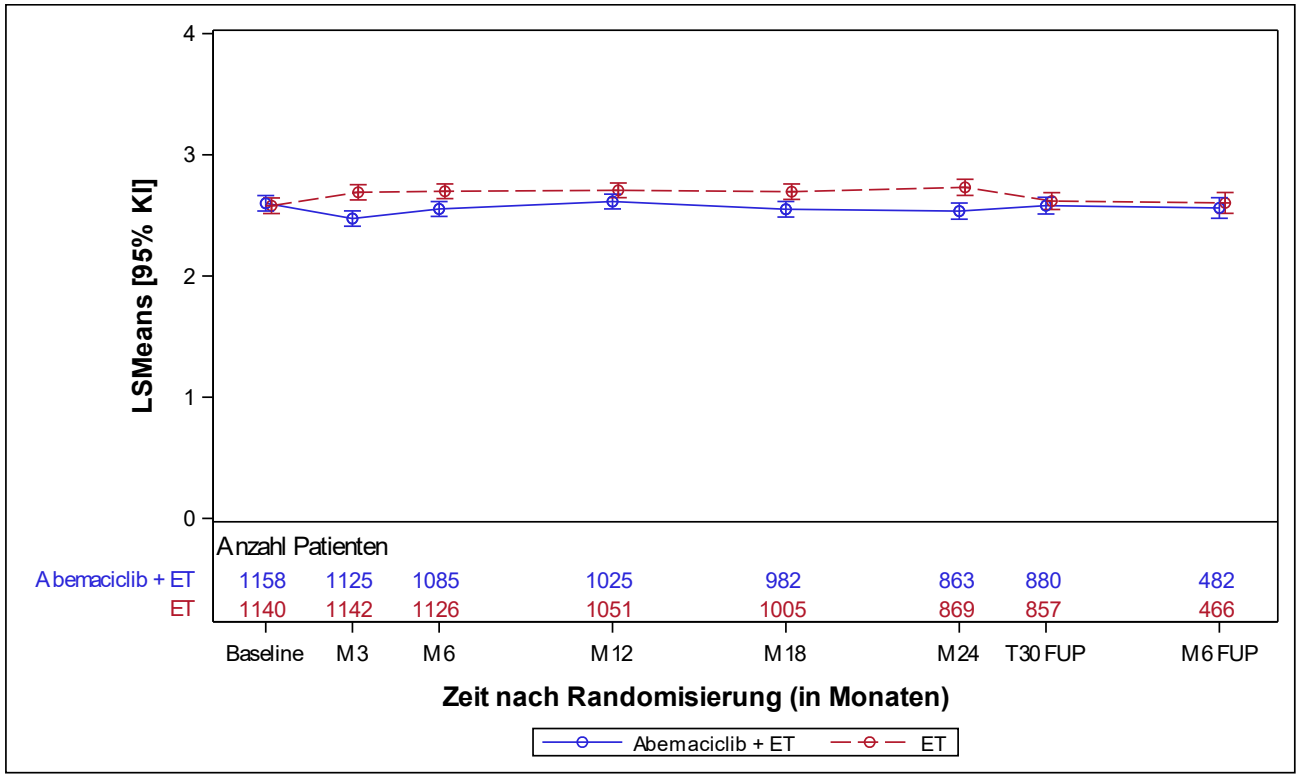
Verlaufskurven - FACIT-Fatigue: I am able to do usual activities
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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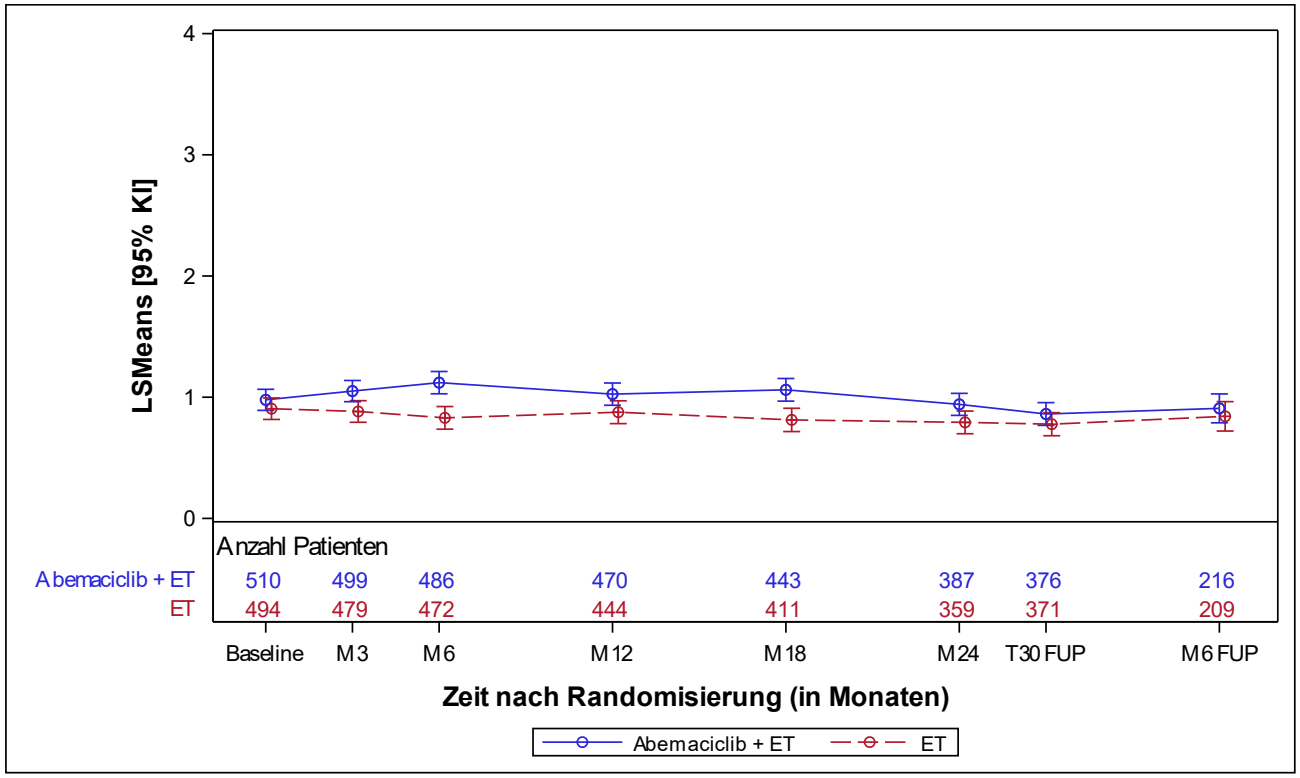
Verlaufskurven - FACIT-Fatigue: I need to sleep during the day
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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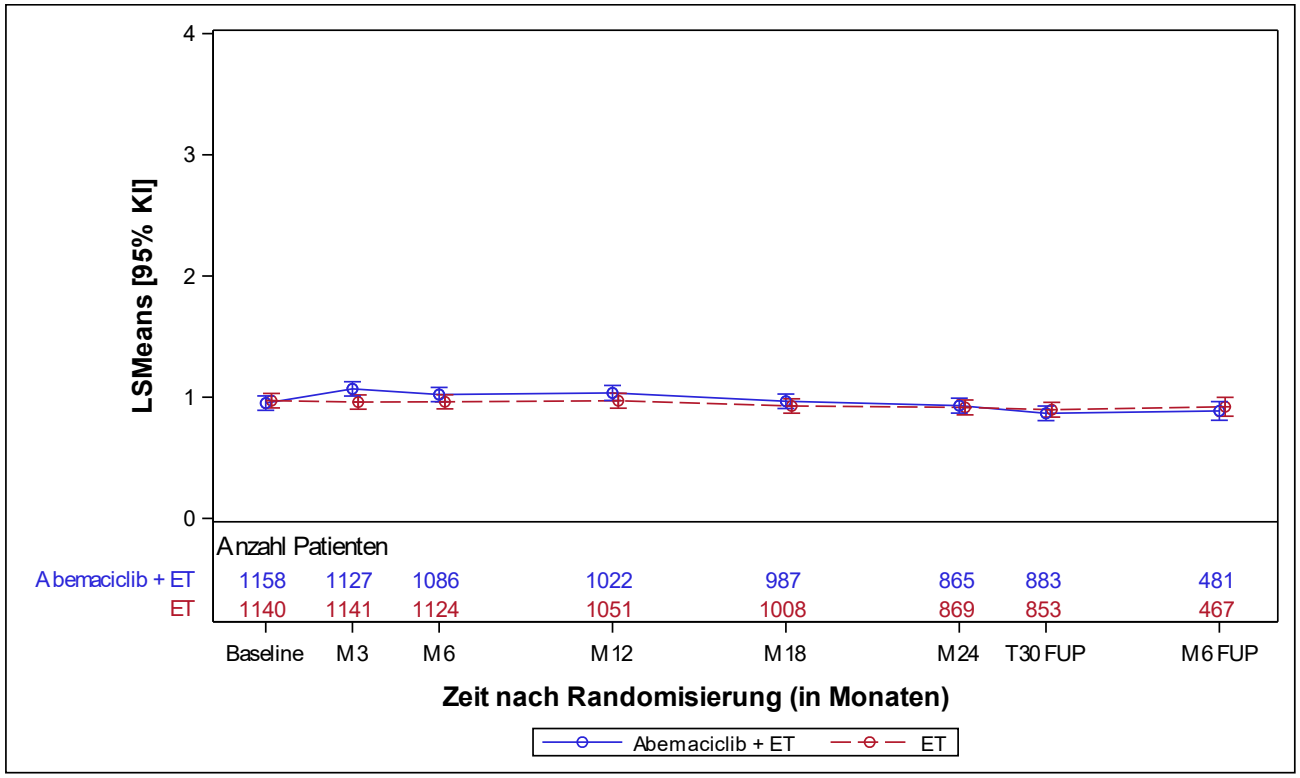
Verlaufskurven - FACIT-Fatigue: I need to sleep during the day
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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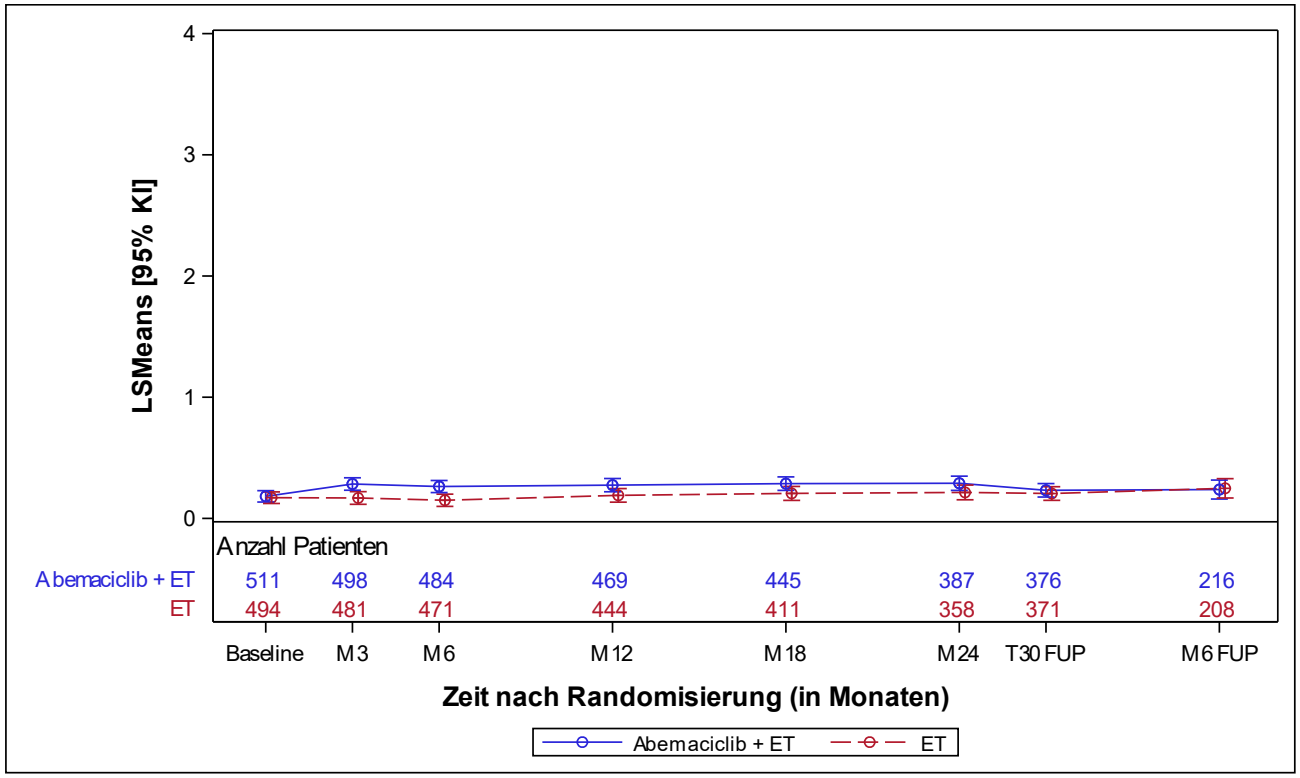
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I am too tired to eat
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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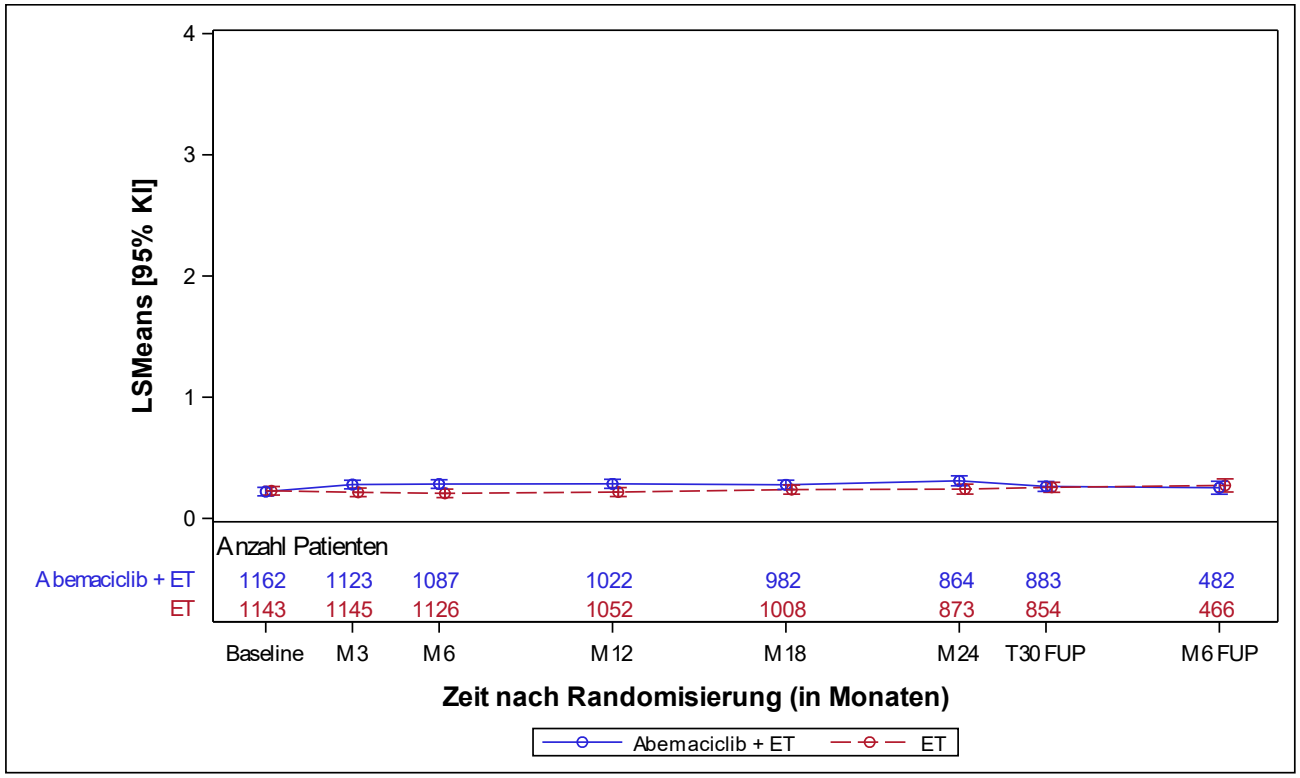
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I am too tired to eat
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
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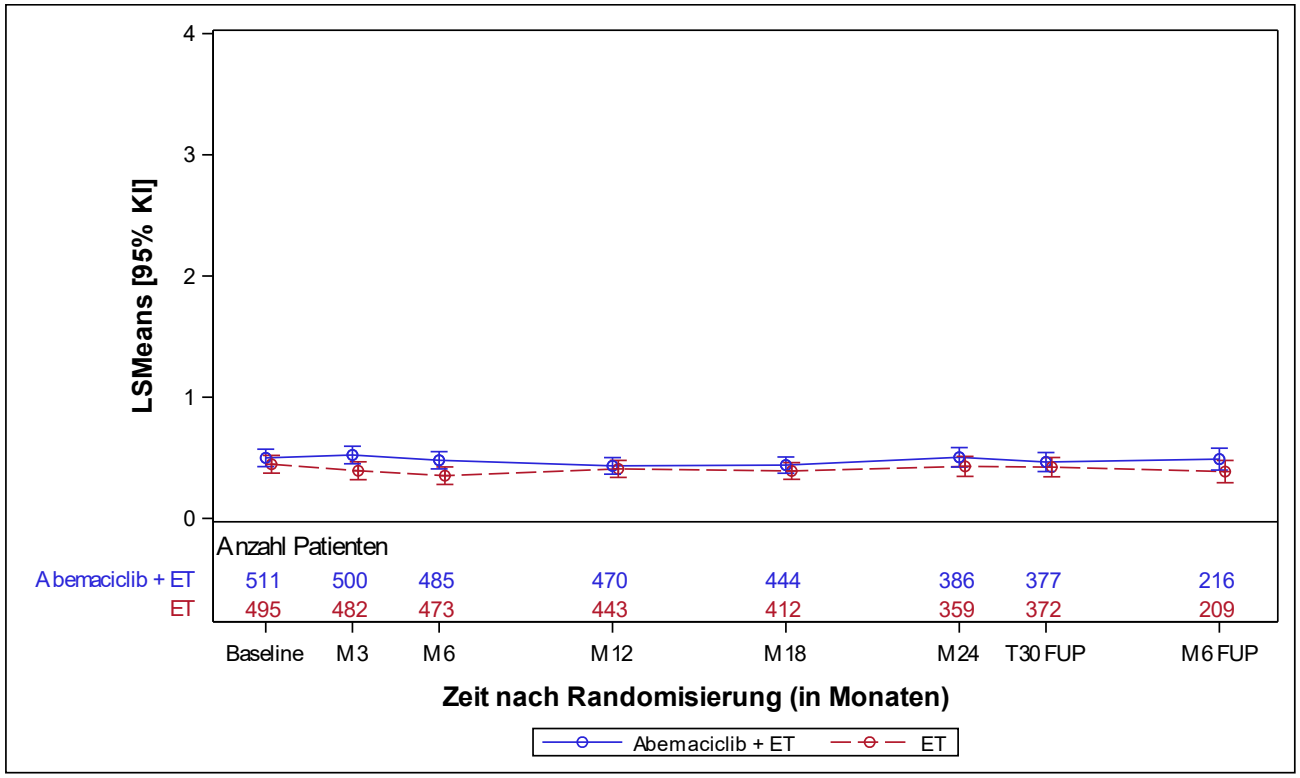
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I need help doing my usual activities
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
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Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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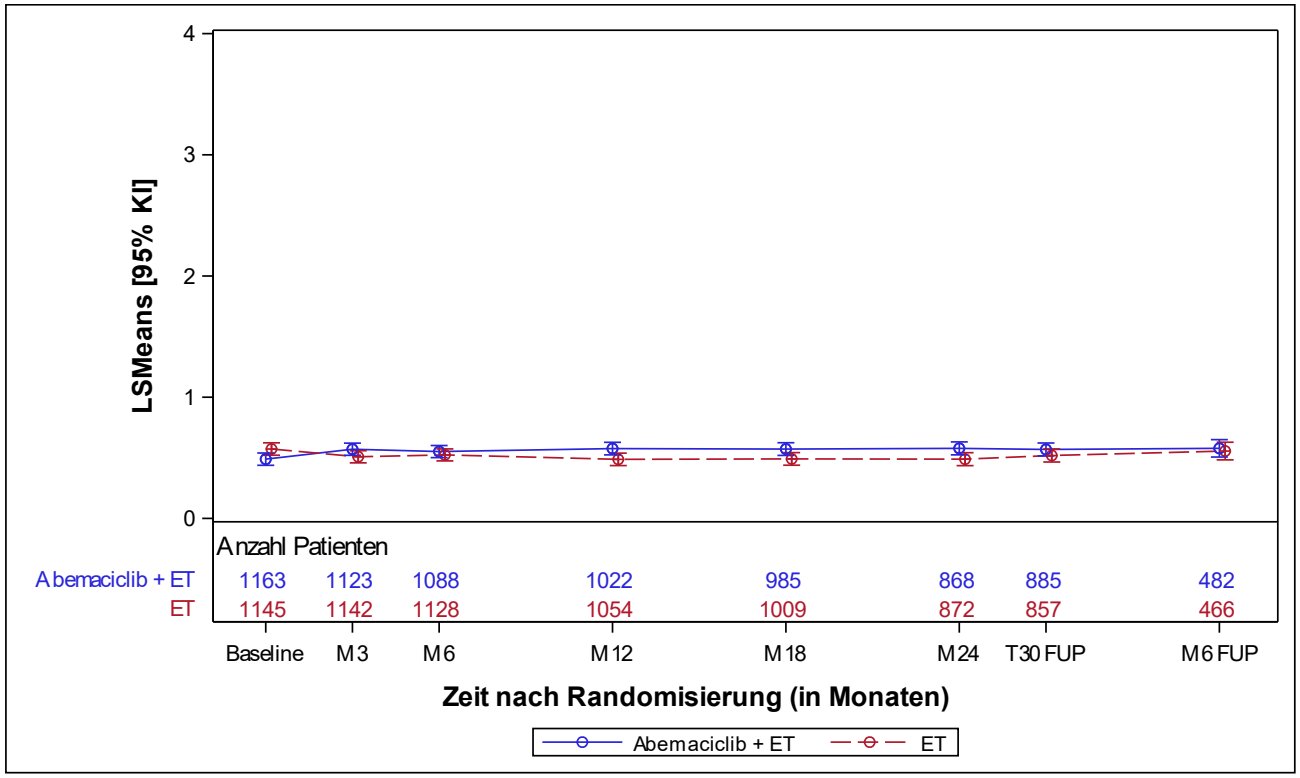
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I need help doing my usual activities
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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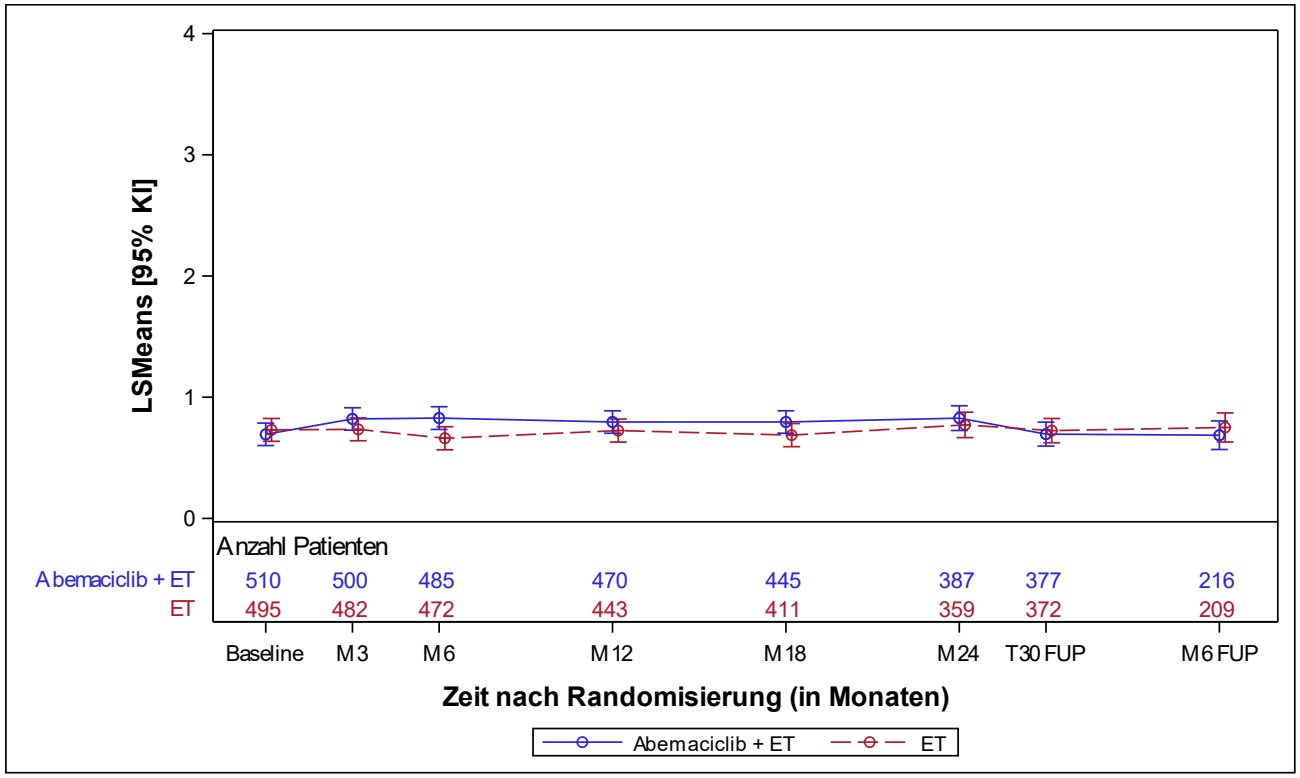
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I am frustrated by being too tired to do the things I want to do
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
*LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.*
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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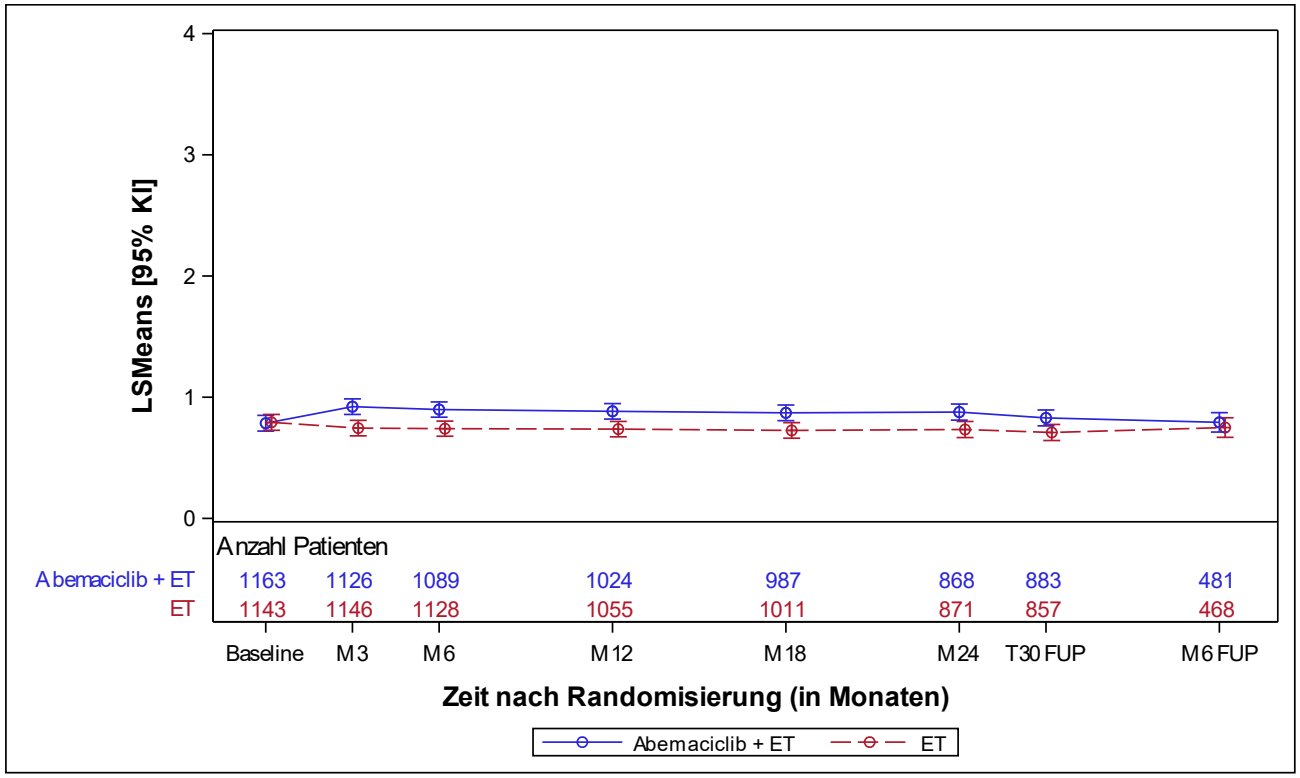
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I am frustrated by being too tired to do the things I want to do
Kohorte 1 Population - Safety - Postmenopausal



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Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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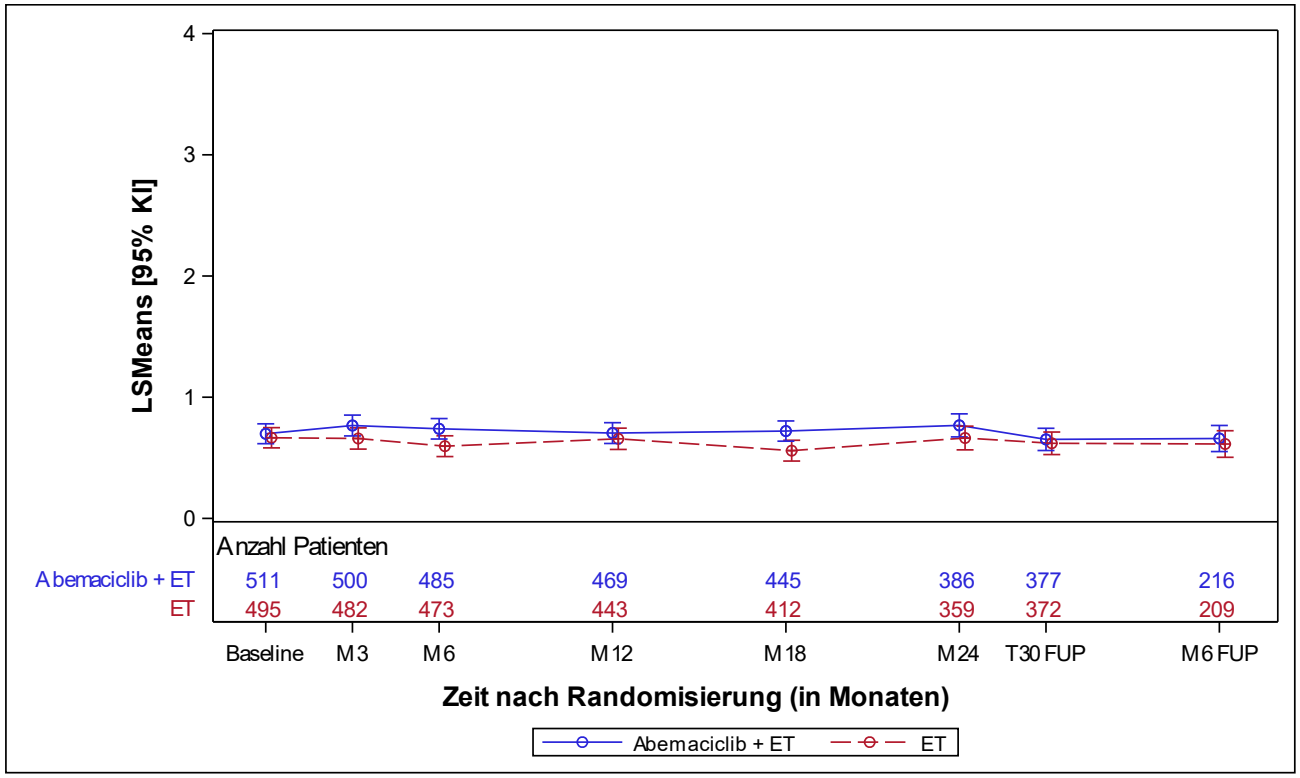
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I have to limit my social activity because I am tired
Kohorte 1 Population - Safety - Prämenopausal



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Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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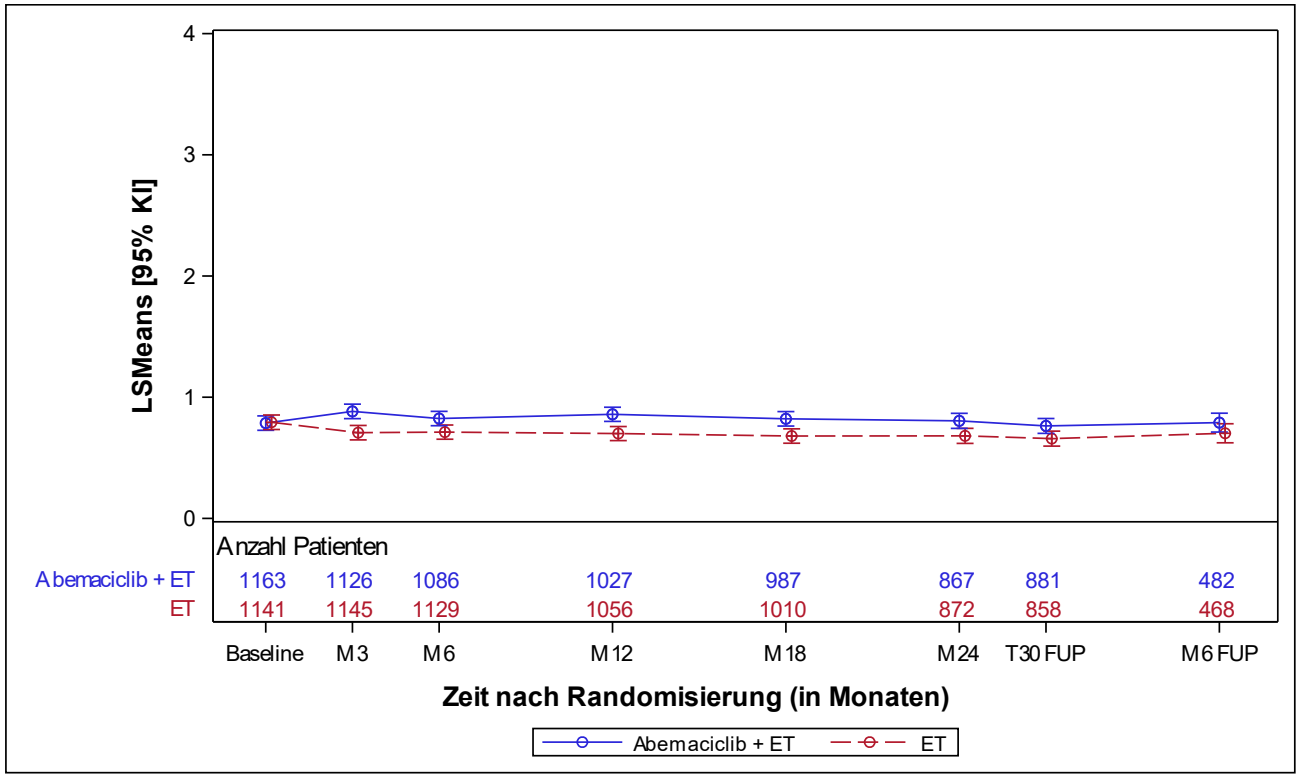
30NOV2021 / 02:40

Verlaufskurven - FACIT-Fatigue: I have to limit my social activity because I am tired
Kohorte 1 Population - Safety - Postmenopausal



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LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
Abkürzungen: ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; FUP: Follow-up; KI: Konfidenzintervall; LSMean: Least Squares Mean; M: Monat; T: Tag
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30NOV2021 / 02:40

Anhang 4-G1.3: Häufige unerwünschte Ereignisse nach SOC und PT

Tabelle 4-121 (Anhang): Häufige unerwünschte Ereignisse nach SOC und PT

Table: Results from binary analysis for adverse events according PT - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Abdominal distension				
15/553 (2,7)	3/535 (0,6)	4,84 [1,41; 16,61] 0,0123[3]	4,94 [1,42; 17,18] 0,0054[4]	2,2 [0,7; 3,6] 0,0054[4]
Abdominal pain				
136/553 (24,6)	26/535 (4,9)	5,06 [3,38; 7,57] <,0001[3]	6,38 [4,12; 9,90] <,0001[4]	19,7 [15,7; 23,8] <,0001[4]
Abdominal pain upper				
68/553 (12,3)	22/535 (4,1)	2,99 [1,88; 4,76] <,0001[3]	3,27 [1,99; 5,37] <,0001[4]	8,2 [5,0; 11,4] <,0001[4]
Alanine aminotransferase increased				
41/553 (7,4)	27/535 (5,0)	1,47 [0,92; 2,35] 0,1095[3]	1,51 [0,91; 2,49] 0,1068[4]	2,4 [-0,5; 5,2] 0,1068[4]
Alopecia				
43/553 (7,8)	10/535 (1,9)	4,16 [2,11; 8,19] <,0001[3]	4,43 [2,20; 8,90] <,0001[4]	5,9 [3,4; 8,4] <,0001[4]
Anaemia				
101/553 (18,3)	23/535 (4,3)	4,25 [2,74; 6,58] <,0001[3]	4,97 [3,11; 7,96] <,0001[4]	14,0 [10,3; 17,6] <,0001[4]
Anxiety				
21/553 (3,8)	25/535 (4,7)	0,81 [0,46; 1,43] 0,4740[3]	0,81 [0,45; 1,46] 0,4731[4]	-0,9 [-3,3; 1,5] 0,4731[4]
Arthralgia				
106/553 (19,2)	142/535 (26,5)	0,72 [0,58; 0,90] 0,0040[3]	0,66 [0,49; 0,87] 0,0037[4]	-7,4 [-12,4; -2,4] 0,0037[4]
Aspartate aminotransferase increased				
42/553 (7,6)	22/535 (4,1)	1,85 [1,12; 3,05] 0,0166[3]	1,92 [1,13; 3,26] 0,0147[4]	3,5 [0,7; 6,3] 0,0147[4]
Asthenia				
57/553 (10,3)	22/535 (4,1)	2,51 [1,56; 4,04] 0,0002[3]	2,68 [1,61; 4,45] <,0001[4]	6,2 [3,2; 9,2] <,0001[4]
Back pain				
60/553 (10,8)	68/535 (12,7)	0,85 [0,62; 1,18] 0,3416[3]	0,84 [0,58; 1,21] 0,3410[4]	-1,9 [-5,7; 2,0] 0,3410[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood cholesterol increased				
10/553 (1,8)	7/535 (1,3)	1,38 [0,53; 3,60] 0,5082[3]	1,39 [0,52; 3,68] 0,5062[4]	0,5 [-1,0; 2,0] 0,5062[4]
Blood creatinine increased				
51/553 (9,2)	2/535 (0,4)	24,67 [6,04; 100,83] <,0001[3]	27,07 [6,56; 111,79] <,0001[4]	8,8 [6,4; 11,3] <,0001[4]
Bone pain				
6/553 (1,1)	13/535 (2,4)	0,45 [0,17; 1,17] 0,0997[3]	0,44 [0,17; 1,17] 0,0904[4]	-1,3 [-2,9; 0,2] 0,0904[4]
Breast pain				
23/553 (4,2)	20/535 (3,7)	1,11 [0,62; 2,00] 0,7219[3]	1,12 [0,61; 2,06] 0,7217[4]	0,4 [-1,9; 2,7] 0,7217[4]
Cellulitis				
15/553 (2,7)	5/535 (0,9)	2,90 [1,06; 7,93] 0,0377[3]	2,96 [1,07; 8,19] 0,0291[4]	1,8 [0,2; 3,4] 0,0291[4]
Chills				
14/553 (2,5)	2/535 (0,4)	6,77 [1,55; 29,66] 0,0111[3]	6,92 [1,57; 30,60] 0,0031[4]	2,2 [0,8; 3,6] 0,0031[4]
Conjunctivitis				
10/553 (1,8)	6/535 (1,1)	1,61 [0,59; 4,41] 0,3516[3]	1,62 [0,59; 4,50] 0,3468[4]	0,7 [-0,7; 2,1] 0,3468[4]
Constipation				
78/553 (14,1)	43/535 (8,0)	1,75 [1,23; 2,50] 0,0018[3]	1,88 [1,27; 2,78] 0,0015[4]	6,1 [2,4; 9,8] 0,0015[4]
Cough				
66/553 (11,9)	28/535 (5,2)	2,28 [1,49; 3,49] 0,0001[3]	2,45 [1,55; 3,88] <,0001[4]	6,7 [3,4; 10,0] <,0001[4]
Cystitis				
19/553 (3,4)	10/535 (1,9)	1,84 [0,86; 3,92] 0,1147[3]	1,87 [0,86; 4,06] 0,1087[4]	1,6 [-0,3; 3,5] 0,1087[4]
Decreased appetite				
49/553 (8,9)	7/535 (1,3)	6,77 [3,10; 14,82] <,0001[3]	7,33 [3,29; 16,34] <,0001[4]	7,6 [5,0; 10,1] <,0001[4]
Depression				
26/553 (4,7)	17/535 (3,2)	1,48 [0,81; 2,70] 0,2003[3]	1,50 [0,81; 2,80] 0,1971[4]	1,5 [-0,8; 3,8] 0,1971[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Diarrhoea				
444/553 (80,3)	31/535 (5,8)	13,86 [9,82; 19,55] <,0001[3]	66,23 [43,56; 100,68] <,0001[4]	74,5 [70,6; 78,4] <,0001[4]
Dizziness				
46/553 (8,3)	29/535 (5,4)	1,53 [0,98; 2,40] 0,0617[3]	1,58 [0,98; 2,56] 0,0593[4]	2,9 [-0,1; 5,9] 0,0593[4]
Dry eye				
21/553 (3,8)	7/535 (1,3)	2,90 [1,24; 6,77] 0,0137[3]	2,98 [1,26; 7,06] 0,0095[4]	2,5 [0,6; 4,4] 0,0095[4]
Dry mouth				
13/553 (2,4)	4/535 (0,7)	3,14 [1,03; 9,58] 0,0439[3]	3,20 [1,04; 9,86] 0,0330[4]	1,6 [0,1; 3,1] 0,0330[4]
Dry skin				
29/553 (5,2)	15/535 (2,8)	1,87 [1,01; 3,45] 0,0449[3]	1,92 [1,02; 3,62] 0,0411[4]	2,4 [0,1; 4,8] 0,0411[4]
Dysgeusia				
15/553 (2,7)	1/535 (0,2)	14,51 [1,92; 109,48] 0,0095[3]	14,89 [1,96; 113,11] 0,0005[4]	2,5 [1,1; 3,9] 0,0005[4]
Dyspepsia				
55/553 (9,9)	14/535 (2,6)	3,80 [2,14; 6,75] <,0001[3]	4,11 [2,26; 7,48] <,0001[4]	7,3 [4,5; 10,2] <,0001[4]
Dyspnoea				
34/553 (6,1)	11/535 (2,1)	2,99 [1,53; 5,84] 0,0013[3]	3,12 [1,56; 6,23] 0,0007[4]	4,1 [1,8; 6,4] 0,0007[4]
Eczema				
5/553 (0,9)	14/535 (2,6)	0,35 [0,13; 0,95] 0,0400[3]	0,34 [0,12; 0,95] 0,0311[4]	-1,7 [-3,3; -0,1] 0,0311[4]
Erythema				
13/553 (2,4)	3/535 (0,6)	4,19 [1,20; 14,63] 0,0246[3]	4,27 [1,21; 15,07] 0,0142[4]	1,8 [0,4; 3,2] 0,0142[4]
Fatigue				
146/553 (26,4)	65/535 (12,1)	2,17 [1,66; 2,84] <,0001[3]	2,59 [1,88; 3,58] <,0001[4]	14,3 [9,7; 18,9] <,0001[4]
Gamma-glutamyltransferase increased				
15/553 (2,7)	5/535 (0,9)	2,90 [1,06; 7,93] 0,0377[3]	2,96 [1,07; 8,19] 0,0291[4]	1,8 [0,2; 3,4] 0,0291[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Gastritis				
16/553 (2,9)	6/535 (1,1)	2,58 [1,02; 6,54] 0,0460[3]	2,63 [1,02; 6,76] 0,0379[4]	1,8 [0,1; 3,4] 0,0379[4]
Gastroenteritis				
15/553 (2,7)	8/535 (1,5)	1,81 [0,78; 4,24] 0,1696[3]	1,84 [0,77; 4,37] 0,1629[4]	1,2 [-0,5; 2,9] 0,1629[4]
Gastrooesophageal reflux disease				
15/553 (2,7)	8/535 (1,5)	1,81 [0,78; 4,24] 0,1696[3]	1,84 [0,77; 4,37] 0,1629[4]	1,2 [-0,5; 2,9] 0,1629[4]
Haemorrhoids				
21/553 (3,8)	9/535 (1,7)	2,26 [1,04; 4,88] 0,0387[3]	2,31 [1,05; 5,08] 0,0332[4]	2,1 [0,2; 4,0] 0,0332[4]
Headache				
108/553 (19,5)	92/535 (17,2)	1,14 [0,88; 1,46] 0,3211[3]	1,17 [0,86; 1,59] 0,3205[4]	2,3 [-2,3; 6,9] 0,3205[4]
Hepatic steatosis				
13/553 (2,4)	12/535 (2,2)	1,05 [0,48; 2,28] 0,9055[3]	1,05 [0,47; 2,32] 0,9055[4]	0,1 [-1,7; 1,9] 0,9055[4]
Hot flush				
98/553 (17,7)	123/535 (23,0)	0,77 [0,61; 0,98] 0,0315[3]	0,72 [0,54; 0,97] 0,0308[4]	-5,3 [-10,0; -0,5] 0,0308[4]
Hypertension				
27/553 (4,9)	19/535 (3,6)	1,37 [0,77; 2,44] 0,2777[3]	1,39 [0,77; 2,54] 0,2754[4]	1,3 [-1,1; 3,7] 0,2754[4]
Hypertriglyceridaemia				
12/553 (2,2)	7/535 (1,3)	1,66 [0,66; 4,18] 0,2835[3]	1,67 [0,65; 4,28] 0,2781[4]	0,9 [-0,7; 2,4] 0,2781[4]
Hypokalaemia				
18/553 (3,3)	1/535 (0,2)	17,41 [2,33; 129,99] 0,0053[3]	17,97 [2,39; 135,06] 0,0001[4]	3,1 [1,5; 4,6] 0,0001[4]
Hypothyroidism				
7/553 (1,3)	14/535 (2,6)	0,48 [0,20; 1,19] 0,1135[3]	0,48 [0,19; 1,19] 0,1054[4]	-1,4 [-3,0; 0,3] 0,1054[4]
Influenza				
29/553 (5,2)	25/535 (4,7)	1,12 [0,67; 1,89] 0,6647[3]	1,13 [0,65; 1,95] 0,6645[4]	0,6 [-2,0; 3,2] 0,6645[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Influenza like illness				
40/553 (7,2)	23/535 (4,3)	1,68 [1,02; 2,77] 0,0410[3]	1,74 [1,02; 2,94] 0,0383[4]	2,9 [0,2; 5,7] 0,0383[4]
Insomnia				
48/553 (8,7)	46/535 (8,6)	1,01 [0,69; 1,49] 0,9617[3]	1,01 [0,66; 1,54] 0,9617[4]	0,1 [-3,3; 3,4] 0,9617[4]
Lacrimation increased				
28/553 (5,1)	1/535 (0,2)	27,09 [3,70; 198,39] 0,0012[3]	28,48 [3,86; 210,08] <,0001[4]	4,9 [3,0; 6,7] <,0001[4]
Leukopenia				
53/553 (9,6)	8/535 (1,5)	6,41 [3,08; 13,35] <,0001[3]	6,98 [3,29; 14,83] <,0001[4]	8,1 [5,4; 10,7] <,0001[4]
Lymphocyte count decreased				
57/553 (10,3)	15/535 (2,8)	3,68 [2,11; 6,41] <,0001[3]	3,98 [2,23; 7,13] <,0001[4]	7,5 [4,6; 10,4] <,0001[4]
Lymphoedema				
78/553 (14,1)	52/535 (9,7)	1,45 [1,04; 2,02] 0,0271[3]	1,53 [1,05; 2,21] 0,0258[4]	4,4 [0,5; 8,2] 0,0258[4]
Lymphopenia				
19/553 (3,4)	6/535 (1,1)	3,06 [1,23; 7,61] 0,0159[3]	3,14 [1,24; 7,92] 0,0109[4]	2,3 [0,6; 4,1] 0,0109[4]
Malaise				
24/553 (4,3)	9/535 (1,7)	2,58 [1,21; 5,50] 0,0141[3]	2,65 [1,22; 5,76] 0,0106[4]	2,7 [0,6; 4,7] 0,0106[4]
Mucosal inflammation				
12/553 (2,2)	3/535 (0,6)	3,87 [1,10; 13,64] 0,0352[3]	3,93 [1,10; 14,02] 0,0229[4]	1,6 [0,2; 3,0] 0,0229[4]
Muscle spasms				
36/553 (6,5)	30/535 (5,6)	1,16 [0,73; 1,86] 0,5335[3]	1,17 [0,71; 1,93] 0,5330[4]	0,9 [-1,9; 3,7] 0,5330[4]
Musculoskeletal chest pain				
12/553 (2,2)	12/535 (2,2)	0,97 [0,44; 2,13] 0,9347[3]	0,97 [0,43; 2,17] 0,9347[4]	-0,1 [-1,8; 1,7] 0,9347[4]
Myalgia				
39/553 (7,1)	30/535 (5,6)	1,26 [0,79; 1,99] 0,3296[3]	1,28 [0,78; 2,09] 0,3282[4]	1,4 [-1,4; 4,3] 0,3282[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Nail disorder				
15/553 (2,7)	2/535 (0,4)	7,26 [1,67; 31,58] 0,0083[3]	7,43 [1,69; 32,65] 0,0019[4]	2,3 [0,9; 3,8] 0,0019[4]
Nasopharyngitis				
82/553 (14,8)	52/535 (9,7)	1,53 [1,10; 2,11] 0,0112[3]	1,62 [1,12; 2,34] 0,0104[4]	5,1 [1,2; 9,0] 0,0104[4]
Nausea				
154/553 (27,8)	40/535 (7,5)	3,72 [2,69; 5,16] <,0001[3]	4,78 [3,29; 6,93] <,0001[4]	20,4 [16,0; 24,7] <,0001[4]
Neck pain				
12/553 (2,2)	6/535 (1,1)	1,93 [0,73; 5,12] 0,1835[3]	1,96 [0,73; 5,25] 0,1753[4]	1,0 [-0,5; 2,6] 0,1753[4]
Neuropathy peripheral				
10/553 (1,8)	9/535 (1,7)	1,07 [0,44; 2,62] 0,8739[3]	1,08 [0,43; 2,67] 0,8739[4]	0,1 [-1,4; 1,7] 0,8739[4]
Neutropenia				
104/553 (18,8)	17/535 (3,2)	5,92 [3,59; 9,75] <,0001[3]	7,06 [4,16; 11,97] <,0001[4]	15,6 [12,0; 19,2] <,0001[4]
Neutrophil count decreased				
138/553 (25,0)	22/535 (4,1)	6,07 [3,93; 9,37] <,0001[3]	7,75 [4,86; 12,38] <,0001[4]	20,8 [16,9; 24,8] <,0001[4]
Oedema				
10/553 (1,8)	2/535 (0,4)	4,84 [1,06; 21,97] 0,0412[3]	4,91 [1,07; 22,50] 0,0235[4]	1,4 [0,2; 2,7] 0,0235[4]
Oedema peripheral				
43/553 (7,8)	22/535 (4,1)	1,89 [1,15; 3,12] 0,0125[3]	1,97 [1,16; 3,33] 0,0108[4]	3,7 [0,9; 6,5] 0,0108[4]
Onychoclasis				
14/553 (2,5)	4/535 (0,7)	3,39 [1,12; 10,22] 0,0305[3]	3,45 [1,13; 10,54] 0,0211[4]	1,8 [0,3; 3,3] 0,0211[4]
Oropharyngeal pain				
24/553 (4,3)	14/535 (2,6)	1,66 [0,87; 3,17] 0,1262[3]	1,69 [0,86; 3,30] 0,1217[4]	1,7 [-0,4; 3,9] 0,1217[4]
Osteoporosis				
10/553 (1,8)	9/535 (1,7)	1,07 [0,44; 2,62] 0,8739[3]	1,08 [0,43; 2,67] 0,8739[4]	0,1 [-1,4; 1,7] 0,8739[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Pain				
14/553 (2,5)	8/535 (1,5)	1,69 [0,72; 4,00] 0,2304[3]	1,71 [0,71; 4,11] 0,2247[4]	1,0 [-0,6; 2,7] 0,2247[4]
Pain in extremity				
55/553 (9,9)	52/535 (9,7)	1,02 [0,71; 1,47] 0,9004[3]	1,03 [0,69; 1,53] 0,9003[4]	0,2 [-3,3; 3,8] 0,9003[4]
Peripheral sensory neuropathy				
12/553 (2,2)	11/535 (2,1)	1,06 [0,47; 2,37] 0,8961[3]	1,06 [0,46; 2,42] 0,8961[4]	0,1 [-1,6; 1,8] 0,8961[4]
Peripheral swelling				
10/553 (1,8)	9/535 (1,7)	1,07 [0,44; 2,62] 0,8739[3]	1,08 [0,43; 2,67] 0,8739[4]	0,1 [-1,4; 1,7] 0,8739[4]
Platelet count decreased				
38/553 (6,9)	8/535 (1,5)	4,60 [2,16; 9,76] <,0001[3]	4,86 [2,25; 10,52] <,0001[4]	5,4 [3,0; 7,7] <,0001[4]
Pneumonia				
12/553 (2,2)	5/535 (0,9)	2,32 [0,82; 6,55] 0,1112[3]	2,35 [0,82; 6,72] 0,1005[4]	1,2 [-0,2; 2,7] 0,1005[4]
Procedural pain				
20/553 (3,6)	10/535 (1,9)	1,93 [0,91; 4,10] 0,0844[3]	1,97 [0,91; 4,25] 0,0784[4]	1,7 [-0,2; 3,7] 0,0784[4]
Productive cough				
11/553 (2,0)	3/535 (0,6)	3,55 [1,00; 12,64] 0,0509[3]	3,60 [1,00; 12,97] 0,0366[4]	1,4 [0,1; 2,8] 0,0366[4]
Pruritus				
51/553 (9,2)	20/535 (3,7)	2,47 [1,49; 4,08] 0,0004[3]	2,62 [1,54; 4,45] 0,0003[4]	5,5 [2,6; 8,4] 0,0003[4]
Pyrexia				
58/553 (10,5)	25/535 (4,7)	2,24 [1,43; 3,53] 0,0005[3]	2,39 [1,47; 3,88] 0,0003[4]	5,8 [2,7; 8,9] 0,0003[4]
Rash				
44/553 (8,0)	17/535 (3,2)	2,50 [1,45; 4,33] 0,0010[3]	2,63 [1,49; 4,67] 0,0006[4]	4,8 [2,1; 7,5] 0,0006[4]
Rectal haemorrhage				
11/553 (2,0)	2/535 (0,4)	5,32 [1,18; 23,89] 0,0292[3]	5,41 [1,19; 24,52] 0,0142[4]	1,6 [0,3; 2,9] 0,0142[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Rhinitis allergic				
16/553 (2,9)	10/535 (1,9)	1,55 [0,71; 3,38] 0,2729[3]	1,56 [0,70; 3,48] 0,2688[4]	1,0 [-0,8; 2,8] 0,2688[4]
Sinusitis				
20/553 (3,6)	7/535 (1,3)	2,76 [1,18; 6,48] 0,0194[3]	2,83 [1,19; 6,75] 0,0144[4]	2,3 [0,5; 4,1] 0,0144[4]
Skin infection				
11/553 (2,0)	5/535 (0,9)	2,13 [0,74; 6,08] 0,1587[3]	2,15 [0,74; 6,23] 0,1485[4]	1,1 [-0,4; 2,5] 0,1485[4]
Stomatitis				
48/553 (8,7)	11/535 (2,1)	4,22 [2,22; 8,04] <,0001[3]	4,53 [2,33; 8,82] <,0001[4]	6,6 [4,0; 9,3] <,0001[4]
Thrombocytopenia				
18/553 (3,3)	7/535 (1,3)	2,49 [1,05; 5,91] 0,0389[3]	2,54 [1,05; 6,13] 0,0322[4]	1,9 [0,2; 3,7] 0,0322[4]
Toothache				
15/553 (2,7)	7/535 (1,3)	2,07 [0,85; 5,04] 0,1081[3]	2,10 [0,85; 5,20] 0,1000[4]	1,4 [-0,3; 3,1] 0,1000[4]
Upper respiratory tract infection				
46/553 (8,3)	44/535 (8,2)	1,01 [0,68; 1,50] 0,9551[3]	1,01 [0,66; 1,56] 0,9551[4]	0,1 [-3,2; 3,4] 0,9551[4]
Urinary tract infection				
48/553 (8,7)	22/535 (4,1)	2,11 [1,29; 3,45] 0,0028[3]	2,22 [1,32; 3,73] 0,0021[4]	4,6 [1,7; 7,5] 0,0021[4]
Urticaria				
11/553 (2,0)	3/535 (0,6)	3,55 [1,00; 12,64] 0,0509[3]	3,60 [1,00; 12,97] 0,0366[4]	1,4 [0,1; 2,8] 0,0366[4]
Vaginal discharge				
7/553 (1,3)	21/535 (3,9)	0,32 [0,14; 0,75] 0,0088[3]	0,31 [0,13; 0,74] 0,0056[4]	-2,7 [-4,6; -0,8] 0,0056[4]
Vaginal infection				
14/553 (2,5)	7/535 (1,3)	1,93 [0,79; 4,76] 0,1504[3]	1,96 [0,78; 4,89] 0,1426[4]	1,2 [-0,4; 2,8] 0,1426[4]
Vertigo				
15/553 (2,7)	11/535 (2,1)	1,32 [0,61; 2,85] 0,4800[3]	1,33 [0,60; 2,92] 0,4785[4]	0,7 [-1,2; 2,5] 0,4785[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Vitamin D deficiency				
8/553 (1,4)	13/535 (2,4)	0,60 [0,25; 1,42] 0,2441[3]	0,59 [0,24; 1,43] 0,2386[4]	-1,0 [-2,6; 0,7] 0,2386[4]
Vomiting				
82/553 (14,8)	15/535 (2,8)	5,29 [3,09; 9,05] <,0001[3]	6,04 [3,43; 10,61] <,0001[4]	12,0 [8,7; 15,3] <,0001[4]
Vulvovaginal dryness				
20/553 (3,6)	19/535 (3,6)	1,02 [0,55; 1,89] 0,9539[3]	1,02 [0,54; 1,93] 0,9539[4]	0,1 [-2,1; 2,3] 0,9539[4]
Weight decreased				
10/553 (1,8)	5/535 (0,9)	1,93 [0,67; 5,62] 0,2253[3]	1,95 [0,66; 5,75] 0,2166[4]	0,9 [-0,5; 2,3] 0,2166[4]
Weight increased				
12/553 (2,2)	9/535 (1,7)	1,29 [0,55; 3,04] 0,5600[3]	1,30 [0,54; 3,10] 0,5588[4]	0,5 [-1,1; 2,1] 0,5588[4]
White blood cell count decreased				
140/553 (25,3)	31/535 (5,8)	4,37 [3,02; 6,33] <,0001[3]	5,51 [3,66; 8,31] <,0001[4]	19,5 [15,4; 23,7] <,0001[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttiraep_premp_safc1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Results from binary analysis for adverse events according PT - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Abdominal discomfort				
19/1283 (1,5)	7/1265 (0,6)	2,68 [1,13; 6,34] 0,0254[3]	2,70 [1,13; 6,45] 0,0198[4]	0,9 [0,2; 1,7] 0,0198[4]
Abdominal distension				
33/1283 (2,6)	11/1265 (0,9)	2,96 [1,50; 5,83] 0,0017[3]	3,01 [1,51; 5,98] 0,0010[4]	1,7 [0,7; 2,7] 0,0010[4]
Abdominal pain				
311/1283 (24,2)	62/1265 (4,9)	4,95 [3,81; 6,42] <,0001[3]	6,21 [4,67; 8,26] <,0001[4]	19,3 [16,7; 22,0] <,0001[4]
Abdominal pain upper				
124/1283 (9,7)	44/1265 (3,5)	2,78 [1,99; 3,88] <,0001[3]	2,97 [2,09; 4,23] <,0001[4]	6,2 [4,3; 8,1] <,0001[4]
Alanine aminotransferase increased				
154/1283 (12,0)	67/1265 (5,3)	2,27 [1,72; 2,99] <,0001[3]	2,44 [1,81; 3,29] <,0001[4]	6,7 [4,5; 8,9] <,0001[4]
Alopecia				
150/1283 (11,7)	34/1265 (2,7)	4,35 [3,02; 6,26] <,0001[3]	4,79 [3,27; 7,02] <,0001[4]	9,0 [7,0; 11,0] <,0001[4]
Anaemia				
329/1283 (25,6)	46/1265 (3,6)	7,05 [5,23; 9,51] <,0001[3]	9,14 [6,64; 12,58] <,0001[4]	22,0 [19,4; 24,6] <,0001[4]
Anxiety				
36/1283 (2,8)	55/1265 (4,3)	0,65 [0,43; 0,98] 0,0377[3]	0,64 [0,41; 0,97] 0,0360[4]	-1,5 [-3,0; -0,1] 0,0360[4]
Arthralgia				
342/1283 (26,7)	488/1265 (38,6)	0,69 [0,62; 0,77] <,0001[3]	0,58 [0,49; 0,68] <,0001[4]	-11,9 [-15,5; -8,3] <,0001[4]
Arthritis				
11/1283 (0,9)	18/1265 (1,4)	0,60 [0,29; 1,27] 0,1832[3]	0,60 [0,28; 1,27] 0,1784[4]	-0,6 [-1,4; 0,3] 0,1784[4]
Aspartate aminotransferase increased				
146/1283 (11,4)	65/1265 (5,1)	2,21 [1,67; 2,94] <,0001[3]	2,37 [1,75; 3,21] <,0001[4]	6,2 [4,1; 8,4] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Asthenia				
146/1283 (11,4)	67/1265 (5,3)	2,15 [1,63; 2,84] <,0001[3]	2,30 [1,70; 3,10] <,0001[4]	6,1 [4,0; 8,2] <,0001[4]
Axillary pain				
24/1283 (1,9)	18/1265 (1,4)	1,31 [0,72; 2,41] 0,3764[3]	1,32 [0,71; 2,45] 0,3749[4]	0,4 [-0,5; 1,4] 0,3749[4]
Back pain				
114/1283 (8,9)	148/1265 (11,7)	0,76 [0,60; 0,96] 0,0199[3]	0,74 [0,57; 0,95] 0,0194[4]	-2,8 [-5,2; -0,5] 0,0194[4]
Blood alkaline phosphatase increased				
59/1283 (4,6)	39/1265 (3,1)	1,49 [1,00; 2,22] 0,0484[3]	1,52 [1,00; 2,29] 0,0467[4]	1,5 [0,0; 3,0] 0,0467[4]
Blood bilirubin increased				
17/1283 (1,3)	8/1265 (0,6)	2,10 [0,91; 4,84] 0,0832[3]	2,11 [0,91; 4,91] 0,0762[4]	0,7 [-0,1; 1,5] 0,0762[4]
Blood cholesterol increased				
14/1283 (1,1)	21/1265 (1,7)	0,66 [0,34; 1,29] 0,2209[3]	0,65 [0,33; 1,29] 0,2174[4]	-0,6 [-1,5; 0,3] 0,2174[4]
Blood creatinine increased				
150/1283 (11,7)	14/1265 (1,1)	10,56 [6,14; 18,17] <,0001[3]	11,83 [6,80; 20,58] <,0001[4]	10,6 [8,7; 12,4] <,0001[4]
Bone pain				
32/1283 (2,5)	48/1265 (3,8)	0,66 [0,42; 1,02] 0,0619[3]	0,65 [0,41; 1,02] 0,0599[4]	-1,3 [-2,7; 0,1] 0,0599[4]
Breast pain				
42/1283 (3,3)	57/1265 (4,5)	0,73 [0,49; 1,07] 0,1092[3]	0,72 [0,48; 1,08] 0,1075[4]	-1,2 [-2,7; 0,3] 0,1075[4]
Bronchitis				
24/1283 (1,9)	28/1265 (2,2)	0,85 [0,49; 1,45] 0,5411[3]	0,84 [0,49; 1,46] 0,5406[4]	-0,3 [-1,4; 0,8] 0,5406[4]
COVID-19				
33/1283 (2,6)	8/1265 (0,6)	4,07 [1,89; 8,77] 0,0003[3]	4,15 [1,91; 9,02] <,0001[4]	1,9 [1,0; 2,9] <,0001[4]
Cataract				
25/1283 (1,9)	11/1265 (0,9)	2,24 [1,11; 4,53] 0,0249[3]	2,27 [1,11; 4,62] 0,0210[4]	1,1 [0,2; 2,0] 0,0210[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Cellulitis				
27/1283 (2,1)	20/1265 (1,6)	1,33 [0,75; 2,36] 0,3280[3]	1,34 [0,75; 2,40] 0,3262[4]	0,5 [-0,5; 1,6] 0,3262[4]
Chest pain				
27/1283 (2,1)	25/1265 (2,0)	1,06 [0,62; 1,82] 0,8191[3]	1,07 [0,62; 1,85] 0,8191[4]	0,1 [-1,0; 1,2] 0,8191[4]
Chills				
19/1283 (1,5)	10/1265 (0,8)	1,87 [0,87; 4,01] 0,1063[3]	1,89 [0,87; 4,07] 0,1005[4]	0,7 [-0,1; 1,5] 0,1005[4]
Conjunctivitis				
22/1283 (1,7)	13/1265 (1,0)	1,67 [0,84; 3,30] 0,1408[3]	1,68 [0,84; 3,35] 0,1363[4]	0,7 [-0,2; 1,6] 0,1363[4]
Constipation				
152/1283 (11,8)	70/1265 (5,5)	2,14 [1,63; 2,81] <,0001[3]	2,29 [1,71; 3,08] <,0001[4]	6,3 [4,1; 8,5] <,0001[4]
Contusion				
21/1283 (1,6)	18/1265 (1,4)	1,15 [0,62; 2,15] 0,6605[3]	1,15 [0,61; 2,17] 0,6602[4]	0,2 [-0,7; 1,2] 0,6602[4]
Cough				
185/1283 (14,4)	111/1265 (8,8)	1,64 [1,32; 2,05] <,0001[3]	1,75 [1,37; 2,25] <,0001[4]	5,6 [3,2; 8,1] <,0001[4]
Cystitis				
37/1283 (2,9)	32/1265 (2,5)	1,14 [0,71; 1,82] 0,5821[3]	1,14 [0,71; 1,85] 0,5818[4]	0,4 [-0,9; 1,6] 0,5818[4]
Decreased appetite				
163/1283 (12,7)	41/1265 (3,2)	3,92 [2,81; 5,47] <,0001[3]	4,34 [3,06; 6,18] <,0001[4]	9,5 [7,4; 11,5] <,0001[4]
Deep vein thrombosis				
21/1283 (1,6)	3/1265 (0,2)	6,90 [2,06; 23,08] 0,0017[3]	7,00 [2,08; 23,53] 0,0003[4]	1,4 [0,7; 2,1] 0,0003[4]
Dehydration				
26/1283 (2,0)	3/1265 (0,2)	8,55 [2,59; 28,16] 0,0004[3]	8,70 [2,63; 28,82] <,0001[4]	1,8 [1,0; 2,6] <,0001[4]
Depression				
50/1283 (3,9)	49/1265 (3,9)	1,01 [0,68; 1,48] 0,9754[3]	1,01 [0,67; 1,50] 0,9754[4]	0,0 [-1,5; 1,5] 0,9754[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Dermatitis				
18/1283 (1,4)	7/1265 (0,6)	2,54 [1,06; 6,05] 0,0360[3]	2,56 [1,06; 6,14] 0,0296[4]	0,8 [0,1; 1,6] 0,0296[4]
Diarrhoea				
1059/1283 (82,5)	110/1265 (8,7)	9,49 [7,93; 11,37] <,0001[3]	49,64 [38,93; 63,29] <,0001[4]	73,8 [71,3; 76,4] <,0001[4]
Dizziness				
137/1283 (10,7)	83/1265 (6,6)	1,63 [1,25; 2,11] 0,0003[3]	1,70 [1,28; 2,26] 0,0002[4]	4,1 [1,9; 6,3] 0,0002[4]
Dry eye				
38/1283 (3,0)	11/1265 (0,9)	3,41 [1,75; 6,63] 0,0003[3]	3,48 [1,77; 6,84] 0,0001[4]	2,1 [1,0; 3,2] 0,0001[4]
Dry mouth				
45/1283 (3,5)	16/1265 (1,3)	2,77 [1,58; 4,88] 0,0004[3]	2,84 [1,60; 5,05] 0,0002[4]	2,2 [1,1; 3,4] 0,0002[4]
Dry skin				
51/1283 (4,0)	25/1265 (2,0)	2,01 [1,25; 3,23] 0,0037[3]	2,05 [1,26; 3,33] 0,0030[4]	2,0 [0,7; 3,3] 0,0030[4]
Dysgeusia				
60/1283 (4,7)	5/1265 (0,4)	11,83 [4,77; 29,36] <,0001[3]	12,36 [4,95; 30,89] <,0001[4]	4,3 [3,1; 5,5] <,0001[4]
Dyspepsia				
96/1283 (7,5)	31/1265 (2,5)	3,05 [2,05; 4,54] <,0001[3]	3,22 [2,13; 4,86] <,0001[4]	5,0 [3,4; 6,7] <,0001[4]
Dyspnoea				
93/1283 (7,2)	51/1265 (4,0)	1,80 [1,29; 2,51] 0,0005[3]	1,86 [1,31; 2,64] 0,0004[4]	3,2 [1,4; 5,0] 0,0004[4]
Dysuria				
24/1283 (1,9)	13/1265 (1,0)	1,82 [0,93; 3,56] 0,0800[3]	1,84 [0,93; 3,62] 0,0753[4]	0,8 [-0,1; 1,8] 0,0753[4]
Eczema				
13/1283 (1,0)	16/1265 (1,3)	0,80 [0,39; 1,66] 0,5503[3]	0,80 [0,38; 1,67] 0,5495[4]	-0,3 [-1,1; 0,6] 0,5495[4]
Epistaxis				
23/1283 (1,8)	3/1265 (0,2)	7,56 [2,28; 25,11] 0,0010[3]	7,68 [2,30; 25,64] <,0001[4]	1,6 [0,8; 2,3] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Erythema				
17/1283 (1,3)	16/1265 (1,3)	1,05 [0,53; 2,06] 0,8931[3]	1,05 [0,53; 2,08] 0,8931[4]	0,1 [-0,8; 0,9] 0,8931[4]
Fall				
44/1283 (3,4)	28/1265 (2,2)	1,55 [0,97; 2,47] 0,0664[3]	1,57 [0,97; 2,54] 0,0640[4]	1,2 [-0,1; 2,5] 0,0640[4]
Fatigue				
394/1283 (30,7)	149/1265 (11,8)	2,61 [2,20; 3,10] <,0001[3]	3,32 [2,70; 4,09] <,0001[4]	18,9 [15,8; 22,0] <,0001[4]
Flatulence				
42/1283 (3,3)	8/1265 (0,6)	5,18 [2,44; 10,98] <,0001[3]	5,32 [2,49; 11,37] <,0001[4]	2,6 [1,6; 3,7] <,0001[4]
Gamma-glutamyltransferase increased				
42/1283 (3,3)	16/1265 (1,3)	2,59 [1,46; 4,58] 0,0011[3]	2,64 [1,48; 4,72] 0,0007[4]	2,0 [0,9; 3,2] 0,0007[4]
Gastritis				
30/1283 (2,3)	21/1265 (1,7)	1,41 [0,81; 2,45] 0,2241[3]	1,42 [0,81; 2,49] 0,2217[4]	0,7 [-0,4; 1,8] 0,2217[4]
Gastroenteritis				
18/1283 (1,4)	13/1265 (1,0)	1,37 [0,67; 2,77] 0,3896[3]	1,37 [0,67; 2,81] 0,3876[4]	0,4 [-0,5; 1,2] 0,3876[4]
Gastrointestinal pain				
17/1283 (1,3)	0/1265 (0,0)	34,51 [2,08; 573,23] 0,0135[3]	34,97 [2,10; 582,17] <,0001[4]	1,3 [0,7; 2,0] <,0001[4]
Gastrooesophageal reflux disease				
41/1283 (3,2)	23/1265 (1,8)	1,76 [1,06; 2,91] 0,0285[3]	1,78 [1,06; 2,99] 0,0263[4]	1,4 [0,2; 2,6] 0,0263[4]
Haemorrhoids				
27/1283 (2,1)	14/1265 (1,1)	1,90 [1,00; 3,61] 0,0493[3]	1,92 [1,00; 3,68] 0,0454[4]	1,0 [0,0; 2,0] 0,0454[4]
Headache				
222/1283 (17,3)	147/1265 (11,6)	1,49 [1,23; 1,81] <,0001[3]	1,59 [1,27; 1,99] <,0001[4]	5,7 [3,0; 8,4] <,0001[4]
Hepatic steatosis				
23/1283 (1,8)	22/1265 (1,7)	1,03 [0,58; 1,84] 0,9183[3]	1,03 [0,57; 1,86] 0,9183[4]	0,1 [-1,0; 1,1] 0,9183[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Herpes zoster				
23/1283 (1,8)	23/1265 (1,8)	0,99 [0,56; 1,75] 0,9614[3]	0,99 [0,55; 1,77] 0,9614[4]	-0,0 [-1,1; 1,0] 0,9614[4]
Hot flush				
143/1283 (11,1)	214/1265 (16,9)	0,66 [0,54; 0,80] <,0001[3]	0,62 [0,49; 0,77] <,0001[4]	-5,8 [-8,5; -3,1] <,0001[4]
Hypercalcaemia				
27/1283 (2,1)	17/1265 (1,3)	1,57 [0,86; 2,86] 0,1441[3]	1,58 [0,86; 2,91] 0,1406[4]	0,8 [-0,2; 1,8] 0,1406[4]
Hypercholesterolaemia				
15/1283 (1,2)	24/1265 (1,9)	0,62 [0,32; 1,17] 0,1384[3]	0,61 [0,32; 1,17] 0,1344[4]	-0,7 [-1,7; 0,2] 0,1344[4]
Hyperglycaemia				
20/1283 (1,6)	29/1265 (2,3)	0,68 [0,39; 1,20] 0,1804[3]	0,67 [0,38; 1,20] 0,1776[4]	-0,7 [-1,8; 0,3] 0,1776[4]
Hyperhidrosis				
17/1283 (1,3)	21/1265 (1,7)	0,80 [0,42; 1,51] 0,4863[3]	0,80 [0,42; 1,51] 0,4854[4]	-0,3 [-1,3; 0,6] 0,4854[4]
Hyperkalaemia				
14/1283 (1,1)	6/1265 (0,5)	2,30 [0,89; 5,97] 0,0867[3]	2,31 [0,89; 6,04] 0,0777[4]	0,6 [-0,1; 1,3] 0,0777[4]
Hypersensitivity				
13/1283 (1,0)	11/1265 (0,9)	1,17 [0,52; 2,59] 0,7076[3]	1,17 [0,52; 2,61] 0,7073[4]	0,1 [-0,6; 0,9] 0,7073[4]
Hypertension				
55/1283 (4,3)	71/1265 (5,6)	0,76 [0,54; 1,08] 0,1240[3]	0,75 [0,52; 1,08] 0,1227[4]	-1,3 [-3,0; 0,4] 0,1227[4]
Hypertriglyceridaemia				
22/1283 (1,7)	28/1265 (2,2)	0,77 [0,45; 1,35] 0,3655[3]	0,77 [0,44; 1,35] 0,3642[4]	-0,5 [-1,6; 0,6] 0,3642[4]
Hyperuricaemia				
20/1283 (1,6)	10/1265 (0,8)	1,97 [0,93; 4,20] 0,0780[3]	1,99 [0,93; 4,26] 0,0722[4]	0,8 [-0,1; 1,6] 0,0722[4]
Hypoalbuminaemia				
14/1283 (1,1)	6/1265 (0,5)	2,30 [0,89; 5,97] 0,0867[3]	2,31 [0,89; 6,04] 0,0777[4]	0,6 [-0,1; 1,3] 0,0777[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Hypokalaemia				
57/1283 (4,4)	16/1265 (1,3)	3,51 [2,03; 6,08] <,0001[3]	3,63 [2,07; 6,35] <,0001[4]	3,2 [1,9; 4,5] <,0001[4]
Hyponatraemia				
19/1283 (1,5)	8/1265 (0,6)	2,34 [1,03; 5,33] 0,0426[3]	2,36 [1,03; 5,42] 0,0365[4]	0,8 [0,1; 1,6] 0,0365[4]
Hypotension				
23/1283 (1,8)	7/1265 (0,6)	3,24 [1,40; 7,52] 0,0062[3]	3,28 [1,40; 7,67] 0,0037[4]	1,2 [0,4; 2,1] 0,0037[4]
Hypothyroidism				
16/1283 (1,2)	19/1265 (1,5)	0,83 [0,43; 1,61] 0,5810[3]	0,83 [0,42; 1,62] 0,5805[4]	-0,3 [-1,2; 0,6] 0,5805[4]
Influenza				
47/1283 (3,7)	43/1265 (3,4)	1,08 [0,72; 1,62] 0,7181[3]	1,08 [0,71; 1,65] 0,7181[4]	0,3 [-1,2; 1,7] 0,7181[4]
Influenza like illness				
56/1283 (4,4)	42/1265 (3,3)	1,31 [0,89; 1,95] 0,1719[3]	1,33 [0,88; 2,00] 0,1704[4]	1,0 [-0,4; 2,5] 0,1704[4]
Insomnia				
94/1283 (7,3)	90/1265 (7,1)	1,03 [0,78; 1,36] 0,8363[3]	1,03 [0,76; 1,39] 0,8363[4]	0,2 [-1,8; 2,2] 0,8363[4]
Joint stiffness				
12/1283 (0,9)	30/1265 (2,4)	0,39 [0,20; 0,77] 0,0061[3]	0,39 [0,20; 0,76] 0,0044[4]	-1,4 [-2,4; -0,4] 0,0044[4]
Lacrimation increased				
72/1283 (5,6)	5/1265 (0,4)	14,20 [5,75; 35,03] <,0001[3]	14,98 [6,03; 37,22] <,0001[4]	5,2 [3,9; 6,5] <,0001[4]
Leukopenia				
186/1283 (14,5)	25/1265 (2,0)	7,34 [4,87; 11,06] <,0001[3]	8,41 [5,50; 12,87] <,0001[4]	12,5 [10,4; 14,6] <,0001[4]
Lymphocyte count decreased				
111/1283 (8,7)	29/1265 (2,3)	3,77 [2,53; 5,64] <,0001[3]	4,04 [2,66; 6,12] <,0001[4]	6,4 [4,6; 8,1] <,0001[4]
Lymphoedema				
153/1283 (11,9)	101/1265 (8,0)	1,49 [1,18; 1,90] 0,0010[3]	1,56 [1,20; 2,03] 0,0009[4]	3,9 [1,6; 6,3] 0,0009[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Lymphopenia				
68/1283 (5,3)	9/1265 (0,7)	7,45 [3,73; 14,87] <,0001[3]	7,81 [3,88; 15,72] <,0001[4]	4,6 [3,3; 5,9] <,0001[4]
Malaise				
33/1283 (2,6)	12/1265 (0,9)	2,71 [1,41; 5,23] 0,0029[3]	2,76 [1,42; 5,36] 0,0019[4]	1,6 [0,6; 2,6] 0,0019[4]
Mastitis				
10/1283 (0,8)	17/1265 (1,3)	0,58 [0,27; 1,26] 0,1695[3]	0,58 [0,26; 1,26] 0,1641[4]	-0,6 [-1,4; 0,2] 0,1641[4]
Memory impairment				
17/1283 (1,3)	9/1265 (0,7)	1,86 [0,83; 4,16] 0,1296[3]	1,87 [0,83; 4,22] 0,1234[4]	0,6 [-0,2; 1,4] 0,1234[4]
Mucosal inflammation				
37/1283 (2,9)	9/1265 (0,7)	4,05 [1,96; 8,36] 0,0002[3]	4,14 [1,99; 8,62] <,0001[4]	2,2 [1,1; 3,2] <,0001[4]
Muscle spasms				
72/1283 (5,6)	48/1265 (3,8)	1,48 [1,04; 2,11] 0,0316[3]	1,51 [1,04; 2,19] 0,0304[4]	1,8 [0,2; 3,5] 0,0304[4]
Muscular weakness				
17/1283 (1,3)	8/1265 (0,6)	2,10 [0,91; 4,84] 0,0832[3]	2,11 [0,91; 4,91] 0,0762[4]	0,7 [-0,1; 1,5] 0,0762[4]
Musculoskeletal chest pain				
38/1283 (3,0)	29/1265 (2,3)	1,29 [0,80; 2,08] 0,2925[3]	1,30 [0,80; 2,12] 0,2911[4]	0,7 [-0,6; 1,9] 0,2911[4]
Musculoskeletal pain				
15/1283 (1,2)	24/1265 (1,9)	0,62 [0,32; 1,17] 0,1384[3]	0,61 [0,32; 1,17] 0,1344[4]	-0,7 [-1,7; 0,2] 0,1344[4]
Musculoskeletal stiffness				
16/1283 (1,2)	18/1265 (1,4)	0,88 [0,45; 1,71] 0,6991[3]	0,87 [0,44; 1,72] 0,6989[4]	-0,2 [-1,1; 0,7] 0,6989[4]
Myalgia				
71/1283 (5,5)	82/1265 (6,5)	0,85 [0,63; 1,16] 0,3143[3]	0,85 [0,61; 1,17] 0,3137[4]	-0,9 [-2,8; 0,9] 0,3137[4]
Nail disorder				
23/1283 (1,8)	2/1265 (0,2)	11,34 [2,68; 47,99] 0,0010[3]	11,53 [2,71; 49,00] <,0001[4]	1,6 [0,9; 2,4] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Nasal congestion				
17/1283 (1,3)	13/1265 (1,0)	1,29 [0,63; 2,64] 0,4878[3]	1,29 [0,63; 2,67] 0,4866[4]	0,3 [-0,5; 1,1] 0,4866[4]
Nasopharyngitis				
105/1283 (8,2)	90/1265 (7,1)	1,15 [0,88; 1,51] 0,3105[3]	1,16 [0,87; 1,56] 0,3100[4]	1,1 [-1,0; 3,1] 0,3100[4]
Nausea				
383/1283 (29,9)	97/1265 (7,7)	3,89 [3,16; 4,80] <,0001[3]	5,12 [4,03; 6,51] <,0001[4]	22,2 [19,3; 25,1] <,0001[4]
Neck pain				
27/1283 (2,1)	31/1265 (2,5)	0,86 [0,52; 1,43] 0,5584[3]	0,86 [0,51; 1,44] 0,5580[4]	-0,3 [-1,5; 0,8] 0,5580[4]
Neuropathy peripheral				
39/1283 (3,0)	36/1265 (2,8)	1,07 [0,68; 1,67] 0,7722[3]	1,07 [0,68; 1,70] 0,7722[4]	0,2 [-1,1; 1,5] 0,7722[4]
Neutropenia				
295/1283 (23,0)	29/1265 (2,3)	10,03 [6,90; 14,57] <,0001[3]	12,73 [8,61; 18,80] <,0001[4]	20,7 [18,3; 23,1] <,0001[4]
Neutrophil count decreased				
281/1283 (21,9)	22/1265 (1,7)	12,59 [8,22; 19,30] <,0001[3]	15,84 [10,19; 24,65] <,0001[4]	20,2 [17,8; 22,5] <,0001[4]
Night sweats				
10/1283 (0,8)	14/1265 (1,1)	0,70 [0,31; 1,58] 0,3949[3]	0,70 [0,31; 1,59] 0,3925[4]	-0,3 [-1,1; 0,4] 0,3925[4]
Oedema				
16/1283 (1,2)	8/1265 (0,6)	1,97 [0,85; 4,59] 0,1153[3]	1,98 [0,85; 4,65] 0,1083[4]	0,6 [-0,1; 1,4] 0,1083[4]
Oedema peripheral				
93/1283 (7,2)	48/1265 (3,8)	1,91 [1,36; 2,68] 0,0002[3]	1,98 [1,39; 2,83] 0,0001[4]	3,5 [1,7; 5,2] 0,0001[4]
Onychoclasis				
22/1283 (1,7)	3/1265 (0,2)	7,23 [2,17; 24,10] 0,0013[3]	7,34 [2,19; 24,58] 0,0002[4]	1,5 [0,7; 2,2] 0,0002[4]
Oral herpes				
16/1283 (1,2)	5/1265 (0,4)	3,16 [1,16; 8,59] 0,0245[3]	3,18 [1,16; 8,71] 0,0174[4]	0,9 [0,2; 1,6] 0,0174[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Oropharyngeal pain				
49/1283 (3,8)	31/1265 (2,5)	1,56 [1,00; 2,43] 0,0497[3]	1,58 [1,00; 2,50] 0,0476[4]	1,4 [0,0; 2,7] 0,0476[4]
Osteoarthritis				
15/1283 (1,2)	24/1265 (1,9)	0,62 [0,32; 1,17] 0,1384[3]	0,61 [0,32; 1,17] 0,1344[4]	-0,7 [-1,7; 0,2] 0,1344[4]
Osteopenia				
20/1283 (1,6)	26/1265 (2,1)	0,76 [0,43; 1,35] 0,3483[3]	0,75 [0,42; 1,36] 0,3466[4]	-0,5 [-1,5; 0,5] 0,3466[4]
Osteoporosis				
30/1283 (2,3)	47/1265 (3,7)	0,63 [0,40; 0,99] 0,0444[3]	0,62 [0,39; 0,99] 0,0423[4]	-1,4 [-2,7; -0,0] 0,0423[4]
Pain				
29/1283 (2,3)	31/1265 (2,5)	0,92 [0,56; 1,52] 0,7516[3]	0,92 [0,55; 1,54] 0,7515[4]	-0,2 [-1,4; 1,0] 0,7515[4]
Pain in extremity				
126/1283 (9,8)	140/1265 (11,1)	0,89 [0,71; 1,11] 0,3039[3]	0,88 [0,68; 1,13] 0,3036[4]	-1,2 [-3,6; 1,1] 0,3036[4]
Palpitations				
27/1283 (2,1)	12/1265 (0,9)	2,22 [1,13; 4,36] 0,0208[3]	2,24 [1,13; 4,45] 0,0175[4]	1,2 [0,2; 2,1] 0,0175[4]
Paraesthesia				
31/1283 (2,4)	30/1265 (2,4)	1,02 [0,62; 1,67] 0,9412[3]	1,02 [0,61; 1,69] 0,9412[4]	0,0 [-1,1; 1,2] 0,9412[4]
Paronychia				
15/1283 (1,2)	4/1265 (0,3)	3,70 [1,23; 11,11] 0,0198[3]	3,73 [1,23; 11,27] 0,0123[4]	0,9 [0,2; 1,5] 0,0123[4]
Peripheral sensory neuropathy				
16/1283 (1,2)	13/1265 (1,0)	1,21 [0,59; 2,51] 0,6022[3]	1,22 [0,58; 2,54] 0,6016[4]	0,2 [-0,6; 1,0] 0,6016[4]
Peripheral swelling				
30/1283 (2,3)	25/1265 (2,0)	1,18 [0,70; 2,00] 0,5301[3]	1,19 [0,69; 2,03] 0,5296[4]	0,4 [-0,8; 1,5] 0,5296[4]
Platelet count decreased				
116/1283 (9,0)	9/1265 (0,7)	12,71 [6,48; 24,93] <,0001[3]	13,87 [7,01; 27,46] <,0001[4]	8,3 [6,7; 10,0] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Pneumonia				
31/1283 (2,4)	19/1265 (1,5)	1,61 [0,91; 2,83] 0,0996[3]	1,62 [0,91; 2,89] 0,0962[4]	0,9 [-0,2; 2,0] 0,0962[4]
Pneumonitis				
18/1283 (1,4)	3/1265 (0,2)	5,92 [1,75; 20,03] 0,0043[3]	5,99 [1,76; 20,37] 0,0011[4]	1,2 [0,5; 1,9] 0,0011[4]
Procedural pain				
34/1283 (2,7)	25/1265 (2,0)	1,34 [0,80; 2,23] 0,2600[3]	1,35 [0,80; 2,28] 0,2582[4]	0,7 [-0,5; 1,8] 0,2582[4]
Productive cough				
21/1283 (1,6)	13/1265 (1,0)	1,59 [0,80; 3,17] 0,1844[3]	1,60 [0,80; 3,21] 0,1803[4]	0,6 [-0,3; 1,5] 0,1803[4]
Pruritus				
107/1283 (8,3)	58/1265 (4,6)	1,82 [1,33; 2,48] 0,0002[3]	1,89 [1,36; 2,63] 0,0001[4]	3,8 [1,9; 5,7] 0,0001[4]
Pyrexia				
98/1283 (7,6)	42/1265 (3,3)	2,30 [1,62; 3,27] <,0001[3]	2,41 [1,66; 3,49] <,0001[4]	4,3 [2,6; 6,1] <,0001[4]
Rash				
113/1283 (8,8)	37/1265 (2,9)	3,01 [2,09; 4,33] <,0001[3]	3,21 [2,19; 4,69] <,0001[4]	5,9 [4,1; 7,7] <,0001[4]
Rash maculo-papular				
22/1283 (1,7)	3/1265 (0,2)	7,23 [2,17; 24,10] 0,0013[3]	7,34 [2,19; 24,58] 0,0002[4]	1,5 [0,7; 2,2] 0,0002[4]
Respiratory tract infection				
15/1283 (1,2)	9/1265 (0,7)	1,64 [0,72; 3,74] 0,2367[3]	1,65 [0,72; 3,79] 0,2318[4]	0,5 [-0,3; 1,2] 0,2318[4]
Rhinitis allergic				
22/1283 (1,7)	23/1265 (1,8)	0,94 [0,53; 1,68] 0,8429[3]	0,94 [0,52; 1,70] 0,8429[4]	-0,1 [-1,1; 0,9] 0,8429[4]
Sciatica				
12/1283 (0,9)	15/1265 (1,2)	0,79 [0,37; 1,68] 0,5380[3]	0,79 [0,37; 1,69] 0,5370[4]	-0,3 [-1,0; 0,5] 0,5370[4]
Seroma				
16/1283 (1,2)	5/1265 (0,4)	3,16 [1,16; 8,59] 0,0245[3]	3,18 [1,16; 8,71] 0,0174[4]	0,9 [0,2; 1,6] 0,0174[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Sinusitis				
30/1283 (2,3)	32/1265 (2,5)	0,92 [0,57; 1,51] 0,7540[3]	0,92 [0,56; 1,53] 0,7539[4]	-0,2 [-1,4; 1,0] 0,7539[4]
Stomatitis				
68/1283 (5,3)	12/1265 (0,9)	5,59 [3,04; 10,27] <,0001[3]	5,84 [3,15; 10,85] <,0001[4]	4,4 [3,0; 5,7] <,0001[4]
Syncope				
14/1283 (1,1)	8/1265 (0,6)	1,73 [0,73; 4,10] 0,2166[3]	1,73 [0,72; 4,15] 0,2107[4]	0,5 [-0,3; 1,2] 0,2107[4]
Taste disorder				
21/1283 (1,6)	2/1265 (0,2)	10,35 [2,43; 44,06] 0,0016[3]	10,51 [2,46; 44,91] <,0001[4]	1,5 [0,8; 2,2] <,0001[4]
Tendonitis				
9/1283 (0,7)	18/1265 (1,4)	0,49 [0,22; 1,09] 0,0817[3]	0,49 [0,22; 1,09] 0,0754[4]	-0,7 [-1,5; 0,1] 0,0754[4]
Thrombocytopenia				
86/1283 (6,7)	9/1265 (0,7)	9,42 [4,76; 18,64] <,0001[3]	10,03 [5,02; 20,01] <,0001[4]	6,0 [4,5; 7,4] <,0001[4]
Tooth extraction				
8/1283 (0,6)	13/1265 (1,0)	0,61 [0,25; 1,46] 0,2643[3]	0,60 [0,25; 1,46] 0,2593[4]	-0,4 [-1,1; 0,3] 0,2593[4]
Toothache				
18/1283 (1,4)	19/1265 (1,5)	0,93 [0,49; 1,77] 0,8346[3]	0,93 [0,49; 1,79] 0,8345[4]	-0,1 [-1,0; 0,8] 0,8345[4]
Tremor				
15/1283 (1,2)	7/1265 (0,6)	2,11 [0,86; 5,16] 0,1009[3]	2,13 [0,86; 5,23] 0,0930[4]	0,6 [-0,1; 1,3] 0,0930[4]
Trigger finger				
12/1283 (0,9)	14/1265 (1,1)	0,85 [0,39; 1,82] 0,6672[3]	0,84 [0,39; 1,83] 0,6669[4]	-0,2 [-1,0; 0,6] 0,6669[4]
Upper respiratory tract infection				
107/1283 (8,3)	88/1265 (7,0)	1,20 [0,91; 1,57] 0,1899[3]	1,22 [0,91; 1,63] 0,1891[4]	1,4 [-0,7; 3,4] 0,1891[4]
Urinary tract infection				
117/1283 (9,1)	69/1265 (5,5)	1,67 [1,25; 2,23] 0,0005[3]	1,74 [1,28; 2,37] 0,0004[4]	3,7 [1,7; 5,7] 0,0004[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Urticaria				
13/1283 (1,0)	10/1265 (0,8)	1,28 [0,56; 2,91] 0,5533[3]	1,28 [0,56; 2,94] 0,5523[4]	0,2 [-0,5; 1,0] 0,5523[4]
Vertigo				
40/1283 (3,1)	27/1265 (2,1)	1,46 [0,90; 2,37] 0,1233[3]	1,48 [0,90; 2,42] 0,1209[4]	1,0 [-0,3; 2,2] 0,1209[4]
Viral infection				
15/1283 (1,2)	2/1265 (0,2)	7,39 [1,69; 32,27] 0,0078[3]	7,47 [1,70; 32,73] 0,0017[4]	1,0 [0,4; 1,6] 0,0017[4]
Vision blurred				
29/1283 (2,3)	10/1265 (0,8)	2,86 [1,40; 5,84] 0,0040[3]	2,90 [1,41; 5,98] 0,0025[4]	1,5 [0,5; 2,4] 0,0025[4]
Vitamin B12 deficiency				
16/1283 (1,2)	4/1265 (0,3)	3,94 [1,32; 11,76] 0,0139[3]	3,98 [1,33; 11,94] 0,0078[4]	0,9 [0,2; 1,6] 0,0078[4]
Vitamin D deficiency				
16/1283 (1,2)	14/1265 (1,1)	1,13 [0,55; 2,30] 0,7428[3]	1,13 [0,55; 2,32] 0,7426[4]	0,1 [-0,7; 1,0] 0,7426[4]
Vomiting				
222/1283 (17,3)	53/1265 (4,2)	4,13 [3,09; 5,52] <,0001[3]	4,78 [3,51; 6,53] <,0001[4]	13,1 [10,8; 15,5] <,0001[4]
Vulvovaginal dryness				
25/1283 (1,9)	40/1265 (3,2)	0,62 [0,38; 1,01] 0,0546[3]	0,61 [0,37; 1,01] 0,0521[4]	-1,2 [-2,4; 0,0] 0,0521[4]
Weight decreased				
55/1283 (4,3)	15/1265 (1,2)	3,62 [2,05; 6,36] <,0001[3]	3,73 [2,10; 6,64] <,0001[4]	3,1 [1,8; 4,4] <,0001[4]
Weight increased				
19/1283 (1,5)	30/1265 (2,4)	0,62 [0,35; 1,10] 0,1050[3]	0,62 [0,35; 1,11] 0,1017[4]	-0,9 [-2,0; 0,2] 0,1017[4]
White blood cell count decreased				
284/1283 (22,1)	50/1265 (4,0)	5,60 [4,19; 7,49] <,0001[3]	6,91 [5,06; 9,44] <,0001[4]	18,2 [15,7; 20,7] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 3: from Z-test; 4: from Chi^2-test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk				

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttiraep_posmp_safc1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Results from binary analysis for adverse events according PT - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Abdominal distension				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Abdominal pain				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Alanine aminotransferase increased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Anaemia				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Anxiety				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Aortic stenosis				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Arthralgia				
1/10 (10,0)	4/9 (44,4)	[2]	[2]	[2]
Aspartate aminotransferase increased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Atrial fibrillation				
0/10 (0,0)	2/9 (22,2)	[2]	[2]	[2]
Blood creatinine increased				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Blood lactic acid increased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Body temperature increased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Cataract				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Cellulitis streptococcal				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Chest discomfort				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Chest pain				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Conjunctivitis				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Constipation				
3/10 (30,0)	0/9 (0,0)	[2]	[2]	[2]
Contusion				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Coronary artery disease				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Cough				
4/10 (40,0)	0/9 (0,0)	[2]	[2]	[2]
Decreased appetite				
3/10 (30,0)	0/9 (0,0)	[2]	[2]	[2]
Dermatitis acneiform				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Diarrhoea				
6/10 (60,0)	0/9 (0,0)	[2]	[2]	[2]
Dizziness				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Dry mouth				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Dry throat				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Dyspnoea				
2/10 (20,0)	1/9 (11,1)	[2]	[2]	[2]
Fatigue				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
6/10 (60,0)	3/9 (33,3)	[2]	[2]	[2]
Finger amputation				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Flank pain				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Gamma-glutamyltransferase increased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Gastrooesophageal reflux disease				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Haematuria				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Haemoptysis				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Helicobacter infection				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Hot flush				
1/10 (10,0)	2/9 (22,2)	[2]	[2]	[2]
Hyperhidrosis				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Hyperthyroidism				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Hypoalbuminaemia				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Hyponatraemia				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Hypotension				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Influenza				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Influenza like illness				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Inguinal hernia				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Insomnia				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Iron deficiency anaemia				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Irritability				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Joint range of motion decreased				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Joint swelling				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Lacrimation increased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Left ventricular dysfunction				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Libido decreased				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Lymphangitis				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Lymphocyte count decreased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Lymphoedema				
2/10 (20,0)	2/9 (22,2)	[2]	[2]	[2]
Mood swings				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Muscle spasms				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Musculoskeletal chest pain				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
0/10 (0,0)	2/9 (22,2)	[2]	[2]	[2]
Myalgia				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Nasal congestion				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Nasal dryness				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Nausea				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Neck pain				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Nephrolithiasis				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Neutropenia				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Neutrophil count decreased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Oedema peripheral				
1/10 (10,0)	1/9 (11,1)	[2]	[2]	[2]
Oropharyngeal pain				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Osteopenia				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Pain in extremity				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Palpitations				
1/10 (10,0)	2/9 (22,2)	[2]	[2]	[2]
Peau d'orange				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Peripheral swelling				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Platelet count decreased				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Pneumonia				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Pneumonitis				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Polyneuropathy				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Postoperative respiratory failure				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Primary progressive aphasia				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Pruritus				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Pulmonary embolism				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Pyrexia				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Radius fracture				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Rash				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Rhinorrhoea				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Seasonal allergy				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Sinus bradycardia				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Skin infection				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Skin laceration				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Stomatitis				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Subcutaneous haematoma				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Syncope				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Taste disorder				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Tendon injury				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Tendonitis				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Thrombophlebitis superficial				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Urinary tract infection				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Vertigo				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Viral infection				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Vitamin D deficiency				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Vomiting				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Weight decreased				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Weight increased				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
0/10 (0,0)	1/9 (11,1)	2	2	2
White blood cell count decreased				
2/10 (20,0)	0/9 (0,0)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to appropriate comparator by GBA: Tamoxifen; 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Results from binary analysis for adverse events according SOC - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
184/553 (33,3)	55/535 (10,3)	3,24 [2,45; 4,27] <,0001[3]	4,35 [3,13; 6,06] <,0001[4]	23,0 [18,3; 27,7] <,0001[4]
Cardiac disorders				
20/553 (3,6)	15/535 (2,8)	1,29 [0,67; 2,49] 0,4488[3]	1,30 [0,66; 2,57] 0,4474[4]	0,8 [-1,3; 2,9] 0,4474[4]
Ear and labyrinth disorders				
27/553 (4,9)	30/535 (5,6)	0,87 [0,52; 1,44] 0,5919[3]	0,86 [0,51; 1,47] 0,5916[4]	-0,7 [-3,4; 1,9] 0,5916[4]
Endocrine disorders				
8/553 (1,4)	20/535 (3,7)	0,39 [0,17; 0,87] 0,0218[3]	0,38 [0,17; 0,87] 0,0170[4]	-2,3 [-4,2; -0,4] 0,0170[4]
Eye disorders				
78/553 (14,1)	32/535 (6,0)	2,36 [1,59; 3,50] <,0001[3]	2,58 [1,68; 3,97] <,0001[4]	8,1 [4,6; 11,7] <,0001[4]
Gastrointestinal disorders				
496/553 (89,7)	177/535 (33,1)	2,71 [2,40; 3,07] <,0001[3]	17,60 [12,68; 24,43] <,0001[4]	56,6 [51,9; 61,3] <,0001[4]
General disorders and administration site conditions				
310/553 (56,1)	165/535 (30,8)	1,82 [1,57; 2,11] <,0001[3]	2,86 [2,23; 3,67] <,0001[4]	25,2 [19,5; 30,9] <,0001[4]
Hepatobiliary disorders				
33/553 (6,0)	18/535 (3,4)	1,77 [1,01; 3,11] 0,0456[3]	1,82 [1,01; 3,28] 0,0423[4]	2,6 [0,1; 5,1] 0,0423[4]
Immune system disorders				
11/553 (2,0)	11/535 (2,1)	0,97 [0,42; 2,21] 0,9375[3]	0,97 [0,42; 2,25] 0,9375[4]	-0,1 [-1,7; 1,6] 0,9375[4]
Infections and infestations				
299/553 (54,1)	222/535 (41,5)	1,30 [1,15; 1,48] <,0001[3]	1,66 [1,31; 2,11] <,0001[4]	12,6 [6,7; 18,5] <,0001[4]
Injury, poisoning and procedural complications				
86/553 (15,6)	69/535 (12,9)	1,21 [0,90; 1,62] 0,2116[3]	1,24 [0,88; 1,75] 0,2105[4]	2,7 [-1,5; 6,8] 0,2105[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Investigations				
268/553 (48,5)	99/535 (18,5)	2,62 [2,15; 3,19] <,0001[3]	4,14 [3,15; 5,45] <,0001[4]	30,0 [24,6; 35,3] <,0001[4]
Metabolism and nutrition disorders				
113/553 (20,4)	51/535 (9,5)	2,14 [1,57; 2,92] <,0001[3]	2,44 [1,71; 3,48] <,0001[4]	10,9 [6,7; 15,1] <,0001[4]
Musculoskeletal and connective tissue disorders				
247/553 (44,7)	269/535 (50,3)	0,89 [0,78; 1,01] 0,0640[3]	0,80 [0,63; 1,01] 0,0637[4]	-5,6 [-11,5; 0,3] 0,0637[4]
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
19/553 (3,4)	18/535 (3,4)	1,02 [0,54; 1,92] 0,9483[3]	1,02 [0,53; 1,97] 0,9483[4]	0,1 [-2,1; 2,2] 0,9483[4]
Nervous system disorders				
199/553 (36,0)	152/535 (28,4)	1,27 [1,06; 1,51] 0,0079[3]	1,42 [1,10; 1,83] 0,0075[4]	7,6 [2,0; 13,1] 0,0075[4]
Psychiatric disorders				
107/553 (19,3)	102/535 (19,1)	1,01 [0,80; 1,30] 0,9055[3]	1,02 [0,75; 1,38] 0,9055[4]	0,3 [-4,4; 5,0] 0,9055[4]
Renal and urinary disorders				
37/553 (6,7)	26/535 (4,9)	1,38 [0,85; 2,24] 0,1984[3]	1,40 [0,84; 2,35] 0,1961[4]	1,8 [-0,9; 4,6] 0,1961[4]
Reproductive system and breast disorders				
95/553 (17,2)	109/535 (20,4)	0,84 [0,66; 1,08] 0,1778[3]	0,81 [0,60; 1,10] 0,1771[4]	-3,2 [-7,8; 1,4] 0,1771[4]
Respiratory, thoracic and mediastinal disorders				
157/553 (28,4)	74/535 (13,8)	2,05 [1,60; 2,63] <,0001[3]	2,47 [1,82; 3,36] <,0001[4]	14,6 [9,8; 19,3] <,0001[4]
Skin and subcutaneous tissue disorders				
220/553 (39,8)	107/535 (20,0)	1,99 [1,63; 2,42] <,0001[3]	2,64 [2,01; 3,47] <,0001[4]	19,8 [14,5; 25,1] <,0001[4]
Surgical and medical procedures				
31/553 (5,6)	32/535 (6,0)	0,94 [0,58; 1,51] 0,7909[3]	0,93 [0,56; 1,55] 0,7909[4]	-0,4 [-3,2; 2,4] 0,7909[4]
Vascular disorders				
186/553 (33,6)	188/535 (35,1)	0,96 [0,81; 1,13] 0,6012[3]	0,94 [0,73; 1,20] 0,6012[4]	-1,5 [-7,2; 4,1] 0,6012[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 3: from Z-test; 4: from Chi^2-test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class				

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Table: Results from binary analysis for adverse events according SOC - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
587/1283 (45,8)	113/1265 (8,9)	5,12 [4,25; 6,17] <,0001[3]	8,60 [6,88; 10,74] <,0001[4]	36,8 [33,7; 40,0] <,0001[4]
Cardiac disorders				
90/1283 (7,0)	58/1265 (4,6)	1,53 [1,11; 2,11] 0,0094[3]	1,57 [1,12; 2,20] 0,0087[4]	2,4 [0,6; 4,2] 0,0087[4]
Ear and labyrinth disorders				
51/1283 (4,0)	56/1265 (4,4)	0,90 [0,62; 1,30] 0,5699[3]	0,89 [0,61; 1,32] 0,5697[4]	-0,5 [-2,0; 1,1] 0,5697[4]
Endocrine disorders				
24/1283 (1,9)	31/1265 (2,5)	0,76 [0,45; 1,29] 0,3154[3]	0,76 [0,44; 1,30] 0,3138[4]	-0,6 [-1,7; 0,5] 0,3138[4]
Eye disorders				
195/1283 (15,2)	66/1265 (5,2)	2,91 [2,23; 3,81] <,0001[3]	3,26 [2,43; 4,36] <,0001[4]	10,0 [7,7; 12,3] <,0001[4]
Gastrointestinal disorders				
1142/1283 (89,0)	408/1265 (32,3)	2,76 [2,54; 3,00] <,0001[3]	17,01 [13,78; 21,01] <,0001[4]	56,8 [53,7; 59,8] <,0001[4]
General disorders and administration site conditions				
713/1283 (55,6)	406/1265 (32,1)	1,73 [1,58; 1,90] <,0001[3]	2,65 [2,25; 3,11] <,0001[4]	23,5 [19,7; 27,2] <,0001[4]
Hepatobiliary disorders				
60/1283 (4,7)	54/1265 (4,3)	1,10 [0,76; 1,57] 0,6188[3]	1,10 [0,76; 1,60] 0,6186[4]	0,4 [-1,2; 2,0] 0,6186[4]
Immune system disorders				
30/1283 (2,3)	30/1265 (2,4)	0,99 [0,60; 1,63] 0,9558[3]	0,99 [0,59; 1,64] 0,9558[4]	-0,0 [-1,2; 1,1] 0,9558[4]
Infections and infestations				
600/1283 (46,8)	462/1265 (36,5)	1,28 [1,17; 1,41] <,0001[3]	1,53 [1,30; 1,79] <,0001[4]	10,2 [6,4; 14,1] <,0001[4]
Injury, poisoning and procedural complications				
217/1283 (16,9)	184/1265 (14,5)	1,16 [0,97; 1,39] 0,1013[3]	1,20 [0,97; 1,48] 0,1008[4]	2,4 [-0,5; 5,2] 0,1008[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Investigations				
621/1283 (48,4)	275/1265 (21,7)	2,23 [1,98; 2,51] <,0001[3]	3,38 [2,84; 4,01] <,0001[4]	26,7 [23,1; 30,2] <,0001[4]
Metabolism and nutrition disorders				
358/1283 (27,9)	202/1265 (16,0)	1,75 [1,50; 2,04] <,0001[3]	2,04 [1,68; 2,47] <,0001[4]	11,9 [8,8; 15,1] <,0001[4]
Musculoskeletal and connective tissue disorders				
624/1283 (48,6)	744/1265 (58,8)	0,83 [0,77; 0,89] <,0001[3]	0,66 [0,57; 0,78] <,0001[4]	-10,2 [-14,0; -6,3] <,0001[4]
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
37/1283 (2,9)	36/1265 (2,8)	1,01 [0,64; 1,59] 0,9541[3]	1,01 [0,64; 1,61] 0,9541[4]	0,0 [-1,3; 1,3] 0,9541[4]
Nervous system disorders				
494/1283 (38,5)	344/1265 (27,2)	1,42 [1,26; 1,59] <,0001[3]	1,68 [1,42; 1,98] <,0001[4]	11,3 [7,7; 14,9] <,0001[4]
Psychiatric disorders				
202/1283 (15,7)	214/1265 (16,9)	0,93 [0,78; 1,11] 0,4234[3]	0,92 [0,74; 1,13] 0,4233[4]	-1,2 [-4,0; 1,7] 0,4233[4]
Renal and urinary disorders				
99/1283 (7,7)	69/1265 (5,5)	1,41 [1,05; 1,90] 0,0222[3]	1,45 [1,05; 1,99] 0,0214[4]	2,3 [0,3; 4,2] 0,0214[4]
Reproductive system and breast disorders				
121/1283 (9,4)	166/1265 (13,1)	0,72 [0,58; 0,90] 0,0034[3]	0,69 [0,54; 0,88] 0,0032[4]	-3,7 [-6,1; -1,2] 0,0032[4]
Respiratory, thoracic and mediastinal disorders				
373/1283 (29,1)	249/1265 (19,7)	1,48 [1,28; 1,70] <,0001[3]	1,67 [1,39; 2,01] <,0001[4]	9,4 [6,1; 12,7] <,0001[4]
Skin and subcutaneous tissue disorders				
506/1283 (39,4)	279/1265 (22,1)	1,79 [1,58; 2,02] <,0001[3]	2,30 [1,93; 2,74] <,0001[4]	17,4 [13,9; 20,9] <,0001[4]
Surgical and medical procedures				
66/1283 (5,1)	71/1265 (5,6)	0,92 [0,66; 1,27] 0,6003[3]	0,91 [0,65; 1,29] 0,6002[4]	-0,5 [-2,2; 1,3] 0,6002[4]
Vascular disorders				
386/1283 (30,1)	370/1265 (29,2)	1,03 [0,91; 1,16] 0,6439[3]	1,04 [0,88; 1,23] 0,6439[4]	0,8 [-2,7; 4,4] 0,6439[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 3: from Z-test; 4: from Chi^2-test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class				

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt.sas
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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Results from binary analysis for adverse events according SOC - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
3/10 (30,0)	1/9 (11,1)	[2]	[2]	[2]
Cardiac disorders				
1/10 (10,0)	2/9 (22,2)	[2]	[2]	[2]
Ear and labyrinth disorders				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Endocrine disorders				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Eye disorders				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Gastrointestinal disorders				
7/10 (70,0)	1/9 (11,1)	[2]	[2]	[2]
General disorders and administration site conditions				
6/10 (60,0)	4/9 (44,4)	[2]	[2]	[2]
Immune system disorders				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Infections and infestations				
4/10 (40,0)	2/9 (22,2)	[2]	[2]	[2]
Injury, poisoning and procedural complications				
0/10 (0,0)	3/9 (33,3)	[2]	[2]	[2]
Investigations				
5/10 (50,0)	1/9 (11,1)	[2]	[2]	[2]
Metabolism and nutrition disorders				
4/10 (40,0)	0/9 (0,0)	[2]	[2]	[2]
Musculoskeletal and connective tissue disorders				
3/10 (30,0)	6/9 (66,7)	[2]	[2]	[2]
Nervous system disorders				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
2/10 (20,0)	2/9 (22,2)	2	2	2
Psychiatric disorders				
2/10 (20,0)	2/9 (22,2)	2	2	2
Renal and urinary disorders				
0/10 (0,0)	2/9 (22,2)	2	2	2
Respiratory, thoracic and mediastinal disorders				
6/10 (60,0)	1/9 (11,1)	2	2	2
Skin and subcutaneous tissue disorders				
4/10 (40,0)	1/9 (11,1)	2	2	2
Surgical and medical procedures				
0/10 (0,0)	1/9 (11,1)	2	2	2
Vascular disorders				
2/10 (20,0)	5/9 (55,6)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to appropriate comparator by GBA: Tamoxifen; 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Results from binary analysis for serious adverse events according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
No events in category				
-	-	-	-	-

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Results from binary analysis for serious adverse events according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Pneumonia				
15/1283 (1,2)	7/1265 (0,6)	2,11 [0,86; 5,16] 0,1009[3]	2,13 [0,86; 5,23] 0,0930[4]	0,6 [-0,1; 1,3] 0,0930[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Results from binary analysis for serious adverse events according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aortic stenosis				
0/10 (0,0)	1/9 (11,1)	2	2	2
Cellulitis streptococcal				
1/10 (10,0)	0/9 (0,0)	2	2	2
Coronary artery disease				
0/10 (0,0)	1/9 (11,1)	2	2	2
Hyponatraemia				
1/10 (10,0)	0/9 (0,0)	2	2	2
Pneumonitis				
1/10 (10,0)	0/9 (0,0)	2	2	2
Pulmonary embolism				
1/10 (10,0)	0/9 (0,0)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to appropriate comparator by GBA: Tamoxifen; 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Results from binary analysis for serious adverse events according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Infections and infestations				
18/553 (3,3)	10/535 (1,9)	1,74 [0,81; 3,74] 0,1546[3]	1,77 [0,81; 3,86] 0,1490[4]	1,4 [-0,5; 3,3] 0,1490[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Results from binary analysis for serious adverse events according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Cardiac disorders				
16/1283 (1,2)	8/1265 (0,6)	1,97 [0,85; 4,59] 0,1153[3]	1,98 [0,85; 4,65] 0,1083[4]	0,6 [-0,1; 1,4] 0,1083[4]
Gastrointestinal disorders				
31/1283 (2,4)	14/1265 (1,1)	2,18 [1,17; 4,08] 0,0146[3]	2,21 [1,17; 4,18] 0,0121[4]	1,3 [0,3; 2,3] 0,0121[4]
Infections and infestations				
69/1283 (5,4)	34/1265 (2,7)	2,00 [1,34; 2,99] 0,0007[3]	2,06 [1,35; 3,13] 0,0006[4]	2,7 [1,2; 4,2] 0,0006[4]
Injury, poisoning and procedural complications				
17/1283 (1,3)	15/1265 (1,2)	1,12 [0,56; 2,23] 0,7524[3]	1,12 [0,56; 2,25] 0,7523[4]	0,1 [-0,7; 1,0] 0,7523[4]
Nervous system disorders				
13/1283 (1,0)	13/1265 (1,0)	0,99 [0,46; 2,12] 0,9711[3]	0,99 [0,46; 2,13] 0,9711[4]	-0,0 [-0,8; 0,8] 0,9711[4]
Respiratory, thoracic and mediastinal disorders				
16/1283 (1,2)	9/1265 (0,7)	1,75 [0,78; 3,95] 0,1760[3]	1,76 [0,78; 4,00] 0,1702[4]	0,5 [-0,2; 1,3] 0,1702[4]
Vascular disorders				
16/1283 (1,2)	6/1265 (0,5)	2,63 [1,03; 6,70] 0,0427[3]	2,65 [1,03; 6,79] 0,0350[4]	0,8 [0,1; 1,5] 0,0350[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Results from binary analysis for serious adverse events according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Cardiac disorders				
0/10 (0,0)	1/9 (11,1)	2	2	2
Infections and infestations				
1/10 (10,0)	0/9 (0,0)	2	2	2
Metabolism and nutrition disorders				
1/10 (10,0)	0/9 (0,0)	2	2	2
Respiratory, thoracic and mediastinal disorders				
2/10 (20,0)	0/9 (0,0)	2	2	2
Vascular disorders				
0/10 (0,0)	1/9 (11,1)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to appropriate comparator by GBA: Tamoxifen; 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Alanine aminotransferase increased				
11/553 (2,0)	1/535 (0,2)	10,64 [1,38; 82,14] 0,0233[3]	10,84 [1,39; 84,24] 0,0044[4]	1,8 [0,6; 3,0] 0,0044[4]
Aspartate aminotransferase increased				
10/553 (1,8)	1/535 (0,2)	9,67 [1,24; 75,32] 0,0302[3]	9,83 [1,25; 77,09] 0,0075[4]	1,6 [0,5; 2,8] 0,0075[4]
Diarrhoea				
30/553 (5,4)	2/535 (0,4)	14,51 [3,49; 60,42] 0,0002[3]	15,29 [3,63; 64,29] <,0001[4]	5,1 [3,1; 7,0] <,0001[4]
Leukopenia				
14/553 (2,5)	0/535 (0,0)	28,06 [1,68; 469,17] 0,0203[3]	28,78 [1,71; 483,76] 0,0002[4]	2,5 [1,2; 3,8] 0,0002[4]
Lymphocyte count decreased				
24/553 (4,3)	0/535 (0,0)	47,41 [2,89; 777,61] 0,0069[3]	49,56 [3,01; 816,98] <,0001[4]	4,3 [2,6; 6,0] <,0001[4]
Neutropenia				
42/553 (7,6)	6/535 (1,1)	6,77 [2,90; 15,80] <,0001[3]	7,25 [3,05; 17,19] <,0001[4]	6,5 [4,1; 8,9] <,0001[4]
Neutrophil count decreased				
57/553 (10,3)	5/535 (0,9)	11,03 [4,46; 27,30] <,0001[3]	12,18 [4,84; 30,64] <,0001[4]	9,4 [6,7; 12,0] <,0001[4]
White blood cell count decreased				
44/553 (8,0)	5/535 (0,9)	8,51 [3,40; 21,31] <,0001[3]	9,16 [3,60; 23,29] <,0001[4]	7,0 [4,6; 9,4] <,0001[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Alanine aminotransferase increased				
35/1283 (2,7)	6/1265 (0,5)	5,75 [2,43; 13,63] <,0001[3]	5,88 [2,47; 14,04] <,0001[4]	2,3 [1,3; 3,2] <,0001[4]
Anaemia				
38/1283 (3,0)	5/1265 (0,4)	7,49 [2,96; 18,98] <,0001[3]	7,69 [3,02; 19,61] <,0001[4]	2,6 [1,6; 3,6] <,0001[4]
Aspartate aminotransferase increased				
22/1283 (1,7)	4/1265 (0,3)	5,42 [1,87; 15,69] 0,0018[3]	5,50 [1,89; 16,01] 0,0004[4]	1,4 [0,6; 2,2] 0,0004[4]
Diarrhoea				
125/1283 (9,7)	2/1265 (0,2)	61,62 [15,28; 248,59] <,0001[3]	68,17 [16,82; 276,22] <,0001[4]	9,6 [7,9; 11,2] <,0001[4]
Fatigue				
34/1283 (2,7)	2/1265 (0,2)	16,76 [4,04; 69,62] 0,0001[3]	17,19 [4,12; 71,71] <,0001[4]	2,5 [1,6; 3,4] <,0001[4]
Gamma-glutamyltransferase increased				
20/1283 (1,6)	5/1265 (0,4)	3,94 [1,48; 10,48] 0,0059[3]	3,99 [1,49; 10,67] 0,0029[4]	1,2 [0,4; 1,9] 0,0029[4]
Hypertension				
17/1283 (1,3)	20/1265 (1,6)	0,84 [0,44; 1,59] 0,5896[3]	0,84 [0,44; 1,60] 0,5891[4]	-0,3 [-1,2; 0,7] 0,5891[4]
Hypokalaemia				
18/1283 (1,4)	5/1265 (0,4)	3,55 [1,32; 9,53] 0,0119[3]	3,59 [1,33; 9,69] 0,0072[4]	1,0 [0,3; 1,7] 0,0072[4]
Leukopenia				
47/1283 (3,7)	2/1265 (0,2)	23,17 [5,64; 95,19] <,0001[3]	24,01 [5,82; 99,07] <,0001[4]	3,5 [2,5; 4,6] <,0001[4]
Lymphocyte count decreased				
42/1283 (3,3)	5/1265 (0,4)	8,28 [3,29; 20,87] <,0001[3]	8,53 [3,36; 21,63] <,0001[4]	2,9 [1,8; 3,9] <,0001[4]
Lymphopenia				
22/1283 (1,7)	1/1265 (0,1)	21,69 [2,93; 160,68] 0,0026[3]	22,05 [2,97; 163,85] <,0001[4]	1,6 [0,9; 2,4] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Neutropenia				
139/1283 (10,8)	4/1265 (0,3)	34,26 [12,72; 92,30] <,0001[3]	38,30 [14,13; 103,83] <,0001[4]	10,5 [8,8; 12,2] <,0001[4]
Neutrophil count decreased				
128/1283 (10,0)	3/1265 (0,2)	42,07 [13,43; 131,82] <,0001[3]	46,62 [14,80; 146,87] <,0001[4]	9,7 [8,1; 11,4] <,0001[4]
Platelet count decreased				
13/1283 (1,0)	0/1265 (0,0)	26,62 [1,58; 447,34] 0,0226[3]	26,89 [1,60; 452,88] 0,0003[4]	1,0 [0,5; 1,6] 0,0003[4]
White blood cell count decreased				
98/1283 (7,6)	3/1265 (0,2)	32,21 [10,24; 101,33] <,0001[3]	34,79 [11,00; 110,04] <,0001[4]	7,4 [5,9; 8,9] <,0001[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttirgr3p_posmp_safc1.rtf
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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aortic stenosis				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Atrial fibrillation				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Cellulitis streptococcal				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Coronary artery disease				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Finger amputation				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Haematuria				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Hypoalbuminaemia				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Hyponatraemia				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Lymphocyte count decreased				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Neutropenia				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Platelet count decreased				
2/10 (20,0)	0/9 (0,0)	[2]	[2]	[2]
Pneumonitis				
1/10 (10,0)	0/9 (0,0)	[2]	[2]	[2]
Postoperative respiratory failure				
0/10 (0,0)	1/9 (11,1)	[2]	[2]	[2]
Pulmonary embolism				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
1/10 (10,0)	0/9 (0,0)	2	2	2
Radius fracture				
0/10 (0,0)	1/9 (11,1)	2	2	2
Tendon injury				
0/10 (0,0)	1/9 (11,1)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to appropriate comparator by GBA: Tamoxifen; 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
62/553 (11,2)	8/535 (1,5)	7,50 [3,63; 15,51] <,0001[3]	8,32 [3,94; 17,55] <,0001[4]	9,7 [6,9; 12,5] <,0001[4]
Gastrointestinal disorders				
40/553 (7,2)	4/535 (0,7)	9,67 [3,49; 26,85] <,0001[3]	10,35 [3,68; 29,14] <,0001[4]	6,5 [4,2; 8,8] <,0001[4]
Infections and infestations				
21/553 (3,8)	10/535 (1,9)	2,03 [0,97; 4,27] 0,0617[3]	2,07 [0,97; 4,44] 0,0560[4]	1,9 [-0,0; 3,9] 0,0560[4]
Investigations				
105/553 (19,0)	9/535 (1,7)	11,29 [5,77; 22,06] <,0001[3]	13,70 [6,85; 27,37] <,0001[4]	17,3 [13,9; 20,8] <,0001[4]
Metabolism and nutrition disorders				
11/553 (2,0)	5/535 (0,9)	2,13 [0,74; 6,08] 0,1587[3]	2,15 [0,74; 6,23] 0,1485[4]	1,1 [-0,4; 2,5] 0,1485[4]
Vascular disorders				
10/553 (1,8)	9/535 (1,7)	1,07 [0,44; 2,62] 0,8739[3]	1,08 [0,43; 2,67] 0,8739[4]	0,1 [-1,4; 1,7] 0,8739[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttirgr3s_premp_safc1.rtf
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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
209/1283 (16,3)	13/1265 (1,0)	15,85 [9,10; 27,61] <,0001[3]	18,74 [10,64; 33,01] <,0001[4]	15,3 [13,2; 17,4] <,0001[4]
Cardiac disorders				
14/1283 (1,1)	11/1265 (0,9)	1,25 [0,57; 2,75] 0,5712[3]	1,26 [0,57; 2,78] 0,5704[4]	0,2 [-0,5; 1,0] 0,5704[4]
Eye disorders				
14/1283 (1,1)	6/1265 (0,5)	2,30 [0,89; 5,97] 0,0867[3]	2,31 [0,89; 6,04] 0,0777[4]	0,6 [-0,1; 1,3] 0,0777[4]
Gastrointestinal disorders				
148/1283 (11,5)	18/1265 (1,4)	8,11 [5,00; 13,14] <,0001[3]	9,03 [5,50; 14,83] <,0001[4]	10,1 [8,2; 12,0] <,0001[4]
General disorders and administration site conditions				
53/1283 (4,1)	7/1265 (0,6)	7,47 [3,41; 16,36] <,0001[3]	7,74 [3,51; 17,10] <,0001[4]	3,6 [2,4; 4,7] <,0001[4]
Infections and infestations				
69/1283 (5,4)	36/1265 (2,8)	1,89 [1,27; 2,81] 0,0016[3]	1,94 [1,29; 2,93] 0,0013[4]	2,5 [1,0; 4,1] 0,0013[4]
Injury, poisoning and procedural complications				
16/1283 (1,2)	16/1265 (1,3)	0,99 [0,50; 1,96] 0,9679[3]	0,99 [0,49; 1,98] 0,9679[4]	-0,0 [-0,9; 0,8] 0,9679[4]
Investigations				
246/1283 (19,2)	29/1265 (2,3)	8,36 [5,74; 12,19] <,0001[3]	10,11 [6,82; 14,99] <,0001[4]	16,9 [14,6; 19,2] <,0001[4]
Metabolism and nutrition disorders				
64/1283 (5,0)	22/1265 (1,7)	2,87 [1,78; 4,63] <,0001[3]	2,97 [1,82; 4,85] <,0001[4]	3,2 [1,9; 4,6] <,0001[4]
Musculoskeletal and connective tissue disorders				
13/1283 (1,0)	24/1265 (1,9)	0,53 [0,27; 1,04] 0,0667[3]	0,53 [0,27; 1,04] 0,0622[4]	-0,9 [-1,8; 0,0] 0,0622[4]
Nervous system disorders				
26/1283 (2,0)	17/1265 (1,3)	1,51 [0,82; 2,77] 0,1843[3]	1,52 [0,82; 2,81] 0,1810[4]	0,7 [-0,3; 1,7] 0,1810[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Respiratory, thoracic and mediastinal disorders				
23/1283 (1,8)	10/1265 (0,8)	2,27 [1,08; 4,75] 0,0297[3]	2,29 [1,09; 4,83] 0,0253[4]	1,0 [0,1; 1,9] 0,0253[4]
Surgical and medical procedures				
14/1283 (1,1)	9/1265 (0,7)	1,53 [0,67; 3,53] 0,3147[3]	1,54 [0,66; 3,57] 0,3109[4]	0,4 [-0,4; 1,1] 0,3109[4]
Vascular disorders				
29/1283 (2,3)	30/1265 (2,4)	0,95 [0,58; 1,58] 0,8520[3]	0,95 [0,57; 1,60] 0,8520[4]	-0,1 [-1,3; 1,1] 0,8520[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
2/10 (20,0)	0/9 (0,0)	2	2	2
Cardiac disorders				
0/10 (0,0)	1/9 (11,1)	2	2	2
Infections and infestations				
1/10 (10,0)	0/9 (0,0)	2	2	2
Injury, poisoning and procedural complications				
0/10 (0,0)	2/9 (22,2)	2	2	2
Investigations				
2/10 (20,0)	0/9 (0,0)	2	2	2
Metabolism and nutrition disorders				
2/10 (20,0)	0/9 (0,0)	2	2	2
Renal and urinary disorders				
0/10 (0,0)	1/9 (11,1)	2	2	2
Respiratory, thoracic and mediastinal disorders				
2/10 (20,0)	0/9 (0,0)	2	2	2
Surgical and medical procedures				
0/10 (0,0)	1/9 (11,1)	2	2	2
Vascular disorders				
0/10 (0,0)	1/9 (11,1)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to appropriate comparator by GBA: Tamoxifen; 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttirgr3s_men_safc1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Anhang 4-G2: Ergänzende Subgruppenanalysen der Studie MONARCH-E

Anhang 4-G2.1: Gesamtüberleben - Subgruppenanalysen

Tabelle 4-122 (Anhang): Gesamtüberleben - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen für Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - ITT - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7327)					
Neoadjuvante Chemotherapie	13/217 (6,0)	NE [NE; NE]	7/219 (3,2)	NE [NE; NE]	1,81 [0,72; 4,55] 0,1975
Adjuvante Chemotherapie	4/327 (1,2)	NE [40,11; NE]	4/312 (1,3)	NE [NE; NE]	0,91 [0,23; 3,63] 0,8894
Keine Chemotherapie	0/9 (0,0)	NE [NE; NE]	0/4 (0,0)	NE [NE; NE]	NB
Region (p-Wert des Interaktionsterms: 0,8296)					
Nordamerika / Europa	7/252 (2,8)	NE [NE; NE]	6/233 (2,6)	NE [NE; NE]	1,06 [0,35; 3,14] 0,9226
Asien	2/168 (1,2)	NE [NE; NE]	0/166 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,1658
Andere	8/133 (6,0)	40,1 [40,11; NE]	5/136 (3,7)	NE [NE; NE]	1,71 [0,56; 5,22] 0,3439
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6254)					
< 20 mm	2/141 (1,4)	NE [NE; NE]	3/140 (2,1)	NE [NE; NE]	0,67 [0,11; 3,99] 0,6551
≥ 20 bis < 50 mm	9/255 (3,5)	NE [NE; NE]	5/249 (2,0)	NE [NE; NE]	1,75 [0,58; 5,21] 0,3115
≥ 50 mm	5/145 (3,4)	40,1 [40,11; NE]	3/141 (2,1)	NE [NE; NE]	1,25 [0,28; 5,59] 0,7687
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7695)					
0-3	8/203 (3,9)	NE [40,11; NE]	5/214 (2,3)	NE [NE; NE]	1,65 [0,54; 5,05] 0,3737
4-9	4/242 (1,7)	NE [NE; NE]	4/231 (1,7)	NE [NE; NE]	0,95 [0,24; 3,79] 0,9400
≥ 10	5/108 (4,6)	NE [NE; NE]	2/90 (2,2)	NE [NE; NE]	1,96 [0,38; 10,12] 0,4122
Tumorstadium (p-Wert des Interaktionsterms: 0,9943)					
IIA	2/59 (3,4)	NE [NE; NE]	1/62 (1,6)	NE [NE; NE]	1,90 [0,17; 21,01] 0,5943
IIB	2/53 (3,8)	NE [NE; NE]	3/69 (4,3)	NE [NE; NE]	0,97 [0,16; 5,83] 0,9761

Subgruppe	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
IIIA	5/236 (2,1)	40,1 [NE; NE]	3/214 (1,4)	NE [NE; NE]	1,64 [0,39; 6,95] 0,4995
IIIB	1/18 (5,6)	NE [30,35; NE]	0/15 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,3865
IIIC	7/186 (3,8)	NE [NE; NE]	4/174 (2,3)	NE [NE; NE]	1,60 [0,47; 5,48] 0,4465
Tumorgrading (p-Wert des Interaktionsterms: 0,9839)					
G1	1/47 (2,1)	NE [NE; NE]	0/41 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,2963
G2	5/244 (2,0)	NE [NE; NE]	4/234 (1,7)	NE [NE; NE]	1,17 [0,31; 4,36] 0,8127
G3	10/233 (4,3)	NE [40,11; NE]	6/226 (2,7)	NE [NE; NE]	1,58 [0,57; 4,34] 0,3732
GX	1/29 (3,4)	NE [NE; NE]	1/33 (3,0)	NE [NE; NE]	1,24 [0,08; 19,82] 0,8802
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,8897)					
Negativ	3/49 (6,1)	NE [NE; NE]	1/44 (2,3)	NE [NE; NE]	2,62 [0,27; 25,33] 0,3862
Positiv	14/477 (2,9)	NE [NE; NE]	10/471 (2,1)	NE [NE; NE]	1,36 [0,60; 3,06] 0,4576
Unbekannt	0/4 (0,0)	NE [NE; NE]	0/8 (0,0)	NE [NE; NE]	NB
Ethnizität (p-Wert des Interaktionsterms: 0,7761)					
Weiß	11/323 (3,4)	NE [40,11; NE]	9/324 (2,8)	NE [NE; NE]	1,21 [0,50; 2,91] 0,6770
Asiatisch	3/199 (1,5)	NE [NE; NE]	0/180 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,1049
Andere	3/19 (15,8)	NE [31,79; NE]	1/21 (4,8)	NE [NE; NE]	2,91 [0,30; 28,28] 0,3355
ECOG-PS (p-Wert des Interaktionsterms: 0,9999)					
ECOG-PS 0	17/496 (3,4)	NE [NE; NE]	11/480 (2,3)	NE [NE; NE]	1,47 [0,69; 3,14] 0,3168
ECOG-PS 1	0/57 (0,0)	NE [NE; NE]	0/55 (0,0)	NE [NE; NE]	NB

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
Datenschnitt: 01.04.2021 ITT-Population 1: Aus Log-rank-Test; 2: In Monaten; 3: gemäß ZVT des G-BA: Tamoxifen. Abkürzungen: ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl verstorbener Patienten; N: Gesamtzahl der Patienten in der Analyse; NB = Nicht berechnet; NE: Nicht errechenbar/nicht erreicht.					

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Tabell: Subgruppen für Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - ITT - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
Alter (p-Wert des Interaktionsterms: 0,8110)					
< 65 Jahre	35/918 (3,8)	NE [NE; NE]	40/937 (4,3)	NE [NE; NE]	0,91 [0,58; 1,43] 0,6678
≥ 65 Jahre	19/366 (5,2)	NE [NE; NE]	18/327 (5,5)	NE [NE; NE]	1,00 [0,52; 1,90] 0,9927
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8721)					
Neoadjuvante Chemotherapie	28/430 (6,5)	NE [NE; NE]	31/415 (7,5)	NE [NE; NE]	0,92 [0,55; 1,54] 0,7639
Adjuvante Chemotherapie	23/785 (2,9)	NE [NE; NE]	22/768 (2,9)	NE [NE; NE]	1,03 [0,58; 1,86] 0,9095
Keine Chemotherapie	3/69 (4,3)	NE [NE; NE]	5/81 (6,2)	NE [NE; NE]	0,67 [0,16; 2,81] 0,5806
Region (p-Wert des Interaktionsterms: 0,5333)					
Nordamerika / Europa	27/679 (4,0)	NE [NE; NE]	23/649 (3,5)	NE [NE; NE]	1,15 [0,66; 2,01] 0,6161
Asien	4/203 (2,0)	NE [NE; NE]	7/201 (3,5)	NE [NE; NE]	0,56 [0,16; 1,91] 0,3484
Andere	23/402 (5,7)	NE [NE; NE]	28/414 (6,8)	NE [NE; NE]	0,89 [0,51; 1,54] 0,6659
Primärtumorgröße (p-Wert des Interaktionsterms: 0,0803)					
< 20 mm	8/332 (2,4)	NE [NE; NE]	19/334 (5,7)	NE [NE; NE]	0,43 [0,19; 0,98] 0,0377
≥ 20 bis < 50 mm	27/646 (4,2)	NE [NE; NE]	27/653 (4,1)	NE [NE; NE]	1,03 [0,60; 1,75] 0,9258
≥ 50 mm	19/289 (6,6)	NE [NE; NE]	12/265 (4,5)	NE [NE; NE]	1,50 [0,73; 3,08] 0,2706
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9524)					
0-3	15/427 (3,5)	NE [NE; NE]	17/418 (4,1)	NE [NE; NE]	0,89 [0,44; 1,78] 0,7398
4-9	18/548 (3,3)	NE [NE; NE]	18/543 (3,3)	NE [NE; NE]	1,03 [0,53; 1,97] 0,9393

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
≥ 10	21/309 (6,8)	NE [NE; NE]	23/303 (7,6)	NE [NE; NE]	0,92 [0,51; 1,65] 0,7690
Tumorstadium (p-Wert des Interaktionsterms: 0,4829)					
IIA	2/113 (1,8)	NE [NE; NE]	7/114 (6,1)	NE [36,85; NE]	0,29 [0,06; 1,40] 0,1008
IIB	6/151 (4,0)	NE [NE; NE]	6/136 (4,4)	NE [NE; NE]	0,87 [0,28; 2,71] 0,8160
IIIA	19/495 (3,8)	NE [NE; NE]	14/488 (2,9)	NE [NE; NE]	1,40 [0,70; 2,78] 0,3411
IIIB	3/54 (5,6)	NE [NE; NE]	3/45 (6,7)	NE [NE; NE]	0,91 [0,18; 4,49] 0,9038
IIIC	24/469 (5,1)	NE [NE; NE]	28/479 (5,8)	NE [NE; NE]	0,89 [0,52; 1,54] 0,6803
Tumorgrading (p-Wert des Interaktionsterms: 0,9827)					
G1	5/91 (5,5)	NE [NE; NE]	4/93 (4,3)	NE [NE; NE]	1,25 [0,34; 4,66] 0,7390
G2	25/613 (4,1)	NE [NE; NE]	26/602 (4,3)	NE [NE; NE]	0,99 [0,57; 1,71] 0,9582
G3	24/528 (4,5)	NE [NE; NE]	24/505 (4,8)	NE [NE; NE]	0,96 [0,55; 1,70] 0,8998
GX	0/50 (0,0)	NE [NE; NE]	3/60 (5,0)	NE [NE; NE]	0,00 [0,00; NE] 0,1069
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,8128)					
Negativ	10/157 (6,4)	NE [NE; NE]	15/168 (8,9)	NE [NE; NE]	0,74 [0,33; 1,64] 0,4563
Positiv	42/1089 (3,9)	NE [NE; NE]	42/1067 (3,9)	NE [NE; NE]	1,00 [0,65; 1,53] 0,9937
Unbekannt	0/10 (0,0)	NE [NE; NE]	0/7 (0,0)	NE [NE; NE]	NB
Ethnizität (p-Wert des Interaktionsterms: 0,6501)					
Weiß	49/958 (5,1)	NE [NE; NE]	49/944 (5,2)	NE [NE; NE]	1,01 [0,68; 1,50] 0,9509
Asiatisch	4/250 (1,6)	NE [NE; NE]	7/242 (2,9)	NE [NE; NE]	0,56 [0,16; 1,90] 0,3427

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
Andere	1/63 (1,6)	NE [NE; NE]	1/63 (1,6)	NE [NE; NE]	1,06 [0,07; 16,97] 0,9665
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,5057)					
Tamoxifen	4/114 (3,5)	NE [NE; NE]	7/132 (5,3)	NE [NE; NE]	0,64 [0,19; 2,19] 0,4756
Aromatase-Inhibitor	50/1170 (4,3)	NE [NE; NE]	51/1132 (4,5)	NE [NE; NE]	0,98 [0,66; 1,45] 0,9132
ECOG-PS (p-Wert des Interaktionsterms: 0,1801)					
ECOG-PS 0	41/1070 (3,8)	NE [NE; NE]	48/1020 (4,7)	NE [NE; NE]	0,83 [0,55; 1,26] 0,3829
ECOG-PS 1	13/214 (6,1)	NE [NE; NE]	10/244 (4,1)	NE [NE; NE]	1,56 [0,69; 3,57] 0,2831

Datenschnitt: 01.04.2021
ITT-Population
1: Aus Log-rank-Test; 2: In Monaten; 3: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen.
Abkürzungen: ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl verstorbener Patienten; N: Gesamtzahl der Patienten in der Analyse; NB = Nicht berechnet; NE: Nicht errechenbar/nicht erreicht.

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Anhang 4-G2.2: IDFS - Subgruppenanalysen

Tabelle 4-123 (Anhang): IDFS - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen für IDFS aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - ITT - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,6886)					
Neoadjuvante Chemotherapie	31/217 (14,3)	NE [NE; NE]	51/219 (23,3)	NE [NE; NE]	0,57 [0,36; 0,89] 0,0122
Adjuvante Chemotherapie	13/327 (4,0)	NE [NE; NE]	30/312 (9,6)	NE [NE; NE]	0,40 [0,21; 0,77] 0,0045
Keine Chemotherapie	1/9 (11,1)	NE [14,24; NE]	0/4 (0,0)	NE [NE; NE]	>100 [0,00; NE] 0,4497
Region (p-Wert des Interaktionsterms: 0,8339)					
Nordamerika / Europa	21/252 (8,3)	NE [NE; NE]	37/233 (15,9)	NE [NE; NE]	0,50 [0,30; 0,86] 0,0108
Asien	9/168 (5,4)	NE [NE; NE]	19/166 (11,4)	NE [NE; NE]	0,44 [0,20; 0,98] 0,0396
Andere	15/133 (11,3)	NE [NE; NE]	25/136 (18,4)	NE [NE; NE]	0,60 [0,32; 1,14] 0,1137
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2093)					
< 20 mm	9/141 (6,4)	NE [NE; NE]	21/140 (15,0)	NE [NE; NE]	0,42 [0,19; 0,92] 0,0249
≥ 20 bis < 50 mm	23/255 (9,0)	NE [NE; NE]	32/249 (12,9)	NE [NE; NE]	0,69 [0,40; 1,17] 0,1677
≥ 50 mm	10/145 (6,9)	NE [NE; NE]	27/141 (19,1)	NE [NE; NE]	0,33 [0,16; 0,68] 0,0015
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,2595)					
0-3	19/203 (9,4)	NE [NE; NE]	28/214 (13,1)	NE [NE; NE]	0,71 [0,40; 1,27] 0,2433
4-9	13/242 (5,4)	NE [NE; NE]	35/231 (15,2)	NE [NE; NE]	0,34 [0,18; 0,65] 0,0006
≥ 10	13/108 (12,0)	NE [NE; NE]	18/90 (20,0)	NE [NE; NE]	0,52 [0,26; 1,07] 0,0702
Tumorstadium (p-Wert des Interaktionsterms: 0,3143)					
IIA	6/59 (10,2)	NE [NE; NE]	10/62 (16,1)	NE [NE; NE]	0,61 [0,22; 1,69] 0,3394

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
IIB	5/53 (9,4)	NE [NE; NE]	5/69 (7,2)	NE [NE; NE]	1,49 [0,43; 5,18] 0,5253
IIIA	14/236 (5,9)	NE [NE; NE]	31/214 (14,5)	NE [NE; NE]	0,39 [0,21; 0,73] 0,0024
IIIB	4/18 (22,2)	34,8 [33,96; NE]	3/15 (20,0)	NE [25,68; NE]	0,85 [0,19; 3,88] 0,8341
IIIC	16/186 (8,6)	NE [NE; NE]	32/174 (18,4)	NE [NE; NE]	0,43 [0,24; 0,78] 0,0046
Tumorgrading (p-Wert des Interaktionsterms: 0,7640)					
G1	2/47 (4,3)	NE [NE; NE]	2/41 (4,9)	NE [NE; NE]	0,88 [0,12; 6,25] 0,8968
G2	15/244 (6,1)	NE [NE; NE]	33/234 (14,1)	NE [NE; NE]	0,41 [0,22; 0,75] 0,0027
G3	26/233 (11,2)	NE [NE; NE]	42/226 (18,6)	NE [NE; NE]	0,58 [0,36; 0,95] 0,0284
GX	2/29 (6,9)	NE [NE; NE]	4/33 (12,1)	NE [35,15; NE]	0,67 [0,12; 3,75] 0,6447
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,8101)					
Negativ	6/49 (12,2)	NE [NE; NE]	13/44 (29,5)	NE [NE; NE]	0,37 [0,14; 0,98] 0,0372
Positiv	36/477 (7,5)	NE [NE; NE]	67/471 (14,2)	NE [NE; NE]	0,51 [0,34; 0,77] 0,0010
Unbekannt	0/4 (0,0)	NE [NE; NE]	0/8 (0,0)	NE [NE; NE]	NB
Ethnizität (p-Wert des Interaktionsterms: 0,4375)					
Weiß	31/323 (9,6)	NE [NE; NE]	50/324 (15,4)	NE [NE; NE]	0,60 [0,39; 0,95] 0,0261
Asiatisch	11/199 (5,5)	NE [NE; NE]	25/180 (13,9)	NE [NE; NE]	0,37 [0,18; 0,75] 0,0043
Andere	3/19 (15,8)	NE [NE; NE]	4/21 (19,0)	NE [35,15; NE]	0,92 [0,21; 4,13] 0,9158
ECOG-PS (p-Wert des Interaktionsterms: 0,6008)					
ECOG-PS 0	42/496 (8,5)	NE [NE; NE]	73/480 (15,2)	NE [NE; NE]	0,53 [0,36; 0,78] 0,0009

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
ECOG-PS 1	3/57 (5,3)	NE [NE; NE]	8/55 (14,5)	NE [35,15; NE]	0,39 [0,10; 1,46] 0,1467

Datenschnitt: 01.04.2021
ITT-Population
1: Aus Log-rank-Test; 2: In Monaten; 3: gemäß ZVT des G-BA: Tamoxifen.
Abkürzungen: ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; HR: Hazard Ratio; IDFS: Invasives krankheitsfreies Überleben (invasive disease-free survival); ITT: Intention to Treat; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB = Nicht berechnet; NE: Nicht errechenbar/nicht erreicht.

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Tabelle: Subgruppen für IDFS aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - ITT - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
Alter (p-Wert des Interaktionsterms: 0,4694)					
< 65 Jahre	84/918 (9,2)	NE [NE; NE]	123/937 (13,1)	NE [NE; NE]	0,70 [0,53; 0,92] 0,0105
≥ 65 Jahre	38/366 (10,4)	NE [NE; NE]	42/327 (12,8)	NE [NE; NE]	0,84 [0,54; 1,31] 0,4505
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8460)					
Neoadjuvante Chemotherapie	57/430 (13,3)	NE [NE; NE]	80/415 (19,3)	NE [NE; NE]	0,70 [0,50; 0,99] 0,0421
Adjuvante Chemotherapie	57/785 (7,3)	NE [NE; NE]	71/768 (9,2)	NE [NE; NE]	0,79 [0,56; 1,12] 0,1926
Keine Chemotherapie	8/69 (11,6)	NE [NE; NE]	14/81 (17,3)	NE [NE; NE]	0,62 [0,26; 1,48] 0,2738
Region (p-Wert des Interaktionsterms: 0,6841)					
Nordamerika / Europa	60/679 (8,8)	NE [NE; NE]	74/649 (11,4)	NE [NE; NE]	0,79 [0,56; 1,11] 0,1681
Asien	20/203 (9,9)	NE [NE; NE]	23/201 (11,4)	NE [NE; NE]	0,85 [0,47; 1,54] 0,5900
Andere	42/402 (10,4)	NE [NE; NE]	68/414 (16,4)	NE [NE; NE]	0,65 [0,44; 0,96] 0,0276
Primärtumorgröße (p-Wert des Interaktionsterms: 0,0972)					
< 20 mm	20/332 (6,0)	NE [NE; NE]	45/334 (13,5)	NE [NE; NE]	0,45 [0,27; 0,76] 0,0022
≥ 20 bis < 50 mm	66/646 (10,2)	NE [NE; NE]	76/653 (11,6)	NE [NE; NE]	0,89 [0,64; 1,23] 0,4784
≥ 50 mm	35/289 (12,1)	NE [NE; NE]	42/265 (15,8)	NE [NE; NE]	0,78 [0,50; 1,22] 0,2798
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,6579)					
0-3	30/427 (7,0)	NE [NE; NE]	47/418 (11,2)	NE [NE; NE]	0,62 [0,39; 0,98] 0,0399
4-9	46/548 (8,4)	NE [NE; NE]	57/543 (10,5)	NE [NE; NE]	0,82 [0,56; 1,21] 0,3133

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
≥ 10	46/309 (14,9)	NE [NE; NE]	61/303 (20,1)	NE [NE; NE]	0,75 [0,51; 1,10] 0,1409
Tumorstadium (p-Wert des Interaktionsterms: 0,2523)					
IIA	4/113 (3,5)	NE [NE; NE]	11/114 (9,6)	NE [NE; NE]	0,37 [0,12; 1,15] 0,0721
IIB	13/151 (8,6)	NE [NE; NE]	14/136 (10,3)	NE [NE; NE]	0,81 [0,38; 1,73] 0,5912
IIIA	45/495 (9,1)	NE [NE; NE]	44/488 (9,0)	NE [NE; NE]	1,05 [0,69; 1,60] 0,8086
IIIB	5/54 (9,3)	NE [NE; NE]	7/45 (15,6)	NE [NE; NE]	0,65 [0,21; 2,05] 0,4582
IIIC	55/469 (11,7)	NE [NE; NE]	89/479 (18,6)	NE [NE; NE]	0,63 [0,45; 0,88] 0,0063
Tumorgrading (p-Wert des Interaktionsterms: 0,5502)					
G1	6/91 (6,6)	NE [NE; NE]	9/93 (9,7)	NE [NE; NE]	0,66 [0,24; 1,87] 0,4339
G2	60/613 (9,8)	NE [NE; NE]	74/602 (12,3)	NE [NE; NE]	0,82 [0,58; 1,15] 0,2515
G3	52/528 (9,8)	NE [NE; NE]	68/505 (13,5)	NE [NE; NE]	0,73 [0,51; 1,05] 0,0932
GX	4/50 (8,0)	NE [NE; NE]	13/60 (21,7)	NE [NE; NE]	0,35 [0,11; 1,08] 0,0554
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9643)					
Negativ	24/157 (15,3)	NE [NE; NE]	37/168 (22,0)	NE [NE; NE]	0,69 [0,41; 1,16] 0,1603
Positiv	96/1089 (8,8)	NE [NE; NE]	126/1067 (11,8)	NE [NE; NE]	0,75 [0,58; 0,98] 0,0366
Unbekannt	0/10 (0,0)	NE [NE; NE]	0/7 (0,0)	NE [NE; NE]	NB
Ethnizität (p-Wert des Interaktionsterms: 0,8689)					
Weiß	97/958 (10,1)	NE [NE; NE]	128/944 (13,6)	NE [NE; NE]	0,76 [0,58; 0,98] 0,0367
Asiatisch	20/250 (8,0)	NE [NE; NE]	30/242 (12,4)	NE [NE; NE]	0,65 [0,37; 1,14] 0,1276

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
Andere	4/63 (6,3)	NE [35,15; NE]	5/63 (7,9)	NE [NE; NE]	0,88 [0,23; 3,28] 0,8458
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,1151)					
Tamoxifen	6/114 (5,3)	NE [NE; NE]	18/132 (13,6)	NE [NE; NE]	0,37 [0,15; 0,92] 0,0267
Aromatase-Inhibitor	116/1170 (9,9)	NE [NE; NE]	147/1132 (13,0)	NE [NE; NE]	0,78 [0,61; 0,99] 0,0434
ECOG-PS (p-Wert des Interaktionsterms: 0,1418)					
ECOG-PS 0	95/1070 (8,9)	NE [NE; NE]	134/1020 (13,1)	NE [NE; NE]	0,68 [0,52; 0,88] 0,0036
ECOG-PS 1	27/214 (12,6)	NE [NE; NE]	31/244 (12,7)	NE [NE; NE]	1,05 [0,63; 1,75] 0,8608

Datenschnitt: 01.04.2021
ITT-Population
1: Aus Log-rank-Test; 2: In Monaten; 3: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen.
Abkürzungen: ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; HR: Hazard Ratio; IDFS: Invasives krankheitsfreies Überleben (invasive disease-free survival); ITT: Intention to Treat; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB = Nicht berechnet; NE: Nicht errechenbar/nicht erreicht.

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Anhang 4-G2.3: DRFS - Subgruppenanalysen

Tabelle 4-124 (Anhang): DRFS - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen für DRFS aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - ITT - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,6034)					
Neoadjuvante Chemotherapie	26/217 (12,0)	NE [NE; NE]	39/219 (17,8)	NE [NE; NE]	0,63 [0,39; 1,04] 0,0692
Adjuvante Chemotherapie	12/327 (3,7)	NE [NE; NE]	27/312 (8,7)	NE [NE; NE]	0,41 [0,21; 0,81] 0,0083
Keine Chemotherapie	0/9 (0,0)	NE [NE; NE]	0/4 (0,0)	NE [NE; NE]	NB
Region (p-Wert des Interaktionsterms: 0,9470)					
Nordamerika / Europa	17/252 (6,7)	NE [NE; NE]	30/233 (12,9)	NE [NE; NE]	0,51 [0,28; 0,92] 0,0231
Asien	8/168 (4,8)	NE [NE; NE]	14/166 (8,4)	NE [NE; NE]	0,54 [0,23; 1,28] 0,1556
Andere	13/133 (9,8)	NE [NE; NE]	22/136 (16,2)	NE [NE; NE]	0,59 [0,30; 1,17] 0,1271
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2963)					
< 20 mm	7/141 (5,0)	NE [NE; NE]	17/140 (12,1)	NE [NE; NE]	0,40 [0,17; 0,96] 0,0340
≥ 20 bis < 50 mm	20/255 (7,8)	NE [NE; NE]	27/249 (10,8)	NE [NE; NE]	0,71 [0,40; 1,27] 0,2441
≥ 50 mm	9/145 (6,2)	NE [NE; NE]	22/141 (15,6)	NE [NE; NE]	0,37 [0,17; 0,80] 0,0085
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,6210)					
0-3	14/203 (6,9)	NE [NE; NE]	23/214 (10,7)	NE [NE; NE]	0,63 [0,33; 1,23] 0,1737
4-9	11/242 (4,5)	NE [NE; NE]	26/231 (11,3)	NE [NE; NE]	0,40 [0,20; 0,80] 0,0076
≥ 10	13/108 (12,0)	NE [NE; NE]	17/90 (18,9)	NE [NE; NE]	0,56 [0,27; 1,15] 0,1098
Tumorstadium (p-Wert des Interaktionsterms: 0,7201)					
IIA	6/59 (10,2)	NE [NE; NE]	8/62 (12,9)	NE [NE; NE]	0,77 [0,27; 2,21] 0,6196
IIB	3/53 (5,7)	NE [NE; NE]	4/69 (5,8)	NE [NE; NE]	1,06 [0,24; 4,72] 0,9440

Subgruppe	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
IIIA	11/236 (4,7)	NE [NE; NE]	22/214 (10,3)	NE [NE; NE]	0,43 [0,21; 0,90] 0,0201
IIIB	3/18 (16,7)	34,8 [33,96; NE]	3/15 (20,0)	NE [25,68; NE]	0,59 [0,12; 2,99] 0,5178
IIIC	15/186 (8,1)	NE [NE; NE]	29/174 (16,7)	NE [NE; NE]	0,44 [0,24; 0,83] 0,0089
Tumorgrading (p-Wert des Interaktionsterms: 0,7256)					
G1	1/47 (2,1)	NE [NE; NE]	1/41 (2,4)	NE [NE; NE]	0,83 [0,05; 13,34] 0,8966
G2	13/244 (5,3)	NE [NE; NE]	29/234 (12,4)	NE [NE; NE]	0,40 [0,21; 0,77] 0,0048
G3	22/233 (9,4)	NE [NE; NE]	33/226 (14,6)	NE [NE; NE]	0,63 [0,37; 1,08] 0,0898
GX	2/29 (6,9)	NE [NE; NE]	3/33 (9,1)	NE [35,15; NE]	0,93 [0,15; 5,83] 0,9407
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9983)					
Negativ	5/49 (10,2)	NE [NE; NE]	8/44 (18,2)	NE [NE; NE]	0,49 [0,16; 1,51] 0,2077
Positiv	30/477 (6,3)	NE [NE; NE]	58/471 (12,3)	NE [NE; NE]	0,50 [0,32; 0,77] 0,0015
Unbekannt	0/4 (0,0)	NE [NE; NE]	0/8 (0,0)	NE [NE; NE]	NB
Ethnizität (p-Wert des Interaktionsterms: 0,5887)					
Weiß	25/323 (7,7)	NE [NE; NE]	43/324 (13,3)	NE [NE; NE]	0,57 [0,35; 0,93] 0,0229
Asiatisch	10/199 (5,0)	NE [NE; NE]	19/180 (10,6)	NE [NE; NE]	0,45 [0,21; 0,96] 0,0340
Andere	3/19 (15,8)	NE [NE; NE]	3/21 (14,3)	NE [35,15; NE]	1,22 [0,25; 6,08] 0,8039
ECOG-PS (p-Wert des Interaktionsterms: 0,2980)					
ECOG-PS 0	36/496 (7,3)	NE [NE; NE]	58/480 (12,1)	NE [NE; NE]	0,58 [0,38; 0,87] 0,0087
ECOG-PS 1	2/57 (3,5)	NE [NE; NE]	8/55 (14,5)	NE [35,15; NE]	0,26 [0,06; 1,24] 0,0696

Subgruppe	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
Datenschnitt: 01.04.2021 ITT-Population 1: Aus Log-rank-Test; 2: In Monaten; 3: gemäß ZVT des G-BA: Tamoxifen. Abkürzungen: ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; HR: Hazard Ratio; DRFS: Fernmetastasenfreies Überleben (distant relapse-free survival); ITT: Intention to Treat; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB = Nicht berechnet; NE: Nicht errechenbar/nicht erreicht.					

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Tabelle: Subgruppen für DRFS aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - ITT - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
Alter (p-Wert des Interaktionsterms: 0,3350)					
< 65 Jahre	69/918 (7,5)	NE [NE; NE]	107/937 (11,4)	NE [NE; NE]	0,66 [0,49; 0,89] 0,0068
≥ 65 Jahre	31/366 (8,5)	NE [NE; NE]	33/327 (10,1)	NE [NE; NE]	0,88 [0,54; 1,43] 0,5999
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7144)					
Neoadjuvante Chemotherapie	46/430 (10,7)	NE [NE; NE]	71/415 (17,1)	NE [NE; NE]	0,64 [0,44; 0,93] 0,0181
Adjuvante Chemotherapie	47/785 (6,0)	NE [NE; NE]	58/768 (7,6)	NE [NE; NE]	0,80 [0,55; 1,18] 0,2634
Keine Chemotherapie	7/69 (10,1)	NE [NE; NE]	11/81 (13,6)	NE [NE; NE]	0,68 [0,26; 1,76] 0,4255
Region (p-Wert des Interaktionsterms: 0,8037)					
Nordamerika / Europa	47/679 (6,9)	NE [NE; NE]	61/649 (9,4)	NE [NE; NE]	0,75 [0,51; 1,10] 0,1375
Asien	16/203 (7,9)	NE [NE; NE]	19/201 (9,5)	NE [NE; NE]	0,82 [0,42; 1,60] 0,5613
Andere	37/402 (9,2)	NE [NE; NE]	60/414 (14,5)	NE [NE; NE]	0,65 [0,43; 0,98] 0,0385
Primärtumorgröße (p-Wert des Interaktionsterms: 0,0559)					
< 20 mm	13/332 (3,9)	NE [NE; NE]	37/334 (11,1)	NE [NE; NE]	0,36 [0,19; 0,68] 0,0009
≥ 20 bis < 50 mm	56/646 (8,7)	NE [NE; NE]	69/653 (10,6)	NE [NE; NE]	0,83 [0,58; 1,18] 0,2886
≥ 50 mm	30/289 (10,4)	NE [NE; NE]	33/265 (12,5)	NE [NE; NE]	0,86 [0,52; 1,41] 0,5474
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,5235)					
0-3	24/427 (5,6)	NE [NE; NE]	39/418 (9,3)	NE [NE; NE]	0,60 [0,36; 1,00] 0,0479
4-9	38/548 (6,9)	NE [NE; NE]	45/543 (8,3)	NE [NE; NE]	0,86 [0,56; 1,33] 0,5029

Anhang 4-G2.4: Gesundheitszustand anhand der EQ-5D VAS - Subgruppenanalysen

Tabelle 4-125 (Anhang): EQ-5D VAS - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen für die Veränderung der EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8580)																			
Neoadjuvante Chemotherapie	192 78,41 (14,97)	182 77,24 (16,58)	177 78,72 (16,68)	171 79,19 (16,70)	159 80,32 (15,13)	147 79,35 (17,23)	145 79,10 (16,98)	73 78,27 (17,15)	0,30 (0,88)	190 79,13 (15,28)	171 79,44 (14,90)	173 81,21 (13,74)	148 81,39 (14,01)	142 81,75 (15,58)	117 81,22 (15,66)	132 79,45 (16,02)	77 80,88 (19,39)	0,61 (0,89)	-0,31 [-2,78;2,16] 0,8050 -0,03 [-0,23;0,18]
Adjuvante Chemotherapie	279 76,95 (14,86)	261 78,34 (15,01)	258 79,02 (15,99)	251 79,40 (15,79)	240 79,81 (14,09)	203 82,08 (13,60)	194 81,73 (13,77)	124 82,68 (14,18)	2,61 (0,55)	280 78,16 (15,45)	269 79,34 (14,41)	262 81,34 (14,46)	258 82,15 (13,84)	235 81,94 (15,16)	216 81,51 (15,76)	214 82,89 (12,77)	117 83,13 (13,21)	3,29 (0,55)	-0,68 [-2,21;0,85] 0,3844 -0,07 [-0,24;0,09]
Keine Chemotherapie	7 72,14 (23,95)	7 80,71 (14,56)	6 78,33 (12,50)	6 71,67 (19,41)	5 80,00 (22,64)	5 77,00 (21,10)	6 75,83 (22,23)	2 85,00 (7,07)	NE	1 55,00 (NE)	1 70,00 (NE)	1 75,00 (NE)	1 70,00 (NE)	1 80,00 (NE)	1 75,00 (NE)	1 80,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,8835)																			
Nordamerika / Europa	194 75,25 (14,32)	175 75,42 (15,06)	169 76,30 (16,15)	163 75,85 (16,97)	150 77,33 (15,64)	129 77,60 (17,45)	126 78,72 (16,44)	70 77,04 (18,30)	1,58 (0,82)	191 74,98 (17,16)	170 75,82 (16,14)	166 77,93 (16,73)	148 78,75 (16,15)	133 79,71 (16,76)	125 77,99 (18,97)	126 77,69 (16,49)	63 76,16 (18,55)	2,17 (0,84)	-0,59 [-2,90;1,72] 0,6150 -0,05 [-0,25;0,15]
Asien	162 76,94 (15,21)	160 76,05 (16,23)	157 77,90 (16,04)	154 79,23 (13,83)	144 79,31 (13,14)	128 79,29 (14,30)	134 79,80 (14,61)	69 81,93 (13,07)	1,08 (0,75)	153 79,84 (13,32)	148 79,57 (13,60)	150 81,23 (11,74)	144 81,56 (11,21)	137 81,48 (14,21)	120 81,18 (13,49)	121 82,13 (11,38)	65 83,91 (11,13)	2,25 (0,78)	-1,17 [-3,30;0,96] 0,2815 -0,12 [-0,34;0,10]
Andere	122 81,68 (15,23)	115 84,38 (13,87)	115 84,05 (15,44)	111 84,11 (16,92)	110 84,60 (13,91)	98 87,29 (11,35)	85 84,33 (14,37)	60 84,83 (13,10)	2,72 (0,89)	127 82,19 (13,82)	123 84,00 (11,97)	120 85,95 (11,54)	115 86,19 (12,68)	108 85,02 (14,25)	89 86,45 (11,62)	100 85,79 (12,75)	66 86,39 (15,75)	2,81 (0,87)	-0,09 [-2,54;2,36] 0,9416 -0,01 [-0,26;0,24]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4152)																			
< 20 mm	120 77,38 (13,42)	113 76,96 (15,01)	105 78,82 (14,69)	107 77,50 (17,51)	102 78,73 (14,42)	93 76,90 (17,57)	91 79,76 (15,44)	54 79,89 (14,51)	0,36 (1,00)	121 78,75 (15,08)	108 78,18 (15,33)	112 81,58 (14,32)	103 81,86 (14,28)	99 82,83 (13,77)	86 81,36 (16,81)	82 84,02 (11,48)	48 82,13 (19,12)	1,63 (1,00)	-1,27 [-4,06;1,52] 0,3708 -0,12 [-0,37;0,14]
≥ 20 bis < 50 mm	220 79,03 (14,49)	206 78,82 (16,34)	209 79,95 (15,66)	200 80,33 (15,30)	186 80,49 (14,62)	160 82,86 (13,09)	155 80,99 (15,17)	91 81,96 (15,40)	1,77 (0,68)	225 78,14 (15,83)	215 80,13 (13,88)	213 81,28 (13,94)	199 81,96 (14,52)	183 80,90 (17,11)	167 80,95 (15,56)	178 80,95 (14,99)	92 82,66 (15,76)	2,53 (0,67)	-0,76 [-2,64;1,12] 0,4260 -0,08 [-0,26;0,11]
≥ 50 mm	128 74,74 (17,25)	123 77,33 (15,34)	120 77,25 (18,29)	114 78,81 (16,57)	108 80,23 (14,93)	94 81,37 (15,87)	91 80,80 (15,70)	48 80,29 (16,71)	2,91 (0,97)	120 79,18 (14,69)	113 78,96 (15,25)	106 80,71 (14,60)	100 81,59 (12,37)	93 82,75 (12,84)	77 82,25 (15,12)	83 80,45 (14,54)	50 81,06 (13,35)	2,05 (1,00)	0,86 [-1,89;3,61] 0,5390 0,08 [-0,17;0,33]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,2777)																			
0-3	173 77,53 (14,22)	163 77,02 (15,64)	154 78,16 (15,77)	151 78,58 (16,07)	138 79,04 (15,50)	126 79,33 (17,41)	128 79,14 (16,89)	76 80,17 (16,78)	0,72 (0,84)	187 77,28 (15,84)	172 79,87 (13,89)	167 80,97 (14,28)	158 81,03 (13,83)	153 80,65 (16,40)	130 80,13 (15,41)	132 80,86 (14,70)	69 81,52 (16,26)	2,32 (0,82)	-1,60 [-3,90;0,71] 0,1735 -0,14 [-0,35;0,06]
4-9	210 75,64 (15,99)	198 76,91 (15,79)	197 78,05 (16,49)	190 78,37 (16,61)	184 79,20 (14,14)	162 80,78 (14,55)	153 79,69 (14,05)	81 79,98 (14,54)	2,06 (0,66)	209 79,50 (15,00)	197 79,19 (15,16)	199 81,34 (13,91)	184 81,89 (13,73)	171 82,64 (14,06)	152 81,59 (15,85)	158 81,64 (13,91)	88 83,82 (12,47)	2,62 (0,67)	-0,56 [-2,42;1,29] 0,5500 -0,06 [-0,25;0,13]
≥ 10	95 81,40 (13,69)	89 81,88 (14,81)	90 82,00 (16,09)	87 82,13 (15,30)	82 83,48 (13,57)	67 84,06 (12,45)	64 85,27 (14,50)	42 84,88 (14,05)	2,43 (1,18)	75 78,77 (15,33)	72 78,61 (14,72)	70 81,83 (14,67)	65 83,72 (14,47)	54 82,89 (15,75)	52 83,94 (15,84)	57 83,05 (13,68)	37 79,81 (21,79)	1,41 (1,33)	1,02 [-2,50;4,54] 0,5687 0,09 [-0,21;0,39]
Tumorstadium (p-Wert des Interaktionsterms: 0,4738)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	51 79,16 (12,16)	47 76,79 (15,15)	45 78,93 (15,12)	44 74,18 (19,89)	44 76,11 (16,34)	39 74,05 (19,41)	39 78,00 (16,36)	23 76,74 (17,16)	-2,38 (1,47)	56 77,32 (16,97)	50 79,56 (13,60)	50 81,24 (14,68)	45 79,44 (15,30)	46 79,02 (18,12)	36 80,92 (14,46)	37 84,14 (9,67)	17 84,71 (10,23)	2,01 (1,44)	-4,39 [-8,47;-0,31] 0,0353 -0,41 [-0,80;-0,03]
IIB	42 77,62 (13,12)	40 77,75 (16,89)	38 81,16 (11,61)	38 81,26 (11,97)	32 81,56 (12,91)	31 81,87 (12,29)	28 78,96 (13,27)	22 83,00 (14,74)	2,34 (1,65)	62 77,48 (14,60)	59 81,42 (12,42)	58 81,62 (11,91)	55 81,16 (13,46)	54 79,56 (18,04)	51 78,71 (16,53)	53 79,45 (17,09)	32 80,34 (19,14)	1,96 (1,32)	0,39 [-3,80;4,57] 0,8550 0,04 [-0,35;0,43]
IIIA	208 74,88 (16,45)	200 76,88 (15,76)	197 78,16 (16,70)	189 79,40 (15,69)	183 79,21 (15,25)	160 81,02 (15,17)	154 79,74 (15,08)	83 80,16 (15,53)	2,79 (0,70)	191 78,84 (15,13)	177 78,69 (15,06)	176 80,23 (14,44)	169 81,26 (13,81)	155 82,27 (13,16)	129 81,23 (16,32)	137 81,38 (13,55)	71 84,39 (11,62)	2,98 (0,74)	-0,19 [-2,19;1,81] 0,8523 -0,02 [-0,22;0,18]
IIIB	14 73,79 (20,77)	13 75,69 (18,29)	13 70,69 (20,63)	13 77,77 (12,60)	10 78,00 (12,52)	8 69,75 (27,16)	11 76,55 (21,86)	6 67,50 (10,37)	-0,44 (2,44)	14 85,86 (9,78)	13 86,92 (9,90)	14 85,07 (13,10)	11 83,64 (12,86)	9 86,67 (12,50)	9 83,00 (13,41)	9 81,67 (9,68)	5 68,00 (20,80)	0,29 (2,62)	-0,74 [-8,20;6,73] 0,8422 -0,08 [-0,80;0,64]
IIIC	162 80,61 (13,30)	149 80,01 (15,06)	147 80,16 (16,27)	143 80,15 (16,76)	134 82,29 (13,29)	116 83,72 (12,54)	112 83,53 (14,77)	64 84,80 (14,08)	1,37 (0,86)	147 78,30 (15,87)	141 78,60 (15,40)	137 82,04 (14,63)	126 83,64 (13,76)	114 83,18 (15,45)	109 82,85 (15,13)	111 81,96 (14,94)	69 81,32 (18,48)	1,99 (0,90)	-0,62 [-3,08;1,83] 0,6176 -0,06 [-0,28;0,17]
Tumorgrading (p-Wert des Interaktionsterms: 0,6978)																			
G1	44 78,70 (16,91)	40 78,85 (16,45)	39 80,21 (15,50)	39 78,41 (17,12)	37 81,05 (13,53)	32 82,00 (16,93)	31 81,19 (16,15)	18 84,22 (12,38)	2,22 (1,56)	36 79,14 (15,06)	33 77,36 (15,22)	33 79,27 (14,30)	34 78,85 (18,03)	31 80,23 (17,21)	27 77,96 (18,33)	24 80,21 (13,61)	13 86,85 (11,91)	1,34 (1,72)	0,88 [-3,74;5,50] 0,7050 0,09 [-0,36;0,53]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	208 76,81 (15,42)	194 77,22 (15,69)	196 77,94 (16,78)	185 78,83 (15,69)	177 80,62 (13,40)	159 80,28 (14,43)	160 80,16 (14,26)	83 82,40 (13,50)	1,80 (0,68)	204 78,86 (16,17)	195 79,21 (15,98)	190 81,34 (15,53)	178 82,48 (13,76)	159 83,24 (13,63)	144 82,12 (16,20)	151 81,46 (14,31)	86 82,78 (15,35)	2,33 (0,70)	-0,53 [-2,45;1,39] 0,5849 -0,05 [-0,25;0,14]
G3	198 77,27 (14,20)	188 77,79 (15,75)	181 79,38 (16,07)	178 79,54 (16,73)	165 78,65 (16,24)	142 80,49 (16,33)	134 80,43 (16,97)	85 78,29 (17,56)	1,54 (0,82)	202 77,81 (14,77)	187 79,90 (12,89)	187 81,32 (13,09)	170 81,91 (13,31)	164 80,70 (16,77)	139 81,42 (14,77)	150 81,77 (14,25)	83 81,40 (17,59)	2,62 (0,81)	-1,08 [-3,34;1,18] 0,3480 -0,09 [-0,29;0,10]
GX	28 81,79 (15,03)	28 82,50 (13,02)	25 80,76 (13,76)	26 80,81 (15,29)	25 83,16 (12,21)	22 86,14 (12,04)	20 83,00 (11,85)	13 86,62 (13,06)	1,76 (1,76)	28 79,86 (15,25)	25 79,48 (15,01)	25 83,52 (10,58)	24 80,79 (12,59)	23 82,61 (12,14)	23 80,70 (15,28)	22 82,45 (13,81)	12 79,17 (11,65)	0,95 (1,73)	0,80 [-4,16;5,76] 0,7460 0,09 [-0,44;0,61]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,0622)																			
Negativ	46 75,22 (14,41)	43 75,00 (17,42)	40 75,63 (17,84)	42 74,26 (21,65)	36 79,00 (15,28)	38 76,18 (17,46)	36 71,19 (20,15)	11 72,36 (20,97)	-1,19 (2,13)	39 78,51 (16,00)	36 80,42 (15,18)	35 82,43 (12,39)	30 82,13 (14,13)	30 83,63 (14,63)	26 81,54 (14,27)	31 81,13 (15,42)	15 83,93 (21,01)	3,35 (2,30)	-4,54 [-10,79;1,71] 0,1518 -0,32 [-0,74;0,11]
Positiv	415 77,62 (15,21)	394 78,51 (15,08)	387 79,30 (15,67)	374 79,80 (15,57)	357 80,24 (14,29)	308 81,53 (15,05)	296 81,53 (14,55)	179 81,68 (14,97)	2,09 (0,49)	416 78,76 (14,90)	392 79,43 (14,26)	389 81,51 (13,99)	364 81,97 (13,38)	334 81,62 (15,40)	296 81,92 (15,25)	308 81,76 (14,06)	175 82,14 (15,45)	2,21 (0,49)	-0,13 [-1,48;1,23] 0,8562 -0,01 [-0,15;0,12]
Unbekannt	2 92,50 (3,54)	2 70,00 (42,43)	2 54,50 (64,35)	1 100,00 (NE)	0	0	0	0	NE	8 67,00 (26,76)	7 65,71 (25,24)	7 67,29 (23,20)	6 74,67 (24,43)	6 81,33 (14,51)	8 65,13 (26,25)	4 78,75 (16,01)	2 88,00 (2,83)	1,96 (5,73)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,8143)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	265 76,85 (15,22)	247 78,19 (15,27)	238 78,74 (16,56)	229 78,58 (17,25)	218 79,42 (15,64)	190 80,76 (16,30)	175 80,29 (16,19)	114 80,18 (16,76)	2,05 (0,69)	281 77,25 (16,69)	259 78,62 (15,45)	251 80,53 (15,83)	234 81,22 (15,48)	215 81,60 (16,07)	193 80,81 (17,37)	203 80,42 (15,87)	119 80,66 (18,05)	2,31 (0,67)	-0,27 [-2,17;1,63] 0,7818 -0,02 [-0,19;0,14]
Asiatisch	186 77,69 (14,80)	181 77,22 (15,95)	179 79,16 (15,57)	176 80,33 (13,41)	164 80,45 (13,03)	146 80,73 (14,03)	149 80,67 (14,54)	75 82,56 (12,86)	1,83 (0,69)	165 79,73 (13,09)	160 79,88 (13,30)	161 81,71 (11,57)	155 82,24 (11,18)	144 81,78 (13,94)	124 81,27 (13,37)	129 82,23 (11,18)	66 83,88 (10,96)	2,53 (0,73)	-0,70 [-2,68;1,28] 0,4881 -0,07 [-0,28;0,14]
Andere	16 83,75 (17,46)	14 88,57 (10,64)	15 80,33 (19,04)	14 78,00 (26,90)	15 85,33 (16,09)	13 86,00 (16,22)	14 85,00 (12,25)	9 80,33 (18,19)	-1,60 (2,21)	16 85,81 (13,06)	15 87,33 (12,66)	16 88,00 (10,07)	15 85,60 (13,40)	14 85,71 (15,42)	12 89,17 (7,93)	12 91,58 (6,40)	7 89,14 (15,82)	1,61 (2,25)	-3,22 [-9,68;3,25] 0,3167 -0,35 [-1,03;0,33]
ECOG-PS (p-Wert des Interaktionsterms: 0,1647)																			
ECOG-PS 0	428 77,42 (15,03)	403 77,55 (15,33)	393 78,48 (16,34)	385 78,57 (16,32)	362 79,66 (14,28)	319 80,80 (14,84)	310 80,17 (15,31)	184 81,46 (14,23)	1,38 (0,51)	418 78,81 (15,29)	391 79,43 (14,57)	386 81,35 (14,01)	361 82,20 (13,72)	337 82,08 (15,43)	299 81,89 (15,12)	313 81,58 (14,35)	176 81,72 (16,40)	2,20 (0,51)	-0,82 [-2,24;0,60] 0,2571 -0,08 [-0,21;0,06]
ECOG-PS 1	50 77,90 (15,32)	47 81,23 (17,87)	48 82,23 (14,70)	43 84,93 (13,92)	42 83,05 (16,86)	36 81,64 (19,35)	35 83,63 (15,76)	15 76,47 (26,05)	4,45 (1,48)	53 76,06 (16,16)	50 78,84 (14,77)	50 80,66 (15,29)	46 79,09 (14,98)	41 80,12 (14,06)	35 77,11 (19,61)	34 81,56 (12,42)	18 87,28 (9,26)	3,39 (1,44)	1,06 [-3,06;5,17] 0,6105 0,10 [-0,29;0,49]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung der EQ-5D VAS = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung der EQ-5D VAS haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; EQ-5D: European Quality of Life Questionnaire 5 Dimensions; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler; VAS: Visuelle Analogskala

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t104_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,9353)																			
< 65 Jahre	790 78,36 (16,34)	733 77,57 (15,65)	722 78,78 (15,11)	676 79,40 (15,55)	659 79,21 (14,85)	577 79,21 (15,77)	581 79,69 (15,39)	317 80,46 (13,74)	0,03 (0,37)	822 78,94 (14,94)	776 80,14 (14,39)	769 81,08 (14,44)	713 80,40 (15,27)	672 81,45 (14,55)	593 80,97 (15,32)	585 81,44 (15,33)	311 80,41 (16,02)	1,50 (0,36)	-1,47 [-2,48;-0,45] 0,0048 -0,14 [-0,24;-0,04]
≥ 65 Jahre	300 77,63 (16,37)	274 75,14 (16,73)	258 78,10 (13,91)	252 77,22 (15,48)	231 76,65 (15,74)	217 78,35 (14,65)	217 78,05 (15,39)	113 76,67 (16,08)	-1,40 (0,58)	270 77,27 (14,83)	257 77,37 (16,67)	252 77,87 (14,94)	232 78,97 (13,89)	229 77,49 (15,02)	199 78,81 (16,23)	189 79,15 (14,63)	114 78,75 (15,52)	0,07 (0,60)	-1,46 [-3,11;0,18] 0,0802 -0,15 [-0,31;0,02]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,6090)																			
Neoadjuvante Chemotherapie	358 78,50 (17,25)	326 77,51 (15,75)	315 79,59 (14,01)	293 79,85 (14,57)	276 79,46 (15,51)	230 79,93 (15,54)	246 79,61 (16,67)	124 80,42 (14,27)	-0,35 (0,54)	359 79,37 (14,63)	339 79,74 (15,19)	324 81,13 (14,02)	298 80,02 (15,32)	284 81,38 (13,86)	236 80,18 (16,18)	251 81,65 (13,65)	134 79,25 (15,57)	0,62 (0,54)	-0,97 [-2,46;0,53] 0,2043 -0,09 [-0,24;0,05]
Adjuvante Chemotherapie	673 78,53 (15,66)	628 76,81 (16,04)	617 78,47 (14,92)	588 78,95 (15,51)	571 78,40 (14,80)	524 79,01 (15,20)	508 79,46 (14,74)	281 79,43 (14,43)	-0,29 (0,40)	669 78,40 (15,01)	633 79,68 (14,57)	639 80,20 (14,80)	594 80,68 (14,18)	572 80,50 (15,13)	513 81,14 (14,76)	479 80,96 (15,76)	265 80,88 (16,14)	1,54 (0,40)	-1,83 [-2,94;-0,72] 0,0013 -0,18 [-0,28;-0,07]
Keine Chemotherapie	59 71,97 (17,34)	53 74,30 (16,66)	48 73,79 (17,40)	47 70,53 (19,54)	43 74,58 (16,38)	40 73,00 (17,50)	44 74,80 (15,02)	25 75,16 (15,55)	-1,06 (1,26)	64 75,14 (15,33)	61 75,51 (18,27)	58 76,59 (15,64)	53 73,23 (19,27)	45 73,84 (14,18)	43 73,21 (19,60)	44 75,61 (16,43)	26 74,38 (14,02)	-0,38 (1,22)	-0,68 [-4,15;2,79] 0,6983 -0,07 [-0,42;0,28]
Region (p-Wert des Interaktionsterms: 0,3232)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	539 76,42 (16,87)	476 74,43 (16,74)	461 76,09 (16,19)	430 76,61 (16,92)	407 76,76 (16,10)	372 77,04 (16,39)	373 77,39 (16,24)	196 77,89 (15,99)	-0,36 (0,48)	515 74,97 (15,02)	472 76,94 (15,43)	465 77,14 (15,72)	421 77,01 (16,30)	405 77,87 (15,77)	355 77,43 (16,85)	326 78,69 (15,79)	195 77,72 (16,70)	1,49 (0,49)	-1,85 [-3,19;-0,50] 0,0071 -0,17 [-0,29;-0,05]
Asien	190 81,05 (14,50)	184 77,40 (15,33)	181 79,71 (13,70)	172 79,48 (14,43)	169 79,89 (13,69)	147 80,54 (14,12)	155 80,74 (14,01)	86 80,56 (11,32)	-1,55 (0,68)	189 82,92 (12,65)	186 81,55 (13,37)	184 82,47 (13,16)	173 82,27 (13,01)	169 82,06 (13,49)	145 83,19 (12,05)	149 81,83 (13,75)	79 81,49 (13,48)	-0,02 (0,69)	-1,52 [-3,43;0,38] 0,1164 -0,16 [-0,36;0,04]
Andere	361 79,24 (16,19)	347 80,04 (14,65)	338 81,43 (12,68)	326 81,34 (13,77)	314 80,14 (14,32)	275 80,74 (14,59)	270 80,94 (14,71)	148 80,92 (13,82)	0,41 (0,50)	388 81,12 (14,75)	375 81,57 (14,85)	372 83,15 (13,06)	351 82,61 (13,44)	327 82,81 (13,58)	292 82,70 (14,90)	299 82,79 (14,94)	151 82,06 (15,69)	1,47 (0,48)	-1,06 [-2,43;0,31] 0,1284 -0,11 [-0,25;0,03]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,9109)																			
< 20 mm	275 77,40 (16,71)	248 76,94 (15,60)	242 78,69 (14,43)	237 77,88 (16,26)	228 77,38 (16,12)	202 78,41 (14,92)	200 79,91 (15,21)	100 79,01 (14,54)	-0,33 (0,63)	295 79,24 (14,33)	277 79,83 (14,32)	271 81,13 (13,90)	251 80,50 (14,46)	248 80,92 (14,94)	210 80,65 (16,22)	212 80,50 (16,19)	110 79,31 (15,54)	0,85 (0,61)	-1,19 [-2,90;0,53] 0,1745 -0,11 [-0,28;0,05]
≥ 20 bis < 50 mm	560 79,28 (15,69)	529 77,95 (15,72)	513 79,30 (14,36)	489 79,80 (15,05)	466 79,25 (14,76)	417 80,03 (15,21)	419 79,73 (15,04)	220 80,53 (13,87)	-0,32 (0,43)	564 78,99 (15,02)	538 79,96 (15,14)	531 80,61 (14,60)	493 80,22 (15,49)	472 80,76 (14,28)	421 80,82 (15,14)	400 81,69 (14,21)	224 80,79 (15,35)	1,06 (0,43)	-1,38 [-2,58;-0,18] 0,0241 -0,13 [-0,25;-0,02]
≥ 50 mm	238 76,50 (17,03)	216 74,22 (16,91)	210 76,79 (15,95)	189 77,17 (16,09)	182 77,98 (14,84)	162 77,15 (16,85)	165 77,47 (16,16)	103 77,15 (15,67)	-0,34 (0,68)	222 76,23 (15,25)	207 77,39 (15,69)	209 78,00 (15,60)	191 78,93 (14,23)	174 78,70 (15,87)	153 78,90 (16,11)	154 79,15 (16,40)	88 78,64 (17,81)	1,58 (0,70)	-1,92 [-3,84;0,01] 0,0507 -0,18 [-0,37;0,00]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8810)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	361 76,85 (16,80)	336 75,81 (15,98)	323 78,10 (14,47)	305 78,78 (14,83)	292 77,54 (15,80)	266 77,95 (17,10)	273 78,12 (15,79)	158 79,91 (14,48)	0,15 (0,56)	354 78,22 (15,34)	337 79,42 (15,17)	331 80,38 (14,57)	303 80,33 (14,53)	291 80,85 (14,17)	248 80,93 (14,39)	245 82,07 (13,77)	140 79,18 (15,51)	1,89 (0,56)	-1,74 [-3,30;-0,19] 0,0281 -0,16 [-0,31;-0,02]
4-9	470 79,07 (16,13)	433 78,01 (15,28)	426 78,95 (15,01)	409 78,13 (16,71)	390 78,67 (14,94)	350 79,64 (14,22)	343 80,41 (13,83)	170 79,45 (13,39)	-0,69 (0,46)	479 78,56 (14,87)	455 79,47 (15,09)	454 80,48 (14,16)	425 79,68 (15,16)	405 80,20 (15,67)	364 80,02 (16,48)	347 80,71 (15,64)	190 80,42 (15,87)	0,79 (0,45)	-1,49 [-2,74;-0,23] 0,0202 -0,15 [-0,28;-0,02]
≥ 10	259 78,35 (16,03)	238 76,45 (17,11)	231 78,65 (14,91)	214 80,14 (14,20)	208 79,73 (14,44)	178 79,17 (15,26)	182 78,75 (17,40)	102 78,81 (16,18)	-0,49 (0,68)	259 78,90 (14,50)	241 79,48 (14,80)	236 79,79 (15,59)	217 80,39 (15,15)	205 80,35 (13,78)	180 80,54 (15,31)	182 79,59 (16,07)	95 80,21 (16,58)	0,74 (0,68)	-1,23 [-3,12;0,66] 0,2007 -0,11 [-0,28;0,06]
Tumorstadium (p-Wert des Interaktionsterms: 0,7915)																			
IIA	91 78,27 (16,33)	83 78,04 (13,69)	81 80,00 (12,60)	81 80,06 (12,84)	77 78,36 (14,96)	73 79,71 (13,53)	72 78,90 (15,32)	37 80,65 (13,05)	1,10 (1,04)	95 77,73 (16,58)	92 79,85 (13,87)	89 79,12 (13,88)	84 79,61 (14,91)	79 80,80 (13,14)	69 82,42 (12,93)	72 81,21 (14,08)	37 81,00 (13,68)	1,51 (1,02)	-0,41 [-3,28;2,47] 0,7808 -0,04 [-0,33;0,25]
IIB	129 79,88 (14,63)	121 77,97 (14,70)	114 80,46 (12,40)	110 81,17 (13,40)	109 79,11 (15,28)	96 80,47 (16,94)	102 80,38 (15,15)	64 81,66 (13,45)	-1,02 (0,94)	110 80,83 (13,26)	103 80,84 (16,15)	101 83,04 (14,16)	94 80,64 (14,90)	88 81,06 (14,89)	80 81,04 (13,64)	73 82,74 (12,63)	41 78,68 (17,73)	-0,13 (1,03)	-0,89 [-3,64;1,86] 0,5242 -0,08 [-0,34;0,17]
IIIA	427 77,90 (16,67)	395 76,16 (16,26)	385 78,59 (15,00)	368 77,78 (16,41)	345 77,87 (15,45)	313 78,38 (15,14)	311 78,44 (14,73)	154 78,77 (13,79)	-0,68 (0,47)	427 77,84 (15,39)	402 79,08 (15,34)	408 80,10 (14,23)	381 80,20 (14,20)	360 80,42 (15,52)	324 80,24 (15,77)	305 80,50 (15,93)	172 81,44 (14,63)	1,68 (0,47)	-2,37 [-3,67;-1,07] 0,0004 -0,24 [-0,38;-0,11]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIB	45 76,64 (18,52)	43 79,09 (16,14)	42 77,21 (16,25)	41 77,29 (19,07)	38 79,00 (16,70)	33 78,36 (19,21)	31 80,00 (15,10)	12 82,25 (14,18)	0,50 (1,58)	41 79,07 (14,98)	39 81,41 (15,85)	38 81,16 (15,06)	34 80,06 (15,59)	34 78,09 (16,61)	30 77,67 (22,27)	30 82,97 (17,06)	14 77,86 (21,19)	0,37 (1,63)	0,13 [-4,41;4,66] 0,9552 0,01 [-0,41;0,44]
IIIC	396 78,13 (16,28)	364 76,81 (16,56)	357 77,83 (15,56)	326 79,04 (15,38)	319 79,07 (14,64)	277 78,97 (15,40)	280 79,65 (16,32)	162 78,72 (15,81)	-0,36 (0,55)	417 78,72 (14,46)	395 79,14 (14,65)	383 79,90 (15,27)	350 79,77 (15,78)	338 80,41 (14,14)	287 80,21 (15,68)	293 80,47 (15,09)	160 78,63 (16,71)	0,81 (0,54)	-1,17 [-2,68;0,35] 0,1314 -0,11 [-0,24;0,03]
Tumorgrading (p-Wert des Interaktionsterms: 0,6544)																			
G1	83 78,65 (17,14)	78 76,45 (15,80)	80 77,40 (18,01)	72 78,76 (17,63)	70 76,96 (14,89)	67 76,81 (16,94)	61 79,51 (15,14)	32 79,28 (14,13)	-0,68 (1,19)	83 79,73 (16,52)	81 80,10 (16,29)	78 82,55 (13,25)	70 81,46 (14,70)	70 77,79 (19,68)	64 81,84 (15,94)	53 82,92 (13,10)	34 84,26 (13,66)	1,49 (1,19)	-2,17 [-5,49;1,16] 0,2001 -0,20 [-0,50;0,11]
G2	517 77,44 (16,43)	483 76,08 (16,47)	466 77,79 (14,53)	438 78,26 (15,79)	418 78,86 (14,93)	366 79,02 (15,18)	360 79,18 (15,39)	202 78,90 (14,67)	-0,14 (0,45)	520 77,94 (14,81)	486 78,88 (14,86)	493 79,85 (13,93)	459 79,62 (14,70)	427 79,67 (14,44)	387 79,92 (15,19)	378 79,14 (15,99)	205 78,61 (16,41)	1,04 (0,44)	-1,17 [-2,41;0,06] 0,0625 -0,12 [-0,24;0,01]
G3	442 78,71 (16,01)	404 77,77 (15,37)	390 79,84 (13,95)	373 79,43 (14,46)	360 78,72 (15,18)	323 79,30 (15,60)	342 79,36 (15,20)	175 80,12 (14,69)	-0,16 (0,50)	431 78,33 (14,80)	408 79,51 (15,21)	395 79,53 (15,86)	366 79,63 (15,58)	355 81,36 (14,09)	302 80,89 (15,42)	303 82,33 (14,24)	163 80,02 (16,03)	1,17 (0,51)	-1,33 [-2,74;0,07] 0,0623 -0,13 [-0,26;0,01]
GX	46 80,33 (16,85)	40 79,70 (15,37)	42 78,95 (17,81)	43 79,37 (18,95)	40 78,23 (15,51)	36 80,50 (14,16)	35 78,40 (18,26)	21 79,81 (11,39)	-3,42 (1,52)	54 84,26 (13,75)	54 82,44 (13,50)	52 86,75 (11,58)	47 84,91 (12,24)	46 83,67 (13,40)	37 78,84 (20,05)	38 84,55 (14,18)	21 86,76 (8,03)	0,22 (1,43)	-3,63 [-7,80;0,54] 0,0870 -0,35 [-0,74;0,05]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,3869)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Negativ	134 75,11 (16,26)	128 73,67 (16,77)	118 76,47 (16,13)	112 77,29 (15,72)	105 78,35 (14,66)	89 77,58 (16,00)	94 76,97 (16,04)	59 75,49 (16,51)	-0,02 (0,89)	144 79,37 (15,36)	136 78,30 (16,89)	128 81,69 (14,54)	120 80,37 (16,79)	115 81,44 (16,05)	98 81,10 (14,05)	107 78,58 (16,12)	52 79,06 (14,16)	0,87 (0,85)	-0,89 [-3,33;1,55] 0,4733 -0,09 [-0,32;0,15]
Positiv	925 78,55 (16,33)	850 77,38 (15,80)	832 78,77 (14,62)	791 78,86 (15,60)	762 78,49 (15,26)	681 79,04 (15,27)	685 79,45 (15,34)	361 80,11 (14,06)	-0,43 (0,34)	923 78,29 (14,87)	876 79,49 (14,73)	871 80,05 (14,54)	804 79,88 (14,67)	766 80,18 (14,52)	675 80,11 (15,81)	650 81,08 (15,02)	360 79,92 (16,06)	1,14 (0,34)	-1,57 [-2,51;-0,63] 0,0011 -0,15 [-0,24;-0,06]
Unbekannt	9 74,44 (12,61)	9 70,22 (19,08)	9 79,56 (7,13)	7 83,14 (13,38)	5 88,00 (10,93)	6 78,00 (27,24)	5 78,40 (20,07)	1 90,00 (NE)	0,13 (3,63)	7 89,71 (12,05)	6 92,83 (7,52)	6 92,33 (8,45)	6 93,67 (6,22)	6 95,17 (3,60)	6 96,83 (3,82)	5 98,40 (2,07)	5 95,20 (5,97)	9,23 (4,00)	-9,11 [-21,70;3,48] 0,1426 -0,80 [-1,77;0,17]
Ethnizität (p-Wert des Interaktionsterms: 0,9741)																			
Weiß	796 76,82 (16,64)	726 76,10 (16,11)	712 77,70 (15,04)	672 77,87 (15,94)	638 77,26 (15,47)	577 77,91 (15,81)	573 78,15 (15,77)	319 78,82 (15,20)	-0,29 (0,38)	803 77,31 (15,18)	753 78,59 (15,12)	741 79,25 (14,64)	679 78,74 (15,48)	653 79,36 (15,19)	577 79,34 (16,36)	556 79,96 (15,70)	315 79,13 (16,04)	1,20 (0,37)	-1,49 [-2,53;-0,45] 0,0051 -0,14 [-0,24;-0,04]
Asiatisch	228 80,98 (14,01)	218 77,76 (14,96)	213 80,41 (13,33)	204 80,17 (14,33)	201 80,65 (13,45)	171 80,86 (14,20)	179 81,26 (13,97)	96 80,79 (11,40)	-0,76 (0,63)	218 82,12 (13,06)	213 81,55 (13,28)	212 82,79 (13,00)	201 82,43 (12,78)	192 82,44 (13,30)	163 83,22 (11,92)	166 82,60 (12,92)	85 82,06 (13,23)	0,94 (0,64)	-1,71 [-3,47;0,06] 0,0585 -0,18 [-0,37;0,01]
Andere	55 86,55 (14,26)	52 86,10 (11,36)	46 85,04 (13,51)	44 86,48 (9,65)	42 86,93 (13,79)	36 87,39 (10,92)	40 86,23 (11,34)	14 83,71 (14,98)	-0,03 (1,28)	58 84,34 (14,12)	55 85,13 (16,53)	56 87,04 (15,14)	53 89,17 (11,45)	46 87,52 (12,17)	41 87,00 (12,45)	43 89,16 (11,45)	19 85,95 (23,00)	0,81 (1,20)	-0,84 [-4,33;2,65] 0,6318 -0,09 [-0,46;0,28]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,8421)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Tamoxifen	103 79,85 (15,96)	97 79,11 (15,52)	94 80,30 (13,78)	95 81,39 (13,40)	90 80,11 (14,44)	88 80,60 (14,98)	89 82,48 (13,77)	54 84,57 (11,12)	1,05 (0,96)	122 79,78 (13,93)	119 81,51 (13,86)	117 83,18 (12,90)	106 83,54 (11,95)	98 82,65 (15,35)	90 84,06 (13,56)	88 82,53 (14,53)	55 81,35 (17,45)	2,58 (0,89)	-1,53 [-4,11;1,05] 0,2429 -0,16 [-0,42;0,11]
Aromatase-Inhibitor	987 77,98 (16,38)	910 76,67 (16,02)	886 78,42 (14,90)	833 78,51 (15,76)	800 78,37 (15,19)	706 78,77 (15,52)	709 78,84 (15,55)	376 78,73 (14,75)	-0,51 (0,33)	970 78,37 (15,04)	914 79,18 (15,17)	904 79,91 (14,80)	839 79,61 (15,23)	803 80,18 (14,68)	702 79,96 (15,76)	686 80,66 (15,27)	370 79,76 (15,66)	0,94 (0,33)	-1,45 [-2,37;-0,53] 0,0020 -0,14 [-0,23;-0,05]
ECOG-PS (p-Wert des Interaktionsterms: 0,7510)																			
ECOG-PS 0	921 78,96 (15,77)	848 77,07 (15,95)	830 78,82 (14,84)	792 79,07 (15,37)	759 78,89 (15,04)	683 79,33 (15,18)	677 79,60 (15,48)	363 80,03 (14,19)	-0,74 (0,33)	880 79,24 (14,75)	831 79,93 (14,49)	825 80,49 (14,60)	762 80,36 (14,83)	729 80,71 (14,75)	648 80,72 (15,44)	635 80,76 (15,12)	346 79,99 (15,08)	0,71 (0,34)	-1,46 [-2,39;-0,52] 0,0022 -0,14 [-0,24;-0,05]
ECOG-PS 1	169 73,80 (18,64)	159 76,03 (16,16)	150 77,37 (14,57)	136 77,29 (16,57)	131 76,59 (15,47)	111 76,76 (17,04)	121 77,28 (14,82)	67 76,40 (15,61)	1,63 (0,89)	212 75,60 (15,30)	202 77,50 (16,99)	196 79,44 (14,73)	183 78,77 (15,42)	172 79,31 (14,82)	144 79,08 (16,14)	139 81,42 (15,53)	79 79,87 (19,13)	3,13 (0,79)	-1,50 [-3,84;0,85] 0,2101 -0,13 [-0,33;0,07]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung der EQ-5D VAS = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung der EQ-5D VAS haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; EQ-5D: European Quality of Life Questionnaire 5 Dimensions; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler; VAS: Visuelle Analogskala

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t104_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Anhang 4-G2.5: Symptomatik anhand FACIT-Fatigue - Subgruppenanalysen

Tabelle 4-126 (Anhang): FACIT-Fatigue - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen für die Veränderung des FACIT-Fatigue aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,1980)																			
Neoadjuvante Chemotherapie	190 40,80 (8,46)	178 38,94 (9,44)	173 38,94 (9,84)	166 38,76 (10,04)	153 38,50 (10,48)	143 38,09 (11,15)	140 38,60 (10,93)	71 39,00 (10,01)	-2,22 (0,47)	189 40,71 (8,99)	171 41,18 (8,93)	170 42,19 (7,87)	153 41,84 (8,80)	145 42,59 (8,43)	118 42,27 (9,25)	131 41,62 (9,72)	76 42,08 (9,21)	0,36 (0,48)	-2,58 [-3,90;-1,26] 0,0001 -0,40 [-0,60;-0,19]
Adjuvante Chemotherapie	279 39,96 (9,63)	262 38,86 (9,99)	259 39,66 (10,03)	255 39,85 (9,44)	242 39,73 (9,71)	206 40,35 (10,25)	195 41,74 (8,91)	120 40,69 (9,47)	-0,06 (0,34)	277 40,08 (8,76)	269 40,41 (9,19)	254 41,50 (8,57)	249 41,42 (9,00)	232 41,62 (8,89)	218 40,79 (9,49)	211 41,45 (9,21)	119 40,95 (8,43)	0,95 (0,34)	-1,01 [-1,96;-0,05] 0,0383 -0,18 [-0,34;-0,01]
Keine Chemotherapie	7 43,43 (9,47)	7 39,43 (13,13)	6 37,67 (14,54)	6 41,17 (10,93)	4 34,00 (13,59)	4 40,50 (12,87)	6 39,33 (13,34)	2 44,50 (0,71)	-3,30 (4,49)	1 39,00 (NE)	1 31,00 (NE)	1 40,00 (NE)	1 37,00 (NE)	1 37,00 (NE)	1 30,00 (NE)	1 42,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,6859)																			
Nordamerika / Europa	196 40,41 (9,43)	176 38,27 (10,38)	173 38,46 (10,67)	166 38,70 (10,09)	147 38,67 (11,10)	129 38,94 (11,75)	125 40,80 (10,30)	68 41,03 (9,65)	-1,23 (0,49)	193 39,47 (9,57)	176 39,62 (10,17)	166 40,98 (9,44)	152 40,37 (10,33)	141 41,96 (9,73)	131 40,88 (10,72)	128 41,16 (10,75)	66 41,30 (9,84)	0,82 (0,50)	-2,05 [-3,42;-0,69] 0,0034 -0,30 [-0,50;-0,10]
Asien	161 40,76 (8,21)	160 39,08 (9,04)	156 39,78 (8,47)	154 39,78 (8,67)	147 39,41 (9,02)	128 38,99 (10,03)	134 40,38 (9,66)	67 40,51 (9,80)	-1,25 (0,42)	152 41,41 (7,35)	148 41,52 (7,60)	149 41,97 (7,44)	145 42,41 (7,23)	136 42,06 (7,63)	119 41,96 (8,02)	120 42,16 (7,75)	66 42,11 (6,53)	0,51 (0,43)	-1,76 [-2,94;-0,57] 0,0037 -0,33 [-0,55;-0,11]
Andere	119 39,68 (9,99)	111 39,66 (9,94)	109 40,13 (10,90)	107 40,13 (10,43)	105 39,65 (9,94)	96 40,70 (9,99)	82 39,87 (10,00)	58 38,57 (9,44)	-0,13 (0,55)	122 40,34 (9,23)	117 41,23 (9,01)	110 42,71 (7,42)	106 42,13 (8,67)	101 41,89 (8,65)	87 40,94 (9,18)	95 41,19 (9,34)	63 40,73 (9,57)	0,89 (0,54)	-1,02 [-2,54;0,50] 0,1865 -0,17 [-0,42;0,08]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3395)																			
< 20 mm	117 39,86 (9,01)	109 37,84 (9,69)	104 39,13 (10,08)	107 38,21 (10,76)	99 39,02 (10,44)	87 37,11 (11,94)	87 39,28 (10,75)	52 40,81 (9,21)	-1,28 (0,62)	119 40,58 (8,25)	111 39,97 (9,41)	106 42,01 (8,08)	103 40,73 (9,09)	98 41,67 (8,78)	84 41,85 (9,50)	82 43,26 (8,36)	49 42,69 (8,48)	0,62 (0,61)	-1,91 [-3,61;-0,20] 0,0287 -0,29 [-0,54;-0,03]
≥ 20 bis < 50 mm	221 40,81 (9,24)	208 39,05 (10,24)	209 39,64 (9,81)	203 39,97 (9,55)	184 39,39 (10,02)	164 40,43 (9,94)	153 41,24 (9,40)	90 39,67 (10,23)	-0,97 (0,40)	223 40,09 (8,93)	210 41,14 (8,74)	207 41,91 (8,04)	193 42,19 (8,58)	184 41,83 (8,99)	169 40,77 (9,37)	174 40,67 (9,99)	92 40,71 (9,15)	0,94 (0,40)	-1,91 [-3,03;-0,80] 0,0008 -0,32 [-0,51;-0,13]
≥ 50 mm	126 40,05 (9,45)	121 39,49 (9,29)	116 38,72 (10,59)	109 39,47 (8,94)	107 38,76 (10,05)	93 39,46 (10,73)	92 40,29 (10,20)	45 39,96 (9,36)	-0,88 (0,52)	120 40,69 (9,34)	115 40,57 (9,57)	107 41,41 (9,09)	102 41,30 (9,46)	93 42,60 (8,21)	80 41,76 (9,70)	83 41,80 (9,06)	50 41,68 (8,45)	0,30 (0,53)	-1,18 [-2,64;0,28] 0,1121 -0,20 [-0,45;0,05]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,1576)																			
0-3	172 40,72 (8,79)	159 38,26 (10,00)	155 39,41 (9,51)	151 39,11 (9,41)	135 38,90 (9,80)	124 39,76 (10,46)	124 40,56 (10,24)	73 40,48 (8,86)	-1,44 (0,47)	184 40,34 (8,30)	172 41,28 (8,08)	165 41,92 (8,27)	158 41,15 (8,42)	153 41,44 (8,58)	131 40,92 (8,47)	129 40,63 (9,70)	69 40,48 (8,27)	0,42 (0,46)	-1,86 [-3,16;-0,56] 0,0051 -0,30 [-0,51;-0,09]
4-9	210 39,34 (9,67)	201 38,40 (9,99)	196 38,46 (10,32)	189 38,65 (9,72)	181 37,94 (10,31)	163 38,25 (11,08)	153 39,73 (9,65)	79 39,09 (10,39)	-0,97 (0,42)	207 40,36 (9,41)	196 40,57 (9,36)	191 41,70 (8,10)	179 41,65 (9,12)	170 42,63 (8,11)	151 41,36 (9,78)	157 42,02 (9,26)	87 41,40 (8,76)	1,05 (0,42)	-2,02 [-3,19;-0,84] 0,0008 -0,33 [-0,52;-0,14]
≥ 10	94 41,93 (8,51)	87 41,24 (8,70)	87 41,22 (10,02)	87 41,77 (9,84)	83 42,43 (9,27)	66 41,76 (9,74)	64 41,73 (10,14)	41 41,41 (9,53)	-0,26 (0,63)	76 40,22 (8,58)	73 39,60 (10,52)	69 41,65 (8,92)	66 42,35 (9,52)	55 41,44 (10,68)	55 41,87 (10,65)	57 42,16 (8,97)	39 42,97 (9,46)	0,54 (0,71)	-0,80 [-2,68;1,08] 0,4009 -0,13 [-0,43;0,17]
Tumorstadium (p-Wert des Interaktionsterms: 0,1676)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	50 41,20 (8,30)	45 37,49 (10,53)	44 39,45 (9,83)	43 37,60 (10,64)	42 38,02 (9,33)	36 35,92 (10,93)	36 38,31 (10,48)	21 38,76 (9,32)	-3,05 (0,91)	56 40,09 (8,42)	52 40,17 (8,46)	51 41,41 (9,04)	48 40,25 (8,21)	47 41,89 (8,39)	35 41,69 (8,32)	37 43,16 (7,66)	19 43,21 (6,63)	1,49 (0,87)	-4,54 [-7,04;-2,05] 0,0005 -0,70 [-1,10;-0,31]
IIB	42 41,07 (8,44)	40 39,78 (9,23)	39 41,90 (6,95)	39 40,67 (7,68)	32 41,22 (7,69)	33 41,61 (8,70)	27 44,07 (6,62)	21 42,10 (6,66)	-0,01 (0,86)	61 40,97 (7,16)	57 42,44 (6,91)	55 42,85 (7,11)	52 42,10 (8,06)	53 40,49 (8,32)	52 40,46 (8,05)	51 39,41 (10,54)	30 39,13 (8,31)	-0,45 (0,71)	0,45 [-1,76;2,66] 0,6897 0,08 [-0,31;0,47]
IIIA	210 39,34 (9,57)	203 38,41 (10,23)	197 38,46 (10,21)	189 38,87 (9,61)	179 37,83 (10,36)	160 38,55 (10,81)	154 39,45 (9,90)	80 39,65 (10,05)	-0,84 (0,42)	189 40,10 (9,60)	177 40,51 (9,23)	171 41,66 (7,92)	165 41,07 (9,40)	156 42,37 (8,17)	130 41,08 (9,95)	136 41,55 (9,28)	70 40,76 (9,10)	1,00 (0,45)	-1,84 [-3,05;-0,63] 0,0029 -0,30 [-0,50;-0,10]
IIIB	14 34,71 (13,44)	13 33,85 (11,22)	13 31,92 (14,24)	13 31,38 (12,17)	10 30,00 (13,30)	8 31,50 (15,90)	11 35,82 (13,47)	6 31,00 (10,43)	-2,74 (1,71)	14 43,43 (8,30)	14 45,57 (5,06)	14 43,71 (5,80)	11 43,18 (7,14)	9 46,33 (3,57)	10 43,80 (4,47)	9 43,33 (5,61)	5 39,60 (7,70)	0,49 (1,77)	-3,23 [-8,54;2,08] 0,2218 -0,48 [-1,21;0,25]
IIIC	159 41,75 (8,38)	145 40,26 (8,83)	144 40,53 (9,75)	142 41,18 (9,35)	135 41,59 (9,45)	115 41,70 (9,99)	112 42,03 (9,81)	64 41,23 (9,73)	-0,70 (0,49)	146 40,21 (8,70)	140 39,91 (10,07)	133 41,41 (9,14)	126 42,40 (9,00)	113 41,82 (9,92)	110 41,53 (10,11)	110 41,75 (9,68)	71 42,61 (9,02)	0,54 (0,51)	-1,25 [-2,64;0,14] 0,0779 -0,20 [-0,43;0,02]
Tumorgrading (p-Wert des Interaktionsterms: 0,8283)																			
G1	44 42,36 (8,43)	42 40,81 (8,78)	38 40,47 (9,17)	37 41,30 (8,66)	36 40,97 (9,40)	31 39,97 (10,45)	32 40,03 (9,69)	18 39,94 (10,69)	-1,54 (0,78)	37 41,68 (9,23)	36 42,08 (8,26)	31 43,10 (6,88)	32 43,00 (7,78)	30 43,13 (8,59)	28 40,36 (11,10)	24 42,50 (8,56)	12 45,50 (6,37)	0,70 (0,85)	-2,24 [-4,55;0,06] 0,0566 -0,43 [-0,87;0,01]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	207 40,04 (9,55)	193 39,01 (9,81)	194 38,81 (10,50)	188 39,22 (9,87)	179 39,18 (10,00)	159 39,00 (10,63)	161 40,45 (9,80)	82 41,22 (9,52)	-0,74 (0,44)	204 40,00 (9,66)	193 40,24 (10,17)	189 41,50 (8,82)	178 41,20 (9,95)	161 42,04 (8,86)	147 41,61 (10,05)	148 41,80 (9,42)	85 41,12 (9,66)	0,73 (0,45)	-1,47 [-2,72;-0,22] 0,0211 -0,23 [-0,42;-0,03]
G3	198 39,97 (9,17)	185 38,14 (10,19)	182 39,54 (9,82)	177 39,07 (9,79)	160 38,49 (10,41)	142 39,45 (11,13)	129 40,23 (10,44)	81 38,25 (9,67)	-1,15 (0,44)	197 40,21 (8,16)	185 40,54 (8,30)	179 41,47 (8,24)	167 41,64 (8,09)	162 41,49 (8,77)	138 40,85 (8,65)	148 40,93 (9,70)	85 41,13 (8,32)	0,68 (0,44)	-1,83 [-3,05;-0,60] 0,0037 -0,29 [-0,49;-0,10]
GX	27 42,15 (7,00)	27 40,44 (8,32)	24 40,33 (8,88)	25 41,12 (9,10)	24 41,42 (8,81)	21 41,86 (8,22)	19 41,95 (8,88)	12 45,33 (5,97)	-0,70 (1,05)	28 41,61 (6,56)	26 43,08 (6,82)	25 44,16 (5,43)	25 41,64 (7,91)	24 43,08 (7,62)	23 42,78 (8,01)	23 42,52 (8,14)	13 41,08 (6,42)	0,64 (1,01)	-1,35 [-4,29;1,59] 0,3611 -0,25 [-0,78;0,28]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,0518)																			
Negativ	46 38,17 (9,79)	42 35,19 (10,66)	40 37,45 (11,52)	41 36,98 (11,41)	38 35,76 (10,85)	38 35,82 (11,96)	35 33,40 (12,68)	12 37,17 (10,36)	-2,10 (1,15)	39 39,67 (7,88)	35 40,34 (9,88)	34 41,21 (9,00)	30 43,37 (6,65)	31 44,32 (6,95)	26 42,85 (8,27)	31 42,03 (9,69)	15 43,20 (5,72)	2,56 (1,24)	-4,65 [-8,03;-1,28] 0,0075 -0,60 [-1,04;-0,16]
Positiv	412 40,51 (9,16)	389 39,18 (9,75)	383 39,46 (9,90)	371 39,60 (9,57)	348 39,46 (10,01)	304 39,77 (10,54)	291 41,03 (9,37)	173 40,23 (9,69)	-0,86 (0,29)	412 40,37 (8,96)	392 40,76 (9,02)	378 41,92 (8,17)	359 41,36 (9,03)	332 41,62 (8,90)	299 41,19 (9,44)	302 41,40 (9,38)	173 41,18 (8,97)	0,57 (0,29)	-1,43 [-2,25;-0,62] 0,0006 -0,24 [-0,38;-0,10]
Unbekannt	2 41,50 (0,71)	2 44,50 (6,36)	2 45,50 (3,54)	1 49,00 (NE)	1 48,00 (NE)	1 49,00 (NE)	1 50,00 (NE)	0	NE	7 37,43 (10,16)	6 35,83 (13,01)	7 37,86 (10,37)	6 39,00 (13,11)	6 44,50 (8,73)	7 36,43 (13,56)	4 41,00 (13,34)	2 37,00 (9,90)	0,11 (2,08)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,3047)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	265 40,01 (9,92)	243 38,65 (10,45)	237 38,72 (11,05)	227 38,97 (10,35)	211 38,81 (11,07)	188 39,37 (11,34)	171 40,26 (10,42)	111 40,07 (9,68)	-0,94 (0,41)	276 39,74 (9,70)	254 40,10 (10,05)	241 41,59 (8,84)	229 40,66 (9,96)	217 41,57 (9,54)	196 40,52 (10,40)	201 41,05 (10,25)	119 40,98 (9,79)	0,66 (0,40)	-1,60 [-2,71;-0,48] 0,0050 -0,24 [-0,41;-0,07]
Asiatisch	186 40,78 (8,14)	182 39,42 (8,87)	179 40,31 (8,28)	177 40,34 (8,55)	167 39,90 (8,71)	147 39,67 (9,71)	150 40,89 (9,37)	72 40,51 (9,52)	-0,75 (0,39)	165 41,30 (7,37)	161 41,47 (7,42)	160 42,13 (7,36)	156 42,54 (7,17)	143 42,16 (7,54)	123 41,91 (8,07)	127 41,89 (8,13)	67 41,97 (6,39)	0,63 (0,41)	-1,37 [-2,49;-0,26] 0,0161 -0,26 [-0,47;-0,05]
Andere	15 40,47 (9,39)	14 38,64 (9,34)	13 38,92 (10,14)	14 36,00 (11,87)	14 37,64 (9,75)	12 38,58 (12,78)	14 39,86 (10,08)	9 38,33 (11,18)	-2,04 (1,44)	16 40,56 (7,31)	16 42,88 (6,62)	16 42,75 (7,02)	15 44,87 (6,88)	13 45,46 (5,44)	12 45,92 (3,68)	11 44,64 (6,28)	7 43,29 (8,36)	3,26 (1,46)	-5,30 [-9,53;-1,06] 0,0164 -0,90 [-1,62;-0,18]
ECOG-PS (p-Wert des Interaktionsterms: 0,5984)																			
ECOG-PS 0	426 40,39 (9,11)	398 38,95 (9,60)	391 39,28 (10,11)	382 39,31 (9,70)	358 39,01 (10,11)	316 39,35 (10,69)	306 40,27 (10,02)	178 40,21 (9,63)	-1,13 (0,29)	415 40,61 (8,66)	391 40,76 (9,09)	374 42,02 (8,10)	358 42,03 (8,54)	336 42,29 (8,47)	301 41,71 (9,09)	311 41,69 (9,21)	176 41,35 (8,79)	0,75 (0,30)	-1,88 [-2,70;-1,06] <,0001 -0,31 [-0,45;-0,17]
ECOG-PS 1	50 40,00 (9,82)	49 38,49 (11,39)	47 39,89 (9,19)	45 40,62 (9,67)	41 40,83 (9,53)	37 40,16 (10,73)	35 41,66 (9,47)	15 38,93 (10,12)	0,46 (0,96)	52 38,10 (9,95)	50 40,12 (9,20)	51 40,00 (9,43)	45 37,84 (10,82)	42 39,43 (10,18)	36 37,67 (11,37)	32 39,81 (10,90)	19 41,74 (8,40)	0,25 (0,96)	0,21 [-2,48;2,91] 0,8746 0,03 [-0,36;0,42]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACIT-Fatigue Score = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACIT-Fatigue Score haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t115_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des FACIT-Fatigue aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,3048)																			
< 65 Jahre	787 40,22 (9,37)	731 38,56 (9,86)	712 39,06 (9,91)	660 39,63 (9,54)	644 39,39 (9,60)	568 39,69 (9,36)	576 40,16 (9,35)	321 40,50 (9,31)	-0,95 (0,22)	808 39,46 (9,76)	750 40,09 (9,26)	743 39,99 (9,49)	694 40,46 (9,19)	655 40,89 (9,21)	582 40,98 (9,27)	576 40,83 (9,65)	305 40,24 (10,04)	0,64 (0,22)	-1,59 [-2,21;-0,97] <,0001 -0,25 [-0,35;-0,15]
≥ 65 Jahre	288 40,20 (9,47)	259 37,63 (9,83)	245 39,10 (8,83)	229 38,49 (8,81)	214 38,03 (9,74)	193 39,11 (9,18)	203 39,67 (9,66)	113 39,73 (8,49)	-2,08 (0,36)	269 39,78 (9,04)	251 40,49 (8,73)	245 40,32 (8,86)	231 40,03 (8,27)	225 39,74 (8,84)	194 40,15 (8,91)	186 39,61 (8,96)	109 39,34 (9,53)	-0,22 (0,37)	-1,86 [-2,87;-0,85] 0,0003 -0,31 [-0,47;-0,14]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,2246)																			
Neoadjuvante Chemotherapie	354 40,61 (9,36)	323 38,74 (9,51)	307 39,44 (9,61)	280 39,88 (9,15)	261 39,34 (9,94)	223 40,31 (8,86)	238 39,72 (9,77)	123 40,88 (8,53)	-1,53 (0,34)	352 38,99 (9,86)	325 40,16 (9,32)	312 39,91 (9,26)	292 39,88 (9,56)	272 40,71 (8,65)	229 40,33 (9,81)	248 40,53 (9,70)	131 38,92 (10,10)	0,26 (0,34)	-1,78 [-2,74;-0,83] 0,0003 -0,28 [-0,42;-0,13]
Adjuvante Chemotherapie	663 40,13 (9,43)	615 38,30 (9,98)	601 39,01 (9,71)	561 39,33 (9,37)	555 38,93 (9,52)	500 39,45 (9,40)	498 40,35 (9,27)	284 40,14 (9,30)	-0,97 (0,24)	659 39,94 (9,34)	614 40,33 (8,94)	617 40,20 (9,36)	583 40,77 (8,58)	561 40,69 (9,30)	501 41,13 (8,84)	468 40,60 (9,46)	256 40,73 (9,83)	0,52 (0,24)	-1,49 [-2,16;-0,83] <,0001 -0,24 [-0,35;-0,13]
Keine Chemotherapie	58 38,78 (9,22)	52 35,87 (10,29)	49 37,47 (9,07)	48 36,21 (10,16)	42 38,79 (9,73)	38 36,21 (10,18)	43 38,14 (9,18)	27 39,37 (9,64)	-3,20 (0,80)	66 38,45 (10,31)	62 38,90 (10,07)	59 39,69 (9,51)	50 38,18 (9,49)	47 38,85 (9,77)	46 39,15 (9,60)	46 39,87 (8,91)	27 38,41 (9,32)	0,45 (0,76)	-3,65 [-5,84;-1,45] 0,0014 -0,59 [-0,95;-0,23]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2017)																			

Anhang 4-G2.6: Symptomatik anhand FACT-ES - Subgruppenanalysen

Tabelle 4-127 (Anhang): FACT-ES - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen für die Veränderung des FACT-ES 19 aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,1859)																			
Neoadjuvante Chemotherapie	196 60,98 (9,23)	189 58,46 (9,74)	181 57,51 (11,57)	176 57,40 (12,13)	165 56,47 (11,93)	149 56,83 (12,07)	146 58,75 (11,46)	75 58,89 (10,41)	-3,32 (0,52)	193 59,98 (9,85)	181 58,44 (10,02)	179 59,45 (9,83)	156 59,34 (10,20)	146 59,01 (10,33)	120 59,15 (10,49)	135 59,01 (10,59)	77 59,84 (9,92)	-1,65 (0,53)	-1,67 [-3,12;-0,22] 0,0244 -0,23 [-0,43;-0,03]
Adjuvante Chemotherapie	288 59,69 (9,75)	273 56,96 (10,95)	270 56,83 (11,05)	266 56,42 (11,11)	254 55,92 (11,65)	214 56,37 (12,12)	205 58,04 (10,22)	128 55,93 (11,45)	-2,93 (0,40)	284 59,74 (9,73)	275 59,02 (9,90)	269 58,71 (9,82)	261 58,53 (10,07)	240 57,63 (11,05)	221 57,21 (11,61)	219 58,16 (11,30)	121 57,33 (11,49)	-1,51 (0,41)	-1,42 [-2,55;-0,30] 0,0134 -0,21 [-0,37;-0,04]
Keine Chemotherapie	7 67,43 (10,53)	7 60,43 (11,72)	6 58,00 (12,46)	6 58,83 (11,62)	5 57,40 (9,74)	5 57,20 (8,81)	6 63,00 (8,15)	2 66,50 (0,71)	-5,46 (2,04)	1 63,00 (NE)	1 49,00 (NE)	1 51,00 (NE)	1 48,00 (NE)	1 52,00 (NE)	1 43,00 (NE)	1 48,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,0970)																			
Nordamerika / Europa	204 60,35 (8,94)	188 57,14 (9,93)	181 56,46 (10,84)	178 56,23 (11,23)	162 55,78 (11,33)	139 56,38 (11,73)	134 58,96 (10,57)	75 57,97 (10,10)	-3,18 (0,48)	197 59,08 (10,13)	183 57,87 (10,59)	176 58,85 (9,83)	155 58,80 (10,38)	142 57,64 (11,21)	132 56,59 (12,16)	132 57,33 (11,57)	66 58,52 (11,45)	-1,09 (0,49)	-2,09 [-3,43;-0,74] 0,0024 -0,31 [-0,50;-0,11]
Asien	163 60,93 (8,92)	162 57,53 (10,12)	159 56,75 (10,59)	156 56,22 (11,03)	150 55,71 (11,01)	130 55,93 (11,41)	137 58,24 (10,33)	69 57,77 (11,34)	-4,13 (0,54)	153 61,54 (8,32)	151 60,36 (8,82)	151 59,77 (9,44)	146 59,40 (9,37)	137 59,07 (9,60)	120 59,64 (10,13)	122 59,53 (10,54)	66 59,17 (10,30)	-2,19 (0,56)	-1,94 [-3,47;-0,41] 0,0129 -0,28 [-0,50;-0,06]
Andere	124 59,46 (11,34)	119 58,50 (11,83)	117 58,62 (12,64)	114 58,64 (12,48)	112 57,28 (13,13)	99 57,67 (13,25)	86 57,85 (11,58)	61 55,33 (12,04)	-1,67 (0,67)	128 58,99 (10,56)	123 58,13 (10,08)	122 58,22 (10,25)	117 58,09 (10,67)	108 57,60 (11,62)	90 57,31 (11,15)	101 58,61 (10,84)	66 57,24 (11,14)	-1,54 (0,66)	-0,13 [-1,98;1,72] 0,8887 -0,02 [-0,26;0,23]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3665)																			
< 20 mm	121 60,39 (9,39)	115 58,17 (9,30)	109 56,29 (10,92)	112 55,25 (11,37)	105 55,05 (11,66)	93 53,05 (12,80)	90 56,66 (10,61)	54 57,81 (8,81)	-4,14 (0,59)	123 58,54 (9,35)	116 57,51 (10,01)	116 57,11 (9,83)	107 56,54 (10,51)	101 56,24 (10,62)	86 56,41 (11,29)	85 57,85 (11,02)	50 57,70 (10,83)	-2,36 (0,59)	-1,78 [-3,44;-0,13] 0,0350 -0,27 [-0,52;-0,02]
≥ 20 bis < 50 mm	230 60,23 (9,54)	220 56,96 (11,59)	219 57,25 (11,37)	214 57,26 (11,66)	197 56,43 (11,97)	171 57,84 (11,57)	165 59,25 (10,46)	97 57,49 (12,60)	-2,81 (0,49)	227 59,68 (10,19)	218 58,74 (10,16)	217 59,23 (10,19)	201 59,29 (10,08)	187 58,32 (11,28)	172 57,89 (11,63)	181 58,53 (11,35)	93 58,39 (11,07)	-1,03 (0,49)	-1,77 [-3,14;-0,41] 0,0109 -0,24 [-0,42;-0,06]
≥ 50 mm	128 60,38 (10,18)	124 58,23 (9,81)	120 57,47 (11,59)	114 57,56 (11,43)	113 56,32 (11,46)	95 57,46 (11,65)	93 58,53 (11,34)	48 55,40 (10,79)	-2,85 (0,58)	123 61,31 (9,37)	118 59,86 (9,54)	111 60,24 (8,81)	105 59,64 (9,36)	96 59,45 (9,67)	80 58,93 (10,54)	85 58,47 (10,40)	51 58,16 (11,08)	-2,10 (0,59)	-0,75 [-2,37;0,88] 0,3646 -0,11 [-0,36;0,13]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,2973)																			
0-3	177 60,75 (9,50)	168 57,93 (9,68)	161 57,53 (10,50)	158 56,92 (11,37)	144 56,69 (11,48)	129 56,81 (11,67)	131 58,74 (10,64)	77 58,83 (9,61)	-3,07 (0,51)	190 59,80 (9,07)	180 58,69 (9,34)	176 58,83 (9,25)	164 58,43 (9,02)	156 57,17 (10,08)	134 56,99 (9,76)	134 57,09 (10,40)	71 57,31 (10,74)	-2,44 (0,50)	-0,63 [-2,03;0,77] 0,3761 -0,09 [-0,30;0,11]
4-9	216 59,44 (10,22)	207 56,54 (11,56)	204 55,98 (12,14)	198 55,99 (11,80)	193 55,02 (11,79)	169 55,95 (12,12)	158 58,36 (10,76)	85 56,21 (12,45)	-3,24 (0,49)	210 59,73 (10,48)	201 58,86 (9,88)	200 59,23 (10,07)	186 59,22 (10,48)	173 58,61 (11,04)	153 58,21 (12,16)	160 59,12 (11,50)	87 58,83 (11,37)	-0,90 (0,50)	-2,35 [-3,72;-0,97] 0,0008 -0,33 [-0,52;-0,13]
≥ 10	98 61,48 (8,15)	94 59,44 (9,16)	92 58,89 (10,30)	92 58,52 (11,07)	87 57,76 (11,83)	70 57,61 (12,56)	68 57,91 (10,87)	43 55,84 (10,75)	-3,01 (0,69)	78 60,24 (9,49)	76 58,68 (11,49)	73 58,71 (10,53)	68 58,60 (11,60)	58 59,33 (11,76)	55 58,96 (12,11)	61 59,69 (10,98)	40 58,95 (10,51)	-1,44 (0,78)	-1,56 [-3,62;0,49] 0,1345 -0,23 [-0,53;0,07]
Tumorstadium (p-Wert des Interaktionsterms: 0,4647)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 60,17 (10,57)	49 57,71 (9,88)	48 55,50 (11,27)	47 54,49 (11,67)	46 53,76 (12,17)	39 52,92 (13,18)	39 55,72 (11,28)	23 57,78 (9,74)	-4,98 (0,87)	57 58,42 (8,97)	54 57,69 (8,93)	54 58,44 (8,30)	48 56,94 (9,01)	47 57,23 (7,62)	35 56,80 (10,03)	37 58,49 (10,71)	19 58,89 (9,02)	-1,79 (0,85)	-3,19 [-5,61;-0,76] 0,0105 -0,50 [-0,88;-0,12]
IIB	45 60,18 (8,71)	44 57,75 (10,71)	41 59,66 (9,17)	42 58,33 (11,15)	35 58,31 (9,96)	34 57,94 (10,10)	31 60,35 (10,15)	22 60,00 (9,81)	-2,17 (1,16)	64 60,08 (9,34)	61 58,80 (9,95)	61 58,08 (9,87)	56 58,48 (9,17)	55 55,89 (10,84)	54 55,63 (10,21)	54 55,52 (10,67)	32 56,41 (11,07)	-3,57 (0,96)	1,40 [-1,59;4,39] 0,3548 0,18 [-0,20;0,56]
IIIA	213 59,48 (10,36)	207 56,58 (11,55)	202 55,97 (12,32)	196 56,07 (11,60)	190 55,28 (12,04)	165 55,90 (12,08)	157 58,24 (10,56)	86 56,84 (11,78)	-3,06 (0,49)	192 59,55 (10,21)	182 58,58 (9,60)	179 59,08 (9,66)	172 59,10 (9,97)	158 58,44 (10,59)	131 57,61 (11,69)	140 58,59 (10,88)	70 57,30 (11,94)	-1,06 (0,52)	-2,00 [-3,39;-0,60] 0,0051 -0,28 [-0,48;-0,08]
IIIB	14 56,43 (13,73)	13 55,69 (9,88)	13 54,46 (11,84)	13 54,62 (12,78)	10 48,80 (7,74)	8 52,50 (13,01)	11 57,36 (13,33)	6 49,50 (12,86)	-1,99 (2,31)	14 64,57 (7,69)	14 64,93 (8,34)	14 64,50 (7,91)	11 63,36 (8,12)	9 64,22 (11,55)	10 66,00 (4,08)	9 65,00 (6,56)	5 63,60 (6,11)	0,85 (2,36)	-2,84 [-10,41;4,72] 0,4234 -0,32 [-1,04;0,41]
IIIC	166 61,78 (7,82)	155 59,10 (9,08)	152 58,70 (10,01)	149 58,34 (11,27)	142 58,06 (11,45)	121 58,55 (11,83)	118 59,10 (10,64)	67 57,01 (11,00)	-3,01 (0,51)	150 60,21 (9,79)	145 58,77 (10,76)	140 58,80 (10,56)	130 58,75 (11,10)	118 58,67 (11,87)	112 58,80 (11,74)	115 59,13 (11,54)	72 59,61 (10,55)	-1,52 (0,54)	-1,48 [-2,95;-0,01] 0,0481 -0,22 [-0,45;-0,00]
Tumorgrading (p-Wert des Interaktionsterms: 0,1708)																			
G1	45 63,16 (7,58)	43 61,77 (7,22)	40 59,48 (9,10)	40 59,20 (8,88)	39 58,72 (9,81)	33 58,21 (11,76)	33 60,06 (9,19)	18 57,61 (13,83)	-2,14 (1,17)	38 58,74 (10,12)	36 57,89 (10,00)	34 55,50 (10,92)	36 55,92 (11,67)	31 54,58 (12,85)	28 54,54 (13,05)	25 55,52 (12,22)	13 56,46 (11,14)	-3,50 (1,27)	1,36 [-2,12;4,84] 0,4381 0,17 [-0,26;0,61]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	213 59,93 (9,75)	202 57,50 (10,12)	201 56,66 (11,49)	196 56,12 (11,80)	188 55,90 (11,62)	165 55,75 (12,18)	166 57,89 (10,86)	87 57,36 (10,50)	-3,15 (0,44)	208 60,15 (10,24)	200 59,55 (10,68)	197 60,27 (9,50)	183 59,70 (10,32)	163 59,20 (10,86)	148 58,78 (11,70)	155 59,52 (11,11)	87 58,25 (10,81)	-0,76 (0,45)	-2,38 [-3,62;-1,15] 0,0002 -0,37 [-0,56;-0,18]
G3	205 59,74 (9,90)	196 56,69 (11,20)	191 56,94 (11,27)	187 56,95 (11,60)	172 55,47 (12,04)	148 56,67 (12,22)	138 58,33 (10,84)	87 55,70 (11,29)	-3,08 (0,53)	202 59,37 (9,43)	193 57,90 (9,34)	191 58,11 (9,89)	172 58,22 (9,73)	167 57,16 (10,40)	141 57,13 (10,42)	151 57,44 (10,89)	85 58,38 (11,42)	-2,12 (0,53)	-0,96 [-2,42;0,51] 0,2003 -0,13 [-0,32;0,07]
GX	28 62,93 (8,05)	28 58,64 (11,20)	25 58,28 (12,44)	25 57,88 (12,33)	25 58,68 (12,72)	22 59,59 (9,90)	20 60,65 (11,09)	13 64,31 (7,76)	-4,10 (1,12)	29 62,90 (7,20)	27 60,81 (7,62)	26 60,50 (8,79)	26 60,50 (8,29)	25 62,60 (7,87)	24 60,50 (10,66)	24 61,00 (9,27)	13 60,08 (9,23)	-2,23 (1,09)	-1,88 [-5,03;1,27] 0,2365 -0,32 [-0,84;0,20]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,2608)																			
Negativ	46 58,35 (10,57)	43 54,81 (11,26)	40 54,05 (13,22)	42 53,95 (14,68)	39 52,21 (14,05)	38 53,61 (13,17)	36 52,81 (12,46)	12 54,33 (12,50)	-4,79 (1,14)	39 57,46 (9,27)	36 56,22 (9,47)	35 57,80 (8,83)	30 57,27 (8,33)	31 57,39 (9,43)	25 57,04 (8,26)	31 57,23 (9,67)	15 59,20 (10,65)	0,40 (1,21)	-5,20 [-8,51;-1,89] 0,0025 -0,68 [-1,12;-0,24]
Positiv	427 60,39 (9,57)	409 57,75 (10,50)	402 57,31 (11,10)	392 57,09 (11,25)	372 56,51 (11,50)	319 56,84 (12,00)	305 58,84 (10,47)	183 57,07 (11,19)	-2,97 (0,34)	422 60,09 (9,78)	406 59,07 (9,78)	400 59,19 (9,83)	374 58,88 (10,21)	341 58,10 (10,92)	304 57,98 (11,44)	314 58,61 (11,14)	176 57,99 (11,10)	-1,78 (0,34)	-1,18 [-2,13;-0,24] 0,0139 -0,17 [-0,30;-0,03]
Unbekannt	2 65,50 (6,36)	2 59,50 (12,02)	2 64,00 (5,66)	1 65,00 (NE)	1 64,00 (NE)	1 67,00 (NE)	1 68,00 (NE)	0	NE	8 57,13 (12,21)	7 52,43 (17,77)	8 55,38 (13,52)	6 57,67 (15,19)	6 59,00 (14,89)	8 52,75 (14,50)	4 51,25 (16,52)	2 67,00 (7,07)	-0,21 (2,58)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,8209)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	276 59,46 (10,03)	261 56,85 (10,66)	251 56,31 (11,51)	245 56,13 (11,52)	230 55,51 (11,85)	200 56,14 (12,13)	183 57,87 (10,86)	120 56,20 (11,10)	-3,00 (0,42)	285 58,55 (10,31)	267 57,50 (10,39)	261 57,89 (10,02)	241 57,80 (10,48)	224 56,87 (11,08)	200 56,06 (11,79)	209 57,08 (11,13)	122 57,35 (11,00)	-1,51 (0,42)	-1,49 [-2,66;-0,32] 0,0127 -0,21 [-0,38;-0,05]
Asiatisch	188 61,47 (8,87)	185 58,66 (10,25)	182 58,09 (10,81)	179 57,82 (11,36)	171 57,08 (11,26)	149 57,18 (11,66)	153 59,02 (10,27)	75 58,17 (11,16)	-3,26 (0,51)	166 61,83 (8,49)	164 60,55 (9,00)	162 60,27 (9,56)	157 60,12 (9,54)	144 59,50 (9,79)	124 59,75 (10,24)	130 59,67 (10,51)	67 59,28 (10,25)	-1,98 (0,55)	-1,28 [-2,76;0,20] 0,0894 -0,18 [-0,39;0,03]
Andere	16 60,19 (10,35)	15 58,47 (8,31)	15 57,80 (12,24)	15 55,47 (12,92)	15 54,87 (13,14)	13 55,62 (14,57)	14 58,29 (12,69)	9 60,33 (11,90)	-3,92 (1,85)	17 60,18 (8,08)	16 61,13 (6,83)	17 60,88 (8,27)	16 60,06 (9,50)	14 61,86 (14,18)	12 63,67 (6,83)	12 66,17 (10,86)	7 65,71 (13,45)	0,75 (1,84)	-4,67 [-10,06;0,72] 0,0865 -0,61 [-1,29;0,07]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-ES 19 Score = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-ES 19 Score haben.
Abkürzungen: B: Baseline; ET: Endokrine Therapie; FACT-ES: Functional Assessment of Cancer Therapy - Endokrine Symptome; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t113_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des FACT-ES 19 aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,0911)																			
< 65 Jahre	804 62,73 (9,00)	759 60,37 (9,74)	744 60,21 (10,11)	700 60,13 (10,12)	675 59,99 (10,12)	589 59,60 (10,37)	603 61,17 (9,65)	330 61,25 (9,50)	-2,42 (0,23)	831 61,97 (9,11)	792 61,45 (9,56)	783 60,77 (9,85)	730 60,42 (9,87)	692 60,79 (9,83)	609 60,89 (9,88)	606 61,48 (9,79)	318 60,65 (9,48)	-1,27 (0,22)	-1,16 [-1,78;-0,54] 0,0003 -0,18 [-0,28;-0,08]
≥ 65 Jahre	303 66,28 (7,12)	285 64,41 (7,68)	266 65,33 (7,12)	255 64,08 (7,61)	238 63,56 (8,36)	218 63,67 (8,08)	227 65,28 (7,75)	121 63,93 (7,48)	-2,09 (0,29)	278 66,45 (7,16)	267 65,17 (7,53)	259 65,28 (6,92)	247 65,10 (7,18)	240 64,26 (7,73)	208 64,29 (7,90)	197 64,43 (7,65)	115 63,96 (8,02)	-1,76 (0,30)	-0,33 [-1,15;0,49] 0,4312 -0,07 [-0,23;0,10]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,6042)																			
Neoadjuvante Chemotherapie	363 64,39 (8,63)	335 61,58 (9,52)	324 62,09 (9,51)	302 61,59 (9,44)	279 61,14 (9,79)	234 61,15 (9,73)	254 62,90 (8,75)	130 62,46 (8,28)	-2,58 (0,33)	365 62,72 (9,01)	347 62,18 (9,46)	331 61,34 (9,43)	310 61,13 (9,65)	290 61,50 (9,54)	244 61,41 (9,98)	259 62,09 (9,80)	138 61,09 (9,73)	-1,49 (0,33)	-1,09 [-2,01;-0,17] 0,0202 -0,17 [-0,32;-0,03]
Adjuvante Chemotherapie	685 63,20 (8,78)	655 61,32 (9,32)	635 61,02 (9,84)	602 60,82 (9,81)	588 60,69 (9,90)	533 60,35 (10,11)	531 61,73 (9,75)	295 61,45 (9,51)	-2,16 (0,23)	678 63,06 (8,67)	649 62,21 (8,99)	652 61,85 (9,36)	613 61,50 (9,35)	596 61,47 (9,46)	528 61,57 (9,39)	498 61,92 (9,26)	269 61,45 (9,02)	-1,42 (0,23)	-0,73 [-1,38;-0,09] 0,0264 -0,12 [-0,23;-0,01]
Keine Chemotherapie	59 65,27 (7,14)	54 62,61 (9,52)	51 64,86 (7,83)	51 63,14 (9,11)	46 62,57 (8,85)	40 62,73 (9,22)	45 65,53 (6,51)	26 65,42 (6,76)	-2,46 (0,58)	66 65,45 (9,92)	63 65,37 (9,99)	59 65,46 (9,16)	54 65,46 (9,31)	46 65,61 (8,05)	45 65,76 (7,65)	46 65,93 (7,71)	26 64,65 (8,18)	-0,72 (0,56)	-1,75 [-3,34;-0,16] 0,0316 -0,39 [-0,74;-0,04]
Region (p-Wert des Interaktionsterms: 0,1633)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	548 63,01 (8,96)	496 60,14 (9,90)	481 60,36 (9,86)	447 60,48 (9,81)	419 59,73 (10,21)	375 59,58 (10,60)	392 60,81 (9,90)	211 60,77 (9,58)	-2,94 (0,25)	527 62,02 (9,21)	490 61,10 (9,85)	479 60,38 (9,74)	441 60,13 (9,87)	421 59,96 (9,90)	373 60,35 (9,89)	344 60,65 (9,97)	201 60,72 (9,91)	-1,86 (0,26)	-1,08 [-1,78;-0,37] 0,0027 -0,18 [-0,30;-0,06]
Asien	195 65,93 (7,17)	190 63,83 (8,19)	185 62,82 (9,55)	178 62,30 (9,50)	173 62,05 (9,63)	152 61,41 (9,65)	163 63,72 (8,67)	87 62,08 (8,76)	-2,92 (0,43)	193 65,80 (7,38)	190 64,99 (8,08)	188 64,94 (7,98)	180 63,96 (8,87)	176 64,39 (8,23)	149 63,83 (8,29)	155 64,91 (7,56)	81 62,85 (8,31)	-1,08 (0,43)	-1,84 [-3,04;-0,64] 0,0027 -0,31 [-0,51;-0,11]
Andere	364 63,56 (8,79)	358 62,06 (8,98)	344 62,56 (9,31)	330 61,55 (9,51)	321 61,86 (9,22)	280 61,82 (9,09)	275 63,57 (8,58)	153 63,56 (8,30)	-1,07 (0,32)	389 63,21 (8,81)	379 62,75 (8,64)	375 62,29 (9,24)	356 62,24 (8,99)	335 62,41 (9,07)	295 62,48 (9,39)	304 62,59 (9,23)	151 61,89 (8,68)	-0,92 (0,31)	-0,16 [-1,03;0,72] 0,7294 -0,03 [-0,17;0,12]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3038)																			
< 20 mm	280 62,41 (9,24)	258 60,51 (9,80)	254 60,17 (10,48)	245 60,10 (10,38)	235 59,89 (10,21)	210 59,67 (10,80)	210 61,33 (9,94)	106 60,83 (9,44)	-2,47 (0,36)	297 62,95 (9,11)	284 62,33 (9,50)	275 62,53 (9,52)	259 61,98 (10,05)	250 61,63 (10,10)	214 61,93 (9,95)	219 62,38 (9,91)	108 61,50 (9,24)	-1,00 (0,35)	-1,47 [-2,47;-0,48] 0,0038 -0,24 [-0,41;-0,08]
≥ 20 bis < 50 mm	569 63,90 (8,68)	547 61,77 (9,29)	521 61,92 (9,80)	502 61,42 (9,66)	476 61,33 (9,76)	424 61,30 (9,88)	433 62,72 (9,48)	232 62,16 (9,28)	-2,09 (0,26)	572 63,06 (8,66)	549 62,39 (9,25)	543 62,02 (9,12)	511 61,54 (9,52)	492 61,82 (9,27)	437 61,64 (9,60)	417 62,30 (9,40)	231 61,68 (8,92)	-1,38 (0,26)	-0,71 [-1,42;0,00] 0,0516 -0,12 [-0,23;0,00]
≥ 50 mm	241 64,54 (7,96)	224 61,59 (9,27)	219 62,15 (8,38)	195 61,78 (8,67)	188 61,04 (9,54)	160 60,29 (9,19)	173 62,33 (8,30)	105 62,60 (8,36)	-2,55 (0,38)	229 63,09 (9,17)	215 62,14 (8,90)	214 60,53 (9,97)	197 61,08 (8,68)	183 61,21 (9,12)	158 61,55 (8,83)	159 61,51 (8,69)	90 60,78 (9,99)	-2,05 (0,39)	-0,50 [-1,58;0,58] 0,3654 -0,08 [-0,26;0,10]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8672)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	368 63,01 (9,27)	348 60,41 (9,73)	337 60,93 (9,94)	314 61,08 (9,47)	305 60,44 (10,12)	273 59,93 (10,20)	285 61,23 (9,84)	166 61,58 (9,23)	-2,25 (0,32)	359 62,77 (8,67)	343 61,90 (9,00)	339 61,34 (9,07)	313 61,46 (9,13)	301 61,77 (9,01)	258 61,55 (8,97)	255 62,22 (8,92)	142 61,84 (9,87)	-1,28 (0,32)	-0,97 [-1,85;-0,08] 0,0319 -0,16 [-0,31;-0,01]
4-9	475 63,82 (8,58)	447 61,77 (9,36)	435 61,46 (9,84)	418 61,09 (9,93)	395 61,17 (9,81)	353 61,01 (10,13)	357 62,74 (9,20)	176 61,73 (9,44)	-2,44 (0,29)	486 63,03 (9,17)	466 62,37 (9,60)	465 61,91 (9,79)	440 61,54 (10,11)	419 61,45 (10,08)	376 61,59 (10,07)	358 62,21 (10,05)	191 61,72 (8,71)	-1,38 (0,28)	-1,07 [-1,86;-0,27] 0,0086 -0,17 [-0,30;-0,04]
≥ 10	264 64,46 (7,90)	249 62,41 (8,85)	238 62,64 (8,90)	223 61,52 (9,49)	213 61,14 (9,38)	181 61,25 (9,25)	188 63,06 (8,73)	109 62,95 (8,17)	-2,23 (0,36)	264 63,64 (8,60)	250 63,08 (8,82)	238 62,66 (9,08)	224 61,95 (8,69)	212 62,01 (8,82)	183 62,36 (9,16)	190 62,17 (8,76)	100 60,73 (9,26)	-1,63 (0,36)	-0,60 [-1,59;0,40] 0,2394 -0,10 [-0,27;0,07]
Tumorstadium (p-Wert des Interaktionsterms: 0,6960)																			
IIA	93 61,16 (9,68)	88 59,99 (9,73)	86 59,35 (10,46)	81 59,21 (10,49)	81 58,65 (10,48)	76 58,59 (10,94)	76 59,86 (10,68)	39 60,08 (9,84)	-1,98 (0,59)	95 61,71 (9,10)	92 61,42 (9,05)	89 61,16 (9,26)	85 61,86 (8,52)	79 61,67 (8,69)	70 61,41 (8,41)	74 61,96 (8,48)	37 61,78 (8,25)	-0,32 (0,59)	-1,66 [-3,31;-0,01] 0,0487 -0,29 [-0,58;-0,00]
IIB	133 63,57 (9,85)	125 60,91 (10,10)	117 62,00 (9,95)	116 61,71 (9,65)	113 61,39 (10,29)	100 60,18 (10,94)	110 62,12 (10,35)	68 61,90 (9,72)	-2,44 (0,55)	112 64,02 (7,98)	106 62,01 (9,66)	105 62,19 (8,52)	98 60,42 (10,52)	93 61,15 (9,25)	84 61,01 (9,89)	80 61,64 (9,80)	44 60,27 (11,19)	-2,93 (0,60)	0,49 [-1,12;2,10] 0,5523 0,08 [-0,18;0,33]
IIIA	430 63,59 (8,55)	407 61,55 (9,35)	394 61,30 (9,69)	373 60,78 (9,95)	349 60,95 (9,81)	312 60,85 (9,95)	321 62,21 (9,01)	158 61,14 (9,70)	-2,32 (0,31)	436 63,08 (8,72)	414 62,43 (9,00)	421 61,77 (9,57)	396 61,72 (9,33)	376 61,61 (9,43)	334 61,78 (9,46)	316 62,46 (9,46)	172 61,66 (8,53)	-1,28 (0,30)	-1,05 [-1,89;-0,20] 0,0151 -0,17 [-0,30;-0,03]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIB	47 64,96 (10,05)	45 63,11 (10,64)	45 63,44 (11,04)	44 62,55 (10,11)	41 63,07 (9,79)	36 61,86 (11,44)	31 63,19 (10,26)	15 65,07 (7,39)	-1,46 (0,73)	41 64,63 (9,34)	40 64,28 (9,26)	39 63,31 (9,16)	34 64,38 (9,11)	34 63,79 (8,98)	31 64,13 (7,30)	30 65,07 (7,34)	14 65,29 (7,22)	-0,23 (0,79)	-1,23 [-3,37;0,91] 0,2560 -0,24 [-0,66;0,18]
IIIC	402 64,27 (7,87)	378 61,69 (8,95)	366 61,97 (9,17)	339 61,72 (9,08)	327 61,01 (9,47)	281 61,10 (9,13)	290 62,95 (8,77)	169 62,86 (8,04)	-2,44 (0,30)	423 63,01 (9,15)	405 62,48 (9,41)	386 61,96 (9,57)	362 61,51 (9,60)	348 61,72 (9,78)	296 61,76 (9,98)	302 61,90 (9,60)	165 61,30 (9,70)	-1,41 (0,29)	-1,04 [-1,85;-0,22] 0,0124 -0,17 [-0,31;-0,04]
Tumorgrading (p-Wert des Interaktionsterms: 0,8912)																			
G1	82 62,76 (8,80)	80 62,51 (9,07)	81 61,04 (10,68)	74 61,46 (9,52)	71 60,80 (10,73)	65 60,66 (9,14)	62 62,63 (8,17)	31 59,81 (9,68)	-1,46 (0,67)	84 64,58 (8,46)	82 64,52 (8,41)	79 63,86 (8,09)	70 62,99 (9,13)	73 63,01 (9,04)	63 64,16 (8,00)	55 63,47 (8,61)	34 63,68 (6,33)	-0,92 (0,67)	-0,54 [-2,41;1,33] 0,5699 -0,09 [-0,39;0,22]
G2	525 63,95 (8,44)	498 61,22 (9,58)	479 61,60 (9,64)	452 61,00 (9,74)	430 60,87 (9,63)	371 60,99 (9,89)	374 62,64 (9,05)	212 62,41 (8,83)	-2,42 (0,27)	532 62,34 (9,09)	504 61,77 (9,26)	503 60,93 (9,73)	477 60,80 (9,70)	446 60,85 (9,75)	402 60,66 (9,67)	391 61,32 (9,55)	211 60,64 (8,82)	-1,61 (0,26)	-0,81 [-1,54;-0,07] 0,0324 -0,13 [-0,25;-0,01]
G3	451 63,55 (8,97)	422 61,50 (9,32)	405 61,56 (9,50)	383 61,25 (9,51)	370 60,79 (9,88)	332 60,33 (10,12)	357 61,64 (10,04)	186 61,90 (9,20)	-2,31 (0,29)	435 63,23 (8,74)	415 62,23 (9,21)	404 62,06 (9,36)	379 61,83 (9,36)	364 62,01 (9,22)	313 62,21 (9,65)	316 62,80 (9,40)	165 62,11 (10,09)	-1,28 (0,30)	-1,04 [-1,86;-0,22] 0,0128 -0,17 [-0,30;-0,04]
GX	47 64,60 (7,70)	42 62,74 (8,11)	43 62,70 (9,76)	44 63,00 (9,89)	40 63,85 (8,38)	37 62,54 (9,31)	37 64,54 (6,45)	22 61,41 (9,53)	-2,37 (0,75)	54 67,24 (6,69)	54 66,07 (9,10)	53 66,64 (6,36)	48 65,54 (7,52)	46 64,80 (8,23)	37 65,57 (7,46)	39 64,72 (7,85)	21 63,19 (9,61)	-1,58 (0,70)	-0,79 [-2,83;1,25] 0,4447 -0,15 [-0,55;0,24]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,2385)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Negativ	137 63,61 (8,70)	132 61,18 (9,49)	124 61,11 (10,49)	116 60,83 (9,91)	107 61,21 (9,58)	93 60,82 (9,97)	100 62,75 (8,76)	63 60,83 (9,38)	-2,52 (0,47)	148 63,52 (8,54)	138 63,18 (9,40)	133 62,86 (8,94)	126 61,98 (9,36)	121 61,97 (9,73)	102 61,62 (9,50)	114 61,43 (8,98)	56 61,23 (9,06)	-1,49 (0,45)	-1,04 [-2,33;0,25] 0,1148 -0,19 [-0,42;0,05]
Positiv	939 63,60 (8,70)	881 61,35 (9,37)	855 61,44 (9,61)	814 61,05 (9,66)	782 60,74 (9,89)	690 60,49 (9,96)	708 62,13 (9,48)	377 62,18 (8,98)	-2,34 (0,20)	934 63,01 (8,92)	897 62,26 (9,17)	885 61,73 (9,46)	829 61,54 (9,46)	790 61,65 (9,42)	694 61,78 (9,56)	668 62,35 (9,46)	363 61,52 (9,22)	-1,39 (0,20)	-0,96 [-1,52;-0,40] 0,0008 -0,15 [-0,25;-0,06]
Unbekannt	9 67,00 (5,39)	9 62,44 (12,05)	9 66,00 (7,62)	7 70,29 (4,86)	5 70,20 (5,81)	6 66,67 (9,33)	5 68,60 (5,27)	1 68,00 (NE)	1,30 (1,57)	7 63,86 (9,39)	6 69,00 (6,57)	6 64,17 (7,68)	6 67,67 (4,32)	6 66,00 (4,38)	6 65,83 (7,03)	5 66,00 (5,79)	5 66,40 (4,62)	2,90 (1,62)	-1,60 [-6,62;3,43] 0,5052 -0,33 [-1,27;0,61]
Ethnizität (p-Wert des Interaktionsterms: 0,1285)																			
Weiß	808 62,88 (8,94)	755 60,52 (9,52)	735 60,86 (9,52)	693 60,55 (9,55)	660 60,05 (9,75)	585 60,11 (9,88)	599 61,40 (9,42)	340 61,72 (8,99)	-2,36 (0,21)	817 62,51 (9,00)	772 61,71 (9,33)	759 61,14 (9,48)	705 60,70 (9,62)	674 60,79 (9,54)	597 61,13 (9,72)	579 61,33 (9,70)	320 61,04 (9,37)	-1,54 (0,21)	-0,82 [-1,40;-0,25] 0,0050 -0,14 [-0,24;-0,04]
Asiatisch	233 66,32 (7,34)	225 64,47 (8,28)	218 63,83 (9,61)	210 63,44 (9,50)	205 63,32 (9,61)	176 62,30 (9,71)	187 64,24 (8,57)	97 62,44 (8,96)	-2,35 (0,41)	222 65,40 (7,64)	218 64,97 (8,05)	216 65,02 (8,16)	208 64,34 (8,78)	201 64,71 (8,28)	167 64,05 (8,34)	172 65,11 (7,68)	88 63,23 (8,30)	-0,67 (0,42)	-1,67 [-2,82;-0,53] 0,0043 -0,27 [-0,45;-0,08]
Andere	54 65,17 (7,30)	52 63,35 (8,71)	48 62,60 (9,77)	44 62,07 (8,99)	42 63,40 (8,74)	36 63,47 (8,95)	38 67,16 (6,75)	13 65,00 (12,09)	-1,12 (1,01)	57 63,18 (9,99)	57 62,09 (10,73)	55 61,11 (10,72)	52 62,90 (8,87)	46 61,48 (10,98)	42 61,81 (9,96)	43 63,56 (9,07)	19 61,74 (10,19)	-2,67 (0,97)	1,55 [-1,24;4,35] 0,2719 0,21 [-0,16;0,58]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,5797)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Tamoxifen	104 61,16 (8,79)	99 58,79 (9,80)	98 59,07 (10,25)	96 58,96 (10,29)	94 57,50 (11,55)	90 56,94 (11,34)	91 58,58 (10,83)	55 58,42 (10,69)	-2,61 (0,63)	124 61,55 (8,86)	122 61,28 (9,12)	119 60,13 (9,72)	110 60,15 (10,34)	103 59,83 (8,95)	94 60,48 (10,27)	92 60,88 (9,10)	56 60,25 (8,93)	-1,22 (0,58)	-1,39 [-3,07;0,30] 0,1058 -0,22 [-0,48;0,05]
Aromatase-Inhibitor	1003 63,97 (8,62)	945 61,75 (9,31)	912 61,83 (9,58)	859 61,44 (9,57)	819 61,31 (9,52)	717 61,17 (9,69)	739 62,75 (9,05)	396 62,46 (8,72)	-2,29 (0,19)	985 63,29 (8,86)	937 62,53 (9,24)	923 62,12 (9,35)	867 61,79 (9,35)	829 61,91 (9,50)	723 61,92 (9,42)	711 62,38 (9,42)	377 61,72 (9,26)	-1,43 (0,19)	-0,87 [-1,40;-0,33] 0,0015 -0,14 [-0,23;-0,06]
ECOG-PS (p-Wert des Interaktionsterms: 0,5645)																			
ECOG-PS 0	933 63,71 (8,67)	878 61,54 (9,39)	853 61,45 (9,78)	814 61,01 (9,75)	780 60,88 (9,81)	692 60,83 (9,93)	704 62,20 (9,35)	382 62,02 (9,14)	-2,42 (0,20)	897 63,31 (8,71)	855 62,45 (9,11)	844 61,89 (9,37)	792 61,65 (9,32)	758 61,73 (9,44)	671 61,74 (9,58)	663 62,05 (9,48)	352 61,28 (9,35)	-1,58 (0,20)	-0,84 [-1,39;-0,28] 0,0030 -0,14 [-0,23;-0,05]
ECOG-PS 1	174 63,63 (8,69)	166 61,09 (9,43)	157 62,17 (9,08)	141 62,23 (9,18)	133 61,17 (9,84)	115 59,91 (10,16)	126 62,83 (9,30)	69 61,72 (8,77)	-1,73 (0,48)	212 62,18 (9,50)	204 62,11 (9,73)	198 61,89 (9,57)	185 61,41 (10,15)	174 61,48 (9,54)	146 61,82 (9,29)	140 62,97 (8,94)	81 62,60 (8,64)	-0,62 (0,43)	-1,11 [-2,37;0,15] 0,0853 -0,18 [-0,38;0,02]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-ES 19 Score = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-ES 19 Score haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-ES: Functional Assessment of Cancer Therapy - Endokrine Symptome; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t113_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des ESS 18 aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,2810)																			
Neoadjuvante Chemotherapie	196 58,23 (8,59)	189 55,46 (9,20)	181 54,71 (10,76)	176 54,65 (11,31)	165 53,95 (11,09)	149 54,20 (11,20)	146 56,18 (10,60)	75 56,51 (9,66)	-3,24 (0,49)	193 57,21 (9,08)	181 55,71 (9,25)	179 56,71 (9,08)	156 56,54 (9,44)	146 56,16 (9,60)	120 56,23 (9,71)	135 56,13 (9,88)	77 57,01 (9,11)	-1,67 (0,50)	-1,57 [-2,94;-0,20] 0,0251 -0,23 [-0,43;-0,03]
Adjuvante Chemotherapie	288 57,09 (9,10)	273 54,14 (10,30)	270 53,97 (10,52)	266 53,71 (10,42)	254 53,18 (10,99)	214 53,58 (11,34)	205 55,45 (9,50)	128 53,51 (10,78)	-3,05 (0,38)	284 57,18 (8,98)	275 56,36 (9,25)	269 56,07 (9,24)	261 55,94 (9,44)	240 54,98 (10,25)	221 54,76 (10,81)	219 55,51 (10,55)	121 54,88 (10,70)	-1,57 (0,39)	-1,48 [-2,55;-0,41] 0,0067 -0,23 [-0,39;-0,06]
Keine Chemotherapie	7 63,86 (10,29)	7 56,86 (11,39)	6 54,67 (12,23)	6 56,00 (10,95)	5 54,60 (9,34)	5 54,80 (8,23)	6 60,00 (7,80)	2 65,00 (1,41)	-4,91 (1,96)	1 60,00 (NE)	1 46,00 (NE)	1 51,00 (NE)	1 47,00 (NE)	1 51,00 (NE)	1 42,00 (NE)	1 46,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,0690)																			
Nordamerika / Europa	204 57,59 (8,48)	188 54,29 (9,42)	181 53,82 (10,29)	178 53,68 (10,51)	162 53,35 (10,62)	139 53,88 (10,95)	134 56,53 (9,84)	75 55,73 (9,65)	-2,98 (0,45)	197 56,42 (9,39)	183 55,28 (9,84)	176 56,15 (9,21)	155 56,23 (9,62)	142 55,06 (10,36)	132 54,08 (11,25)	132 54,76 (10,80)	66 56,02 (10,59)	-1,03 (0,46)	-1,95 [-3,21;-0,69] 0,0025 -0,30 [-0,50;-0,11]
Asien	163 58,40 (8,21)	162 54,60 (9,48)	159 53,74 (9,96)	156 53,40 (10,35)	150 52,87 (10,46)	130 53,09 (10,71)	137 55,50 (9,56)	69 55,12 (10,55)	-4,42 (0,51)	153 58,90 (7,62)	151 57,57 (8,19)	151 57,14 (8,72)	146 56,64 (8,75)	137 56,14 (8,89)	120 56,88 (9,38)	122 56,64 (9,78)	66 56,55 (9,51)	-2,34 (0,53)	-2,08 [-3,53;-0,64] 0,0049 -0,32 [-0,54;-0,10]
Andere	124 56,74 (10,48)	119 55,55 (11,12)	117 55,70 (11,87)	114 55,77 (11,64)	112 54,54 (12,19)	99 54,81 (12,28)	86 55,24 (10,72)	61 53,02 (11,24)	-1,71 (0,64)	128 56,37 (9,70)	123 55,46 (9,40)	122 55,53 (9,62)	117 55,40 (10,01)	108 54,96 (10,85)	90 54,77 (10,44)	101 55,86 (10,19)	66 54,56 (10,34)	-1,57 (0,63)	-0,14 [-1,90;1,62] 0,8776 -0,02 [-0,27;0,23]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,5323)																			
< 20 mm	121 57,74 (8,91)	115 55,29 (8,98)	109 53,62 (10,32)	112 52,65 (10,78)	105 52,55 (10,87)	93 50,68 (11,92)	90 54,42 (9,79)	54 55,46 (8,37)	-4,04 (0,56)	123 55,91 (8,71)	116 55,08 (9,40)	116 54,72 (9,15)	107 54,10 (9,78)	101 53,69 (9,92)	86 53,99 (10,46)	85 55,15 (10,28)	50 55,22 (10,04)	-2,14 (0,56)	-1,90 [-3,46;-0,35] 0,0166 -0,31 [-0,56;-0,06]
≥ 20 bis < 50 mm	230 57,53 (8,83)	220 54,08 (10,89)	219 54,38 (10,74)	214 54,52 (10,88)	197 53,69 (11,33)	171 55,03 (10,86)	165 56,56 (9,78)	97 55,06 (11,75)	-2,83 (0,46)	227 57,07 (9,37)	218 55,99 (9,43)	217 56,45 (9,59)	201 56,52 (9,44)	187 55,55 (10,47)	172 55,18 (10,87)	181 55,75 (10,64)	93 55,77 (10,29)	-1,20 (0,47)	-1,63 [-2,93;-0,33] 0,0138 -0,23 [-0,42;-0,05]
≥ 50 mm	128 57,73 (9,46)	124 55,25 (9,11)	120 54,55 (10,91)	114 54,72 (10,62)	113 53,65 (10,69)	95 54,56 (10,85)	93 55,74 (10,53)	48 53,02 (10,21)	-3,03 (0,55)	123 58,55 (8,61)	118 57,06 (8,85)	111 57,50 (8,15)	105 56,99 (8,71)	96 56,67 (8,89)	80 56,33 (9,60)	85 55,80 (9,56)	51 55,51 (10,21)	-2,08 (0,56)	-0,95 [-2,49;0,60] 0,2299 -0,15 [-0,40;0,10]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,2509)																			
0-3	177 57,99 (8,90)	168 54,96 (9,10)	161 54,76 (9,83)	158 54,25 (10,57)	144 54,05 (10,69)	129 54,12 (10,90)	131 56,12 (9,88)	77 56,25 (9,12)	-3,03 (0,48)	190 57,14 (8,45)	180 56,02 (8,70)	176 56,10 (8,69)	164 55,73 (8,41)	156 54,47 (9,36)	134 54,43 (9,05)	134 54,45 (9,64)	71 54,75 (9,92)	-2,42 (0,46)	-0,61 [-1,92;0,70] 0,3633 -0,10 [-0,30;0,11]
4-9	216 56,89 (9,51)	207 53,72 (10,92)	204 53,16 (11,49)	198 53,29 (11,06)	193 52,47 (11,09)	169 53,25 (11,36)	158 55,78 (10,04)	85 54,06 (11,68)	-3,32 (0,47)	210 57,13 (9,64)	201 56,22 (9,23)	200 56,58 (9,38)	186 56,54 (9,77)	173 55,89 (10,24)	153 55,55 (11,33)	160 56,36 (10,80)	87 56,18 (10,58)	-0,99 (0,48)	-2,33 [-3,64;-1,02] 0,0005 -0,34 [-0,53;-0,15]
≥ 10	98 58,67 (7,58)	94 56,45 (8,58)	92 55,88 (9,73)	92 55,66 (10,41)	87 54,85 (11,20)	70 54,79 (11,58)	68 55,34 (9,96)	43 53,28 (10,02)	-3,04 (0,65)	78 57,51 (8,62)	76 55,88 (10,58)	73 56,11 (9,78)	68 56,06 (10,83)	58 56,52 (10,90)	55 56,35 (11,15)	61 56,82 (10,16)	40 56,38 (9,66)	-1,42 (0,73)	-1,62 [-3,55;0,31] 0,0987 -0,25 [-0,55;0,05]
Tumorstadium (p-Wert des Interaktionsterms: 0,3963)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 57,44 (9,99)	49 54,80 (9,44)	48 52,79 (10,44)	47 52,00 (10,91)	46 51,26 (11,27)	39 50,64 (12,24)	39 53,54 (10,50)	23 55,26 (9,23)	-4,80 (0,81)	57 55,82 (8,42)	54 55,35 (8,37)	54 56,04 (7,64)	48 54,56 (8,32)	47 54,70 (6,87)	35 54,66 (9,20)	37 55,92 (9,86)	19 56,47 (8,27)	-1,60 (0,79)	-3,20 [-5,45;-0,95] 0,0057 -0,54 [-0,92;-0,16]
IIB	45 57,44 (8,02)	44 54,61 (10,12)	41 56,76 (8,52)	42 55,43 (10,39)	35 55,57 (9,42)	34 55,21 (9,69)	31 57,35 (9,89)	22 57,27 (9,38)	-2,25 (1,09)	64 57,30 (8,63)	61 55,80 (9,19)	61 55,16 (9,46)	56 55,45 (8,65)	55 53,13 (10,08)	54 52,93 (9,56)	54 52,91 (9,85)	32 53,91 (9,95)	-3,57 (0,90)	1,32 [-1,49;4,12] 0,3539 0,18 [-0,20;0,56]
IIIA	213 56,92 (9,66)	207 53,73 (10,90)	202 53,13 (11,69)	196 53,38 (10,85)	190 52,76 (11,28)	165 53,21 (11,30)	157 55,68 (9,84)	86 54,64 (11,09)	-3,12 (0,46)	192 56,97 (9,41)	182 55,97 (8,99)	179 56,40 (9,01)	172 56,45 (9,26)	158 55,77 (9,80)	131 55,04 (10,90)	140 55,91 (10,24)	70 54,76 (11,16)	-1,13 (0,49)	-1,99 [-3,32;-0,66] 0,0034 -0,29 [-0,49;-0,10]
IIIB	14 53,57 (12,68)	13 52,92 (8,74)	13 51,85 (10,90)	13 52,00 (11,88)	10 46,30 (7,13)	8 49,63 (11,81)	11 54,64 (12,02)	6 47,50 (12,63)	-2,45 (1,77)	14 61,50 (7,14)	14 61,71 (8,00)	14 61,57 (6,99)	11 60,36 (7,58)	9 61,33 (10,36)	10 62,90 (3,90)	9 61,78 (6,63)	5 60,80 (5,22)	1,30 (1,82)	-3,75 [-9,39;1,88] 0,1769 -0,54 [-1,28;0,19]
IIIC	166 59,02 (7,27)	155 56,18 (8,49)	152 55,83 (9,43)	149 55,52 (10,58)	142 55,17 (10,82)	121 55,66 (10,99)	118 56,47 (9,77)	67 54,49 (10,19)	-3,04 (0,49)	150 57,54 (8,99)	145 56,04 (9,94)	140 56,19 (9,81)	130 56,16 (10,39)	118 55,84 (11,07)	112 56,09 (10,82)	115 56,27 (10,71)	72 56,88 (9,82)	-1,61 (0,51)	-1,44 [-2,83;-0,05] 0,0422 -0,23 [-0,45;-0,01]
Tumorgrading (p-Wert des Interaktionsterms: 0,2360)																			
G1	45 60,16 (6,98)	43 58,51 (6,83)	40 56,48 (8,53)	40 56,28 (8,22)	39 56,03 (9,01)	33 55,52 (10,83)	33 57,42 (8,29)	18 55,11 (12,84)	-2,07 (1,12)	38 56,11 (9,49)	36 55,42 (9,47)	34 53,32 (10,37)	36 53,64 (11,04)	31 52,42 (11,95)	28 52,25 (12,32)	25 53,20 (11,32)	13 54,00 (10,38)	-3,19 (1,22)	1,12 [-2,21;4,46] 0,5041 0,15 [-0,28;0,58]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	213 57,27 (9,12)	202 54,62 (9,54)	201 53,86 (10,80)	196 53,44 (11,06)	188 53,36 (10,91)	165 53,07 (11,38)	166 55,31 (10,08)	87 54,99 (9,92)	-3,15 (0,42)	208 57,47 (9,35)	200 56,79 (9,83)	197 57,50 (8,77)	183 56,87 (9,60)	163 56,36 (10,08)	148 56,03 (10,89)	155 56,63 (10,43)	87 55,51 (10,09)	-0,91 (0,43)	-2,24 [-3,42;-1,07] 0,0002 -0,37 [-0,56;-0,17]
G3	205 57,12 (9,23)	196 53,82 (10,56)	191 54,14 (10,64)	187 54,25 (10,84)	172 52,75 (11,32)	148 53,93 (11,44)	138 55,72 (10,09)	87 53,32 (10,58)	-3,16 (0,49)	202 56,79 (8,76)	193 55,28 (8,78)	191 55,47 (9,33)	172 55,67 (9,09)	167 54,53 (9,68)	141 54,66 (9,57)	151 54,78 (10,13)	85 55,87 (10,53)	-2,13 (0,50)	-1,03 [-2,40;0,35] 0,1431 -0,15 [-0,34;0,05]
GX	28 60,29 (7,44)	28 55,79 (10,41)	25 55,16 (12,03)	25 54,92 (11,62)	25 55,64 (11,94)	22 56,73 (8,96)	20 58,15 (10,29)	13 61,69 (7,05)	-4,17 (1,07)	29 59,97 (6,90)	27 57,85 (7,29)	26 57,69 (8,16)	26 57,73 (7,75)	25 59,24 (7,29)	24 57,63 (10,07)	24 58,33 (8,57)	13 57,69 (8,20)	-2,13 (1,04)	-2,04 [-5,03;0,95] 0,1768 -0,36 [-0,89;0,16]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,4377)																			
Negativ	46 55,83 (9,99)	43 52,19 (10,71)	40 51,23 (12,28)	42 51,36 (13,62)	39 49,82 (13,23)	38 51,24 (12,22)	36 50,86 (11,50)	12 51,92 (11,57)	-4,77 (1,07)	39 55,05 (8,61)	36 53,33 (8,95)	35 54,94 (8,28)	30 54,47 (7,76)	31 54,45 (8,86)	25 54,12 (7,45)	31 54,29 (9,05)	15 56,47 (10,01)	-0,12 (1,14)	-4,65 [-7,77;-1,53] 0,0040 -0,65 [-1,08;-0,21]
Positiv	427 57,70 (8,91)	409 54,81 (9,88)	402 54,46 (10,49)	392 54,33 (10,53)	372 53,80 (10,79)	319 54,07 (11,20)	305 56,17 (9,73)	183 54,63 (10,48)	-3,02 (0,32)	422 57,42 (9,04)	406 56,39 (9,09)	400 56,53 (9,17)	374 56,23 (9,49)	341 55,39 (10,11)	304 55,39 (10,60)	314 55,90 (10,36)	176 55,41 (10,27)	-1,77 (0,32)	-1,25 [-2,14;-0,36] 0,0060 -0,19 [-0,32;-0,05]
Unbekannt	2 64,00 (5,66)	2 57,00 (11,31)	2 61,00 (5,66)	1 63,00 (NE)	1 61,00 (NE)	1 65,00 (NE)	1 65,00 (NE)	0	NE	8 54,88 (10,80)	7 50,43 (16,29)	8 52,75 (12,67)	6 54,50 (15,53)	6 56,00 (14,14)	8 49,88 (13,98)	4 47,75 (15,97)	2 63,50 (7,78)	0,78 (3,59)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,8046)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	276 56,76 (9,42)	261 53,95 (10,02)	251 53,59 (10,85)	245 53,47 (10,76)	230 52,97 (11,06)	200 53,50 (11,31)	183 55,43 (10,16)	120 53,93 (10,53)	-2,91 (0,40)	285 55,94 (9,52)	267 54,93 (9,66)	261 55,26 (9,38)	241 55,21 (9,77)	224 54,31 (10,31)	200 53,57 (10,97)	209 54,44 (10,40)	122 54,79 (10,23)	-1,48 (0,39)	-1,43 [-2,53;-0,32] 0,0113 -0,21 [-0,38;-0,05]
Asiatisch	188 58,84 (8,17)	185 55,71 (9,65)	182 55,05 (10,23)	179 54,96 (10,68)	171 54,21 (10,72)	149 54,31 (10,96)	153 56,24 (9,53)	75 55,59 (10,40)	-3,50 (0,49)	166 59,17 (7,81)	164 57,74 (8,35)	162 57,60 (8,85)	157 57,34 (8,92)	144 56,55 (9,10)	124 56,98 (9,48)	130 56,79 (9,79)	67 56,66 (9,47)	-2,13 (0,52)	-1,36 [-2,78;0,05] 0,0585 -0,20 [-0,41;0,01]
Andere	16 57,63 (9,39)	15 55,87 (7,91)	15 54,93 (11,39)	15 53,20 (11,94)	15 52,67 (12,09)	13 53,38 (13,27)	14 55,86 (11,43)	9 57,89 (10,43)	-3,78 (1,74)	17 57,12 (7,24)	16 58,19 (6,59)	17 58,06 (7,91)	16 57,69 (8,60)	14 59,00 (12,78)	12 61,00 (5,74)	12 63,33 (9,38)	7 62,71 (11,98)	0,93 (1,73)	-4,71 [-9,78;0,35] 0,0669 -0,65 [-1,34;0,03]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des ESS 18 Score = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des ESS 18 Score haben.
Abkürzungen: B: Baseline; ET: Endokrine Therapie; ESS: Endocrine symptom scale; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t114_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des ESS 18 aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,0916)																			
< 65 Jahre	804 60,13 (8,29)	759 57,71 (9,01)	744 57,61 (9,39)	700 57,59 (9,42)	675 57,53 (9,41)	589 57,21 (9,66)	603 58,79 (8,89)	330 59,06 (8,75)	-2,28 (0,21)	831 59,49 (8,46)	792 59,09 (8,83)	783 58,49 (9,10)	730 58,27 (9,16)	692 58,57 (9,09)	609 58,64 (9,14)	606 59,14 (9,03)	318 58,36 (8,80)	-1,04 (0,21)	-1,24 [-1,82;-0,67] <,0001 -0,21 [-0,31;-0,11]
≥ 65 Jahre	303 63,55 (6,47)	285 61,69 (7,06)	266 62,55 (6,51)	255 61,50 (7,00)	238 61,03 (7,62)	218 61,24 (7,38)	227 62,78 (7,03)	121 61,72 (6,89)	-1,89 (0,27)	278 63,81 (6,40)	267 62,78 (6,78)	259 62,95 (6,17)	247 62,76 (6,39)	240 62,00 (6,96)	208 61,98 (7,17)	197 62,04 (6,82)	115 61,50 (7,31)	-1,41 (0,28)	-0,48 [-1,23;0,27] 0,2101 -0,10 [-0,27;0,06]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,6280)																			
Neoadjuvante Chemotherapie	363 61,72 (7,91)	335 58,87 (8,84)	324 59,40 (8,80)	302 58,97 (8,74)	279 58,66 (9,10)	234 58,68 (8,97)	254 60,46 (8,03)	130 60,21 (7,66)	-2,40 (0,31)	365 60,18 (8,38)	347 59,75 (8,78)	331 59,05 (8,70)	310 58,92 (8,91)	290 59,30 (8,78)	244 59,12 (9,28)	259 59,73 (9,07)	138 58,76 (9,01)	-1,22 (0,31)	-1,18 [-2,03;-0,33] 0,0068 -0,20 [-0,35;-0,06]
Adjuvante Chemotherapie	685 60,60 (8,09)	655 58,67 (8,62)	635 58,42 (9,15)	602 58,29 (9,16)	588 58,21 (9,19)	533 57,99 (9,44)	531 59,35 (8,99)	295 59,30 (8,79)	-2,02 (0,22)	678 60,59 (7,99)	649 59,91 (8,27)	652 59,57 (8,62)	613 59,34 (8,65)	596 59,23 (8,75)	528 59,33 (8,66)	498 59,60 (8,46)	269 59,13 (8,32)	-1,18 (0,22)	-0,84 [-1,44;-0,24] 0,0061 -0,15 [-0,26;-0,04]
Keine Chemotherapie	59 62,51 (6,70)	54 59,89 (8,92)	51 61,82 (7,46)	51 60,71 (8,50)	46 60,02 (8,05)	40 60,18 (8,55)	45 62,89 (5,89)	26 63,00 (5,87)	-2,22 (0,53)	66 62,62 (9,16)	63 62,68 (9,11)	59 62,98 (8,62)	54 63,02 (8,51)	46 63,22 (7,21)	45 63,31 (6,91)	46 63,20 (7,12)	26 62,15 (7,80)	-0,40 (0,51)	-1,82 [-3,29;-0,35] 0,0160 -0,44 [-0,79;-0,08]
Region (p-Wert des Interaktionsterms: 0,0808)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	548 60,50 (8,26)	496 57,58 (9,21)	481 57,85 (9,19)	447 58,02 (9,14)	419 57,39 (9,50)	375 57,36 (9,86)	392 58,61 (9,20)	211 58,83 (8,96)	-2,73 (0,23)	527 59,64 (8,57)	490 58,90 (9,09)	479 58,31 (9,04)	441 58,17 (9,15)	421 57,98 (9,16)	373 58,33 (9,12)	344 58,49 (9,18)	201 58,54 (9,21)	-1,52 (0,24)	-1,21 [-1,86;-0,55] 0,0003 -0,22 [-0,34;-0,10]
Asien	195 63,02 (6,65)	190 60,87 (7,60)	185 59,99 (8,88)	178 59,50 (8,87)	173 59,25 (9,03)	152 58,74 (8,99)	163 61,04 (8,02)	87 59,78 (8,01)	-2,78 (0,40)	193 63,04 (6,76)	190 62,43 (7,45)	188 62,45 (7,28)	180 61,54 (8,26)	176 61,87 (7,56)	149 61,34 (7,73)	155 62,37 (7,01)	81 60,35 (7,85)	-0,84 (0,41)	-1,94 [-3,06;-0,81] 0,0008 -0,34 [-0,54;-0,14]
Andere	364 60,88 (8,06)	358 59,38 (8,29)	344 59,80 (8,61)	330 59,00 (8,86)	321 59,38 (8,48)	280 59,33 (8,47)	275 61,00 (7,79)	153 61,07 (7,57)	-0,99 (0,30)	389 60,62 (8,12)	379 60,27 (7,97)	375 59,81 (8,53)	356 59,86 (8,28)	335 60,02 (8,39)	295 60,02 (8,72)	304 60,09 (8,43)	151 59,46 (7,90)	-0,76 (0,29)	-0,24 [-1,05;0,57] 0,5679 -0,04 [-0,18;0,10]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2765)																			
< 20 mm	280 59,83 (8,61)	258 57,88 (9,15)	254 57,53 (9,73)	245 57,58 (9,64)	235 57,45 (9,44)	210 57,28 (10,00)	210 58,93 (9,17)	106 58,65 (8,75)	-2,33 (0,34)	297 60,45 (8,46)	284 59,91 (8,79)	275 60,18 (8,82)	259 59,78 (9,28)	250 59,41 (9,34)	214 59,61 (9,20)	219 59,92 (9,15)	108 59,19 (8,62)	-0,80 (0,33)	-1,53 [-2,46;-0,61] 0,0012 -0,27 [-0,43;-0,11]
≥ 20 bis < 50 mm	569 61,24 (7,96)	547 59,06 (8,58)	521 59,23 (9,12)	502 58,88 (9,00)	476 58,83 (9,03)	424 58,87 (9,21)	433 60,27 (8,72)	232 59,97 (8,57)	-1,94 (0,24)	572 60,55 (7,99)	549 60,07 (8,51)	543 59,75 (8,39)	511 59,31 (8,84)	492 59,57 (8,53)	437 59,40 (8,85)	417 59,97 (8,59)	231 59,35 (8,18)	-1,11 (0,24)	-0,83 [-1,50;-0,17] 0,0143 -0,15 [-0,26;-0,03]
≥ 50 mm	241 61,90 (7,25)	224 58,99 (8,57)	219 59,62 (7,73)	195 59,19 (8,09)	188 58,56 (8,97)	160 57,91 (8,51)	173 59,96 (7,64)	105 60,37 (7,62)	-2,37 (0,36)	229 60,57 (8,46)	215 59,75 (8,23)	214 58,28 (9,22)	197 58,99 (7,92)	183 59,04 (8,41)	158 59,31 (8,20)	159 59,25 (8,01)	90 58,46 (9,34)	-1,74 (0,37)	-0,63 [-1,64;0,37] 0,2168 -0,11 [-0,30;0,07]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9268)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	368 60,43 (8,51)	348 57,88 (9,01)	337 58,32 (9,25)	314 58,59 (8,90)	305 58,07 (9,38)	273 57,66 (9,48)	285 58,89 (9,08)	166 59,38 (8,47)	-2,06 (0,29)	359 60,21 (8,07)	343 59,54 (8,33)	339 59,07 (8,36)	313 59,26 (8,41)	301 59,47 (8,29)	258 59,25 (8,35)	255 59,78 (8,26)	142 59,44 (9,10)	-1,02 (0,30)	-1,04 [-1,85;-0,22] 0,0132 -0,18 [-0,33;-0,04]
4-9	475 61,14 (7,89)	447 59,06 (8,69)	435 58,81 (9,12)	418 58,56 (9,22)	395 58,61 (9,15)	353 58,54 (9,44)	357 60,29 (8,47)	176 59,60 (8,79)	-2,26 (0,27)	486 60,52 (8,42)	466 60,00 (8,85)	465 59,61 (9,07)	440 59,34 (9,36)	419 59,25 (9,28)	376 59,34 (9,25)	358 59,86 (9,18)	191 59,35 (8,06)	-1,13 (0,26)	-1,13 [-1,87;-0,39] 0,0028 -0,19 [-0,32;-0,07]
≥ 10	264 61,83 (7,31)	249 59,61 (8,22)	238 59,92 (8,29)	223 58,85 (8,78)	213 58,66 (8,64)	181 58,80 (8,56)	188 60,59 (7,99)	109 60,67 (7,48)	-2,17 (0,33)	264 61,16 (7,98)	250 60,72 (8,10)	238 60,34 (8,34)	224 59,74 (8,02)	212 59,83 (8,18)	183 60,13 (8,48)	190 59,92 (8,05)	100 58,56 (8,65)	-1,37 (0,33)	-0,80 [-1,73;0,12] 0,0896 -0,15 [-0,32;0,02]
Tumorstadium (p-Wert des Interaktionsterms: 0,6625)																			
IIA	93 58,61 (8,99)	88 57,42 (9,01)	86 56,74 (9,70)	81 56,75 (9,92)	81 56,26 (9,64)	76 56,33 (10,22)	76 57,51 (9,88)	39 58,05 (9,11)	-1,82 (0,56)	95 59,22 (8,63)	92 58,98 (8,41)	89 58,93 (8,65)	85 59,69 (7,84)	79 59,44 (8,00)	70 59,04 (7,89)	74 59,41 (7,85)	37 59,46 (7,57)	-0,10 (0,55)	-1,72 [-3,26;-0,17] 0,0297 -0,32 [-0,61;-0,03]
IIB	133 61,01 (9,03)	125 58,37 (9,36)	117 59,35 (9,31)	116 59,34 (9,16)	113 59,09 (9,59)	100 57,99 (10,31)	110 59,80 (9,55)	68 59,76 (8,84)	-2,16 (0,51)	112 61,34 (7,40)	106 59,67 (8,88)	105 59,89 (7,68)	98 58,24 (9,69)	93 58,89 (8,41)	84 58,70 (9,11)	80 59,19 (9,02)	44 58,11 (10,21)	-2,51 (0,56)	0,35 [-1,14;1,84] 0,6465 0,06 [-0,19;0,31]
IIIA	430 60,95 (7,83)	407 58,88 (8,63)	394 58,70 (8,94)	373 58,27 (9,21)	349 58,43 (9,12)	312 58,40 (9,25)	321 59,81 (8,27)	158 58,94 (8,97)	-2,16 (0,28)	436 60,58 (7,96)	414 60,07 (8,24)	421 59,48 (8,85)	396 59,53 (8,59)	376 59,38 (8,66)	334 59,51 (8,69)	316 60,07 (8,65)	172 59,28 (7,92)	-1,05 (0,28)	-1,11 [-1,90;-0,33] 0,0054 -0,19 [-0,32;-0,06]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIB	47 62,09 (9,12)	45 60,29 (9,86)	45 60,62 (10,17)	44 59,73 (9,43)	41 60,44 (9,03)	36 59,28 (10,71)	31 60,58 (9,71)	15 62,40 (7,05)	-1,24 (0,68)	41 61,98 (8,64)	40 61,68 (8,69)	39 60,97 (8,41)	34 61,97 (8,50)	34 61,44 (8,28)	31 61,90 (6,66)	30 62,67 (6,48)	14 62,64 (6,32)	0,09 (0,73)	-1,33 [-3,32;0,66] 0,1864 -0,28 [-0,71;0,14]
IIIC	402 61,62 (7,28)	378 58,97 (8,35)	366 59,28 (8,58)	339 59,08 (8,40)	327 58,50 (8,77)	281 58,67 (8,41)	290 60,49 (8,05)	169 60,65 (7,41)	-2,34 (0,28)	423 60,52 (8,51)	405 60,14 (8,72)	386 59,66 (8,83)	362 59,31 (8,92)	348 59,50 (9,09)	296 59,53 (9,25)	302 59,65 (8,85)	165 58,98 (9,02)	-1,16 (0,27)	-1,18 [-1,94;-0,43] 0,0022 -0,21 [-0,35;-0,08]
Tumorgrading (p-Wert des Interaktionsterms: 0,8541)																			
G1	82 60,21 (7,96)	80 59,86 (8,31)	81 58,41 (10,00)	74 58,89 (8,92)	71 58,32 (9,99)	65 58,38 (8,51)	62 60,24 (7,48)	31 57,65 (8,74)	-1,39 (0,63)	84 62,08 (7,90)	82 62,07 (7,69)	79 61,47 (7,52)	70 60,66 (8,25)	73 60,68 (8,42)	63 61,73 (7,66)	55 60,91 (7,93)	34 61,09 (5,72)	-0,80 (0,62)	-0,59 [-2,34;1,15] 0,5028 -0,10 [-0,41;0,20]
G2	525 61,33 (7,78)	498 58,57 (8,89)	479 58,98 (8,94)	452 58,45 (9,02)	430 58,39 (8,93)	371 58,55 (9,17)	374 60,22 (8,28)	212 60,19 (8,26)	-2,28 (0,25)	532 59,91 (8,42)	504 59,49 (8,52)	503 58,72 (9,02)	477 58,72 (9,02)	446 58,69 (9,02)	402 58,55 (8,91)	391 59,08 (8,71)	211 58,40 (8,23)	-1,34 (0,24)	-0,94 [-1,63;-0,26] 0,0069 -0,17 [-0,29;-0,05]
G3	451 60,90 (8,30)	422 58,79 (8,65)	405 58,88 (8,82)	383 58,72 (8,89)	370 58,32 (9,17)	332 57,96 (9,44)	357 59,24 (9,29)	186 59,74 (8,39)	-2,13 (0,27)	435 60,66 (8,07)	415 59,82 (8,55)	404 59,72 (8,58)	379 59,56 (8,65)	364 59,75 (8,48)	313 59,84 (8,94)	316 60,33 (8,68)	165 59,74 (9,25)	-1,02 (0,28)	-1,11 [-1,87;-0,35] 0,0042 -0,19 [-0,32;-0,06]
GX	47 61,85 (6,67)	42 60,10 (7,32)	43 59,91 (9,08)	44 60,23 (9,29)	40 61,28 (7,68)	37 60,03 (8,58)	37 62,00 (5,92)	22 59,14 (8,85)	-2,10 (0,69)	54 64,35 (5,90)	54 63,39 (8,24)	53 64,17 (5,73)	48 62,94 (6,80)	46 62,39 (7,41)	37 62,86 (6,72)	39 62,33 (7,40)	21 60,71 (9,06)	-1,26 (0,65)	-0,84 [-2,73;1,05] 0,3817 -0,18 [-0,57;0,22]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,3069)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Negativ	137 61,07 (7,91)	132 58,63 (8,70)	124 58,60 (9,65)	116 58,29 (9,22)	107 58,78 (8,76)	93 58,35 (9,16)	100 60,26 (8,07)	63 58,70 (8,57)	-2,36 (0,44)	148 60,95 (7,90)	138 60,79 (8,62)	133 60,50 (8,12)	126 59,81 (8,66)	121 59,77 (9,02)	102 59,30 (8,81)	114 59,11 (8,32)	56 58,95 (8,52)	-1,20 (0,43)	-1,16 [-2,37;0,06] 0,0613 -0,22 [-0,46;0,01]
Positiv	939 60,96 (8,02)	881 58,66 (8,70)	855 58,78 (8,94)	814 58,51 (9,00)	782 58,27 (9,20)	690 58,11 (9,29)	708 59,74 (8,73)	377 59,97 (8,31)	-2,19 (0,19)	934 60,52 (8,25)	897 59,91 (8,46)	885 59,46 (8,75)	829 59,35 (8,74)	790 59,42 (8,67)	694 59,54 (8,81)	668 60,00 (8,67)	363 59,18 (8,51)	-1,14 (0,19)	-1,05 [-1,57;-0,53] <,0001 -0,18 [-0,27;-0,09]
Unbekannt	9 63,44 (4,93)	9 59,44 (11,77)	9 63,44 (6,62)	7 66,86 (4,53)	5 66,60 (5,77)	6 64,00 (8,44)	5 65,40 (4,98)	1 66,00 (NE)	2,38 (1,74)	7 61,00 (8,49)	6 66,00 (6,16)	6 61,00 (7,13)	6 65,00 (4,34)	6 63,67 (4,63)	6 62,50 (6,80)	5 62,80 (5,54)	5 63,60 (4,39)	2,85 (1,88)	-0,47 [-6,19;5,25] 0,8588 -0,09 [-1,02;0,85]
Ethnizität (p-Wert des Interaktionsterms: 0,0609)																			
Weiß	808 60,35 (8,23)	755 57,95 (8,83)	735 58,30 (8,87)	693 58,11 (8,90)	660 57,71 (9,04)	585 57,83 (9,21)	599 59,11 (8,68)	340 59,62 (8,30)	-2,19 (0,19)	817 60,03 (8,34)	772 59,42 (8,60)	759 58,92 (8,77)	705 58,61 (8,90)	674 58,66 (8,83)	597 58,94 (8,97)	579 59,04 (8,93)	320 58,77 (8,67)	-1,25 (0,19)	-0,94 [-1,48;-0,41] 0,0006 -0,17 [-0,27;-0,07]
Asiatisch	233 63,37 (6,83)	225 61,48 (7,70)	218 60,92 (8,90)	210 60,58 (8,84)	205 60,42 (8,99)	176 59,55 (9,02)	187 61,52 (7,91)	97 60,05 (8,18)	-2,23 (0,38)	222 62,69 (6,98)	218 62,42 (7,40)	216 62,55 (7,40)	208 61,85 (8,18)	201 62,18 (7,59)	167 61,56 (7,78)	172 62,54 (7,07)	88 60,69 (7,80)	-0,48 (0,39)	-1,75 [-2,83;-0,68] 0,0014 -0,30 [-0,49;-0,12]
Andere	54 62,26 (6,60)	52 60,48 (8,06)	48 59,69 (9,05)	44 59,20 (8,60)	42 60,74 (8,30)	36 60,83 (8,21)	38 64,29 (6,18)	13 62,00 (11,75)	-1,10 (0,92)	57 60,63 (9,31)	57 59,33 (9,97)	55 58,53 (9,89)	52 60,33 (8,13)	46 58,93 (10,06)	42 59,29 (9,06)	43 60,91 (8,02)	19 59,32 (9,20)	-2,50 (0,88)	1,40 [-1,13;3,93] 0,2741 0,21 [-0,16;0,58]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,6266)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Tamoxifen	104 58,54 (7,97)	99 56,03 (9,06)	98 56,20 (9,59)	96 56,10 (9,66)	94 54,90 (10,71)	90 54,48 (10,60)	91 56,07 (10,03)	55 56,42 (10,01)	-2,64 (0,59)	124 58,95 (8,15)	122 58,63 (8,27)	119 57,55 (8,88)	110 57,55 (9,41)	103 57,33 (8,17)	94 57,77 (9,48)	92 58,14 (8,39)	56 57,61 (8,14)	-1,23 (0,54)	-1,41 [-2,99;0,17] 0,0797 -0,23 [-0,50;0,03]
Aromatase-Inhibitor	1003 61,33 (7,94)	945 59,08 (8,62)	912 59,20 (8,88)	859 58,92 (8,89)	819 58,85 (8,82)	717 58,78 (8,98)	739 60,35 (8,29)	396 60,24 (8,02)	-2,12 (0,18)	985 60,78 (8,19)	937 60,20 (8,53)	923 59,86 (8,63)	867 59,64 (8,65)	829 59,71 (8,76)	723 59,71 (8,69)	711 60,07 (8,64)	377 59,43 (8,58)	-1,14 (0,18)	-0,98 [-1,48;-0,49] <,0001 -0,18 [-0,26;-0,09]
ECOG-PS (p-Wert des Interaktionsterms: 0,6606)																			
ECOG-PS 0	933 61,06 (7,97)	878 58,86 (8,69)	853 58,80 (9,10)	814 58,45 (9,07)	780 58,39 (9,11)	692 58,42 (9,24)	704 59,79 (8,59)	382 59,80 (8,41)	-2,25 (0,18)	897 60,76 (8,05)	855 60,09 (8,41)	844 59,61 (8,64)	792 59,47 (8,62)	758 59,50 (8,71)	671 59,46 (8,86)	663 59,71 (8,71)	352 58,98 (8,66)	-1,30 (0,19)	-0,96 [-1,47;-0,45] 0,0003 -0,17 [-0,26;-0,08]
ECOG-PS 1	174 61,08 (8,04)	166 58,45 (8,82)	157 59,52 (8,37)	141 59,70 (8,56)	133 58,72 (9,13)	115 57,56 (9,46)	126 60,39 (8,67)	69 59,62 (8,19)	-1,65 (0,45)	212 59,79 (8,80)	204 59,75 (8,96)	198 59,56 (8,91)	185 59,14 (9,36)	174 59,24 (8,78)	146 59,60 (8,54)	140 60,51 (8,20)	81 60,14 (7,94)	-0,51 (0,40)	-1,13 [-2,31;0,05] 0,0598 -0,19 [-0,39;0,01]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des ESS 18 Score = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des ESS 18 Score haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; ESS: Endocrine symptom scale; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t114_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Anhang 4-G2.7: Gesundheitsbezogene Lebensqualität anhand FACT-B - Subgruppenanalysen

Tabelle 4-128 (Anhang): FACT-B - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen für die Veränderung des FACT-B (Gesamtscore) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,1311)																			
Neoadjuvante Chemotherapie	196 108,27 (16,60)	188 105,86 (18,63)	181 105,39 (20,16)	176 104,09 (20,51)	164 103,32 (19,50)	149 103,76 (20,77)	147 101,61 (20,84)	75 102,15 (21,16)	-4,19 (0,89)	193 106,44 (18,29)	181 106,06 (18,46)	178 107,85 (17,65)	155 109,01 (19,00)	144 110,10 (18,19)	120 109,89 (19,21)	135 106,36 (20,02)	77 106,04 (19,84)	0,18 (0,90)	-4,37 [-6,87;-1,87] 0,0006 -0,35 [-0,55;-0,15]
Adjuvante Chemotherapie	286 105,13 (17,07)	271 104,96 (17,86)	266 105,80 (18,90)	263 105,85 (18,39)	252 105,21 (18,95)	212 105,51 (19,65)	203 104,82 (19,29)	125 103,74 (17,58)	0,19 (0,68)	283 105,42 (16,57)	275 106,59 (17,69)	266 107,56 (17,06)	261 108,00 (17,93)	237 108,64 (17,45)	221 106,87 (18,05)	216 106,31 (18,32)	119 107,11 (17,53)	1,83 (0,68)	-1,64 [-3,52;0,25] 0,0882 -0,14 [-0,31;0,02]
Keine Chemotherapie	7 111,14 (28,33)	7 107,29 (24,59)	6 101,67 (23,61)	6 104,83 (25,73)	5 103,20 (26,83)	5 96,20 (26,62)	6 105,33 (23,34)	2 118,00 (16,97)	-4,54 (2,36)	1 116,00 (NE)	1 93,00 (NE)	1 93,00 (NE)	1 89,00 (NE)	1 89,00 (NE)	1 90,00 (NE)	1 97,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,5631)																			
Nordamerika / Europa	203 109,30 (15,86)	187 107,96 (17,45)	180 107,79 (18,90)	176 106,55 (19,12)	160 106,61 (18,79)	138 106,14 (20,62)	134 107,03 (19,30)	72 106,88 (18,13)	-2,04 (0,82)	197 107,78 (17,00)	183 106,67 (18,77)	172 109,02 (17,19)	154 109,66 (19,28)	137 111,30 (19,21)	132 109,63 (19,55)	131 107,11 (20,20)	65 108,52 (20,57)	0,37 (0,84)	-2,40 [-4,72;-0,09] 0,0414 -0,20 [-0,40;-0,01]
Asien	162 102,85 (17,07)	161 101,14 (17,27)	157 101,25 (17,96)	155 101,25 (18,71)	149 100,43 (18,02)	129 100,33 (19,16)	136 100,13 (19,41)	69 102,30 (18,55)	-2,18 (0,86)	152 104,00 (17,33)	150 104,23 (17,13)	151 104,46 (17,51)	146 106,45 (16,98)	137 106,13 (16,67)	120 105,57 (18,09)	121 103,88 (18,63)	65 105,63 (15,91)	0,60 (0,88)	-2,79 [-5,21;-0,36] 0,0244 -0,26 [-0,48;-0,03]
Andere	124 106,60 (18,33)	118 106,98 (19,82)	116 108,02 (21,24)	114 108,25 (19,76)	112 106,71 (20,66)	99 108,29 (20,08)	86 103,34 (21,31)	61 100,16 (19,98)	-0,22 (1,18)	128 105,10 (17,42)	124 108,42 (17,65)	122 109,63 (16,65)	117 108,94 (18,59)	108 110,20 (16,68)	90 108,41 (17,26)	100 108,18 (17,44)	66 105,92 (18,66)	2,89 (1,15)	-3,11 [-6,36;0,13] 0,0601 -0,24 [-0,49;0,01]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3728)																			
< 20 mm	121 106,02 (15,46)	115 104,81 (17,07)	109 103,66 (19,55)	110 103,20 (20,75)	105 103,73 (20,14)	93 101,84 (21,07)	91 102,20 (20,02)	53 104,04 (17,68)	-2,69 (1,06)	123 105,68 (18,12)	116 105,92 (18,91)	114 107,73 (16,18)	107 106,41 (18,03)	99 108,78 (17,60)	85 108,73 (17,99)	84 108,79 (17,79)	50 107,14 (19,81)	0,97 (1,06)	-3,66 [-6,62;-0,70] 0,0155 -0,31 [-0,56;-0,06]
≥ 20 bis < 50 mm	228 107,42 (17,42)	217 105,01 (19,56)	216 107,52 (19,36)	213 105,79 (19,12)	195 104,94 (19,24)	169 105,83 (19,44)	163 103,90 (19,80)	95 102,36 (20,85)	-1,62 (0,80)	227 104,85 (17,24)	218 105,72 (17,60)	216 107,64 (17,34)	200 109,06 (18,14)	185 109,07 (17,69)	172 106,83 (18,53)	180 105,25 (18,95)	93 106,33 (18,85)	1,63 (0,80)	-3,25 [-5,48;-1,01] 0,0045 -0,27 [-0,45;-0,08]
≥ 50 mm	128 105,52 (18,06)	124 106,26 (17,18)	119 103,84 (19,43)	114 105,67 (18,04)	112 103,79 (18,28)	95 105,18 (20,33)	93 104,40 (20,20)	48 103,92 (16,70)	-1,12 (1,01)	122 108,28 (16,33)	118 108,14 (17,87)	110 107,99 (18,43)	105 109,55 (18,96)	95 109,77 (17,98)	81 109,75 (19,24)	84 106,44 (19,94)	49 107,41 (16,16)	0,10 (1,04)	-1,22 [-4,08;1,65] 0,4038 -0,11 [-0,35;0,14]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,2825)																			
0-3	177 107,63 (16,62)	169 106,66 (17,89)	160 106,09 (19,68)	157 105,48 (19,59)	143 105,68 (18,72)	129 106,33 (21,38)	131 103,37 (20,95)	77 104,53 (17,71)	-1,71 (0,93)	190 106,68 (16,39)	181 107,80 (17,72)	175 108,58 (17,31)	163 108,78 (17,50)	154 108,05 (17,54)	136 107,99 (18,18)	135 105,79 (19,37)	71 106,79 (18,21)	0,63 (0,90)	-2,34 [-4,89;0,21] 0,0723 -0,19 [-0,39;0,02]
4-9	214 104,89 (18,08)	203 102,41 (19,07)	200 103,90 (19,48)	196 103,60 (19,59)	191 102,47 (19,31)	167 103,37 (19,80)	157 102,41 (20,05)	82 100,88 (20,78)	-2,17 (0,79)	210 105,81 (18,04)	201 105,96 (17,71)	197 106,93 (17,15)	186 107,91 (18,32)	170 110,23 (17,16)	151 108,29 (18,35)	159 106,36 (18,76)	86 106,73 (18,35)	1,20 (0,80)	-3,37 [-5,58;-1,16] 0,0029 -0,29 [-0,48;-0,10]
≥ 10	98 107,86 (15,60)	94 109,37 (16,07)	93 108,34 (18,71)	92 107,84 (18,16)	87 106,78 (19,67)	70 104,73 (18,88)	68 106,26 (17,99)	43 105,65 (17,33)	-0,32 (1,20)	77 103,94 (17,24)	75 103,88 (19,18)	73 107,30 (17,63)	68 108,40 (20,40)	58 108,83 (19,86)	55 106,49 (19,87)	58 107,34 (18,73)	39 106,41 (19,47)	2,11 (1,36)	-2,43 [-6,02;1,17] 0,1841 -0,20 [-0,50;0,10]
Tumorstadium (p-Wert des Interaktionsterms: 0,3749)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 108,40 (15,29)	49 105,37 (18,55)	48 103,48 (20,28)	45 101,93 (20,94)	46 102,26 (20,71)	39 100,77 (21,72)	39 100,64 (20,64)	23 101,26 (16,34)	-5,23 (1,64)	57 107,35 (16,83)	54 108,20 (16,72)	54 109,83 (16,20)	48 107,00 (15,86)	46 110,65 (14,16)	36 109,39 (16,49)	37 111,19 (15,23)	19 111,11 (13,25)	1,60 (1,59)	-6,83 [-11,36;-2,30] 0,0035 -0,57 [-0,96;-0,19]
IIB	45 107,44 (14,82)	44 107,11 (18,89)	41 111,63 (15,84)	42 106,52 (17,38)	35 107,09 (16,26)	34 108,88 (17,86)	31 106,16 (15,99)	22 105,05 (16,56)	0,23 (1,85)	64 106,75 (15,50)	62 108,08 (17,06)	60 109,12 (17,23)	55 109,11 (19,05)	55 107,07 (16,85)	54 107,13 (17,70)	55 103,87 (19,99)	32 107,50 (19,59)	-0,42 (1,53)	0,65 [-4,12;5,42] 0,7869 0,05 [-0,33;0,43]
IIIA	211 104,94 (18,90)	204 103,38 (18,91)	197 104,02 (19,48)	194 104,62 (18,89)	187 103,15 (19,21)	163 104,18 (19,79)	156 102,39 (19,90)	83 102,52 (20,26)	-1,49 (0,77)	193 105,66 (18,47)	183 105,85 (17,54)	177 106,49 (17,49)	173 107,12 (18,25)	155 108,95 (17,64)	131 108,11 (18,51)	140 105,88 (19,23)	71 106,18 (19,20)	0,85 (0,82)	-2,33 [-4,54;-0,12] 0,0386 -0,21 [-0,40;-0,01]
IIIB	14 100,50 (20,95)	13 99,69 (20,86)	13 93,85 (27,09)	13 91,38 (19,69)	10 89,80 (13,58)	8 84,88 (27,47)	11 91,45 (24,55)	6 88,67 (12,75)	-8,37 (3,24)	14 113,07 (15,62)	14 112,07 (18,91)	14 112,64 (17,21)	11 112,00 (25,25)	9 116,11 (19,90)	10 106,50 (21,83)	9 103,56 (21,26)	5 93,80 (20,02)	-2,49 (3,41)	-5,88 [-15,95;4,19] 0,2408 -0,46 [-1,19;0,27]
IIIC	166 108,20 (15,21)	155 107,97 (16,64)	153 107,73 (18,71)	150 107,60 (19,51)	142 107,27 (19,33)	121 106,75 (19,72)	118 106,39 (20,17)	67 105,70 (19,17)	-0,75 (0,98)	148 104,43 (16,68)	143 104,87 (19,28)	139 107,05 (17,49)	129 109,77 (18,49)	117 109,22 (19,36)	111 107,61 (19,41)	111 106,64 (19,01)	69 106,55 (18,21)	2,28 (1,04)	-3,02 [-5,84;-0,21] 0,0351 -0,24 [-0,46;-0,02]
Tumorgrading (p-Wert des Interaktionsterms: 0,6855)																			
G1	45 108,60 (16,45)	42 107,14 (16,77)	40 106,75 (18,02)	40 104,93 (17,41)	39 106,41 (17,28)	33 105,24 (17,20)	33 105,73 (17,08)	18 105,56 (19,88)	-2,09 (1,58)	38 105,29 (15,55)	36 109,14 (14,78)	33 107,03 (15,57)	36 109,14 (18,70)	30 110,70 (18,34)	28 103,04 (21,19)	25 107,20 (19,62)	13 108,85 (18,77)	2,48 (1,74)	-4,57 [-9,26;0,11] 0,0555 -0,43 [-0,87;0,01]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	212 107,14 (17,35)	201 105,62 (18,52)	200 105,97 (19,20)	195 105,61 (19,14)	186 104,85 (19,48)	164 104,15 (19,55)	166 104,32 (19,65)	84 105,26 (18,13)	-2,04 (0,79)	207 106,35 (17,76)	200 105,54 (19,42)	194 107,51 (18,07)	181 107,66 (18,85)	159 109,20 (18,24)	147 107,86 (19,63)	152 105,39 (19,82)	85 105,40 (19,36)	-0,14 (0,81)	-1,90 [-4,12;0,31] 0,0920 -0,17 [-0,36;0,03]
G3	204 105,12 (16,61)	196 104,52 (18,39)	188 104,54 (20,23)	184 104,43 (20,16)	171 103,39 (19,91)	147 105,20 (21,66)	137 101,72 (21,08)	87 99,36 (19,29)	-1,07 (0,90)	203 105,50 (17,15)	194 106,53 (17,16)	191 107,92 (17,18)	173 109,21 (17,84)	167 108,46 (17,52)	143 108,78 (16,99)	153 106,59 (18,24)	86 108,09 (17,91)	1,95 (0,89)	-3,03 [-5,52;-0,54] 0,0173 -0,24 [-0,43;-0,04]
GX	28 107,89 (19,89)	27 106,67 (17,87)	25 108,52 (17,71)	26 106,96 (18,30)	25 105,68 (15,74)	22 104,18 (20,04)	20 105,20 (20,49)	13 113,69 (16,06)	-1,39 (1,88)	28 105,82 (17,61)	26 107,23 (17,16)	26 107,69 (14,83)	26 105,88 (18,20)	25 111,60 (16,04)	23 108,48 (17,00)	22 109,59 (17,51)	12 103,42 (15,96)	2,04 (1,85)	-3,44 [-8,75;1,87] 0,1994 -0,35 [-0,88;0,18]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,2165)																			
Negativ	46 104,33 (15,81)	43 100,60 (17,11)	41 101,71 (23,76)	42 100,38 (22,73)	39 97,44 (20,76)	37 97,70 (21,59)	36 91,64 (19,77)	12 98,83 (21,47)	-6,13 (2,07)	39 106,46 (15,32)	36 106,83 (14,48)	35 106,14 (14,87)	30 110,23 (13,75)	31 110,65 (15,44)	26 109,23 (15,90)	31 109,32 (17,28)	15 112,20 (13,02)	1,95 (2,23)	-8,08 [-14,14;-2,01] 0,0097 -0,58 [-1,01;-0,14]
Positiv	426 106,42 (17,41)	407 105,51 (18,40)	398 105,65 (19,00)	388 105,21 (18,99)	370 104,88 (18,95)	319 105,15 (19,96)	305 104,23 (19,67)	182 103,21 (18,93)	-1,25 (0,57)	421 105,76 (17,39)	406 106,28 (18,09)	396 107,87 (17,32)	373 107,97 (18,50)	337 108,57 (17,96)	303 107,79 (18,53)	311 105,85 (19,00)	174 105,67 (18,79)	0,96 (0,57)	-2,21 [-3,80;-0,63] 0,0063 -0,19 [-0,32;-0,05]
Unbekannt	2 117,00 (12,73)	2 114,00 (33,94)	2 123,00 (21,21)	1 140,00 (NE)	1 136,00 (NE)	1 133,00 (NE)	1 140,00 (NE)	0	NE	8 100,13 (23,68)	7 98,86 (29,64)	8 103,13 (25,34)	6 106,00 (28,38)	6 116,33 (19,54)	8 100,75 (27,41)	4 104,25 (33,39)	2 120,00 (15,56)	3,93 (3,20)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,3105)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	275 108,26 (16,80)	258 107,02 (18,49)	249 107,16 (19,57)	243 106,29 (18,76)	228 105,23 (19,78)	199 105,60 (20,47)	183 104,72 (19,82)	117 103,53 (18,77)	-2,20 (0,71)	285 106,87 (17,16)	268 106,92 (18,57)	257 108,80 (17,32)	241 108,43 (19,10)	219 109,74 (18,29)	200 108,62 (18,83)	208 106,81 (19,22)	121 106,33 (19,84)	0,38 (0,70)	-2,58 [-4,54;-0,61] 0,0103 -0,22 [-0,38;-0,05]
Asiatisch	187 103,65 (17,07)	184 103,08 (17,47)	180 103,34 (18,66)	178 104,00 (19,28)	170 103,28 (18,90)	148 103,22 (19,83)	152 101,93 (19,71)	75 103,49 (18,53)	-0,48 (0,88)	165 103,88 (17,56)	163 104,70 (17,34)	162 105,28 (17,68)	157 107,83 (17,62)	144 107,01 (16,94)	124 105,79 (18,51)	129 104,14 (18,52)	66 105,68 (15,62)	1,41 (0,93)	-1,89 [-4,41;0,63] 0,1408 -0,16 [-0,37;0,05]
Andere	16 105,94 (23,29)	15 103,87 (22,67)	15 104,73 (24,58)	15 99,80 (25,85)	15 103,40 (17,53)	13 106,85 (20,73)	14 104,79 (23,25)	9 100,22 (26,48)	-2,47 (2,62)	17 105,12 (17,84)	16 108,13 (14,78)	17 108,18 (12,54)	16 109,75 (13,68)	14 119,00 (13,39)	12 112,42 (9,96)	11 120,45 (12,96)	7 117,00 (14,64)	8,59 (2,72)	-11,05 [-18,77;-3,34] 0,0065 -0,99 [-1,70;-0,29]
ECOG-PS (p-Wert des Interaktionsterms: 0,1205)																			
ECOG-PS 0	439 106,17 (17,02)	417 104,85 (18,03)	404 104,85 (19,40)	399 104,13 (19,16)	376 103,40 (19,06)	328 103,88 (19,86)	320 102,74 (19,80)	187 102,94 (18,96)	-2,28 (0,56)	424 106,76 (17,02)	405 106,97 (17,95)	394 108,28 (16,98)	371 109,20 (18,11)	339 109,78 (17,62)	306 108,88 (18,38)	318 106,76 (19,01)	177 107,00 (18,51)	0,98 (0,57)	-3,26 [-4,82;-1,70] <,0001 -0,28 [-0,41;-0,15]
ECOG-PS 1	50 109,14 (17,82)	49 109,67 (19,62)	49 111,61 (18,81)	46 113,91 (18,74)	45 113,24 (18,55)	38 111,50 (22,00)	36 110,28 (20,94)	15 107,60 (19,13)	4,83 (1,91)	53 98,62 (17,68)	52 101,52 (17,57)	51 102,73 (18,82)	46 101,28 (18,69)	43 104,05 (17,96)	36 99,42 (17,43)	34 102,03 (18,01)	19 103,79 (17,95)	1,48 (1,87)	3,34 [-2,08;8,76] 0,2236 0,25 [-0,14;0,63]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B Gesamtscore = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B Gesamtscore haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t105_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des FACT-B (Gesamtscore) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,6422)																			
< 65 Jahre	803 108,26 (18,08)	757 107,32 (18,70)	743 107,20 (19,64)	696 106,66 (19,12)	669 106,88 (19,29)	592 106,49 (18,83)	600 106,10 (19,38)	329 106,70 (18,80)	-1,70 (0,43)	831 106,98 (18,06)	791 107,97 (17,91)	782 107,84 (18,02)	727 107,65 (18,39)	691 108,55 (18,35)	609 108,25 (18,66)	605 107,12 (19,58)	319 105,90 (18,92)	0,44 (0,42)	-2,14 [-3,32;-0,95] 0,0004 -0,17 [-0,27;-0,08]
≥ 65 Jahre	302 108,44 (18,54)	282 105,65 (18,98)	263 107,35 (17,40)	254 106,70 (18,60)	238 105,79 (20,06)	214 104,41 (20,03)	226 106,02 (19,20)	119 104,72 (17,91)	-3,19 (0,66)	279 109,92 (17,32)	266 109,58 (17,99)	257 109,91 (16,93)	246 109,94 (16,62)	240 107,95 (18,35)	211 107,73 (18,08)	197 107,55 (17,38)	117 108,00 (18,60)	-1,61 (0,68)	-1,58 [-3,45;0,30] 0,0989 -0,14 [-0,30;0,03]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9233)																			
Neoadjuvante Chemotherapie	362 109,93 (17,94)	335 108,01 (19,08)	323 108,62 (19,27)	298 106,50 (19,85)	277 106,37 (20,44)	236 106,25 (19,66)	253 105,53 (19,95)	129 106,09 (17,25)	-3,53 (0,63)	365 106,77 (17,97)	345 107,25 (17,19)	331 106,87 (17,69)	307 106,59 (17,89)	291 107,06 (17,30)	248 107,24 (18,06)	260 106,34 (18,97)	139 102,61 (18,83)	-1,04 (0,62)	-2,49 [-4,23;-0,75] 0,0051 -0,21 [-0,35;-0,06]
Adjuvante Chemotherapie	683 107,45 (18,52)	650 106,49 (18,65)	632 106,70 (19,12)	601 107,10 (18,54)	584 106,95 (19,00)	530 106,14 (19,01)	527 106,50 (19,19)	292 106,16 (19,45)	-1,07 (0,46)	678 108,08 (17,75)	648 109,08 (18,09)	649 109,13 (17,81)	611 109,23 (17,85)	593 109,27 (18,76)	527 109,00 (18,58)	495 107,94 (19,15)	270 108,43 (18,70)	0,77 (0,47)	-1,84 [-3,13;-0,55] 0,0051 -0,15 [-0,26;-0,05]
Keine Chemotherapie	60 108,42 (15,40)	54 104,33 (18,54)	51 105,31 (16,92)	51 102,67 (18,67)	46 103,46 (19,96)	40 101,45 (18,08)	46 104,17 (17,47)	27 106,78 (15,10)	-5,81 (1,40)	67 109,30 (19,25)	64 107,31 (20,04)	59 108,02 (17,53)	55 106,25 (19,39)	47 105,70 (18,87)	45 102,58 (19,29)	47 104,64 (18,40)	27 106,63 (17,84)	-3,83 (1,35)	-1,98 [-5,84;1,88] 0,3119 -0,18 [-0,53;0,17]
Region (p-Wert des Interaktionsterms: 0,2724)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	548 109,82 (18,66)	493 107,85 (19,36)	478 108,12 (19,64)	445 107,86 (19,26)	414 108,40 (19,51)	375 106,98 (19,88)	390 107,15 (19,81)	209 109,18 (18,57)	-2,87 (0,48)	529 108,91 (18,03)	489 109,99 (18,06)	479 109,80 (17,69)	437 109,39 (18,57)	421 109,27 (18,90)	375 110,26 (18,82)	343 108,78 (19,38)	205 108,89 (19,04)	-0,32 (0,49)	-2,55 [-3,90;-1,21] 0,0002 -0,23 [-0,35;-0,11]
Asien	195 107,09 (18,48)	190 105,78 (19,99)	185 105,12 (20,81)	177 104,99 (20,50)	173 104,58 (21,11)	152 103,58 (20,97)	163 102,80 (20,38)	87 100,59 (18,40)	-2,11 (0,92)	192 106,82 (18,31)	189 106,20 (18,70)	187 106,32 (18,64)	179 107,32 (18,87)	174 107,07 (19,58)	149 105,38 (18,70)	155 105,66 (18,64)	81 101,64 (18,78)	-0,34 (0,93)	-1,77 [-4,35;0,80] 0,1766 -0,14 [-0,34;0,06]
Andere	362 106,69 (17,18)	356 106,08 (17,23)	343 107,17 (17,16)	328 105,98 (17,63)	320 105,35 (18,37)	279 105,83 (16,98)	273 106,50 (17,75)	152 105,24 (17,93)	-0,94 (0,64)	389 106,55 (17,50)	379 107,36 (17,23)	373 107,51 (17,32)	357 107,26 (16,71)	336 107,99 (16,91)	296 106,78 (17,74)	304 106,27 (18,82)	150 105,75 (18,15)	0,30 (0,62)	-1,24 [-2,99;0,51] 0,1658 -0,10 [-0,24;0,04]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2828)																			
< 20 mm	279 108,84 (18,54)	257 107,60 (18,95)	253 108,33 (19,42)	244 106,81 (19,72)	231 106,40 (20,18)	208 105,28 (20,64)	207 107,01 (20,04)	106 106,90 (18,97)	-2,49 (0,71)	298 108,55 (17,29)	282 108,64 (17,62)	275 109,59 (17,10)	257 108,64 (17,53)	248 108,60 (17,62)	216 109,18 (17,40)	220 107,76 (18,52)	111 106,92 (17,90)	-0,61 (0,69)	-1,88 [-3,83;0,07] 0,0591 -0,16 [-0,32;0,01]
≥ 20 bis < 50 mm	568 107,91 (18,58)	543 106,87 (18,82)	519 107,55 (18,98)	499 107,07 (18,68)	474 106,92 (19,48)	423 107,06 (18,53)	431 106,78 (19,33)	231 105,53 (18,85)	-1,38 (0,52)	572 107,80 (18,08)	549 108,33 (17,98)	542 108,35 (17,72)	509 108,21 (18,40)	492 108,66 (18,42)	438 108,01 (18,97)	415 107,48 (19,76)	230 105,99 (18,98)	-0,04 (0,51)	-1,34 [-2,77;0,09] 0,0653 -0,11 [-0,23;0,01]
≥ 50 mm	241 108,76 (16,98)	224 105,90 (18,72)	218 105,52 (18,81)	194 105,76 (18,86)	188 106,58 (18,54)	162 104,79 (18,48)	174 103,86 (18,43)	103 106,73 (18,07)	-3,07 (0,76)	229 106,13 (18,58)	215 107,78 (18,49)	212 106,26 (18,86)	197 107,44 (17,77)	184 107,21 (19,29)	158 106,77 (18,98)	159 105,62 (18,22)	91 106,70 (20,05)	0,26 (0,78)	-3,33 [-5,47;-1,19] 0,0023 -0,28 [-0,46;-0,10]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8696)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	366 108,28 (19,19)	346 106,90 (19,07)	333 107,71 (19,73)	311 106,89 (19,39)	300 106,46 (20,35)	273 105,47 (20,26)	284 105,59 (20,51)	166 107,45 (19,20)	-1,99 (0,63)	360 107,68 (17,59)	341 107,81 (17,24)	340 108,21 (16,62)	310 107,81 (17,39)	301 108,85 (17,29)	260 108,54 (18,15)	255 108,20 (18,66)	142 106,61 (18,58)	-0,09 (0,64)	-1,90 [-3,66;-0,15] 0,0338 -0,16 [-0,30;-0,01]
4-9	475 107,99 (17,32)	444 106,55 (18,26)	436 106,58 (18,79)	417 105,75 (18,71)	396 106,20 (19,08)	352 106,30 (18,18)	355 106,86 (18,39)	173 105,67 (17,18)	-2,03 (0,55)	485 107,59 (18,34)	465 108,77 (18,53)	462 108,56 (18,19)	437 108,11 (19,04)	418 108,08 (19,19)	377 107,47 (18,99)	357 106,69 (19,79)	192 106,61 (19,15)	-0,17 (0,54)	-1,87 [-3,38;-0,35] 0,0157 -0,16 [-0,28;-0,03]
≥ 10	264 108,95 (18,38)	249 107,39 (19,37)	237 107,82 (18,68)	222 108,10 (18,87)	211 107,54 (19,06)	181 105,94 (19,41)	187 105,32 (19,24)	109 105,03 (19,74)	-2,30 (0,75)	265 108,02 (17,61)	251 108,40 (17,77)	237 108,13 (18,60)	226 109,04 (16,68)	212 108,39 (18,15)	183 108,84 (18,03)	190 106,93 (18,19)	102 105,98 (18,78)	-0,03 (0,75)	-2,27 [-4,36;-0,18] 0,0337 -0,19 [-0,36;-0,01]
Tumorgrading (p-Wert des Interaktionsterms: 0,9619)																			
G1	81 108,06 (18,29)	78 108,45 (19,15)	80 107,44 (19,70)	73 107,44 (19,26)	68 107,28 (20,64)	62 107,32 (16,92)	62 107,42 (18,90)	31 106,74 (16,57)	-0,45 (1,36)	84 110,05 (17,57)	82 111,39 (18,37)	78 111,00 (17,49)	70 112,03 (15,29)	74 107,86 (20,57)	64 111,08 (18,77)	55 110,76 (17,54)	34 110,85 (17,02)	0,90 (1,34)	-1,35 [-5,13;2,43] 0,4817 -0,11 [-0,42;0,20]
G2	526 108,61 (17,71)	498 106,38 (19,34)	480 106,79 (19,31)	451 106,37 (19,53)	432 106,23 (19,81)	373 105,08 (19,66)	374 105,61 (19,63)	211 105,80 (18,99)	-2,86 (0,53)	533 107,39 (18,10)	505 107,82 (18,07)	503 107,68 (18,00)	474 107,62 (18,33)	446 107,29 (18,72)	402 107,19 (18,49)	392 105,34 (19,75)	214 105,35 (19,35)	-0,72 (0,52)	-2,15 [-3,60;-0,69] 0,0039 -0,18 [-0,30;-0,06]
G3	449 108,03 (18,95)	419 107,16 (18,32)	401 108,05 (18,86)	381 107,04 (18,30)	365 107,01 (19,21)	332 106,45 (19,03)	353 106,50 (19,01)	184 106,73 (18,45)	-1,35 (0,56)	436 107,43 (17,97)	413 108,44 (17,76)	403 108,48 (17,72)	378 108,42 (18,12)	363 109,89 (17,06)	315 109,15 (18,55)	314 109,21 (18,51)	165 107,67 (18,80)	0,71 (0,57)	-2,06 [-3,64;-0,48] 0,0105 -0,17 [-0,30;-0,04]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
GX	47 107,94 (16,72)	42 106,62 (16,73)	43 104,28 (17,60)	43 105,37 (19,34)	40 106,48 (17,19)	37 107,84 (19,16)	37 104,49 (20,28)	22 104,36 (19,10)	-3,27 (1,85)	53 109,42 (15,28)	53 107,89 (16,81)	52 109,00 (16,24)	48 106,21 (16,27)	45 107,56 (20,45)	37 103,76 (16,60)	39 105,18 (16,44)	21 103,38 (15,23)	-2,02 (1,76)	-1,25 [-6,32;3,81] 0,6242 -0,10 [-0,49;0,29]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,7862)																			
Negativ	137 104,73 (17,35)	131 102,81 (19,82)	123 102,67 (20,65)	116 103,44 (19,60)	105 102,93 (20,83)	92 102,08 (19,51)	100 102,63 (18,70)	63 100,05 (18,58)	-2,71 (1,03)	149 106,64 (17,46)	139 107,12 (18,02)	133 108,26 (17,86)	125 108,38 (18,20)	121 107,67 (17,92)	103 106,46 (19,88)	114 103,82 (19,59)	56 102,48 (18,56)	-0,21 (0,98)	-2,50 [-5,31;0,30] 0,0799 -0,21 [-0,44;0,02]
Positiv	937 108,54 (18,24)	877 107,02 (18,51)	853 107,44 (18,73)	809 106,68 (18,71)	780 106,74 (19,13)	692 106,02 (18,95)	704 106,28 (19,34)	375 107,01 (18,36)	-2,09 (0,39)	934 107,59 (17,92)	895 108,35 (17,87)	883 108,08 (17,76)	826 107,98 (17,90)	789 108,27 (18,43)	696 108,14 (18,36)	668 107,50 (18,90)	366 106,71 (18,78)	-0,07 (0,39)	-2,02 [-3,11;-0,93] 0,0003 -0,17 [-0,26;-0,08]
Unbekannt	9 112,00 (22,72)	9 114,78 (15,72)	9 123,22 (12,27)	7 127,00 (18,48)	3 139,33 (3,06)	6 121,33 (22,90)	5 116,60 (22,41)	1 131,00 (NE)	7,03 (3,76)	7 118,29 (18,16)	6 122,67 (10,63)	6 119,17 (10,78)	6 125,83 (8,33)	6 120,00 (10,14)	6 119,33 (11,84)	5 121,20 (14,45)	5 125,20 (7,05)	7,88 (3,89)	-0,86 [-12,36;10,65] 0,8760 -0,07 [-1,01;0,86]
Ethnizität (p-Wert des Interaktionsterms: 0,4642)																			
Weiß	806 108,23 (18,05)	751 106,97 (18,24)	734 107,32 (18,32)	691 106,35 (18,40)	653 106,44 (19,13)	585 106,02 (18,54)	593 106,12 (18,99)	336 107,04 (18,37)	-2,44 (0,41)	819 108,08 (17,72)	772 108,90 (17,69)	757 109,05 (17,33)	703 108,18 (17,80)	675 108,56 (18,11)	600 108,67 (18,22)	577 107,46 (18,92)	323 107,37 (18,62)	-0,26 (0,40)	-2,18 [-3,31;-1,06] 0,0001 -0,19 [-0,29;-0,09]
Asiatisch	233 108,27 (18,82)	225 106,69 (20,05)	218 107,02 (20,79)	209 107,36 (20,82)	204 107,18 (21,12)	176 105,64 (21,04)	187 104,79 (20,69)	97 102,80 (19,14)	-0,90 (0,89)	221 106,56 (18,59)	216 106,88 (18,76)	215 106,49 (19,04)	207 108,56 (19,04)	199 108,18 (19,73)	167 106,27 (18,86)	172 106,59 (19,08)	88 102,76 (19,56)	0,61 (0,91)	-1,51 [-4,00;0,99] 0,2364 -0,11 [-0,30;0,07]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Andere	54 109,61 (17,43)	51 106,67 (20,66)	46 107,87 (20,86)	42 108,38 (18,63)	42 105,43 (17,86)	36 107,28 (20,48)	40 110,08 (17,60)	14 107,14 (17,68)	-1,69 (1,78)	57 108,77 (17,84)	57 107,25 (18,53)	55 108,15 (16,48)	51 107,59 (17,17)	46 106,57 (16,69)	42 108,86 (20,08)	44 108,86 (20,48)	19 107,58 (19,56)	-1,38 (1,70)	-0,31 [-5,19;4,57] 0,9004 -0,02 [-0,40;0,35]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,2878)																			
Tamoxifen	103 106,28 (17,10)	97 105,72 (17,54)	98 105,34 (19,47)	95 105,51 (17,43)	93 105,74 (19,07)	90 105,23 (18,01)	91 105,79 (19,13)	55 105,95 (18,74)	-0,34 (1,13)	124 105,38 (16,61)	122 105,91 (16,31)	120 106,24 (17,31)	109 106,97 (15,92)	103 105,54 (16,86)	94 107,45 (17,31)	92 104,18 (17,11)	56 103,00 (19,09)	0,06 (1,04)	-0,40 [-3,44;2,63] 0,7937 -0,03 [-0,30;0,23]
Aromatase-Inhibitor	1002 108,52 (18,30)	942 106,99 (18,91)	908 107,45 (19,03)	855 106,80 (19,14)	814 106,69 (19,55)	716 106,03 (19,31)	735 106,11 (19,36)	393 106,21 (18,57)	-2,30 (0,38)	986 108,02 (18,06)	935 108,69 (18,12)	919 108,62 (17,82)	864 108,39 (18,23)	828 108,75 (18,49)	726 108,20 (18,66)	710 107,62 (19,27)	380 106,97 (18,77)	-0,12 (0,39)	-2,18 [-3,25;-1,12] <,0001 -0,18 [-0,27;-0,09]
ECOG-PS (p-Wert des Interaktionsterms: 0,4901)																			
ECOG-PS 0	931 109,24 (17,76)	874 107,71 (18,53)	849 108,01 (18,92)	809 107,19 (18,80)	774 107,26 (19,31)	692 106,63 (19,05)	700 106,69 (19,09)	380 107,34 (18,38)	-2,14 (0,39)	898 108,52 (17,74)	854 109,15 (17,74)	841 109,00 (17,42)	790 108,78 (17,56)	757 108,88 (18,30)	674 108,22 (18,32)	663 106,97 (19,09)	355 106,02 (18,74)	-0,45 (0,40)	-1,69 [-2,79;-0,60] 0,0025 -0,14 [-0,23;-0,05]
ECOG-PS 1	174 103,37 (19,73)	165 102,42 (19,54)	157 103,10 (19,43)	141 103,72 (19,76)	133 102,71 (20,13)	114 101,75 (19,38)	126 102,64 (20,31)	68 99,65 (18,37)	-1,77 (0,96)	212 104,33 (18,30)	203 105,11 (18,39)	198 105,59 (19,01)	183 105,84 (19,57)	174 106,29 (18,40)	146 107,62 (19,40)	139 108,46 (18,92)	81 108,42 (19,27)	1,68 (0,87)	-3,45 [-6,00;-0,89] 0,0083 -0,27 [-0,47;-0,07]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B Gesamtscore = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B Gesamtscore haben. Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler																		

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t105_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: BCS aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Region (p-Wert des Interaktionsterms: 0,9118)																			
Nordamerika / Europa	203 24,00 (5,33)	188 24,38 (5,45)	180 24,29 (5,31)	177 23,84 (5,44)	160 23,80 (5,39)	138 23,49 (5,37)	134 23,54 (5,28)	74 23,55 (5,12)	0,10 (0,24)	197 23,49 (5,76)	183 23,79 (5,75)	175 24,45 (5,76)	155 24,65 (5,59)	139 24,99 (5,79)	132 24,57 (5,50)	131 24,26 (5,36)	65 25,45 (4,85)	0,77 (0,25)	-0,67 [-1,35;0,01] 0,0533 -0,19 [-0,39;0,00]
Asien	163 22,08 (5,14)	162 22,88 (5,09)	158 22,44 (5,11)	156 22,06 (5,39)	150 21,51 (5,15)	130 21,46 (5,34)	137 21,46 (5,60)	69 21,14 (5,71)	-0,24 (0,26)	153 22,56 (4,77)	151 22,93 (4,97)	151 23,01 (5,11)	146 22,97 (5,17)	138 22,74 (4,82)	120 22,83 (5,06)	122 22,98 (5,12)	66 23,62 (4,72)	0,37 (0,27)	-0,61 [-1,35;0,14] 0,1088 -0,18 [-0,40;0,04]
Andere	124 23,13 (5,93)	119 23,98 (5,80)	117 25,08 (6,25)	114 24,67 (6,01)	112 24,33 (6,72)	99 24,54 (6,26)	86 22,63 (5,82)	61 21,84 (6,15)	0,90 (0,34)	128 22,80 (5,55)	124 23,99 (5,66)	122 24,63 (5,36)	117 24,38 (5,36)	108 24,55 (5,09)	90 24,01 (5,39)	101 24,77 (5,14)	66 24,39 (5,55)	1,46 (0,33)	-0,56 [-1,50;0,38] 0,2386 -0,15 [-0,40;0,10]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,8985)																			
< 20 mm	121 22,83 (4,99)	115 23,71 (4,80)	109 23,36 (5,47)	110 23,12 (5,82)	105 22,76 (5,58)	93 22,38 (5,91)	91 22,37 (5,96)	54 22,74 (5,53)	0,31 (0,34)	123 22,69 (5,97)	116 23,28 (6,05)	115 23,73 (5,72)	107 23,22 (5,20)	101 23,52 (5,34)	85 23,89 (5,16)	84 24,32 (5,15)	50 24,72 (5,53)	0,88 (0,34)	-0,57 [-1,51;0,37] 0,2319 -0,15 [-0,40;0,10]
≥ 20 bis < 50 mm	229 23,54 (5,52)	220 24,12 (5,67)	218 24,44 (5,64)	215 23,67 (5,47)	196 23,54 (6,00)	170 23,56 (5,73)	164 22,85 (5,39)	96 22,55 (5,73)	0,25 (0,23)	227 22,65 (5,25)	218 23,39 (5,17)	217 23,99 (5,24)	201 24,10 (5,53)	185 24,06 (5,31)	172 23,48 (5,50)	181 23,76 (5,26)	93 24,24 (5,05)	0,93 (0,23)	-0,68 [-1,33;-0,03] 0,0391 -0,19 [-0,38;-0,01]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
≥ 50 mm	128 22,79 (5,74)	124 23,32 (5,50)	119 23,35 (5,51)	114 23,32 (5,69)	112 22,60 (5,70)	95 22,84 (5,60)	93 22,46 (5,45)	48 21,27 (5,78)	0,05 (0,30)	123 23,99 (5,04)	119 24,22 (5,36)	111 24,39 (5,73)	105 24,63 (5,37)	96 24,67 (5,34)	81 24,54 (5,28)	85 24,07 (5,36)	50 24,62 (4,87)	0,45 (0,31)	-0,41 [-1,27;0,45] 0,3534 -0,12 [-0,37;0,13]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,3509)																			
0-3	177 23,28 (5,50)	169 23,65 (5,42)	160 23,79 (5,56)	158 23,43 (5,64)	143 23,51 (5,33)	129 23,24 (5,56)	131 22,56 (5,42)	77 22,12 (5,65)	0,28 (0,27)	190 23,17 (5,24)	181 23,94 (5,38)	176 24,45 (5,34)	164 24,20 (5,18)	155 23,87 (5,33)	136 23,99 (5,22)	135 23,78 (5,40)	71 24,89 (4,68)	0,97 (0,26)	-0,70 [-1,43;0,03] 0,0595 -0,20 [-0,40;0,01]
4-9	215 22,88 (5,66)	206 23,53 (5,52)	202 23,58 (5,64)	197 22,93 (5,66)	192 22,65 (5,91)	168 22,85 (5,97)	158 22,40 (5,73)	84 22,11 (5,90)	-0,04 (0,24)	210 22,88 (5,49)	201 23,26 (5,46)	199 23,66 (5,58)	186 23,74 (5,54)	172 24,15 (5,39)	151 23,79 (5,39)	159 24,03 (5,11)	86 24,42 (5,34)	0,79 (0,25)	-0,83 [-1,52;-0,15] 0,0170 -0,23 [-0,42;-0,04]
≥ 10	98 23,45 (5,04)	94 24,47 (5,34)	93 24,54 (5,56)	92 24,49 (5,61)	87 23,54 (6,30)	70 23,20 (5,54)	68 22,74 (5,69)	43 22,65 (5,55)	0,50 (0,36)	78 22,97 (5,66)	76 23,42 (5,79)	73 23,93 (5,51)	68 24,15 (5,69)	58 24,28 (5,34)	55 23,42 (5,65)	60 24,23 (5,38)	40 23,90 (5,29)	0,58 (0,41)	-0,08 [-1,15;1,00] 0,8879 -0,02 [-0,32;0,28]
Tumorstadium (p-Wert des Interaktionsterms: 0,1070)																			
IIA	52 23,90 (5,29)	49 23,69 (4,89)	48 23,92 (5,40)	46 23,04 (6,11)	46 22,78 (5,83)	39 22,36 (5,90)	39 22,49 (5,87)	23 22,26 (5,56)	-0,35 (0,49)	57 22,70 (5,87)	54 23,76 (5,71)	54 24,65 (5,15)	48 23,33 (4,80)	46 24,13 (5,43)	36 23,69 (5,21)	37 24,92 (4,80)	19 26,32 (3,64)	1,37 (0,48)	-1,71 [-3,08;-0,35] 0,0142 -0,48 [-0,86;-0,10]
IIB	45 22,91 (5,02)	44 24,00 (5,64)	41 25,17 (4,73)	42 23,79 (5,48)	35 23,80 (5,40)	34 23,71 (5,15)	31 22,97 (3,89)	22 22,55 (5,41)	0,64 (0,56)	64 23,44 (4,87)	62 24,84 (4,36)	61 24,34 (5,32)	56 24,82 (5,86)	55 23,62 (5,28)	54 24,00 (5,63)	55 23,53 (5,76)	32 24,91 (5,12)	0,57 (0,46)	0,07 [-1,36;1,50] 0,9256 0,02 [-0,36;0,40]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIA	212 22,94 (5,85)	206 23,59 (5,46)	199 23,54 (5,63)	195 23,01 (5,55)	188 22,76 (5,87)	164 22,72 (5,98)	157 22,49 (5,56)	85 22,13 (6,01)	-0,00 (0,25)	193 22,99 (5,41)	183 22,99 (5,38)	179 23,39 (5,67)	173 23,56 (5,49)	157 23,79 (5,36)	131 23,67 (5,27)	140 23,81 (5,15)	71 24,01 (5,57)	0,48 (0,26)	-0,48 [-1,18;0,22] 0,1806 -0,13 [-0,33;0,06]
IIIB	14 21,71 (7,29)	13 22,69 (6,64)	13 20,77 (7,44)	13 21,31 (5,17)	10 20,50 (3,57)	8 19,13 (5,96)	11 19,64 (6,67)	6 19,83 (5,74)	-0,91 (0,88)	14 25,57 (4,13)	14 27,57 (4,26)	14 26,93 (4,39)	11 27,82 (4,92)	10 28,40 (2,84)	10 25,60 (4,55)	9 24,56 (5,34)	5 23,80 (2,95)	1,34 (0,92)	-2,25 [-5,21;0,70] 0,1273 -0,65 [-1,39;0,09]
IIIC	166 23,39 (4,97)	156 24,10 (5,45)	153 24,16 (5,59)	150 24,19 (5,71)	142 23,73 (5,93)	121 23,82 (5,42)	118 22,72 (5,85)	67 22,42 (5,63)	0,53 (0,27)	149 22,68 (5,53)	144 23,22 (5,85)	139 24,08 (5,41)	129 24,06 (5,28)	117 24,22 (5,39)	111 23,77 (5,49)	113 24,01 (5,30)	70 24,31 (5,01)	1,11 (0,28)	-0,58 [-1,35;0,18] 0,1345 -0,17 [-0,39;0,05]
Tumorgrading (p-Wert des Interaktionsterms: 0,6637)																			
G1	45 23,96 (4,80)	43 24,14 (5,28)	40 24,00 (4,92)	40 23,90 (4,64)	39 24,03 (5,38)	33 23,39 (4,97)	33 23,85 (5,20)	18 23,89 (6,56)	0,66 (0,55)	38 21,11 (5,47)	36 23,11 (5,06)	34 22,85 (5,97)	36 23,25 (5,76)	32 23,91 (5,08)	28 22,50 (6,33)	25 23,28 (5,88)	13 23,46 (5,70)	1,44 (0,60)	-0,78 [-2,43;0,87] 0,3512 -0,21 [-0,64;0,22]
G2	212 23,70 (5,35)	201 24,17 (5,27)	200 24,30 (5,38)	195 23,60 (5,56)	186 23,43 (5,59)	164 23,07 (5,67)	166 23,05 (5,36)	86 23,08 (5,25)	-0,10 (0,24)	207 23,62 (5,36)	200 23,76 (5,74)	196 24,14 (5,62)	182 24,13 (5,45)	160 24,42 (5,25)	147 24,01 (5,35)	153 24,10 (5,26)	85 24,35 (5,07)	0,29 (0,25)	-0,39 [-1,07;0,29] 0,2660 -0,11 [-0,30;0,08]
G3	205 22,31 (5,55)	197 23,09 (5,55)	190 23,36 (5,92)	186 23,07 (5,90)	172 22,60 (6,16)	148 22,91 (6,03)	138 21,67 (5,72)	87 20,84 (5,74)	0,48 (0,26)	203 22,84 (5,49)	194 23,59 (5,25)	191 24,12 (5,25)	173 24,31 (5,26)	167 23,86 (5,42)	143 23,86 (5,24)	153 23,90 (5,28)	86 24,90 (5,11)	1,27 (0,26)	-0,80 [-1,52;-0,08] 0,0295 -0,22 [-0,41;-0,02]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
GX	28 23,64 (6,38)	28 24,96 (6,02)	25 23,76 (5,72)	26 24,00 (6,20)	25 23,04 (5,56)	22 23,36 (5,63)	20 21,90 (6,61)	13 23,54 (5,81)	-0,44 (0,54)	29 22,48 (4,70)	27 22,56 (6,01)	26 23,88 (5,57)	26 21,88 (5,68)	25 23,44 (5,94)	23 23,87 (5,07)	23 24,26 (4,56)	13 23,62 (4,66)	0,66 (0,53)	-1,10 [-2,63;0,42] 0,1511 -0,39 [-0,91;0,14]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,2151)																			
Negativ	46 21,61 (5,11)	43 22,47 (4,81)	41 22,61 (6,16)	42 21,76 (6,62)	39 21,21 (6,65)	37 20,73 (6,47)	36 18,83 (5,72)	12 20,75 (6,05)	-0,39 (0,63)	39 22,51 (4,94)	36 22,78 (4,50)	35 23,31 (5,08)	30 23,47 (5,67)	31 23,26 (5,12)	26 24,12 (4,28)	31 24,35 (4,71)	15 26,53 (4,53)	1,63 (0,68)	-2,02 [-3,86;-0,19] 0,0313 -0,48 [-0,91;-0,04]
Positiv	427 23,17 (5,51)	410 23,81 (5,52)	400 23,90 (5,55)	390 23,51 (5,55)	371 23,25 (5,68)	320 23,20 (5,61)	306 22,78 (5,42)	183 22,16 (5,71)	0,28 (0,17)	422 22,98 (5,45)	407 23,58 (5,53)	399 24,00 (5,51)	374 23,94 (5,33)	339 24,01 (5,39)	303 23,73 (5,44)	313 23,88 (5,33)	175 24,16 (5,13)	0,75 (0,17)	-0,47 [-0,94;0,01] 0,0530 -0,13 [-0,27;0,00]
Unbekannt	2 27,50 (7,78)	2 29,00 (7,07)	2 30,50 (2,12)	1 34,00 (NE)	1 34,00 (NE)	1 33,00 (NE)	1 34,00 (NE)	0	NE	8 24,13 (6,71)	7 22,43 (8,22)	8 25,38 (6,37)	6 25,17 (9,26)	6 26,17 (4,88)	8 23,88 (5,91)	4 25,00 (5,94)	2 28,50 (0,71)	0,54 (0,84)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,3455)																			
Weiß	275 23,67 (5,60)	260 24,13 (5,57)	250 24,38 (5,64)	244 23,86 (5,52)	228 23,61 (5,85)	199 23,58 (5,68)	183 22,80 (5,42)	119 22,67 (5,47)	0,15 (0,21)	285 23,20 (5,72)	268 23,70 (5,83)	260 24,42 (5,67)	241 24,35 (5,58)	221 24,59 (5,48)	200 24,21 (5,30)	208 24,29 (5,12)	121 24,76 (5,24)	0,95 (0,21)	-0,80 [-1,39;-0,21] 0,0081 -0,22 [-0,39;-0,06]
Asiatisch	188 22,44 (5,04)	185 23,30 (5,15)	181 23,12 (5,25)	179 22,88 (5,62)	171 22,40 (5,68)	149 22,22 (5,66)	153 22,09 (5,69)	75 21,59 (5,74)	0,22 (0,26)	166 22,64 (4,84)	164 23,05 (4,96)	162 23,31 (5,30)	157 23,34 (5,33)	145 23,00 (4,94)	124 22,90 (5,29)	130 22,97 (5,11)	67 23,49 (4,54)	0,44 (0,28)	-0,23 [-0,97;0,52] 0,5510 -0,06 [-0,27;0,15]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Andere	16 22,00 (7,84)	15 23,07 (6,60)	15 23,60 (7,75)	15 22,40 (7,69)	15 22,87 (6,13)	13 23,85 (6,57)	14 23,43 (6,56)	9 22,33 (8,35)	0,92 (0,94)	17 23,06 (4,41)	16 25,13 (4,83)	17 24,06 (3,58)	16 24,19 (3,35)	14 25,86 (6,04)	12 25,08 (5,47)	12 29,00 (5,20)	7 28,00 (5,66)	2,60 (0,94)	-1,68 [-4,42;1,06] 0,2192 -0,43 [-1,10;0,25]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B BCS = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B BCS haben.
Abkürzungen: B: Baseline; BCS: Mammakarzinomspezifische Subskala; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t106_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: BCS aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,3769)																			
< 65 Jahre	804 23,74 (5,65)	758 24,43 (5,53)	746 24,50 (5,67)	698 24,07 (5,70)	673 24,04 (5,88)	596 23,88 (5,68)	603 23,83 (5,55)	330 23,90 (5,41)	0,42 (0,13)	832 23,36 (5,63)	791 24,27 (5,41)	783 24,22 (5,38)	732 24,23 (5,47)	694 24,49 (5,54)	611 24,32 (5,52)	606 24,42 (5,62)	319 23,94 (5,54)	0,90 (0,13)	-0,48 [-0,83;-0,13] 0,0080 -0,13 [-0,23;-0,03]
≥ 65 Jahre	303 24,44 (5,09)	284 24,97 (5,14)	266 25,01 (5,07)	257 24,07 (5,29)	239 24,24 (5,53)	218 23,97 (5,25)	227 23,96 (5,06)	120 24,08 (4,92)	-0,30 (0,20)	279 24,96 (5,52)	266 24,67 (5,21)	260 25,42 (4,94)	246 25,29 (5,07)	240 24,74 (5,33)	211 24,74 (5,22)	198 24,55 (5,59)	118 25,11 (5,54)	-0,13 (0,21)	-0,17 [-0,75;0,41] 0,5609 -0,05 [-0,21;0,11]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8495)																			
Neoadjuvante Chemotherapie	362 24,48 (5,53)	335 24,93 (5,66)	324 24,82 (5,74)	300 23,91 (5,66)	279 24,00 (6,09)	236 23,82 (5,56)	254 23,79 (5,40)	129 23,89 (4,95)	-0,27 (0,19)	365 23,75 (5,61)	345 24,43 (5,13)	332 24,23 (5,33)	309 24,03 (5,24)	292 24,30 (5,18)	248 24,40 (5,13)	261 24,41 (5,15)	139 23,41 (5,35)	0,33 (0,18)	-0,59 [-1,11;-0,08] 0,0235 -0,17 [-0,31;-0,02]
Adjuvante Chemotherapie	685 23,52 (5,58)	653 24,33 (5,36)	637 24,48 (5,47)	604 24,20 (5,63)	587 24,16 (5,74)	536 23,98 (5,64)	530 23,86 (5,52)	294 23,89 (5,56)	0,61 (0,14)	679 23,62 (5,70)	648 24,32 (5,48)	652 24,53 (5,37)	614 24,63 (5,49)	595 24,61 (5,65)	528 24,43 (5,66)	496 24,44 (5,86)	271 24,53 (5,63)	0,88 (0,14)	-0,27 [-0,66;0,12] 0,1788 -0,07 [-0,18;0,03]
Keine Chemotherapie	60 25,28 (3,95)	54 25,35 (4,75)	51 25,27 (4,59)	51 23,51 (4,67)	46 23,76 (4,40)	42 23,45 (4,65)	46 24,37 (4,25)	27 24,78 (3,45)	-1,13 (0,42)	67 25,25 (5,11)	64 24,50 (5,47)	59 26,03 (4,01)	55 25,60 (4,89)	47 25,45 (5,19)	46 24,48 (4,61)	47 24,77 (5,49)	27 25,85 (5,40)	-0,31 (0,40)	-0,82 [-1,98;0,34] 0,1630 -0,25 [-0,60;0,10]
Region (p-Wert des Interaktionsterms: 0,6228)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	548 24,22 (5,67)	494 24,68 (5,55)	482 24,78 (5,50)	446 24,14 (5,53)	417 24,34 (5,81)	381 24,02 (5,76)	392 23,94 (5,39)	210 24,24 (5,35)	-0,07 (0,15)	529 23,84 (5,74)	489 24,45 (5,50)	480 24,54 (5,30)	440 24,58 (5,52)	422 24,52 (5,53)	377 24,67 (5,53)	345 24,45 (5,87)	206 24,88 (5,79)	0,49 (0,15)	-0,56 [-0,97;-0,14] 0,0088 -0,16 [-0,28;-0,04]
Asien	195 24,25 (5,55)	190 24,72 (5,74)	185 24,14 (6,20)	178 24,02 (6,19)	173 23,86 (6,12)	152 23,10 (5,91)	163 23,44 (5,85)	87 22,18 (5,15)	-0,12 (0,27)	192 23,85 (6,02)	189 24,15 (5,56)	187 24,35 (5,72)	179 24,48 (5,85)	175 24,47 (5,87)	149 23,56 (5,96)	155 24,32 (5,42)	81 22,54 (5,42)	0,47 (0,27)	-0,58 [-1,32;0,16] 0,1219 -0,16 [-0,36;0,04]
Andere	364 23,33 (5,20)	358 24,35 (5,10)	345 24,69 (5,14)	331 24,01 (5,34)	322 23,89 (5,58)	281 24,19 (5,06)	275 24,02 (5,20)	153 24,55 (5,08)	0,83 (0,19)	390 23,61 (5,33)	379 24,37 (5,07)	376 24,57 (5,09)	359 24,39 (4,98)	337 24,64 (5,24)	296 24,55 (5,01)	304 24,51 (5,41)	150 24,31 (5,12)	0,94 (0,18)	-0,11 [-0,63;0,41] 0,6743 -0,03 [-0,17;0,11]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,1905)																			
< 20 mm	280 23,78 (5,68)	258 24,34 (5,86)	255 24,84 (5,83)	245 24,22 (5,64)	233 23,82 (6,04)	211 23,58 (5,87)	209 24,05 (5,45)	106 24,17 (5,54)	0,36 (0,22)	298 23,76 (5,42)	282 24,23 (5,38)	276 24,56 (5,25)	259 24,22 (5,55)	249 24,26 (5,66)	216 24,28 (5,47)	221 24,44 (5,52)	111 23,84 (5,15)	0,55 (0,21)	-0,19 [-0,78;0,40] 0,5308 -0,05 [-0,22;0,11]
≥ 20 bis < 50 mm	568 23,90 (5,57)	544 24,67 (5,34)	522 24,69 (5,44)	501 24,17 (5,64)	475 24,26 (5,77)	425 24,31 (5,51)	432 24,08 (5,60)	231 23,76 (5,39)	0,37 (0,15)	573 23,85 (5,72)	549 24,34 (5,37)	544 24,51 (5,33)	511 24,63 (5,34)	494 24,74 (5,41)	439 24,53 (5,54)	416 24,49 (5,88)	231 24,29 (5,59)	0,59 (0,15)	-0,22 [-0,65;0,21] 0,3124 -0,06 [-0,18;0,06]
≥ 50 mm	242 24,17 (5,19)	225 24,53 (5,15)	219 24,28 (5,30)	196 23,77 (5,38)	190 24,16 (5,42)	165 23,49 (5,30)	175 23,36 (4,91)	105 24,26 (4,86)	-0,09 (0,23)	229 23,44 (5,79)	215 24,53 (5,33)	213 24,37 (5,34)	198 24,46 (5,39)	184 24,36 (5,50)	159 24,29 (5,24)	159 24,29 (5,13)	91 24,56 (6,02)	0,86 (0,23)	-0,95 [-1,59;-0,31] 0,0036 -0,27 [-0,45;-0,09]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8090)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	368 23,83 (5,59)	348 24,49 (5,55)	337 24,75 (5,39)	314 24,20 (5,47)	303 24,24 (5,85)	277 23,87 (5,81)	288 24,00 (5,46)	167 24,38 (5,60)	0,50 (0,18)	360 23,80 (5,30)	341 24,38 (5,11)	340 24,56 (5,05)	312 24,60 (5,38)	302 25,06 (4,86)	261 24,77 (4,98)	255 24,86 (5,18)	143 24,47 (5,24)	0,77 (0,19)	-0,28 [-0,79;0,24] 0,2955 -0,08 [-0,22;0,07]
4-9	475 23,84 (5,51)	445 24,40 (5,35)	436 24,37 (5,61)	419 23,80 (5,60)	397 23,92 (5,69)	355 23,93 (5,27)	355 23,82 (5,33)	174 23,71 (5,01)	0,11 (0,17)	485 23,82 (5,80)	465 24,36 (5,43)	463 24,65 (5,29)	439 24,62 (5,43)	419 24,36 (5,78)	377 24,25 (5,63)	358 24,22 (5,95)	192 24,30 (5,71)	0,57 (0,16)	-0,46 [-0,91;0,00] 0,0512 -0,13 [-0,25;0,00]
≥ 10	264 24,25 (5,41)	249 25,00 (5,41)	239 24,94 (5,53)	222 24,42 (5,72)	212 24,19 (5,91)	182 23,92 (5,78)	187 23,77 (5,53)	109 23,67 (5,21)	0,09 (0,23)	266 23,59 (5,82)	251 24,38 (5,58)	240 24,20 (5,65)	227 24,10 (5,33)	213 24,23 (5,70)	184 24,30 (5,68)	191 24,32 (5,51)	102 23,86 (5,72)	0,55 (0,23)	-0,46 [-1,10;0,18] 0,1556 -0,12 [-0,29;0,05]
Tumorstadium (p-Wert des Interaktionsterms: 0,1331)																			
IIA	93 23,88 (5,98)	88 24,40 (6,10)	86 24,93 (5,48)	82 24,39 (5,45)	81 24,04 (5,83)	77 24,62 (5,64)	76 24,70 (5,79)	39 24,51 (5,90)	0,69 (0,32)	95 23,28 (5,04)	90 23,48 (5,35)	90 23,77 (4,68)	85 23,27 (5,31)	81 24,16 (5,08)	71 23,55 (5,15)	74 23,99 (4,81)	37 23,70 (5,03)	0,28 (0,32)	0,41 [-0,48;1,30] 0,3678 0,13 [-0,15;0,42]
IIB	133 23,64 (5,79)	126 24,90 (5,67)	118 24,79 (5,26)	116 24,45 (5,44)	113 24,40 (5,87)	101 23,62 (5,72)	110 24,37 (5,29)	67 24,42 (5,61)	0,69 (0,32)	113 24,33 (5,49)	107 24,40 (5,09)	106 24,51 (4,90)	98 24,62 (5,50)	94 25,35 (4,89)	85 24,78 (5,17)	81 25,16 (5,79)	45 24,27 (5,73)	0,43 (0,35)	0,26 [-0,68;1,21] 0,5874 0,07 [-0,18;0,32]
IIIA	429 23,93 (5,34)	404 24,36 (5,12)	394 24,42 (5,32)	373 23,60 (5,54)	350 23,83 (5,66)	315 23,77 (5,37)	320 23,41 (5,17)	156 23,41 (5,12)	-0,01 (0,17)	436 23,79 (5,66)	414 24,41 (5,30)	419 24,73 (5,20)	394 24,68 (5,25)	378 24,45 (5,70)	335 24,48 (5,49)	316 24,46 (5,78)	172 24,59 (5,53)	0,74 (0,17)	-0,74 [-1,22;-0,27] 0,0022 -0,21 [-0,34;-0,08]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIB	47 23,53 (6,11)	45 24,20 (6,52)	45 24,69 (6,49)	44 24,00 (6,77)	41 24,93 (6,52)	36 23,36 (5,23)	31 24,52 (5,85)	15 25,20 (4,90)	0,64 (0,53)	41 24,98 (6,19)	40 25,98 (5,69)	39 26,15 (5,83)	35 26,80 (5,62)	34 25,76 (5,65)	31 25,16 (5,80)	30 25,27 (6,21)	14 24,93 (7,32)	1,03 (0,57)	-0,39 [-1,95;1,17] 0,6201 -0,11 [-0,53;0,31]
IIIC	403 24,10 (5,44)	378 24,79 (5,40)	367 24,75 (5,70)	338 24,42 (5,56)	325 24,20 (5,78)	283 24,06 (5,76)	291 23,95 (5,56)	171 24,07 (5,18)	0,20 (0,19)	424 23,56 (5,75)	404 24,35 (5,45)	387 24,30 (5,55)	364 24,32 (5,46)	345 24,43 (5,48)	298 24,41 (5,52)	302 24,29 (5,52)	168 23,93 (5,52)	0,62 (0,18)	-0,41 [-0,92;0,10] 0,1167 -0,11 [-0,25;0,03]
Tumorgrading (p-Wert des Interaktionsterms: 0,8106)																			
G1	82 23,07 (5,75)	79 24,57 (5,17)	81 24,43 (5,71)	74 23,55 (5,42)	70 23,06 (6,59)	66 23,33 (5,56)	63 23,14 (5,68)	32 23,09 (4,96)	0,44 (0,41)	84 24,68 (5,26)	82 25,45 (5,54)	78 25,24 (5,18)	71 25,34 (4,85)	74 24,23 (5,69)	65 25,05 (5,08)	55 25,36 (5,19)	34 24,76 (5,90)	0,56 (0,40)	-0,12 [-1,25;1,02] 0,8404 -0,03 [-0,34;0,27]
G2	526 24,15 (5,49)	499 24,67 (5,49)	481 24,70 (5,63)	452 24,01 (5,77)	433 24,15 (5,87)	375 23,87 (5,73)	374 23,87 (5,42)	211 23,93 (5,36)	0,04 (0,16)	534 23,67 (5,85)	505 24,21 (5,38)	505 24,39 (5,38)	477 24,39 (5,54)	447 24,34 (5,68)	403 24,15 (5,60)	392 23,82 (5,83)	214 24,02 (5,76)	0,46 (0,16)	-0,42 [-0,86;0,02] 0,0621 -0,11 [-0,24;0,01]
G3	450 23,88 (5,50)	420 24,54 (5,51)	405 24,66 (5,44)	383 24,27 (5,40)	367 24,26 (5,58)	334 24,02 (5,34)	356 24,00 (5,34)	185 24,08 (5,34)	0,45 (0,17)	436 23,52 (5,48)	413 24,35 (5,24)	405 24,46 (5,24)	379 24,38 (5,31)	365 24,90 (5,12)	315 24,75 (5,30)	316 25,08 (5,46)	166 24,45 (5,41)	0,93 (0,17)	-0,48 [-0,96;0,00] 0,0512 -0,13 [-0,26;0,00]
GX	47 23,43 (5,46)	42 23,98 (4,64)	43 23,98 (4,82)	44 23,84 (5,79)	40 23,88 (5,36)	37 24,41 (6,02)	37 23,89 (5,85)	22 24,18 (4,74)	0,29 (0,48)	53 24,77 (4,88)	53 23,92 (5,36)	52 24,63 (4,90)	48 24,77 (5,12)	45 24,07 (6,00)	37 23,46 (5,09)	39 24,18 (4,49)	21 24,43 (4,35)	0,10 (0,46)	0,19 [-1,14;1,52] 0,7765 0,06 [-0,34;0,45]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,8506)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Negativ	137 23,30 (5,66)	131 23,60 (5,82)	124 24,07 (5,59)	116 23,67 (5,40)	105 23,51 (6,17)	93 23,43 (5,47)	100 23,87 (5,07)	63 23,11 (5,33)	0,33 (0,30)	149 23,50 (5,51)	139 24,23 (5,26)	134 24,90 (5,03)	126 24,41 (5,54)	122 23,91 (5,22)	103 24,18 (5,30)	114 23,75 (5,23)	56 23,41 (5,04)	0,70 (0,29)	-0,37 [-1,20;0,45] 0,3748 -0,11 [-0,34;0,13]
Positiv	939 23,95 (5,49)	880 24,64 (5,37)	858 24,59 (5,52)	813 24,02 (5,61)	784 24,06 (5,72)	698 23,85 (5,56)	708 23,80 (5,46)	377 24,06 (5,30)	0,21 (0,12)	935 23,70 (5,65)	895 24,30 (5,37)	885 24,37 (5,35)	830 24,43 (5,36)	790 24,56 (5,53)	698 24,40 (5,49)	669 24,45 (5,66)	367 24,27 (5,65)	0,63 (0,12)	-0,42 [-0,75;-0,09] 0,0133 -0,11 [-0,21;-0,02]
Unbekannt	9 25,22 (6,48)	9 25,33 (4,53)	9 28,56 (4,80)	7 29,71 (4,42)	4 32,75 (3,77)	6 28,17 (6,43)	5 27,40 (5,59)	1 28,00 (NE)	2,25 (1,23)	7 26,57 (5,47)	6 28,67 (1,86)	6 27,00 (2,10)	6 30,33 (2,94)	6 27,00 (4,00)	6 28,83 (3,71)	5 29,00 (3,39)	5 28,40 (2,88)	3,16 (1,25)	-0,90 [-4,67;2,86] 0,6139 -0,24 [-1,18;0,69]
Ethnizität (p-Wert des Interaktionsterms: 0,6039)																			
Weiß	808 23,66 (5,50)	754 24,39 (5,28)	737 24,58 (5,29)	694 23,79 (5,28)	657 23,77 (5,63)	593 23,80 (5,37)	597 23,70 (5,28)	338 24,13 (5,19)	0,17 (0,12)	819 23,74 (5,52)	772 24,37 (5,29)	760 24,55 (5,18)	706 24,36 (5,26)	676 24,46 (5,35)	602 24,55 (5,27)	579 24,35 (5,54)	323 24,67 (5,41)	0,63 (0,12)	-0,46 [-0,80;-0,12] 0,0074 -0,13 [-0,23;-0,04]
Asiatisch	233 24,68 (5,58)	225 25,03 (5,65)	218 24,84 (6,20)	210 24,90 (6,39)	205 24,84 (6,29)	176 23,89 (6,08)	187 24,05 (5,86)	97 22,94 (5,57)	0,32 (0,26)	221 23,87 (5,99)	216 24,30 (5,60)	215 24,55 (5,70)	207 24,80 (5,90)	200 24,86 (6,00)	167 23,90 (5,99)	172 24,61 (5,61)	88 22,88 (5,73)	0,66 (0,26)	-0,34 [-1,06;0,39] 0,3582 -0,09 [-0,27;0,10]
Andere	54 24,67 (4,93)	51 25,41 (6,33)	47 24,40 (5,84)	43 24,53 (5,95)	42 24,95 (5,79)	36 26,50 (5,74)	40 25,63 (5,29)	14 26,50 (4,40)	0,85 (0,58)	58 24,47 (5,56)	57 24,96 (5,28)	56 24,34 (5,44)	53 25,34 (5,33)	47 24,70 (5,32)	42 25,14 (5,62)	44 25,73 (6,23)	19 23,68 (6,50)	0,18 (0,55)	0,67 [-0,93;2,27] 0,4070 0,16 [-0,21;0,53]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,2942)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Tamoxifen	103 22,50 (5,20)	97 23,34 (4,90)	98 23,68 (5,22)	95 23,24 (5,58)	93 23,89 (6,09)	90 23,46 (5,65)	91 23,32 (5,52)	55 22,24 (5,81)	0,81 (0,32)	124 23,37 (5,34)	122 23,92 (4,89)	120 23,72 (4,94)	109 23,94 (5,19)	103 23,25 (5,11)	94 23,90 (4,95)	92 23,58 (4,61)	56 23,00 (5,45)	0,48 (0,30)	0,32 [-0,54;1,19] 0,4646 0,10 [-0,16;0,36]
Aromatase-Inhibitor	1004 24,08 (5,52)	945 24,70 (5,47)	914 24,73 (5,54)	860 24,17 (5,59)	819 24,11 (5,76)	724 23,96 (5,55)	739 23,94 (5,41)	395 24,18 (5,17)	0,17 (0,12)	987 23,81 (5,68)	935 24,43 (5,42)	923 24,62 (5,34)	869 24,56 (5,41)	831 24,71 (5,51)	728 24,49 (5,50)	712 24,56 (5,72)	381 24,44 (5,55)	0,65 (0,12)	-0,48 [-0,80;-0,16] 0,0034 -0,13 [-0,22;-0,04]
ECOG-PS (p-Wert des Interaktionsterms: 0,5985)																			
ECOG-PS 0	932 24,11 (5,47)	876 24,66 (5,40)	854 24,74 (5,55)	813 24,19 (5,58)	778 24,19 (5,79)	699 24,04 (5,59)	703 24,03 (5,40)	380 24,32 (5,30)	0,26 (0,12)	898 23,85 (5,63)	854 24,49 (5,32)	844 24,60 (5,21)	794 24,50 (5,33)	759 24,54 (5,55)	676 24,36 (5,46)	664 24,38 (5,67)	356 24,05 (5,59)	0,55 (0,12)	-0,29 [-0,62;0,04] 0,0857 -0,08 [-0,17;0,01]
ECOG-PS 1	175 22,98 (5,66)	166 24,15 (5,62)	158 24,06 (5,32)	142 23,40 (5,63)	134 23,51 (5,74)	115 23,07 (5,32)	127 22,97 (5,46)	70 21,93 (4,72)	0,11 (0,28)	213 23,39 (5,68)	203 23,86 (5,50)	199 24,15 (5,66)	184 24,47 (5,63)	175 24,62 (5,21)	146 24,75 (5,37)	140 24,76 (5,33)	81 25,14 (5,33)	1,05 (0,26)	-0,94 [-1,70;-0,19] 0,0143 -0,25 [-0,45;-0,05]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B BCS = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B BCS haben.
Abkürzungen: B: Baseline; BCS: Mammakarzinomspezifische Subskala; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t106_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: PWB aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8943)																			
Neoadjuvante Chemotherapie	196 23,85 (3,85)	189 22,51 (4,62)	181 22,79 (4,66)	177 22,67 (4,70)	165 22,45 (4,89)	150 22,83 (4,92)	147 22,90 (5,10)	75 22,69 (5,36)	-1,13 (0,24)	193 23,34 (4,52)	181 23,22 (4,36)	179 23,43 (4,08)	156 23,80 (4,25)	145 24,01 (3,78)	121 23,73 (4,44)	136 22,96 (4,92)	77 23,26 (5,32)	-0,23 (0,25)	-0,90 [-1,58;-0,21] 0,0106 -0,26 [-0,46;-0,06]
Adjuvante Chemotherapie	288 23,08 (4,48)	274 22,38 (4,79)	270 22,60 (4,86)	266 22,71 (4,78)	254 22,67 (4,47)	214 22,90 (4,83)	205 23,33 (4,32)	128 23,15 (4,30)	-0,29 (0,17)	284 23,17 (4,09)	276 23,37 (4,14)	269 23,61 (4,07)	261 23,56 (4,40)	241 23,71 (4,30)	222 23,35 (4,56)	219 23,22 (4,67)	121 23,17 (4,10)	0,30 (0,17)	-0,58 [-1,06;-0,10] 0,0176 -0,20 [-0,36;-0,03]
Keine Chemotherapie	7 25,00 (3,61)	7 23,00 (4,40)	6 21,83 (4,45)	6 22,83 (4,54)	5 22,20 (6,50)	5 22,00 (5,96)	6 23,33 (5,50)	2 25,50 (2,12)	-1,87 (0,76)	1 22,00 (NE)	1 23,00 (NE)	1 18,00 (NE)	1 22,00 (NE)	1 23,00 (NE)	1 21,00 (NE)	1 21,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,9708)																			
Nordamerika / Europa	204 23,69 (3,81)	189 22,23 (4,59)	182 22,33 (4,94)	179 22,39 (4,91)	162 22,33 (4,82)	140 22,42 (5,21)	135 23,43 (4,54)	75 22,95 (4,61)	-1,08 (0,23)	197 23,12 (4,36)	183 22,85 (4,73)	176 23,17 (4,26)	155 23,12 (4,76)	141 23,61 (4,49)	134 23,10 (4,98)	133 22,73 (5,20)	66 22,64 (5,73)	-0,18 (0,24)	-0,89 [-1,55;-0,24] 0,0078 -0,27 [-0,46;-0,07]
Asien	163 23,35 (4,23)	162 22,46 (4,65)	158 22,85 (4,26)	156 23,06 (4,17)	150 22,99 (4,17)	130 23,19 (4,47)	137 23,28 (4,71)	69 23,87 (4,36)	-0,29 (0,21)	153 23,37 (3,66)	151 23,52 (3,53)	151 23,68 (4,08)	146 24,05 (3,68)	138 24,03 (3,83)	120 24,03 (3,86)	122 23,34 (4,47)	66 23,94 (3,47)	0,42 (0,22)	-0,71 [-1,32;-0,11] 0,0202 -0,26 [-0,48;-0,04]
Andere	124 23,06 (4,89)	119 22,77 (4,99)	117 22,95 (5,14)	114 22,66 (5,17)	112 22,38 (5,01)	99 23,04 (4,87)	86 22,52 (4,80)	61 22,10 (5,06)	-0,51 (0,30)	128 23,25 (4,77)	124 23,73 (4,16)	122 23,85 (3,79)	117 23,83 (4,47)	108 23,84 (3,95)	90 23,29 (4,57)	101 23,35 (4,49)	66 23,05 (4,28)	0,14 (0,29)	-0,65 [-1,48;0,17] 0,1208 -0,20 [-0,44;0,05]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4896)																			
< 20 mm	121 23,13 (3,91)	115 22,32 (4,38)	109 22,14 (4,64)	112 22,13 (5,15)	105 22,56 (4,59)	94 21,86 (5,21)	91 23,00 (4,58)	54 23,17 (4,46)	-0,67 (0,27)	123 22,80 (4,39)	116 22,89 (4,13)	116 23,28 (3,79)	107 23,45 (3,74)	102 23,75 (3,78)	87 23,20 (4,49)	85 23,67 (3,88)	50 23,04 (4,37)	0,15 (0,27)	-0,82 [-1,58;-0,06] 0,0338 -0,27 [-0,53;-0,02]
≥ 20 bis < 50 mm	230 23,77 (4,07)	221 22,39 (5,14)	220 23,06 (4,67)	215 22,85 (4,63)	197 22,53 (4,69)	171 23,02 (4,64)	165 23,12 (4,67)	97 22,69 (5,00)	-0,84 (0,22)	227 23,22 (4,22)	218 23,32 (4,38)	217 23,67 (4,17)	201 23,87 (4,64)	187 23,74 (4,39)	172 23,45 (4,63)	182 22,97 (5,02)	93 23,05 (5,03)	0,14 (0,22)	-0,98 [-1,58;-0,38] 0,0015 -0,30 [-0,48;-0,11]
≥ 50 mm	128 23,04 (4,87)	124 22,51 (4,35)	119 22,23 (5,08)	114 22,79 (4,55)	113 22,52 (4,77)	95 23,37 (4,95)	93 23,38 (4,88)	48 23,13 (4,48)	-0,44 (0,27)	123 23,75 (4,19)	119 23,66 (4,07)	111 23,50 (4,25)	105 23,45 (4,32)	95 24,08 (3,88)	81 23,80 (4,39)	85 22,92 (4,98)	51 23,59 (4,14)	-0,10 (0,27)	-0,34 [-1,10;0,42] 0,3772 -0,11 [-0,36;0,14]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,1702)																			
0-3	177 23,72 (3,89)	169 22,68 (4,36)	160 22,74 (4,49)	159 22,94 (4,40)	144 23,01 (4,09)	130 23,33 (4,43)	131 23,22 (4,87)	77 23,51 (4,10)	-0,61 (0,23)	190 23,10 (4,14)	181 23,39 (3,87)	176 23,52 (4,03)	164 23,67 (3,76)	155 23,65 (3,85)	136 23,40 (4,10)	135 22,70 (5,00)	71 22,69 (5,02)	0,00 (0,22)	-0,61 [-1,24;0,01] 0,0547 -0,20 [-0,41;0,00]
4-9	216 23,15 (4,48)	207 21,88 (5,10)	204 22,38 (4,86)	198 22,43 (4,78)	193 22,10 (4,83)	169 22,41 (4,92)	159 23,13 (4,29)	85 22,42 (4,99)	-0,75 (0,20)	210 23,32 (4,38)	201 23,31 (4,25)	200 23,60 (4,03)	186 23,67 (4,42)	174 24,08 (4,08)	153 23,68 (4,60)	160 23,41 (4,48)	87 23,64 (4,23)	0,29 (0,21)	-1,05 [-1,61;-0,48] 0,0003 -0,35 [-0,54;-0,16]
≥ 10	98 23,46 (4,33)	94 23,26 (4,27)	93 23,18 (5,02)	92 22,84 (5,18)	87 22,92 (5,09)	70 23,07 (5,46)	68 23,10 (5,17)	43 23,26 (5,08)	-0,41 (0,38)	78 23,32 (4,29)	76 23,12 (4,94)	73 23,37 (4,38)	68 23,53 (5,34)	58 23,52 (4,83)	55 23,11 (5,23)	61 23,28 (4,93)	40 23,18 (4,62)	-0,28 (0,42)	-0,13 [-1,25;0,99] 0,8212 -0,03 [-0,33;0,26]
Tumorstadium (p-Wert des Interaktionsterms: 0,0557)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 24,29 (3,37)	49 22,88 (4,28)	48 22,71 (4,17)	47 22,68 (4,65)	46 22,93 (4,00)	40 21,95 (4,64)	39 23,00 (4,14)	23 23,09 (4,41)	-1,27 (0,41)	57 22,93 (4,12)	54 22,85 (4,11)	54 23,11 (4,22)	48 23,31 (3,45)	47 23,72 (3,26)	36 23,22 (4,30)	37 23,38 (3,90)	19 23,37 (2,81)	-0,12 (0,40)	-1,15 [-2,28;-0,02] 0,0466 -0,39 [-0,77;-0,01]
IIB	45 23,84 (3,23)	44 22,91 (4,64)	41 24,02 (3,55)	42 23,38 (3,71)	35 23,31 (3,90)	34 24,15 (3,05)	31 23,58 (4,09)	22 23,86 (3,09)	-0,40 (0,47)	64 23,53 (3,78)	62 23,74 (3,92)	61 23,75 (3,41)	56 23,86 (3,96)	55 23,27 (3,61)	54 23,56 (3,57)	55 22,31 (5,56)	32 22,28 (5,61)	-0,51 (0,38)	0,10 [-1,10;1,30] 0,8634 0,03 [-0,35;0,42]
IIIA	213 23,20 (4,43)	207 21,96 (5,06)	201 22,52 (4,87)	196 22,73 (4,74)	190 22,25 (4,81)	165 22,96 (4,68)	158 23,13 (4,41)	86 22,95 (4,54)	-0,58 (0,20)	193 23,19 (4,45)	183 23,32 (4,05)	180 23,54 (3,93)	173 23,45 (4,33)	158 23,94 (3,92)	133 23,48 (4,58)	141 23,17 (4,46)	71 23,52 (4,15)	0,29 (0,21)	-0,86 [-1,45;-0,28] 0,0036 -0,29 [-0,49;-0,10]
IIIB	14 21,36 (7,20)	13 20,38 (5,74)	13 18,92 (7,10)	13 18,46 (6,08)	10 19,50 (6,13)	8 18,63 (8,37)	11 20,82 (7,82)	6 17,17 (5,12)	-1,89 (0,70)	14 24,29 (3,12)	14 25,71 (1,73)	14 25,64 (1,74)	11 25,64 (2,66)	10 26,20 (2,44)	10 24,80 (2,62)	9 24,00 (3,74)	5 22,00 (5,57)	1,16 (0,74)	-3,05 [-5,19;-0,91] 0,0069 -1,10 [-1,87;-0,32]
IIIC	166 23,51 (4,12)	156 22,99 (4,21)	153 22,82 (4,74)	150 22,82 (4,78)	142 22,95 (4,66)	121 22,93 (5,21)	118 23,36 (4,97)	67 23,27 (5,17)	-0,47 (0,27)	149 23,17 (4,38)	144 23,03 (4,71)	139 23,34 (4,60)	129 23,75 (4,89)	117 23,76 (4,90)	111 23,40 (5,05)	114 23,28 (5,04)	71 23,35 (4,89)	0,06 (0,28)	-0,53 [-1,29;0,24] 0,1770 -0,15 [-0,37;0,07]
Tumorgrading (p-Wert des Interaktionsterms: 0,9679)																			
G1	45 24,09 (3,85)	43 23,09 (3,48)	40 23,18 (4,42)	40 23,48 (4,03)	39 23,10 (4,15)	33 22,45 (5,82)	33 22,97 (4,50)	18 22,61 (5,34)	-0,86 (0,44)	38 23,58 (4,45)	36 23,75 (4,20)	34 23,65 (3,95)	36 23,67 (4,33)	32 23,59 (4,59)	28 22,43 (5,01)	25 23,44 (4,43)	13 25,00 (3,37)	0,03 (0,48)	-0,89 [-2,19;0,40] 0,1739 -0,30 [-0,74;0,13]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	213 23,35 (4,52)	202 22,17 (4,94)	202 22,50 (4,95)	196 22,52 (4,83)	188 22,58 (4,59)	165 22,82 (4,73)	167 23,32 (4,43)	87 23,59 (4,26)	-0,66 (0,22)	207 23,25 (4,42)	200 23,36 (4,56)	196 23,46 (4,60)	182 23,55 (4,75)	161 24,02 (4,30)	148 23,45 (5,03)	154 23,12 (4,95)	86 23,00 (4,79)	0,04 (0,23)	-0,71 [-1,33;-0,09] 0,0259 -0,22 [-0,41;-0,03]
G3	205 23,28 (4,06)	197 22,42 (4,80)	190 22,61 (4,77)	187 22,53 (4,84)	172 22,27 (4,94)	149 22,83 (4,97)	138 22,88 (5,08)	87 22,07 (5,05)	-0,67 (0,22)	203 23,05 (4,08)	194 23,08 (3,93)	192 23,40 (3,69)	173 23,62 (3,88)	168 23,52 (3,96)	143 23,47 (4,02)	153 22,92 (4,72)	86 23,16 (4,66)	0,07 (0,22)	-0,75 [-1,37;-0,13] 0,0183 -0,23 [-0,43;-0,04]
GX	28 23,82 (4,05)	28 23,64 (3,82)	25 23,60 (3,76)	26 23,96 (4,04)	25 23,92 (3,67)	22 23,91 (3,74)	20 23,95 (4,01)	13 25,92 (1,89)	0,05 (0,50)	29 23,83 (4,25)	27 23,89 (3,80)	26 24,77 (2,58)	26 24,35 (4,41)	25 24,88 (3,05)	24 24,83 (3,06)	24 24,04 (4,23)	13 23,08 (3,93)	0,50 (0,48)	-0,45 [-1,84;0,95] 0,5216 -0,17 [-0,69;0,35]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,3071)																			
Negativ	46 23,43 (4,56)	43 21,56 (5,63)	41 21,93 (5,87)	42 21,95 (5,92)	39 21,44 (5,35)	38 21,84 (5,55)	36 21,00 (6,27)	12 21,33 (6,18)	-1,75 (0,52)	39 23,74 (3,40)	36 23,11 (4,32)	35 23,77 (3,54)	30 24,23 (3,65)	31 24,29 (3,84)	26 24,35 (3,71)	31 23,74 (4,67)	15 24,67 (3,13)	0,19 (0,57)	-1,95 [-3,48;-0,41] 0,0138 -0,55 [-0,98;-0,12]
Positiv	427 23,43 (4,24)	410 22,54 (4,62)	401 22,73 (4,69)	392 22,72 (4,61)	372 22,73 (4,58)	320 22,99 (4,83)	306 23,38 (4,47)	183 23,16 (4,65)	-0,54 (0,15)	422 23,22 (4,31)	407 23,38 (4,16)	400 23,64 (3,99)	374 23,61 (4,33)	341 23,76 (4,17)	305 23,49 (4,48)	315 23,04 (4,77)	176 23,05 (4,74)	0,11 (0,15)	-0,64 [-1,06;-0,22] 0,0027 -0,21 [-0,34;-0,07]
Unbekannt	2 22,50 (3,54)	2 19,00 (9,90)	2 23,50 (3,54)	1 26,00 (NE)	1 25,00 (NE)	1 20,00 (NE)	1 26,00 (NE)	0	NE	8 20,75 (6,30)	7 19,43 (7,04)	8 18,75 (7,36)	6 21,00 (8,29)	6 23,67 (4,23)	8 19,63 (7,31)	4 22,00 (7,79)	2 23,00 (4,24)	-0,26 (1,23)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,0519)																			

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	276 23,47 (4,39)	261 22,37 (4,90)	252 22,47 (5,11)	246 22,45 (5,01)	230 22,21 (5,06)	201 22,64 (5,04)	184 23,08 (4,58)	120 22,63 (4,78)	-0,93 (0,20)	285 23,13 (4,44)	268 23,07 (4,56)	261 23,24 (4,18)	241 23,15 (4,77)	223 23,46 (4,34)	202 23,01 (4,92)	210 22,82 (4,92)	122 22,66 (5,10)	-0,27 (0,20)	-0,66 [-1,22;-0,11] 0,0198 -0,20 [-0,36;-0,03]
Asiatisch	188 23,39 (4,11)	185 22,64 (4,50)	181 23,13 (4,19)	179 23,27 (4,07)	171 23,16 (4,08)	149 23,37 (4,41)	153 23,41 (4,65)	75 23,83 (4,24)	-0,13 (0,20)	166 23,30 (3,71)	164 23,57 (3,73)	162 23,78 (4,05)	157 24,21 (3,68)	145 24,14 (3,78)	124 23,95 (3,92)	130 23,24 (4,64)	67 23,96 (3,45)	0,53 (0,21)	-0,65 [-1,22;-0,09] 0,0237 -0,24 [-0,45;-0,03]
Andere	16 22,94 (4,40)	15 21,80 (4,48)	15 20,60 (5,40)	15 19,60 (6,92)	15 21,80 (5,13)	13 21,62 (6,92)	14 22,07 (5,46)	9 21,44 (6,65)	-1,64 (0,89)	17 23,06 (6,47)	16 24,06 (3,21)	17 24,88 (2,64)	16 25,00 (2,31)	14 25,86 (2,68)	12 25,33 (2,31)	12 26,25 (1,86)	7 25,86 (2,67)	1,90 (0,88)	-3,55 [-6,12;-0,98] 0,0086 -0,96 [-1,66;-0,25]
ECOG-PS (p-Wert des Interaktionsterms: 0,4120)																			
ECOG-PS 0	441 23,39 (4,28)	421 22,41 (4,69)	408 22,58 (4,82)	403 22,60 (4,76)	379 22,50 (4,67)	331 22,87 (4,81)	322 23,12 (4,72)	190 23,06 (4,68)	-0,71 (0,15)	425 23,37 (4,17)	406 23,42 (4,09)	397 23,61 (3,94)	372 23,81 (4,18)	344 23,94 (4,04)	308 23,73 (4,26)	321 23,21 (4,63)	179 23,20 (4,65)	0,09 (0,15)	-0,79 [-1,20;-0,38] 0,0002 -0,26 [-0,39;-0,12]
ECOG-PS 1	50 23,64 (3,96)	49 22,73 (4,89)	49 23,37 (4,31)	46 23,50 (4,45)	45 23,24 (4,57)	38 22,76 (5,38)	36 23,44 (4,22)	15 22,33 (5,04)	-0,10 (0,53)	53 22,17 (4,85)	52 22,46 (5,07)	52 22,87 (4,98)	46 22,30 (5,30)	43 22,93 (4,58)	36 21,31 (5,91)	35 22,20 (5,78)	19 23,32 (4,19)	0,20 (0,52)	-0,30 [-1,78;1,19] 0,6916 -0,08 [-0,47;0,31]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B PWB = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B PWB haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; PWB: körperliches Wohlbefinden; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t107_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: PWB aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,1114)																			
< 65 Jahre	805 23,39 (4,22)	761 22,40 (4,74)	746 22,49 (4,63)	702 22,66 (4,50)	678 22,58 (4,68)	597 22,67 (4,62)	605 22,97 (4,69)	331 23,21 (4,58)	-0,77 (0,11)	832 23,06 (4,24)	792 23,09 (4,24)	784 23,21 (4,13)	731 23,13 (4,26)	696 23,37 (4,13)	611 23,47 (4,23)	607 23,19 (4,62)	319 23,23 (4,36)	-0,02 (0,11)	-0,75 [-1,06;-0,44] <,0001 -0,24 [-0,33;-0,14]
≥ 65 Jahre	304 23,58 (4,22)	285 22,14 (4,59)	267 22,74 (4,20)	258 22,75 (4,59)	242 22,14 (4,84)	221 22,49 (4,43)	227 23,00 (4,65)	121 22,82 (4,45)	-1,20 (0,17)	279 23,35 (4,17)	268 23,46 (4,25)	262 23,59 (4,07)	248 23,66 (3,73)	241 23,34 (4,13)	211 23,22 (4,48)	198 23,49 (4,00)	118 23,36 (4,79)	-0,10 (0,18)	-1,11 [-1,59;-0,62] <,0001 -0,37 [-0,53;-0,20]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,3049)																			
Neoadjuvante Chemotherapie	363 23,71 (4,04)	336 22,40 (4,88)	324 22,72 (4,46)	301 22,56 (4,73)	281 22,36 (5,18)	238 22,71 (4,58)	254 22,86 (4,55)	130 23,26 (4,36)	-1,14 (0,17)	365 22,87 (4,32)	347 23,07 (4,21)	333 22,99 (4,03)	309 22,98 (4,30)	293 23,11 (4,18)	248 23,02 (4,64)	261 22,87 (4,67)	139 22,68 (4,37)	-0,25 (0,17)	-0,89 [-1,36;-0,42] 0,0002 -0,28 [-0,42;-0,13]
Adjuvante Chemotherapie	686 23,28 (4,31)	656 22,31 (4,65)	638 22,49 (4,60)	608 22,77 (4,41)	593 22,54 (4,48)	538 22,63 (4,58)	532 23,06 (4,73)	295 23,08 (4,65)	-0,66 (0,12)	679 23,21 (4,17)	649 23,19 (4,17)	653 23,37 (4,21)	614 23,38 (4,01)	597 23,48 (4,15)	528 23,64 (4,08)	497 23,43 (4,43)	271 23,56 (4,53)	0,11 (0,12)	-0,77 [-1,10;-0,45] <,0001 -0,25 [-0,36;-0,15]
Keine Chemotherapie	60 23,60 (4,17)	54 22,22 (4,15)	51 22,35 (3,79)	51 22,43 (4,63)	46 22,09 (4,89)	42 21,98 (4,36)	46 22,63 (4,80)	27 22,63 (4,35)	-2,08 (0,40)	67 23,84 (4,12)	64 23,75 (5,12)	60 24,37 (3,30)	56 23,61 (4,65)	47 23,38 (3,52)	46 22,74 (4,64)	47 23,66 (3,68)	27 23,33 (4,39)	-0,67 (0,39)	-1,41 [-2,51;-0,31] 0,0128 -0,45 [-0,80;-0,10]
Region (p-Wert des Interaktionsterms: 0,0579)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	550 23,38 (4,35)	498 21,92 (5,12)	483 22,13 (4,88)	451 22,54 (4,74)	425 22,33 (4,90)	385 22,43 (4,81)	394 22,78 (4,87)	212 22,98 (4,74)	-1,15 (0,14)	529 22,84 (4,42)	491 22,97 (4,45)	483 23,06 (4,17)	441 23,11 (4,35)	424 23,10 (4,42)	377 23,23 (4,48)	346 23,06 (4,57)	206 23,37 (4,34)	-0,04 (0,14)	-1,12 [-1,50;-0,74] <,0001 -0,35 [-0,47;-0,23]
Asien	195 23,90 (3,86)	190 22,99 (4,09)	185 23,21 (3,95)	178 23,14 (4,21)	173 23,12 (4,27)	152 23,26 (4,10)	163 23,20 (4,27)	87 23,13 (4,23)	-0,70 (0,21)	192 23,83 (3,65)	189 23,43 (4,17)	187 23,52 (4,18)	179 23,64 (3,91)	175 23,89 (4,01)	149 23,71 (4,11)	155 23,79 (3,85)	81 23,25 (4,74)	-0,16 (0,22)	-0,54 [-1,14;0,06] 0,0797 -0,18 [-0,38;0,02]
Andere	364 23,28 (4,18)	358 22,56 (4,33)	345 22,80 (4,23)	331 22,64 (4,37)	322 22,29 (4,69)	281 22,54 (4,45)	275 23,12 (4,63)	153 23,27 (4,45)	-0,61 (0,16)	390 23,19 (4,18)	380 23,34 (3,99)	376 23,53 (4,00)	359 23,27 (3,99)	338 23,42 (3,78)	296 23,46 (4,15)	304 23,22 (4,65)	150 23,12 (4,54)	0,03 (0,15)	-0,64 [-1,07;-0,20] 0,0041 -0,21 [-0,35;-0,07]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3784)																			
< 20 mm	280 23,07 (4,52)	258 22,11 (4,64)	255 22,23 (4,63)	245 22,01 (4,93)	236 21,97 (5,05)	211 22,15 (4,99)	210 22,80 (4,69)	106 22,84 (4,94)	-0,97 (0,19)	298 22,94 (4,30)	284 23,21 (4,10)	277 23,40 (3,86)	259 23,38 (4,11)	252 23,82 (3,82)	216 23,73 (4,04)	221 23,13 (4,88)	111 23,25 (4,43)	0,23 (0,19)	-1,20 [-1,73;-0,67] <,0001 -0,37 [-0,54;-0,21]
≥ 20 bis < 50 mm	569 23,68 (4,11)	547 22,53 (4,67)	521 22,75 (4,45)	504 23,01 (4,33)	479 22,71 (4,60)	428 22,98 (4,24)	433 23,31 (4,60)	232 23,19 (4,34)	-0,82 (0,13)	573 23,24 (4,23)	549 23,18 (4,34)	545 23,45 (4,09)	512 23,24 (4,19)	494 23,22 (4,19)	439 23,28 (4,50)	417 23,32 (4,41)	231 23,24 (4,44)	-0,15 (0,13)	-0,67 [-1,03;-0,30] 0,0003 -0,21 [-0,33;-0,10]
≥ 50 mm	243 23,28 (4,11)	226 21,96 (4,88)	221 22,49 (4,52)	198 22,77 (4,36)	191 22,52 (4,42)	166 22,50 (4,59)	175 22,42 (4,82)	106 23,01 (4,71)	-0,93 (0,19)	229 23,03 (4,14)	216 23,07 (4,24)	214 22,69 (4,50)	198 23,06 (4,11)	184 23,03 (4,34)	159 23,19 (4,10)	159 23,18 (4,09)	91 23,20 (4,71)	-0,19 (0,20)	-0,74 [-1,29;-0,19] 0,0085 -0,24 [-0,42;-0,06]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7681)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	369 23,35 (4,18)	349 22,28 (4,75)	337 22,58 (4,44)	315 22,68 (4,29)	306 22,58 (4,56)	278 22,60 (4,59)	288 22,78 (5,00)	168 23,43 (4,33)	-0,84 (0,16)	360 23,20 (3,98)	344 23,06 (4,17)	341 23,20 (3,89)	313 23,25 (3,91)	304 23,29 (3,94)	261 23,29 (4,39)	255 23,28 (4,47)	143 23,47 (4,51)	-0,11 (0,16)	-0,72 [-1,16;-0,28] 0,0014 -0,24 [-0,38;-0,09]
4-9	476 23,43 (4,22)	448 22,40 (4,65)	438 22,53 (4,65)	421 22,65 (4,67)	400 22,32 (4,82)	357 22,70 (4,58)	356 23,21 (4,46)	175 22,88 (4,56)	-0,89 (0,15)	485 23,02 (4,46)	465 23,25 (4,38)	464 23,46 (4,19)	439 23,11 (4,51)	420 23,45 (4,21)	377 23,22 (4,58)	359 23,32 (4,68)	192 23,28 (4,29)	0,02 (0,14)	-0,91 [-1,31;-0,50] <,0001 -0,29 [-0,41;-0,16]
≥ 10	264 23,58 (4,28)	249 22,28 (4,72)	238 22,56 (4,41)	224 22,76 (4,57)	214 22,56 (4,76)	183 22,49 (4,54)	188 22,83 (4,57)	109 22,97 (4,83)	-0,97 (0,19)	266 23,25 (4,10)	251 23,24 (4,09)	241 23,17 (4,30)	227 23,58 (3,67)	213 23,29 (4,24)	184 23,93 (3,47)	191 23,14 (4,08)	102 22,94 (4,78)	-0,08 (0,19)	-0,89 [-1,43;-0,35] 0,0012 -0,28 [-0,45;-0,11]
Tumorstadium (p-Wert des Interaktionsterms: 0,1459)																			
IIA	93 23,25 (4,24)	88 22,43 (4,35)	86 22,55 (4,40)	82 22,04 (4,52)	82 22,24 (5,07)	77 22,61 (4,86)	76 22,64 (5,13)	39 22,95 (4,94)	-0,81 (0,35)	95 22,55 (4,53)	92 23,16 (4,16)	90 22,70 (4,14)	85 23,21 (4,19)	81 23,62 (3,43)	71 23,56 (3,75)	74 22,93 (5,13)	37 23,14 (5,20)	0,12 (0,35)	-0,93 [-1,90;0,05] 0,0618 -0,27 [-0,56;0,01]
IIB	133 23,97 (3,78)	126 23,06 (4,49)	117 23,19 (3,88)	116 23,36 (3,81)	113 23,37 (4,01)	101 23,11 (4,29)	110 23,40 (4,93)	68 24,04 (3,63)	-0,87 (0,25)	113 23,76 (3,62)	107 22,98 (4,37)	106 23,55 (4,08)	99 22,87 (4,17)	94 22,45 (4,66)	85 22,89 (5,13)	81 23,09 (4,39)	45 22,60 (4,79)	-0,87 (0,27)	-0,00 [-0,73;0,72] 0,9898 -0,00 [-0,25;0,25]
IIIA	431 23,21 (4,07)	408 21,99 (4,77)	397 22,32 (4,65)	376 22,27 (4,78)	354 21,99 (4,84)	318 22,42 (4,56)	321 22,73 (4,63)	157 22,64 (4,66)	-1,01 (0,15)	436 23,03 (4,38)	414 23,23 (4,21)	421 23,46 (4,13)	395 23,37 (4,01)	378 23,52 (3,97)	335 23,30 (4,46)	317 23,47 (4,55)	172 23,45 (4,29)	0,15 (0,15)	-1,16 [-1,58;-0,73] <,0001 -0,36 [-0,50;-0,23]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIB	47 23,70 (4,35)	45 22,78 (5,30)	45 23,13 (5,05)	44 23,07 (4,60)	41 22,68 (5,19)	36 23,19 (4,73)	31 23,97 (4,32)	15 25,07 (2,96)	-0,62 (0,36)	41 23,61 (4,64)	40 24,25 (3,48)	39 23,85 (3,37)	35 23,46 (4,79)	34 24,65 (3,27)	31 24,10 (4,49)	30 23,93 (4,86)	14 24,50 (4,64)	0,37 (0,38)	-0,99 [-2,04;0,06] 0,0652 -0,40 [-0,82;0,02]
IIIC	403 23,54 (4,47)	378 22,38 (4,69)	366 22,55 (4,53)	340 23,04 (4,40)	328 22,71 (4,61)	284 22,62 (4,58)	292 23,05 (4,56)	171 23,00 (4,73)	-0,84 (0,16)	424 23,15 (4,08)	405 23,10 (4,33)	388 23,15 (4,18)	363 23,24 (4,22)	348 23,25 (4,33)	298 23,55 (3,96)	302 23,11 (4,22)	168 23,17 (4,43)	-0,11 (0,15)	-0,73 [-1,15;-0,30] 0,0009 -0,23 [-0,37;-0,10]
Tumorgrading (p-Wert des Interaktionsterms: 0,5424)																			
G1	83 22,73 (4,70)	81 22,68 (4,30)	82 22,44 (4,79)	75 22,96 (4,24)	72 22,69 (4,62)	67 23,09 (4,27)	63 23,11 (4,76)	32 22,81 (4,22)	0,00 (0,33)	84 23,32 (4,72)	82 23,67 (4,27)	79 23,68 (3,94)	71 23,96 (3,95)	74 23,42 (4,95)	65 23,92 (4,07)	55 24,16 (4,13)	34 24,03 (3,55)	0,54 (0,33)	-0,54 [-1,46;0,39] 0,2529 -0,18 [-0,48;0,13]
G2	526 23,39 (4,36)	500 22,12 (5,03)	481 22,39 (4,72)	454 22,46 (4,75)	435 22,22 (4,81)	377 22,42 (4,46)	375 22,77 (4,68)	212 23,14 (4,52)	-1,04 (0,14)	534 23,00 (4,22)	505 22,98 (4,19)	507 23,16 (4,13)	476 23,05 (4,17)	448 23,28 (4,02)	403 23,13 (4,34)	392 22,94 (4,43)	214 22,79 (4,77)	-0,15 (0,14)	-0,89 [-1,27;-0,50] <,0001 -0,28 [-0,40;-0,16]
G3	451 23,57 (4,00)	421 22,48 (4,40)	405 22,82 (4,20)	385 22,85 (4,32)	371 22,69 (4,58)	335 22,71 (4,73)	357 23,18 (4,67)	186 23,15 (4,57)	-0,82 (0,14)	436 23,15 (4,18)	416 23,23 (4,24)	405 23,24 (4,18)	381 23,34 (4,16)	367 23,33 (4,14)	315 23,52 (4,38)	317 23,37 (4,61)	166 23,68 (4,20)	-0,03 (0,15)	-0,79 [-1,20;-0,39] 0,0001 -0,26 [-0,39;-0,13]
GX	47 24,15 (3,18)	42 22,79 (4,23)	43 22,07 (4,68)	44 23,27 (4,21)	40 23,00 (4,89)	37 23,30 (4,36)	37 22,86 (4,64)	22 22,91 (5,16)	-1,61 (0,42)	53 24,15 (3,48)	53 23,94 (4,63)	52 24,56 (3,61)	48 23,48 (3,92)	45 24,20 (3,74)	37 24,30 (3,26)	39 24,59 (3,43)	21 24,24 (3,58)	0,06 (0,40)	-1,66 [-2,83;-0,50] 0,0055 -0,57 [-0,97;-0,17]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,4982)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Negativ	137 22,75 (4,58)	132 21,54 (5,04)	123 21,83 (5,13)	116 22,33 (4,49)	107 22,50 (4,59)	93 22,45 (4,41)	100 22,92 (4,66)	63 22,21 (4,95)	-0,94 (0,28)	149 23,34 (4,11)	139 23,01 (4,56)	134 23,28 (4,57)	127 23,29 (4,22)	122 23,16 (4,44)	103 22,80 (4,86)	115 22,43 (5,22)	56 22,36 (5,17)	-0,57 (0,27)	-0,37 [-1,14;0,39] 0,3395 -0,11 [-0,35;0,12]
Positiv	941 23,50 (4,17)	883 22,39 (4,63)	859 22,60 (4,44)	818 22,66 (4,54)	789 22,42 (4,75)	701 22,58 (4,62)	710 22,94 (4,71)	378 23,24 (4,47)	-0,89 (0,10)	935 23,07 (4,25)	897 23,19 (4,21)	888 23,29 (4,06)	830 23,24 (4,14)	793 23,37 (4,11)	698 23,46 (4,21)	669 23,39 (4,33)	367 23,36 (4,38)	0,04 (0,10)	-0,93 [-1,21;-0,65] <,0001 -0,30 [-0,39;-0,21]
Unbekannt	9 24,78 (3,63)	9 21,78 (6,22)	9 24,67 (2,92)	7 25,57 (3,21)	5 26,80 (1,30)	6 24,50 (3,08)	5 24,20 (3,27)	1 26,00 (NE)	-0,15 (0,65)	7 24,43 (2,99)	6 25,67 (2,25)	6 24,83 (1,72)	6 26,17 (0,98)	6 25,00 (2,10)	6 25,67 (2,16)	5 26,20 (2,05)	5 26,60 (0,89)	1,61 (0,73)	-1,76 [-3,84;0,33] 0,0929 -0,86 [-1,84;0,12]
Ethnizität (p-Wert des Interaktionsterms: 0,1132)																			
Weiß	810 23,28 (4,32)	758 22,14 (4,77)	739 22,29 (4,59)	697 22,42 (4,63)	665 22,15 (4,85)	596 22,39 (4,63)	599 22,72 (4,76)	340 23,04 (4,61)	-1,02 (0,11)	819 23,04 (4,27)	774 23,16 (4,26)	763 23,31 (3,97)	707 23,11 (4,26)	679 23,25 (4,17)	602 23,36 (4,33)	580 23,11 (4,63)	323 23,23 (4,48)	-0,05 (0,11)	-0,97 [-1,28;-0,67] <,0001 -0,31 [-0,41;-0,21]
Asiatisch	233 23,96 (3,75)	225 23,07 (4,15)	218 23,48 (3,87)	211 23,39 (4,08)	205 23,41 (4,12)	176 23,40 (4,13)	187 23,49 (4,29)	97 23,27 (4,27)	-0,47 (0,19)	221 23,61 (3,81)	217 23,41 (4,14)	215 23,47 (4,25)	207 23,73 (3,84)	200 23,79 (4,01)	167 23,71 (4,00)	172 23,80 (3,93)	88 23,26 (4,61)	-0,05 (0,20)	-0,42 [-0,97;0,12] 0,1292 -0,14 [-0,33;0,04]
Andere	54 23,96 (3,90)	51 22,59 (4,98)	46 22,80 (5,26)	43 23,37 (3,99)	42 22,62 (4,99)	36 22,81 (4,85)	40 24,35 (4,87)	14 23,36 (5,12)	-0,86 (0,45)	58 23,21 (4,61)	57 23,05 (4,39)	56 23,59 (4,22)	53 23,75 (3,72)	47 23,28 (4,18)	42 23,50 (4,25)	44 23,93 (4,10)	19 24,16 (4,23)	-0,09 (0,43)	-0,76 [-2,00;0,47] 0,2220 -0,23 [-0,60;0,14]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,8343)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Tamoxifen	104 23,36 (3,63)	99 22,79 (4,18)	99 22,37 (4,85)	96 23,01 (4,13)	94 22,17 (4,96)	91 22,51 (4,26)	91 22,80 (4,51)	55 23,07 (4,17)	-0,51 (0,32)	124 23,06 (3,75)	122 23,33 (3,96)	120 23,58 (3,87)	110 23,94 (3,62)	103 23,89 (3,74)	94 24,12 (4,05)	92 23,38 (4,60)	56 22,57 (5,66)	0,30 (0,29)	-0,81 [-1,66;0,04] 0,0614 -0,25 [-0,51;0,01]
Aromatase-Inhibitor	1005 23,45 (4,27)	947 22,28 (4,75)	914 22,57 (4,48)	864 22,65 (4,56)	826 22,50 (4,69)	727 22,63 (4,61)	741 22,99 (4,70)	397 23,11 (4,60)	-0,93 (0,10)	987 23,14 (4,28)	938 23,17 (4,28)	926 23,27 (4,15)	869 23,18 (4,20)	834 23,30 (4,17)	728 23,31 (4,32)	713 23,25 (4,46)	381 23,36 (4,27)	-0,09 (0,10)	-0,84 [-1,12;-0,57] <,0001 -0,27 [-0,36;-0,18]
ECOG-PS (p-Wert des Interaktionsterms: 0,9099)																			
ECOG-PS 0	934 23,68 (4,06)	880 22,50 (4,66)	855 22,67 (4,50)	818 22,80 (4,50)	785 22,61 (4,65)	702 22,79 (4,46)	705 23,07 (4,65)	382 23,32 (4,36)	-0,96 (0,10)	898 23,40 (4,10)	856 23,36 (4,08)	847 23,51 (3,98)	793 23,47 (4,00)	761 23,49 (3,98)	676 23,55 (4,21)	665 23,29 (4,48)	356 23,20 (4,42)	-0,15 (0,10)	-0,80 [-1,09;-0,52] <,0001 -0,26 [-0,35;-0,17]
ECOG-PS 1	175 22,15 (4,79)	166 21,41 (4,82)	158 21,93 (4,58)	142 22,04 (4,58)	135 21,63 (5,02)	116 21,58 (5,05)	127 22,42 (4,77)	70 21,97 (5,32)	-0,57 (0,25)	213 22,03 (4,54)	204 22,48 (4,81)	199 22,46 (4,58)	186 22,38 (4,60)	176 22,82 (4,69)	146 22,74 (4,65)	140 23,14 (4,48)	81 23,53 (4,72)	0,51 (0,23)	-1,07 [-1,74;-0,40] 0,0019 -0,32 [-0,52;-0,12]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B PWB = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B PWB haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; PWB: körperliches Wohlbefinden; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t107_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: SWB aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,3123)																			
Neoadjuvante Chemotherapie	196 22,72 (4,55)	189 21,88 (4,85)	181 21,10 (5,72)	177 21,20 (5,60)	165 21,04 (5,30)	150 20,88 (5,35)	147 20,48 (5,40)	75 21,05 (4,58)	-1,57 (0,24)	193 22,36 (5,05)	181 21,50 (5,44)	179 21,65 (5,74)	156 21,75 (5,44)	145 21,92 (5,11)	121 21,83 (5,61)	136 21,69 (5,04)	77 21,27 (5,13)	-0,82 (0,25)	-0,75 [-1,44;-0,06] 0,0326 -0,22 [-0,42;-0,02]
Adjuvante Chemotherapie	287 22,08 (5,15)	273 21,58 (4,86)	269 21,59 (5,54)	265 21,36 (5,50)	253 21,18 (5,29)	213 21,45 (5,31)	204 20,65 (5,51)	128 20,98 (4,65)	-0,66 (0,20)	284 21,98 (5,12)	276 21,58 (5,29)	268 21,49 (5,01)	261 21,77 (4,80)	241 21,63 (4,79)	222 21,33 (4,73)	219 21,01 (4,90)	121 21,17 (5,07)	-0,44 (0,20)	-0,22 [-0,77;0,34] 0,4454 -0,06 [-0,23;0,10]
Keine Chemotherapie	7 21,57 (5,94)	7 21,14 (6,31)	6 18,83 (6,79)	6 20,83 (6,62)	5 16,80 (9,12)	5 14,80 (13,33)	6 20,67 (8,76)	2 26,50 (2,12)	-1,60 (1,02)	1 25,00 (NE)	1 17,00 (NE)	1 21,00 (NE)	1 16,00 (NE)	1 15,00 (NE)	1 17,00 (NE)	1 22,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,7388)																			
Nordamerika / Europa	204 23,63 (4,54)	189 23,10 (4,37)	182 22,89 (5,32)	179 22,48 (5,31)	162 22,35 (4,97)	140 22,09 (5,08)	135 21,93 (5,29)	75 22,17 (4,06)	-1,15 (0,22)	197 23,35 (4,06)	183 22,50 (4,83)	175 22,84 (4,55)	155 22,78 (4,47)	141 22,62 (4,51)	134 22,49 (4,64)	133 22,25 (4,65)	66 22,12 (4,40)	-0,84 (0,22)	-0,30 [-0,91;0,31] 0,3307 -0,10 [-0,29;0,10]
Asien	162 20,59 (5,03)	161 19,77 (5,16)	157 19,45 (5,52)	155 19,31 (5,68)	149 19,16 (5,56)	129 19,57 (5,75)	136 19,11 (5,49)	69 20,16 (4,74)	-1,24 (0,29)	153 20,56 (5,66)	151 19,98 (5,69)	151 19,87 (5,62)	146 20,48 (5,41)	138 20,39 (5,19)	120 20,12 (5,50)	122 19,87 (5,31)	66 19,91 (5,33)	-0,67 (0,29)	-0,57 [-1,38;0,24] 0,1646 -0,16 [-0,38;0,06]
Andere	124 22,47 (4,76)	119 22,07 (4,37)	117 21,54 (5,51)	114 22,11 (4,98)	112 21,79 (4,91)	99 21,79 (5,41)	86 20,80 (5,37)	61 20,72 (4,93)	-0,71 (0,30)	128 22,16 (5,31)	124 22,01 (5,22)	122 21,79 (5,39)	117 21,96 (4,99)	108 22,26 (4,71)	90 21,84 (4,66)	101 21,69 (4,54)	66 21,59 (5,27)	-0,34 (0,30)	-0,37 [-1,20;0,47] 0,3838 -0,11 [-0,36;0,14]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4423)																			
< 20 mm	121 22,67 (4,41)	115 21,77 (4,75)	109 21,23 (5,48)	112 20,68 (6,05)	105 20,85 (5,42)	94 21,04 (5,07)	91 20,74 (5,10)	54 20,98 (4,21)	-1,61 (0,28)	123 22,58 (5,04)	116 22,00 (5,16)	115 22,05 (5,25)	107 21,61 (5,33)	102 22,32 (4,77)	87 21,99 (4,83)	85 22,01 (4,61)	50 21,90 (4,99)	-0,63 (0,28)	-0,98 [-1,77;-0,19] 0,0150 -0,31 [-0,57;-0,06]
≥ 20 bis < 50 mm	229 22,24 (5,20)	220 21,51 (5,05)	219 21,80 (5,44)	214 21,59 (5,53)	196 21,20 (5,04)	170 21,39 (5,27)	164 20,48 (5,62)	97 20,80 (4,91)	-0,66 (0,22)	227 21,84 (4,99)	218 21,24 (5,29)	217 21,35 (5,32)	201 21,71 (4,86)	187 21,71 (4,81)	172 21,14 (5,01)	182 21,10 (4,71)	93 21,43 (4,92)	-0,46 (0,22)	-0,20 [-0,81;0,42] 0,5253 -0,06 [-0,24;0,12]
≥ 50 mm	128 22,30 (4,88)	124 21,98 (4,65)	119 20,82 (6,01)	114 21,43 (4,91)	113 21,13 (5,73)	95 20,83 (6,27)	93 20,52 (5,63)	48 21,48 (4,63)	-1,32 (0,34)	123 22,36 (5,37)	119 21,74 (5,66)	111 21,58 (5,39)	105 22,15 (5,14)	95 21,14 (5,23)	81 21,86 (5,40)	85 21,04 (5,68)	51 20,47 (5,11)	-0,87 (0,35)	-0,45 [-1,41;0,51] 0,3595 -0,12 [-0,36;0,13]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,6054)																			
0-3	177 22,42 (5,25)	169 21,91 (4,77)	160 21,48 (5,74)	159 21,36 (5,11)	144 21,07 (5,30)	130 21,45 (5,67)	131 20,40 (5,71)	77 21,48 (4,08)	-1,11 (0,28)	190 22,42 (4,83)	181 21,77 (5,21)	176 21,72 (5,37)	164 21,75 (5,46)	155 21,25 (5,46)	136 21,31 (5,62)	135 21,41 (5,12)	71 21,42 (5,35)	-0,88 (0,27)	-0,23 [-1,00;0,53] 0,5500 -0,06 [-0,27;0,14]
4-9	215 22,29 (4,96)	206 21,25 (5,11)	203 21,21 (5,54)	197 21,24 (5,73)	192 20,96 (5,22)	168 21,09 (5,19)	158 20,42 (5,58)	85 20,52 (4,89)	-1,18 (0,22)	210 22,18 (4,88)	201 21,63 (4,96)	199 21,44 (5,40)	186 21,77 (4,55)	174 22,07 (4,39)	153 21,66 (4,33)	160 21,26 (4,57)	87 21,10 (4,63)	-0,59 (0,22)	-0,59 [-1,20;0,02] 0,0575 -0,18 [-0,38;0,01]
≥ 10	98 22,23 (4,26)	94 22,29 (4,45)	93 21,47 (5,66)	92 21,26 (5,89)	87 21,34 (5,77)	70 20,61 (6,01)	68 21,31 (4,93)	43 21,40 (4,99)	-0,66 (0,34)	78 21,33 (6,14)	76 20,71 (6,49)	73 21,44 (4,92)	68 21,66 (5,34)	58 21,93 (4,83)	55 21,49 (5,49)	61 21,00 (5,59)	40 21,05 (5,65)	0,01 (0,38)	-0,66 [-1,67;0,35] 0,1974 -0,20 [-0,49;0,10]
Tumorstadium (p-Wert des Interaktionsterms: 0,2927)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 22,81 (4,21)	49 21,76 (5,06)	48 20,44 (6,35)	47 20,21 (5,51)	46 19,76 (5,95)	40 20,05 (6,00)	39 19,67 (5,66)	23 20,35 (3,39)	-2,37 (0,45)	57 23,18 (3,98)	54 22,39 (3,83)	54 22,37 (4,62)	48 21,00 (5,26)	47 22,15 (4,31)	36 22,25 (4,20)	37 22,38 (3,46)	19 22,47 (4,10)	-1,17 (0,44)	-1,20 [-2,45;0,05] 0,0596 -0,37 [-0,74;0,01]
IIB	45 21,82 (5,63)	44 21,93 (4,62)	41 22,32 (4,92)	42 21,48 (4,95)	35 21,57 (4,14)	34 22,09 (5,01)	31 20,23 (5,10)	22 21,09 (4,31)	-0,09 (0,50)	64 21,56 (5,66)	62 20,97 (6,08)	61 21,52 (5,41)	56 21,20 (5,56)	55 20,91 (5,41)	54 20,43 (5,82)	55 20,85 (5,25)	32 21,78 (5,08)	-0,49 (0,42)	0,40 [-0,89;1,70] 0,5382 0,12 [-0,26;0,50]
IIIA	212 21,97 (5,23)	206 21,09 (5,23)	200 21,02 (5,59)	195 21,33 (5,43)	189 20,93 (5,11)	164 21,16 (5,40)	157 20,35 (5,62)	86 20,79 (4,82)	-0,99 (0,22)	193 22,19 (4,88)	183 21,78 (4,90)	179 21,49 (5,36)	173 21,77 (4,72)	158 21,82 (4,82)	133 21,68 (4,42)	141 21,35 (4,88)	71 21,25 (4,73)	-0,54 (0,23)	-0,45 [-1,07;0,17] 0,1521 -0,14 [-0,34;0,05]
IIIB	14 23,21 (4,08)	13 22,15 (4,78)	13 22,00 (3,32)	13 20,31 (4,87)	10 20,00 (5,64)	8 18,88 (4,39)	11 20,18 (6,16)	6 20,67 (3,93)	-2,85 (1,41)	14 23,93 (3,77)	14 19,71 (8,27)	14 21,29 (7,13)	11 20,73 (8,43)	10 22,00 (8,47)	10 19,80 (8,77)	9 19,89 (6,99)	5 17,80 (9,15)	-2,66 (1,44)	-0,19 [-4,32;3,95] 0,9275 -0,03 [-0,75;0,69]
IIIC	166 22,72 (4,59)	156 22,37 (4,34)	153 21,82 (5,74)	150 21,62 (5,93)	142 21,69 (5,66)	121 21,33 (5,73)	118 21,38 (5,34)	67 21,75 (4,92)	-0,83 (0,28)	149 21,76 (5,54)	144 21,33 (5,68)	139 21,35 (5,29)	129 22,31 (4,82)	117 21,79 (4,67)	111 21,69 (5,19)	114 21,14 (5,15)	71 20,80 (5,31)	-0,39 (0,29)	-0,43 [-1,23;0,37] 0,2872 -0,12 [-0,34;0,10]
Tumorgrading (p-Wert des Interaktionsterms: 0,7541)																			
G1	45 22,07 (4,75)	43 21,51 (5,22)	40 21,30 (5,92)	40 20,50 (6,83)	39 20,97 (5,44)	33 21,48 (5,07)	33 20,61 (5,85)	18 21,61 (4,03)	-1,14 (0,46)	38 22,42 (5,31)	36 21,94 (5,26)	33 21,52 (6,20)	36 22,47 (4,35)	32 22,84 (4,27)	28 21,68 (5,00)	25 22,20 (4,70)	13 22,38 (4,89)	-0,04 (0,51)	-1,10 [-2,47;0,27] 0,1127 -0,35 [-0,79;0,08]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	Abemaciclib+ET[1] M3 N MW (SD)	Abemaciclib+ET[1] M6 N MW (SD)	Abemaciclib+ET[1] M12 N MW (SD)	Abemaciclib+ET[1] M18 N MW (SD)	Abemaciclib+ET[1] M24 N MW (SD)	Abemaciclib+ET[1] T30 FUP[2] N MW (SD)	Abemaciclib+ET[1] M6 FUP[3] N MW (SD)	Abemaciclib+ET[1] PB LSM (SE)	ET[1] B N MW (SD)	ET[1] M3 N MW (SD)	ET[1] M6 N MW (SD)	ET[1] M12 N MW (SD)	ET[1] M18 N MW (SD)	ET[1] M24 N MW (SD)	ET[1] T30 FUP[2] N MW (SD)	ET[1] M6 FUP[3] N MW (SD)	ET[1] PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	213 22,59 (4,71)	202 21,86 (4,88)	202 21,26 (5,58)	196 21,66 (5,13)	188 21,36 (5,32)	165 21,10 (5,49)	167 20,86 (5,33)	87 20,84 (4,95)	-1,21 (0,23)	207 22,25 (4,75)	200 21,24 (5,74)	196 21,55 (5,15)	182 21,60 (5,03)	161 21,61 (4,92)	148 21,43 (4,96)	154 20,89 (5,21)	86 20,76 (5,46)	-0,91 (0,23)	-0,30 [-0,94;0,34] 0,3580 -0,09 [-0,28;0,10]
G3	204 22,15 (5,16)	196 21,69 (4,70)	189 21,47 (5,57)	186 21,30 (5,55)	171 20,90 (5,36)	148 21,35 (5,41)	137 20,26 (5,54)	87 20,89 (4,44)	-0,88 (0,25)	203 22,10 (5,39)	194 21,83 (4,88)	192 21,71 (5,38)	173 21,88 (5,31)	168 21,53 (5,14)	143 21,66 (5,29)	153 21,56 (4,64)	86 21,91 (4,74)	-0,40 (0,25)	-0,48 [-1,19;0,22] 0,1792 -0,13 [-0,33;0,06]
GX	28 22,07 (5,23)	28 20,79 (5,54)	25 21,36 (6,27)	26 19,65 (6,16)	25 20,28 (5,64)	22 19,27 (6,97)	20 20,40 (6,44)	13 23,00 (4,30)	-1,02 (0,49)	29 21,31 (5,30)	27 21,11 (5,75)	26 20,50 (4,93)	26 21,00 (4,31)	25 22,40 (4,08)	24 20,75 (4,56)	24 20,96 (5,51)	13 18,38 (3,82)	-0,72 (0,47)	-0,31 [-1,67;1,06] 0,6523 -0,12 [-0,64;0,40]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,0506)																			
Negativ	46 23,30 (3,75)	43 21,40 (4,66)	41 21,24 (5,17)	42 20,81 (4,80)	39 19,90 (5,62)	38 19,87 (5,00)	36 19,36 (4,65)	12 20,67 (4,33)	-2,62 (0,46)	39 22,18 (4,56)	36 22,64 (4,17)	35 21,46 (5,95)	30 22,73 (4,03)	31 22,29 (3,74)	26 21,77 (4,27)	31 22,42 (3,80)	15 22,53 (4,72)	-0,53 (0,50)	-2,09 [-3,44;-0,74] 0,0028 -0,67 [-1,11;-0,23]
Positiv	426 22,14 (5,06)	409 21,59 (4,91)	400 21,25 (5,70)	391 21,21 (5,64)	371 21,06 (5,31)	319 21,17 (5,58)	305 20,49 (5,58)	183 21,02 (4,61)	-0,93 (0,17)	422 22,13 (5,15)	407 21,36 (5,45)	399 21,53 (5,28)	374 21,59 (5,15)	341 21,55 (5,02)	305 21,44 (5,11)	315 21,11 (5,05)	176 20,96 (5,14)	-0,67 (0,17)	-0,26 [-0,73;0,21] 0,2760 -0,07 [-0,21;0,06]
Unbekannt	2 24,00 (5,66)	2 23,00 (7,07)	2 23,00 (7,07)	1 28,00 (NE)	1 28,00 (NE)	1 28,00 (NE)	1 28,00 (NE)	0	NE	8 20,75 (5,23)	7 23,86 (2,97)	8 22,50 (3,25)	6 23,33 (3,78)	6 23,67 (3,83)	8 21,38 (6,00)	4 21,50 (5,92)	2 25,50 (0,71)	1,52 (0,44)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,8668)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	276 23,36 (4,40)	261 22,69 (4,42)	252 22,34 (5,29)	246 22,19 (5,09)	230 21,87 (5,05)	201 21,70 (5,28)	184 21,45 (5,24)	120 21,47 (4,46)	-1,19 (0,18)	285 22,91 (4,43)	268 22,31 (4,85)	260 22,43 (4,75)	241 22,38 (4,55)	223 22,26 (4,68)	202 22,26 (4,69)	210 21,86 (4,64)	122 21,76 (4,85)	-0,76 (0,18)	-0,43 [-0,94;0,08] 0,0990 -0,14 [-0,31;0,03]
Asiatisch	187 20,66 (5,30)	184 20,33 (5,16)	180 19,82 (5,85)	178 19,98 (5,89)	170 19,88 (5,65)	148 20,30 (5,80)	152 19,37 (5,67)	75 20,48 (4,75)	-0,82 (0,29)	166 20,68 (5,95)	164 20,09 (5,87)	162 20,02 (5,78)	157 20,83 (5,44)	145 20,64 (5,23)	124 20,27 (5,55)	130 20,08 (5,27)	67 20,04 (5,39)	-0,52 (0,30)	-0,31 [-1,13;0,52] 0,4655 -0,08 [-0,29;0,13]
Andere	16 22,63 (5,15)	15 20,80 (5,25)	15 21,93 (4,62)	15 21,80 (5,49)	15 21,93 (4,08)	13 22,38 (3,97)	14 22,21 (4,85)	9 20,78 (5,76)	-0,76 (0,68)	17 22,65 (4,65)	16 21,69 (5,68)	17 21,47 (6,30)	16 20,50 (6,82)	14 23,93 (3,29)	12 20,33 (3,73)	12 23,58 (4,70)	7 21,14 (4,81)	-0,36 (0,70)	-0,39 [-2,39;1,60] 0,6891 -0,14 [-0,80;0,53]
ECOG-PS (p-Wert des Interaktionsterms: 0,0948)																			
ECOG-PS 0	440 22,30 (4,81)	420 21,58 (4,90)	407 21,23 (5,58)	402 21,08 (5,46)	378 20,87 (5,36)	330 20,95 (5,46)	321 20,43 (5,44)	190 20,98 (4,60)	-1,21 (0,16)	425 22,35 (4,90)	406 21,67 (5,38)	396 21,75 (5,16)	372 22,00 (4,86)	344 21,86 (4,87)	308 21,77 (4,88)	321 21,37 (4,91)	179 21,37 (5,04)	-0,64 (0,16)	-0,57 [-1,01;-0,12] 0,0123 -0,17 [-0,30;-0,04]
ECOG-PS 1	50 22,58 (5,89)	49 22,65 (4,49)	49 22,43 (5,92)	46 23,09 (5,97)	45 22,80 (5,02)	38 22,71 (5,83)	36 21,94 (6,00)	15 22,13 (4,93)	0,49 (0,58)	53 20,43 (6,20)	52 20,48 (4,95)	52 20,06 (6,15)	46 19,72 (6,01)	43 20,63 (5,18)	36 19,17 (5,94)	35 20,40 (5,33)	19 19,63 (5,35)	-0,63 (0,57)	1,12 [-0,50;2,75] 0,1721 0,27 [-0,12;0,66]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B SWB = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B SWB haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler; SWB: soziales und familiäres Wohlbefinden

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t108_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: SWB aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,7925)																			
< 65 Jahre	805 22,63 (5,12)	761 22,36 (5,15)	746 21,96 (5,16)	702 21,87 (5,32)	678 21,85 (5,19)	597 21,61 (5,22)	604 21,55 (5,52)	331 21,73 (5,42)	-0,75 (0,13)	832 22,63 (4,96)	792 22,10 (5,28)	784 22,10 (5,19)	731 21,88 (5,19)	696 21,91 (5,03)	610 21,79 (5,32)	607 21,58 (5,52)	319 21,04 (5,49)	-0,76 (0,12)	0,01 [-0,33;0,36] 0,9466 0,00 [-0,09;0,10]
≥ 65 Jahre	304 22,57 (5,35)	285 21,69 (6,25)	268 21,67 (5,97)	257 22,12 (5,53)	242 21,73 (5,94)	221 21,46 (6,21)	227 21,89 (5,70)	121 21,12 (5,80)	-0,73 (0,21)	279 22,73 (5,33)	268 22,19 (5,53)	260 22,10 (5,56)	248 22,03 (5,50)	241 21,38 (5,91)	211 21,53 (5,66)	198 21,81 (5,15)	118 21,58 (5,86)	-0,87 (0,21)	0,13 [-0,45;0,72] 0,6514 0,04 [-0,13;0,20]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,4028)																			
Neoadjuvante Chemotherapie	363 22,82 (5,13)	336 22,30 (5,20)	325 22,30 (5,17)	300 22,19 (5,33)	281 21,70 (5,67)	238 21,55 (5,49)	253 21,70 (5,74)	130 21,40 (5,21)	-0,82 (0,19)	365 22,38 (4,94)	347 21,56 (5,47)	333 21,61 (5,37)	309 21,61 (5,21)	293 21,39 (5,38)	248 21,37 (5,57)	261 21,62 (5,56)	139 20,34 (5,99)	-1,04 (0,18)	0,22 [-0,29;0,74] 0,3941 0,06 [-0,08;0,21]
Adjuvante Chemotherapie	686 22,55 (5,15)	656 22,24 (5,45)	638 21,76 (5,41)	608 21,91 (5,30)	593 21,97 (5,12)	538 21,66 (5,41)	532 21,73 (5,46)	295 21,60 (5,69)	-0,68 (0,14)	679 22,80 (5,11)	649 22,45 (5,18)	651 22,48 (5,06)	614 22,19 (5,12)	597 22,12 (5,11)	527 22,08 (5,14)	497 21,77 (5,27)	271 21,64 (5,27)	-0,56 (0,14)	-0,13 [-0,50;0,25] 0,5091 -0,04 [-0,14;0,07]
Keine Chemotherapie	60 22,03 (5,81)	54 20,63 (7,12)	51 20,76 (6,28)	51 20,78 (6,48)	46 20,72 (6,79)	42 20,52 (6,68)	46 20,28 (5,81)	27 22,11 (5,29)	-1,13 (0,47)	67 22,69 (5,03)	64 21,88 (6,03)	60 20,75 (6,63)	56 20,70 (6,83)	47 19,77 (6,12)	46 19,57 (6,89)	47 20,40 (6,36)	27 20,96 (6,29)	-1,80 (0,45)	0,67 [-0,62;1,97] 0,3047 0,18 [-0,17;0,53]
Region (p-Wert des Interaktionsterms: 0,9651)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	550 23,59 (4,59)	498 23,40 (4,57)	484 22,90 (4,93)	451 23,16 (4,73)	425 23,08 (4,53)	385 22,64 (5,04)	393 22,73 (4,98)	212 23,09 (4,70)	-0,70 (0,14)	529 23,57 (4,48)	491 23,37 (4,66)	483 23,28 (4,74)	441 22,81 (4,99)	424 22,82 (4,87)	376 23,19 (4,76)	346 22,98 (4,83)	206 22,32 (5,18)	-0,72 (0,14)	0,02 [-0,36;0,40] 0,9235 0,01 [-0,11;0,13]
Asien	195 20,59 (6,33)	190 20,18 (6,58)	185 19,81 (6,18)	177 19,75 (6,28)	173 19,46 (6,58)	152 19,36 (6,34)	163 18,92 (6,79)	87 19,09 (6,47)	-0,82 (0,29)	192 20,96 (5,68)	189 20,15 (6,21)	187 20,35 (5,95)	179 20,25 (5,69)	175 19,69 (5,95)	149 19,54 (5,91)	155 19,61 (5,55)	81 18,73 (6,13)	-0,84 (0,29)	0,02 [-0,78;0,82] 0,9595 0,01 [-0,19;0,20]
Andere	364 22,21 (4,99)	358 21,54 (5,58)	345 21,56 (5,20)	331 21,44 (5,25)	322 21,44 (5,26)	281 21,30 (5,25)	275 21,70 (5,00)	153 20,87 (5,37)	-0,80 (0,19)	390 22,26 (5,20)	380 21,49 (5,30)	374 21,45 (5,25)	359 21,66 (5,16)	338 21,54 (5,06)	296 20,95 (5,41)	304 21,15 (5,62)	150 20,95 (5,40)	-0,88 (0,18)	0,08 [-0,44;0,60] 0,7694 0,02 [-0,12;0,16]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,5781)																			
< 20 mm	280 23,09 (4,50)	258 22,64 (4,58)	255 22,32 (4,60)	245 22,44 (4,81)	236 22,24 (4,84)	211 21,68 (5,44)	209 22,11 (4,99)	106 21,87 (5,13)	-0,92 (0,20)	298 23,24 (4,71)	284 22,25 (5,72)	277 22,38 (5,24)	259 22,27 (5,20)	252 21,74 (5,55)	216 21,98 (5,38)	221 22,19 (5,30)	111 21,86 (5,32)	-1,16 (0,19)	0,24 [-0,31;0,79] 0,3929 0,07 [-0,09;0,23]
≥ 20 bis < 50 mm	569 22,27 (5,56)	547 21,90 (5,96)	522 21,79 (5,63)	503 21,72 (5,51)	479 21,66 (5,76)	428 21,63 (5,60)	433 21,49 (5,82)	232 21,24 (5,75)	-0,57 (0,15)	573 22,49 (5,09)	549 22,00 (5,13)	544 22,08 (5,14)	512 21,73 (5,46)	494 21,83 (5,14)	438 21,68 (5,36)	417 21,58 (5,39)	231 21,03 (5,53)	-0,63 (0,15)	0,06 [-0,36;0,48] 0,7865 0,02 [-0,10;0,13]
≥ 50 mm	243 22,87 (4,98)	226 22,37 (5,16)	221 21,58 (5,62)	198 21,95 (5,74)	191 21,92 (4,92)	166 21,48 (5,32)	175 21,53 (5,60)	106 21,95 (5,49)	-0,87 (0,23)	229 22,29 (5,43)	216 22,19 (5,46)	213 21,74 (5,75)	198 21,90 (4,83)	184 21,69 (5,26)	159 21,38 (5,67)	159 21,03 (5,76)	91 20,69 (6,11)	-0,75 (0,24)	-0,13 [-0,79;0,54] 0,7107 -0,03 [-0,21;0,15]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,6671)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	369 22,82 (5,06)	349 22,15 (5,31)	338 21,97 (5,45)	314 21,80 (5,45)	306 21,57 (5,61)	278 21,29 (5,79)	287 21,36 (5,63)	168 21,48 (5,52)	-1,05 (0,19)	360 22,69 (5,04)	344 21,76 (5,53)	341 21,73 (5,36)	313 21,54 (5,39)	304 21,65 (5,32)	261 21,77 (5,29)	255 21,64 (5,53)	143 21,13 (5,37)	-1,02 (0,19)	-0,03 [-0,55;0,49] 0,9218 -0,01 [-0,15;0,14]
4-9	476 22,38 (5,17)	448 21,90 (5,65)	438 21,63 (5,43)	421 21,76 (5,46)	400 21,78 (5,39)	357 21,70 (5,40)	356 21,80 (5,47)	175 21,79 (5,55)	-0,60 (0,16)	485 22,58 (5,21)	465 22,42 (5,40)	464 22,11 (5,37)	439 22,03 (5,28)	420 21,75 (5,32)	377 21,70 (5,58)	359 21,49 (5,47)	192 21,11 (5,74)	-0,68 (0,16)	0,08 [-0,37;0,53] 0,7272 0,02 [-0,10;0,15]
≥ 10	264 22,73 (5,36)	249 22,72 (5,37)	238 22,23 (5,23)	224 22,47 (5,09)	214 22,26 (5,06)	183 21,74 (5,25)	188 21,78 (5,66)	109 21,36 (5,52)	-0,53 (0,21)	266 22,74 (4,78)	251 22,08 (4,94)	239 22,63 (4,96)	227 22,22 (5,05)	213 22,00 (5,14)	183 21,69 (5,24)	191 21,92 (5,23)	102 21,41 (5,66)	-0,60 (0,21)	0,08 [-0,52;0,67] 0,8001 0,02 [-0,15;0,19]
Tumorstadium (p-Wert des Interaktionsterms: 0,6609)																			
IIA	93 23,46 (4,22)	88 22,49 (4,57)	86 22,50 (4,51)	82 22,30 (4,66)	82 22,28 (4,70)	77 21,56 (5,13)	75 22,17 (4,52)	39 21,64 (4,62)	-1,14 (0,31)	95 22,82 (4,85)	92 21,65 (5,58)	90 21,97 (5,07)	85 21,74 (5,24)	81 21,98 (4,72)	71 22,11 (4,92)	74 22,28 (4,85)	37 21,27 (4,66)	-1,08 (0,30)	-0,06 [-0,91;0,79] 0,8863 -0,02 [-0,31;0,27]
IIB	133 22,35 (5,65)	126 22,17 (5,61)	118 21,91 (5,70)	116 21,77 (5,61)	113 21,39 (5,87)	101 21,82 (5,74)	110 20,93 (6,46)	68 22,22 (5,35)	-0,74 (0,31)	113 23,04 (4,53)	107 22,24 (4,63)	106 21,80 (5,01)	99 21,27 (5,78)	94 21,66 (5,00)	85 21,47 (5,18)	81 21,23 (5,62)	45 20,67 (5,85)	-1,34 (0,34)	0,61 [-0,30;1,52] 0,1903 0,17 [-0,08;0,42]
IIIA	431 22,63 (4,98)	408 22,05 (5,33)	397 21,73 (5,41)	376 21,88 (5,32)	354 21,92 (5,20)	318 21,84 (5,21)	321 21,69 (5,35)	157 21,64 (5,40)	-0,65 (0,17)	436 22,40 (5,53)	414 22,30 (5,57)	421 21,84 (5,56)	395 21,86 (5,43)	378 21,74 (5,40)	335 21,56 (5,76)	317 21,14 (5,66)	172 20,89 (5,93)	-0,73 (0,17)	0,09 [-0,39;0,57] 0,7247 0,02 [-0,11;0,16]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIB	47 21,70 (5,66)	45 20,58 (7,12)	45 21,22 (6,36)	43 20,98 (7,09)	41 19,80 (7,23)	36 19,58 (7,62)	31 20,77 (6,03)	15 20,40 (8,56)	-1,21 (0,61)	41 22,93 (4,90)	40 22,55 (4,96)	39 22,18 (4,89)	35 21,83 (5,06)	34 20,76 (5,59)	31 20,77 (5,87)	30 21,53 (6,47)	14 22,36 (5,02)	-1,00 (0,66)	-0,20 [-1,99;1,59] 0,8208 -0,05 [-0,47;0,37]
IIIC	403 22,62 (5,32)	378 22,48 (5,48)	366 22,02 (5,28)	340 22,13 (5,26)	328 22,05 (5,25)	284 21,47 (5,49)	292 21,86 (5,61)	171 21,40 (5,59)	-0,67 (0,18)	424 22,76 (4,73)	405 21,98 (5,28)	386 22,50 (5,13)	363 22,23 (4,95)	348 21,93 (5,28)	297 21,97 (5,14)	302 22,15 (5,12)	168 21,48 (5,42)	-0,61 (0,17)	-0,07 [-0,55;0,42] 0,7939 -0,02 [-0,15;0,12]
Tumorgrading (p-Wert des Interaktionsterms: 0,7179)																			
G1	83 23,22 (4,29)	81 22,00 (6,22)	82 21,85 (5,75)	75 22,32 (4,88)	72 22,74 (4,78)	67 22,19 (5,59)	63 22,35 (4,57)	32 22,66 (4,35)	-0,77 (0,37)	84 22,77 (5,15)	82 22,32 (5,20)	79 22,61 (4,88)	71 22,65 (5,17)	74 21,70 (5,69)	64 22,47 (5,04)	55 22,20 (5,20)	34 22,76 (4,63)	-0,38 (0,37)	-0,39 [-1,44;0,65] 0,4593 -0,11 [-0,42;0,19]
G2	526 22,62 (5,04)	500 22,26 (5,30)	482 21,84 (5,41)	453 21,87 (5,57)	435 21,67 (5,47)	377 21,36 (5,66)	375 21,64 (5,56)	212 21,36 (5,84)	-0,83 (0,16)	534 22,61 (5,02)	505 22,12 (5,42)	507 22,04 (5,30)	476 21,94 (5,10)	448 21,54 (5,42)	403 21,61 (5,36)	392 21,24 (5,45)	214 20,89 (5,75)	-0,88 (0,16)	0,05 [-0,40;0,49] 0,8324 0,01 [-0,11;0,13]
G3	451 22,54 (5,46)	421 22,11 (5,56)	405 22,03 (5,33)	385 21,98 (5,17)	371 21,86 (5,37)	335 21,60 (5,34)	356 21,65 (5,58)	186 21,68 (5,35)	-0,67 (0,16)	436 22,82 (4,96)	416 22,13 (5,31)	403 22,17 (5,24)	381 21,86 (5,38)	367 22,21 (4,85)	315 22,00 (5,39)	317 22,32 (5,19)	166 21,71 (5,27)	-0,70 (0,16)	0,03 [-0,42;0,47] 0,9031 0,01 [-0,12;0,14]
GX	47 21,96 (5,47)	42 22,07 (5,31)	43 20,91 (5,10)	44 21,50 (6,18)	40 21,45 (5,95)	37 22,05 (5,30)	37 20,38 (6,88)	22 21,09 (5,41)	-0,31 (0,61)	53 21,57 (5,89)	53 21,81 (5,21)	52 21,21 (6,01)	48 20,88 (6,13)	45 20,69 (6,39)	37 19,14 (6,21)	39 19,28 (6,62)	21 17,48 (6,55)	-1,08 (0,58)	0,77 [-0,89;2,43] 0,3601 0,18 [-0,21;0,58]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,0768)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Negativ	137 21,84 (5,37)	132 21,55 (5,34)	124 20,52 (5,68)	116 20,93 (5,73)	107 20,76 (6,07)	93 20,45 (6,13)	100 20,12 (6,19)	63 20,35 (5,59)	-0,99 (0,30)	149 22,31 (5,07)	139 21,78 (5,54)	134 21,93 (5,35)	127 21,93 (5,13)	122 21,70 (5,06)	103 21,13 (5,62)	115 21,43 (4,64)	56 20,32 (5,86)	-0,57 (0,28)	-0,42 [-1,22;0,39] 0,3122 -0,12 [-0,35;0,11]
Positiv	941 22,66 (5,12)	883 22,16 (5,52)	859 21,95 (5,34)	817 21,99 (5,33)	789 21,87 (5,30)	701 21,63 (5,42)	709 21,80 (5,48)	378 21,69 (5,52)	-0,73 (0,12)	935 22,67 (5,07)	897 22,15 (5,29)	887 22,07 (5,26)	830 21,88 (5,31)	793 21,75 (5,34)	697 21,75 (5,40)	669 21,64 (5,53)	367 21,25 (5,54)	-0,82 (0,12)	0,09 [-0,23;0,41] 0,5891 0,02 [-0,07;0,12]
Unbekannt	9 22,22 (8,96)	9 25,56 (2,60)	9 26,67 (1,66)	7 25,43 (4,83)	5 27,20 (1,10)	6 24,67 (5,35)	5 23,40 (5,73)	1 28,00 (NE)	2,29 (1,34)	7 24,71 (6,16)	6 23,67 (5,24)	6 23,00 (8,88)	6 24,17 (6,01)	6 22,83 (4,71)	6 24,67 (4,13)	5 21,20 (10,80)	5 23,80 (4,09)	-0,01 (1,45)	2,30 [-1,95;6,55] 0,2645 0,55 [-0,40;1,51]
Ethnizität (p-Wert des Interaktionsterms: 0,5555)																			
Weiß	810 23,13 (4,73)	758 22,70 (4,98)	739 22,38 (5,00)	697 22,45 (4,95)	665 22,42 (4,85)	596 22,11 (5,18)	598 22,31 (4,95)	340 22,13 (5,05)	-0,78 (0,12)	819 23,09 (4,80)	774 22,57 (5,10)	761 22,58 (4,98)	707 22,40 (4,95)	679 22,31 (4,92)	601 22,30 (5,08)	580 22,20 (5,19)	323 21,76 (5,27)	-0,80 (0,12)	0,02 [-0,30;0,34] 0,9005 0,01 [-0,09;0,10]
Asiatisch	233 20,98 (6,35)	225 20,50 (6,78)	218 20,29 (6,34)	210 20,30 (6,44)	205 20,09 (6,62)	176 19,94 (6,26)	187 19,42 (6,86)	97 19,75 (6,46)	-0,64 (0,28)	221 21,04 (5,79)	217 20,64 (6,08)	215 20,48 (6,00)	207 20,64 (5,84)	200 20,15 (6,13)	167 19,80 (6,13)	172 19,88 (5,86)	88 19,07 (6,30)	-0,65 (0,29)	0,01 [-0,78;0,80] 0,9820 0,00 [-0,18;0,19]
Andere	54 21,70 (4,81)	51 21,47 (4,75)	47 21,49 (5,21)	43 21,49 (4,95)	42 20,60 (5,12)	36 20,08 (5,63)	40 21,45 (5,18)	14 20,07 (6,87)	-0,69 (0,50)	58 22,57 (4,62)	57 21,51 (4,92)	56 21,71 (5,20)	53 20,28 (6,14)	47 20,45 (5,07)	42 20,98 (5,51)	44 21,20 (5,55)	19 21,26 (5,17)	-1,16 (0,47)	0,47 [-0,89;1,83] 0,4959 0,13 [-0,24;0,50]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,3295)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Tamoxifen	104 22,28 (4,99)	99 21,87 (5,27)	99 21,77 (5,61)	96 21,76 (5,32)	94 21,48 (5,54)	91 21,59 (5,55)	91 21,60 (5,81)	55 22,09 (4,53)	-0,37 (0,30)	124 21,46 (5,22)	122 21,06 (5,16)	120 21,29 (5,13)	110 20,92 (5,15)	103 20,44 (5,47)	94 20,53 (5,31)	92 20,33 (5,32)	56 20,18 (5,68)	-0,82 (0,28)	0,45 [-0,36;1,25] 0,2750 0,15 [-0,12;0,41]
Aromatase-Inhibitor	1005 22,64 (5,20)	947 22,21 (5,50)	915 21,90 (5,37)	863 21,96 (5,39)	826 21,86 (5,37)	727 21,57 (5,50)	740 21,65 (5,54)	397 21,50 (5,64)	-0,79 (0,11)	987 22,81 (5,01)	938 22,26 (5,35)	924 22,21 (5,29)	869 22,05 (5,27)	834 21,94 (5,23)	727 21,87 (5,41)	713 21,81 (5,43)	381 21,33 (5,57)	-0,77 (0,12)	-0,02 [-0,34;0,30] 0,8949 -0,01 [-0,09;0,08]
ECOG-PS (p-Wert des Interaktionsterms: 0,1291)																			
ECOG-PS 0	934 22,81 (5,08)	880 22,39 (5,38)	856 22,09 (5,30)	817 22,12 (5,25)	785 22,04 (5,27)	702 21,75 (5,44)	704 21,81 (5,49)	382 21,85 (5,47)	-0,74 (0,12)	898 22,83 (4,92)	856 22,28 (5,33)	845 22,15 (5,28)	793 21,98 (5,25)	761 21,86 (5,22)	675 21,62 (5,42)	665 21,54 (5,42)	356 21,04 (5,69)	-0,92 (0,12)	0,18 [-0,15;0,50] 0,2874 0,05 [-0,04;0,14]
ECOG-PS 1	175 21,54 (5,60)	166 21,07 (5,83)	158 20,75 (5,70)	142 20,89 (5,98)	135 20,57 (5,89)	116 20,48 (5,80)	127 20,72 (5,92)	70 20,07 (5,61)	-0,77 (0,29)	213 21,94 (5,52)	204 21,46 (5,33)	199 21,90 (5,27)	186 21,65 (5,35)	176 21,40 (5,50)	146 22,20 (5,36)	140 22,14 (5,48)	81 21,84 (5,12)	-0,15 (0,26)	-0,61 [-1,37;0,14] 0,1123 -0,16 [-0,36;0,04]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B SWB = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B SWB haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler; SWB: soziales und familiäres Wohlbefinden

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t108_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: EWB aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,0728)																			
Neoadjuvante Chemotherapie	196 18,30 (4,04)	188 18,15 (4,16)	181 18,17 (4,24)	177 17,81 (4,31)	165 17,75 (4,16)	150 17,97 (4,04)	147 17,57 (4,37)	75 17,19 (4,85)	-0,39 (0,21)	193 17,78 (4,29)	181 17,93 (4,42)	179 18,15 (4,22)	155 18,21 (4,02)	145 18,65 (4,12)	121 18,53 (4,09)	136 17,67 (4,49)	77 17,22 (4,73)	-0,07 (0,21)	-0,32 [-0,90;0,26] 0,2802 -0,11 [-0,31;0,09]
Adjuvante Chemotherapie	288 17,80 (4,10)	274 18,02 (4,19)	268 18,16 (4,09)	265 18,20 (4,05)	254 18,02 (4,07)	214 17,85 (4,22)	205 17,82 (4,38)	126 17,13 (4,00)	0,10 (0,16)	284 17,79 (4,10)	276 17,97 (4,09)	267 18,26 (3,77)	261 18,28 (3,82)	240 18,38 (3,66)	222 18,16 (3,81)	219 18,06 (4,05)	121 18,17 (3,82)	0,32 (0,16)	-0,23 [-0,67;0,22] 0,3176 -0,08 [-0,25;0,08]
Keine Chemotherapie	7 17,57 (5,91)	7 18,57 (3,82)	6 17,50 (3,73)	6 17,33 (4,59)	5 19,80 (5,02)	5 17,60 (2,88)	6 19,67 (3,27)	2 21,50 (3,54)	1,65 (0,54)	1 21,00 (NE)	1 11,00 (NE)	1 17,00 (NE)	1 14,00 (NE)	1 18,00 (NE)	1 14,00 (NE)	1 16,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,4963)																			
Nordamerika / Europa	204 18,26 (3,81)	189 18,56 (3,92)	181 18,34 (4,25)	178 18,17 (4,17)	162 18,24 (3,95)	140 18,19 (4,34)	135 18,09 (4,32)	73 17,78 (4,03)	-0,00 (0,19)	197 18,05 (4,01)	183 17,93 (4,31)	174 18,39 (4,13)	154 18,41 (4,05)	141 18,70 (3,98)	134 18,40 (4,00)	133 17,76 (4,58)	66 17,89 (4,66)	0,00 (0,20)	-0,00 [-0,55;0,54] 0,9923 -0,00 [-0,20;0,19]
Asien	163 17,56 (4,19)	162 17,23 (4,16)	158 17,46 (4,05)	156 17,30 (4,15)	150 17,29 (3,96)	130 17,21 (4,04)	137 17,26 (4,21)	69 16,94 (4,27)	-0,31 (0,21)	153 17,58 (4,32)	151 17,70 (4,17)	151 17,91 (3,87)	146 18,04 (3,66)	137 18,03 (3,72)	120 17,86 (4,01)	122 17,66 (4,14)	66 17,79 (4,01)	0,05 (0,21)	-0,36 [-0,95;0,23] 0,2262 -0,14 [-0,36;0,08]
Andere	124 18,12 (4,43)	118 18,47 (4,42)	116 18,81 (3,98)	114 18,82 (4,00)	112 18,36 (4,46)	99 18,37 (3,83)	86 18,00 (4,63)	61 16,77 (4,73)	0,18 (0,26)	128 17,65 (4,27)	124 18,26 (4,19)	122 18,34 (3,78)	117 18,28 (3,97)	108 18,76 (3,77)	90 18,66 (3,63)	101 18,40 (3,80)	66 17,73 (3,99)	0,48 (0,26)	-0,30 [-1,03;0,43] 0,4200 -0,10 [-0,35;0,15]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6672)																			
< 20 mm	121 17,80 (3,88)	115 17,93 (4,17)	109 17,89 (4,29)	112 18,07 (4,27)	105 17,75 (4,18)	94 17,54 (4,14)	91 17,02 (4,23)	53 17,23 (4,15)	-0,32 (0,25)	123 17,89 (4,24)	116 18,14 (4,20)	116 18,25 (3,65)	107 18,22 (3,96)	100 18,33 (3,88)	87 18,63 (3,89)	85 18,35 (4,25)	50 17,60 (4,80)	0,14 (0,25)	-0,47 [-1,17;0,24] 0,1926 -0,17 [-0,42;0,08]
≥ 20 bis < 50 mm	230 18,23 (4,01)	220 17,90 (4,42)	218 18,33 (4,15)	214 17,98 (4,16)	197 18,02 (4,17)	171 18,08 (4,10)	165 17,97 (4,32)	96 16,98 (4,37)	-0,15 (0,19)	227 17,61 (4,02)	218 17,66 (4,20)	216 18,24 (3,93)	200 18,22 (3,73)	187 18,30 (3,81)	172 18,06 (3,91)	182 17,61 (4,28)	93 17,90 (4,06)	0,15 (0,19)	-0,30 [-0,81;0,22] 0,2600 -0,11 [-0,29;0,08]
≥ 50 mm	128 17,80 (4,43)	124 18,49 (3,70)	119 17,97 (4,06)	114 18,06 (4,08)	113 17,90 (3,88)	95 17,89 (4,10)	93 18,11 (4,49)	48 17,69 (4,30)	0,19 (0,24)	123 18,11 (4,45)	119 18,34 (4,35)	110 18,23 (4,34)	105 18,41 (4,18)	96 18,97 (3,83)	81 18,52 (3,91)	85 18,20 (4,01)	51 17,88 (3,92)	0,15 (0,25)	0,04 [-0,63;0,72] 0,9038 0,02 [-0,23;0,26]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,1938)																			
0-3	177 18,22 (3,98)	169 18,59 (3,76)	160 18,29 (3,94)	158 18,37 (3,90)	144 18,06 (4,05)	130 18,08 (4,20)	131 17,87 (4,37)	77 17,23 (4,42)	-0,08 (0,21)	190 18,26 (3,91)	181 18,48 (4,02)	175 18,59 (3,77)	163 18,58 (3,47)	156 18,69 (3,65)	136 18,71 (3,50)	135 18,09 (4,08)	71 18,32 (4,01)	0,09 (0,20)	-0,18 [-0,74;0,39] 0,5435 -0,06 [-0,27;0,14]
4-9	216 17,60 (4,23)	206 17,41 (4,53)	202 17,77 (4,34)	198 17,55 (4,36)	193 17,46 (4,24)	169 17,85 (4,08)	159 17,33 (4,36)	83 17,01 (4,48)	-0,17 (0,19)	210 17,43 (4,48)	201 17,63 (4,32)	199 17,98 (4,04)	186 18,02 (4,07)	172 18,45 (3,85)	153 18,10 (4,10)	160 17,74 (4,41)	87 17,56 (4,35)	0,31 (0,19)	-0,47 [-1,01;0,06] 0,0832 -0,17 [-0,36;0,02]
≥ 10	98 18,46 (4,00)	94 18,64 (3,85)	93 18,75 (3,97)	92 18,49 (4,05)	87 18,78 (3,81)	70 17,64 (4,14)	68 18,49 (4,28)	43 17,47 (3,97)	0,14 (0,29)	78 17,63 (3,91)	76 17,50 (4,37)	73 17,90 (4,09)	68 18,06 (4,31)	58 18,00 (4,27)	55 17,71 (4,31)	61 17,93 (4,05)	40 17,40 (4,27)	-0,12 (0,32)	0,26 [-0,60;1,11] 0,5556 0,09 [-0,21;0,39]
Tumorstadium (p-Wert des Interaktionsterms: 0,7237)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 17,54 (3,98)	49 18,12 (3,72)	48 17,81 (4,12)	46 18,20 (3,73)	46 17,57 (4,27)	40 17,45 (4,37)	39 17,26 (3,88)	23 16,35 (4,58)	-0,25 (0,39)	57 18,60 (3,72)	54 18,98 (3,75)	54 18,69 (3,56)	48 18,90 (3,10)	47 19,04 (3,61)	36 19,25 (3,60)	37 19,46 (3,58)	19 18,37 (4,69)	0,29 (0,38)	-0,55 [-1,62;0,53] 0,3157 -0,19 [-0,57;0,18]
IIB	45 18,42 (3,50)	44 18,30 (4,52)	41 19,17 (3,03)	42 17,98 (3,73)	35 17,91 (4,22)	34 18,53 (3,90)	31 19,13 (3,24)	22 17,23 (3,41)	0,07 (0,40)	64 18,08 (3,63)	62 17,98 (4,08)	60 18,78 (3,84)	55 18,38 (3,63)	55 18,42 (3,50)	54 18,59 (3,28)	55 17,58 (4,09)	32 18,50 (4,37)	0,02 (0,33)	0,05 [-0,97;1,07] 0,9269 0,02 [-0,36;0,40]
IIIA	213 17,72 (4,42)	207 17,78 (4,21)	199 17,89 (4,23)	196 17,87 (4,29)	190 17,79 (4,13)	165 17,93 (3,86)	158 17,34 (4,34)	84 17,19 (4,67)	-0,02 (0,19)	193 17,49 (4,58)	183 17,79 (4,22)	179 17,98 (4,09)	173 17,84 (4,00)	158 18,39 (3,84)	133 18,11 (4,10)	141 17,66 (4,42)	71 17,51 (4,46)	0,20 (0,20)	-0,22 [-0,76;0,31] 0,4150 -0,08 [-0,28;0,11]
IIIB	14 15,86 (5,22)	13 16,31 (5,88)	13 14,69 (6,85)	13 15,23 (4,57)	10 14,20 (3,79)	8 13,88 (6,69)	11 15,09 (6,14)	6 16,17 (1,72)	-1,30 (0,70)	14 19,71 (2,73)	14 19,07 (3,83)	14 18,93 (2,79)	11 19,18 (4,53)	9 19,33 (3,43)	10 18,80 (3,74)	9 19,00 (2,35)	5 17,00 (1,87)	0,14 (0,72)	-1,45 [-3,64;0,74] 0,1859 -0,53 [-1,26;0,21]
IIIC	166 18,57 (3,69)	155 18,55 (3,96)	153 18,60 (3,85)	150 18,45 (4,13)	142 18,49 (3,93)	121 18,10 (4,19)	118 18,35 (4,47)	67 17,55 (4,32)	-0,02 (0,23)	149 17,57 (4,09)	144 17,60 (4,47)	139 18,01 (4,05)	129 18,42 (4,05)	117 18,34 (4,11)	111 17,97 (4,07)	114 17,78 (4,27)	71 17,69 (3,91)	0,10 (0,24)	-0,12 [-0,79;0,54] 0,7175 -0,04 [-0,26;0,18]
Tumorgrading (p-Wert des Interaktionsterms: 0,7802)																			
G1	45 18,49 (3,59)	43 18,44 (4,46)	40 18,78 (3,72)	40 18,10 (4,06)	39 18,46 (4,15)	33 18,30 (2,90)	33 18,45 (3,40)	18 17,72 (3,58)	-0,11 (0,42)	38 18,18 (3,85)	36 18,64 (3,52)	34 18,06 (3,86)	36 18,69 (3,73)	30 18,73 (3,67)	28 17,07 (4,61)	25 18,24 (3,94)	13 17,00 (4,71)	-0,31 (0,47)	0,20 [-1,06;1,46] 0,7541 0,07 [-0,36;0,50]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	213 18,02 (3,96)	202 18,15 (3,92)	201 18,17 (4,12)	196 17,97 (4,09)	188 17,99 (3,90)	165 17,89 (3,89)	167 17,78 (4,31)	85 17,99 (4,18)	-0,01 (0,19)	207 17,69 (4,24)	200 17,61 (4,53)	194 18,36 (3,87)	181 17,91 (4,14)	162 18,30 (3,91)	148 18,04 (4,14)	154 17,58 (4,18)	86 17,93 (3,96)	0,04 (0,20)	-0,05 [-0,60;0,49] 0,8423 -0,02 [-0,21;0,17]
G3	205 17,94 (4,17)	197 17,99 (4,31)	189 17,92 (4,32)	186 18,10 (4,27)	172 17,79 (4,24)	149 17,84 (4,61)	138 17,57 (4,63)	87 16,14 (4,41)	-0,12 (0,20)	203 17,85 (4,15)	194 18,12 (4,11)	192 18,06 (4,04)	173 18,53 (3,68)	168 18,57 (3,85)	143 18,81 (3,42)	153 18,07 (4,35)	86 17,94 (4,50)	0,28 (0,20)	-0,41 [-0,96;0,14] 0,1458 -0,14 [-0,34;0,05]
GX	28 17,39 (5,36)	27 17,59 (4,61)	25 18,80 (3,57)	26 17,92 (4,17)	25 17,68 (4,83)	22 17,68 (4,17)	20 17,55 (4,43)	13 18,31 (4,70)	0,16 (0,45)	29 17,79 (4,45)	27 18,30 (3,53)	26 18,62 (3,96)	26 18,12 (3,80)	25 18,88 (3,61)	24 18,13 (4,13)	24 18,58 (3,93)	13 16,85 (3,58)	0,75 (0,44)	-0,59 [-1,85;0,66] 0,3492 -0,25 [-0,77;0,27]
Ethnizität (p-Wert des Interaktionsterms: 0,6440)																			
Weiß	276 18,09 (4,07)	260 18,31 (4,18)	250 18,31 (4,23)	245 18,22 (4,09)	230 17,96 (4,23)	201 17,97 (4,17)	184 17,80 (4,39)	118 17,25 (4,29)	-0,07 (0,17)	285 17,92 (4,08)	268 17,98 (4,27)	259 18,25 (3,97)	241 18,17 (4,01)	223 18,54 (3,93)	202 18,33 (3,90)	210 17,81 (4,33)	122 17,54 (4,35)	0,00 (0,17)	-0,08 [-0,54;0,39] 0,7446 -0,03 [-0,19;0,14]
Asiatisch	188 17,76 (4,10)	185 17,66 (4,15)	181 17,90 (4,05)	179 17,79 (4,21)	171 17,82 (4,08)	149 17,69 (4,15)	153 17,72 (4,26)	75 17,17 (4,24)	0,01 (0,20)	166 17,55 (4,31)	164 17,79 (4,15)	162 18,03 (4,00)	157 18,27 (3,79)	144 18,24 (3,77)	124 17,95 (4,05)	130 17,80 (4,15)	67 17,81 (3,99)	0,20 (0,21)	-0,19 [-0,77;0,39] 0,5208 -0,07 [-0,28;0,14]
Andere	16 18,25 (5,36)	15 18,53 (4,31)	15 18,53 (4,17)	15 18,00 (4,39)	15 18,33 (3,72)	13 18,31 (3,61)	14 17,36 (5,05)	9 16,67 (6,22)	-0,23 (0,81)	17 17,94 (4,46)	16 18,25 (4,02)	17 18,18 (3,56)	16 19,25 (3,44)	14 19,71 (2,97)	12 20,25 (2,56)	12 20,42 (2,78)	7 21,00 (2,52)	1,25 (0,82)	-1,48 [-3,88;0,92] 0,2136 -0,44 [-1,11;0,24]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B EWB = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B EWB haben. Abkürzungen: B: Baseline; ET: Endokrine Therapie; EWB: emotionales Wohlbefinden; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler																		

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t109_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: EWB aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,5043)																			
< 65 Jahre	804 18,53 (3,99)	760 18,67 (4,01)	745 18,77 (4,10)	699 18,62 (4,12)	672 18,76 (3,76)	593 18,53 (3,97)	603 18,36 (4,08)	330 18,64 (4,03)	0,03 (0,09)	831 18,31 (4,22)	792 18,55 (4,14)	783 18,59 (3,94)	731 18,52 (4,00)	693 18,70 (4,09)	610 18,59 (3,97)	605 18,29 (4,20)	319 18,34 (3,98)	0,11 (0,09)	-0,07 [-0,33;0,19] 0,5855 -0,03 [-0,12;0,07]
≥ 65 Jahre	303 18,59 (4,01)	283 18,63 (4,00)	266 18,97 (3,64)	256 18,77 (3,98)	241 18,78 (3,88)	217 18,57 (3,73)	226 18,61 (3,91)	120 18,65 (3,88)	-0,10 (0,14)	279 19,19 (3,88)	267 19,38 (3,82)	260 19,38 (3,68)	247 19,46 (3,47)	241 19,19 (3,74)	211 19,11 (3,71)	197 18,80 (3,78)	117 18,43 (4,04)	-0,01 (0,15)	-0,09 [-0,49;0,32] 0,6718 -0,04 [-0,20;0,13]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7418)																			
Neoadjuvante Chemotherapie	363 18,90 (3,98)	336 18,93 (4,11)	325 19,15 (3,98)	300 18,60 (4,22)	279 18,75 (3,89)	238 18,58 (4,07)	254 18,14 (4,19)	130 18,56 (4,23)	-0,24 (0,14)	365 18,30 (4,30)	347 18,40 (4,20)	331 18,44 (3,86)	309 18,42 (3,92)	292 18,54 (4,00)	248 18,42 (3,97)	260 18,04 (4,19)	139 17,40 (4,14)	-0,17 (0,14)	-0,07 [-0,47;0,33] 0,7230 -0,03 [-0,17;0,12]
Adjuvante Chemotherapie	684 18,35 (4,02)	653 18,52 (3,98)	635 18,64 (4,05)	604 18,73 (4,01)	588 18,78 (3,75)	532 18,55 (3,87)	529 18,52 (4,02)	293 18,69 (3,92)	0,13 (0,10)	678 18,67 (3,98)	648 19,02 (3,93)	652 18,92 (3,93)	613 18,90 (3,87)	595 18,97 (4,02)	528 18,89 (3,89)	495 18,63 (4,11)	270 18,84 (3,76)	0,21 (0,10)	-0,08 [-0,35;0,20] 0,5858 -0,03 [-0,14;0,08]
Keine Chemotherapie	60 18,67 (3,63)	54 18,70 (3,60)	51 18,94 (2,94)	51 18,29 (4,08)	46 18,61 (3,77)	40 18,13 (3,31)	46 18,96 (3,24)	27 18,48 (3,58)	-0,23 (0,31)	67 18,40 (4,93)	64 18,14 (4,65)	60 19,18 (3,52)	56 19,14 (3,92)	47 18,66 (3,82)	45 18,44 (3,79)	47 18,26 (3,57)	27 18,44 (4,64)	-0,04 (0,30)	-0,20 [-1,06;0,66] 0,6487 -0,08 [-0,43;0,27]
Region (p-Wert des Interaktionsterms: 0,3190)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	550 18,51 (4,23)	497 18,49 (4,29)	483 18,68 (4,13)	449 18,35 (4,34)	420 18,68 (3,99)	379 18,37 (4,10)	393 18,22 (4,24)	211 18,88 (3,95)	-0,15 (0,11)	529 18,60 (4,25)	491 18,88 (4,04)	481 18,78 (3,91)	441 18,70 (3,92)	423 18,92 (4,07)	376 18,85 (4,00)	343 18,45 (4,10)	205 18,35 (4,20)	0,02 (0,11)	-0,17 [-0,48;0,14] 0,2718 -0,07 [-0,19;0,05]
Asien	195 18,91 (3,53)	190 19,03 (3,56)	185 18,94 (3,89)	178 18,90 (3,83)	173 18,98 (3,64)	152 18,77 (3,65)	163 18,44 (3,76)	87 18,02 (3,74)	0,00 (0,18)	192 18,58 (3,96)	189 18,66 (3,93)	187 18,84 (3,82)	179 19,09 (3,74)	174 19,07 (3,79)	149 18,66 (3,77)	155 18,55 (3,96)	81 18,10 (3,81)	0,18 (0,18)	-0,18 [-0,68;0,33] 0,4912 -0,07 [-0,27;0,13]
Andere	362 18,41 (3,86)	356 18,70 (3,82)	343 18,95 (3,82)	328 18,97 (3,83)	320 18,75 (3,60)	279 18,65 (3,76)	273 18,73 (3,88)	152 18,67 (4,14)	0,24 (0,14)	389 18,42 (4,13)	379 18,66 (4,20)	375 18,75 (3,92)	358 18,67 (3,93)	337 18,57 (4,03)	296 18,59 (3,87)	304 18,32 (4,20)	150 18,51 (3,81)	0,08 (0,14)	0,16 [-0,23;0,55] 0,4188 0,06 [-0,08;0,20]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,8731)																			
< 20 mm	279 18,81 (3,92)	257 19,02 (3,89)	253 19,04 (3,76)	244 18,53 (4,31)	234 18,81 (3,67)	208 18,47 (4,11)	209 18,63 (3,79)	106 18,43 (3,97)	-0,17 (0,15)	298 18,69 (3,89)	284 18,93 (3,99)	276 19,12 (3,66)	258 18,74 (4,00)	251 18,73 (3,93)	216 18,94 (3,57)	220 18,21 (4,06)	111 18,11 (3,81)	-0,10 (0,15)	-0,07 [-0,49;0,35] 0,7461 -0,03 [-0,19;0,14]
≥ 20 bis < 50 mm	569 18,50 (4,02)	546 18,61 (3,99)	522 18,84 (4,06)	503 18,90 (3,95)	476 18,88 (3,80)	426 18,83 (3,72)	432 18,54 (4,08)	232 18,75 (3,89)	0,13 (0,11)	572 18,57 (4,23)	549 18,80 (4,10)	543 18,75 (3,90)	511 18,89 (3,76)	492 18,92 (3,96)	439 18,72 (4,06)	415 18,58 (4,12)	230 18,39 (3,99)	0,12 (0,11)	0,01 [-0,30;0,32] 0,9445 0,00 [-0,11;0,12]
≥ 50 mm	242 18,38 (4,05)	225 18,41 (4,13)	220 18,60 (3,93)	195 18,18 (4,12)	189 18,53 (3,89)	163 18,04 (3,91)	174 17,94 (4,16)	104 18,63 (4,17)	-0,08 (0,17)	229 18,20 (4,36)	215 18,44 (4,14)	214 18,41 (4,21)	199 18,49 (4,05)	184 18,67 (4,24)	158 18,52 (3,91)	159 18,28 (4,14)	91 18,56 (4,30)	0,19 (0,18)	-0,27 [-0,75;0,22] 0,2819 -0,10 [-0,28;0,08]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,0633)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	367 18,59 (3,96)	347 18,78 (3,90)	335 18,84 (4,36)	313 18,69 (4,20)	302 18,76 (3,86)	274 18,38 (4,12)	285 18,21 (4,20)	167 18,95 (3,84)	-0,06 (0,14)	360 18,47 (4,33)	343 18,79 (4,04)	341 18,98 (3,80)	313 18,82 (3,85)	303 19,05 (3,85)	260 18,99 (3,85)	255 18,75 (3,84)	142 18,42 (4,12)	0,21 (0,14)	-0,27 [-0,65;0,11] 0,1593 -0,10 [-0,25;0,04]
4-9	476 18,55 (3,98)	447 18,72 (3,96)	438 18,90 (3,68)	419 18,74 (3,88)	398 18,79 (3,70)	354 18,66 (3,76)	356 18,73 (3,93)	174 18,58 (3,89)	0,10 (0,12)	485 18,51 (4,18)	465 18,57 (4,14)	463 18,66 (3,84)	439 18,50 (4,01)	419 18,50 (4,19)	377 18,44 (4,02)	357 18,22 (4,30)	192 18,56 (3,73)	-0,08 (0,12)	0,18 [-0,15;0,52] 0,2840 0,07 [-0,06;0,20]
≥ 10	264 18,50 (4,07)	249 18,38 (4,23)	238 18,65 (3,98)	223 18,48 (4,29)	213 18,71 (3,86)	182 18,56 (3,85)	188 18,19 (3,96)	109 18,27 (4,33)	-0,10 (0,16)	265 18,67 (3,87)	251 19,09 (4,00)	239 18,74 (4,11)	226 19,19 (3,69)	212 19,14 (3,81)	184 18,93 (3,73)	190 18,36 (4,07)	102 17,89 (4,27)	0,17 (0,16)	-0,27 [-0,72;0,19] 0,2511 -0,10 [-0,27;0,07]
Tumorstadium (p-Wert des Interaktionsterms: 0,5241)																			
IIA	92 18,73 (4,08)	87 18,91 (3,68)	84 18,83 (4,20)	81 18,40 (4,27)	80 18,53 (3,65)	76 18,41 (4,23)	75 18,15 (4,43)	39 19,00 (3,81)	-0,24 (0,26)	95 18,16 (4,95)	92 18,39 (4,66)	90 18,84 (3,82)	84 18,43 (3,98)	80 18,69 (3,50)	71 18,52 (3,77)	74 17,85 (4,01)	37 17,43 (3,72)	-0,00 (0,26)	-0,24 [-0,96;0,48] 0,5152 -0,10 [-0,38;0,19]
IIB	133 18,86 (3,79)	126 19,12 (3,71)	118 19,45 (4,05)	116 19,05 (4,19)	113 19,19 (3,80)	101 19,31 (3,60)	109 18,50 (4,18)	68 19,46 (3,70)	0,04 (0,23)	113 19,11 (4,14)	107 19,51 (3,43)	106 19,20 (3,72)	99 19,01 (3,77)	94 19,34 (4,08)	85 19,27 (4,30)	81 19,28 (3,88)	44 18,77 (4,29)	0,00 (0,25)	0,04 [-0,61;0,70] 0,8964 0,02 [-0,23;0,27]
IIIA	431 18,55 (3,91)	407 18,69 (3,92)	397 18,85 (3,69)	374 18,65 (3,84)	352 18,63 (3,74)	314 18,46 (3,81)	321 18,51 (3,99)	156 18,35 (3,90)	0,02 (0,13)	436 18,53 (4,25)	414 18,50 (4,08)	420 18,72 (3,91)	395 18,58 (4,03)	377 18,56 (4,27)	334 18,58 (3,95)	315 18,29 (4,24)	172 18,73 (3,63)	-0,03 (0,13)	0,05 [-0,30;0,40] 0,7768 0,02 [-0,11;0,15]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIB	47 17,34 (4,52)	45 17,53 (4,67)	45 18,40 (4,63)	44 17,95 (4,62)	41 18,32 (3,80)	36 17,67 (4,37)	31 18,55 (3,80)	15 18,47 (4,14)	0,29 (0,39)	41 18,63 (4,03)	40 19,30 (3,91)	39 19,21 (3,69)	35 19,23 (4,04)	34 19,06 (4,35)	31 18,87 (3,76)	30 18,70 (4,50)	14 18,79 (4,14)	0,70 (0,42)	-0,40 [-1,54;0,74] 0,4856 -0,15 [-0,57;0,27]
IIIC	402 18,56 (4,05)	377 18,55 (4,17)	365 18,62 (4,14)	338 18,71 (4,20)	325 18,89 (3,88)	281 18,51 (3,95)	291 18,37 (3,99)	170 18,52 (4,20)	-0,04 (0,13)	423 18,45 (3,88)	404 18,89 (4,05)	386 18,67 (3,97)	363 18,91 (3,74)	347 18,99 (3,77)	298 18,76 (3,81)	301 18,44 (4,01)	168 18,04 (4,29)	0,16 (0,13)	-0,20 [-0,57;0,17] 0,2892 -0,07 [-0,21;0,06]
Tumorgrading (p-Wert des Interaktionsterms: 0,2629)																			
G1	82 18,99 (4,06)	80 19,30 (3,18)	81 18,84 (4,02)	74 18,66 (4,66)	70 18,94 (3,81)	63 18,41 (3,76)	62 18,68 (3,90)	31 18,03 (4,35)	-0,15 (0,29)	84 18,93 (4,00)	82 19,12 (4,05)	79 18,68 (4,65)	71 19,41 (3,74)	74 18,77 (4,33)	65 19,43 (3,78)	55 18,80 (4,50)	34 18,65 (4,03)	0,15 (0,28)	-0,30 [-1,10;0,49] 0,4532 -0,12 [-0,42;0,19]
G2	526 18,59 (4,00)	499 18,56 (4,16)	482 18,84 (3,86)	454 18,68 (4,09)	434 18,78 (3,84)	375 18,53 (3,92)	375 18,42 (4,08)	212 18,67 (4,13)	-0,05 (0,12)	533 18,55 (4,17)	505 18,57 (4,14)	504 18,58 (3,90)	477 18,49 (3,93)	447 18,49 (4,17)	402 18,50 (3,94)	392 18,11 (4,21)	214 18,42 (3,74)	-0,17 (0,11)	0,13 [-0,19;0,45] 0,4328 0,05 [-0,07;0,17]
G3	450 18,45 (3,98)	420 18,63 (3,98)	403 18,83 (4,13)	382 18,63 (3,98)	367 18,74 (3,75)	333 18,59 (3,93)	355 18,40 (4,04)	185 18,77 (3,75)	0,10 (0,12)	436 18,38 (4,24)	415 18,98 (3,97)	405 18,99 (3,83)	379 18,98 (3,86)	365 19,26 (3,72)	315 18,91 (3,98)	314 18,73 (3,99)	165 18,22 (4,41)	0,37 (0,13)	-0,27 [-0,62;0,08] 0,1271 -0,10 [-0,23;0,03]
GX	47 18,21 (4,05)	42 18,79 (3,85)	43 18,44 (4,05)	43 18,74 (4,07)	40 18,55 (3,81)	37 18,49 (3,96)	37 18,35 (3,93)	22 18,23 (4,12)	-0,01 (0,35)	53 19,00 (3,55)	53 18,28 (4,39)	52 19,29 (2,97)	48 18,69 (3,78)	45 18,58 (3,86)	37 18,24 (2,77)	39 18,46 (3,12)	21 18,95 (2,38)	-0,08 (0,34)	0,07 [-0,90;1,03] 0,8931 0,03 [-0,37;0,42]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,7765)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Negativ	137 18,05 (3,58)	132 18,00 (4,08)	124 18,12 (4,13)	116 18,42 (3,87)	106 17,99 (3,97)	92 17,55 (4,01)	100 18,01 (3,76)	63 17,35 (4,10)	-0,29 (0,23)	149 18,33 (3,96)	139 18,41 (4,16)	133 18,41 (4,04)	126 18,48 (4,10)	121 18,76 (3,80)	103 18,38 (3,98)	114 17,61 (4,48)	56 17,68 (3,95)	-0,03 (0,22)	-0,26 [-0,89;0,37] 0,4243 -0,09 [-0,33;0,14]
Positiv	939 18,60 (4,06)	880 18,71 (4,01)	856 18,87 (3,97)	814 18,63 (4,12)	785 18,82 (3,75)	695 18,61 (3,87)	707 18,44 (4,07)	376 18,83 (3,92)	0,03 (0,09)	934 18,49 (4,18)	896 18,79 (4,07)	886 18,79 (3,87)	830 18,77 (3,86)	792 18,78 (4,05)	697 18,74 (3,92)	668 18,50 (4,04)	366 18,42 (3,99)	0,11 (0,09)	-0,08 [-0,32;0,16] 0,4972 -0,03 [-0,12;0,06]
Unbekannt	9 18,00 (4,24)	9 19,33 (3,84)	9 19,89 (3,66)	7 21,00 (3,42)	3 22,33 (2,08)	6 20,33 (4,84)	5 18,00 (5,24)	1 23,00 (NE)	0,76 (1,00)	7 20,86 (3,89)	6 20,00 (4,34)	6 20,67 (3,44)	6 21,00 (1,41)	6 21,17 (2,14)	6 20,00 (2,10)	5 20,80 (0,84)	5 21,60 (1,82)	0,67 (1,04)	0,09 [-3,10;3,28] 0,9533 0,03 [-0,91;0,96]
Ethnizität (p-Wert des Interaktionsterms: 0,8352)																			
Weiß	808 18,40 (4,11)	755 18,52 (4,06)	738 18,71 (3,98)	694 18,46 (4,18)	659 18,61 (3,89)	588 18,40 (3,99)	596 18,27 (4,17)	338 18,64 (4,09)	-0,06 (0,09)	819 18,50 (4,18)	773 18,76 (4,08)	761 18,80 (3,80)	707 18,58 (3,94)	678 18,70 (4,08)	601 18,66 (3,95)	577 18,36 (4,14)	323 18,34 (4,06)	0,01 (0,09)	-0,07 [-0,33;0,19] 0,6054 -0,03 [-0,12;0,07]
Asiatisch	233 18,98 (3,50)	225 19,14 (3,59)	218 19,17 (3,85)	210 19,19 (3,79)	204 19,23 (3,56)	176 19,01 (3,59)	187 18,68 (3,71)	97 18,45 (3,82)	0,24 (0,17)	221 18,53 (4,01)	217 18,69 (3,97)	215 18,78 (4,01)	207 19,29 (3,75)	199 19,26 (3,84)	167 18,81 (3,79)	172 18,65 (4,01)	88 18,35 (3,90)	0,33 (0,17)	-0,09 [-0,56;0,39] 0,7195 -0,03 [-0,22;0,15]
Andere	54 19,00 (3,97)	51 18,59 (4,71)	47 19,04 (4,39)	42 19,33 (3,52)	42 18,67 (3,37)	36 18,67 (4,04)	40 19,23 (3,46)	14 19,71 (2,23)	-0,20 (0,36)	57 19,09 (4,10)	57 18,82 (4,60)	55 18,95 (4,03)	52 18,92 (3,83)	46 18,76 (3,74)	42 19,31 (3,88)	44 18,59 (4,18)	19 18,47 (3,96)	-0,20 (0,34)	-0,00 [-0,98;0,98] 0,9970 -0,00 [-0,37;0,37]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,7204)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Tamoxifen	104 18,47 (4,04)	99 18,03 (4,45)	99 18,10 (4,42)	96 17,78 (4,24)	94 18,39 (3,82)	91 18,11 (3,94)	91 18,26 (3,98)	55 17,96 (4,46)	-0,21 (0,25)	124 17,87 (4,13)	122 18,13 (4,10)	120 17,94 (4,32)	110 18,03 (3,80)	103 18,07 (3,84)	94 18,18 (3,98)	92 17,62 (4,07)	56 17,82 (3,51)	-0,01 (0,23)	-0,20 [-0,86;0,46] 0,5563 -0,08 [-0,34;0,18]
Aromatase-Inhibitor	1003 18,56 (3,99)	944 18,73 (3,95)	912 18,90 (3,93)	859 18,76 (4,05)	819 18,81 (3,79)	719 18,60 (3,90)	738 18,45 (4,04)	395 18,74 (3,91)	0,02 (0,08)	986 18,62 (4,15)	937 18,84 (4,07)	923 18,89 (3,82)	868 18,85 (3,90)	831 18,92 (4,02)	727 18,79 (3,90)	710 18,52 (4,11)	380 18,44 (4,05)	0,09 (0,08)	-0,07 [-0,30;0,17] 0,5709 -0,03 [-0,11;0,06]
ECOG-PS (p-Wert des Interaktionsterms: 0,5649)																			
ECOG-PS 0	933 18,67 (3,89)	878 18,81 (3,93)	854 18,90 (3,94)	814 18,70 (4,06)	779 18,85 (3,75)	695 18,59 (3,93)	703 18,46 (4,03)	382 18,75 (3,97)	-0,00 (0,09)	898 18,58 (4,12)	855 18,81 (4,04)	845 18,88 (3,79)	794 18,82 (3,83)	759 18,84 (4,01)	675 18,72 (3,89)	663 18,31 (4,16)	355 18,32 (4,00)	0,04 (0,09)	-0,04 [-0,28;0,20] 0,7404 -0,02 [-0,11;0,08]
ECOG-PS 1	174 17,92 (4,45)	165 17,89 (4,33)	157 18,39 (4,20)	141 18,46 (4,20)	134 18,28 (4,01)	115 18,26 (3,72)	126 18,27 (4,10)	68 18,06 (4,04)	0,02 (0,20)	212 18,33 (4,30)	204 18,55 (4,20)	198 18,39 (4,29)	184 18,49 (4,13)	175 18,77 (3,99)	146 18,74 (4,01)	139 18,92 (3,83)	81 18,53 (3,96)	0,25 (0,18)	-0,23 [-0,76;0,31] 0,4045 -0,09 [-0,29;0,12]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B EWB = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B EWB haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; EWB: emotionales Wohlbefinden; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t109_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: FWB aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,1538)																			
Neoadjuvante Chemotherapie	196 19,96 (5,06)	188 19,32 (5,57)	181 19,54 (5,49)	177 19,50 (5,50)	165 19,27 (5,53)	150 19,23 (6,06)	147 18,71 (5,89)	75 19,00 (5,04)	-0,74 (0,25)	193 19,62 (5,32)	181 20,04 (5,38)	179 20,19 (5,15)	155 20,72 (5,13)	145 21,12 (5,12)	121 21,25 (5,40)	136 19,88 (5,72)	77 19,65 (6,25)	0,41 (0,25)	-1,15 [-1,84;-0,45] 0,0012 -0,33 [-0,53;-0,13]
Adjuvante Chemotherapie	287 19,47 (5,10)	272 19,62 (4,97)	267 19,65 (5,54)	264 19,86 (5,16)	253 20,25 (5,20)	213 20,23 (5,35)	204 20,18 (5,22)	126 20,40 (5,04)	0,45 (0,20)	283 19,67 (5,22)	275 19,88 (5,36)	267 20,58 (5,19)	261 20,74 (5,25)	240 21,12 (4,81)	222 20,50 (4,95)	217 20,20 (5,10)	120 20,19 (5,23)	0,76 (0,20)	-0,31 [-0,87;0,25] 0,2822 -0,09 [-0,25;0,07]
Keine Chemotherapie	7 18,71 (7,95)	7 19,00 (6,53)	6 18,67 (7,20)	6 19,17 (6,97)	5 18,80 (6,98)	5 18,60 (7,89)	6 19,83 (5,64)	2 20,50 (4,95)	0,36 (1,46)	1 22,00 (NE)	1 19,00 (NE)	1 21,00 (NE)	1 17,00 (NE)	1 16,00 (NE)	1 20,00 (NE)	1 16,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,2361)																			
Nordamerika / Europa	204 19,76 (5,08)	188 19,78 (4,89)	181 19,90 (5,15)	178 19,70 (5,22)	162 20,11 (5,16)	140 19,96 (5,67)	135 20,13 (5,20)	73 20,55 (4,65)	0,17 (0,24)	197 19,78 (4,80)	183 19,61 (5,35)	174 20,39 (4,89)	154 20,73 (5,13)	141 21,45 (4,95)	134 20,89 (5,15)	133 20,20 (5,58)	66 20,67 (6,01)	0,57 (0,25)	-0,40 [-1,08;0,27] 0,2428 -0,12 [-0,31;0,08]
Asien	162 19,40 (5,15)	161 18,92 (5,40)	157 19,15 (5,32)	155 19,52 (5,35)	149 19,56 (5,37)	129 19,05 (5,87)	136 19,14 (5,71)	69 20,19 (5,06)	-0,22 (0,26)	152 19,85 (5,34)	150 19,94 (5,60)	151 19,99 (5,42)	146 20,90 (5,33)	137 20,99 (5,08)	120 20,73 (5,49)	121 19,88 (5,50)	65 20,11 (5,53)	0,43 (0,26)	-0,65 [-1,37;0,08] 0,0795 -0,20 [-0,42;0,02]
Andere	124 19,82 (5,20)	118 19,81 (5,49)	116 19,72 (6,32)	114 19,99 (5,44)	112 19,86 (5,64)	99 20,56 (5,41)	86 19,38 (5,78)	61 18,74 (5,40)	0,00 (0,33)	128 19,23 (5,80)	124 20,43 (5,04)	122 21,02 (5,21)	117 20,50 (5,15)	108 20,80 (4,69)	90 20,61 (4,55)	100 20,13 (4,82)	66 19,17 (5,34)	0,95 (0,32)	-0,95 [-1,85;-0,05] 0,0390 -0,26 [-0,51;-0,01]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4674)																			
< 20 mm	121 19,59 (4,95)	115 19,08 (4,90)	109 19,05 (5,34)	112 19,21 (5,29)	105 19,81 (5,25)	94 18,93 (5,81)	91 19,07 (5,52)	53 20,13 (4,36)	-0,39 (0,32)	123 19,72 (5,11)	116 19,62 (5,54)	116 20,72 (4,59)	107 19,91 (5,50)	100 21,10 (5,26)	87 20,76 (5,35)	85 20,51 (5,33)	50 19,88 (5,94)	0,40 (0,32)	-0,78 [-1,67;0,10] 0,0815 -0,22 [-0,48;0,03]
≥ 20 bis < 50 mm	229 19,76 (5,32)	218 19,34 (5,72)	217 19,93 (5,50)	213 19,74 (5,35)	196 19,79 (5,57)	170 19,96 (5,55)	164 19,65 (5,69)	96 19,40 (5,59)	-0,04 (0,23)	227 19,54 (5,20)	218 20,11 (5,12)	216 20,34 (5,40)	200 21,19 (4,83)	187 21,18 (4,62)	172 20,69 (4,85)	181 19,93 (5,20)	93 19,71 (5,74)	0,72 (0,23)	-0,76 [-1,40;-0,13] 0,0191 -0,22 [-0,40;-0,04]
≥ 50 mm	128 19,58 (5,07)	124 19,96 (4,69)	119 19,46 (5,79)	114 20,07 (5,21)	113 19,84 (5,16)	95 20,24 (5,74)	93 19,94 (5,31)	48 20,35 (4,79)	0,23 (0,29)	122 19,93 (5,53)	118 19,94 (5,72)	110 20,45 (5,31)	105 20,91 (5,39)	96 20,99 (5,20)	81 21,02 (5,48)	84 19,98 (5,74)	50 20,80 (5,08)	0,57 (0,30)	-0,34 [-1,16;0,48] 0,4112 -0,10 [-0,35;0,14]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9024)																			
0-3	177 19,98 (5,08)	169 19,84 (5,02)	160 19,79 (5,63)	158 19,51 (5,63)	144 20,17 (5,23)	130 20,13 (6,11)	131 19,31 (5,97)	77 20,19 (4,61)	-0,15 (0,26)	190 19,74 (5,11)	181 20,22 (5,28)	175 20,40 (5,28)	163 20,61 (5,25)	156 20,76 (5,17)	136 20,59 (5,24)	135 19,81 (5,70)	71 19,46 (5,93)	0,36 (0,25)	-0,51 [-1,23;0,21] 0,1639 -0,15 [-0,35;0,06]
4-9	215 19,12 (5,25)	204 18,63 (5,47)	201 19,06 (5,51)	197 19,38 (5,22)	192 19,45 (5,28)	168 19,38 (5,34)	158 19,33 (5,24)	83 19,07 (5,43)	-0,07 (0,23)	210 20,00 (5,07)	201 20,12 (5,00)	199 20,36 (5,17)	186 20,72 (5,09)	172 21,41 (4,54)	153 20,91 (4,95)	160 19,98 (5,24)	87 20,20 (5,26)	0,50 (0,23)	-0,57 [-1,21;0,07] 0,0805 -0,17 [-0,36;0,02]
≥ 10	98 20,26 (4,85)	94 20,72 (4,79)	93 20,40 (5,33)	92 20,76 (4,86)	87 20,20 (5,73)	70 20,20 (5,69)	68 20,63 (5,32)	43 20,88 (4,94)	0,36 (0,36)	77 18,51 (5,97)	75 18,80 (6,31)	73 20,66 (4,93)	68 21,00 (5,42)	58 21,10 (5,30)	55 20,76 (5,30)	59 20,90 (4,68)	39 20,44 (5,99)	1,56 (0,41)	-1,20 [-2,27;-0,12] 0,0290 -0,34 [-0,64;-0,04]
Tumorstadium (p-Wert des Interaktionsterms: 0,3587)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 19,87 (4,93)	49 18,92 (5,72)	48 18,60 (5,73)	46 18,39 (5,48)	46 19,22 (5,82)	40 18,78 (5,74)	39 18,23 (5,64)	23 19,22 (3,63)	-0,97 (0,44)	57 19,95 (4,76)	54 20,22 (4,60)	54 21,02 (4,43)	48 20,46 (4,96)	47 21,96 (4,22)	36 20,97 (4,62)	37 21,05 (4,88)	19 20,58 (3,89)	0,85 (0,42)	-1,82 [-3,03;-0,61] 0,0035 -0,57 [-0,96;-0,19]
IIB	45 20,44 (4,11)	44 19,98 (4,75)	41 20,95 (4,53)	42 19,90 (4,84)	35 20,49 (4,00)	34 20,41 (5,39)	31 20,26 (4,70)	22 20,32 (4,76)	-0,06 (0,48)	64 20,14 (4,49)	62 20,55 (4,51)	60 21,00 (5,35)	55 20,95 (4,54)	55 20,85 (4,26)	54 20,56 (4,60)	55 19,60 (5,53)	32 20,03 (5,99)	-0,01 (0,40)	-0,05 [-1,29;1,20] 0,9415 -0,01 [-0,40;0,37]
IIIA	212 19,26 (5,37)	205 19,17 (5,28)	198 19,14 (5,53)	195 19,59 (5,11)	189 19,69 (5,29)	164 19,62 (5,42)	157 19,29 (5,22)	84 19,67 (5,44)	0,09 (0,22)	193 19,80 (5,31)	183 19,97 (5,20)	179 20,21 (5,32)	173 20,49 (5,10)	158 21,00 (4,75)	133 21,01 (4,99)	141 19,95 (5,15)	71 19,89 (5,36)	0,49 (0,24)	-0,40 [-1,04;0,24] 0,2198 -0,12 [-0,32;0,07]
IIIB	14 18,36 (6,11)	13 18,15 (5,57)	13 17,46 (7,05)	13 16,08 (5,09)	10 15,60 (3,86)	8 14,38 (7,56)	11 15,73 (7,28)	6 14,83 (3,66)	-2,00 (1,16)	14 19,57 (7,64)	14 20,00 (8,08)	14 19,86 (7,25)	11 18,64 (9,98)	9 19,89 (9,06)	10 17,50 (8,54)	9 16,11 (9,24)	5 13,20 (10,45)	-0,55 (1,05)	-1,45 [-4,68;1,78] 0,3659 -0,34 [-1,06;0,38]
IIIC	166 20,02 (5,02)	155 20,05 (5,12)	153 20,32 (5,47)	150 20,52 (5,52)	142 20,41 (5,58)	121 20,57 (5,83)	118 20,58 (5,77)	67 20,72 (5,00)	0,35 (0,29)	148 19,15 (5,44)	143 19,52 (5,87)	139 20,27 (4,97)	129 21,22 (5,15)	117 21,11 (5,30)	111 20,78 (5,24)	112 20,44 (5,15)	70 20,37 (5,60)	1,03 (0,31)	-0,67 [-1,51;0,17] 0,1158 -0,18 [-0,40;0,04]
Tumorgrading (p-Wert des Interaktionsterms: 0,3831)																			
G1	45 20,00 (4,87)	42 20,02 (4,34)	40 19,50 (5,37)	40 18,95 (4,41)	39 19,85 (4,34)	33 19,61 (5,04)	33 19,85 (4,70)	18 19,72 (4,81)	-0,30 (0,46)	38 20,00 (5,27)	36 21,69 (4,39)	34 21,56 (4,16)	36 21,06 (5,47)	30 21,80 (5,11)	28 19,36 (5,37)	25 20,04 (5,90)	13 21,00 (4,32)	1,22 (0,51)	-1,52 [-2,89;-0,15] 0,0307 -0,49 [-0,92;-0,05]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	213 19,53 (5,17)	202 19,35 (5,43)	201 19,71 (5,52)	196 19,78 (5,41)	188 19,70 (5,59)	165 19,35 (5,45)	167 19,38 (5,44)	85 19,92 (5,26)	-0,01 (0,24)	207 19,55 (5,57)	200 19,58 (5,89)	194 20,03 (5,46)	181 20,50 (5,36)	162 20,83 (5,19)	148 20,78 (5,58)	153 19,85 (5,69)	86 19,57 (6,14)	0,40 (0,24)	-0,42 [-1,08;0,25] 0,2193 -0,12 [-0,31;0,07]
G3	204 19,54 (5,15)	196 19,42 (5,28)	188 19,30 (5,67)	185 19,57 (5,50)	171 19,88 (5,31)	148 20,32 (5,94)	137 19,47 (5,96)	87 19,43 (5,00)	0,09 (0,25)	203 19,66 (5,04)	194 19,91 (4,99)	192 20,70 (4,99)	173 20,88 (5,07)	168 21,10 (4,70)	143 20,97 (4,67)	153 20,14 (5,07)	86 20,19 (5,50)	0,72 (0,25)	-0,63 [-1,31;0,06] 0,0726 -0,18 [-0,37;0,02]
GX	28 20,96 (5,01)	27 20,22 (4,73)	25 21,00 (4,71)	26 21,42 (4,23)	25 20,76 (5,55)	22 19,95 (6,69)	20 21,40 (4,62)	13 22,92 (3,57)	-0,05 (0,59)	28 19,93 (4,56)	26 20,38 (4,66)	26 19,92 (5,40)	26 20,54 (4,62)	25 22,00 (4,45)	24 20,96 (4,34)	23 21,04 (3,93)	12 20,33 (4,27)	0,72 (0,58)	-0,77 [-2,45;0,91] 0,3615 -0,25 [-0,77;0,28]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,8798)																			
Negativ	46 18,52 (5,13)	43 18,16 (5,43)	41 19,02 (5,76)	42 18,62 (5,53)	39 17,79 (5,80)	38 17,87 (5,84)	36 16,97 (5,67)	12 18,75 (4,88)	-0,61 (0,56)	39 20,36 (4,25)	36 19,92 (4,27)	35 19,17 (5,88)	30 21,23 (4,16)	31 22,23 (4,14)	26 21,54 (4,57)	31 20,77 (4,92)	15 19,40 (4,72)	0,18 (0,61)	-0,79 [-2,45;0,87] 0,3467 -0,21 [-0,64;0,22]
Positiv	426 19,73 (5,14)	407 19,56 (5,24)	399 19,58 (5,53)	390 19,75 (5,27)	371 19,99 (5,27)	319 19,94 (5,60)	305 19,76 (5,50)	182 19,85 (5,07)	-0,00 (0,17)	421 19,65 (5,31)	406 20,00 (5,41)	398 20,61 (5,03)	373 20,68 (5,28)	341 20,91 (4,97)	305 20,72 (5,10)	313 19,99 (5,31)	175 19,92 (5,75)	0,63 (0,17)	-0,63 [-1,09;-0,17] 0,0077 -0,18 [-0,32;-0,05]
Unbekannt	2 22,50 (0,71)	2 21,00 (7,07)	2 23,50 (6,36)	1 28,00 (NE)	1 27,00 (NE)	1 28,00 (NE)	1 28,00 (NE)	0	NE	8 16,00 (6,68)	7 16,57 (7,70)	8 17,75 (7,17)	6 18,17 (5,56)	6 22,83 (6,05)	8 18,00 (7,29)	4 18,25 (10,72)	2 22,00 (7,07)	2,00 (1,48)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,2691)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	276 19,70 (5,03)	259 19,63 (5,15)	250 19,66 (5,36)	245 19,59 (5,16)	230 19,74 (5,42)	201 19,73 (5,66)	184 19,66 (5,30)	118 19,64 (5,09)	-0,07 (0,21)	285 19,71 (5,08)	268 19,85 (5,21)	259 20,60 (5,06)	241 20,38 (5,03)	223 20,96 (4,91)	202 20,69 (4,99)	210 20,07 (5,41)	122 19,75 (5,82)	0,41 (0,20)	-0,47 [-1,04;0,09] 0,1005 -0,14 [-0,30;0,03]
Asiatisch	187 19,50 (5,31)	184 19,26 (5,32)	180 19,44 (5,67)	178 20,07 (5,30)	170 20,07 (5,33)	148 19,76 (5,85)	152 19,44 (5,87)	75 20,43 (5,08)	0,15 (0,26)	165 19,64 (5,68)	163 20,04 (5,61)	162 20,14 (5,39)	157 21,18 (5,39)	144 21,03 (5,04)	124 20,71 (5,46)	129 19,91 (5,37)	66 20,12 (5,49)	0,70 (0,27)	-0,55 [-1,29;0,19] 0,1454 -0,16 [-0,37;0,05]
Andere	16 20,13 (6,01)	15 19,67 (6,70)	15 20,07 (6,89)	15 18,00 (6,75)	15 18,47 (5,37)	13 20,69 (5,04)	14 19,71 (5,36)	9 19,00 (4,61)	-0,60 (0,65)	17 18,41 (4,49)	16 19,00 (6,11)	17 19,59 (5,30)	16 20,81 (5,88)	14 23,64 (3,63)	12 21,42 (3,65)	11 21,64 (3,50)	7 21,00 (3,74)	2,99 (0,70)	-3,59 [-5,59;-1,58] 0,0013 -1,27 [-2,01;-0,54]
ECOG-PS (p-Wert des Interaktionsterms: 0,3223)																			
ECOG-PS 0	440 19,58 (5,13)	418 19,42 (5,19)	405 19,52 (5,46)	401 19,55 (5,31)	378 19,67 (5,40)	330 19,59 (5,69)	321 19,37 (5,40)	188 19,79 (5,03)	-0,18 (0,16)	424 20,06 (5,04)	405 20,22 (5,27)	396 20,78 (4,99)	371 21,01 (5,04)	343 21,34 (4,92)	308 20,92 (5,09)	320 20,16 (5,45)	178 20,02 (5,73)	0,54 (0,17)	-0,72 [-1,17;-0,26] 0,0021 -0,21 [-0,34;-0,08]
ECOG-PS 1	50 20,38 (5,05)	49 20,10 (5,57)	49 20,20 (6,06)	46 21,11 (5,22)	45 21,33 (4,84)	38 21,61 (5,46)	36 21,36 (6,49)	15 21,07 (5,40)	1,60 (0,55)	53 16,42 (5,80)	52 17,75 (5,54)	51 17,69 (5,71)	46 18,43 (5,90)	43 19,21 (4,51)	36 19,36 (5,09)	34 19,18 (4,09)	19 19,58 (4,86)	1,05 (0,54)	0,55 [-1,02;2,11] 0,4902 0,14 [-0,25;0,53]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B FWB = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B FWB haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FWB: funktionales Wohlbefinden; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t110_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung der FACT-B-Subskala: FWB aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,6034)																			
< 65 Jahre	804 19,94 (5,45)	760 19,43 (5,62)	745 19,48 (5,52)	699 19,47 (5,64)	672 19,67 (5,27)	593 19,70 (5,34)	603 19,36 (5,64)	329 19,13 (5,81)	-0,52 (0,13)	831 19,63 (5,65)	792 19,98 (5,21)	783 19,72 (5,35)	730 19,94 (5,42)	693 20,13 (5,34)	610 20,12 (5,46)	606 19,62 (5,56)	319 19,36 (5,61)	0,12 (0,13)	-0,64 [-0,99;-0,28] 0,0005 -0,17 [-0,27;-0,08]
≥ 65 Jahre	303 19,26 (6,21)	283 18,19 (6,05)	266 19,08 (5,84)	256 19,03 (5,34)	241 18,75 (5,96)	217 18,21 (6,25)	226 18,50 (5,97)	120 17,75 (6,10)	-0,99 (0,21)	279 19,69 (5,66)	267 19,95 (5,32)	261 19,37 (5,68)	247 19,56 (5,52)	241 19,29 (5,62)	211 19,13 (5,33)	197 18,89 (5,49)	117 19,40 (5,07)	-0,45 (0,22)	-0,55 [-1,14;0,04] 0,0691 -0,15 [-0,31;0,01]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9070)																			
Neoadjuvante Chemotherapie	363 20,05 (5,70)	336 19,48 (5,58)	325 19,71 (5,40)	300 19,33 (5,88)	279 19,63 (5,64)	238 19,70 (5,71)	254 19,02 (6,17)	129 18,96 (5,61)	-0,78 (0,19)	365 19,48 (5,54)	347 19,89 (5,19)	332 19,59 (5,34)	309 19,59 (5,48)	292 19,81 (5,32)	248 20,02 (5,26)	261 19,33 (5,49)	139 18,78 (5,29)	-0,13 (0,19)	-0,65 [-1,17;-0,13] 0,0137 -0,18 [-0,33;-0,04]
Adjuvante Chemotherapie	684 19,68 (5,65)	653 19,04 (5,81)	635 19,32 (5,62)	604 19,50 (5,36)	588 19,42 (5,35)	532 19,27 (5,53)	529 19,27 (5,51)	293 18,68 (6,05)	-0,54 (0,14)	678 19,79 (5,64)	648 20,10 (5,26)	652 19,83 (5,41)	612 20,20 (5,28)	595 20,08 (5,47)	528 20,00 (5,42)	495 19,68 (5,44)	270 19,81 (5,57)	0,15 (0,14)	-0,69 [-1,08;-0,30] 0,0005 -0,19 [-0,29;-0,08]
Keine Chemotherapie	60 18,83 (5,63)	54 17,43 (6,10)	51 17,98 (6,49)	51 17,65 (5,80)	46 18,28 (6,04)	40 17,35 (6,31)	46 17,93 (5,88)	27 18,78 (6,03)	-1,28 (0,50)	67 19,12 (6,28)	64 19,05 (5,24)	60 17,68 (5,89)	56 17,41 (6,30)	47 18,45 (5,23)	45 17,42 (6,13)	47 17,55 (6,59)	27 18,04 (5,01)	-1,14 (0,48)	-0,14 [-1,51;1,22] 0,8379 -0,04 [-0,38;0,31]
Region (p-Wert des Interaktionsterms: 0,8401)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	550 20,11 (5,64)	497 19,35 (5,70)	483 19,71 (5,51)	449 19,73 (5,79)	420 19,92 (5,37)	379 19,59 (5,77)	393 19,48 (5,81)	210 19,77 (5,74)	-0,76 (0,15)	529 20,07 (5,36)	491 20,39 (5,25)	482 20,06 (5,33)	441 20,25 (5,59)	423 20,00 (5,49)	376 20,36 (5,54)	344 19,80 (5,45)	205 19,89 (5,39)	-0,18 (0,15)	-0,59 [-1,00;-0,17] 0,0062 -0,17 [-0,29;-0,05]
Asien	195 19,43 (6,23)	190 18,87 (6,41)	185 19,03 (6,30)	178 19,21 (5,82)	173 19,16 (6,03)	152 19,09 (6,30)	163 18,80 (6,16)	87 18,16 (6,18)	-0,41 (0,30)	192 19,59 (6,20)	189 19,81 (5,66)	187 19,25 (6,06)	179 19,86 (5,95)	174 19,93 (6,23)	149 19,90 (5,66)	155 19,39 (6,03)	81 19,02 (5,82)	0,09 (0,30)	-0,50 [-1,32;0,33] 0,2383 -0,12 [-0,32;0,08]
Andere	362 19,39 (5,38)	356 18,86 (5,48)	343 19,09 (5,33)	328 18,91 (5,05)	320 18,93 (5,26)	279 19,01 (5,03)	273 18,80 (5,37)	152 17,72 (5,81)	-0,60 (0,19)	389 19,10 (5,71)	379 19,50 (4,96)	375 19,27 (5,22)	357 19,34 (4,94)	337 19,80 (4,87)	296 19,22 (5,14)	304 19,06 (5,39)	150 18,85 (5,34)	0,12 (0,18)	-0,72 [-1,22;-0,21] 0,0057 -0,20 [-0,35;-0,06]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3019)																			
< 20 mm	279 20,05 (5,48)	257 19,42 (5,72)	253 19,78 (5,54)	244 19,55 (5,63)	234 19,48 (5,65)	208 19,47 (5,88)	209 19,40 (5,96)	106 19,58 (5,44)	-0,72 (0,22)	298 19,93 (5,47)	284 20,14 (5,30)	277 20,00 (5,56)	257 20,03 (5,36)	251 20,18 (5,21)	216 20,25 (5,11)	221 19,70 (5,35)	111 19,86 (5,12)	-0,13 (0,21)	-0,59 [-1,18;0,00] 0,0506 -0,16 [-0,33;0,00]
≥ 20 bis < 50 mm	569 19,53 (5,97)	546 19,15 (5,77)	522 19,53 (5,57)	503 19,31 (5,56)	476 19,40 (5,56)	426 19,37 (5,63)	432 19,33 (5,68)	232 18,53 (6,31)	-0,44 (0,16)	572 19,67 (5,75)	549 20,01 (5,15)	543 19,59 (5,32)	511 19,78 (5,50)	492 19,93 (5,38)	439 19,85 (5,49)	415 19,52 (5,63)	230 19,00 (5,62)	0,00 (0,16)	-0,44 [-0,88;-0,01] 0,0437 -0,12 [-0,24;-0,00]
≥ 50 mm	242 20,05 (5,13)	225 18,64 (5,86)	220 18,69 (5,77)	195 19,23 (5,57)	189 19,42 (5,09)	163 19,02 (5,42)	174 18,49 (5,57)	103 18,38 (5,61)	-1,02 (0,23)	229 19,17 (5,69)	215 19,57 (5,41)	214 19,13 (5,60)	199 19,67 (5,48)	184 19,45 (5,84)	158 19,40 (5,79)	159 18,84 (5,69)	91 19,69 (5,50)	-0,02 (0,24)	-1,00 [-1,66;-0,34] 0,0030 -0,28 [-0,46;-0,09]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,6830)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	367 19,64 (5,77)	347 19,14 (5,72)	335 19,54 (5,74)	313 19,51 (5,53)	302 19,20 (5,68)	274 19,16 (5,94)	285 19,13 (5,85)	167 18,97 (6,10)	-0,51 (0,20)	360 19,51 (5,74)	343 19,95 (5,25)	341 19,73 (5,16)	313 19,65 (5,63)	303 19,94 (5,32)	260 19,72 (5,66)	255 19,67 (5,84)	142 19,04 (5,58)	0,04 (0,20)	-0,55 [-1,11;0,00] 0,0503 -0,15 [-0,29;0,00]
4-9	476 19,77 (5,45)	447 19,12 (5,64)	438 19,18 (5,61)	419 18,89 (5,63)	398 19,43 (5,40)	354 19,35 (5,30)	356 19,27 (5,64)	173 18,57 (5,71)	-0,75 (0,17)	485 19,66 (5,76)	465 20,17 (5,23)	464 19,62 (5,58)	438 19,91 (5,50)	419 19,98 (5,48)	377 19,86 (5,29)	358 19,41 (5,54)	192 19,36 (5,60)	-0,03 (0,16)	-0,72 [-1,18;-0,26] 0,0020 -0,20 [-0,33;-0,07]
≥ 10	264 19,88 (5,93)	249 19,00 (6,06)	238 19,51 (5,39)	223 20,00 (5,42)	213 19,73 (5,32)	182 19,40 (5,81)	188 18,84 (5,79)	109 18,76 (5,99)	-0,69 (0,22)	265 19,80 (5,32)	251 19,62 (5,23)	239 19,51 (5,55)	226 19,98 (5,07)	212 19,74 (5,46)	184 20,08 (5,45)	190 19,19 (5,16)	102 19,87 (5,07)	-0,12 (0,22)	-0,57 [-1,18;0,05] 0,0695 -0,16 [-0,33;0,01]
Tumorgrading (p-Wert des Interaktionsterms: 0,5800)																			
G1	82 20,02 (5,28)	80 19,88 (6,42)	81 19,94 (6,16)	74 19,96 (5,30)	70 20,04 (5,56)	63 19,94 (5,33)	62 19,81 (5,62)	31 19,35 (4,98)	-0,13 (0,41)	84 20,35 (5,61)	82 20,83 (4,85)	79 20,39 (5,30)	70 20,90 (4,35)	74 19,74 (6,15)	65 20,45 (5,63)	55 20,24 (5,48)	34 20,65 (6,31)	0,22 (0,40)	-0,35 [-1,48;0,78] 0,5378 -0,10 [-0,40;0,21]
G2	526 19,86 (5,55)	499 18,81 (5,82)	482 19,09 (5,63)	454 19,39 (5,45)	434 19,40 (5,40)	375 19,00 (5,76)	375 18,95 (5,86)	211 18,69 (5,88)	-0,86 (0,16)	533 19,57 (5,63)	505 19,95 (5,18)	505 19,50 (5,39)	477 19,83 (5,40)	447 19,62 (5,39)	402 19,80 (5,18)	392 19,22 (5,40)	214 19,23 (5,49)	-0,07 (0,15)	-0,79 [-1,22;-0,36] 0,0003 -0,22 [-0,34;-0,10]
G3	450 19,54 (5,94)	420 19,29 (5,61)	403 19,66 (5,49)	382 19,30 (5,71)	367 19,34 (5,63)	333 19,47 (5,59)	355 19,20 (5,59)	185 18,84 (6,16)	-0,40 (0,18)	436 19,56 (5,70)	415 19,84 (5,45)	405 19,67 (5,52)	379 19,84 (5,58)	365 20,29 (5,28)	315 19,97 (5,67)	315 19,68 (5,60)	165 19,52 (5,05)	0,10 (0,18)	-0,51 [-1,00;-0,02] 0,0433 -0,14 [-0,27;-0,00]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	ET[1] B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
GX	47 20,19 (5,15)	42 19,00 (5,28)	43 18,88 (5,36)	43 18,37 (5,98)	40 19,60 (4,88)	37 19,59 (5,31)	37 19,00 (6,26)	22 17,95 (5,53)	-1,52 (0,61)	53 19,92 (5,39)	53 19,92 (4,54)	52 19,31 (5,44)	48 18,40 (6,03)	45 20,02 (5,68)	37 18,62 (5,85)	39 18,67 (6,61)	21 18,29 (6,63)	-0,98 (0,58)	-0,53 [-2,20;1,13] 0,5270 -0,13 [-0,52;0,27]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,3353)																			
Negativ	137 18,79 (5,81)	132 18,23 (5,97)	124 18,29 (6,03)	116 18,09 (6,23)	106 18,29 (5,80)	92 18,25 (6,15)	100 17,71 (6,36)	63 17,03 (6,82)	-0,89 (0,34)	149 19,17 (6,02)	139 19,68 (5,06)	134 19,71 (5,50)	126 20,19 (5,54)	121 20,09 (5,28)	103 19,97 (5,55)	114 18,67 (5,37)	56 18,71 (5,90)	0,36 (0,32)	-1,26 [-2,18;-0,33] 0,0078 -0,32 [-0,55;-0,08]
Positiv	939 19,80 (5,63)	880 19,08 (5,71)	856 19,41 (5,51)	814 19,41 (5,41)	785 19,50 (5,39)	695 19,32 (5,54)	707 19,25 (5,61)	376 19,01 (5,71)	-0,63 (0,12)	934 19,66 (5,58)	896 19,95 (5,22)	886 19,55 (5,43)	829 19,73 (5,42)	792 19,83 (5,45)	697 19,82 (5,36)	669 19,50 (5,58)	366 19,39 (5,40)	-0,09 (0,12)	-0,54 [-0,87;-0,22] 0,0011 -0,15 [-0,24;-0,06]
Unbekannt	9 21,78 (6,89)	9 22,78 (3,73)	9 23,44 (5,96)	7 25,29 (3,99)	3 27,67 (0,58)	6 23,67 (6,31)	5 23,60 (5,86)	1 26,00 (NE)	2,55 (1,02)	7 21,71 (7,32)	6 24,67 (4,18)	6 23,67 (4,23)	6 24,17 (4,71)	6 24,00 (3,69)	6 20,17 (10,65)	5 24,00 (3,32)	5 24,80 (3,11)	2,68 (1,00)	-0,13 [-3,17;2,91] 0,9298 -0,04 [-0,98;0,89]
Ethnizität (p-Wert des Interaktionsterms: 0,8166)																			
Weiß	808 19,74 (5,49)	755 19,18 (5,52)	738 19,36 (5,33)	694 19,23 (5,44)	659 19,41 (5,31)	588 19,28 (5,42)	596 19,08 (5,60)	337 18,90 (5,66)	-0,74 (0,12)	819 19,70 (5,44)	773 20,06 (5,05)	762 19,79 (5,20)	707 19,78 (5,34)	678 19,90 (5,23)	601 19,84 (5,30)	578 19,43 (5,34)	323 19,37 (5,30)	-0,09 (0,12)	-0,66 [-1,00;-0,32] 0,0001 -0,19 [-0,29;-0,09]
Asiatisch	233 19,67 (6,23)	225 18,95 (6,52)	218 19,24 (6,38)	210 19,65 (5,78)	204 19,67 (5,96)	176 19,41 (6,15)	187 19,14 (6,21)	97 18,39 (6,38)	-0,24 (0,28)	221 19,51 (6,28)	217 19,94 (5,66)	215 19,21 (6,26)	207 20,09 (5,82)	199 20,11 (6,13)	167 20,04 (5,65)	172 19,66 (5,99)	88 19,20 (6,04)	0,25 (0,28)	-0,49 [-1,27;0,28] 0,2129 -0,12 [-0,30;0,07]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Andere	54 20,28 (5,86)	51 18,61 (5,62)	47 20,47 (5,20)	42 20,00 (5,25)	42 18,60 (5,63)	36 19,22 (6,22)	40 19,43 (5,62)	14 17,50 (8,20)	-0,67 (0,54)	57 19,60 (6,35)	57 18,89 (5,94)	55 19,67 (4,91)	51 19,76 (5,41)	46 19,41 (5,00)	42 19,93 (5,90)	44 19,41 (6,23)	19 20,00 (5,73)	-0,18 (0,51)	-0,48 [-1,95;0,98] 0,5139 -0,12 [-0,50;0,25]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,0901)																			
Tamoxifen	104 19,83 (5,45)	99 19,91 (5,23)	99 19,53 (5,76)	96 19,81 (5,01)	94 19,89 (5,02)	91 19,68 (5,36)	91 19,80 (5,66)	55 20,58 (5,16)	0,06 (0,33)	124 19,61 (5,51)	122 19,48 (4,99)	120 19,72 (4,89)	110 20,30 (4,94)	103 19,89 (5,35)	94 20,71 (5,11)	92 19,28 (5,28)	56 19,43 (5,96)	0,16 (0,30)	-0,10 [-0,98;0,77] 0,8206 -0,03 [-0,29;0,23]
Aromatase-Inhibitor	1003 19,75 (5,69)	944 19,01 (5,81)	912 19,36 (5,59)	859 19,30 (5,62)	819 19,37 (5,53)	719 19,25 (5,67)	738 19,04 (5,75)	394 18,51 (5,97)	-0,73 (0,12)	986 19,65 (5,67)	937 20,03 (5,27)	924 19,62 (5,50)	867 19,79 (5,50)	831 19,92 (5,43)	727 19,76 (5,47)	711 19,46 (5,58)	380 19,37 (5,40)	-0,05 (0,12)	-0,68 [-1,01;-0,36] <,0001 -0,18 [-0,27;-0,10]
ECOG-PS (p-Wert des Interaktionsterms: 0,6472)																			
ECOG-PS 0	933 19,95 (5,61)	878 19,33 (5,72)	854 19,64 (5,47)	814 19,43 (5,56)	779 19,60 (5,43)	695 19,47 (5,66)	703 19,30 (5,73)	381 19,07 (5,84)	-0,62 (0,12)	898 19,87 (5,63)	855 20,23 (5,15)	846 19,84 (5,39)	793 20,04 (5,36)	759 20,20 (5,34)	675 20,01 (5,41)	663 19,46 (5,48)	355 19,37 (5,30)	-0,03 (0,12)	-0,59 [-0,93;-0,26] 0,0005 -0,16 [-0,25;-0,07]
ECOG-PS 1	174 18,69 (5,91)	165 17,87 (5,83)	157 17,95 (6,11)	141 18,89 (5,54)	134 18,42 (5,67)	115 18,29 (5,39)	126 18,12 (5,72)	68 17,03 (6,06)	-0,75 (0,29)	212 18,69 (5,62)	204 18,86 (5,47)	198 18,72 (5,57)	184 19,02 (5,73)	175 18,66 (5,60)	146 19,20 (5,51)	140 19,36 (5,86)	81 19,38 (6,16)	0,09 (0,26)	-0,84 [-1,60;-0,08] 0,0300 -0,22 [-0,42;-0,02]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B FWB = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B FWB haben. Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FWB: funktionales Wohlbefinden; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler																		

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t110_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des FACT-G (Gesamtscore) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,1049)																			
Neoadjuvante Chemotherapie	196 84,84 (12,82)	188 81,83 (14,68)	181 81,60 (15,63)	177 81,18 (15,63)	165 80,51 (15,14)	150 80,91 (16,24)	147 79,67 (16,67)	75 79,93 (16,39)	-3,95 (0,71)	193 83,09 (14,29)	181 82,70 (14,50)	179 83,42 (14,37)	155 84,45 (14,84)	144 85,63 (14,21)	121 85,33 (15,44)	136 82,21 (16,09)	77 81,40 (16,36)	-0,63 (0,72)	-3,32 [-5,31;-1,33] 0,0011 -0,33 [-0,53;-0,13]
Adjuvante Chemotherapie	287 82,38 (13,50)	272 81,58 (14,34)	267 81,94 (15,00)	264 82,09 (14,80)	253 82,10 (14,50)	213 82,38 (15,50)	204 81,94 (15,51)	126 81,60 (13,88)	-0,37 (0,55)	283 82,64 (13,44)	275 82,89 (14,17)	266 83,91 (13,50)	261 84,35 (14,45)	240 84,83 (13,87)	222 83,34 (14,22)	217 82,57 (14,68)	120 82,82 (14,37)	0,98 (0,55)	-1,35 [-2,88;0,19] 0,0847 -0,14 [-0,31;0,02]
Keine Chemotherapie	7 82,86 (22,63)	7 81,71 (19,83)	6 76,83 (18,76)	6 80,17 (21,48)	5 77,60 (23,38)	5 73,00 (23,26)	6 83,50 (20,87)	2 94,00 (12,73)	-1,13 (1,90)	1 90,00 (NE)	1 70,00 (NE)	1 77,00 (NE)	1 69,00 (NE)	1 72,00 (NE)	1 72,00 (NE)	1 75,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,4856)																			
Nordamerika / Europa	204 85,34 (12,44)	188 83,70 (13,60)	181 83,44 (14,81)	178 82,69 (15,18)	162 83,03 (14,72)	140 82,66 (16,44)	135 83,57 (15,49)	73 83,37 (13,89)	-2,10 (0,67)	197 84,29 (12,91)	183 82,89 (14,77)	173 84,75 (13,47)	154 85,02 (15,11)	140 86,31 (14,86)	134 84,89 (15,51)	133 82,93 (16,36)	66 83,32 (17,37)	-0,40 (0,69)	-1,71 [-3,59;0,18] 0,0754 -0,18 [-0,37;0,02]
Asien	162 80,82 (13,74)	161 78,30 (14,40)	157 78,87 (14,59)	155 79,19 (15,09)	149 78,97 (14,58)	129 78,95 (15,64)	136 78,72 (15,88)	69 81,16 (14,80)	-2,00 (0,70)	152 81,42 (14,33)	150 81,31 (13,94)	151 81,44 (14,38)	146 83,47 (13,86)	137 83,41 (13,73)	120 82,73 (14,85)	121 80,91 (15,06)	65 81,94 (13,27)	0,27 (0,73)	-2,28 [-4,27;-0,28] 0,0252 -0,25 [-0,48;-0,03]
Andere	124 83,47 (14,06)	118 83,08 (15,41)	116 82,97 (16,43)	114 83,58 (15,05)	112 82,38 (15,10)	99 83,76 (15,16)	86 80,71 (16,87)	61 78,33 (15,78)	-1,08 (0,92)	128 82,30 (14,26)	124 84,43 (13,88)	122 85,00 (13,40)	117 84,56 (14,80)	108 85,66 (13,03)	90 84,40 (13,09)	100 83,52 (13,72)	66 81,53 (14,68)	1,41 (0,90)	-2,50 [-5,04;0,05] 0,0542 -0,24 [-0,49;0,00]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3294)																			
< 20 mm	121 83,19 (12,48)	115 81,10 (13,81)	109 80,30 (15,32)	112 80,09 (16,16)	105 80,97 (15,70)	94 79,37 (16,31)	91 79,82 (15,56)	53 81,36 (13,71)	-3,02 (0,85)	123 82,99 (14,16)	116 82,65 (14,69)	115 84,17 (12,60)	107 83,19 (14,56)	100 85,43 (14,07)	87 84,57 (14,71)	85 84,54 (14,10)	50 82,42 (16,14)	0,10 (0,84)	-3,13 [-5,48;-0,77] 0,0096 -0,33 [-0,59;-0,08]
≥ 20 bis < 50 mm	229 83,96 (13,66)	218 81,07 (15,60)	217 83,06 (15,16)	213 82,11 (15,13)	196 81,51 (14,71)	170 82,40 (15,28)	164 81,16 (16,04)	96 79,86 (16,52)	-1,79 (0,65)	227 82,21 (13,84)	218 82,33 (14,08)	216 83,66 (14,16)	200 84,97 (14,36)	187 84,94 (13,84)	172 83,34 (14,48)	181 81,58 (15,32)	93 82,10 (15,62)	0,68 (0,65)	-2,47 [-4,28;-0,66] 0,0076 -0,25 [-0,44;-0,07]
≥ 50 mm	128 82,73 (14,01)	124 82,94 (13,41)	119 80,49 (15,45)	114 82,35 (14,23)	113 81,40 (14,21)	95 82,34 (16,33)	93 81,94 (16,52)	48 82,65 (12,51)	-1,21 (0,82)	122 84,25 (13,24)	118 83,91 (14,53)	110 83,70 (14,57)	105 84,92 (15,07)	95 85,13 (14,33)	81 85,21 (15,34)	84 82,37 (15,96)	50 83,00 (13,04)	-0,37 (0,84)	-0,84 [-3,16;1,48] 0,4754 -0,09 [-0,34;0,16]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,2944)																			
0-3	177 84,34 (13,29)	169 83,01 (14,25)	160 82,30 (15,53)	158 82,13 (15,41)	144 82,32 (14,73)	130 83,00 (16,97)	131 80,80 (17,01)	77 82,42 (13,50)	-1,97 (0,76)	190 83,52 (13,05)	181 83,85 (14,11)	175 84,19 (13,74)	163 84,59 (14,00)	155 84,32 (14,15)	136 84,00 (14,67)	135 82,01 (15,84)	71 81,90 (15,53)	-0,35 (0,73)	-1,62 [-3,69;0,46] 0,1269 -0,16 [-0,36;0,05]
4-9	215 82,10 (14,00)	204 79,09 (15,25)	201 80,33 (15,35)	197 80,59 (15,47)	192 79,94 (14,86)	168 80,67 (15,27)	158 80,15 (15,98)	83 78,90 (16,39)	-2,14 (0,63)	210 82,93 (14,40)	201 82,70 (13,97)	198 83,38 (13,95)	186 84,18 (14,39)	172 85,98 (13,19)	153 84,35 (14,41)	160 82,39 (14,93)	87 82,51 (14,37)	0,46 (0,64)	-2,60 [-4,36;-0,84] 0,0038 -0,28 [-0,47;-0,09]
≥ 10	98 84,41 (12,14)	94 84,90 (12,44)	93 83,81 (14,53)	92 83,35 (14,19)	87 83,24 (14,86)	70 81,53 (15,43)	68 83,53 (14,33)	43 83,00 (13,79)	-0,78 (0,97)	77 80,92 (13,71)	75 80,45 (15,39)	73 83,37 (13,87)	68 84,25 (16,55)	58 84,55 (15,84)	55 83,07 (15,56)	59 83,36 (14,66)	39 82,38 (16,52)	1,52 (1,11)	-2,30 [-5,22;0,63] 0,1225 -0,24 [-0,54;0,06]
Tumorstadium (p-Wert des Interaktionsterms: 0,4818)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 84,50 (12,12)	49 81,67 (15,10)	48 79,56 (16,07)	46 79,24 (15,92)	46 79,48 (16,06)	40 78,23 (16,75)	39 78,15 (15,82)	23 79,00 (12,68)	-4,84 (1,30)	57 84,65 (12,40)	54 84,44 (12,43)	54 85,19 (12,52)	48 83,67 (12,74)	47 86,87 (11,32)	36 85,69 (13,31)	37 86,27 (12,33)	19 84,79 (10,51)	0,11 (1,25)	-4,96 [-8,54;-1,38] 0,0071 -0,53 [-0,91;-0,14]
IIB	45 84,53 (11,20)	44 83,11 (14,71)	41 86,46 (12,37)	42 82,74 (13,36)	35 83,29 (12,27)	34 85,18 (14,01)	31 83,19 (13,06)	22 82,50 (12,33)	-0,45 (1,49)	64 83,31 (13,03)	62 83,24 (14,28)	60 84,95 (13,74)	55 84,31 (14,87)	55 83,45 (13,23)	54 83,13 (13,54)	55 80,35 (15,84)	32 82,59 (16,89)	-0,98 (1,23)	0,52 [-3,32;4,36] 0,7881 0,05 [-0,33;0,43]
IIIA	212 82,09 (14,73)	205 79,96 (15,23)	198 80,48 (15,33)	195 81,53 (14,92)	189 80,63 (14,72)	164 81,61 (15,33)	157 80,04 (16,01)	84 80,50 (15,79)	-1,47 (0,61)	193 82,67 (14,96)	183 82,86 (14,01)	178 83,23 (14,34)	173 83,56 (14,35)	157 85,08 (13,95)	133 84,28 (14,60)	141 82,13 (15,35)	71 82,17 (14,86)	0,41 (0,64)	-1,88 [-3,61;-0,14] 0,0345 -0,21 [-0,41;-0,02]
IIIB	14 78,79 (15,96)	13 77,00 (15,86)	13 73,08 (20,06)	13 70,08 (15,20)	10 69,30 (11,50)	8 65,75 (22,04)	11 71,82 (19,97)	6 68,83 (9,02)	-7,55 (2,76)	14 87,50 (12,51)	14 84,50 (16,16)	14 85,71 (15,18)	11 84,18 (21,15)	9 87,33 (18,03)	10 80,90 (19,75)	9 79,00 (18,61)	5 70,00 (17,96)	-3,27 (2,87)	-4,28 [-12,79;4,23] 0,3099 -0,39 [-1,12;0,33]
IIIC	166 84,81 (12,19)	155 83,93 (13,00)	153 83,57 (14,79)	150 83,41 (15,50)	142 83,54 (15,03)	121 82,93 (15,99)	118 83,67 (16,27)	67 83,28 (15,24)	-1,17 (0,81)	148 81,72 (13,10)	143 81,66 (15,21)	139 82,97 (13,70)	129 85,71 (14,94)	117 85,00 (15,10)	111 83,85 (15,36)	112 82,77 (15,28)	70 82,40 (15,49)	1,07 (0,86)	-2,24 [-4,57;0,08] 0,0588 -0,22 [-0,44;0,01]
Tumorgrading (p-Wert des Interaktionsterms: 0,8087)																			
G1	45 84,64 (13,06)	42 83,21 (12,93)	40 82,75 (14,44)	40 81,03 (14,34)	39 82,38 (12,81)	33 81,85 (13,87)	33 81,88 (13,94)	18 81,67 (14,52)	-2,48 (1,29)	38 84,18 (12,79)	36 86,03 (11,93)	33 84,39 (12,44)	36 85,89 (14,66)	30 86,77 (14,46)	28 80,54 (16,25)	25 83,92 (15,25)	13 85,38 (14,32)	0,90 (1,43)	-3,39 [-7,22;0,44] 0,0823 -0,39 [-0,82;0,05]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	213 83,48 (13,61)	202 81,52 (15,01)	201 81,62 (15,35)	196 81,93 (15,37)	188 81,63 (15,43)	165 81,16 (15,35)	167 81,35 (15,85)	85 82,25 (14,56)	-1,93 (0,64)	207 82,73 (14,02)	200 81,78 (15,43)	194 83,43 (14,43)	181 83,54 (14,94)	161 84,72 (14,39)	148 83,70 (15,87)	153 81,40 (15,93)	86 81,26 (16,14)	-0,40 (0,65)	-1,54 [-3,33;0,26] 0,0927 -0,16 [-0,36;0,03]
G3	204 82,85 (13,05)	196 81,47 (14,58)	188 81,24 (15,67)	185 81,43 (15,56)	171 80,81 (15,14)	148 82,28 (17,02)	137 80,11 (17,03)	87 78,52 (15,18)	-1,58 (0,72)	203 82,66 (13,67)	194 82,94 (13,55)	192 83,88 (13,78)	173 84,91 (14,39)	168 84,71 (13,89)	143 84,92 (13,31)	153 82,69 (14,75)	86 83,20 (14,72)	0,71 (0,72)	-2,29 [-4,28;-0,29] 0,0247 -0,22 [-0,42;-0,03]
GX	28 84,25 (15,40)	27 82,00 (13,42)	25 84,76 (13,31)	26 82,96 (13,03)	25 82,64 (11,55)	22 80,82 (16,09)	20 83,30 (15,24)	13 90,15 (11,53)	-0,94 (1,45)	28 83,25 (14,71)	26 84,69 (13,50)	26 83,81 (12,06)	26 84,00 (13,84)	25 88,16 (11,79)	24 84,67 (13,16)	23 85,57 (13,39)	12 79,42 (12,14)	1,72 (1,42)	-2,66 [-6,74;1,42] 0,1958 -0,35 [-0,88;0,18]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,2115)																			
Negativ	46 82,72 (12,41)	43 78,14 (14,39)	41 79,10 (18,50)	42 78,62 (17,78)	39 76,23 (15,52)	38 76,82 (15,87)	36 72,81 (15,80)	12 78,08 (17,00)	-5,68 (1,59)	39 83,95 (13,21)	36 84,06 (11,94)	35 82,83 (13,10)	30 86,77 (10,29)	31 87,39 (12,14)	26 85,12 (13,37)	31 84,97 (14,10)	15 85,67 (11,22)	0,36 (1,71)	-6,04 [-10,69;-1,39] 0,0116 -0,56 [-1,00;-0,13]
Positiv	426 83,26 (13,68)	407 81,76 (14,60)	399 81,74 (14,99)	390 81,68 (14,98)	371 81,70 (14,73)	319 81,98 (15,89)	305 81,47 (15,97)	182 81,07 (14,89)	-1,51 (0,46)	421 82,77 (13,81)	406 82,69 (14,38)	397 83,96 (13,75)	373 84,03 (14,82)	340 84,58 (14,16)	305 83,99 (14,63)	313 82,06 (15,18)	175 81,58 (15,47)	0,24 (0,47)	-1,75 [-3,04;-0,47] 0,0076 -0,18 [-0,32;-0,05]
Unbekannt	2 89,50 (4,95)	2 85,00 (26,87)	2 92,50 (19,09)	1 106,00 (NE)	1 102,00 (NE)	1 100,00 (NE)	1 106,00 (NE)	0	NE	8 76,00 (17,31)	7 76,43 (21,85)	8 77,75 (19,20)	6 80,83 (19,21)	6 90,17 (16,07)	8 76,88 (21,92)	4 79,25 (28,29)	2 91,50 (14,85)	3,56 (2,81)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,2644)																			

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	276 84,62 (12,90)	259 83,01 (14,50)	250 82,74 (15,23)	245 82,41 (14,79)	230 81,79 (15,20)	201 82,03 (16,11)	184 81,99 (15,88)	118 80,92 (14,77)	-2,30 (0,57)	285 83,67 (13,26)	268 83,22 (14,51)	258 84,50 (13,60)	241 84,08 (14,92)	222 85,17 (14,28)	202 84,30 (14,87)	210 82,57 (15,50)	122 81,71 (16,25)	-0,55 (0,56)	-1,75 [-3,32;-0,18] 0,0293 -0,18 [-0,35;-0,02]
Asiatisch	187 81,25 (13,93)	184 79,83 (14,36)	180 80,26 (15,15)	178 81,11 (15,28)	170 80,92 (14,82)	148 81,07 (15,86)	152 79,88 (16,07)	75 81,91 (14,71)	-0,73 (0,71)	165 81,22 (14,68)	163 81,64 (14,20)	162 81,97 (14,39)	157 84,49 (14,29)	144 84,03 (13,80)	124 82,89 (14,99)	129 81,18 (15,03)	66 82,12 (13,23)	0,99 (0,76)	-1,72 [-3,78;0,33] 0,0997 -0,18 [-0,39;0,03]
Andere	16 83,94 (17,13)	15 80,80 (17,36)	15 81,13 (17,55)	15 77,40 (18,97)	15 80,53 (12,86)	13 83,00 (15,22)	14 81,36 (17,38)	9 77,89 (18,62)	-3,11 (1,93)	17 82,06 (15,08)	16 83,00 (12,44)	17 84,12 (12,59)	16 85,56 (13,31)	14 93,14 (8,20)	12 87,33 (6,72)	11 92,09 (9,19)	7 89,00 (10,91)	6,26 (2,00)	-9,36 [-15,06;-3,67] 0,0021 -1,14 [-1,86;-0,42]
ECOG-PS (p-Wert des Interaktionsterms: 0,1973)																			
ECOG-PS 0	440 83,15 (13,37)	418 81,34 (14,48)	405 81,30 (15,25)	401 81,06 (15,16)	378 80,80 (14,88)	330 81,11 (15,69)	321 80,51 (15,97)	188 80,90 (14,86)	-2,22 (0,45)	424 83,65 (13,42)	405 83,38 (14,11)	395 84,36 (13,43)	371 85,14 (14,20)	342 85,67 (13,89)	308 84,77 (14,58)	320 82,78 (15,30)	178 82,46 (15,36)	0,20 (0,46)	-2,42 [-3,68;-1,16] 0,0002 -0,26 [-0,39;-0,12]
ECOG-PS 1	50 85,36 (13,77)	49 84,55 (14,74)	49 85,35 (15,18)	46 87,26 (14,52)	45 86,69 (13,63)	38 86,39 (17,24)	36 85,72 (16,48)	15 83,67 (15,06)	2,70 (1,55)	53 76,34 (14,89)	52 78,19 (14,93)	51 78,55 (15,83)	46 78,00 (16,10)	43 80,51 (14,07)	36 77,50 (13,94)	34 78,91 (13,99)	19 80,42 (13,26)	0,43 (1,53)	2,27 [-2,14;6,68] 0,3097 0,21 [-0,18;0,59]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-G Gesamtscore = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-G Gesamtscore haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-G: Functional Assessment of Cancer Therapy - General; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t111_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des FACT-G (Gesamtscore) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,3013)																			
< 65 Jahre	804 84,51 (14,08)	760 82,88 (14,91)	744 82,71 (15,47)	699 82,60 (14,95)	672 82,84 (14,87)	593 82,57 (14,71)	602 82,25 (15,30)	329 82,78 (15,16)	-2,07 (0,35)	831 83,63 (14,22)	792 83,72 (14,07)	783 83,61 (14,23)	728 83,46 (14,55)	693 84,09 (14,28)	609 83,94 (14,72)	605 82,70 (15,41)	319 81,96 (14,91)	-0,50 (0,34)	-1,57 [-2,53;-0,62] 0,0013 -0,16 [-0,26;-0,06]
≥ 65 Jahre	303 84,03 (15,15)	283 80,67 (15,49)	265 82,45 (14,18)	255 82,66 (14,83)	241 81,44 (16,13)	217 80,66 (16,28)	226 82,02 (15,92)	120 80,47 (14,90)	-2,94 (0,54)	279 84,95 (13,97)	267 84,97 (14,46)	258 84,38 (13,96)	247 84,68 (13,35)	241 83,19 (14,99)	211 82,98 (14,62)	197 83,01 (13,62)	117 82,85 (14,61)	-1,46 (0,55)	-1,48 [-3,00;0,03] 0,0550 -0,16 [-0,32;0,00]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8612)																			
Neoadjuvante Chemotherapie	363 85,48 (14,21)	336 83,11 (15,19)	324 83,84 (15,06)	299 82,63 (15,56)	279 82,37 (15,72)	238 82,55 (15,54)	253 81,73 (16,09)	129 82,19 (14,17)	-3,16 (0,51)	365 83,02 (14,43)	347 82,92 (13,85)	331 82,63 (13,96)	308 82,62 (14,26)	292 82,82 (13,93)	248 82,83 (14,77)	260 81,92 (15,36)	139 79,20 (14,97)	-1,46 (0,50)	-1,70 [-3,11;-0,29] 0,0180 -0,18 [-0,32;-0,03]
Adjuvante Chemotherapie	684 83,90 (14,55)	653 82,13 (14,98)	634 82,24 (15,17)	604 82,91 (14,44)	588 82,74 (14,79)	532 82,14 (14,96)	529 82,61 (15,20)	293 82,16 (15,65)	-1,70 (0,37)	678 84,46 (13,79)	648 84,76 (14,15)	650 84,57 (14,14)	611 84,62 (14,01)	595 84,66 (14,58)	527 84,58 (14,40)	495 83,50 (14,73)	270 83,89 (14,59)	-0,11 (0,37)	-1,59 [-2,62;-0,56] 0,0026 -0,16 [-0,27;-0,06]
Keine Chemotherapie	60 83,13 (13,17)	54 78,98 (15,59)	51 80,04 (14,89)	51 79,16 (16,27)	46 79,70 (17,42)	40 78,05 (15,26)	46 79,80 (14,99)	27 82,00 (13,99)	-4,70 (1,18)	67 84,04 (16,27)	64 82,81 (15,90)	60 81,98 (15,02)	56 80,86 (16,24)	47 80,26 (15,62)	45 78,04 (16,30)	47 79,87 (15,21)	27 80,78 (14,19)	-3,50 (1,13)	-1,20 [-4,43;2,04] 0,4658 -0,13 [-0,48;0,22]
Region (p-Wert des Interaktionsterms: 0,2713)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	550 85,60 (14,43)	497 83,15 (15,23)	481 83,40 (15,45)	449 83,75 (15,14)	420 83,98 (15,10)	379 83,01 (15,49)	392 83,20 (15,89)	210 84,82 (14,77)	-2,77 (0,39)	529 85,07 (13,93)	491 85,61 (13,96)	481 85,18 (14,03)	439 84,87 (14,60)	423 84,82 (14,86)	375 85,60 (14,85)	343 84,33 (14,96)	205 83,99 (14,58)	-0,85 (0,40)	-1,92 [-3,01;-0,83] 0,0006 -0,21 [-0,33;-0,09]
Asien	195 82,84 (14,95)	190 81,07 (16,21)	185 80,98 (16,49)	177 80,95 (15,96)	173 80,72 (16,47)	152 80,48 (16,53)	163 79,36 (16,08)	87 78,40 (15,41)	-1,97 (0,75)	192 82,97 (14,55)	189 82,04 (14,97)	187 81,97 (14,98)	179 82,84 (14,87)	174 82,58 (15,52)	149 81,81 (14,74)	155 81,34 (15,05)	81 79,10 (15,29)	-0,78 (0,76)	-1,19 [-3,29;0,92] 0,2680 -0,11 [-0,31;0,09]
Andere	362 83,35 (13,85)	356 81,71 (14,22)	343 82,47 (13,84)	328 81,97 (13,89)	320 81,44 (14,50)	279 81,62 (13,83)	273 82,42 (14,28)	152 80,63 (14,83)	-1,78 (0,51)	389 82,95 (14,20)	379 82,99 (13,86)	373 82,94 (13,78)	357 82,88 (13,44)	337 83,31 (13,31)	296 82,23 (14,22)	304 81,76 (14,86)	150 81,44 (14,64)	-0,65 (0,49)	-1,13 [-2,52;0,26] 0,1121 -0,12 [-0,26;0,03]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4915)																			
< 20 mm	279 85,04 (14,34)	257 83,23 (14,72)	253 83,44 (15,02)	244 82,57 (15,44)	234 82,50 (15,53)	208 81,74 (16,36)	208 82,97 (15,93)	106 82,73 (15,20)	-2,82 (0,57)	298 84,80 (13,70)	284 84,52 (14,08)	276 84,91 (13,68)	257 84,42 (13,74)	251 84,43 (13,88)	216 84,89 (13,72)	220 83,31 (14,78)	111 83,08 (14,28)	-1,13 (0,56)	-1,69 [-3,26;-0,12] 0,0344 -0,18 [-0,34;-0,01]
≥ 20 bis < 50 mm	569 83,98 (14,75)	546 82,18 (15,26)	520 82,87 (15,08)	502 82,91 (14,59)	476 82,63 (15,31)	426 82,77 (14,61)	432 82,67 (15,30)	232 81,71 (15,33)	-1,74 (0,41)	572 83,95 (14,29)	549 83,99 (14,06)	542 83,84 (14,01)	510 83,60 (14,67)	492 83,90 (14,47)	438 83,49 (14,98)	415 82,99 (15,30)	230 81,69 (14,94)	-0,65 (0,41)	-1,09 [-2,23;0,06] 0,0622 -0,11 [-0,23;0,01]
≥ 50 mm	242 84,65 (13,56)	225 81,41 (15,23)	220 81,40 (15,40)	195 82,06 (15,12)	189 82,43 (14,57)	163 81,31 (14,71)	174 80,47 (15,30)	103 82,29 (15,00)	-2,94 (0,62)	229 82,69 (14,66)	215 83,25 (14,80)	213 81,92 (15,18)	198 83,10 (14,04)	184 82,84 (15,36)	158 82,46 (15,35)	159 81,33 (14,60)	91 82,14 (15,48)	-0,66 (0,63)	-2,28 [-4,02;-0,54] 0,0105 -0,24 [-0,42;-0,06]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9388)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	367 84,47 (14,95)	347 82,41 (15,26)	334 82,96 (15,92)	312 82,69 (15,38)	302 82,11 (15,93)	274 81,61 (15,94)	284 81,52 (16,37)	167 82,93 (15,27)	-2,50 (0,51)	360 83,88 (14,34)	343 83,54 (13,96)	341 83,65 (13,43)	312 83,30 (13,80)	303 83,89 (14,04)	260 83,76 (14,97)	255 83,33 (15,17)	142 82,11 (15,05)	-0,85 (0,52)	-1,65 [-3,08;-0,22] 0,0234 -0,17 [-0,31;-0,02]
4-9	476 84,12 (13,69)	447 82,13 (14,79)	438 82,24 (14,82)	419 82,00 (14,72)	398 82,32 (14,95)	354 82,36 (14,48)	356 83,01 (14,67)	173 81,91 (14,24)	-2,13 (0,44)	485 83,77 (14,40)	465 84,41 (14,56)	463 83,85 (14,46)	437 83,50 (15,07)	419 83,70 (14,93)	377 83,22 (14,98)	357 82,46 (15,37)	192 82,31 (14,82)	-0,74 (0,44)	-1,39 [-2,61;-0,17] 0,0257 -0,14 [-0,27;-0,02]
≥ 10	264 84,69 (14,81)	249 82,38 (15,44)	237 82,93 (14,62)	223 83,67 (14,58)	213 83,27 (14,70)	182 82,14 (15,31)	188 81,63 (15,54)	109 81,36 (16,26)	-2,32 (0,60)	265 84,44 (13,50)	251 84,02 (13,77)	237 83,95 (14,63)	226 84,93 (13,23)	212 84,14 (14,17)	183 84,57 (13,70)	190 82,61 (14,01)	102 82,12 (14,63)	-0,62 (0,60)	-1,71 [-3,37;-0,04] 0,0446 -0,18 [-0,35;-0,00]
Tumorstadium (p-Wert des Interaktionsterms: 0,0791)																			
IIA	92 85,85 (14,81)	87 84,13 (13,89)	84 84,54 (14,95)	81 82,90 (15,22)	80 82,69 (15,90)	76 82,80 (16,95)	74 82,73 (17,71)	39 83,41 (15,98)	-2,67 (0,97)	95 83,36 (15,39)	92 83,27 (13,92)	90 83,52 (13,20)	84 83,31 (13,44)	80 84,39 (11,11)	71 84,32 (12,55)	74 82,84 (15,15)	37 81,14 (14,19)	-1,26 (0,96)	-1,41 [-4,11;1,29] 0,3027 -0,15 [-0,44;0,14]
IIB	133 84,70 (15,32)	126 83,93 (14,41)	117 84,73 (14,65)	116 83,74 (15,05)	113 83,63 (15,73)	101 83,58 (15,17)	109 82,17 (15,70)	68 85,47 (14,02)	-1,76 (0,83)	113 86,65 (13,60)	107 85,03 (13,02)	106 84,42 (13,05)	99 82,32 (14,63)	94 83,31 (15,36)	85 83,31 (16,79)	81 83,51 (15,72)	44 80,98 (16,62)	-3,04 (0,91)	1,28 [-1,16;3,71] 0,3020 0,13 [-0,12;0,38]
IIIA	431 84,09 (13,34)	407 81,52 (14,67)	397 81,91 (15,00)	374 81,49 (14,67)	352 81,63 (15,17)	314 82,00 (14,41)	321 81,97 (14,99)	155 80,72 (14,33)	-2,47 (0,48)	436 83,43 (14,69)	414 84,12 (14,57)	420 83,71 (14,57)	393 83,73 (14,65)	377 83,86 (15,37)	334 83,31 (15,28)	315 82,30 (15,39)	172 82,49 (14,88)	-0,42 (0,47)	-2,05 [-3,37;-0,73] 0,0024 -0,21 [-0,34;-0,07]

Subgruppe	Abemaciclib+ET[1] B N MW (SD)	Abemaciclib+ET[1] M3 N MW (SD)	Abemaciclib+ET[1] M6 N MW (SD)	Abemaciclib+ET[1] M12 N MW (SD)	Abemaciclib+ET[1] M18 N MW (SD)	Abemaciclib+ET[1] M24 N MW (SD)	Abemaciclib+ET[1] T30 FUP[2] N MW (SD)	Abemaciclib+ET[1] M6 FUP[3] N MW (SD)	Abemaciclib+ET[1] PB LSM (SE)	ET[1] B N MW (SD)	ET[1] M3 N MW (SD)	ET[1] M6 N MW (SD)	ET[1] M12 N MW (SD)	ET[1] M18 N MW (SD)	ET[1] M24 N MW (SD)	ET[1] T30 FUP[2] N MW (SD)	ET[1] M6 FUP[3] N MW (SD)	ET[1] PB LSM (SE)	Abemaciclib+ET vs. ET[1] Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIIB	47 82,47 (14,43)	45 79,53 (17,54)	45 80,82 (16,86)	43 81,30 (17,21)	41 79,44 (16,13)	36 78,56 (17,55)	31 82,61 (15,53)	15 83,33 (17,50)	-2,74 (1,37)	41 85,59 (14,80)	40 87,38 (13,23)	39 85,87 (12,40)	35 85,51 (15,21)	34 85,50 (13,29)	31 83,39 (15,99)	30 84,13 (18,02)	14 85,07 (16,89)	0,07 (1,45)	-2,81 [-6,78;1,17] 0,1636 -0,30 [-0,72;0,12]
IIIC	402 84,55 (15,02)	377 82,50 (15,66)	364 82,63 (15,24)	338 83,65 (14,74)	325 83,39 (14,79)	281 81,90 (15,19)	291 82,28 (15,43)	170 81,81 (15,83)	-2,18 (0,48)	423 83,76 (13,39)	404 83,56 (14,23)	384 83,57 (14,45)	362 84,15 (13,87)	347 83,78 (14,07)	297 84,10 (13,80)	301 82,96 (14,05)	168 82,18 (14,39)	-0,52 (0,47)	-1,66 [-2,99;-0,33] 0,0143 -0,17 [-0,31;-0,03]
Tumorgrading (p-Wert des Interaktionsterms: 0,9557)																			
G1	82 85,18 (13,97)	80 83,95 (15,77)	81 83,17 (15,75)	74 83,97 (15,43)	70 84,39 (15,15)	63 84,11 (13,53)	62 84,18 (14,83)	31 83,39 (13,26)	-1,08 (1,07)	84 85,37 (13,96)	82 85,94 (14,05)	79 85,37 (14,11)	70 86,76 (12,15)	74 83,64 (16,52)	64 86,09 (14,89)	55 85,40 (13,92)	34 86,09 (12,36)	0,44 (1,06)	-1,52 [-4,50;1,45] 0,3131 -0,16 [-0,46;0,15]
G2	526 84,46 (14,04)	499 81,73 (15,53)	481 82,13 (15,35)	453 82,38 (15,25)	434 82,07 (15,46)	375 81,28 (15,49)	375 81,78 (15,86)	211 81,86 (15,64)	-2,84 (0,43)	533 83,73 (14,16)	505 83,62 (14,33)	504 83,28 (14,26)	475 83,28 (14,35)	447 82,92 (14,70)	402 83,04 (14,53)	392 81,52 (15,34)	214 81,33 (15,22)	-1,22 (0,42)	-1,63 [-2,81;-0,44] 0,0071 -0,17 [-0,29;-0,05]
G3	450 84,11 (15,02)	420 82,55 (14,59)	402 83,38 (14,86)	382 82,76 (14,39)	367 82,63 (15,16)	333 82,38 (15,15)	354 82,43 (15,09)	185 82,52 (14,80)	-1,78 (0,45)	436 83,91 (14,39)	415 84,17 (14,16)	403 84,03 (14,22)	379 84,04 (14,55)	365 85,07 (13,54)	315 84,40 (14,93)	314 84,12 (14,68)	165 83,19 (14,72)	-0,24 (0,46)	-1,54 [-2,80;-0,29] 0,0159 -0,16 [-0,29;-0,03]
GX	47 84,51 (12,92)	42 82,64 (13,76)	43 80,30 (14,36)	43 81,67 (15,52)	40 82,60 (13,46)	37 83,43 (14,50)	37 80,59 (16,17)	22 80,18 (15,78)	-3,60 (1,54)	53 84,64 (12,41)	53 83,96 (13,08)	52 84,37 (12,96)	48 81,44 (13,33)	45 83,49 (15,83)	37 80,30 (13,49)	39 81,00 (14,16)	21 78,95 (13,35)	-2,04 (1,47)	-1,56 [-5,78;2,66] 0,4656 -0,15 [-0,54;0,25]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,7301)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Negativ	137 81,43 (13,86)	132 79,33 (15,72)	123 78,62 (16,68)	116 79,77 (15,91)	106 79,58 (16,16)	92 78,66 (15,62)	100 78,76 (15,19)	63 76,94 (15,48)	-3,04 (0,85)	149 83,14 (14,26)	139 82,89 (14,23)	133 83,33 (14,37)	126 83,98 (14,31)	121 83,74 (14,47)	103 82,27 (16,07)	114 80,06 (15,43)	56 79,07 (15,28)	-0,86 (0,81)	-2,18 [-4,49;0,13] 0,0639 -0,22 [-0,45;0,01]
Positiv	939 84,58 (14,38)	880 82,36 (14,92)	855 82,86 (14,81)	813 82,67 (14,62)	785 82,61 (14,97)	695 82,19 (15,01)	706 82,46 (15,45)	376 82,86 (14,85)	-2,27 (0,31)	934 83,89 (14,13)	896 84,07 (14,13)	885 83,68 (14,13)	827 83,58 (14,23)	792 83,73 (14,50)	696 83,75 (14,50)	668 83,06 (14,87)	366 82,44 (14,64)	-0,72 (0,32)	-1,55 [-2,43;-0,68] 0,0005 -0,16 [-0,25;-0,07]
Unbekannt	9 86,78 (18,40)	9 89,44 (12,61)	9 94,67 (9,75)	7 97,29 (15,07)	3 105,00 (2,65)	6 93,17 (17,03)	5 89,20 (17,54)	1 103,00 (NE)	5,30 (2,66)	7 91,71 (13,31)	6 94,00 (9,34)	6 92,17 (9,20)	6 95,50 (7,15)	6 93,00 (6,54)	6 90,50 (11,29)	5 92,20 (11,37)	5 96,80 (4,55)	4,87 (2,77)	0,43 [-7,74;8,60] 0,9124 0,05 [-0,88;0,99]
Ethnizität (p-Wert des Interaktionsterms: 0,4408)																			
Weiß	808 84,57 (14,19)	755 82,57 (14,62)	737 82,78 (14,56)	694 82,57 (14,60)	659 82,61 (14,97)	588 82,22 (14,73)	595 82,40 (15,27)	337 82,82 (14,91)	-2,61 (0,33)	819 84,34 (13,99)	773 84,54 (13,96)	759 84,46 (13,69)	705 83,86 (14,16)	678 84,14 (14,29)	600 84,13 (14,50)	577 83,11 (14,86)	323 82,70 (14,58)	-0,89 (0,33)	-1,71 [-2,63;-0,80] 0,0002 -0,18 [-0,28;-0,09]
Asiatisch	233 83,59 (15,12)	225 81,66 (16,33)	218 82,18 (16,40)	209 82,44 (16,03)	204 82,36 (16,35)	176 81,76 (16,35)	187 80,74 (16,37)	97 79,87 (15,58)	-1,18 (0,72)	221 82,69 (14,74)	217 82,68 (14,92)	215 81,94 (15,37)	207 83,75 (14,88)	199 83,31 (15,50)	167 82,37 (14,81)	172 81,98 (15,29)	88 79,89 (15,65)	-0,08 (0,73)	-1,10 [-3,12;0,92] 0,2844 -0,10 [-0,28;0,08]
Andere	54 84,94 (13,56)	51 81,25 (15,99)	46 83,52 (16,50)	42 83,98 (14,01)	42 80,48 (13,97)	36 80,78 (16,54)	40 84,45 (13,81)	14 80,64 (15,49)	-2,51 (1,34)	57 84,35 (14,43)	57 82,28 (14,56)	55 83,76 (13,04)	51 82,27 (13,55)	46 81,72 (13,06)	42 83,71 (15,66)	44 83,14 (15,33)	19 83,89 (15,43)	-1,60 (1,28)	-0,91 [-4,58;2,76] 0,6239 -0,09 [-0,47;0,28]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,3984)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Tamoxifen	104 83,93 (13,62)	99 82,60 (14,44)	99 81,77 (15,89)	96 82,36 (13,36)	94 81,94 (14,44)	91 81,89 (14,26)	91 82,47 (15,23)	55 83,71 (14,35)	-1,19 (0,92)	124 82,01 (13,14)	122 81,99 (13,29)	120 82,53 (13,87)	110 83,18 (12,44)	103 82,29 (13,78)	94 83,54 (13,83)	92 80,61 (13,99)	56 80,00 (15,65)	-0,35 (0,85)	-0,83 [-3,31;1,64] 0,5066 -0,09 [-0,35;0,17]
Aromatase-Inhibitor	1003 84,42 (14,46)	944 82,25 (15,16)	910 82,74 (15,06)	858 82,65 (15,08)	819 82,53 (15,31)	719 82,08 (15,28)	737 82,15 (15,50)	394 81,94 (15,22)	-2,45 (0,31)	986 84,21 (14,27)	937 84,30 (14,27)	921 83,97 (14,20)	865 83,84 (14,48)	831 84,05 (14,54)	726 83,71 (14,81)	710 83,06 (15,09)	380 82,53 (14,69)	-0,80 (0,31)	-1,65 [-2,51;-0,79] 0,0002 -0,17 [-0,26;-0,08]
ECOG-PS (p-Wert des Interaktionsterms: 0,4124)																			
ECOG-PS 0	933 85,12 (13,99)	878 83,04 (14,84)	852 83,30 (14,95)	813 83,02 (14,71)	779 83,08 (14,95)	695 82,59 (15,07)	702 82,65 (15,29)	381 82,99 (14,89)	-2,37 (0,32)	898 84,67 (13,92)	855 84,68 (14,03)	843 84,36 (13,82)	791 84,31 (13,92)	759 84,38 (14,28)	674 83,87 (14,49)	663 82,58 (14,94)	355 81,95 (14,67)	-1,03 (0,32)	-1,34 [-2,23;-0,46] 0,0029 -0,14 [-0,23;-0,05]
ECOG-PS 1	174 80,39 (15,73)	165 78,27 (15,82)	157 79,06 (15,69)	141 80,30 (15,85)	134 78,92 (16,28)	115 78,83 (15,39)	126 79,63 (16,21)	68 77,51 (15,60)	-1,96 (0,77)	212 80,96 (14,81)	204 81,35 (14,53)	198 81,43 (15,34)	184 81,45 (15,45)	175 81,60 (15,05)	146 82,88 (15,63)	139 83,69 (15,18)	81 83,28 (15,52)	0,65 (0,70)	-2,61 [-4,65;-0,56] 0,0126 -0,26 [-0,46;-0,06]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-G Gesamtscore = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-G Gesamtscore haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-G: Functional Assessment of Cancer Therapy - General; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t111_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des TOI aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,4145)																			
Neoadjuvante Chemotherapie	196 67,25 (11,50)	188 65,85 (13,05)	181 66,12 (13,64)	176 65,11 (14,09)	164 64,61 (13,47)	149 64,88 (14,40)	147 63,55 (14,17)	75 63,91 (14,46)	-2,15 (0,61)	193 66,31 (12,82)	181 66,62 (12,50)	178 68,09 (11,55)	155 69,05 (12,50)	144 69,59 (11,88)	120 69,54 (12,42)	135 67,03 (13,52)	77 67,55 (13,77)	1,03 (0,62)	-3,19 [-4,90;-1,47] 0,0003 -0,37 [-0,57;-0,17]
Adjuvante Chemotherapie	286 65,30 (11,99)	271 65,40 (12,37)	266 66,13 (13,01)	263 66,33 (12,63)	252 66,05 (12,98)	212 66,25 (13,43)	203 66,40 (12,50)	125 65,68 (12,26)	0,76 (0,45)	283 65,60 (11,60)	275 66,94 (12,04)	267 67,88 (11,80)	261 67,95 (12,34)	237 68,68 (11,88)	221 67,36 (12,34)	216 67,19 (12,53)	119 67,76 (11,53)	1,93 (0,46)	-1,18 [-2,45;0,09] 0,0684 -0,15 [-0,32;0,01]
Keine Chemotherapie	7 72,00 (17,10)	7 67,57 (15,33)	6 65,33 (16,46)	6 66,67 (16,31)	5 66,60 (17,44)	5 63,80 (18,25)	6 65,00 (12,74)	2 70,00 (11,31)	NE	1 70,00 (NE)	1 65,00 (NE)	1 55,00 (NE)	1 59,00 (NE)	1 56,00 (NE)	1 59,00 (NE)	1 59,00 (NE)	0	NE	NE
Region (p-Wert des Interaktionsterms: 0,5359)																			
Nordamerika / Europa	203 67,42 (11,32)	187 66,31 (12,46)	180 66,63 (13,20)	176 65,94 (13,39)	160 66,14 (13,22)	138 65,83 (14,08)	134 67,06 (12,81)	72 66,96 (12,86)	-0,85 (0,58)	197 66,39 (12,41)	183 66,25 (12,98)	173 67,91 (12,19)	154 68,46 (13,44)	137 70,09 (13,16)	132 68,70 (13,36)	131 67,14 (13,97)	65 68,60 (14,11)	1,18 (0,59)	-2,03 [-3,66;-0,40] 0,0146 -0,25 [-0,44;-0,05]
Asien	162 64,75 (11,30)	161 64,17 (11,52)	157 64,36 (11,67)	155 64,67 (12,19)	149 64,00 (11,72)	129 63,58 (13,02)	136 63,79 (12,97)	69 65,20 (12,49)	-0,69 (0,56)	152 65,77 (11,08)	150 66,39 (11,02)	151 66,68 (11,26)	146 67,92 (11,07)	137 67,74 (10,68)	120 67,59 (11,49)	121 66,25 (12,38)	65 67,83 (10,03)	1,23 (0,58)	-1,91 [-3,49;-0,33] 0,0179 -0,27 [-0,49;-0,05]
Andere	124 66,01 (13,42)	118 66,47 (14,33)	116 67,69 (15,17)	114 67,32 (14,36)	112 66,57 (14,89)	99 68,13 (14,37)	86 64,53 (14,19)	61 62,67 (13,83)	0,35 (0,80)	128 65,29 (12,78)	124 68,15 (12,35)	122 69,51 (11,38)	117 68,70 (12,58)	108 69,19 (11,56)	90 67,91 (12,15)	100 68,11 (12,05)	66 66,61 (12,88)	2,58 (0,79)	-2,23 [-4,45;-0,01] 0,0493 -0,25 [-0,50;-0,00]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3962)																			
< 20 mm	121 65,55 (11,04)	115 65,11 (11,50)	109 64,54 (12,99)	110 64,50 (14,03)	105 65,13 (13,40)	93 63,20 (14,97)	91 64,44 (13,90)	53 65,92 (12,18)	-0,70 (0,74)	123 65,22 (12,48)	116 65,78 (12,93)	115 67,66 (11,03)	107 66,58 (11,82)	99 68,27 (11,77)	85 68,06 (12,08)	84 68,45 (11,94)	50 67,64 (12,85)	1,46 (0,74)	-2,16 [-4,22;-0,10] 0,0400 -0,26 [-0,52;-0,01]
≥ 20 bis < 50 mm	228 67,00 (11,94)	217 65,68 (13,71)	216 67,46 (13,24)	213 66,27 (13,11)	195 65,78 (13,34)	169 66,40 (13,19)	163 65,52 (12,92)	95 64,60 (14,06)	-0,70 (0,55)	227 65,40 (12,10)	218 66,82 (11,98)	216 68,00 (11,68)	200 69,13 (12,43)	185 69,07 (11,98)	172 67,62 (12,51)	180 66,58 (12,96)	93 67,00 (13,09)	1,84 (0,55)	-2,54 [-4,06;-1,02] 0,0011 -0,31 [-0,49;-0,12]
≥ 50 mm	128 65,41 (12,70)	124 65,79 (12,04)	119 65,04 (13,69)	114 66,18 (12,61)	112 64,87 (12,91)	95 66,45 (13,88)	93 65,77 (13,18)	48 64,75 (12,56)	-0,09 (0,67)	122 67,67 (11,56)	118 67,84 (11,92)	110 68,25 (12,52)	105 68,99 (12,75)	95 69,71 (11,81)	81 69,37 (12,75)	84 67,04 (13,77)	49 69,06 (10,92)	0,95 (0,69)	-1,04 [-2,93;0,84] 0,2770 -0,14 [-0,39;0,11]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,4003)																			
0-3	177 66,98 (11,21)	169 66,17 (12,30)	160 66,31 (13,18)	157 65,82 (13,39)	143 66,63 (12,30)	129 66,75 (14,10)	131 65,10 (13,74)	77 65,82 (12,32)	-0,56 (0,62)	190 66,01 (11,60)	181 67,55 (11,69)	175 68,30 (11,74)	163 68,45 (11,49)	154 68,20 (11,40)	136 67,98 (11,84)	135 66,28 (13,28)	71 67,04 (12,22)	1,40 (0,60)	-1,96 [-3,65;-0,27] 0,0230 -0,24 [-0,44;-0,03]
4-9	214 65,06 (12,67)	203 63,84 (13,28)	200 65,03 (13,42)	196 64,83 (13,19)	191 64,12 (13,45)	167 64,47 (13,99)	157 64,74 (12,96)	82 63,45 (14,09)	-0,80 (0,54)	210 66,20 (12,32)	201 66,70 (12,07)	198 67,60 (11,51)	186 68,12 (12,61)	170 69,74 (11,72)	151 68,51 (12,52)	159 67,38 (12,70)	86 68,15 (12,45)	1,50 (0,55)	-2,30 [-3,81;-0,79] 0,0029 -0,29 [-0,48;-0,10]
≥ 10	98 67,16 (11,32)	94 68,45 (11,41)	93 68,12 (13,04)	92 68,09 (13,04)	87 66,66 (13,95)	70 66,47 (13,13)	68 66,47 (13,12)	43 66,79 (12,40)	0,39 (0,87)	77 64,78 (12,74)	75 65,35 (13,67)	73 67,96 (12,18)	68 68,68 (13,93)	58 68,90 (13,54)	55 67,29 (13,48)	58 68,28 (12,58)	39 67,77 (13,01)	2,08 (0,99)	-1,69 [-4,29;0,91] 0,2017 -0,20 [-0,49;0,10]
Tumorstadium (p-Wert des Interaktionsterms: 0,1367)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
IIA	52 68,06 (10,96)	49 65,49 (12,69)	48 65,23 (12,96)	45 63,84 (14,40)	46 64,93 (13,20)	39 63,18 (14,34)	39 63,72 (13,74)	23 64,57 (11,39)	-2,69 (1,08)	57 65,58 (12,09)	54 66,83 (11,75)	54 68,78 (11,44)	48 67,10 (10,66)	46 69,65 (9,91)	36 67,89 (11,21)	37 69,35 (10,74)	19 70,26 (8,33)	2,33 (1,04)	-5,03 [-8,01;-2,05] 0,0011 -0,64 [-1,03;-0,26]
IIB	45 67,20 (9,82)	44 66,89 (12,62)	41 70,15 (10,53)	42 67,07 (11,92)	35 67,60 (10,76)	34 68,26 (11,30)	31 66,81 (9,81)	22 66,73 (11,35)	0,18 (1,23)	64 67,11 (10,02)	62 69,13 (10,25)	60 68,92 (11,05)	55 69,55 (12,23)	55 67,75 (10,73)	54 68,11 (11,61)	55 65,44 (14,20)	32 67,22 (13,46)	0,01 (1,02)	0,17 [-3,00;3,34] 0,9156 0,02 [-0,36;0,40]
IIIA	211 65,31 (12,83)	204 64,57 (13,12)	197 65,21 (13,35)	194 65,43 (12,84)	187 64,56 (13,50)	163 65,14 (13,94)	156 64,79 (12,84)	83 64,63 (13,70)	-0,46 (0,54)	193 65,98 (12,61)	183 66,28 (11,86)	178 67,12 (11,64)	173 67,50 (12,52)	155 68,81 (11,60)	131 68,31 (12,54)	140 66,90 (12,82)	71 67,42 (12,68)	1,22 (0,57)	-1,68 [-3,22;-0,15] 0,0317 -0,21 [-0,41;-0,02]
IIIB	14 61,43 (17,67)	13 61,23 (16,07)	13 57,15 (19,68)	13 55,85 (13,89)	10 55,60 (10,91)	8 52,13 (20,37)	11 56,18 (17,48)	6 51,83 (13,00)	-4,52 (1,89)	14 69,43 (12,08)	14 73,29 (11,66)	14 72,43 (10,29)	11 72,09 (15,42)	9 75,00 (10,44)	10 67,90 (12,31)	9 64,67 (14,54)	5 59,00 (14,61)	0,44 (2,00)	-4,96 [-10,72;0,80] 0,0885 -0,66 [-1,40;0,08]
IIIC	166 66,92 (10,77)	155 67,08 (11,69)	153 67,30 (12,98)	150 67,53 (13,44)	142 67,08 (13,27)	121 67,32 (13,40)	118 66,66 (13,83)	67 66,40 (13,14)	0,32 (0,66)	148 64,99 (12,29)	143 65,77 (13,40)	139 67,69 (12,24)	129 69,04 (12,67)	117 69,09 (13,47)	111 67,95 (13,13)	111 67,65 (12,91)	69 68,06 (12,49)	2,35 (0,70)	-2,03 [-3,94;-0,12] 0,0370 -0,24 [-0,46;-0,01]
Tumorgrading (p-Wert des Interaktionsterms: 0,6482)																			
G1	45 68,04 (11,31)	42 67,17 (10,79)	40 66,68 (11,74)	40 66,33 (10,55)	39 66,97 (11,86)	33 65,45 (13,63)	33 66,67 (11,71)	18 66,22 (14,65)	-0,71 (1,10)	38 64,68 (11,52)	36 68,56 (10,76)	34 68,06 (10,89)	36 67,97 (13,13)	30 69,27 (12,77)	28 64,29 (14,66)	25 66,76 (13,63)	13 69,46 (11,27)	2,83 (1,20)	-3,54 [-6,79;-0,29] 0,0330 -0,48 [-0,92;-0,04]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
G2	212 66,55 (12,10)	201 65,64 (12,87)	200 66,61 (13,22)	195 65,96 (13,13)	186 65,61 (13,13)	164 65,18 (13,44)	166 65,72 (12,86)	84 66,51 (12,26)	-0,80 (0,55)	207 66,42 (12,62)	200 66,70 (13,26)	194 67,58 (12,65)	181 68,15 (12,88)	159 69,33 (12,31)	147 68,37 (13,27)	152 66,97 (13,55)	85 66,80 (12,96)	0,71 (0,56)	-1,51 [-3,04;0,03] 0,0540 -0,19 [-0,38;0,00]
G3	204 65,07 (11,69)	196 64,86 (12,92)	188 65,18 (13,89)	184 65,13 (14,02)	171 64,71 (13,93)	147 66,01 (14,67)	137 63,93 (14,06)	87 62,33 (13,56)	-0,10 (0,60)	203 65,55 (11,85)	194 66,58 (11,44)	191 68,18 (11,20)	173 68,80 (11,74)	167 68,43 (11,49)	143 68,30 (11,28)	153 66,95 (12,51)	86 68,24 (12,46)	2,08 (0,60)	-2,18 [-3,85;-0,50] 0,0110 -0,25 [-0,45;-0,06]
GX	28 68,43 (12,78)	27 68,48 (11,97)	25 68,36 (11,49)	26 69,38 (12,35)	25 67,72 (10,68)	22 67,23 (12,62)	20 67,25 (13,46)	13 72,38 (8,94)	-0,52 (1,29)	28 66,18 (11,15)	26 66,85 (11,64)	26 68,58 (9,18)	26 66,77 (12,74)	25 70,32 (11,18)	23 69,70 (10,16)	22 69,55 (10,30)	12 67,83 (10,12)	1,92 (1,28)	-2,44 [-6,11;1,23] 0,1878 -0,36 [-0,89;0,17]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,5894)																			
Negativ	46 63,57 (12,48)	43 62,19 (12,83)	41 63,56 (15,97)	42 62,33 (15,56)	39 60,44 (14,59)	37 60,51 (15,38)	36 56,81 (14,58)	12 60,83 (14,73)	-2,83 (1,41)	39 66,62 (9,48)	36 65,81 (9,88)	35 66,26 (9,62)	30 68,93 (10,63)	31 69,77 (10,27)	26 70,00 (9,94)	31 68,87 (11,74)	15 70,60 (9,16)	1,84 (1,52)	-4,67 [-8,81;-0,53] 0,0277 -0,49 [-0,92;-0,06]
Positiv	426 66,30 (11,94)	407 65,83 (12,70)	398 66,22 (13,03)	388 66,00 (12,99)	370 65,92 (12,96)	319 66,09 (13,68)	305 65,89 (12,84)	182 65,13 (13,07)	-0,28 (0,39)	421 65,85 (12,22)	406 66,97 (12,22)	397 68,21 (11,69)	373 68,21 (12,34)	337 68,69 (12,04)	303 68,01 (12,38)	311 66,86 (12,95)	174 67,13 (12,71)	1,50 (0,39)	-1,78 [-2,86;-0,69] 0,0013 -0,22 [-0,36;-0,09]
Unbekannt	2 72,50 (4,95)	2 69,00 (24,04)	2 77,50 (12,02)	1 88,00 (NE)	1 86,00 (NE)	1 81,00 (NE)	1 88,00 (NE)	0	NE	8 60,88 (18,76)	7 58,43 (21,13)	8 61,88 (19,19)	6 64,33 (22,98)	6 72,67 (13,92)	8 61,50 (19,22)	4 65,25 (22,94)	2 73,50 (12,02)	1,89 (2,85)	NE
Ethnizität (p-Wert des Interaktionsterms: 0,1644)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Weiß	275 66,82 (12,33)	258 66,03 (13,31)	249 66,57 (13,93)	243 65,91 (13,39)	228 65,49 (14,07)	199 65,93 (14,30)	183 65,50 (13,20)	117 64,86 (13,23)	-0,90 (0,50)	285 66,04 (12,60)	268 66,63 (13,01)	258 68,20 (12,20)	241 67,88 (13,24)	219 69,03 (12,59)	200 68,00 (12,90)	208 67,16 (13,29)	121 67,08 (13,72)	1,10 (0,50)	-2,00 [-3,39;-0,61] 0,0048 -0,24 [-0,41;-0,07]
Asiatisch	187 65,27 (11,12)	184 65,13 (11,55)	180 65,63 (11,88)	178 66,25 (12,37)	170 65,59 (12,09)	148 65,26 (13,22)	152 64,87 (13,00)	75 65,84 (12,37)	0,28 (0,55)	165 65,56 (11,27)	163 66,67 (11,09)	162 67,23 (11,44)	157 68,73 (11,42)	144 68,16 (10,74)	124 67,56 (11,79)	129 66,16 (12,27)	66 67,73 (9,72)	1,68 (0,59)	-1,39 [-2,99;0,20] 0,0865 -0,18 [-0,39;0,03]
Andere	16 65,06 (16,08)	15 64,53 (15,91)	15 64,27 (18,26)	15 60,00 (19,31)	15 63,13 (13,92)	13 66,15 (16,20)	14 65,21 (15,85)	9 62,78 (17,75)	-1,35 (2,04)	17 64,53 (13,04)	16 68,19 (10,41)	17 68,53 (6,74)	16 70,00 (7,41)	14 75,36 (10,67)	12 71,83 (8,96)	11 76,27 (8,67)	7 74,86 (9,51)	6,98 (2,08)	-8,33 [-14,28;-2,39] 0,0076 -0,97 [-1,68;-0,26]
ECOG-PS (p-Wert des Interaktionsterms: 0,1895)																			
ECOG-PS 0	439 65,99 (11,85)	417 65,34 (12,44)	404 65,66 (13,26)	399 65,23 (13,14)	376 64,82 (13,09)	328 65,22 (13,75)	320 64,73 (13,14)	187 64,88 (13,05)	-0,92 (0,38)	424 66,52 (11,99)	405 67,23 (12,23)	395 68,34 (11,56)	371 68,88 (12,34)	339 69,41 (11,84)	306 68,75 (12,21)	318 67,40 (12,96)	177 67,82 (12,54)	1,43 (0,39)	-2,35 [-3,41;-1,28] <,0001 -0,29 [-0,43;-0,16]
ECOG-PS 1	50 67,80 (12,43)	49 67,96 (14,40)	49 69,84 (13,00)	46 71,26 (13,16)	45 71,13 (13,02)	38 69,47 (14,58)	36 69,36 (13,81)	15 67,33 (13,82)	3,59 (1,29)	53 60,87 (11,84)	52 63,54 (11,51)	51 64,80 (12,30)	46 64,02 (12,05)	43 65,67 (11,75)	36 62,58 (12,67)	34 64,38 (12,11)	19 66,26 (11,50)	2,34 (1,27)	1,25 [-2,41;4,92] 0,4983 0,14 [-0,25;0,52]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B TOI = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B TOI haben.
Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler; TOI: Trial Outcome Index

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t112_mmrm_safc1_premp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Tabelle: Subgruppen für die Veränderung des TOI aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Alter (p-Wert des Interaktionsterms: 0,7437)																			
< 65 Jahre	803 67,08 (12,62)	757 66,27 (12,90)	743 66,48 (13,27)	696 66,18 (13,17)	669 66,27 (13,38)	592 66,29 (13,06)	601 66,18 (13,30)	329 66,30 (12,76)	-0,93 (0,30)	831 66,04 (12,52)	791 67,32 (12,19)	782 67,15 (12,28)	727 67,25 (12,43)	691 67,98 (12,46)	610 67,91 (12,63)	606 67,21 (13,28)	319 66,53 (12,89)	1,05 (0,30)	-1,98 [-2,81;-1,16] <,0001 -0,23 [-0,33;-0,14]
≥ 65 Jahre	302 67,30 (12,64)	282 65,34 (12,63)	263 66,79 (11,70)	255 65,82 (12,49)	238 65,25 (13,61)	214 64,50 (13,20)	226 65,51 (13,01)	119 64,97 (11,93)	-2,42 (0,46)	279 68,00 (11,96)	266 68,03 (12,05)	260 68,43 (11,30)	246 68,50 (11,29)	240 67,40 (12,16)	211 67,09 (12,16)	197 66,94 (11,82)	117 67,91 (12,75)	-0,70 (0,48)	-1,72 [-3,02;-0,42] 0,0096 -0,22 [-0,38;-0,05]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7679)																			
Neoadjuvante Chemotherapie	362 68,22 (12,42)	335 66,79 (13,15)	323 67,21 (13,07)	299 65,75 (13,63)	277 65,92 (14,44)	236 66,17 (13,41)	254 65,67 (13,51)	129 66,12 (11,77)	-2,34 (0,44)	365 66,10 (12,33)	345 67,32 (11,55)	332 66,81 (12,00)	307 66,55 (12,19)	291 67,19 (11,81)	248 67,45 (12,07)	261 66,61 (12,58)	139 64,87 (12,54)	0,07 (0,43)	-2,40 [-3,62;-1,19] 0,0001 -0,29 [-0,43;-0,14]
Adjuvante Chemotherapie	683 66,52 (12,88)	650 65,70 (12,77)	632 66,30 (12,92)	601 66,46 (12,75)	584 66,19 (13,04)	530 65,90 (13,05)	527 66,25 (13,16)	292 65,84 (13,06)	-0,55 (0,32)	678 66,60 (12,47)	648 67,61 (12,36)	651 67,75 (12,24)	611 68,17 (12,13)	593 68,19 (12,70)	528 68,07 (12,70)	495 67,54 (13,22)	270 67,91 (13,08)	1,15 (0,32)	-1,70 [-2,60;-0,81] 0,0002 -0,20 [-0,31;-0,10]
Keine Chemotherapie	60 67,72 (10,48)	54 65,00 (11,35)	51 65,61 (10,86)	51 63,59 (11,68)	46 64,13 (12,43)	40 62,68 (12,04)	46 64,93 (12,47)	27 66,19 (10,70)	-4,44 (1,02)	67 68,21 (12,16)	64 67,30 (13,33)	59 68,12 (10,19)	55 66,58 (12,13)	47 67,28 (11,72)	45 64,67 (12,46)	47 65,98 (11,76)	27 67,22 (11,18)	-2,04 (0,98)	-2,40 [-5,20;0,40] 0,0927 -0,30 [-0,65;0,05]
Region (p-Wert des Interaktionsterms: 0,2477)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Nordamerika / Europa	548 67,72 (13,10)	493 65,94 (13,75)	478 66,57 (13,57)	445 66,35 (13,45)	414 66,60 (13,69)	375 65,97 (13,93)	391 66,20 (13,58)	209 67,19 (13,05)	-2,03 (0,35)	529 66,75 (12,78)	489 67,76 (12,74)	480 67,69 (12,13)	437 67,89 (12,84)	421 67,58 (13,09)	376 68,27 (13,00)	344 67,30 (13,41)	205 68,17 (13,13)	0,34 (0,35)	-2,37 [-3,34;-1,40] <,0001 -0,29 [-0,41;-0,17]
Asien	195 67,58 (12,49)	190 66,58 (12,95)	185 66,38 (13,49)	178 66,37 (13,49)	173 66,14 (14,01)	152 65,45 (13,73)	163 65,44 (13,52)	87 63,47 (11,94)	-1,23 (0,63)	192 67,27 (12,16)	189 67,39 (12,32)	187 67,12 (12,51)	179 67,98 (12,43)	174 68,31 (13,02)	149 67,17 (12,57)	155 67,50 (12,26)	81 64,81 (12,78)	0,35 (0,63)	-1,58 [-3,34;0,17] 0,0773 -0,18 [-0,38;0,02]
Andere	362 66,03 (11,90)	356 65,82 (11,38)	343 66,64 (11,49)	328 65,57 (12,07)	320 65,16 (12,79)	279 65,82 (11,59)	273 66,04 (12,54)	152 65,65 (12,01)	-0,36 (0,44)	389 65,88 (12,00)	379 67,21 (11,28)	375 67,38 (11,74)	357 66,97 (11,14)	336 67,89 (11,07)	296 67,24 (11,84)	304 66,79 (12,74)	150 66,29 (12,38)	1,11 (0,42)	-1,47 [-2,66;-0,29] 0,0150 -0,18 [-0,32;-0,03]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2430)																			
< 20 mm	279 66,94 (13,17)	257 65,94 (13,31)	253 66,97 (13,54)	244 65,83 (13,57)	231 65,35 (14,27)	208 65,15 (14,19)	208 66,26 (13,78)	106 66,59 (13,11)	-1,34 (0,51)	298 66,62 (12,10)	282 67,50 (11,95)	276 68,03 (11,77)	257 67,63 (11,99)	248 68,23 (11,97)	216 68,25 (11,91)	221 67,27 (12,96)	111 66,95 (12,43)	0,64 (0,50)	-1,98 [-3,39;-0,57] 0,0059 -0,23 [-0,39;-0,07]
≥ 20 bis < 50 mm	568 67,13 (12,81)	543 66,36 (12,71)	519 66,93 (12,69)	500 66,45 (12,82)	474 66,36 (13,24)	423 66,64 (12,75)	431 66,75 (13,21)	231 65,52 (12,66)	-0,94 (0,36)	572 66,75 (12,49)	549 67,53 (12,28)	543 67,55 (12,01)	509 67,62 (12,38)	492 67,91 (12,39)	439 67,65 (12,87)	415 67,32 (13,39)	230 66,53 (12,91)	0,47 (0,35)	-1,41 [-2,39;-0,43] 0,0050 -0,17 [-0,28;-0,05]
≥ 50 mm	241 67,47 (11,59)	224 65,08 (12,69)	218 65,40 (12,42)	194 65,67 (12,69)	188 66,12 (12,69)	162 65,08 (12,48)	174 64,35 (12,50)	103 66,09 (12,14)	-2,06 (0,52)	229 65,65 (12,79)	215 67,15 (12,28)	213 66,20 (12,60)	197 67,07 (12,05)	184 66,84 (13,04)	158 66,89 (12,55)	159 66,31 (11,90)	91 67,45 (13,49)	0,74 (0,53)	-2,80 [-4,27;-1,34] 0,0002 -0,35 [-0,53;-0,17]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,6587)																			

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
0-3	366 66,84 (13,16)	346 65,94 (13,22)	333 66,93 (12,85)	312 66,41 (12,89)	300 66,12 (13,65)	273 65,71 (13,69)	285 66,00 (14,06)	166 66,95 (13,02)	-0,86 (0,44)	360 66,51 (11,91)	341 67,31 (11,79)	340 67,51 (11,21)	310 67,46 (11,71)	301 68,22 (11,47)	260 67,79 (12,24)	255 67,81 (12,60)	142 66,99 (12,76)	0,69 (0,44)	-1,55 [-2,77;-0,34] 0,0125 -0,19 [-0,33;-0,04]
4-9	475 67,05 (12,19)	444 65,93 (12,42)	436 66,07 (12,99)	417 65,27 (12,97)	396 65,62 (13,35)	352 65,95 (12,49)	355 66,32 (12,56)	173 65,32 (11,55)	-1,53 (0,38)	485 66,50 (12,86)	465 67,78 (12,45)	463 67,76 (12,24)	437 67,60 (12,92)	418 67,83 (12,92)	377 67,33 (12,92)	358 66,94 (13,51)	192 66,94 (13,02)	0,60 (0,38)	-2,13 [-3,19;-1,07] <,0001 -0,25 [-0,38;-0,13]
≥ 10	264 67,72 (12,65)	249 66,28 (13,05)	237 66,95 (12,69)	222 67,16 (13,11)	211 66,55 (13,37)	181 65,72 (13,49)	187 65,38 (13,18)	109 65,40 (13,31)	-1,62 (0,52)	265 66,62 (12,26)	251 67,24 (12,13)	239 66,87 (12,85)	226 67,65 (11,28)	212 67,26 (12,54)	184 68,31 (12,07)	190 66,65 (12,28)	102 66,68 (12,78)	0,42 (0,52)	-2,04 [-3,50;-0,58] 0,0061 -0,24 [-0,41;-0,07]
Tumorgrading (p-Wert des Interaktionsterms: 0,6213)																			
G1	81 65,74 (13,57)	78 66,99 (12,45)	80 66,78 (13,78)	73 66,41 (12,64)	68 65,72 (14,65)	62 66,45 (11,86)	62 66,27 (13,53)	31 65,74 (11,25)	0,55 (0,94)	84 68,35 (12,52)	82 69,95 (12,14)	78 69,55 (11,56)	70 70,11 (10,99)	74 67,39 (14,39)	65 69,42 (12,51)	55 69,76 (11,71)	34 69,44 (12,51)	1,23 (0,93)	-0,68 [-3,30;1,93] 0,6070 -0,08 [-0,39;0,22]
G2	526 67,40 (12,47)	498 65,59 (13,27)	480 66,15 (13,15)	452 65,83 (13,31)	432 65,77 (13,58)	373 65,22 (13,28)	374 65,56 (13,34)	211 65,77 (12,62)	-1,95 (0,37)	533 66,24 (12,60)	505 67,13 (12,03)	504 67,06 (12,13)	474 67,20 (12,45)	446 67,27 (12,30)	402 67,08 (12,43)	392 65,99 (13,23)	214 66,04 (13,49)	0,30 (0,36)	-2,25 [-3,26;-1,24] <,0001 -0,27 [-0,39;-0,15]
G3	449 67,04 (12,80)	419 66,39 (12,57)	401 67,19 (12,43)	381 66,43 (12,80)	365 66,36 (13,17)	332 66,24 (13,16)	354 66,44 (13,01)	184 66,29 (12,71)	-0,78 (0,40)	436 66,23 (12,29)	413 67,36 (12,27)	405 67,38 (12,10)	378 67,58 (12,14)	363 68,48 (11,92)	315 68,24 (12,75)	315 68,11 (12,89)	165 67,67 (12,30)	1,03 (0,40)	-1,80 [-2,92;-0,69] 0,0015 -0,21 [-0,35;-0,08]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
GX	47 67,77 (11,11)	42 65,76 (11,09)	43 64,93 (12,28)	43 65,26 (12,33)	40 66,48 (12,55)	37 67,30 (13,15)	37 65,76 (13,84)	22 65,05 (12,90)	-2,82 (1,22)	53 68,85 (10,32)	53 67,79 (11,93)	52 68,50 (11,36)	48 66,65 (10,74)	45 68,29 (13,36)	37 66,38 (10,98)	39 67,44 (10,75)	21 66,95 (9,73)	-0,82 (1,16)	-2,00 [-5,33;1,33] 0,2368 -0,24 [-0,63;0,16]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,6491)																			
Negativ	137 64,84 (12,77)	131 63,31 (14,08)	123 64,11 (14,07)	116 64,09 (13,26)	105 64,21 (14,12)	92 64,09 (13,29)	100 64,50 (12,84)	63 62,35 (13,01)	-1,49 (0,73)	149 66,00 (11,75)	139 66,93 (12,04)	134 67,88 (11,98)	125 67,97 (12,39)	121 67,19 (12,18)	103 66,95 (13,40)	114 64,81 (13,74)	56 64,48 (13,05)	0,43 (0,70)	-1,92 [-3,91;0,06] 0,0575 -0,23 [-0,46;0,01]
Positiv	937 67,27 (12,55)	877 66,14 (12,53)	853 66,62 (12,65)	810 66,08 (12,86)	780 66,03 (13,25)	692 65,76 (13,01)	705 66,03 (13,24)	375 66,46 (12,38)	-1,35 (0,27)	934 66,43 (12,45)	895 67,42 (12,11)	884 67,23 (12,07)	826 67,36 (12,08)	789 67,77 (12,44)	697 67,67 (12,41)	669 67,34 (12,74)	366 67,02 (12,82)	0,62 (0,27)	-1,97 [-2,72;-1,21] <,0001 -0,23 [-0,33;-0,14]
Unbekannt	9 71,78 (14,22)	9 69,89 (11,98)	9 76,67 (9,73)	7 80,57 (10,80)	3 89,67 (1,53)	6 76,33 (14,79)	5 75,20 (13,48)	1 80,00 (NE)	3,73 (2,41)	7 72,71 (15,14)	6 79,00 (7,77)	6 75,50 (6,75)	6 80,67 (6,12)	6 76,00 (7,01)	6 74,67 (10,88)	5 79,20 (7,05)	5 79,80 (5,72)	7,24 (2,46)	-3,51 [-10,88;3,86] 0,3246 -0,48 [-1,43;0,47]
Ethnizität (p-Wert des Interaktionsterms: 0,4029)																			
Weiß	806 66,69 (12,56)	751 65,72 (12,63)	734 66,24 (12,53)	691 65,44 (12,67)	653 65,38 (13,27)	585 65,47 (12,77)	594 65,53 (13,09)	336 66,24 (12,54)	-1,60 (0,29)	819 66,49 (12,33)	772 67,57 (12,05)	760 67,68 (11,82)	703 67,20 (12,14)	675 67,59 (12,29)	601 67,74 (12,34)	578 66,87 (12,93)	323 67,27 (12,75)	0,52 (0,28)	-2,12 [-2,91;-1,33] <,0001 -0,26 [-0,36;-0,16]
Asiatisch	233 68,30 (12,61)	225 67,05 (12,94)	218 67,56 (13,44)	210 67,93 (13,67)	204 67,88 (13,96)	176 66,69 (13,86)	187 66,68 (13,63)	97 64,60 (12,51)	-0,43 (0,59)	221 66,98 (12,50)	216 67,60 (12,36)	215 67,23 (12,60)	207 68,62 (12,47)	199 68,77 (13,02)	167 67,66 (12,59)	172 68,07 (12,49)	88 65,34 (13,18)	0,88 (0,61)	-1,31 [-2,98;0,36] 0,1229 -0,15 [-0,33;0,04]

Subgruppe	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Andere	54 68,91 (12,62)	51 66,61 (14,12)	46 67,50 (14,11)	42 67,69 (13,15)	42 66,17 (13,56)	36 68,53 (14,00)	40 69,40 (13,01)	14 67,36 (13,25)	-0,89 (1,31)	57 67,18 (12,61)	57 66,91 (12,91)	55 67,60 (11,57)	51 68,75 (11,61)	46 67,43 (11,23)	42 68,57 (13,54)	44 69,07 (13,97)	19 67,84 (13,70)	-0,03 (1,26)	-0,86 [-4,47;2,75] 0,6374 -0,09 [-0,46;0,28]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,1544)																			
Tamoxifen	103 65,60 (11,07)	97 65,93 (11,12)	98 65,54 (12,45)	95 65,98 (11,85)	93 65,88 (13,11)	90 65,58 (12,08)	91 65,92 (13,01)	55 65,89 (12,29)	0,34 (0,80)	124 66,05 (11,49)	122 66,72 (10,69)	120 67,01 (11,20)	109 68,11 (11,19)	103 67,04 (11,25)	94 68,73 (11,49)	92 66,24 (11,75)	56 65,00 (14,26)	0,91 (0,74)	-0,57 [-2,72;1,57] 0,5991 -0,07 [-0,33;0,19]
Aromatase-Inhibitor	1002 67,30 (12,77)	942 66,03 (13,00)	908 66,67 (12,92)	856 66,10 (13,11)	814 66,02 (13,49)	716 65,85 (13,25)	736 66,01 (13,25)	393 65,95 (12,60)	-1,51 (0,27)	986 66,60 (12,52)	935 67,60 (12,33)	922 67,53 (12,16)	864 67,50 (12,28)	828 67,93 (12,51)	727 67,56 (12,64)	711 67,26 (13,08)	380 67,18 (12,62)	0,57 (0,27)	-2,08 [-2,82;-1,34] <,0001 -0,25 [-0,34;-0,16]
ECOG-PS (p-Wert des Interaktionsterms: 0,7383)																			
ECOG-PS 0	931 67,76 (12,37)	874 66,51 (12,71)	849 67,04 (12,76)	810 66,39 (12,96)	774 66,39 (13,42)	692 66,29 (13,06)	701 66,43 (13,15)	380 66,74 (12,41)	-1,37 (0,27)	898 67,11 (12,32)	854 68,06 (11,97)	844 67,98 (11,84)	790 67,98 (11,81)	757 68,21 (12,32)	675 67,92 (12,39)	663 67,12 (12,98)	355 66,63 (12,71)	0,41 (0,28)	-1,78 [-2,54;-1,01] <,0001 -0,21 [-0,31;-0,12]
ECOG-PS 1	174 63,83 (13,45)	165 63,41 (13,16)	157 63,94 (13,18)	141 64,35 (13,07)	133 63,77 (13,40)	114 62,95 (13,15)	126 63,60 (13,42)	68 61,49 (12,45)	-1,10 (0,67)	212 64,08 (12,49)	203 65,14 (12,66)	198 65,32 (12,73)	183 65,78 (13,46)	174 66,16 (12,50)	146 66,68 (13,04)	140 67,26 (12,75)	81 68,05 (13,45)	1,62 (0,60)	-2,72 [-4,49;-0,95] 0,0027 -0,31 [-0,51;-0,11]

	Abemaciclib+ET[1]									ET[1]									Abemaciclib+ET vs. ET[1]
Subgruppe	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: 30 Tage Follow-up; 3: 6 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-B TOI = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-B TOI haben. Abkürzungen: B: Baseline; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; mm: Millimeter; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler; TOI: Trial Outcome Index																			

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_mmrm_qol_sub.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t112_mmrm_safc1_posmp_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
16DEC2021 / 08:56

Anhang 4-G2.8: Unerwünschte Ereignisse - Subgruppenanalysen

Anhang 4-G2.8.1: Unerwünschte Ereignisse (Gesamtraten) - Subgruppenanalysen

Tabelle 4-129 (Anhang): Unerwünschte Ereignisse (Gesamtraten) - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen - Unerwünschtes Ereignis (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Region (p-Wert des Interaktionsterms: 0,4918)					
Nordamerika / Europa	249/252 (98,8)	207/233 (88,8)	1,11 [1,06; 1,17] <,0001[2]	10,43 [3,11; 34,93] <,0001[3]	10,0 [5,7; 14,2] <,0001[3]
Asien	167/168 (99,4)	148/166 (89,2)	1,11 [1,06; 1,18] <,0001[2]	20,31 [2,68; 154,00] <,0001[3]	10,2 [5,4; 15,1] <,0001[3]
Andere	127/133 (95,5)	110/136 (80,9)	1,18 [1,08; 1,29] 0,0003[2]	5,00 [1,99; 12,60] 0,0002[3]	14,6 [7,1; 22,1] 0,0002[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6851)					
< 20 mm	138/141 (97,9)	124/140 (88,6)	1,11 [1,04; 1,18] 0,0023[2]	5,94 [1,69; 20,86] 0,0019[3]	9,3 [3,5; 15,1] 0,0019[3]
≥ 20 bis < 50 mm	250/255 (98,0)	213/249 (85,5)	1,15 [1,09; 1,21] <,0001[2]	8,45 [3,26; 21,92] <,0001[3]	12,5 [7,8; 17,2] <,0001[3]
≥ 50 mm	143/145 (98,6)	124/141 (87,9)	1,12 [1,05; 1,20] 0,0005[2]	9,80 [2,22; 43,27] 0,0003[3]	10,7 [5,0; 16,4] 0,0003[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7034)					
0-3	202/203 (99,5)	191/214 (89,3)	1,11 [1,06; 1,17] <,0001[2]	24,32 [3,25; 181,88] <,0001[3]	10,3 [6,0; 14,5] <,0001[3]
4-9	236/242 (97,5)	199/231 (86,1)	1,13 [1,07; 1,20] <,0001[2]	6,32 [2,59; 15,43] <,0001[3]	11,4 [6,5; 16,2] <,0001[3]
≥ 10	105/108 (97,2)	75/90 (83,3)	1,17 [1,06; 1,29] 0,0020[2]	7,00 [1,96; 25,04] 0,0007[3]	13,9 [5,6; 22,2] 0,0007[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,1175)					
IIA	58/59 (98,3)	56/62 (90,3)	1,09 [1,00; 1,19] 0,0595[2]	6,21 [0,72; 53,27] 0,1149[4]	8,0 [-0,1; 16,0] 0,1149[4]
IIB	53/53 (100,0)	62/69 (89,9)	1,11 [1,02; 1,21] 0,0166[2]	12,84 [0,72; 230,09] 0,0184[4]	10,1 [3,0; 17,3] 0,0184[4]
IIIA	230/236 (97,5)	190/214 (88,8)	1,10 [1,04; 1,16] 0,0004[2]	4,84 [1,94; 12,09] 0,0002[3]	8,7 [4,0; 13,4] 0,0002[3]
IIIB	18/18 (100,0)	13/15 (86,7)	1,15 [0,92; 1,44] 0,2090[2]	6,85 [0,30; 154,61] 0,1989[4]	13,3 [-3,9; 30,5] 0,1989[4]
IIIC	183/186 (98,4)	143/174 (82,2)	1,20 [1,11; 1,29] <,0001[2]	13,22 [3,96; 44,13] <,0001[3]	16,2 [10,2; 22,2] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,0588)					

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
G1	46/47 (97,9)	36/41 (87,8)	1,11 [0,99; 1,26] 0,0802[2]	6,39 [0,71; 57,14] 0,0931[4]	10,1 [-0,8; 20,9] 0,0931[4]
G2	238/244 (97,5)	201/234 (85,9)	1,14 [1,07; 1,20] <,0001[2]	6,51 [2,67; 15,86] <,0001[3]	11,6 [6,8; 16,5] <,0001[3]
G3	231/233 (99,1)	195/226 (86,3)	1,15 [1,09; 1,21] <,0001[2]	18,36 [4,34; 77,70] <,0001[3]	12,9 [8,2; 17,5] <,0001[3]
GX	28/29 (96,6)	32/33 (97,0)	1,00 [0,91; 1,09] 0,9263[2]	0,88 [0,05; 14,65] 1,0000[4]	-0,4 [-9,3; 8,4] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,2057)					
Weiß	317/323 (98,1)	279/324 (86,1)	1,14 [1,09; 1,19] <,0001[2]	8,52 [3,58; 20,28] <,0001[3]	12,0 [8,0; 16,1] <,0001[3]
Asiatisch	196/199 (98,5)	157/180 (87,2)	1,13 [1,07; 1,20] <,0001[2]	9,57 [2,82; 32,46] <,0001[3]	11,3 [6,1; 16,4] <,0001[3]
Andere	18/19 (94,7)	20/21 (95,2)	0,99 [0,86; 1,15] 0,9422[2]	0,90 [0,05; 15,47] 1,0000[4]	-0,5 [-14,1; 13,1] 1,0000[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,9333)					
< 65 Jahre	900/918 (98,0)	828/937 (88,4)	1,11 [1,08; 1,14] <,0001[2]	6,58 [3,96; 10,93] <,0001[3]	9,7 [7,4; 11,9] <,0001[3]
≥ 65 Jahre	360/365 (98,6)	291/328 (88,7)	1,11 [1,07; 1,16] <,0001[2]	9,15 [3,55; 23,59] <,0001[3]	9,9 [6,3; 13,5] <,0001[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,0550)					
Neoadjuvante Chemotherapie	420/430 (97,7)	377/415 (90,8)	1,08 [1,04; 1,11] <,0001[2]	4,23 [2,08; 8,61] <,0001[3]	6,8 [3,7; 10,0] <,0001[3]
Adjuvante Chemotherapie	773/784 (98,6)	677/769 (88,0)	1,12 [1,09; 1,15] <,0001[2]	9,55 [5,07; 18,00] <,0001[3]	10,6 [8,1; 13,0] <,0001[3]
Keine Chemotherapie	67/69 (97,1)	65/81 (80,2)	1,21 [1,08; 1,36] 0,0012[2]	8,25 [1,82; 37,29] 0,0015[3]	16,9 [7,3; 26,4] 0,0015[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,1168)					
< 20 mm	324/331 (97,9)	297/335 (88,7)	1,10 [1,06; 1,15] <,0001[2]	5,92 [2,60; 13,46] <,0001[3]	9,2 [5,5; 13,0] <,0001[3]
≥ 20 bis < 50 mm	636/646 (98,5)	568/653 (87,0)	1,13 [1,10; 1,17] <,0001[2]	9,52 [4,89; 18,51] <,0001[3]	11,5 [8,7; 14,2] <,0001[3]
≥ 50 mm	283/289 (97,9)	242/265 (91,3)	1,07 [1,03; 1,12] 0,0008[2]	4,48 [1,80; 11,19] 0,0005[3]	6,6 [2,8; 10,4] 0,0005[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,4709)					
0-3	420/427 (98,4)	375/418 (89,7)	1,10 [1,06; 1,14] <,0001[2]	6,88 [3,06; 15,48] <,0001[3]	8,6 [5,5; 11,8] <,0001[3]
4-9	536/549 (97,6)	478/542 (88,2)	1,11 [1,07; 1,14] <,0001[2]	5,52 [3,00; 10,15] <,0001[3]	9,4 [6,4; 12,4] <,0001[3]
≥ 10	304/307 (99,0)	266/305 (87,2)	1,14 [1,09; 1,19] <,0001[2]	14,86 [4,54; 48,63] <,0001[3]	11,8 [7,9; 15,7] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,1930)					
IIA	111/113 (98,2)	104/114 (91,2)	1,08 [1,01; 1,15] 0,0195[2]	5,34 [1,14; 24,93] 0,0184[3]	7,0 [1,3; 12,7] 0,0184[3]
IIB	149/151 (98,7)	123/136 (90,4)	1,09 [1,03; 1,16] 0,0031[2]	7,87 [1,74; 35,56] 0,0018[3]	8,2 [3,0; 13,5] 0,0018[3]
IIIA	482/495 (97,4)	424/488 (86,9)	1,12 [1,08; 1,16] <,0001[2]	5,60 [3,04; 10,30] <,0001[3]	10,5 [7,2; 13,8] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIB	53/54 (98,1)	43/45 (95,6)	1,03 [0,95; 1,10] 0,4716[2]	2,47 [0,22; 28,11] 0,5894[4]	2,6 [-4,4; 9,6] 0,5894[4]
IIIC	463/468 (98,9)	423/480 (88,1)	1,12 [1,08; 1,16] <,0001[2]	12,48 [4,95; 31,42] <,0001[3]	10,8 [7,8; 13,8] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,1885)					
G1	89/91 (97,8)	83/93 (89,2)	1,10 [1,01; 1,18] 0,0198[2]	5,36 [1,14; 25,19] 0,0188[3]	8,6 [1,6; 15,5] 0,0188[3]
G2	600/612 (98,0)	543/603 (90,0)	1,09 [1,06; 1,12] <,0001[2]	5,52 [2,94; 10,38] <,0001[3]	8,0 [5,4; 10,6] <,0001[3]
G3	519/527 (98,5)	442/506 (87,4)	1,13 [1,09; 1,17] <,0001[2]	9,39 [4,46; 19,80] <,0001[3]	11,1 [8,1; 14,2] <,0001[3]
GX	50/51 (98,0)	47/59 (79,7)	1,23 [1,08; 1,41] 0,0025[2]	12,77 [1,60; 102,03] 0,0029[3]	18,4 [7,4; 29,3] 0,0029[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,3333)					
Negativ	154/156 (98,7)	155/169 (91,7)	1,08 [1,03; 1,13] 0,0031[2]	6,95 [1,55; 31,12] 0,0036[3]	7,0 [2,5; 11,5] 0,0036[3]
Positiv	1070/1089 (98,3)	937/1067 (87,8)	1,12 [1,09; 1,15] <,0001[2]	7,81 [4,79; 12,74] <,0001[3]	10,4 [8,3; 12,6] <,0001[3]
Unbekannt	9/10 (90,0)	5/7 (71,4)	1,26 [0,76; 2,10] 0,3764[2]	3,60 [0,26; 50,33] 0,5368[4]	18,6 [-19,7; 56,9] 0,5368[4]
Ethnizität (p-Wert des Interaktionsterms: 0,5520)					
Weiß	940/958 (98,1)	834/944 (88,3)	1,11 [1,08; 1,14] <,0001[2]	6,89 [4,15; 11,44] <,0001[3]	9,8 [7,6; 12,0] <,0001[3]
Asiatisch	246/250 (98,4)	212/242 (87,6)	1,12 [1,07; 1,18] <,0001[2]	8,70 [3,02; 25,10] <,0001[3]	10,8 [6,4; 15,2] <,0001[3]
Andere	61/62 (98,4)	59/64 (92,2)	1,07 [0,99; 1,15] 0,1025[2]	5,17 [0,59; 45,58] 0,2078[4]	6,2 [-1,1; 13,5] 0,2078[4]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,2246)					
Tamoxifen	113/114 (99,1)	113/132 (85,6)	1,16 [1,08; 1,24] <,0001[2]	19,00 [2,50; 144,34] 0,0001[3]	13,5 [7,3; 19,7] 0,0001[3]
Aromatase-Inhibitor	1147/1169 (98,1)	1006/1133 (88,8)	1,11 [1,08; 1,13] <,0001[2]	6,58 [4,15; 10,43] <,0001[3]	9,3 [7,3; 11,3] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,9243)					
ECOG-PS 0	1051/1070 (98,2)	902/1020 (88,4)	1,11 [1,08; 1,14] <,0001[2]	7,24 [4,42; 11,84] <,0001[3]	9,8 [7,7; 11,9] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 1	209/213 (98,1)	217/245 (88,6)	1,11 [1,06; 1,16] <,0001[2]	6,74 [2,32; 19,55] <,0001[3]	9,6 [5,2; 13,9] <,0001[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Schwerwiegendes unerwünschtes Ereignis aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9979)					
Neoadjuvante Chemotherapie	23/217 (10,6)	15/219 (6,8)	1,55 [0,83; 2,88] 0,1694[2]	1,61 [0,82; 3,18] 0,1652[3]	3,7 [-1,5; 9,0] 0,1652[3]
Adjuvante Chemotherapie	38/327 (11,6)	24/312 (7,7)	1,51 [0,93; 2,46] 0,0968[2]	1,58 [0,92; 2,70] 0,0935[3]	3,9 [-0,6; 8,5] 0,0935[3]
Keine Chemotherapie	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (p-Wert des Interaktionsterms: 0,5835)					
Nordamerika / Europa	32/252 (12,7)	22/233 (9,4)	1,34 [0,81; 2,25] 0,2574[2]	1,40 [0,79; 2,48] 0,2547[3]	3,3 [-2,3; 8,8] 0,2547[3]
Asien	18/168 (10,7)	8/166 (4,8)	2,22 [0,99; 4,97] 0,0517[2]	2,37 [1,00; 5,61] 0,0444[3]	5,9 [0,2; 11,6] 0,0444[3]
Andere	13/133 (9,8)	9/136 (6,6)	1,48 [0,65; 3,34] 0,3486[2]	1,53 [0,63; 3,71] 0,3449[3]	3,2 [-3,4; 9,7] 0,3449[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6549)					
< 20 mm	16/141 (11,3)	13/140 (9,3)	1,22 [0,61; 2,44] 0,5709[2]	1,25 [0,58; 2,71] 0,5700[3]	2,1 [-5,0; 9,2] 0,5700[3]
≥ 20 bis < 50 mm	25/255 (9,8)	13/249 (5,2)	1,88 [0,98; 3,59] 0,0563[2]	1,97 [0,99; 3,95] 0,0514[3]	4,6 [0,0; 9,2] 0,0514[3]
≥ 50 mm	21/145 (14,5)	12/141 (8,5)	1,70 [0,87; 3,33] 0,1201[2]	1,82 [0,86; 3,86] 0,1140[3]	6,0 [-1,4; 13,3] 0,1140[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7341)					
0-3	26/203 (12,8)	16/214 (7,5)	1,71 [0,95; 3,10] 0,0749[2]	1,82 [0,94; 3,50] 0,0706[3]	5,3 [-0,5; 11,1] 0,0706[3]
4-9	26/242 (10,7)	15/231 (6,5)	1,65 [0,90; 3,04] 0,1053[2]	1,73 [0,89; 3,36] 0,1005[3]	4,3 [-0,8; 9,3] 0,1005[3]
≥ 10	11/108 (10,2)	8/90 (8,9)	1,15 [0,48; 2,73] 0,7582[2]	1,16 [0,45; 3,03] 0,7578[3]	1,3 [-6,9; 9,5] 0,7578[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,3162)					
IIA	3/59 (5,1)	5/62 (8,1)	0,63 [0,16; 2,52] 0,5143[2]	0,61 [0,14; 2,68] 0,7178[4]	-3,0 [-11,8; 5,8] 0,7178[4]
IIB	2/53 (3,8)	3/69 (4,3)	0,87 [0,15; 5,01] 0,8742[2]	0,86 [0,14; 5,36] 1,0000[4]	-0,6 [-7,6; 6,5] 1,0000[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	33/236 (14,0)	12/214 (5,6)	2,49 [1,32; 4,70] 0,0047[2]	2,74 [1,37; 5,45] 0,0031[3]	8,4 [3,0; 13,8] 0,0031[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	24/186 (12,9)	18/174 (10,3)	1,25 [0,70; 2,22] 0,4514[2]	1,28 [0,67; 2,46] 0,4499[3]	2,6 [-4,1; 9,2] 0,4499[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,9737)					
G1	7/47 (14,9)	3/41 (7,3)	2,04 [0,56; 7,36] 0,2787[2]	2,22 [0,53; 9,20] 0,3267[4]	7,6 [-5,4; 20,5] 0,3267[4]
G2	29/244 (11,9)	19/234 (8,1)	1,46 [0,84; 2,54] 0,1745[2]	1,53 [0,83; 2,81] 0,1709[3]	3,8 [-1,6; 9,1] 0,1709[3]
G3	26/233 (11,2)	17/226 (7,5)	1,48 [0,83; 2,66] 0,1851[2]	1,54 [0,81; 2,93] 0,1813[3]	3,6 [-1,7; 8,9] 0,1813[3]
GX	1/29 (3,4)	0/33 (0,0)	3,40 [0,14; 80,36] 0,4482[2]	3,53 [0,14; 89,98] 0,4677[4]	3,4 [-3,2; 10,1] 0,4677[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,8124)					
Negativ	8/49 (16,3)	6/44 (13,6)	1,20 [0,45; 3,18] 0,7180[2]	1,24 [0,39; 3,89] 0,7172[3]	2,7 [-11,8; 17,2] 0,7172[3]
Positiv	50/477 (10,5)	29/471 (6,2)	1,70 [1,10; 2,64] 0,0176[2]	1,78 [1,11; 2,87] 0,0160[3]	4,3 [0,8; 7,8] 0,0160[3]
Unbekannt	0/4 (0,0)	1/8 (12,5)	0,60 [0,03; 12,15] 0,7393[2]	0,56 [0,02; 16,77] 1,0000[4]	-12,5 [-35,4; 10,4] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,1784)					
Weiß	34/323 (10,5)	29/324 (9,0)	1,18 [0,73; 1,88] 0,4997[2]	1,20 [0,71; 2,02] 0,4991[3]	1,6 [-3,0; 6,1] 0,4991[3]
Asiatisch	23/199 (11,6)	8/180 (4,4)	2,60 [1,19; 5,67] 0,0162[2]	2,81 [1,22; 6,45] 0,0116[3]	7,1 [1,7; 12,5] 0,0116[3]
Andere	3/19 (15,8)	1/21 (4,8)	3,32 [0,38; 29,23] 0,2804[2]	3,75 [0,36; 39,59] 0,3306[4]	11,0 [-7,7; 29,8] 0,3306[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,2996)					
ECOG-PS 0	56/496 (11,3)	37/480 (7,7)	1,46 [0,99; 2,18] 0,0588[2]	1,52 [0,99; 2,36] 0,0567[3]	3,6 [-0,1; 7,2] 0,0567[3]
ECOG-PS 1	7/57 (12,3)	2/55 (3,6)	3,38 [0,73; 15,55] 0,1183[2]	3,71 [0,74; 18,71] 0,1624[4]	8,6 [-1,2; 18,5] 0,1624[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko					

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Tabelle: Subgruppen - Schwerwiegendes unerwünschtes Ereignis aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,9097)					
< 65 Jahre	123/918 (13,4)	80/937 (8,5)	1,57 [1,20; 2,05] 0,0009[2]	1,66 [1,23; 2,23] 0,0008[3]	4,9 [2,0; 7,7] 0,0008[3]
≥ 65 Jahre	77/365 (21,1)	43/328 (13,1)	1,61 [1,14; 2,27] 0,0064[2]	1,77 [1,18; 2,66] 0,0055[3]	8,0 [2,4; 13,5] 0,0055[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9902)					
Neoadjuvante Chemotherapie	68/430 (15,8)	41/415 (9,9)	1,60 [1,11; 2,30] 0,0112[2]	1,71 [1,13; 2,59] 0,0101[3]	5,9 [1,4; 10,4] 0,0101[3]
Adjuvante Chemotherapie	119/784 (15,2)	73/769 (9,5)	1,60 [1,22; 2,10] 0,0008[2]	1,71 [1,25; 2,33] 0,0007[3]	5,7 [2,4; 8,9] 0,0007[3]
Keine Chemotherapie	13/69 (18,8)	9/81 (11,1)	1,70 [0,77; 3,72] 0,1884[2]	1,86 [0,74; 4,65] 0,1823[3]	7,7 [-3,8; 19,2] 0,1823[3]
Region (p-Wert des Interaktionsterms: 0,3370)					
Nordamerika / Europa	116/678 (17,1)	78/650 (12,0)	1,43 [1,09; 1,86] 0,0090[2]	1,51 [1,11; 2,06] 0,0084[3]	5,1 [1,3; 8,9] 0,0084[3]
Asien	36/203 (17,7)	22/201 (10,9)	1,62 [0,99; 2,65] 0,0552[2]	1,75 [0,99; 3,10] 0,0517[3]	6,8 [-0,0; 13,6] 0,0517[3]
Andere	48/402 (11,9)	23/414 (5,6)	2,15 [1,33; 3,47] 0,0017[2]	2,31 [1,37; 3,87] 0,0012[3]	6,4 [2,5; 10,2] 0,0012[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2497)					
< 20 mm	43/331 (13,0)	35/335 (10,4)	1,24 [0,82; 1,89] 0,3088[2]	1,28 [0,80; 2,06] 0,3075[3]	2,5 [-2,3; 7,4] 0,3075[3]
≥ 20 bis < 50 mm	104/646 (16,1)	66/653 (10,1)	1,59 [1,19; 2,13] 0,0016[2]	1,71 [1,23; 2,37] 0,0014[3]	6,0 [2,3; 9,6] 0,0014[3]
≥ 50 mm	51/289 (17,6)	22/265 (8,3)	2,13 [1,33; 3,41] 0,0017[2]	2,37 [1,39; 4,02] 0,0012[3]	9,3 [3,8; 14,9] 0,0012[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,1957)					
0-3	72/427 (16,9)	39/418 (9,3)	1,81 [1,25; 2,60] 0,0015[2]	1,97 [1,30; 2,99] 0,0012[3]	7,5 [3,0; 12,0] 0,0012[3]
4-9	69/549 (12,6)	54/542 (10,0)	1,26 [0,90; 1,76] 0,1751[2]	1,30 [0,89; 1,90] 0,1737[3]	2,6 [-1,1; 6,4] 0,1737[3]
≥ 10	59/307 (19,2)	30/305 (9,8)	1,95 [1,30; 2,94] 0,0014[2]	2,18 [1,36; 3,50] 0,0010[3]	9,4 [3,9; 14,9] 0,0010[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Tumorstadium (p-Wert des Interaktionsterms: 0,5134)					
IIA	14/113 (12,4)	13/114 (11,4)	1,09 [0,53; 2,21] 0,8186[2]	1,10 [0,49; 2,46] 0,8185[3]	1,0 [-7,4; 9,4] 0,8185[3]
IIB	26/151 (17,2)	12/136 (8,8)	1,95 [1,03; 3,71] 0,0417[2]	2,15 [1,04; 4,45] 0,0362[3]	8,4 [0,7; 16,1] 0,0362[3]
IIIA	75/495 (15,2)	46/488 (9,4)	1,61 [1,14; 2,27] 0,0070[2]	1,72 [1,16; 2,54] 0,0063[3]	5,7 [1,6; 9,8] 0,0063[3]
IIIB	6/54 (11,1)	6/45 (13,3)	0,83 [0,29; 2,41] 0,7361[2]	0,81 [0,24; 2,72] 0,7359[3]	-2,2 [-15,2; 10,8] 0,7359[3]
IIIC	79/468 (16,9)	46/480 (9,6)	1,76 [1,25; 2,48] 0,0011[2]	1,92 [1,30; 2,83] 0,0009[3]	7,3 [3,0; 11,6] 0,0009[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,6433)					
G1	16/91 (17,6)	15/93 (16,1)	1,09 [0,57; 2,07] 0,7924[2]	1,11 [0,51; 2,40] 0,7923[3]	1,5 [-9,4; 12,3] 0,7923[3]
G2	102/612 (16,7)	59/603 (9,8)	1,70 [1,26; 2,30] 0,0005[2]	1,84 [1,31; 2,60] 0,0004[3]	6,9 [3,1; 10,7] 0,0004[3]
G3	74/527 (14,0)	43/506 (8,5)	1,65 [1,16; 2,36] 0,0056[2]	1,76 [1,18; 2,62] 0,0049[3]	5,5 [1,7; 9,4] 0,0049[3]
GX	7/51 (13,7)	6/59 (10,2)	1,35 [0,48; 3,76] 0,5660[2]	1,41 [0,44; 4,49] 0,5645[3]	3,6 [-8,6; 15,7] 0,5645[3]
Ethnizität (p-Wert des Interaktionsterms: 0,8090)					
Weiß	148/958 (15,4)	92/944 (9,7)	1,59 [1,24; 2,02] 0,0002[2]	1,69 [1,28; 2,23] 0,0002[3]	5,7 [2,7; 8,7] 0,0002[3]
Asiatisch	42/250 (16,8)	25/242 (10,3)	1,63 [1,02; 2,58] 0,0393[2]	1,75 [1,03; 2,98] 0,0365[3]	6,5 [0,5; 12,5] 0,0365[3]
Andere	9/62 (14,5)	4/64 (6,3)	2,32 [0,75; 7,15] 0,1420[2]	2,55 [0,74; 8,75] 0,1273[3]	8,3 [-2,3; 18,9] 0,1273[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,1185)					
Tamoxifen	20/114 (17,5)	8/132 (6,1)	2,89 [1,33; 6,32] 0,0076[2]	3,30 [1,39; 7,81] 0,0047[3]	11,5 [3,4; 19,6] 0,0047[3]
Aromatase-Inhibitor	180/1169 (15,4)	115/1133 (10,2)	1,52 [1,22; 1,89] 0,0002[2]	1,61 [1,25; 2,07] 0,0002[3]	5,2 [2,5; 8,0] 0,0002[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,1262)					
ECOG-PS 0	149/1070 (13,9)	96/1020 (9,4)	1,48 [1,16; 1,88] 0,0015[2]	1,56 [1,19; 2,04] 0,0013[3]	4,5 [1,8; 7,3] 0,0013[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 1	51/213 (23,9)	27/245 (11,0)	2,17 [1,42; 3,34] 0,0004[2]	2,54 [1,53; 4,23] 0,0002[3]	12,9 [6,0; 19,9] 0,0002[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3 aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,5285)					
Neoadjuvante Chemotherapie	106/217 (48,8)	38/219 (17,4)	2,82 [2,05; 3,87] <,0001[2]	4,55 [2,93; 7,06] <,0001[3]	31,5 [23,2; 39,8] <,0001[3]
Adjuvante Chemotherapie	135/327 (41,3)	35/312 (11,2)	3,68 [2,63; 5,16] <,0001[2]	5,56 [3,68; 8,43] <,0001[3]	30,1 [23,7; 36,4] <,0001[3]
Keine Chemotherapie	3/9 (33,3)	0/4 (0,0)	3,50 [0,22; 55,40] 0,3740[2]	4,85 [0,20; 118,61] 0,4965[4]	33,3 [2,5; 64,1] 0,4965[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,0990)					
< 20 mm	66/141 (46,8)	22/140 (15,7)	2,98 [1,95; 4,54] <,0001[2]	4,72 [2,69; 8,29] <,0001[3]	31,1 [20,9; 41,3] <,0001[3]
≥ 20 bis < 50 mm	111/255 (43,5)	25/249 (10,0)	4,34 [2,91; 6,45] <,0001[2]	6,91 [4,27; 11,18] <,0001[3]	33,5 [26,4; 40,6] <,0001[3]
≥ 50 mm	63/145 (43,4)	26/141 (18,4)	2,36 [1,59; 3,49] <,0001[2]	3,40 [1,99; 5,82] <,0001[3]	25,0 [14,7; 35,3] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8318)					
0-3	98/203 (48,3)	32/214 (15,0)	3,23 [2,28; 4,58] <,0001[2]	5,31 [3,33; 8,46] <,0001[3]	33,3 [25,0; 41,7] <,0001[3]
4-9	96/242 (39,7)	30/231 (13,0)	3,05 [2,11; 4,41] <,0001[2]	4,41 [2,78; 6,99] <,0001[3]	26,7 [19,1; 34,2] <,0001[3]
≥ 10	50/108 (46,3)	11/90 (12,2)	3,79 [2,10; 6,83] <,0001[2]	6,19 [2,97; 12,92] <,0001[3]	34,1 [22,5; 45,7] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,8772)					
IIA	31/59 (52,5)	10/62 (16,1)	3,26 [1,76; 6,04] 0,0002[2]	5,76 [2,47; 13,44] <,0001[3]	36,4 [20,7; 52,1] <,0001[3]
IIB	25/53 (47,2)	13/69 (18,8)	2,50 [1,42; 4,41] 0,0015[2]	3,85 [1,71; 8,64] 0,0008[3]	28,3 [12,0; 44,6] 0,0008[3]
IIIA	92/236 (39,0)	28/214 (13,1)	2,98 [2,04; 4,36] <,0001[2]	4,24 [2,64; 6,83] <,0001[3]	25,9 [18,2; 33,6] <,0001[3]
IIIB	9/18 (50,0)	0/15 (0,0)	16,00 [1,01; 254,05] 0,0494[2]	31,00 [1,61; 596,00] 0,0014[4]	50,0 [26,9; 73,1] 0,0014[4]
IIIC	86/186 (46,2)	22/174 (12,6)	3,66 [2,40; 5,57] <,0001[2]	5,94 [3,49; 10,11] <,0001[3]	33,6 [24,9; 42,3] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,6398)					

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
G1	23/47 (48,9)	7/41 (17,1)	2,87 [1,37; 5,98] 0,0050[2]	4,65 [1,72; 12,58] 0,0017[3]	31,9 [13,5; 50,2] 0,0017[3]
G2	104/244 (42,6)	35/234 (15,0)	2,85 [2,03; 4,00] <,0001[2]	4,22 [2,72; 6,56] <,0001[3]	27,7 [20,0; 35,4] <,0001[3]
G3	106/233 (45,5)	29/226 (12,8)	3,55 [2,45; 5,12] <,0001[2]	5,67 [3,55; 9,05] <,0001[3]	32,7 [24,9; 40,4] <,0001[3]
GX	11/29 (37,9)	2/33 (6,1)	6,26 [1,51; 25,94] 0,0115[2]	9,47 [1,88; 47,61] 0,0021[3]	31,9 [12,4; 51,3] 0,0021[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,3732)					
Negativ	26/49 (53,1)	9/44 (20,5)	2,59 [1,37; 4,92] 0,0035[2]	4,40 [1,75; 11,06] 0,0012[3]	32,6 [14,2; 51,0] 0,0012[3]
Positiv	208/477 (43,6)	59/471 (12,5)	3,48 [2,69; 4,51] <,0001[2]	5,40 [3,89; 7,49] <,0001[3]	31,1 [25,7; 36,4] <,0001[3]
Unbekannt	1/4 (25,0)	2/8 (25,0)	1,00 [0,13; 8,00] 1,0000[2]	1,00 [0,06; 15,99] 1,0000[4]	0,0 [-52,0; 52,0] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,0994)					
Weiß	138/323 (42,7)	51/324 (15,7)	2,71 [2,05; 3,60] <,0001[2]	3,99 [2,75; 5,79] <,0001[3]	27,0 [20,3; 33,7] <,0001[3]
Asiatisch	91/199 (45,7)	17/180 (9,4)	4,84 [3,01; 7,80] <,0001[2]	8,08 [4,56; 14,32] <,0001[3]	36,3 [28,2; 44,4] <,0001[3]
Andere	8/19 (42,1)	4/21 (19,0)	2,21 [0,79; 6,18] 0,1302[2]	3,09 [0,75; 12,78] 0,1120[3]	23,1 [-4,8; 50,9] 0,1120[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,7785)					
ECOG-PS 0	225/496 (45,4)	68/480 (14,2)	3,20 [2,52; 4,07] <,0001[2]	5,03 [3,68; 6,87] <,0001[3]	31,2 [25,8; 36,6] <,0001[3]
ECOG-PS 1	19/57 (33,3)	5/55 (9,1)	3,67 [1,47; 9,13] 0,0053[2]	5,00 [1,71; 14,60] 0,0018[3]	24,2 [9,8; 38,6] 0,0018[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3 aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,1017)					
< 65 Jahre	445/918 (48,5)	142/937 (15,2)	3,20 [2,71; 3,77] <,0001[2]	5,27 [4,22; 6,57] <,0001[3]	33,3 [29,4; 37,3] <,0001[3]
≥ 65 Jahre	200/365 (54,8)	71/328 (21,6)	2,53 [2,02; 3,17] <,0001[2]	4,39 [3,14; 6,13] <,0001[3]	33,1 [26,4; 39,9] <,0001[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7405)					
Neoadjuvante Chemotherapie	233/430 (54,2)	70/415 (16,9)	3,21 [2,55; 4,05] <,0001[2]	5,83 [4,24; 8,02] <,0001[3]	37,3 [31,4; 43,2] <,0001[3]
Adjuvante Chemotherapie	378/784 (48,2)	129/769 (16,8)	2,87 [2,42; 3,42] <,0001[2]	4,62 [3,65; 5,84] <,0001[3]	31,4 [27,1; 35,8] <,0001[3]
Keine Chemotherapie	34/69 (49,3)	14/81 (17,3)	2,85 [1,67; 4,86] 0,0001[2]	4,65 [2,21; 9,79] <,0001[3]	32,0 [17,6; 46,4] <,0001[3]
Region (p-Wert des Interaktionsterms: 0,1677)					
Nordamerika / Europa	334/678 (49,3)	121/650 (18,6)	2,65 [2,21; 3,16] <,0001[2]	4,24 [3,31; 5,44] <,0001[3]	30,6 [25,8; 35,5] <,0001[3]
Asien	124/203 (61,1)	35/201 (17,4)	3,51 [2,55; 4,83] <,0001[2]	7,44 [4,69; 11,80] <,0001[3]	43,7 [35,2; 52,2] <,0001[3]
Andere	187/402 (46,5)	57/414 (13,8)	3,38 [2,60; 4,39] <,0001[2]	5,45 [3,87; 7,66] <,0001[3]	32,7 [26,9; 38,6] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,5510)					
< 20 mm	154/331 (46,5)	56/335 (16,7)	2,78 [2,13; 3,63] <,0001[2]	4,33 [3,03; 6,21] <,0001[3]	29,8 [23,1; 36,5] <,0001[3]
≥ 20 bis < 50 mm	329/646 (50,9)	114/653 (17,5)	2,92 [2,43; 3,50] <,0001[2]	4,91 [3,81; 6,33] <,0001[3]	33,5 [28,6; 38,3] <,0001[3]
≥ 50 mm	154/289 (53,3)	41/265 (15,5)	3,44 [2,55; 4,66] <,0001[2]	6,23 [4,16; 9,35] <,0001[3]	37,8 [30,6; 45,0] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9181)					
0-3	218/427 (51,1)	69/418 (16,5)	3,09 [2,45; 3,91] <,0001[2]	5,28 [3,83; 7,27] <,0001[3]	34,5 [28,6; 40,5] <,0001[3]
4-9	258/549 (47,0)	88/542 (16,2)	2,89 [2,34; 3,57] <,0001[2]	4,57 [3,45; 6,07] <,0001[3]	30,8 [25,6; 36,0] <,0001[3]
≥ 10	169/307 (55,0)	56/305 (18,4)	3,00 [2,32; 3,88] <,0001[2]	5,45 [3,77; 7,86] <,0001[3]	36,7 [29,6; 43,7] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Tumorstadium (p-Wert des Interaktionsterms: 0,1670)					
IIA	46/113 (40,7)	21/114 (18,4)	2,21 [1,41; 3,45] 0,0005[2]	3,04 [1,66; 5,56] 0,0002[3]	22,3 [10,8; 33,8] 0,0002[3]
IIB	78/151 (51,7)	23/136 (16,9)	3,05 [2,04; 4,57] <,0001[2]	5,25 [3,03; 9,10] <,0001[3]	34,7 [24,6; 44,9] <,0001[3]
IIIA	237/495 (47,9)	75/488 (15,4)	3,12 [2,48; 3,91] <,0001[2]	5,06 [3,74; 6,85] <,0001[3]	32,5 [27,1; 38,0] <,0001[3]
IIIB	24/54 (44,4)	12/45 (26,7)	1,67 [0,94; 2,94] 0,0784[2]	2,20 [0,94; 5,15] 0,0671[3]	17,8 [-0,7; 36,3] 0,0671[3]
IIIC	259/468 (55,3)	82/480 (17,1)	3,24 [2,62; 4,01] <,0001[2]	6,01 [4,46; 8,12] <,0001[3]	38,3 [32,6; 43,9] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,7759)					
G1	48/91 (52,7)	18/93 (19,4)	2,73 [1,72; 4,31] <,0001[2]	4,65 [2,41; 8,99] <,0001[3]	33,4 [20,4; 46,4] <,0001[3]
G2	305/612 (49,8)	97/603 (16,1)	3,10 [2,54; 3,78] <,0001[2]	5,18 [3,96; 6,78] <,0001[3]	33,8 [28,8; 38,7] <,0001[3]
G3	265/527 (50,3)	85/506 (16,8)	2,99 [2,42; 3,70] <,0001[2]	5,01 [3,75; 6,69] <,0001[3]	33,5 [28,1; 38,9] <,0001[3]
GX	26/51 (51,0)	13/59 (22,0)	2,31 [1,33; 4,01] 0,0028[2]	3,68 [1,61; 8,40] 0,0016[3]	28,9 [11,6; 46,3] 0,0016[3]
Ethnizität (p-Wert des Interaktionsterms: 0,2110)					
Weiß	468/958 (48,9)	160/944 (16,9)	2,88 [2,47; 3,37] <,0001[2]	4,68 [3,79; 5,79] <,0001[3]	31,9 [27,9; 35,9] <,0001[3]
Asiatisch	141/250 (56,4)	36/242 (14,9)	3,79 [2,75; 5,22] <,0001[2]	7,40 [4,80; 11,42] <,0001[3]	41,5 [33,9; 49,1] <,0001[3]
Andere	32/62 (51,6)	14/64 (21,9)	2,36 [1,40; 3,98] 0,0013[2]	3,81 [1,76; 8,26] 0,0005[3]	29,7 [13,7; 45,8] 0,0005[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,9238)					
ECOG-PS 0	529/1070 (49,4)	169/1020 (16,6)	2,98 [2,57; 3,47] <,0001[2]	4,92 [4,02; 6,04] <,0001[3]	32,9 [29,1; 36,6] <,0001[3]
ECOG-PS 1	116/213 (54,5)	44/245 (18,0)	3,03 [2,26; 4,07] <,0001[2]	5,46 [3,58; 8,34] <,0001[3]	36,5 [28,3; 44,7] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko					

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3 aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Region (p-Wert des Interaktionsterms: 0,4073)					
Nordamerika / Europa	249/252 (98,8)	206/233 (88,4)	1,12 [1,06; 1,17] <,0001[2]	10,88 [3,25; 36,37] <,0001[3]	10,4 [6,1; 14,7] <,0001[3]
Asien	166/168 (98,8)	148/166 (89,2)	1,11 [1,05; 1,17] 0,0003[2]	10,09 [2,30; 44,24] 0,0002[3]	9,7 [4,6; 14,7] 0,0002[3]
Andere	125/133 (94,0)	107/136 (78,7)	1,19 [1,08; 1,32] 0,0004[2]	4,23 [1,86; 9,66] 0,0003[3]	15,3 [7,3; 23,3] 0,0003[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,7437)					
< 20 mm	137/141 (97,2)	123/140 (87,9)	1,11 [1,03; 1,18] 0,0036[2]	4,73 [1,55; 14,45] 0,0030[3]	9,3 [3,2; 15,4] 0,0030[3]
≥ 20 bis < 50 mm	248/255 (97,3)	212/249 (85,1)	1,14 [1,08; 1,21] <,0001[2]	6,18 [2,70; 14,16] <,0001[3]	12,1 [7,3; 17,0] <,0001[3]
≥ 50 mm	143/145 (98,6)	122/141 (86,5)	1,14 [1,06; 1,22] 0,0002[2]	11,14 [2,54; 48,77] <,0001[3]	12,1 [6,1; 18,0] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9181)					
0-3	202/203 (99,5)	188/214 (87,9)	1,13 [1,08; 1,19] <,0001[2]	27,94 [3,75; 207,90] <,0001[3]	11,7 [7,2; 16,1] <,0001[3]
4-9	234/242 (96,7)	198/231 (85,7)	1,13 [1,06; 1,19] <,0001[2]	4,88 [2,20; 10,80] <,0001[3]	11,0 [5,9; 16,0] <,0001[3]
≥ 10	104/108 (96,3)	75/90 (83,3)	1,16 [1,05; 1,28] 0,0044[2]	5,20 [1,66; 16,29] 0,0020[3]	13,0 [4,5; 21,4] 0,0020[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,2147)					
IIA	58/59 (98,3)	55/62 (88,7)	1,11 [1,01; 1,22] 0,0339[2]	7,38 [0,88; 61,96] 0,0620[4]	9,6 [1,1; 18,1] 0,0620[4]
IIB	53/53 (100,0)	61/69 (88,4)	1,13 [1,03; 1,23] 0,0095[2]	14,79 [0,83; 262,29] 0,0096[4]	11,6 [4,0; 19,1] 0,0096[4]
IIIA	228/236 (96,6)	188/214 (87,9)	1,10 [1,04; 1,16] 0,0007[2]	3,94 [1,74; 8,91] 0,0004[3]	8,8 [3,8; 13,7] 0,0004[3]
IIIB	18/18 (100,0)	13/15 (86,7)	1,15 [0,92; 1,44] 0,2090[2]	6,85 [0,30; 154,61] 0,1989[4]	13,3 [-3,9; 30,5] 0,1989[4]
IIIC	182/186 (97,8)	143/174 (82,2)	1,19 [1,11; 1,28] <,0001[2]	9,86 [3,40; 28,59] <,0001[3]	15,7 [9,6; 21,7] <,0001[3]
Ethnizität (p-Wert des Interaktionsterms: 0,1727)					

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Weiß	316/323 (97,8)	276/324 (85,2)	1,15 [1,09; 1,21] <,0001[2]	7,85 [3,50; 17,63] <,0001[3]	12,6 [8,5; 16,8] <,0001[3]
Asiatisch	194/199 (97,5)	156/180 (86,7)	1,12 [1,06; 1,20] 0,0002[2]	5,97 [2,23; 16,01] <,0001[3]	10,8 [5,4; 16,2] <,0001[3]
Andere	18/19 (94,7)	20/21 (95,2)	0,99 [0,86; 1,15] 0,9422[2]	0,90 [0,05; 15,47] 1,0000[4]	-0,5 [-14,1; 13,1] 1,0000[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3 aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,9628)					
< 65 Jahre	894/918 (97,4)	823/937 (87,8)	1,11 [1,08; 1,14] <,0001[2]	5,16 [3,29; 8,09] <,0001[3]	9,6 [7,2; 11,9] <,0001[3]
≥ 65 Jahre	357/365 (97,8)	289/328 (88,1)	1,11 [1,06; 1,16] <,0001[2]	6,02 [2,77; 13,09] <,0001[3]	9,7 [5,9; 13,5] <,0001[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,0585)					
Neoadjuvante Chemotherapie	416/430 (96,7)	375/415 (90,4)	1,07 [1,03; 1,11] 0,0002[2]	3,17 [1,70; 5,92] 0,0001[3]	6,4 [3,1; 9,7] 0,0001[3]
Adjuvante Chemotherapie	769/784 (98,1)	672/769 (87,4)	1,12 [1,09; 1,15] <,0001[2]	7,40 [4,25; 12,87] <,0001[3]	10,7 [8,2; 13,2] <,0001[3]
Keine Chemotherapie	66/69 (95,7)	65/81 (80,2)	1,19 [1,06; 1,34] 0,0039[2]	5,42 [1,51; 19,47] 0,0047[3]	15,4 [5,5; 25,3] 0,0047[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,0841)					
< 20 mm	322/331 (97,3)	294/335 (87,8)	1,11 [1,06; 1,16] <,0001[2]	4,99 [2,38; 10,44] <,0001[3]	9,5 [5,6; 13,4] <,0001[3]
≥ 20 bis < 50 mm	631/646 (97,7)	564/653 (86,4)	1,13 [1,09; 1,17] <,0001[2]	6,64 [3,80; 11,61] <,0001[3]	11,3 [8,4; 14,2] <,0001[3]
≥ 50 mm	281/289 (97,2)	242/265 (91,3)	1,06 [1,02; 1,11] 0,0034[2]	3,34 [1,47; 7,60] 0,0025[3]	5,9 [2,0; 9,8] 0,0025[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,1819)					
0-3	415/427 (97,2)	374/418 (89,5)	1,09 [1,05; 1,13] <,0001[2]	4,07 [2,12; 7,82] <,0001[3]	7,7 [4,4; 11,0] <,0001[3]
4-9	533/549 (97,1)	476/542 (87,8)	1,11 [1,07; 1,14] <,0001[2]	4,62 [2,64; 8,09] <,0001[3]	9,3 [6,2; 12,4] <,0001[3]
≥ 10	303/307 (98,7)	262/305 (85,9)	1,15 [1,10; 1,20] <,0001[2]	12,43 [4,40; 35,10] <,0001[3]	12,8 [8,7; 16,9] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,2846)					
IIA	109/113 (96,5)	104/114 (91,2)	1,06 [0,99; 1,13] 0,1028[2]	2,62 [0,80; 8,61] 0,1013[3]	5,2 [-1,0; 11,4] 0,1013[3]
IIB	147/151 (97,4)	122/136 (89,7)	1,09 [1,02; 1,16] 0,0106[2]	4,22 [1,35; 13,14] 0,0076[3]	7,6 [1,9; 13,4] 0,0076[3]
IIIA	478/495 (96,6)	423/488 (86,7)	1,11 [1,07; 1,16] <,0001[2]	4,32 [2,49; 7,49] <,0001[3]	9,9 [6,5; 13,3] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIB	53/54 (98,1)	42/45 (93,3)	1,05 [0,96; 1,15] 0,2530[2]	3,79 [0,38; 37,73] 0,3271[4]	4,8 [-3,3; 12,9] 0,3271[4]
IIIC	462/468 (98,7)	419/480 (87,3)	1,13 [1,09; 1,17] <,0001[2]	11,21 [4,80; 26,20] <,0001[3]	11,4 [8,3; 14,6] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,0968)					
G1	88/91 (96,7)	82/93 (88,2)	1,10 [1,01; 1,19] 0,0303[2]	3,93 [1,06; 14,61] 0,0291[3]	8,5 [1,0; 16,1] 0,0291[3]
G2	597/612 (97,5)	542/603 (89,9)	1,09 [1,05; 1,12] <,0001[2]	4,48 [2,52; 7,97] <,0001[3]	7,7 [5,0; 10,4] <,0001[3]
G3	514/527 (97,5)	439/506 (86,8)	1,12 [1,08; 1,17] <,0001[2]	6,03 [3,29; 11,08] <,0001[3]	10,8 [7,5; 14,0] <,0001[3]
GX	50/51 (98,0)	45/59 (76,3)	1,29 [1,11; 1,49] 0,0009[2]	15,56 [1,97; 123,07] 0,0009[3]	21,8 [10,3; 33,3] 0,0009[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,6609)					
Negativ	154/156 (98,7)	153/169 (90,5)	1,09 [1,04; 1,15] 0,0011[2]	8,05 [1,82; 35,62] 0,0013[3]	8,2 [3,4; 12,9] 0,0013[3]
Positiv	1061/1089 (97,4)	932/1067 (87,3)	1,12 [1,09; 1,14] <,0001[2]	5,49 [3,62; 8,32] <,0001[3]	10,1 [7,9; 12,3] <,0001[3]
Unbekannt	9/10 (90,0)	5/7 (71,4)	1,26 [0,76; 2,10] 0,3764[2]	3,60 [0,26; 50,33] 0,5368[4]	18,6 [-19,7; 56,9] 0,5368[4]
Ethnizität (p-Wert des Interaktionsterms: 0,3548)					
Weiß	932/958 (97,3)	828/944 (87,7)	1,11 [1,08; 1,14] <,0001[2]	5,02 [3,25; 7,76] <,0001[3]	9,6 [7,2; 11,9] <,0001[3]
Asiatisch	246/250 (98,4)	211/242 (87,2)	1,13 [1,07; 1,19] <,0001[2]	9,04 [3,14; 26,01] <,0001[3]	11,2 [6,7; 15,7] <,0001[3]
Andere	60/62 (96,8)	59/64 (92,2)	1,05 [0,96; 1,14] 0,2605[2]	2,54 [0,47; 13,62] 0,4401[4]	4,6 [-3,3; 12,5] 0,4401[4]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,1470)					
Tamoxifen	113/114 (99,1)	112/132 (84,8)	1,17 [1,08; 1,26] <,0001[2]	20,18 [2,66; 152,92] <,0001[3]	14,3 [7,9; 20,6] <,0001[3]
Aromatase-Inhibitor	1138/1169 (97,3)	1000/1133 (88,3)	1,10 [1,08; 1,13] <,0001[2]	4,88 [3,27; 7,28] <,0001[3]	9,1 [7,0; 11,2] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,7932)					
ECOG-PS 0	1044/1070 (97,6)	896/1020 (87,8)	1,11 [1,08; 1,14] <,0001[2]	5,56 [3,61; 8,56] <,0001[3]	9,7 [7,5; 11,9] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 1	207/213 (97,2)	216/245 (88,2)	1,10 [1,05; 1,16] 0,0002[2]	4,63 [1,88; 11,39] 0,0003[3]	9,0 [4,4; 13,6] 0,0003[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Behandlungsabbruch aufgrund unerwünschter Ereignisse aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,6922)					
Neoadjuvante Chemotherapie	21/217 (9,7)	3/219 (1,4)	7,06 [2,14; 23,34] 0,0013[2]	7,71 [2,27; 26,26] 0,0001[3]	8,3 [4,1; 12,5] 0,0001[3]
Adjuvante Chemotherapie	46/327 (14,1)	3/312 (1,0)	14,63 [4,60; 46,55] <,0001[2]	16,86 [5,19; 54,82] <,0001[3]	13,1 [9,2; 17,0] <,0001[3]
Keine Chemotherapie	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (p-Wert des Interaktionsterms: 0,8591)					
Nordamerika / Europa	42/252 (16,7)	4/233 (1,7)	9,71 [3,54; 26,66] <,0001[2]	11,45 [4,04; 32,48] <,0001[3]	14,9 [10,1; 19,8] <,0001[3]
Asien	18/168 (10,7)	1/166 (0,6)	17,79 [2,40; 131,71] 0,0048[2]	19,80 [2,61; 150,12] <,0001[3]	10,1 [5,3; 14,9] <,0001[3]
Andere	9/133 (6,8)	1/136 (0,7)	9,20 [1,18; 71,64] 0,0340[2]	9,80 [1,22; 78,46] 0,0097[4]	6,0 [1,5; 10,5] 0,0097[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,7231)					
< 20 mm	16/141 (11,3)	2/140 (1,4)	7,94 [1,86; 33,91] 0,0051[2]	8,83 [1,99; 39,18] 0,0007[3]	9,9 [4,3; 15,5] 0,0007[3]
≥ 20 bis < 50 mm	34/255 (13,3)	2/249 (0,8)	16,60 [4,03; 68,36] 0,0001[2]	19,00 [4,51; 80,00] <,0001[3]	12,5 [8,2; 16,8] <,0001[3]
≥ 50 mm	17/145 (11,7)	2/141 (1,4)	8,27 [1,95; 35,12] 0,0042[2]	9,23 [2,09; 40,74] 0,0005[3]	10,3 [4,7; 15,9] 0,0005[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9965)					
0-3	29/203 (14,3)	3/214 (1,4)	10,19 [3,15; 32,93] 0,0001[2]	11,72 [3,51; 39,13] <,0001[3]	12,9 [7,8; 17,9] <,0001[3]
4-9	30/242 (12,4)	3/231 (1,3)	9,55 [2,95; 30,85] 0,0002[2]	10,75 [3,23; 35,76] <,0001[3]	11,1 [6,7; 15,5] <,0001[3]
≥ 10	10/108 (9,3)	0/90 (0,0)	17,53 [1,04; 295,12] 0,0468[2]	19,29 [1,11; 334,01] 0,0022[4]	9,3 [3,8; 14,7] 0,0022[4]
Tumorstadium (p-Wert des Interaktionsterms: 0,8847)					
IIA	7/59 (11,9)	1/62 (1,6)	7,36 [0,93; 57,99] 0,0582[2]	8,21 [0,98; 68,94] 0,0297[4]	10,3 [1,4; 19,1] 0,0297[4]
IIB	9/53 (17,0)	2/69 (2,9)	5,86 [1,32; 25,99] 0,0200[2]	6,85 [1,41; 33,22] 0,0097[4]	14,1 [3,2; 24,9] 0,0097[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	27/236 (11,4)	2/214 (0,9)	12,24 [2,95; 50,87] 0,0006[2]	13,69 [3,22; 58,32] <,0001[3]	10,5 [6,2; 14,8] <,0001[3]
IIIB	3/18 (16,7)	0/15 (0,0)	5,89 [0,33; 105,81] 0,2285[2]	7,00 [0,33; 147,17] 0,2330[4]	16,7 [-0,5; 33,9] 0,2330[4]
IIIC	22/186 (11,8)	1/174 (0,6)	20,58 [2,80; 151,06] 0,0029[2]	23,21 [3,09; 174,14] <,0001[3]	11,3 [6,5; 16,0] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,6338)					
G1	5/47 (10,6)	0/41 (0,0)	9,63 [0,55; 168,96] 0,1214[2]	10,74 [0,58; 200,45] 0,0583[4]	10,6 [1,8; 19,5] 0,0583[4]
G2	34/244 (13,9)	5/234 (2,1)	6,52 [2,60; 16,39] <,0001[2]	7,42 [2,85; 19,31] <,0001[3]	11,8 [7,1; 16,5] <,0001[3]
G3	29/233 (12,4)	1/226 (0,4)	28,13 [3,86; 204,76] 0,0010[2]	31,99 [4,32; 236,92] <,0001[3]	12,0 [7,7; 16,3] <,0001[3]
GX	1/29 (3,4)	0/33 (0,0)	3,40 [0,14; 80,36] 0,4482[2]	3,53 [0,14; 89,98] 0,4677[4]	3,4 [-3,2; 10,1] 0,4677[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,7621)					
Negativ	6/49 (12,2)	1/44 (2,3)	5,39 [0,67; 43,02] 0,1121[2]	6,00 [0,69; 51,96] 0,1146[4]	10,0 [-0,2; 20,2] 0,1146[4]
Positiv	52/477 (10,9)	4/471 (0,8)	12,84 [4,68; 35,21] <,0001[2]	14,28 [5,12; 39,83] <,0001[3]	10,1 [7,1; 13,0] <,0001[3]
Unbekannt	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Ethnizität (p-Wert des Interaktionsterms: 0,8655)					
Weiß	43/323 (13,3)	4/324 (1,2)	10,78 [3,92; 29,69] <,0001[2]	12,29 [4,36; 34,66] <,0001[3]	12,1 [8,2; 16,0] <,0001[3]
Asiatisch	22/199 (11,1)	1/180 (0,6)	19,90 [2,71; 146,14] 0,0033[2]	22,25 [2,97; 166,84] <,0001[3]	10,5 [6,0; 15,0] <,0001[3]
Andere	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,9802)					
ECOG-PS 0	65/496 (13,1)	6/480 (1,3)	10,48 [4,59; 23,97] <,0001[2]	11,91 [5,11; 27,77] <,0001[3]	11,9 [8,7; 15,0] <,0001[3]
ECOG-PS 1	4/57 (7,0)	0/55 (0,0)	8,69 [0,48; 157,70] 0,1437[2]	9,34 [0,49; 177,63] 0,1185[4]	7,0 [0,4; 13,6] 0,1185[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko					

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Tabelle: Subgruppen - Behandlungsabbruch aufgrund unerwünschter Ereignisse aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,1414)					
< 65 Jahre	149/918 (16,2)	5/937 (0,5)	30,42 [12,54; 73,81] <,0001[2]	36,12 [14,74; 88,50] <,0001[3]	15,7 [13,3; 18,1] <,0001[3]
≥ 65 Jahre	133/365 (36,4)	9/328 (2,7)	13,28 [6,87; 25,65] <,0001[2]	20,32 [10,13; 40,75] <,0001[3]	33,7 [28,5; 38,9] <,0001[3]
Region (p-Wert des Interaktionsterms: 0,7141)					
Nordamerika / Europa	181/678 (26,7)	12/650 (1,8)	14,46 [8,14; 25,68] <,0001[2]	19,36 [10,67; 35,14] <,0001[3]	24,9 [21,4; 28,3] <,0001[3]
Asien	48/203 (23,6)	0/201 (0,0)	96,05 [5,96; 1547,07] 0,0013[2]	125,69 [7,69; 2054,44] <,0001[3]	23,6 [17,8; 29,5] <,0001[3]
Andere	53/402 (13,2)	2/414 (0,5)	27,29 [6,70; 111,24] <,0001[2]	31,28 [7,57; 129,29] <,0001[3]	12,7 [9,3; 16,1] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4497)					
< 20 mm	68/331 (20,5)	2/335 (0,6)	34,41 [8,50; 139,25] <,0001[2]	43,05 [10,45; 177,28] <,0001[3]	19,9 [15,5; 24,4] <,0001[3]
≥ 20 bis < 50 mm	144/646 (22,3)	7/653 (1,1)	20,79 [9,82; 44,05] <,0001[2]	26,47 [12,29; 57,03] <,0001[3]	21,2 [17,9; 24,5] <,0001[3]
≥ 50 mm	68/289 (23,5)	5/265 (1,9)	12,47 [5,11; 30,45] <,0001[2]	16,00 [6,34; 40,38] <,0001[3]	21,6 [16,5; 26,8] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,2075)					
IIA	25/113 (22,1)	1/114 (0,9)	25,22 [3,48; 183,00] 0,0014[2]	32,10 [4,27; 241,54] <,0001[3]	21,2 [13,4; 29,1] <,0001[3]
IIB	37/151 (24,5)	2/136 (1,5)	16,66 [4,09; 67,83] <,0001[2]	21,75 [5,13; 92,21] <,0001[3]	23,0 [15,9; 30,2] <,0001[3]
IIIA	117/495 (23,6)	1/488 (0,2)	115,35 [16,18; 822,44] <,0001[2]	150,74 [20,96; 1084,04] <,0001[3]	23,4 [19,7; 27,2] <,0001[3]
IIIB	8/54 (14,8)	1/45 (2,2)	6,67 [0,87; 51,32] 0,0685[2]	7,65 [0,92; 63,72] 0,0374[4]	12,6 [2,2; 23,0] 0,0374[4]
IIIC	95/468 (20,3)	9/480 (1,9)	10,83 [5,53; 21,19] <,0001[2]	13,33 [6,64; 26,76] <,0001[3]	18,4 [14,6; 22,3] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,4311)					

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
G1	18/91 (19,8)	2/93 (2,2)	9,20 [2,20; 38,51] 0,0024[2]	11,22 [2,52; 49,93] 0,0001[3]	17,6 [8,9; 26,3] 0,0001[3]
G2	137/612 (22,4)	4/603 (0,7)	33,75 [12,57; 90,62] <,0001[2]	43,19 [15,87; 117,58] <,0001[3]	21,7 [18,4; 25,1] <,0001[3]
G3	118/527 (22,4)	7/506 (1,4)	16,19 [7,63; 34,35] <,0001[2]	20,57 [9,49; 44,58] <,0001[3]	21,0 [17,3; 24,7] <,0001[3]
GX	9/51 (17,6)	1/59 (1,7)	10,41 [1,37; 79,41] 0,0238[2]	12,43 [1,52; 101,88] 0,0054[4]	16,0 [5,0; 26,9] 0,0054[4]
Ethnizität (p-Wert des Interaktionsterms: 0,8229)					
Weiß	214/958 (22,3)	13/944 (1,4)	16,22 [9,33; 28,19] <,0001[2]	20,60 [11,67; 36,36] <,0001[3]	21,0 [18,2; 23,7] <,0001[3]
Asiatisch	55/250 (22,0)	0/242 (0,0)	107,46 [6,68; 1729,89] 0,0010[2]	137,69 [8,45; 2243,07] <,0001[3]	22,0 [16,9; 27,1] <,0001[3]
Andere	8/62 (12,9)	1/64 (1,6)	8,26 [1,06; 64,10] 0,0435[2]	9,33 [1,13; 77,01] 0,0160[4]	11,3 [2,5; 20,2] 0,0160[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Anhang 4-G2.8.2: Unerwünschte Ereignisse von speziellem Interesse - Subgruppenanalysen

Tabelle 4-130 (Anhang): Unerwünschte Ereignisse von speziellem Interesse - Analyse nicht-interagierender Subgruppen

Tabelle: Subgruppen - Unerwünschtes Ereignis: PT Neutropenie und erniedrigte Neutrophilenzahl (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,1776)					
Neoadjuvante Chemotherapie	82/217 (37,8)	20/219 (9,1)	4,14 [2,63; 6,50] <,0001[2]	6,04 [3,54; 10,32] <,0001[3]	28,7 [21,2; 36,2] <,0001[3]
Adjuvante Chemotherapie	151/327 (46,2)	19/312 (6,1)	7,58 [4,83; 11,91] <,0001[2]	13,23 [7,93; 22,09] <,0001[3]	40,1 [34,1; 46,1] <,0001[3]
Keine Chemotherapie	4/9 (44,4)	0/4 (0,0)	4,50 [0,30; 68,13] 0,2780[2]	7,36 [0,31; 176,41] 0,2280[4]	44,4 [12,0; 76,9] 0,2280[4]
Region (p-Wert des Interaktionsterms: 0,7173)					
Nordamerika / Europa	78/252 (31,0)	11/233 (4,7)	6,56 [3,58; 12,01] <,0001[2]	9,05 [4,67; 17,53] <,0001[3]	26,2 [19,9; 32,6] <,0001[3]
Asien	99/168 (58,9)	19/166 (11,4)	5,15 [3,31; 8,01] <,0001[2]	11,10 [6,29; 19,59] <,0001[3]	47,5 [38,6; 56,4] <,0001[3]
Andere	60/133 (45,1)	9/136 (6,6)	6,82 [3,53; 13,17] <,0001[2]	11,60 [5,44; 24,74] <,0001[3]	38,5 [29,1; 47,9] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4050)					
< 20 mm	56/141 (39,7)	9/140 (6,4)	6,18 [3,18; 12,00] <,0001[2]	9,59 [4,51; 20,40] <,0001[3]	33,3 [24,2; 42,3] <,0001[3]
≥ 20 bis < 50 mm	105/255 (41,2)	21/249 (8,4)	4,88 [3,16; 7,54] <,0001[2]	7,60 [4,56; 12,68] <,0001[3]	32,7 [25,8; 39,7] <,0001[3]
≥ 50 mm	70/145 (48,3)	8/141 (5,7)	8,51 [4,25; 17,03] <,0001[2]	15,52 [7,08; 34,00] <,0001[3]	42,6 [33,6; 51,6] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,3525)					
0-3	85/203 (41,9)	11/214 (5,1)	8,15 [4,48; 14,81] <,0001[2]	13,29 [6,82; 25,92] <,0001[3]	36,7 [29,3; 44,1] <,0001[3]
4-9	104/242 (43,0)	21/231 (9,1)	4,73 [3,07; 7,29] <,0001[2]	7,54 [4,50; 12,62] <,0001[3]	33,9 [26,6; 41,1] <,0001[3]
≥ 10	48/108 (44,4)	7/90 (7,8)	5,71 [2,72; 12,00] <,0001[2]	9,49 [4,02; 22,41] <,0001[3]	36,7 [25,8; 47,5] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9513)					
IIA	20/59 (33,9)	5/62 (8,1)	4,20 [1,69; 10,47] 0,0020[2]	5,85 [2,02; 16,90] 0,0005[3]	25,8 [12,0; 39,7] 0,0005[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	22/53 (41,5)	4/69 (5,8)	7,16 [2,63; 19,53] 0,0001[2]	11,53 [3,66; 36,35] <,0001[3]	35,7 [21,3; 50,1] <,0001[3]
IIIA	107/236 (45,3)	16/214 (7,5)	6,06 [3,71; 9,92] <,0001[2]	10,26 [5,80; 18,15] <,0001[3]	37,9 [30,6; 45,1] <,0001[3]
IIIB	6/18 (33,3)	1/15 (6,7)	5,00 [0,67; 37,06] 0,1153[2]	7,00 [0,74; 66,62] 0,0952[4]	26,7 [1,5; 51,8] 0,0952[4]
IIIC	81/186 (43,5)	13/174 (7,5)	5,83 [3,37; 10,08] <,0001[2]	9,55 [5,06; 18,03] <,0001[3]	36,1 [28,0; 44,2] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,1038)					
G1	21/47 (44,7)	1/41 (2,4)	18,32 [2,58; 130,30] 0,0037[2]	32,31 [4,09; 255,00] <,0001[3]	42,2 [27,3; 57,2] <,0001[3]
G2	97/244 (39,8)	15/234 (6,4)	6,20 [3,71; 10,36] <,0001[2]	9,63 [5,38; 17,25] <,0001[3]	33,3 [26,4; 40,2] <,0001[3]
G3	103/233 (44,2)	15/226 (6,6)	6,66 [4,00; 11,09] <,0001[2]	11,15 [6,21; 19,99] <,0001[3]	37,6 [30,4; 44,7] <,0001[3]
GX	16/29 (55,2)	7/33 (21,2)	2,60 [1,25; 5,42] 0,0108[2]	4,57 [1,51; 13,87] 0,0057[3]	34,0 [11,1; 56,8] 0,0057[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9336)					
Negativ	22/49 (44,9)	4/44 (9,1)	4,94 [1,85; 13,22] 0,0015[2]	8,15 [2,52; 26,30] 0,0001[3]	35,8 [19,5; 52,1] 0,0001[3]
Positiv	207/477 (43,4)	34/471 (7,2)	6,01 [4,28; 8,44] <,0001[2]	9,85 [6,65; 14,60] <,0001[3]	36,2 [31,2; 41,2] <,0001[3]
Unbekannt	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Ethnizität (p-Wert des Interaktionsterms: 0,4655)					
Weiß	126/323 (39,0)	18/324 (5,6)	7,02 [4,39; 11,23] <,0001[2]	10,87 [6,43; 18,39] <,0001[3]	33,5 [27,6; 39,3] <,0001[3]
Asiatisch	102/199 (51,3)	19/180 (10,6)	4,86 [3,11; 7,59] <,0001[2]	8,91 [5,14; 15,46] <,0001[3]	40,7 [32,4; 49,0] <,0001[3]
Andere	7/19 (36,8)	2/21 (9,5)	3,87 [0,91; 16,39] 0,0663[2]	5,54 [0,98; 31,25] 0,0601[4]	27,3 [2,3; 52,4] 0,0601[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,6499)					
ECOG-PS 0	223/496 (45,0)	36/480 (7,5)	5,99 [4,31; 8,33] <,0001[2]	10,07 [6,87; 14,78] <,0001[3]	37,5 [32,5; 42,4] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 1	14/57 (24,6)	3/55 (5,5)	4,50 [1,37; 14,81] 0,0132[2]	5,64 [1,52; 20,93] 0,0048[3]	19,1 [6,4; 31,8] 0,0048[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis: PT Neutropenie und erniedrigte Neutrophilenzahl (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,1312)					
< 65 Jahre	404/918 (44,0)	43/937 (4,6)	9,59 [7,10; 12,96] <,0001[2]	16,34 [11,72; 22,79] <,0001[3]	39,4 [35,9; 42,9] <,0001[3]
≥ 65 Jahre	153/365 (41,9)	8/328 (2,4)	17,19 [8,58; 34,44] <,0001[2]	28,87 [13,89; 60,01] <,0001[3]	39,5 [34,1; 44,8] <,0001[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,5025)					
Neoadjuvante Chemotherapie	202/430 (47,0)	23/415 (5,5)	8,48 [5,63; 12,77] <,0001[2]	15,10 [9,52; 23,95] <,0001[3]	41,4 [36,2; 46,6] <,0001[3]
Adjuvante Chemotherapie	337/784 (43,0)	28/769 (3,6)	11,81 [8,13; 17,13] <,0001[2]	19,95 [13,33; 29,85] <,0001[3]	39,3 [35,6; 43,1] <,0001[3]
Keine Chemotherapie	18/69 (26,1)	0/81 (0,0)	43,34 [2,66; 706,27] 0,0081[2]	58,55 [3,45; 992,81] <,0001[3]	26,1 [15,7; 36,4] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4170)					
< 20 mm	140/331 (42,3)	17/335 (5,1)	8,33 [5,16; 13,47] <,0001[2]	13,71 [8,03; 23,40] <,0001[3]	37,2 [31,4; 43,0] <,0001[3]
≥ 20 bis < 50 mm	280/646 (43,3)	23/653 (3,5)	12,31 [8,16; 18,56] <,0001[2]	20,96 [13,44; 32,67] <,0001[3]	39,8 [35,7; 43,9] <,0001[3]
≥ 50 mm	125/289 (43,3)	9/265 (3,4)	12,74 [6,61; 24,53] <,0001[2]	21,68 [10,72; 43,85] <,0001[3]	39,9 [33,7; 46,0] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7903)					
0-3	174/427 (40,7)	14/418 (3,3)	12,17 [7,18; 20,62] <,0001[2]	19,85 [11,26; 34,98] <,0001[3]	37,4 [32,4; 42,4] <,0001[3]
4-9	247/549 (45,0)	25/542 (4,6)	9,75 [6,58; 14,46] <,0001[2]	16,91 [10,95; 26,14] <,0001[3]	40,4 [35,9; 44,9] <,0001[3]
≥ 10	136/307 (44,3)	12/305 (3,9)	11,26 [6,38; 19,88] <,0001[2]	19,42 [10,45; 36,09] <,0001[3]	40,4 [34,4; 46,3] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9539)					
IIA	43/113 (38,1)	4/114 (3,5)	10,85 [4,03; 29,21] <,0001[2]	16,89 [5,81; 49,12] <,0001[3]	34,5 [25,0; 44,1] <,0001[3]
IIB	69/151 (45,7)	5/136 (3,7)	12,43 [5,17; 29,90] <,0001[2]	22,05 [8,54; 56,93] <,0001[3]	42,0 [33,5; 50,6] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	211/495 (42,6)	18/488 (3,7)	11,56 [7,26; 18,39] <,0001[2]	19,40 [11,73; 32,09] <,0001[3]	38,9 [34,3; 43,6] <,0001[3]
IIIB	27/54 (50,0)	3/45 (6,7)	7,50 [2,43; 23,11] 0,0004[2]	14,00 [3,87; 50,71] <,0001[3]	43,3 [28,1; 58,5] <,0001[3]
IIIC	206/468 (44,0)	21/480 (4,4)	10,06 [6,54; 15,47] <,0001[2]	17,19 [10,70; 27,60] <,0001[3]	39,6 [34,8; 44,5] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,4769)					
G1	33/91 (36,3)	2/93 (2,2)	16,86 [4,17; 68,23] <,0001[2]	25,89 [5,98; 112,01] <,0001[3]	34,1 [23,8; 44,4] <,0001[3]
G2	255/612 (41,7)	26/603 (4,3)	9,66 [6,56; 14,24] <,0001[2]	15,85 [10,37; 24,24] <,0001[3]	37,4 [33,1; 41,6] <,0001[3]
G3	240/527 (45,5)	18/506 (3,6)	12,80 [8,06; 20,34] <,0001[2]	22,67 [13,74; 37,40] <,0001[3]	42,0 [37,4; 46,5] <,0001[3]
GX	28/51 (54,9)	5/59 (8,5)	6,48 [2,70; 15,54] <,0001[2]	13,15 [4,51; 38,31] <,0001[3]	46,4 [31,0; 61,8] <,0001[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9784)					
Negativ	75/156 (48,1)	7/169 (4,1)	11,61 [5,52; 24,41] <,0001[2]	21,43 [9,45; 48,62] <,0001[3]	43,9 [35,5; 52,3] <,0001[3]
Positiv	468/1089 (43,0)	43/1067 (4,0)	10,66 [7,89; 14,40] <,0001[2]	17,95 [12,93; 24,91] <,0001[3]	38,9 [35,8; 42,1] <,0001[3]
Unbekannt	5/10 (50,0)	0/7 (0,0)	8,00 [0,51; 124,90] 0,1381[2]	15,00 [0,68; 332,00] 0,0441[4]	50,0 [19,0; 81,0] 0,0441[4]
Ethnizität (p-Wert des Interaktionsterms: 0,5402)					
Weiß	372/958 (38,8)	37/944 (3,9)	9,91 [7,15; 13,72] <,0001[2]	15,56 [10,93; 22,16] <,0001[3]	34,9 [31,6; 38,2] <,0001[3]
Asiatisch	153/250 (61,2)	13/242 (5,4)	11,39 [6,65; 19,51] <,0001[2]	27,79 [15,04; 51,34] <,0001[3]	55,8 [49,2; 62,5] <,0001[3]
Andere	28/62 (45,2)	1/64 (1,6)	28,90 [4,06; 205,98] 0,0008[2]	51,88 [6,76; 398,13] <,0001[3]	43,6 [30,8; 56,4] <,0001[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,6260)					
Tamoxifen	46/114 (40,4)	6/132 (4,5)	8,88 [3,94; 20,01] <,0001[2]	14,21 [5,77; 34,96] <,0001[3]	35,8 [26,1; 45,5] <,0001[3]
Aromatase-Inhibitor	511/1169 (43,7)	45/1133 (4,0)	11,01 [8,21; 14,76] <,0001[2]	18,78 [13,64; 25,85] <,0001[3]	39,7 [36,7; 42,8] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,4469)					

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 0	465/1070 (43,5)	39/1020 (3,8)	11,37 [8,29; 15,58] <,0001[2]	19,33 [13,73; 27,22] <,0001[3]	39,6 [36,4; 42,8] <,0001[3]
ECOG-PS 1	92/213 (43,2)	12/245 (4,9)	8,82 [4,97; 15,64] <,0001[2]	14,76 [7,78; 28,01] <,0001[3]	38,3 [31,1; 45,5] <,0001[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: PT Neutropenie und erniedrigte Neutrophilenzahl aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,2681)					
Neoadjuvante Chemotherapie	44/217 (20,3)	8/219 (3,7)	5,55 [2,68; 11,51] <,0001[2]	6,71 [3,08; 14,63] <,0001[3]	16,6 [10,7; 22,5] <,0001[3]
Adjuvante Chemotherapie	54/327 (16,5)	3/312 (1,0)	17,17 [5,43; 54,36] <,0001[2]	20,37 [6,30; 65,90] <,0001[3]	15,6 [11,4; 19,7] <,0001[3]
Keine Chemotherapie	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (p-Wert des Interaktionsterms: 0,4772)					
Nordamerika / Europa	31/252 (12,3)	5/233 (2,1)	5,73 [2,27; 14,49] 0,0002[2]	6,40 [2,44; 16,75] <,0001[3]	10,2 [5,7; 14,6] <,0001[3]
Asien	48/168 (28,6)	5/166 (3,0)	9,49 [3,87; 23,23] <,0001[2]	12,88 [4,98; 33,33] <,0001[3]	25,6 [18,3; 32,9] <,0001[3]
Andere	20/133 (15,0)	1/136 (0,7)	20,45 [2,78; 150,22] 0,0030[2]	23,89 [3,16; 180,81] <,0001[3]	14,3 [8,1; 20,5] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2737)					
< 20 mm	27/141 (19,1)	5/140 (3,6)	5,36 [2,13; 13,52] 0,0004[2]	6,39 [2,39; 17,15] <,0001[3]	15,6 [8,4; 22,8] <,0001[3]
≥ 20 bis < 50 mm	43/255 (16,9)	2/249 (0,8)	20,99 [5,14; 85,73] <,0001[2]	25,05 [6,00; 104,63] <,0001[3]	16,1 [11,3; 20,8] <,0001[3]
≥ 50 mm	28/145 (19,3)	4/141 (2,8)	6,81 [2,45; 18,91] 0,0002[2]	8,20 [2,79; 24,05] <,0001[3]	16,5 [9,5; 23,5] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,4376)					
0-3	40/203 (19,7)	3/214 (1,4)	14,06 [4,42; 44,72] <,0001[2]	17,26 [5,25; 56,79] <,0001[3]	18,3 [12,6; 24,0] <,0001[3]
4-9	42/242 (17,4)	5/231 (2,2)	8,02 [3,23; 19,91] <,0001[2]	9,49 [3,68; 24,46] <,0001[3]	15,2 [10,1; 20,3] <,0001[3]
≥ 10	17/108 (15,7)	3/90 (3,3)	4,72 [1,43; 15,60] 0,0109[2]	5,42 [1,53; 19,14] 0,0039[3]	12,4 [4,6; 20,2] 0,0039[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,8391)					
IIA	10/59 (16,9)	2/62 (3,2)	5,25 [1,20; 22,98] 0,0276[2]	6,12 [1,28; 29,26] 0,0116[3]	13,7 [3,2; 24,3] 0,0116[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	11/53 (20,8)	1/69 (1,4)	14,32 [1,91; 107,48] 0,0096[2]	17,81 [2,22; 142,98] 0,0004[3]	19,3 [8,0; 30,6] 0,0004[3]
IIIA	39/236 (16,5)	3/214 (1,4)	11,79 [3,70; 37,59] <,0001[2]	13,92 [4,23; 45,78] <,0001[3]	15,1 [10,1; 20,1] <,0001[3]
IIIB	6/18 (33,3)	0/15 (0,0)	10,95 [0,67; 179,76] 0,0937[2]	16,12 [0,83; 314,64] 0,0213[4]	33,3 [11,6; 55,1] 0,0213[4]
IIIC	32/186 (17,2)	5/174 (2,9)	5,99 [2,39; 15,02] 0,0001[2]	7,02 [2,67; 18,48] <,0001[3]	14,3 [8,4; 20,3] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,8498)					
G1	14/47 (29,8)	0/41 (0,0)	25,38 [1,56; 412,56] 0,0230[2]	35,93 [2,07; 624,63] 0,0001[3]	29,8 [16,7; 42,9] 0,0001[3]
G2	42/244 (17,2)	6/234 (2,6)	6,71 [2,91; 15,49] <,0001[2]	7,90 [3,29; 18,97] <,0001[3]	14,6 [9,5; 19,8] <,0001[3]
G3	40/233 (17,2)	4/226 (1,8)	9,70 [3,53; 26,67] <,0001[2]	11,50 [4,04; 32,73] <,0001[3]	15,4 [10,3; 20,5] <,0001[3]
GX	3/29 (10,3)	1/33 (3,0)	3,41 [0,38; 31,04] 0,2757[2]	3,69 [0,36; 37,63] 0,3321[4]	7,3 [-5,2; 19,8] 0,3321[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,0679)					
Negativ	10/49 (20,4)	2/44 (4,5)	4,49 [1,04; 19,38] 0,0442[2]	5,38 [1,11; 26,13] 0,0227[3]	15,9 [3,0; 28,7] 0,0227[3]
Positiv	88/477 (18,4)	9/471 (1,9)	9,65 [4,92; 18,94] <,0001[2]	11,61 [5,77; 23,36] <,0001[3]	16,5 [12,8; 20,2] <,0001[3]
Unbekannt	0/4 (0,0)	0/8 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,5125)					
Weiß	46/323 (14,2)	5/324 (1,5)	9,23 [3,71; 22,93] <,0001[2]	10,59 [4,15; 27,04] <,0001[3]	12,7 [8,7; 16,7] <,0001[3]
Asiatisch	50/199 (25,1)	5/180 (2,8)	9,05 [3,69; 22,18] <,0001[2]	11,74 [4,57; 30,21] <,0001[3]	22,3 [15,9; 28,8] <,0001[3]
Andere	2/19 (10,5)	1/21 (4,8)	2,21 [0,22; 22,47] 0,5026[2]	2,35 [0,20; 28,27] 0,5962[4]	5,8 [-10,8; 22,3] 0,5962[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,2689)					
ECOG-PS 0	91/496 (18,3)	9/480 (1,9)	9,78 [4,99; 19,18] <,0001[2]	11,76 [5,85; 23,62] <,0001[3]	16,5 [12,9; 20,1] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 1	8/57 (14,0)	2/55 (3,6)	3,86 [0,86; 17,38] 0,0785[2]	4,33 [0,88; 21,37] 0,0941[4]	10,4 [0,1; 20,7] 0,0941[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: PT Neutropenie und erniedrigte Neutrophilenzahl aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,2865)					
< 65 Jahre	187/918 (20,4)	4/937 (0,4)	47,72 [17,80; 127,93] <,0001[2]	59,67 [22,06; 161,41] <,0001[3]	19,9 [17,3; 22,6] <,0001[3]
≥ 65 Jahre	70/365 (19,2)	3/328 (0,9)	20,97 [6,67; 65,95] <,0001[2]	25,71 [8,01; 82,52] <,0001[3]	18,3 [14,1; 22,4] <,0001[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8273)					
Neoadjuvante Chemotherapie	101/430 (23,5)	2/415 (0,5)	48,74 [12,10; 196,27] <,0001[2]	63,39 [15,52; 258,89] <,0001[3]	23,0 [18,9; 27,1] <,0001[3]
Adjuvante Chemotherapie	148/784 (18,9)	5/769 (0,7)	29,03 [11,97; 70,39] <,0001[2]	35,56 [14,49; 87,23] <,0001[3]	18,2 [15,4; 21,0] <,0001[3]
Keine Chemotherapie	8/69 (11,6)	0/81 (0,0)	19,91 [1,17; 338,90] 0,0386[2]	22,53 [1,28; 397,86] 0,0016[4]	11,6 [4,0; 19,1] 0,0016[4]
Region (p-Wert des Interaktionsterms: 0,9888)					
Nordamerika / Europa	109/678 (16,1)	3/650 (0,5)	34,83 [11,12; 109,13] <,0001[2]	41,31 [13,05; 130,81] <,0001[3]	15,6 [12,8; 18,4] <,0001[3]
Asien	80/203 (39,4)	2/201 (1,0)	39,61 [9,87; 158,93] <,0001[2]	64,72 [15,63; 268,01] <,0001[3]	38,4 [31,6; 45,3] <,0001[3]
Andere	68/402 (16,9)	2/414 (0,5)	35,01 [8,64; 141,91] <,0001[2]	41,94 [10,20; 172,39] <,0001[3]	16,4 [12,7; 20,2] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,8562)					
< 20 mm	66/331 (19,9)	2/335 (0,6)	33,40 [8,25; 135,24] <,0001[2]	41,47 [10,06; 170,87] <,0001[3]	19,3 [15,0; 23,7] <,0001[3]
≥ 20 bis < 50 mm	125/646 (19,3)	4/653 (0,6)	31,59 [11,74; 84,98] <,0001[2]	38,93 [14,29; 106,05] <,0001[3]	18,7 [15,6; 21,8] <,0001[3]
≥ 50 mm	64/289 (22,1)	1/265 (0,4)	58,69 [8,20; 420,04] <,0001[2]	75,09 [10,33; 545,63] <,0001[3]	21,8 [16,9; 26,6] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9407)					
0-3	88/427 (20,6)	2/418 (0,5)	43,07 [10,67; 173,81] <,0001[2]	53,99 [13,20; 220,91] <,0001[3]	20,1 [16,2; 24,0] <,0001[3]
4-9	108/549 (19,7)	3/542 (0,6)	35,54 [11,35; 111,24] <,0001[2]	44,00 [13,88; 139,53] <,0001[3]	19,1 [15,7; 22,5] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	61/307 (19,9)	2/305 (0,7)	30,30 [7,48; 122,82] <,0001[2]	37,57 [9,09; 155,18] <,0001[3]	19,2 [14,7; 23,8] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,5250)					
IIA	20/113 (17,7)	0/114 (0,0)	41,36 [2,53; 675,69] 0,0090[2]	50,21 [3,00; 841,23] <,0001[3]	17,7 [10,7; 24,7] <,0001[3]
IIB	36/151 (23,8)	1/136 (0,7)	32,42 [4,51; 233,30] 0,0006[2]	42,26 [5,71; 313,05] <,0001[3]	23,1 [16,2; 30,1] <,0001[3]
IIIA	97/495 (19,6)	1/488 (0,2)	95,63 [13,39; 683,03] <,0001[2]	118,69 [16,48; 854,92] <,0001[3]	19,4 [15,9; 22,9] <,0001[3]
IIIB	9/54 (16,7)	1/45 (2,2)	7,50 [0,99; 56,98] 0,0515[2]	8,80 [1,07; 72,39] 0,0202[4]	14,4 [3,6; 25,3] 0,0202[4]
IIIC	94/468 (20,1)	4/480 (0,8)	24,10 [8,93; 65,03] <,0001[2]	29,91 [10,90; 82,10] <,0001[3]	19,3 [15,5; 23,0] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,8712)					
G1	11/91 (12,1)	0/93 (0,0)	23,50 [1,41; 392,99] 0,0280[2]	26,71 [1,55; 460,48] 0,0005[3]	12,1 [5,4; 18,8] 0,0005[3]
G2	119/612 (19,4)	3/603 (0,5)	39,08 [12,50; 122,23] <,0001[2]	48,28 [15,26; 152,76] <,0001[3]	18,9 [15,8; 22,1] <,0001[3]
G3	114/527 (21,6)	3/506 (0,6)	36,49 [11,67; 114,07] <,0001[2]	46,28 [14,60; 146,71] <,0001[3]	21,0 [17,5; 24,6] <,0001[3]
GX	13/51 (25,5)	1/59 (1,7)	15,04 [2,04; 111,03] 0,0079[2]	19,84 [2,49; 157,98] 0,0002[3]	23,8 [11,4; 36,2] 0,0002[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9962)					
Negativ	41/156 (26,3)	0/169 (0,0)	89,87 [5,58; 1448,66] 0,0015[2]	121,81 [7,42; 1999,97] <,0001[3]	26,3 [19,4; 33,2] <,0001[3]
Positiv	214/1089 (19,7)	6/1067 (0,6)	34,95 [15,59; 78,31] <,0001[2]	43,25 [19,12; 97,82] <,0001[3]	19,1 [16,7; 21,5] <,0001[3]
Unbekannt	2/10 (20,0)	0/7 (0,0)	3,64 [0,20; 65,86] 0,3824[2]	4,41 [0,18; 107,28] 0,4853[4]	20,0 [-4,8; 44,8] 0,4853[4]
Ethnizität (p-Wert des Interaktionsterms: 0,9295)					
Weiß	155/958 (16,2)	5/944 (0,5)	30,55 [12,59; 74,09] <,0001[2]	36,25 [14,80; 88,76] <,0001[3]	15,6 [13,3; 18,0] <,0001[3]
Asiatisch	87/250 (34,8)	2/242 (0,8)	42,11 [10,48; 169,15] <,0001[2]	64,05 [15,55; 263,87] <,0001[3]	34,0 [28,0; 40,0] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Andere	14/62 (22,6)	0/64 (0,0)	29,92 [1,82; 490,96] 0,0173[2]	38,57 [2,24; 662,55] <,0001[3]	22,6 [12,2; 33,0] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,7910)					
ECOG-PS 0	217/1070 (20,3)	6/1020 (0,6)	34,48 [15,39; 77,24] <,0001[2]	42,99 [19,01; 97,25] <,0001[3]	19,7 [17,2; 22,1] <,0001[3]
ECOG-PS 1	40/213 (18,8)	1/245 (0,4)	46,01 [6,38; 331,84] 0,0001[2]	56,42 [7,68; 414,31] <,0001[3]	18,4 [13,1; 23,7] <,0001[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: PT Neutropenie und erniedrigte Neutrophilenzahl aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,4284)					
Neoadjuvante Chemotherapie	63/217 (29,0)	15/219 (6,8)	4,24 [2,49; 7,21] <,0001[2]	5,56 [3,05; 10,14] <,0001[3]	22,2 [15,3; 29,1] <,0001[3]
Adjuvante Chemotherapie	128/327 (39,1)	18/312 (5,8)	6,78 [4,25; 10,84] <,0001[2]	10,51 [6,21; 17,76] <,0001[3]	33,4 [27,5; 39,3] <,0001[3]
Keine Chemotherapie	4/9 (44,4)	0/4 (0,0)	4,50 [0,30; 68,13] 0,2780[2]	7,36 [0,31; 176,41] 0,2280[4]	44,4 [12,0; 76,9] 0,2280[4]
Region (p-Wert des Interaktionsterms: 0,6919)					
Nordamerika / Europa	68/252 (27,0)	9/233 (3,9)	6,99 [3,57; 13,68] <,0001[2]	9,20 [4,47; 18,94] <,0001[3]	23,1 [17,1; 29,1] <,0001[3]
Asien	74/168 (44,0)	15/166 (9,0)	4,87 [2,92; 8,13] <,0001[2]	7,92 [4,30; 14,61] <,0001[3]	35,0 [26,3; 43,7] <,0001[3]
Andere	53/133 (39,8)	9/136 (6,6)	6,02 [3,10; 11,71] <,0001[2]	9,35 [4,37; 19,99] <,0001[3]	33,2 [23,9; 42,5] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,1902)					
< 20 mm	46/141 (32,6)	6/140 (4,3)	7,61 [3,36; 17,25] <,0001[2]	10,81 [4,44; 26,34] <,0001[3]	28,3 [19,9; 36,8] <,0001[3]
≥ 20 bis < 50 mm	87/255 (34,1)	20/249 (8,0)	4,25 [2,70; 6,69] <,0001[2]	5,93 [3,51; 10,03] <,0001[3]	26,1 [19,4; 32,8] <,0001[3]
≥ 50 mm	56/145 (38,6)	6/141 (4,3)	9,08 [4,04; 20,39] <,0001[2]	14,16 [5,85; 34,25] <,0001[3]	34,4 [25,8; 43,0] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,4244)					
0-3	63/203 (31,0)	9/214 (4,2)	7,38 [3,77; 14,44] <,0001[2]	10,25 [4,94; 21,29] <,0001[3]	26,8 [19,9; 33,7] <,0001[3]
4-9	90/242 (37,2)	19/231 (8,2)	4,52 [2,85; 7,17] <,0001[2]	6,61 [3,86; 11,30] <,0001[3]	29,0 [21,9; 36,0] <,0001[3]
≥ 10	42/108 (38,9)	5/90 (5,6)	7,00 [2,89; 16,94] <,0001[2]	10,82 [4,05; 28,87] <,0001[3]	33,3 [23,0; 43,7] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9911)					
IIA	16/59 (27,1)	3/62 (4,8)	5,60 [1,72; 18,25] 0,0042[2]	7,32 [2,01; 26,70] 0,0008[3]	22,3 [9,7; 34,8] 0,0008[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	16/53 (30,2)	4/69 (5,8)	5,21 [1,85; 14,67] 0,0018[2]	7,03 [2,19; 22,59] 0,0003[3]	24,4 [10,9; 37,9] 0,0003[3]
IIIA	89/236 (37,7)	15/214 (7,0)	5,38 [3,22; 9,00] <,0001[2]	8,03 [4,47; 14,45] <,0001[3]	30,7 [23,6; 37,8] <,0001[3]
IIIB	5/18 (27,8)	1/15 (6,7)	4,17 [0,54; 31,88] 0,1692[2]	5,38 [0,55; 52,43] 0,1861[4]	21,1 [-3,1; 45,3] 0,1861[4]
IIIC	68/186 (36,6)	10/174 (5,7)	6,36 [3,39; 11,95] <,0001[2]	9,45 [4,67; 19,12] <,0001[3]	30,8 [23,1; 38,5] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,3415)					
G1	15/47 (31,9)	1/41 (2,4)	13,09 [1,81; 94,81] 0,0109[2]	18,75 [2,35; 149,62] 0,0003[3]	29,5 [15,3; 43,6] 0,0003[3]
G2	80/244 (32,8)	12/234 (5,1)	6,39 [3,58; 11,41] <,0001[2]	9,02 [4,76; 17,10] <,0001[3]	27,7 [21,1; 34,2] <,0001[3]
G3	84/233 (36,1)	13/226 (5,8)	6,27 [3,60; 10,91] <,0001[2]	9,24 [4,97; 17,18] <,0001[3]	30,3 [23,4; 37,2] <,0001[3]
GX	16/29 (55,2)	6/33 (18,2)	3,03 [1,37; 6,72] 0,0062[2]	5,54 [1,76; 17,46] 0,0024[3]	37,0 [14,6; 59,4] 0,0024[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9518)					
Negativ	16/49 (32,7)	3/44 (6,8)	4,79 [1,50; 15,34] 0,0084[2]	6,63 [1,78; 24,69] 0,0020[3]	25,8 [10,7; 40,9] 0,0020[3]
Positiv	171/477 (35,8)	29/471 (6,2)	5,82 [4,01; 8,45] <,0001[2]	8,52 [5,60; 12,96] <,0001[3]	29,7 [24,9; 34,5] <,0001[3]
Unbekannt	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Ethnizität (p-Wert des Interaktionsterms: 0,3132)					
Weiß	113/323 (35,0)	16/324 (4,9)	7,08 [4,30; 11,68] <,0001[2]	10,36 [5,96; 17,99] <,0001[3]	30,0 [24,3; 35,8] <,0001[3]
Asiatisch	75/199 (37,7)	15/180 (8,3)	4,52 [2,70; 7,58] <,0001[2]	6,65 [3,65; 12,14] <,0001[3]	29,4 [21,5; 37,2] <,0001[3]
Andere	5/19 (26,3)	2/21 (9,5)	2,76 [0,61; 12,61] 0,1894[2]	3,39 [0,57; 20,10] 0,2258[4]	16,8 [-6,7; 40,2] 0,2258[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,7097)					
ECOG-PS 0	186/496 (37,5)	31/480 (6,5)	5,81 [4,06; 8,31] <,0001[2]	8,69 [5,79; 13,05] <,0001[3]	31,0 [26,2; 35,8] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 1	9/57 (15,8)	2/55 (3,6)	4,34 [0,98; 19,20] 0,0529[2]	4,97 [1,02; 24,15] 0,0307[3]	12,2 [1,5; 22,8] 0,0307[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: PT Neutropenie und erniedrigte Neutrophilenzahl aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,1948)					
< 65 Jahre	361/918 (39,3)	40/937 (4,3)	9,21 [6,73; 12,61] <,0001[2]	14,53 [10,31; 20,49] <,0001[3]	35,1 [31,6; 38,5] <,0001[3]
≥ 65 Jahre	136/365 (37,3)	8/328 (2,4)	15,28 [7,61; 30,68] <,0001[2]	23,76 [11,41; 49,44] <,0001[3]	34,8 [29,6; 40,1] <,0001[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,5216)					
Neoadjuvante Chemotherapie	183/430 (42,6)	22/415 (5,3)	8,03 [5,27; 12,23] <,0001[2]	13,24 [8,27; 21,18] <,0001[3]	37,3 [32,1; 42,4] <,0001[3]
Adjuvante Chemotherapie	297/784 (37,9)	26/769 (3,4)	11,20 [7,60; 16,52] <,0001[2]	17,43 [11,49; 26,44] <,0001[3]	34,5 [30,9; 38,1] <,0001[3]
Keine Chemotherapie	17/69 (24,6)	0/81 (0,0)	41,00 [2,51; 669,51] 0,0092[2]	54,33 [3,20; 922,96] <,0001[3]	24,6 [14,5; 34,8] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3835)					
< 20 mm	122/331 (36,9)	16/335 (4,8)	7,72 [4,69; 12,70] <,0001[2]	11,64 [6,72; 20,16] <,0001[3]	32,1 [26,4; 37,8] <,0001[3]
≥ 20 bis < 50 mm	254/646 (39,3)	22/653 (3,4)	11,67 [7,65; 17,79] <,0001[2]	18,58 [11,81; 29,25] <,0001[3]	35,9 [31,9; 40,0] <,0001[3]
≥ 50 mm	109/289 (37,7)	8/265 (3,0)	12,49 [6,21; 25,12] <,0001[2]	19,45 [9,26; 40,89] <,0001[3]	34,7 [28,7; 40,7] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7636)					
0-3	153/427 (35,8)	13/418 (3,1)	11,52 [6,65; 19,97] <,0001[2]	17,40 [9,68; 31,28] <,0001[3]	32,7 [27,9; 37,6] <,0001[3]
4-9	222/549 (40,4)	24/542 (4,4)	9,13 [6,10; 13,68] <,0001[2]	14,65 [9,41; 22,83] <,0001[3]	36,0 [31,6; 40,5] <,0001[3]
≥ 10	122/307 (39,7)	11/305 (3,6)	11,02 [6,07; 20,00] <,0001[2]	17,63 [9,26; 33,56] <,0001[3]	36,1 [30,3; 42,0] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9964)					
IIA	36/113 (31,9)	4/114 (3,5)	9,08 [3,34; 24,67] <,0001[2]	12,86 [4,40; 37,61] <,0001[3]	28,3 [19,1; 37,6] <,0001[3]
IIB	59/151 (39,1)	5/136 (3,7)	10,63 [4,39; 25,70] <,0001[2]	16,80 [6,49; 43,49] <,0001[3]	35,4 [27,0; 43,8] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	187/495 (37,8)	17/488 (3,5)	10,84 [6,71; 17,53] <,0001[2]	16,82 [10,03; 28,21] <,0001[3]	34,3 [29,7; 38,9] <,0001[3]
IIIB	25/54 (46,3)	2/45 (4,4)	10,42 [2,61; 41,61] 0,0009[2]	18,53 [4,07; 84,35] <,0001[3]	41,9 [27,3; 56,5] <,0001[3]
IIIC	189/468 (40,4)	20/480 (4,2)	9,69 [6,22; 15,09] <,0001[2]	15,58 [9,60; 25,29] <,0001[3]	36,2 [31,4; 41,0] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,3783)					
G1	31/91 (34,1)	2/93 (2,2)	15,84 [3,90; 64,26] 0,0001[2]	23,51 [5,42; 101,90] <,0001[3]	31,9 [21,7; 42,1] <,0001[3]
G2	224/612 (36,6)	25/603 (4,1)	8,83 [5,93; 13,14] <,0001[2]	13,35 [8,66; 20,58] <,0001[3]	32,5 [28,3; 36,6] <,0001[3]
G3	215/527 (40,8)	16/506 (3,2)	12,90 [7,88; 21,12] <,0001[2]	21,10 [12,45; 35,76] <,0001[3]	37,6 [33,2; 42,1] <,0001[3]
GX	26/51 (51,0)	5/59 (8,5)	6,02 [2,49; 14,51] <,0001[2]	11,23 [3,86; 32,68] <,0001[3]	42,5 [27,1; 58,0] <,0001[3]
Ethnizität (p-Wert des Interaktionsterms: 0,5948)					
Weiß	340/958 (35,5)	35/944 (3,7)	9,57 [6,84; 13,40] <,0001[2]	14,29 [9,94; 20,53] <,0001[3]	31,8 [28,5; 35,0] <,0001[3]
Asiatisch	127/250 (50,8)	12/242 (5,0)	10,24 [5,82; 18,02] <,0001[2]	19,79 [10,53; 37,20] <,0001[3]	45,8 [39,1; 52,6] <,0001[3]
Andere	26/62 (41,9)	1/64 (1,6)	26,84 [3,76; 191,78] 0,0010[2]	45,50 [5,92; 349,52] <,0001[3]	40,4 [27,7; 53,0] <,0001[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,5227)					
Tamoxifen	41/114 (36,0)	6/132 (4,5)	7,91 [3,49; 17,95] <,0001[2]	11,79 [4,78; 29,12] <,0001[3]	31,4 [21,9; 40,9] <,0001[3]
Aromatase-Inhibitor	456/1169 (39,0)	42/1133 (3,7)	10,52 [7,75; 14,28] <,0001[2]	16,61 [11,95; 23,10] <,0001[3]	35,3 [32,3; 38,3] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,2641)					
ECOG-PS 0	418/1070 (39,1)	36/1020 (3,5)	11,07 [7,96; 15,39] <,0001[2]	17,52 [12,29; 24,98] <,0001[3]	35,5 [32,4; 38,7] <,0001[3]
ECOG-PS 1	79/213 (37,1)	12/245 (4,9)	7,57 [4,24; 13,51] <,0001[2]	11,45 [6,02; 21,78] <,0001[3]	32,2 [25,2; 39,2] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko					

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Tabelle: Subgruppen - Unerwünschtes Ereignis: SOC Infektionen (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,2874)					
Neoadjuvante Chemotherapie	108/217 (49,8)	94/219 (42,9)	1,16 [0,95; 1,42] 0,1529[2]	1,32 [0,90; 1,92] 0,1517[3]	6,8 [-2,5; 16,2] 0,1517[3]
Adjuvante Chemotherapie	185/327 (56,6)	127/312 (40,7)	1,39 [1,18; 1,64] <,0001[2]	1,90 [1,39; 2,60] <,0001[3]	15,9 [8,2; 23,5] <,0001[3]
Keine Chemotherapie	6/9 (66,7)	1/4 (25,0)	2,67 [0,46; 15,49] 0,2745[2]	6,00 [0,42; 85,25] 0,2657[4]	41,7 [-10,8; 94,1] 0,2657[4]
Region (p-Wert des Interaktionsterms: 0,8912)					
Nordamerika / Europa	136/252 (54,0)	100/233 (42,9)	1,26 [1,04; 1,52] 0,0163[2]	1,56 [1,09; 2,23] 0,0150[3]	11,0 [2,2; 19,9] 0,0150[3]
Asien	101/168 (60,1)	75/166 (45,2)	1,33 [1,08; 1,64] 0,0071[2]	1,83 [1,18; 2,82] 0,0063[3]	14,9 [4,3; 25,5] 0,0063[3]
Andere	62/133 (46,6)	47/136 (34,6)	1,35 [1,01; 1,81] 0,0462[2]	1,65 [1,01; 2,70] 0,0440[3]	12,1 [0,4; 23,7] 0,0440[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,4491)					
< 20 mm	83/141 (58,9)	58/140 (41,4)	1,42 [1,12; 1,81] 0,0042[2]	2,02 [1,26; 3,25] 0,0035[3]	17,4 [5,9; 28,9] 0,0035[3]
≥ 20 bis < 50 mm	128/255 (50,2)	104/249 (41,8)	1,20 [0,99; 1,45] 0,0592[2]	1,41 [0,99; 2,00] 0,0577[3]	8,4 [-0,2; 17,1] 0,0577[3]
≥ 50 mm	83/145 (57,2)	57/141 (40,4)	1,42 [1,11; 1,81] 0,0054[2]	1,97 [1,23; 3,16] 0,0045[3]	16,8 [5,4; 28,2] 0,0045[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8869)					
0-3	108/203 (53,2)	91/214 (42,5)	1,25 [1,02; 1,53] 0,0299[2]	1,54 [1,04; 2,26] 0,0291[3]	10,7 [1,1; 20,2] 0,0291[3]
4-9	128/242 (52,9)	92/231 (39,8)	1,33 [1,09; 1,62] 0,0050[2]	1,70 [1,18; 2,44] 0,0044[3]	13,1 [4,2; 22,0] 0,0044[3]
≥ 10	63/108 (58,3)	39/90 (43,3)	1,35 [1,01; 1,79] 0,0409[2]	1,83 [1,04; 3,22] 0,0355[3]	15,0 [1,2; 28,8] 0,0355[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,5545)					
IIA	33/59 (55,9)	22/62 (35,5)	1,58 [1,05; 2,36] 0,0276[2]	2,31 [1,11; 4,79] 0,0239[3]	20,4 [3,1; 37,8] 0,0239[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	27/53 (50,9)	34/69 (49,3)	1,03 [0,72; 1,48] 0,8548[2]	1,07 [0,52; 2,19] 0,8551[3]	1,7 [-16,2; 19,6] 0,8551[3]
IIIA	121/236 (51,3)	87/214 (40,7)	1,26 [1,03; 1,55] 0,0259[2]	1,54 [1,06; 2,23] 0,0241[3]	10,6 [1,5; 19,8] 0,0241[3]
IIIB	10/18 (55,6)	5/15 (33,3)	1,67 [0,73; 3,81] 0,2257[2]	2,50 [0,60; 10,34] 0,2018[3]	22,2 [-10,9; 55,3] 0,2018[3]
IIIC	107/186 (57,5)	74/174 (42,5)	1,35 [1,09; 1,67] 0,0053[2]	1,83 [1,20; 2,78] 0,0045[3]	15,0 [4,8; 25,2] 0,0045[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,2818)					
G1	28/47 (59,6)	15/41 (36,6)	1,63 [1,02; 2,60] 0,0406[2]	2,55 [1,08; 6,05] 0,0314[3]	23,0 [2,6; 43,3] 0,0314[3]
G2	130/244 (53,3)	95/234 (40,6)	1,31 [1,08; 1,59] 0,0062[2]	1,67 [1,16; 2,40] 0,0055[3]	12,7 [3,8; 21,6] 0,0055[3]
G3	124/233 (53,2)	90/226 (39,8)	1,34 [1,09; 1,63] 0,0046[2]	1,72 [1,19; 2,49] 0,0040[3]	13,4 [4,4; 22,4] 0,0040[3]
GX	17/29 (58,6)	21/33 (63,6)	0,92 [0,62; 1,37] 0,6875[2]	0,81 [0,29; 2,25] 0,6858[3]	-5,0 [-29,3; 19,3] 0,6858[3]
Ethnizität (p-Wert des Interaktionsterms: 0,9035)					
Weiß	169/323 (52,3)	133/324 (41,0)	1,27 [1,08; 1,51] 0,0044[2]	1,58 [1,15; 2,15] 0,0041[3]	11,3 [3,6; 18,9] 0,0041[3]
Asiatisch	113/199 (56,8)	76/180 (42,2)	1,34 [1,09; 1,66] 0,0056[2]	1,80 [1,20; 2,70] 0,0046[3]	14,6 [4,6; 24,5] 0,0046[3]
Andere	11/19 (57,9)	10/21 (47,6)	1,22 [0,67; 2,19] 0,5164[2]	1,51 [0,43; 5,28] 0,5158[3]	10,3 [-20,5; 41,1] 0,5158[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Tabelle: Subgruppen - Unerwünschtes Ereignis: SOC Infektionen (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,3729)					
< 65 Jahre	442/918 (48,1)	343/937 (36,6)	1,32 [1,18; 1,46] <,0001[2]	1,61 [1,34; 1,94] <,0001[3]	11,5 [7,1; 16,0] <,0001[3]
≥ 65 Jahre	158/365 (43,3)	119/328 (36,3)	1,19 [0,99; 1,44] 0,0619[2]	1,34 [0,99; 1,82] 0,0601[3]	7,0 [-0,3; 14,3] 0,0601[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,4327)					
Neoadjuvante Chemotherapie	202/430 (47,0)	141/415 (34,0)	1,38 [1,17; 1,63] 0,0002[2]	1,72 [1,30; 2,27] 0,0001[3]	13,0 [6,4; 19,6] 0,0001[3]
Adjuvante Chemotherapie	368/784 (46,9)	296/769 (38,5)	1,22 [1,09; 1,37] 0,0008[2]	1,41 [1,16; 1,73] 0,0008[3]	8,4 [3,5; 13,3] 0,0008[3]
Keine Chemotherapie	30/69 (43,5)	25/81 (30,9)	1,41 [0,92; 2,15] 0,1120[2]	1,72 [0,88; 3,37] 0,1101[3]	12,6 [-2,8; 28,0] 0,1101[3]
Region (p-Wert des Interaktionsterms: 0,0832)					
Nordamerika / Europa	347/678 (51,2)	268/650 (41,2)	1,24 [1,10; 1,40] 0,0003[2]	1,49 [1,20; 1,86] 0,0003[3]	9,9 [4,6; 15,3] 0,0003[3]
Asien	102/203 (50,2)	92/201 (45,8)	1,10 [0,90; 1,35] 0,3688[2]	1,20 [0,81; 1,77] 0,3680[3]	4,5 [-5,3; 14,2] 0,3680[3]
Andere	151/402 (37,6)	102/414 (24,6)	1,52 [1,24; 1,88] <,0001[2]	1,84 [1,36; 2,49] <,0001[3]	12,9 [6,6; 19,2] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2290)					
< 20 mm	154/331 (46,5)	107/335 (31,9)	1,46 [1,20; 1,77] 0,0001[2]	1,85 [1,35; 2,54] 0,0001[3]	14,6 [7,3; 21,9] 0,0001[3]
≥ 20 bis < 50 mm	280/646 (43,3)	238/653 (36,4)	1,19 [1,04; 1,36] 0,0114[2]	1,33 [1,07; 1,67] 0,0111[3]	6,9 [1,6; 12,2] 0,0111[3]
≥ 50 mm	158/289 (54,7)	110/265 (41,5)	1,32 [1,10; 1,57] 0,0023[2]	1,70 [1,21; 2,38] 0,0020[3]	13,2 [4,9; 21,4] 0,0020[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9843)					
0-3	201/427 (47,1)	152/418 (36,4)	1,29 [1,10; 1,52] 0,0018[2]	1,56 [1,18; 2,05] 0,0016[3]	10,7 [4,1; 17,3] 0,0016[3]
4-9	252/549 (45,9)	196/542 (36,2)	1,27 [1,10; 1,47] 0,0012[2]	1,50 [1,18; 1,91] 0,0011[3]	9,7 [3,9; 15,5] 0,0011[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	147/307 (47,9)	114/305 (37,4)	1,28 [1,06; 1,54] 0,0092[2]	1,54 [1,12; 2,12] 0,0086[3]	10,5 [2,7; 18,3] 0,0086[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,8578)					
IIA	58/113 (51,3)	44/114 (38,6)	1,33 [0,99; 1,78] 0,0565[2]	1,68 [0,99; 2,84] 0,0539[3]	12,7 [-0,1; 25,6] 0,0539[3]
IIB	68/151 (45,0)	49/136 (36,0)	1,25 [0,94; 1,66] 0,1250[2]	1,45 [0,90; 2,34] 0,1212[3]	9,0 [-2,3; 20,3] 0,1212[3]
IIIA	235/495 (47,5)	171/488 (35,0)	1,35 [1,16; 1,58] <,0001[2]	1,68 [1,30; 2,17] <,0001[3]	12,4 [6,3; 18,5] <,0001[3]
IIIB	21/54 (38,9)	16/45 (35,6)	1,09 [0,65; 1,83] 0,7337[2]	1,15 [0,51; 2,62] 0,7328[3]	3,3 [-15,8; 22,4] 0,7328[3]
IIIC	216/468 (46,2)	181/480 (37,7)	1,22 [1,05; 1,42] 0,0087[2]	1,42 [1,09; 1,83] 0,0084[3]	8,4 [2,2; 14,7] 0,0084[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,7092)					
G1	41/91 (45,1)	27/93 (29,0)	1,55 [1,05; 2,29] 0,0274[2]	2,00 [1,09; 3,69] 0,0244[3]	16,0 [2,3; 29,8] 0,0244[3]
G2	288/612 (47,1)	223/603 (37,0)	1,27 [1,11; 1,45] 0,0004[2]	1,51 [1,20; 1,90] 0,0004[3]	10,1 [4,6; 15,6] 0,0004[3]
G3	244/527 (46,3)	189/506 (37,4)	1,24 [1,07; 1,43] 0,0038[2]	1,45 [1,13; 1,85] 0,0036[3]	8,9 [3,0; 14,9] 0,0036[3]
GX	26/51 (51,0)	21/59 (35,6)	1,43 [0,93; 2,22] 0,1064[2]	1,88 [0,88; 4,04] 0,1038[3]	15,4 [-3,0; 33,8] 0,1038[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,6511)					
Negativ	78/156 (50,0)	71/169 (42,0)	1,19 [0,94; 1,51] 0,1494[2]	1,38 [0,89; 2,14] 0,1488[3]	8,0 [-2,8; 18,8] 0,1488[3]
Positiv	506/1089 (46,5)	376/1067 (35,2)	1,32 [1,19; 1,46] <,0001[2]	1,60 [1,34; 1,90] <,0001[3]	11,2 [7,1; 15,3] <,0001[3]
Unbekannt	6/10 (60,0)	4/7 (57,1)	1,05 [0,46; 2,38] 0,9068[2]	1,13 [0,16; 7,99] 1,0000[4]	2,9 [-44,7; 50,5] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,0990)					
Weiß	446/958 (46,6)	343/944 (36,3)	1,28 [1,15; 1,43] <,0001[2]	1,53 [1,27; 1,83] <,0001[3]	10,2 [5,8; 14,6] <,0001[3]
Asiatisch	116/250 (46,4)	96/242 (39,7)	1,17 [0,95; 1,44] 0,1334[2]	1,32 [0,92; 1,88] 0,1318[3]	6,7 [-2,0; 15,5] 0,1318[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Andere	31/62 (50,0)	15/64 (23,4)	2,13 [1,28; 3,55] 0,0035[2]	3,27 [1,52; 7,01] 0,0020[3]	26,6 [10,4; 42,8] 0,0020[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,9764)					
Tamoxifen	63/114 (55,3)	57/132 (43,2)	1,28 [0,99; 1,65] 0,0590[2]	1,63 [0,98; 2,69] 0,0587[3]	12,1 [-0,4; 24,5] 0,0587[3]
Aromatase-Inhibitor	537/1169 (45,9)	405/1133 (35,7)	1,29 [1,16; 1,42] <,0001[2]	1,53 [1,29; 1,81] <,0001[3]	10,2 [6,2; 14,2] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,6788)					
ECOG-PS 0	499/1070 (46,6)	375/1020 (36,8)	1,27 [1,14; 1,41] <,0001[2]	1,50 [1,26; 1,79] <,0001[3]	9,9 [5,7; 14,1] <,0001[3]
ECOG-PS 1	101/213 (47,4)	87/245 (35,5)	1,34 [1,07; 1,66] 0,0100[2]	1,64 [1,13; 2,38] 0,0098[3]	11,9 [2,9; 20,9] 0,0098[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: SOC Infektionen aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7114)					
Neoadjuvante Chemotherapie	9/217 (4,1)	6/219 (2,7)	1,51 [0,55; 4,18] 0,4237[2]	1,54 [0,54; 4,39] 0,4200[3]	1,4 [-2,0; 4,8] 0,4200[3]
Adjuvante Chemotherapie	12/327 (3,7)	4/312 (1,3)	2,86 [0,93; 8,78] 0,0659[2]	2,93 [0,94; 9,19] 0,0535[3]	2,4 [-0,0; 4,8] 0,0535[3]
Keine Chemotherapie	0/9 (0,0)	0/4 (0,0)	NB	NB	NB
Region (p-Wert des Interaktionsterms: 0,4747)					
Nordamerika / Europa	13/252 (5,2)	6/233 (2,6)	2,00 [0,77; 5,18] 0,1521[2]	2,06 [0,77; 5,51] 0,1429[3]	2,6 [-0,8; 6,0] 0,1429[3]
Asien	3/168 (1,8)	3/166 (1,8)	0,99 [0,20; 4,83] 0,9882[2]	0,99 [0,20; 4,97] 1,0000[4]	-0,0 [-2,9; 2,8] 1,0000[4]
Andere	5/133 (3,8)	1/136 (0,7)	5,11 [0,61; 43,18] 0,1339[2]	5,27 [0,61; 45,75] 0,1174[4]	3,0 [-0,5; 6,6] 0,1174[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6076)					
< 20 mm	5/141 (3,5)	4/140 (2,9)	1,24 [0,34; 4,53] 0,7435[2]	1,25 [0,33; 4,76] 1,0000[4]	0,7 [-3,4; 4,8] 1,0000[4]
≥ 20 bis < 50 mm	9/255 (3,5)	4/249 (1,6)	2,20 [0,69; 7,04] 0,1853[2]	2,24 [0,68; 7,37] 0,1733[3]	1,9 [-0,8; 4,7] 0,1733[3]
≥ 50 mm	7/145 (4,8)	2/141 (1,4)	3,40 [0,72; 16,10] 0,1225[2]	3,53 [0,72; 17,27] 0,1731[4]	3,4 [-0,6; 7,4] 0,1731[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,4432)					
0-3	5/203 (2,5)	5/214 (2,3)	1,05 [0,31; 3,59] 0,9327[2]	1,06 [0,30; 3,70] 1,0000[4]	0,1 [-2,8; 3,1] 1,0000[4]
4-9	10/242 (4,1)	3/231 (1,3)	3,18 [0,89; 11,42] 0,0758[2]	3,28 [0,89; 12,06] 0,0595[3]	2,8 [-0,1; 5,7] 0,0595[3]
≥ 10	6/108 (5,6)	2/90 (2,2)	2,50 [0,52; 12,08] 0,2544[2]	2,59 [0,51; 13,15] 0,2956[4]	3,3 [-2,0; 8,6] 0,2956[4]
Tumorstadium (p-Wert des Interaktionsterms: 0,9492)					
IIA	0/59 (0,0)	3/62 (4,8)	0,15 [0,01; 2,84] 0,2063[2]	0,14 [0,01; 2,83] 0,2442[4]	-4,8 [-10,2; 0,5] 0,2442[4]
IIB	0/53 (0,0)	0/69 (0,0)	NB	NB	NB

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	10/236 (4,2)	2/214 (0,9)	4,53 [1,00; 20,46] 0,0493[2]	4,69 [1,02; 21,65] 0,0299[3]	3,3 [0,4; 6,2] 0,0299[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NB	NB	NB
IIIC	11/186 (5,9)	5/174 (2,9)	2,06 [0,73; 5,80] 0,1724[2]	2,12 [0,72; 6,24] 0,1619[3]	3,0 [-1,2; 7,2] 0,1619[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,7838)					
G1	3/47 (6,4)	1/41 (2,4)	2,62 [0,28; 24,19] 0,3966[2]	2,73 [0,27; 27,29] 0,6199[4]	3,9 [-4,5; 12,4] 0,6199[4]
G2	11/244 (4,5)	4/234 (1,7)	2,64 [0,85; 8,17] 0,0926[2]	2,71 [0,85; 8,65] 0,0793[3]	2,8 [-0,3; 5,9] 0,0793[3]
G3	6/233 (2,6)	5/226 (2,2)	1,16 [0,36; 3,76] 0,7997[2]	1,17 [0,35; 3,88] 0,7995[3]	0,4 [-2,4; 3,2] 0,7995[3]
GX	1/29 (3,4)	0/33 (0,0)	3,40 [0,14; 80,36] 0,4482[2]	3,53 [0,14; 89,98] 0,4677[4]	3,4 [-3,2; 10,1] 0,4677[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,2971)					
Negativ	2/49 (4,1)	3/44 (6,8)	0,60 [0,10; 3,42] 0,5638[2]	0,58 [0,09; 3,65] 0,6646[4]	-2,7 [-12,0; 6,5] 0,6646[4]
Positiv	15/477 (3,1)	5/471 (1,1)	2,96 [1,09; 8,09] 0,0340[2]	3,03 [1,09; 8,39] 0,0256[3]	2,1 [0,3; 3,9] 0,0256[3]
Unbekannt	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Ethnizität (p-Wert des Interaktionsterms: 0,6466)					
Weiß	15/323 (4,6)	7/324 (2,2)	2,15 [0,89; 5,20] 0,0897[2]	2,21 [0,89; 5,48] 0,0814[3]	2,5 [-0,3; 5,3] 0,0814[3]
Asiatisch	3/199 (1,5)	3/180 (1,7)	0,90 [0,18; 4,42] 0,9014[2]	0,90 [0,18; 4,53] 1,0000[4]	-0,2 [-2,7; 2,4] 1,0000[4]
Andere	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,9751)					
ECOG-PS 0	21/496 (4,2)	8/480 (1,7)	2,54 [1,14; 5,68] 0,0231[2]	2,61 [1,14; 5,95] 0,0182[3]	2,6 [0,5; 4,7] 0,0182[3]
ECOG-PS 1	0/57 (0,0)	2/55 (3,6)	0,19 [0,01; 3,93] 0,2849[2]	0,19 [0,01; 3,97] 0,2389[4]	-3,6 [-8,6; 1,3] 0,2389[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class					

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: SOC Infektionen aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,5500)					
< 65 Jahre	44/918 (4,8)	26/937 (2,8)	1,73 [1,07; 2,78] 0,0245[2]	1,76 [1,08; 2,89] 0,0226[3]	2,0 [0,3; 3,8] 0,0226[3]
≥ 65 Jahre	25/365 (6,8)	10/328 (3,0)	2,25 [1,10; 4,61] 0,0271[2]	2,34 [1,11; 4,95] 0,0225[3]	3,8 [0,6; 7,0] 0,0225[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,2967)					
Neoadjuvante Chemotherapie	24/430 (5,6)	13/415 (3,1)	1,78 [0,92; 3,45] 0,0869[2]	1,83 [0,92; 3,64] 0,0820[3]	2,4 [-0,3; 5,2] 0,0820[3]
Adjuvante Chemotherapie	42/784 (5,4)	18/769 (2,3)	2,29 [1,33; 3,94] 0,0028[2]	2,36 [1,35; 4,14] 0,0020[3]	3,0 [1,1; 4,9] 0,0020[3]
Keine Chemotherapie	3/69 (4,3)	5/81 (6,2)	0,70 [0,17; 2,84] 0,6224[2]	0,69 [0,16; 3,00] 0,7264[4]	-1,8 [-8,9; 5,3] 0,7264[4]
Region (p-Wert des Interaktionsterms: 0,1715)					
Nordamerika / Europa	46/678 (6,8)	25/650 (3,8)	1,76 [1,10; 2,84] 0,0192[2]	1,82 [1,10; 3,00] 0,0173[3]	2,9 [0,5; 5,3] 0,0173[3]
Asien	7/203 (3,4)	7/201 (3,5)	0,99 [0,35; 2,77] 0,9850[2]	0,99 [0,34; 2,87] 0,9850[3]	-0,0 [-3,6; 3,5] 0,9850[3]
Andere	16/402 (4,0)	4/414 (1,0)	4,12 [1,39; 12,22] 0,0107[2]	4,25 [1,41; 12,82] 0,0054[3]	3,0 [0,9; 5,1] 0,0054[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,0751)					
< 20 mm	17/331 (5,1)	5/335 (1,5)	3,44 [1,28; 9,22] 0,0140[2]	3,57 [1,30; 9,80] 0,0085[3]	3,6 [0,9; 6,4] 0,0085[3]
≥ 20 bis < 50 mm	33/646 (5,1)	26/653 (4,0)	1,28 [0,78; 2,12] 0,3309[2]	1,30 [0,77; 2,20] 0,3295[3]	1,1 [-1,1; 3,4] 0,3295[3]
≥ 50 mm	19/289 (6,6)	5/265 (1,9)	3,48 [1,32; 9,20] 0,0117[2]	3,66 [1,35; 9,94] 0,0068[3]	4,7 [1,4; 8,0] 0,0068[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8242)					
0-3	27/427 (6,3)	15/418 (3,6)	1,76 [0,95; 3,26] 0,0718[2]	1,81 [0,95; 3,46] 0,0674[3]	2,7 [-0,2; 5,7] 0,0674[3]
4-9	21/549 (3,8)	12/542 (2,2)	1,73 [0,86; 3,48] 0,1254[2]	1,76 [0,86; 3,61] 0,1203[3]	1,6 [-0,4; 3,6] 0,1203[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	21/307 (6,8)	9/305 (3,0)	2,32 [1,08; 4,98] 0,0312[2]	2,41 [1,09; 5,36] 0,0259[3]	3,9 [0,5; 7,3] 0,0259[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,6341)					
IIA	6/113 (5,3)	3/114 (2,6)	2,02 [0,52; 7,87] 0,3122[2]	2,07 [0,51; 8,51] 0,3327[4]	2,7 [-2,4; 7,8] 0,3327[4]
IIB	10/151 (6,6)	9/136 (6,6)	1,00 [0,42; 2,39] 0,9987[2]	1,00 [0,39; 2,54] 0,9987[3]	0,0 [-5,8; 5,8] 0,9987[3]
IIIA	24/495 (4,8)	10/488 (2,0)	2,37 [1,14; 4,90] 0,0202[2]	2,44 [1,15; 5,15] 0,0163[3]	2,8 [0,5; 5,1] 0,0163[3]
IIIB	2/54 (3,7)	1/45 (2,2)	1,67 [0,16; 17,79] 0,6724[2]	1,69 [0,15; 19,30] 1,0000[4]	1,5 [-5,1; 8,1] 1,0000[4]
IIIC	27/468 (5,8)	13/480 (2,7)	2,13 [1,11; 4,08] 0,0224[2]	2,20 [1,12; 4,32] 0,0191[3]	3,1 [0,5; 5,6] 0,0191[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,1246)					
G1	5/91 (5,5)	4/93 (4,3)	1,28 [0,35; 4,61] 0,7083[2]	1,29 [0,34; 4,98] 0,7457[4]	1,2 [-5,0; 7,4] 0,7457[4]
G2	34/612 (5,6)	10/603 (1,7)	3,35 [1,67; 6,72] 0,0007[2]	3,49 [1,71; 7,13] 0,0003[3]	3,9 [1,8; 6,0] 0,0003[3]
G3	26/527 (4,9)	21/506 (4,2)	1,19 [0,68; 2,09] 0,5465[2]	1,20 [0,67; 2,16] 0,5459[3]	0,8 [-1,8; 3,3] 0,5459[3]
GX	3/51 (5,9)	1/59 (1,7)	3,47 [0,37; 32,34] 0,2745[2]	3,63 [0,37; 35,99] 0,3349[4]	4,2 [-3,1; 11,4] 0,3349[4]
Ethnizität (p-Wert des Interaktionsterms: 0,6629)					
Weiß	55/958 (5,7)	28/944 (3,0)	1,94 [1,24; 3,02] 0,0037[2]	1,99 [1,25; 3,17] 0,0031[3]	2,8 [0,9; 4,6] 0,0031[3]
Asiatisch	10/250 (4,0)	8/242 (3,3)	1,21 [0,49; 3,01] 0,6823[2]	1,22 [0,47; 3,14] 0,6818[3]	0,7 [-2,6; 4,0] 0,6818[3]
Andere	4/62 (6,5)	0/64 (0,0)	9,29 [0,51; 168,95] 0,1322[2]	9,92 [0,52; 188,28] 0,0557[4]	6,5 [0,3; 12,6] 0,0557[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,7656)					
ECOG-PS 0	54/1070 (5,0)	26/1020 (2,5)	1,98 [1,25; 3,14] 0,0036[2]	2,03 [1,26; 3,27] 0,0029[3]	2,5 [0,9; 4,1] 0,0029[3]
ECOG-PS 1	15/213 (7,0)	10/245 (4,1)	1,73 [0,79; 3,76] 0,1699[2]	1,78 [0,78; 4,05] 0,1642[3]	3,0 [-1,3; 7,2] 0,1642[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class					

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: SOC Infektionen aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,4046)					
Neoadjuvante Chemotherapie	106/217 (48,8)	91/219 (41,6)	1,18 [0,95; 1,45] 0,1272[2]	1,34 [0,92; 1,96] 0,1259[3]	7,3 [-2,0; 16,6] 0,1259[3]
Adjuvante Chemotherapie	181/327 (55,4)	127/312 (40,7)	1,36 [1,15; 1,60] 0,0003[2]	1,81 [1,32; 2,47] 0,0002[3]	14,6 [7,0; 22,3] 0,0002[3]
Keine Chemotherapie	6/9 (66,7)	1/4 (25,0)	2,67 [0,46; 15,49] 0,2745[2]	6,00 [0,42; 85,25] 0,2657[4]	41,7 [-10,8; 94,1] 0,2657[4]
Region (p-Wert des Interaktionsterms: 0,8375)					
Nordamerika / Europa	133/252 (52,8)	99/233 (42,5)	1,24 [1,03; 1,50] 0,0250[2]	1,51 [1,06; 2,17] 0,0234[3]	10,3 [1,4; 19,1] 0,0234[3]
Asien	100/168 (59,5)	73/166 (44,0)	1,35 [1,09; 1,67] 0,0052[2]	1,87 [1,21; 2,89] 0,0045[3]	15,5 [5,0; 26,1] 0,0045[3]
Andere	60/133 (45,1)	47/136 (34,6)	1,31 [0,97; 1,76] 0,0793[2]	1,56 [0,95; 2,54] 0,0770[3]	10,6 [-1,1; 22,2] 0,0770[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,5419)					
< 20 mm	81/141 (57,4)	57/140 (40,7)	1,41 [1,10; 1,80] 0,0059[2]	1,97 [1,22; 3,16] 0,0050[3]	16,7 [5,2; 28,3] 0,0050[3]
≥ 20 bis < 50 mm	126/255 (49,4)	102/249 (41,0)	1,21 [0,99; 1,46] 0,0583[2]	1,41 [0,99; 2,00] 0,0568[3]	8,4 [-0,2; 17,1] 0,0568[3]
≥ 50 mm	81/145 (55,9)	57/141 (40,4)	1,38 [1,08; 1,77] 0,0103[2]	1,87 [1,17; 2,98] 0,0090[3]	15,4 [4,0; 26,9] 0,0090[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9696)					
0-3	107/203 (52,7)	89/214 (41,6)	1,27 [1,03; 1,56] 0,0238[2]	1,57 [1,06; 2,31] 0,0230[3]	11,1 [1,6; 20,6] 0,0230[3]
4-9	126/242 (52,1)	92/231 (39,8)	1,31 [1,07; 1,60] 0,0084[2]	1,64 [1,14; 2,36] 0,0076[3]	12,2 [3,3; 21,2] 0,0076[3]
≥ 10	60/108 (55,6)	38/90 (42,2)	1,32 [0,98; 1,77] 0,0680[2]	1,71 [0,97; 3,01] 0,0617[3]	13,3 [-0,5; 27,2] 0,0617[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,5007)					
IIA	33/59 (55,9)	21/62 (33,9)	1,65 [1,09; 2,50] 0,0179[2]	2,48 [1,19; 5,17] 0,0147[3]	22,1 [4,8; 39,4] 0,0147[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	27/53 (50,9)	34/69 (49,3)	1,03 [0,72; 1,48] 0,8548[2]	1,07 [0,52; 2,19] 0,8551[3]	1,7 [-16,2; 19,6] 0,8551[3]
IIIA	120/236 (50,8)	87/214 (40,7)	1,25 [1,02; 1,53] 0,0323[2]	1,51 [1,04; 2,19] 0,0303[3]	10,2 [1,0; 19,4] 0,0303[3]
IIIB	10/18 (55,6)	5/15 (33,3)	1,67 [0,73; 3,81] 0,2257[2]	2,50 [0,60; 10,34] 0,2018[3]	22,2 [-10,9; 55,3] 0,2018[3]
IIIC	102/186 (54,8)	72/174 (41,4)	1,33 [1,06; 1,65] 0,0120[2]	1,72 [1,13; 2,61] 0,0107[3]	13,5 [3,2; 23,7] 0,0107[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,3173)					
G1	27/47 (57,4)	15/41 (36,6)	1,57 [0,98; 2,52] 0,0611[2]	2,34 [0,99; 5,53] 0,0506[3]	20,9 [0,4; 41,3] 0,0506[3]
G2	126/244 (51,6)	93/234 (39,7)	1,30 [1,06; 1,59] 0,0099[2]	1,62 [1,13; 2,33] 0,0091[3]	11,9 [3,0; 20,8] 0,0091[3]
G3	123/233 (52,8)	89/226 (39,4)	1,34 [1,10; 1,64] 0,0045[2]	1,72 [1,19; 2,49] 0,0040[3]	13,4 [4,4; 22,4] 0,0040[3]
GX	17/29 (58,6)	21/33 (63,6)	0,92 [0,62; 1,37] 0,6875[2]	0,81 [0,29; 2,25] 0,6858[3]	-5,0 [-29,3; 19,3] 0,6858[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,0835)					
Negativ	21/49 (42,9)	22/44 (50,0)	0,86 [0,55; 1,33] 0,4903[2]	0,75 [0,33; 1,70] 0,4903[3]	-7,1 [-27,4; 13,1] 0,4903[3]
Positiv	257/477 (53,9)	183/471 (38,9)	1,39 [1,20; 1,60] <,0001[2]	1,84 [1,42; 2,38] <,0001[3]	15,0 [8,7; 21,3] <,0001[3]
Unbekannt	2/4 (50,0)	5/8 (62,5)	0,80 [0,26; 2,45] 0,6955[2]	0,60 [0,05; 6,79] 1,0000[4]	-12,5 [-71,9; 46,9] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,7244)					
Weiß	165/323 (51,1)	132/324 (40,7)	1,25 [1,06; 1,49] 0,0088[2]	1,52 [1,11; 2,07] 0,0083[3]	10,3 [2,7; 18,0] 0,0083[3]
Asiatisch	112/199 (56,3)	74/180 (41,1)	1,37 [1,11; 1,69] 0,0039[2]	1,84 [1,23; 2,77] 0,0032[3]	15,2 [5,2; 25,1] 0,0032[3]
Andere	10/19 (52,6)	10/21 (47,6)	1,11 [0,60; 2,05] 0,7513[2]	1,22 [0,35; 4,24] 0,7515[3]	5,0 [-26,0; 36,0] 0,7515[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class					

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: SOC Infektionen aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,3123)					
< 65 Jahre	428/918 (46,6)	340/937 (36,3)	1,28 [1,15; 1,43] <,0001[2]	1,53 [1,27; 1,85] <,0001[3]	10,3 [5,9; 14,8] <,0001[3]
≥ 65 Jahre	148/365 (40,5)	116/328 (35,4)	1,15 [0,95; 1,39] 0,1626[2]	1,25 [0,92; 1,70] 0,1607[3]	5,2 [-2,0; 12,4] 0,1607[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,4544)					
Neoadjuvante Chemotherapie	191/430 (44,4)	137/415 (33,0)	1,35 [1,13; 1,60] 0,0008[2]	1,62 [1,23; 2,14] 0,0007[3]	11,4 [4,9; 17,9] 0,0007[3]
Adjuvante Chemotherapie	357/784 (45,5)	295/769 (38,4)	1,19 [1,06; 1,34] 0,0044[2]	1,34 [1,10; 1,64] 0,0042[3]	7,2 [2,3; 12,1] 0,0042[3]
Keine Chemotherapie	28/69 (40,6)	24/81 (29,6)	1,37 [0,88; 2,13] 0,1618[2]	1,62 [0,82; 3,19] 0,1602[3]	11,0 [-4,3; 26,2] 0,1602[3]
Region (p-Wert des Interaktionsterms: 0,1340)					
Nordamerika / Europa	332/678 (49,0)	262/650 (40,3)	1,21 [1,08; 1,37] 0,0016[2]	1,42 [1,14; 1,77] 0,0015[3]	8,7 [3,3; 14,0] 0,0015[3]
Asien	100/203 (49,3)	92/201 (45,8)	1,08 [0,88; 1,32] 0,4829[2]	1,15 [0,78; 1,70] 0,4825[3]	3,5 [-6,2; 13,2] 0,4825[3]
Andere	144/402 (35,8)	102/414 (24,6)	1,45 [1,17; 1,80] 0,0006[2]	1,71 [1,26; 2,31] 0,0005[3]	11,2 [4,9; 17,4] 0,0005[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,2689)					
< 20 mm	149/331 (45,0)	106/335 (31,6)	1,42 [1,17; 1,73] 0,0005[2]	1,77 [1,29; 2,43] 0,0004[3]	13,4 [6,1; 20,7] 0,0004[3]
≥ 20 bis < 50 mm	270/646 (41,8)	234/653 (35,8)	1,17 [1,02; 1,34] 0,0279[2]	1,29 [1,03; 1,61] 0,0275[3]	6,0 [0,7; 11,3] 0,0275[3]
≥ 50 mm	149/289 (51,6)	109/265 (41,1)	1,25 [1,04; 1,50] 0,0152[2]	1,52 [1,09; 2,13] 0,0140[3]	10,4 [2,2; 18,7] 0,0140[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9736)					
0-3	192/427 (45,0)	149/418 (35,6)	1,26 [1,07; 1,49] 0,0061[2]	1,48 [1,12; 1,94] 0,0058[3]	9,3 [2,7; 15,9] 0,0058[3]
4-9	246/549 (44,8)	195/542 (36,0)	1,25 [1,08; 1,44] 0,0032[2]	1,44 [1,13; 1,84] 0,0030[3]	8,8 [3,0; 14,6] 0,0030[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	138/307 (45,0)	112/305 (36,7)	1,22 [1,01; 1,48] 0,0394[2]	1,41 [1,02; 1,94] 0,0384[3]	8,2 [0,5; 16,0] 0,0384[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,8591)					
IIA	57/113 (50,4)	43/114 (37,7)	1,34 [0,99; 1,80] 0,0562[2]	1,68 [0,99; 2,85] 0,0535[3]	12,7 [-0,1; 25,5] 0,0535[3]
IIB	64/151 (42,4)	49/136 (36,0)	1,18 [0,88; 1,57] 0,2741[2]	1,31 [0,81; 2,10] 0,2712[3]	6,4 [-4,9; 17,6] 0,2712[3]
IIIA	226/495 (45,7)	170/488 (34,8)	1,31 [1,12; 1,53] 0,0006[2]	1,57 [1,22; 2,03] 0,0005[3]	10,8 [4,7; 16,9] 0,0005[3]
IIIB	21/54 (38,9)	16/45 (35,6)	1,09 [0,65; 1,83] 0,7337[2]	1,15 [0,51; 2,62] 0,7328[3]	3,3 [-15,8; 22,4] 0,7328[3]
IIIC	206/468 (44,0)	177/480 (36,9)	1,19 [1,02; 1,39] 0,0255[2]	1,35 [1,04; 1,75] 0,0251[3]	7,1 [0,9; 13,4] 0,0251[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,6943)					
G1	38/91 (41,8)	25/93 (26,9)	1,55 [1,03; 2,35] 0,0370[2]	1,95 [1,05; 3,62] 0,0335[3]	14,9 [1,3; 28,4] 0,0335[3]
G2	277/612 (45,3)	222/603 (36,8)	1,23 [1,07; 1,41] 0,0029[2]	1,42 [1,13; 1,79] 0,0028[3]	8,4 [2,9; 14,0] 0,0028[3]
G3	235/527 (44,6)	186/506 (36,8)	1,21 [1,05; 1,41] 0,0109[2]	1,38 [1,08; 1,78] 0,0104[3]	7,8 [1,9; 13,8] 0,0104[3]
GX	25/51 (49,0)	21/59 (35,6)	1,38 [0,88; 2,14] 0,1567[2]	1,74 [0,81; 3,74] 0,1546[3]	13,4 [-4,9; 31,8] 0,1546[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,8062)					
Negativ	76/156 (48,7)	69/169 (40,8)	1,19 [0,94; 1,52] 0,1535[2]	1,38 [0,89; 2,14] 0,1529[3]	7,9 [-2,9; 18,7] 0,1529[3]
Positiv	484/1089 (44,4)	372/1067 (34,9)	1,27 [1,15; 1,42] <,0001[2]	1,49 [1,26; 1,78] <,0001[3]	9,6 [5,5; 13,7] <,0001[3]
Unbekannt	6/10 (60,0)	4/7 (57,1)	1,05 [0,46; 2,38] 0,9068[2]	1,13 [0,16; 7,99] 1,0000[4]	2,9 [-44,7; 50,5] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,1006)					
Weiß	427/958 (44,6)	337/944 (35,7)	1,25 [1,12; 1,40] <,0001[2]	1,45 [1,20; 1,74] <,0001[3]	8,9 [4,5; 13,3] <,0001[3]
Asiatisch	112/250 (44,8)	96/242 (39,7)	1,13 [0,92; 1,39] 0,2507[2]	1,23 [0,86; 1,77] 0,2494[3]	5,1 [-3,6; 13,8] 0,2494[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Andere	30/62 (48,4)	15/64 (23,4)	2,06 [1,24; 3,44] 0,0055[2]	3,06 [1,43; 6,57] 0,0035[3]	24,9 [8,7; 41,1] 0,0035[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,9510)					
Tamoxifen	62/114 (54,4)	57/132 (43,2)	1,26 [0,97; 1,63] 0,0797[2]	1,57 [0,95; 2,60] 0,0795[3]	11,2 [-1,2; 23,7] 0,0795[3]
Aromatase-Inhibitor	514/1169 (44,0)	399/1133 (35,2)	1,25 [1,13; 1,38] <,0001[2]	1,44 [1,22; 1,71] <,0001[3]	8,8 [4,8; 12,7] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,6038)					
ECOG-PS 0	480/1070 (44,9)	372/1020 (36,5)	1,23 [1,11; 1,37] 0,0001[2]	1,42 [1,19; 1,69] <,0001[3]	8,4 [4,2; 12,6] <,0001[3]
ECOG-PS 1	96/213 (45,1)	84/245 (34,3)	1,31 [1,05; 1,65] 0,0188[2]	1,57 [1,08; 2,29] 0,0184[3]	10,8 [1,8; 19,7] 0,0184[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Tabelle: Subgruppen - Schwerwiegendes unerwünschtes Ereignis: SOC Infektionen aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9999)					
Neoadjuvante Chemotherapie	7/217 (3,2)	4/219 (1,8)	1,77 [0,52; 5,95] 0,3585[2]	1,79 [0,52; 6,21] 0,3516[3]	1,4 [-1,5; 4,3] 0,3516[3]
Adjuvante Chemotherapie	11/327 (3,4)	6/312 (1,9)	1,75 [0,65; 4,67] 0,2647[2]	1,78 [0,65; 4,86] 0,2579[3]	1,4 [-1,0; 3,9] 0,2579[3]
Keine Chemotherapie	0/9 (0,0)	0/4 (0,0)	NB	NB	NB
Region (p-Wert des Interaktionsterms: 0,5023)					
Nordamerika / Europa	8/252 (3,2)	6/233 (2,6)	1,23 [0,43; 3,50] 0,6942[2]	1,24 [0,42; 3,63] 0,6936[3]	0,6 [-2,4; 3,6] 0,6936[3]
Asien	5/168 (3,0)	3/166 (1,8)	1,65 [0,40; 6,78] 0,4896[2]	1,67 [0,39; 7,09] 0,7233[4]	1,2 [-2,1; 4,4] 0,7233[4]
Andere	5/133 (3,8)	1/136 (0,7)	5,11 [0,61; 43,18] 0,1339[2]	5,27 [0,61; 45,75] 0,1174[4]	3,0 [-0,5; 6,6] 0,1174[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,0919)					
< 20 mm	2/141 (1,4)	5/140 (3,6)	0,40 [0,08; 2,01] 0,2648[2]	0,39 [0,07; 2,04] 0,2820[4]	-2,2 [-5,8; 1,5] 0,2820[4]
≥ 20 bis < 50 mm	10/255 (3,9)	4/249 (1,6)	2,44 [0,78; 7,68] 0,1270[2]	2,50 [0,77; 8,08] 0,1138[3]	2,3 [-0,5; 5,2] 0,1138[3]
≥ 50 mm	6/145 (4,1)	1/141 (0,7)	5,83 [0,71; 47,85] 0,1004[2]	6,04 [0,72; 50,85] 0,1207[4]	3,4 [-0,1; 7,0] 0,1207[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,5100)					
0-3	6/203 (3,0)	6/214 (2,8)	1,05 [0,35; 3,22] 0,9261[2]	1,06 [0,33; 3,33] 0,9261[3]	0,2 [-3,1; 3,4] 0,9261[3]
4-9	6/242 (2,5)	2/231 (0,9)	2,86 [0,58; 14,04] 0,1947[2]	2,91 [0,58; 14,57] 0,2859[4]	1,6 [-0,7; 3,9] 0,2859[4]
≥ 10	6/108 (5,6)	2/90 (2,2)	2,50 [0,52; 12,08] 0,2544[2]	2,59 [0,51; 13,15] 0,2956[4]	3,3 [-2,0; 8,6] 0,2956[4]
Tumorstadium (p-Wert des Interaktionsterms: 0,8408)					
IIA	0/59 (0,0)	3/62 (4,8)	0,15 [0,01; 2,84] 0,2063[2]	0,14 [0,01; 2,83] 0,2442[4]	-4,8 [-10,2; 0,5] 0,2442[4]
IIB	1/53 (1,9)	0/69 (0,0)	3,89 [0,16; 93,60] 0,4027[2]	3,97 [0,16; 99,46] 0,4344[4]	1,9 [-1,8; 5,5] 0,4344[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	7/236 (3,0)	1/214 (0,5)	6,35 [0,79; 51,17] 0,0827[2]	6,51 [0,79; 53,36] 0,0705[4]	2,5 [0,1; 4,8] 0,0705[4]
IIIB	0/18 (0,0)	0/15 (0,0)	NB	NB	NB
IIIC	10/186 (5,4)	6/174 (3,4)	1,56 [0,58; 4,20] 0,3796[2]	1,59 [0,57; 4,47] 0,3750[3]	1,9 [-2,3; 6,2] 0,3750[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,8403)					
G1	1/47 (2,1)	1/41 (2,4)	0,87 [0,06; 13,51] 0,9222[2]	0,87 [0,05; 14,36] 1,0000[4]	-0,3 [-6,6; 6,0] 1,0000[4]
G2	8/244 (3,3)	3/234 (1,3)	2,56 [0,69; 9,52] 0,1616[2]	2,61 [0,68; 9,96] 0,1456[3]	2,0 [-0,7; 4,7] 0,1456[3]
G3	8/233 (3,4)	6/226 (2,7)	1,29 [0,46; 3,67] 0,6288[2]	1,30 [0,45; 3,82] 0,6277[3]	0,8 [-2,4; 3,9] 0,6277[3]
GX	1/29 (3,4)	0/33 (0,0)	3,40 [0,14; 80,36] 0,4482[2]	3,53 [0,14; 89,98] 0,4677[4]	3,4 [-3,2; 10,1] 0,4677[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9098)					
Negativ	3/49 (6,1)	3/44 (6,8)	0,90 [0,19; 4,22] 0,8916[2]	0,89 [0,17; 4,66] 1,0000[4]	-0,7 [-10,7; 9,3] 1,0000[4]
Positiv	12/477 (2,5)	5/471 (1,1)	2,37 [0,84; 6,67] 0,1024[2]	2,41 [0,84; 6,88] 0,0916[3]	1,5 [-0,2; 3,1] 0,0916[3]
Unbekannt	0/4 (0,0)	0/8 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,9865)					
Weiß	11/323 (3,4)	7/324 (2,2)	1,58 [0,62; 4,02] 0,3401[2]	1,60 [0,61; 4,17] 0,3356[3]	1,2 [-1,3; 3,8] 0,3356[3]
Asiatisch	6/199 (3,0)	3/180 (1,7)	1,81 [0,46; 7,13] 0,3968[2]	1,83 [0,45; 7,44] 0,5076[4]	1,3 [-1,7; 4,4] 0,5076[4]
Andere	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,5160)					
ECOG-PS 0	16/496 (3,2)	8/480 (1,7)	1,94 [0,84; 4,48] 0,1231[2]	1,97 [0,83; 4,64] 0,1159[3]	1,6 [-0,4; 3,5] 0,1159[3]
ECOG-PS 1	2/57 (3,5)	2/55 (3,6)	0,96 [0,14; 6,61] 0,9710[2]	0,96 [0,13; 7,09] 1,0000[4]	-0,1 [-7,0; 6,7] 1,0000[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class					

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Tabelle: Subgruppen - Schwerwiegendes unerwünschtes Ereignis: SOC Infektionen aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,4685)					
< 65 Jahre	44/918 (4,8)	25/937 (2,7)	1,80 [1,11; 2,91] 0,0173[2]	1,84 [1,11; 3,03] 0,0156[3]	2,1 [0,4; 3,8] 0,0156[3]
≥ 65 Jahre	25/365 (6,8)	9/328 (2,7)	2,50 [1,18; 5,27] 0,0164[2]	2,61 [1,20; 5,67] 0,0125[3]	4,1 [1,0; 7,2] 0,0125[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,1971)					
Neoadjuvante Chemotherapie	26/430 (6,0)	12/415 (2,9)	2,09 [1,07; 4,09] 0,0311[2]	2,16 [1,08; 4,34] 0,0269[3]	3,2 [0,4; 5,9] 0,0269[3]
Adjuvante Chemotherapie	42/784 (5,4)	18/769 (2,3)	2,29 [1,33; 3,94] 0,0028[2]	2,36 [1,35; 4,14] 0,0020[3]	3,0 [1,1; 4,9] 0,0020[3]
Keine Chemotherapie	1/69 (1,4)	4/81 (4,9)	0,29 [0,03; 2,56] 0,2677[2]	0,28 [0,03; 2,59] 0,3747[4]	-3,5 [-9,0; 2,0] 0,3747[4]
Region (p-Wert des Interaktionsterms: 0,1281)					
Nordamerika / Europa	42/678 (6,2)	25/650 (3,8)	1,61 [0,99; 2,61] 0,0532[2]	1,65 [0,99; 2,74] 0,0506[3]	2,3 [0,0; 4,7] 0,0506[3]
Asien	7/203 (3,4)	5/201 (2,5)	1,39 [0,45; 4,30] 0,5714[2]	1,40 [0,44; 4,49] 0,5695[3]	1,0 [-2,3; 4,3] 0,5695[3]
Andere	20/402 (5,0)	4/414 (1,0)	5,15 [1,78; 14,93] 0,0026[2]	5,37 [1,82; 15,84] 0,0007[3]	4,0 [1,7; 6,3] 0,0007[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8691)					
0-3	25/427 (5,9)	14/418 (3,3)	1,75 [0,92; 3,32] 0,0873[2]	1,79 [0,92; 3,50] 0,0826[3]	2,5 [-0,3; 5,3] 0,0826[3]
4-9	27/549 (4,9)	12/542 (2,2)	2,22 [1,14; 4,34] 0,0195[2]	2,28 [1,15; 4,56] 0,0162[3]	2,7 [0,5; 4,9] 0,0162[3]
≥ 10	17/307 (5,5)	8/305 (2,6)	2,11 [0,92; 4,82] 0,0760[2]	2,18 [0,92; 5,12] 0,0686[3]	2,9 [-0,2; 6,0] 0,0686[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,1905)					
IIA	5/113 (4,4)	2/114 (1,8)	2,52 [0,50; 12,73] 0,2628[2]	2,59 [0,49; 13,65] 0,2803[4]	2,7 [-1,8; 7,2] 0,2803[4]
IIB	8/151 (5,3)	9/136 (6,6)	0,80 [0,32; 2,02] 0,6370[2]	0,79 [0,30; 2,11] 0,6363[3]	-1,3 [-6,8; 4,2] 0,6363[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	31/495 (6,3)	9/488 (1,8)	3,40 [1,63; 7,06] 0,0011[2]	3,56 [1,67; 7,55] 0,0005[3]	4,4 [2,0; 6,9] 0,0005[3]
IIIB	3/54 (5,6)	2/45 (4,4)	1,25 [0,22; 7,16] 0,8021[2]	1,26 [0,20; 7,92] 1,0000[4]	1,1 [-7,5; 9,7] 1,0000[4]
IIIC	22/468 (4,7)	12/480 (2,5)	1,88 [0,94; 3,76] 0,0736[2]	1,92 [0,94; 3,93] 0,0685[3]	2,2 [-0,2; 4,6] 0,0685[3]
Ethnizität (p-Wert des Interaktionsterms: 0,7666)					
Weiß	56/958 (5,8)	27/944 (2,9)	2,04 [1,30; 3,21] 0,0019[2]	2,11 [1,32; 3,37] 0,0014[3]	3,0 [1,2; 4,8] 0,0014[3]
Asiatisch	10/250 (4,0)	7/242 (2,9)	1,38 [0,54; 3,57] 0,5035[2]	1,40 [0,52; 3,74] 0,5013[3]	1,1 [-2,1; 4,3] 0,5013[3]
Andere	3/62 (4,8)	0/64 (0,0)	7,22 [0,38; 137,01] 0,1879[2]	7,59 [0,38; 150,00] 0,1162[4]	4,8 [-0,5; 10,2] 0,1162[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,6051)					
ECOG-PS 0	52/1070 (4,9)	26/1020 (2,5)	1,91 [1,20; 3,03] 0,0063[2]	1,95 [1,21; 3,15] 0,0053[3]	2,3 [0,7; 3,9] 0,0053[3]
ECOG-PS 1	17/213 (8,0)	8/245 (3,3)	2,44 [1,08; 5,55] 0,0327[2]	2,57 [1,09; 6,08] 0,0267[3]	4,7 [0,5; 9,0] 0,0267[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Tabelle: Subgruppen - Unerwünschtes Ereignis: PT Diarrhoe (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8118)					
Neoadjuvante Chemotherapie	174/217 (80,2)	11/219 (5,0)	15,96 [8,94; 28,50] <,0001[2]	76,52 [38,30; 152,88] <,0001[3]	75,2 [69,1; 81,2] <,0001[3]
Adjuvante Chemotherapie	264/327 (80,7)	20/312 (6,4)	12,59 [8,22; 19,31] <,0001[2]	61,18 [36,02; 103,93] <,0001[3]	74,3 [69,3; 79,4] <,0001[3]
Keine Chemotherapie	6/9 (66,7)	0/4 (0,0)	6,50 [0,45; 93,73] 0,1692[2]	16,71 [0,68; 409,09] 0,0699[4]	66,7 [35,9; 97,5] 0,0699[4]
Region (p-Wert des Interaktionsterms: 0,0851)					
Nordamerika / Europa	208/252 (82,5)	20/233 (8,6)	9,62 [6,30; 14,68] <,0001[2]	50,35 [28,70; 88,32] <,0001[3]	74,0 [68,0; 79,9] <,0001[3]
Asien	152/168 (90,5)	8/166 (4,8)	18,77 [9,53; 36,98] <,0001[2]	187,63 [78,02; 451,18] <,0001[3]	85,7 [80,2; 91,2] <,0001[3]
Andere	84/133 (63,2)	3/136 (2,2)	28,63 [9,28; 88,33] <,0001[2]	76,00 [22,95; 251,65] <,0001[3]	61,0 [52,4; 69,5] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,1289)					
< 20 mm	115/141 (81,6)	8/140 (5,7)	14,27 [7,25; 28,10] <,0001[2]	72,98 [31,79; 167,52] <,0001[3]	75,8 [68,4; 83,3] <,0001[3]
≥ 20 bis < 50 mm	198/255 (77,6)	19/249 (7,6)	10,18 [6,57; 15,75] <,0001[2]	42,05 [24,19; 73,09] <,0001[3]	70,0 [63,9; 76,1] <,0001[3]
≥ 50 mm	123/145 (84,8)	4/141 (2,8)	29,90 [11,35; 78,76] <,0001[2]	191,49 [64,20; 571,15] <,0001[3]	82,0 [75,5; 88,4] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9068)					
0-3	164/203 (80,8)	12/214 (5,6)	14,41 [8,28; 25,07] <,0001[2]	70,79 [35,90; 139,59] <,0001[3]	75,2 [68,9; 81,4] <,0001[3]
4-9	195/242 (80,6)	13/231 (5,6)	14,32 [8,41; 24,37] <,0001[2]	69,57 [36,54; 132,46] <,0001[3]	75,0 [69,1; 80,8] <,0001[3]
≥ 10	85/108 (78,7)	6/90 (6,7)	11,81 [5,42; 25,73] <,0001[2]	51,74 [20,06; 133,48] <,0001[3]	72,0 [62,8; 81,3] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,8542)					
IIA	47/59 (79,7)	5/62 (8,1)	9,88 [4,22; 23,12] <,0001[2]	44,65 [14,68; 135,82] <,0001[3]	71,6 [59,3; 83,9] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	40/53 (75,5)	5/69 (7,2)	10,42 [4,42; 24,56] <,0001[2]	39,38 [13,05; 118,85] <,0001[3]	68,2 [55,1; 81,3] <,0001[3]
IIIA	191/236 (80,9)	11/214 (5,1)	15,74 [8,83; 28,09] <,0001[2]	78,33 [39,36; 155,89] <,0001[3]	75,8 [70,0; 81,6] <,0001[3]
IIIB	15/18 (83,3)	1/15 (6,7)	12,50 [1,86; 83,97] 0,0094[2]	70,00 [6,49; 754,44] <,0001[3]	76,7 [55,3; 98,0] <,0001[3]
IIIC	150/186 (80,6)	9/174 (5,2)	15,59 [8,22; 29,57] <,0001[2]	76,39 [35,61; 163,86] <,0001[3]	75,5 [68,9; 82,0] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,8698)					
G1	38/47 (80,9)	2/41 (4,9)	16,57 [4,26; 64,50] <,0001[2]	82,33 [16,69; 406,16] <,0001[3]	76,0 [62,9; 89,0] <,0001[3]
G2	204/244 (83,6)	16/234 (6,8)	12,23 [7,59; 19,69] <,0001[2]	69,49 [37,74; 127,94] <,0001[3]	76,8 [71,1; 82,4] <,0001[3]
G3	183/233 (78,5)	11/226 (4,9)	16,14 [9,03; 28,83] <,0001[2]	71,54 [36,17; 141,46] <,0001[3]	73,7 [67,7; 79,6] <,0001[3]
GX	19/29 (65,5)	2/33 (6,1)	10,81 [2,75; 42,50] 0,0007[2]	29,45 [5,82; 149,12] <,0001[3]	59,5 [40,3; 78,6] <,0001[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,4113)					
Negativ	40/49 (81,6)	3/44 (6,8)	11,97 [3,98; 35,98] <,0001[2]	60,74 [15,32; 240,80] <,0001[3]	74,8 [61,7; 88,0] <,0001[3]
Positiv	385/477 (80,7)	24/471 (5,1)	15,84 [10,70; 23,45] <,0001[2]	77,94 [48,74; 124,64] <,0001[3]	75,6 [71,6; 79,7] <,0001[3]
Unbekannt	2/4 (50,0)	1/8 (12,5)	4,00 [0,50; 31,98] 0,1912[2]	7,00 [0,40; 123,35] 0,2364[4]	37,5 [-16,6; 91,6] 0,2364[4]
Ethnizität (p-Wert des Interaktionsterms: 0,4635)					
Weiß	246/323 (76,2)	21/324 (6,5)	11,75 [7,74; 17,85] <,0001[2]	46,10 [27,65; 76,84] <,0001[3]	69,7 [64,3; 75,0] <,0001[3]
Asiatisch	171/199 (85,9)	8/180 (4,4)	19,33 [9,80; 38,15] <,0001[2]	131,30 [58,19; 296,26] <,0001[3]	81,5 [75,8; 87,2] <,0001[3]
Andere	15/19 (78,9)	1/21 (4,8)	16,58 [2,41; 113,85] 0,0043[2]	75,00 [7,59; 741,57] <,0001[3]	74,2 [53,7; 94,7] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko					

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Tabelle: Subgruppen - Unerwünschtes Ereignis: PT Diarrhoe (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7383)					
Neoadjuvante Chemotherapie	352/430 (81,9)	37/415 (8,9)	9,18 [6,73; 12,53] <,0001[2]	46,10 [30,37; 69,98] <,0001[3]	72,9 [68,4; 77,5] <,0001[3]
Adjuvante Chemotherapie	651/784 (83,0)	68/769 (8,8)	9,39 [7,47; 11,81] <,0001[2]	50,46 [36,97; 68,87] <,0001[3]	74,2 [70,9; 77,5] <,0001[3]
Keine Chemotherapie	56/69 (81,2)	5/81 (6,2)	13,15 [5,58; 30,97] <,0001[2]	65,48 [22,07; 194,28] <,0001[3]	75,0 [64,4; 85,6] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,5685)					
< 20 mm	272/331 (82,2)	27/335 (8,1)	10,20 [7,08; 14,69] <,0001[2]	52,59 [32,42; 85,31] <,0001[3]	74,1 [69,1; 79,2] <,0001[3]
≥ 20 bis < 50 mm	528/646 (81,7)	53/653 (8,1)	10,07 [7,76; 13,07] <,0001[2]	50,66 [35,89; 71,49] <,0001[3]	73,6 [70,0; 77,3] <,0001[3]
≥ 50 mm	247/289 (85,5)	28/265 (10,6)	8,09 [5,68; 11,52] <,0001[2]	49,78 [29,88; 82,92] <,0001[3]	74,9 [69,4; 80,4] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8134)					
0-3	346/427 (81,0)	33/418 (7,9)	10,26 [7,37; 14,29] <,0001[2]	49,84 [32,42; 76,61] <,0001[3]	73,1 [68,6; 77,7] <,0001[3]
4-9	462/549 (84,2)	51/542 (9,4)	8,94 [6,87; 11,64] <,0001[2]	51,13 [35,38; 73,89] <,0001[3]	74,7 [70,8; 78,7] <,0001[3]
≥ 10	251/307 (81,8)	26/305 (8,5)	9,59 [6,62; 13,90] <,0001[2]	48,10 [29,31; 78,93] <,0001[3]	73,2 [67,9; 78,6] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,5363)					
IIA	87/113 (77,0)	11/114 (9,6)	7,98 [4,51; 14,12] <,0001[2]	31,33 [14,65; 67,03] <,0001[3]	67,3 [57,9; 76,8] <,0001[3]
IIB	122/151 (80,8)	8/136 (5,9)	13,74 [6,98; 27,02] <,0001[2]	67,31 [29,61; 152,99] <,0001[3]	74,9 [67,5; 82,3] <,0001[3]
IIIA	422/495 (85,3)	39/488 (8,0)	10,67 [7,88; 14,45] <,0001[2]	66,55 [44,13; 100,37] <,0001[3]	77,3 [73,3; 81,2] <,0001[3]
IIIB	41/54 (75,9)	5/45 (11,1)	6,83 [2,95; 15,83] <,0001[2]	25,23 [8,24; 77,30] <,0001[3]	64,8 [50,2; 79,5] <,0001[3]
IIIC	386/468 (82,5)	46/480 (9,6)	8,61 [6,52; 11,36] <,0001[2]	44,41 [30,18; 65,35] <,0001[3]	72,9 [68,6; 77,2] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Tumorgrading (p-Wert des Interaktionsterms: 0,4291)					
G1	78/91 (85,7)	8/93 (8,6)	9,96 [5,11; 19,43] <,0001[2]	63,75 [25,08; 162,03] <,0001[3]	77,1 [67,9; 86,3] <,0001[3]
G2	516/612 (84,3)	56/603 (9,3)	9,08 [7,06; 11,68] <,0001[2]	52,50 [36,97; 74,57] <,0001[3]	75,0 [71,3; 78,7] <,0001[3]
G3	422/527 (80,1)	44/506 (8,7)	9,21 [6,92; 12,25] <,0001[2]	42,20 [28,98; 61,46] <,0001[3]	71,4 [67,2; 75,6] <,0001[3]
GX	41/51 (80,4)	1/59 (1,7)	47,43 [6,76; 332,72] 0,0001[2]	237,80 [29,29; 1930,62] <,0001[3]	78,7 [67,3; 90,1] <,0001[3]
Ethnizität (p-Wert des Interaktionsterms: 0,0559)					
Weiß	791/958 (82,6)	92/944 (9,7)	8,47 [6,96; 10,31] <,0001[2]	43,86 [33,41; 57,59] <,0001[3]	72,8 [69,8; 75,9] <,0001[3]
Asiatisch	204/250 (81,6)	11/242 (4,5)	17,95 [10,05; 32,07] <,0001[2]	93,13 [46,98; 184,61] <,0001[3]	77,1 [71,6; 82,5] <,0001[3]
Andere	52/62 (83,9)	6/64 (9,4)	8,95 [4,14; 19,31] <,0001[2]	50,27 [17,09; 147,89] <,0001[3]	74,5 [62,9; 86,1] <,0001[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,4084)					
Tamoxifen	86/114 (75,4)	8/132 (6,1)	12,45 [6,31; 24,56] <,0001[2]	47,61 [20,71; 109,45] <,0001[3]	69,4 [60,5; 78,3] <,0001[3]
Aromatase-Inhibitor	973/1169 (83,2)	102/1133 (9,0)	9,25 [7,67; 11,15] <,0001[2]	50,18 [38,89; 64,74] <,0001[3]	74,2 [71,5; 76,9] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,5859)					
ECOG-PS 0	893/1070 (83,5)	92/1020 (9,0)	9,25 [7,60; 11,26] <,0001[2]	50,89 [38,92; 66,54] <,0001[3]	74,4 [71,6; 77,3] <,0001[3]
ECOG-PS 1	166/213 (77,9)	18/245 (7,3)	10,61 [6,76; 16,64] <,0001[2]	44,54 [24,96; 79,47] <,0001[3]	70,6 [64,1; 77,0] <,0001[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: PT Diarrhoe aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9380)					
Neoadjuvante Chemotherapie	10/217 (4,6)	0/219 (0,0)	21,19 [1,25; 359,42] 0,0345[2]	22,21 [1,29; 381,50] 0,0008[4]	4,6 [1,8; 7,4] 0,0008[4]
Adjuvante Chemotherapie	18/327 (5,5)	2/312 (0,6)	8,59 [2,01; 36,70] 0,0037[2]	9,03 [2,08; 39,24] 0,0004[3]	4,9 [2,2; 7,5] 0,0004[3]
Keine Chemotherapie	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (p-Wert des Interaktionsterms: 0,7188)					
Nordamerika / Europa	18/252 (7,1)	1/233 (0,4)	16,64 [2,24; 123,69] 0,0060[2]	17,85 [2,36; 134,78] 0,0001[3]	6,7 [3,4; 10,0] 0,0001[3]
Asien	5/168 (3,0)	1/166 (0,6)	4,94 [0,58; 41,84] 0,1428[2]	5,06 [0,58; 43,80] 0,2146[4]	2,4 [-0,5; 5,2] 0,2146[4]
Andere	7/133 (5,3)	0/136 (0,0)	15,34 [0,88; 265,86] 0,0607[2]	16,19 [0,92; 286,30] 0,0067[4]	5,3 [1,5; 9,1] 0,0067[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,9829)					
< 20 mm	9/141 (6,4)	1/140 (0,7)	8,94 [1,15; 69,60] 0,0365[2]	9,48 [1,18; 75,84] 0,0193[4]	5,7 [1,4; 9,9] 0,0193[4]
≥ 20 bis < 50 mm	13/255 (5,1)	0/249 (0,0)	26,37 [1,58; 441,16] 0,0228[2]	27,78 [1,64; 469,89] 0,0003[3]	5,1 [2,4; 7,8] 0,0003[3]
≥ 50 mm	7/145 (4,8)	1/141 (0,7)	6,81 [0,85; 54,62] 0,0711[2]	7,10 [0,86; 58,48] 0,0667[4]	4,1 [0,4; 7,9] 0,0667[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9318)					
0-3	11/203 (5,4)	1/214 (0,5)	11,60 [1,51; 89,01] 0,0184[2]	12,20 [1,56; 95,40] 0,0025[3]	5,0 [1,7; 8,2] 0,0025[3]
4-9	11/242 (4,5)	0/231 (0,0)	21,96 [1,30; 370,51] 0,0321[2]	23,00 [1,35; 392,59] 0,0010[3]	4,5 [1,9; 7,2] 0,0010[3]
≥ 10	8/108 (7,4)	1/90 (1,1)	6,67 [0,85; 52,30] 0,0711[2]	7,12 [0,87; 58,05] 0,0417[4]	6,3 [0,9; 11,7] 0,0417[4]
Tumorstadium (p-Wert des Interaktionsterms: 0,9038)					
IIA	4/59 (6,8)	1/62 (1,6)	4,20 [0,48; 36,53] 0,1930[2]	4,44 [0,48; 40,90] 0,1997[4]	5,2 [-2,0; 12,3] 0,1997[4]
IIB	2/53 (3,8)	0/69 (0,0)	6,48 [0,32; 132,22] 0,2245[2]	6,75 [0,32; 143,57] 0,1867[4]	3,8 [-1,4; 8,9] 0,1867[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	9/236 (3,8)	0/214 (0,0)	17,24 [1,01; 294,37] 0,0493[2]	17,91 [1,04; 309,68] 0,0039[4]	3,8 [1,4; 6,3] 0,0039[4]
IIIB	0/18 (0,0)	0/15 (0,0)	NB	NB	NB
IIIC	14/186 (7,5)	1/174 (0,6)	13,10 [1,74; 98,55] 0,0125[2]	14,08 [1,83; 108,26] 0,0010[3]	7,0 [3,0; 10,9] 0,0010[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,2012)					
G1	0/47 (0,0)	0/41 (0,0)	NB	NB	NB
G2	14/244 (5,7)	1/234 (0,4)	13,43 [1,78; 101,29] 0,0118[2]	14,18 [1,85; 108,74] 0,0009[3]	5,3 [2,3; 8,3] 0,0009[3]
G3	16/233 (6,9)	1/226 (0,4)	15,52 [2,08; 116,06] 0,0076[2]	16,59 [2,18; 126,17] 0,0003[3]	6,4 [3,1; 9,8] 0,0003[3]
GX	0/29 (0,0)	0/33 (0,0)	NB	NB	NB
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9940)					
Negativ	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positiv	27/477 (5,7)	1/471 (0,2)	26,66 [3,64; 195,40] 0,0012[2]	28,20 [3,82; 208,39] <,0001[3]	5,4 [3,3; 7,6] <,0001[3]
Unbekannt	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Ethnizität (p-Wert des Interaktionsterms: 0,5692)					
Weiß	22/323 (6,8)	1/324 (0,3)	22,07 [2,99; 162,75] 0,0024[2]	23,61 [3,16; 176,22] <,0001[3]	6,5 [3,7; 9,3] <,0001[3]
Asiatisch	5/199 (2,5)	1/180 (0,6)	4,52 [0,53; 38,35] 0,1664[2]	4,61 [0,53; 39,87] 0,2186[4]	2,0 [-0,5; 4,4] 0,2186[4]
Andere	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: PT Diarrhoe aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,6734)					
< 65 Jahre	77/918 (8,4)	1/937 (0,1)	78,59 [10,95; 563,88] <,0001[2]	85,70 [11,89; 617,50] <,0001[3]	8,3 [6,5; 10,1] <,0001[3]
≥ 65 Jahre	48/365 (13,2)	1/328 (0,3)	43,13 [5,99; 310,74] 0,0002[2]	49,51 [6,79; 360,88] <,0001[3]	12,8 [9,3; 16,4] <,0001[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9540)					
Neoadjuvante Chemotherapie	48/430 (11,2)	1/415 (0,2)	46,33 [6,42; 334,08] 0,0001[2]	52,02 [7,15; 378,72] <,0001[3]	10,9 [7,9; 13,9] <,0001[3]
Adjuvante Chemotherapie	73/784 (9,3)	1/769 (0,1)	71,60 [9,98; 513,87] <,0001[2]	78,85 [10,93; 568,81] <,0001[3]	9,2 [7,1; 11,2] <,0001[3]
Keine Chemotherapie	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (p-Wert des Interaktionsterms: 0,9994)					
Nordamerika / Europa	67/678 (9,9)	2/650 (0,3)	32,12 [7,90; 130,54] <,0001[2]	35,53 [8,67; 145,64] <,0001[3]	9,6 [7,3; 11,9] <,0001[3]
Asien	13/203 (6,4)	0/201 (0,0)	26,74 [1,60; 446,72] 0,0222[2]	28,56 [1,69; 483,76] 0,0003[3]	6,4 [3,0; 9,8] 0,0003[3]
Andere	45/402 (11,2)	0/414 (0,0)	93,71 [5,79; 1515,99] 0,0014[2]	105,51 [6,48; 1718,80] <,0001[3]	11,2 [8,1; 14,3] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,7882)					
< 20 mm	27/331 (8,2)	0/335 (0,0)	55,66 [3,41; 908,76] 0,0048[2]	60,60 [3,68; 997,72] <,0001[3]	8,2 [5,2; 11,1] <,0001[3]
≥ 20 bis < 50 mm	68/646 (10,5)	1/653 (0,2)	68,74 [9,57; 493,54] <,0001[2]	76,71 [10,62; 554,17] <,0001[3]	10,4 [8,0; 12,8] <,0001[3]
≥ 50 mm	28/289 (9,7)	1/265 (0,4)	25,67 [3,52; 187,39] 0,0014[2]	28,32 [3,83; 209,69] <,0001[3]	9,3 [5,8; 12,8] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9946)					
0-3	51/427 (11,9)	1/418 (0,2)	49,93 [6,93; 359,61] 0,0001[2]	56,56 [7,78; 411,30] <,0001[3]	11,7 [8,6; 14,8] <,0001[3]
4-9	44/549 (8,0)	1/542 (0,2)	43,44 [6,01; 314,16] 0,0002[2]	47,14 [6,47; 343,39] <,0001[3]	7,8 [5,5; 10,1] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	30/307 (9,8)	0/305 (0,0)	60,60 [3,72; 986,65] 0,0039[2]	67,15 [4,09; 1103,41] <,0001[3]	9,8 [6,5; 13,1] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9968)					
IIA	11/113 (9,7)	0/114 (0,0)	23,20 [1,38; 389,08] 0,0288[2]	25,69 [1,50; 441,49] 0,0006[3]	9,7 [4,3; 15,2] 0,0006[3]
IIB	16/151 (10,6)	0/136 (0,0)	29,74 [1,80; 491,08] 0,0177[2]	33,24 [1,97; 559,68] <,0001[3]	10,6 [5,7; 15,5] <,0001[3]
IIIA	35/495 (7,1)	1/488 (0,2)	34,51 [4,75; 250,87] 0,0005[2]	37,05 [5,06; 271,57] <,0001[3]	6,9 [4,6; 9,2] <,0001[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	60/468 (12,8)	1/480 (0,2)	61,54 [8,56; 442,21] <,0001[2]	70,44 [9,72; 510,51] <,0001[3]	12,6 [9,6; 15,7] <,0001[3]
Ethnizität (p-Wert des Interaktionsterms: 0,9998)					
Weiß	103/958 (10,8)	2/944 (0,2)	50,75 [12,56; 205,05] <,0001[2]	56,74 [13,96; 230,64] <,0001[3]	10,5 [8,6; 12,5] <,0001[3]
Asiatisch	14/250 (5,6)	0/242 (0,0)	28,08 [1,68; 468,05] 0,0202[2]	29,74 [1,76; 501,31] 0,0002[3]	5,6 [2,7; 8,5] 0,0002[3]
Andere	6/62 (9,7)	0/64 (0,0)	13,41 [0,77; 233,15] 0,0748[2]	14,84 [0,82; 269,32] 0,0125[4]	9,7 [2,3; 17,0] 0,0125[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,9752)					
ECOG-PS 0	105/1070 (9,8)	2/1020 (0,2)	50,05 [12,39; 202,22] <,0001[2]	55,38 [13,63; 225,00] <,0001[3]	9,6 [7,8; 11,4] <,0001[3]
ECOG-PS 1	20/213 (9,4)	0/245 (0,0)	47,13 [2,87; 774,60] 0,0070[2]	52,02 [3,13; 865,51] <,0001[3]	9,4 [5,5; 13,3] <,0001[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: PT Diarrhoe aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,8200)					
Neoadjuvante Chemotherapie	173/217 (79,7)	11/219 (5,0)	15,87 [8,89; 28,34] <,0001[2]	74,35 [37,26; 148,35] <,0001[3]	74,7 [68,6; 80,8] <,0001[3]
Adjuvante Chemotherapie	264/327 (80,7)	20/312 (6,4)	12,59 [8,22; 19,31] <,0001[2]	61,18 [36,02; 103,93] <,0001[3]	74,3 [69,3; 79,4] <,0001[3]
Keine Chemotherapie	5/9 (55,6)	0/4 (0,0)	5,50 [0,37; 80,92] 0,2140[2]	11,00 [0,46; 263,53] 0,1049[4]	55,6 [23,1; 88,0] 0,1049[4]
Region (p-Wert des Interaktionsterms: 0,0805)					
Nordamerika / Europa	206/252 (81,7)	20/233 (8,6)	9,52 [6,24; 14,54] <,0001[2]	47,69 [27,28; 83,40] <,0001[3]	73,2 [67,2; 79,1] <,0001[3]
Asien	152/168 (90,5)	8/166 (4,8)	18,77 [9,53; 36,98] <,0001[2]	187,63 [78,02; 451,18] <,0001[3]	85,7 [80,2; 91,2] <,0001[3]
Andere	84/133 (63,2)	3/136 (2,2)	28,63 [9,28; 88,33] <,0001[2]	76,00 [22,95; 251,65] <,0001[3]	61,0 [52,4; 69,5] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,1338)					
< 20 mm	114/141 (80,9)	8/140 (5,7)	14,15 [7,19; 27,86] <,0001[2]	69,67 [30,44; 159,42] <,0001[3]	75,1 [67,6; 82,7] <,0001[3]
≥ 20 bis < 50 mm	198/255 (77,6)	19/249 (7,6)	10,18 [6,57; 15,75] <,0001[2]	42,05 [24,19; 73,09] <,0001[3]	70,0 [63,9; 76,1] <,0001[3]
≥ 50 mm	122/145 (84,1)	4/141 (2,8)	29,66 [11,26; 78,13] <,0001[2]	181,67 [61,12; 540,05] <,0001[3]	81,3 [74,8; 87,8] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9118)					
0-3	163/203 (80,3)	12/214 (5,6)	14,32 [8,23; 24,92] <,0001[2]	68,60 [34,85; 135,04] <,0001[3]	74,7 [68,4; 81,0] <,0001[3]
4-9	194/242 (80,2)	13/231 (5,6)	14,24 [8,37; 24,24] <,0001[2]	67,78 [35,64; 128,87] <,0001[3]	74,5 [68,7; 80,4] <,0001[3]
≥ 10	85/108 (78,7)	6/90 (6,7)	11,81 [5,42; 25,73] <,0001[2]	51,74 [20,06; 133,48] <,0001[3]	72,0 [62,8; 81,3] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,8604)					
IIA	47/59 (79,7)	5/62 (8,1)	9,88 [4,22; 23,12] <,0001[2]	44,65 [14,68; 135,82] <,0001[3]	71,6 [59,3; 83,9] <,0001[3]
IIB	40/53 (75,5)	5/69 (7,2)	10,42 [4,42; 24,56] <,0001[2]	39,38 [13,05; 118,85] <,0001[3]	68,2 [55,1; 81,3] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	190/236 (80,5)	11/214 (5,1)	15,66 [8,78; 27,95] <,0001[2]	76,23 [38,35; 151,51] <,0001[3]	75,4 [69,5; 81,2] <,0001[3]
IIIB	15/18 (83,3)	1/15 (6,7)	12,50 [1,86; 83,97] 0,0094[2]	70,00 [6,49; 754,44] <,0001[3]	76,7 [55,3; 98,0] <,0001[3]
IIIC	149/186 (80,1)	9/174 (5,2)	15,49 [8,16; 29,38] <,0001[2]	73,83 [34,48; 158,09] <,0001[3]	74,9 [68,3; 81,5] <,0001[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,8610)					
G1	38/47 (80,9)	2/41 (4,9)	16,57 [4,26; 64,50] <,0001[2]	82,33 [16,69; 406,16] <,0001[3]	76,0 [62,9; 89,0] <,0001[3]
G2	202/244 (82,8)	16/234 (6,8)	12,11 [7,52; 19,50] <,0001[2]	65,53 [35,72; 120,22] <,0001[3]	75,9 [70,2; 81,7] <,0001[3]
G3	183/233 (78,5)	11/226 (4,9)	16,14 [9,03; 28,83] <,0001[2]	71,54 [36,17; 141,46] <,0001[3]	73,7 [67,7; 79,6] <,0001[3]
GX	19/29 (65,5)	2/33 (6,1)	10,81 [2,75; 42,50] 0,0007[2]	29,45 [5,82; 149,12] <,0001[3]	59,5 [40,3; 78,6] <,0001[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,4132)					
Negativ	40/49 (81,6)	3/44 (6,8)	11,97 [3,98; 35,98] <,0001[2]	60,74 [15,32; 240,80] <,0001[3]	74,8 [61,7; 88,0] <,0001[3]
Positiv	384/477 (80,5)	24/471 (5,1)	15,80 [10,67; 23,39] <,0001[2]	76,90 [48,11; 122,92] <,0001[3]	75,4 [71,3; 79,5] <,0001[3]
Unbekannt	2/4 (50,0)	1/8 (12,5)	4,00 [0,50; 31,98] 0,1912[2]	7,00 [0,40; 123,35] 0,2364[4]	37,5 [-16,6; 91,6] 0,2364[4]
Ethnizität (p-Wert des Interaktionsterms: 0,4517)					
Weiß	244/323 (75,5)	21/324 (6,5)	11,66 [7,67; 17,71] <,0001[2]	44,56 [26,76; 74,20] <,0001[3]	69,1 [63,7; 74,5] <,0001[3]
Asiatisch	171/199 (85,9)	8/180 (4,4)	19,33 [9,80; 38,15] <,0001[2]	131,30 [58,19; 296,26] <,0001[3]	81,5 [75,8; 87,2] <,0001[3]
Andere	15/19 (78,9)	1/21 (4,8)	16,58 [2,41; 113,85] 0,0043[2]	75,00 [7,59; 741,57] <,0001[3]	74,2 [53,7; 94,7] <,0001[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: PT Diarrhoe aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7490)					
Neoadjuvante Chemotherapie	348/430 (80,9)	36/415 (8,7)	9,33 [6,80; 12,79] <,0001[2]	44,68 [29,41; 67,86] <,0001[3]	72,3 [67,7; 76,9] <,0001[3]
Adjuvante Chemotherapie	650/784 (82,9)	68/769 (8,8)	9,38 [7,46; 11,79] <,0001[2]	50,01 [36,65; 68,23] <,0001[3]	74,1 [70,8; 77,4] <,0001[3]
Keine Chemotherapie	56/69 (81,2)	5/81 (6,2)	13,15 [5,58; 30,97] <,0001[2]	65,48 [22,07; 194,28] <,0001[3]	75,0 [64,4; 85,6] <,0001[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,5224)					
< 20 mm	272/331 (82,2)	27/335 (8,1)	10,20 [7,08; 14,69] <,0001[2]	52,59 [32,42; 85,31] <,0001[3]	74,1 [69,1; 79,2] <,0001[3]
≥ 20 bis < 50 mm	525/646 (81,3)	52/653 (8,0)	10,21 [7,84; 13,28] <,0001[2]	50,15 [35,50; 70,84] <,0001[3]	73,3 [69,7; 77,0] <,0001[3]
≥ 50 mm	245/289 (84,8)	28/265 (10,6)	8,02 [5,63; 11,43] <,0001[2]	47,13 [28,41; 78,20] <,0001[3]	74,2 [68,7; 79,8] <,0001[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7586)					
0-3	343/427 (80,3)	32/418 (7,7)	10,49 [7,50; 14,69] <,0001[2]	49,26 [31,97; 75,90] <,0001[3]	72,7 [68,1; 77,2] <,0001[3]
4-9	461/549 (84,0)	51/542 (9,4)	8,92 [6,85; 11,62] <,0001[2]	50,43 [34,92; 72,84] <,0001[3]	74,6 [70,6; 78,5] <,0001[3]
≥ 10	250/307 (81,4)	26/305 (8,5)	9,55 [6,59; 13,85] <,0001[2]	47,06 [28,71; 77,15] <,0001[3]	72,9 [67,5; 78,3] <,0001[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,5873)					
IIA	87/113 (77,0)	11/114 (9,6)	7,98 [4,51; 14,12] <,0001[2]	31,33 [14,65; 67,03] <,0001[3]	67,3 [57,9; 76,8] <,0001[3]
IIB	119/151 (78,8)	8/136 (5,9)	13,40 [6,81; 26,37] <,0001[2]	59,50 [26,36; 134,28] <,0001[3]	72,9 [65,3; 80,5] <,0001[3]
IIIA	422/495 (85,3)	39/488 (8,0)	10,67 [7,88; 14,45] <,0001[2]	66,55 [44,13; 100,37] <,0001[3]	77,3 [73,3; 81,2] <,0001[3]
IIIB	41/54 (75,9)	5/45 (11,1)	6,83 [2,95; 15,83] <,0001[2]	25,23 [8,24; 77,30] <,0001[3]	64,8 [50,2; 79,5] <,0001[3]
IIIC	384/468 (82,1)	45/480 (9,4)	8,75 [6,61; 11,60] <,0001[2]	44,19 [30,00; 65,09] <,0001[3]	72,7 [68,3; 77,0] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Tumorgrading (p-Wert des Interaktionsterms: 0,4318)					
G1	77/91 (84,6)	8/93 (8,6)	9,84 [5,04; 19,19] <,0001[2]	58,44 [23,25; 146,90] <,0001[3]	76,0 [66,7; 85,4] <,0001[3]
G2	515/612 (84,2)	56/603 (9,3)	9,06 [7,04; 11,66] <,0001[2]	51,86 [36,54; 73,61] <,0001[3]	74,9 [71,2; 78,6] <,0001[3]
G3	419/527 (79,5)	43/506 (8,5)	9,36 [7,01; 12,49] <,0001[2]	41,77 [28,64; 60,92] <,0001[3]	71,0 [66,8; 75,2] <,0001[3]
GX	41/51 (80,4)	1/59 (1,7)	47,43 [6,76; 332,72] 0,0001[2]	237,80 [29,29; 1930,62] <,0001[3]	78,7 [67,3; 90,1] <,0001[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9984)					
Negativ	125/156 (80,1)	14/169 (8,3)	9,67 [5,82; 16,07] <,0001[2]	44,64 [22,76; 87,56] <,0001[3]	71,8 [64,3; 79,4] <,0001[3]
Positiv	896/1089 (82,3)	92/1067 (8,6)	9,54 [7,83; 11,62] <,0001[2]	49,20 [37,77; 64,09] <,0001[3]	73,7 [70,8; 76,5] <,0001[3]
Unbekannt	8/10 (80,0)	0/7 (0,0)	12,36 [0,83; 184,49] 0,0682[2]	51,00 [2,10; 1240,17] 0,0023[4]	80,0 [55,2; 100,0] 0,0023[4]
Ethnizität (p-Wert des Interaktionsterms: 0,0581)					
Weiß	786/958 (82,0)	91/944 (9,6)	8,51 [6,99; 10,37] <,0001[2]	42,84 [32,64; 56,22] <,0001[3]	72,4 [69,3; 75,5] <,0001[3]
Asiatisch	204/250 (81,6)	11/242 (4,5)	17,95 [10,05; 32,07] <,0001[2]	93,13 [46,98; 184,61] <,0001[3]	77,1 [71,6; 82,5] <,0001[3]
Andere	52/62 (83,9)	6/64 (9,4)	8,95 [4,14; 19,31] <,0001[2]	50,27 [17,09; 147,89] <,0001[3]	74,5 [62,9; 86,1] <,0001[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,4161)					
Tamoxifen	86/114 (75,4)	8/132 (6,1)	12,45 [6,31; 24,56] <,0001[2]	47,61 [20,71; 109,45] <,0001[3]	69,4 [60,5; 78,3] <,0001[3]
Aromatase-Inhibitor	968/1169 (82,8)	101/1133 (8,9)	9,29 [7,70; 11,21] <,0001[2]	49,21 [38,15; 63,48] <,0001[3]	73,9 [71,2; 76,6] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,6009)					
ECOG-PS 0	888/1070 (83,0)	91/1020 (8,9)	9,30 [7,63; 11,34] <,0001[2]	49,81 [38,10; 65,11] <,0001[3]	74,1 [71,2; 76,9] <,0001[3]
ECOG-PS 1	166/213 (77,9)	18/245 (7,3)	10,61 [6,76; 16,64] <,0001[2]	44,54 [24,96; 79,47] <,0001[3]	70,6 [64,1; 77,0] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko					

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Tabelle: Subgruppen - Unerwünschtes Ereignis: Hepatische Ereignisse (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,5818)					
Neoadjuvante Chemotherapie	18/217 (8,3)	8/219 (3,7)	2,27 [1,01; 5,11] 0,0476[2]	2,39 [1,01; 5,61] 0,0407[3]	4,6 [0,2; 9,1] 0,0407[3]
Adjuvante Chemotherapie	36/327 (11,0)	25/312 (8,0)	1,37 [0,84; 2,23] 0,2002[2]	1,42 [0,83; 2,43] 0,1976[3]	3,0 [-1,5; 7,5] 0,1976[3]
Keine Chemotherapie	0/9 (0,0)	0/4 (0,0)	NB	NB	NB
Region (p-Wert des Interaktionsterms: 0,1947)					
Nordamerika / Europa	20/252 (7,9)	6/233 (2,6)	3,08 [1,26; 7,54] 0,0137[2]	3,26 [1,29; 8,27] 0,0088[3]	5,4 [1,5; 9,3] 0,0088[3]
Asien	25/168 (14,9)	18/166 (10,8)	1,37 [0,78; 2,42] 0,2736[2]	1,44 [0,75; 2,75] 0,2706[3]	4,0 [-3,1; 11,2] 0,2706[3]
Andere	9/133 (6,8)	9/136 (6,6)	1,02 [0,42; 2,50] 0,9609[2]	1,02 [0,39; 2,67] 0,9609[3]	0,1 [-5,8; 6,1] 0,9609[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6476)					
< 20 mm	15/141 (10,6)	8/140 (5,7)	1,86 [0,82; 4,25] 0,1401[2]	1,96 [0,80; 4,79] 0,1322[3]	4,9 [-1,5; 11,3] 0,1322[3]
≥ 20 bis < 50 mm	26/255 (10,2)	14/249 (5,6)	1,81 [0,97; 3,39] 0,0623[2]	1,91 [0,97; 3,74] 0,0575[3]	4,6 [-0,1; 9,3] 0,0575[3]
≥ 50 mm	12/145 (8,3)	10/141 (7,1)	1,17 [0,52; 2,61] 0,7076[2]	1,18 [0,49; 2,83] 0,7072[3]	1,2 [-5,0; 7,4] 0,7072[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,4545)					
0-3	21/203 (10,3)	10/214 (4,7)	2,21 [1,07; 4,59] 0,0324[2]	2,35 [1,08; 5,13] 0,0273[3]	5,7 [0,6; 10,7] 0,0273[3]
4-9	20/242 (8,3)	16/231 (6,9)	1,19 [0,63; 2,25] 0,5840[2]	1,21 [0,61; 2,40] 0,5833[3]	1,3 [-3,4; 6,1] 0,5833[3]
≥ 10	13/108 (12,0)	7/90 (7,8)	1,55 [0,64; 3,71] 0,3281[2]	1,62 [0,62; 4,26] 0,3220[3]	4,3 [-4,0; 12,5] 0,3220[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9565)					
IIA	8/59 (13,6)	5/62 (8,1)	1,68 [0,58; 4,85] 0,3362[2]	1,79 [0,55; 5,82] 0,3292[3]	5,5 [-5,6; 16,6] 0,3292[3]
IIB	5/53 (9,4)	3/69 (4,3)	2,17 [0,54; 8,68] 0,2733[2]	2,29 [0,52; 10,06] 0,2921[4]	5,1 [-4,1; 14,3] 0,2921[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	21/236 (8,9)	14/214 (6,5)	1,36 [0,71; 2,61] 0,3540[2]	1,40 [0,69; 2,82] 0,3513[3]	2,4 [-2,6; 7,3] 0,3513[3]
IIIB	1/18 (5,6)	1/15 (6,7)	0,83 [0,06; 12,22] 0,8942[2]	0,82 [0,05; 14,39] 1,0000[4]	-1,1 [-17,6; 15,4] 1,0000[4]
IIIC	18/186 (9,7)	10/174 (5,7)	1,68 [0,80; 3,55] 0,1703[2]	1,76 [0,79; 3,92] 0,1641[3]	3,9 [-1,5; 9,4] 0,1641[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,6473)					
G1	8/47 (17,0)	0/41 (0,0)	14,88 [0,88; 250,04] 0,0608[2]	17,86 [1,00; 319,85] 0,0064[4]	17,0 [6,3; 27,8] 0,0064[4]
G2	14/244 (5,7)	13/234 (5,6)	1,03 [0,50; 2,15] 0,9313[2]	1,03 [0,48; 2,25] 0,9313[3]	0,2 [-4,0; 4,3] 0,9313[3]
G3	25/233 (10,7)	17/226 (7,5)	1,43 [0,79; 2,57] 0,2367[2]	1,48 [0,78; 2,82] 0,2334[3]	3,2 [-2,0; 8,5] 0,2334[3]
GX	7/29 (24,1)	3/33 (9,1)	2,66 [0,76; 9,33] 0,1279[2]	3,18 [0,74; 13,70] 0,1672[4]	15,0 [-3,4; 33,5] 0,1672[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,0866)					
Negativ	7/49 (14,3)	1/44 (2,3)	6,29 [0,80; 49,09] 0,0796[2]	7,17 [0,84; 60,79] 0,0617[4]	12,0 [1,3; 22,8] 0,0617[4]
Positiv	46/477 (9,6)	32/471 (6,8)	1,42 [0,92; 2,19] 0,1127[2]	1,46 [0,91; 2,34] 0,1104[3]	2,8 [-0,6; 6,3] 0,1104[3]
Unbekannt	0/4 (0,0)	0/8 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,7843)					
Weiß	23/323 (7,1)	12/324 (3,7)	1,92 [0,97; 3,80] 0,0598[2]	1,99 [0,97; 4,08] 0,0547[3]	3,4 [-0,1; 6,9] 0,0547[3]
Asiatisch	28/199 (14,1)	18/180 (10,0)	1,41 [0,81; 2,46] 0,2293[2]	1,47 [0,78; 2,77] 0,2256[3]	4,1 [-2,5; 10,6] 0,2256[3]
Andere	3/19 (15,8)	2/21 (9,5)	1,66 [0,31; 8,88] 0,5549[2]	1,78 [0,26; 12,01] 0,6544[4]	6,3 [-14,4; 26,9] 0,6544[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,9175)					
ECOG-PS 0	51/496 (10,3)	31/480 (6,5)	1,59 [1,04; 2,44] 0,0334[2]	1,66 [1,04; 2,64] 0,0313[3]	3,8 [0,4; 7,3] 0,0313[3]
ECOG-PS 1	3/57 (5,3)	2/55 (3,6)	1,45 [0,25; 8,33] 0,6789[2]	1,47 [0,24; 9,17] 1,0000[4]	1,6 [-6,0; 9,2] 1,0000[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko					

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Tabelle: Subgruppen - Unerwünschtes Ereignis: Hepatische Ereignisse (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,7772)					
< 65 Jahre	143/918 (15,6)	77/937 (8,2)	1,90 [1,46; 2,46] <,0001[2]	2,06 [1,54; 2,76] <,0001[3]	7,4 [4,4; 10,3] <,0001[3]
≥ 65 Jahre	48/365 (13,2)	21/328 (6,4)	2,05 [1,26; 3,35] 0,0040[2]	2,21 [1,29; 3,78] 0,0031[3]	6,7 [2,4; 11,1] 0,0031[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7449)					
Neoadjuvante Chemotherapie	73/430 (17,0)	33/415 (8,0)	2,13 [1,45; 3,15] 0,0001[2]	2,37 [1,53; 3,66] <,0001[3]	9,0 [4,6; 13,4] <,0001[3]
Adjuvante Chemotherapie	107/784 (13,6)	59/769 (7,7)	1,78 [1,32; 2,41] 0,0002[2]	1,90 [1,36; 2,66] 0,0001[3]	6,0 [2,9; 9,0] 0,0001[3]
Keine Chemotherapie	11/69 (15,9)	6/81 (7,4)	2,15 [0,84; 5,52] 0,1106[2]	2,37 [0,83; 6,79] 0,1003[3]	8,5 [-1,8; 18,9] 0,1003[3]
Region (p-Wert des Interaktionsterms: 0,6270)					
Nordamerika / Europa	73/678 (10,8)	33/650 (5,1)	2,12 [1,43; 3,15] 0,0002[2]	2,26 [1,47; 3,45] 0,0001[3]	5,7 [2,8; 8,6] 0,0001[3]
Asien	53/203 (26,1)	25/201 (12,4)	2,10 [1,36; 3,24] 0,0008[2]	2,49 [1,47; 4,20] 0,0005[3]	13,7 [6,1; 21,2] 0,0005[3]
Andere	65/402 (16,2)	40/414 (9,7)	1,67 [1,16; 2,42] 0,0063[2]	1,80 [1,18; 2,75] 0,0055[3]	6,5 [1,9; 11,1] 0,0055[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,7432)					
< 20 mm	48/331 (14,5)	28/335 (8,4)	1,74 [1,12; 2,70] 0,0142[2]	1,86 [1,14; 3,05] 0,0127[3]	6,1 [1,3; 11,0] 0,0127[3]
≥ 20 bis < 50 mm	99/646 (15,3)	52/653 (8,0)	1,92 [1,40; 2,64] <,0001[2]	2,09 [1,47; 2,98] <,0001[3]	7,4 [3,9; 10,8] <,0001[3]
≥ 50 mm	40/289 (13,8)	16/265 (6,0)	2,29 [1,32; 3,99] 0,0034[2]	2,50 [1,36; 4,58] 0,0023[3]	7,8 [2,9; 12,7] 0,0023[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,4994)					
0-3	62/427 (14,5)	27/418 (6,5)	2,25 [1,46; 3,46] 0,0002[2]	2,46 [1,53; 3,95] 0,0001[3]	8,1 [4,0; 12,1] 0,0001[3]
4-9	87/549 (15,8)	44/542 (8,1)	1,95 [1,39; 2,75] 0,0001[2]	2,13 [1,45; 3,13] <,0001[3]	7,7 [3,9; 11,6] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	42/307 (13,7)	27/305 (8,9)	1,55 [0,98; 2,44] 0,0618[2]	1,63 [0,98; 2,72] 0,0590[3]	4,8 [-0,2; 9,8] 0,0590[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9565)					
IIA	19/113 (16,8)	10/114 (8,8)	1,92 [0,93; 3,94] 0,0766[2]	2,10 [0,93; 4,75] 0,0695[3]	8,0 [-0,6; 16,7] 0,0695[3]
IIB	17/151 (11,3)	10/136 (7,4)	1,53 [0,73; 3,23] 0,2630[2]	1,60 [0,71; 3,62] 0,2578[3]	3,9 [-2,8; 10,6] 0,2578[3]
IIIA	81/495 (16,4)	38/488 (7,8)	2,10 [1,46; 3,03] <,0001[2]	2,32 [1,54; 3,48] <,0001[3]	8,6 [4,5; 12,6] <,0001[3]
IIIB	9/54 (16,7)	4/45 (8,9)	1,88 [0,62; 5,69] 0,2667[2]	2,05 [0,59; 7,17] 0,2539[3]	7,8 [-5,2; 20,7] 0,2539[3]
IIIC	64/468 (13,7)	36/480 (7,5)	1,82 [1,24; 2,69] 0,0024[2]	1,95 [1,27; 3,00] 0,0020[3]	6,2 [2,3; 10,1] 0,0020[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,3329)					
G1	13/91 (14,3)	3/93 (3,2)	4,43 [1,31; 15,03] 0,0170[2]	5,00 [1,37; 18,19] 0,0078[3]	11,1 [3,0; 19,1] 0,0078[3]
G2	80/612 (13,1)	49/603 (8,1)	1,61 [1,15; 2,25] 0,0057[2]	1,70 [1,17; 2,47] 0,0051[3]	4,9 [1,5; 8,4] 0,0051[3]
G3	87/527 (16,5)	38/506 (7,5)	2,20 [1,53; 3,15] <,0001[2]	2,44 [1,63; 3,64] <,0001[3]	9,0 [5,1; 12,9] <,0001[3]
GX	11/51 (21,6)	7/59 (11,9)	1,82 [0,76; 4,34] 0,1783[2]	2,04 [0,73; 5,74] 0,1701[3]	9,7 [-4,3; 23,7] 0,1701[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,7132)					
Negativ	25/156 (16,0)	15/169 (8,9)	1,81 [0,99; 3,30] 0,0544[2]	1,96 [0,99; 3,87] 0,0500[3]	7,1 [-0,0; 14,3] 0,0500[3]
Positiv	164/1089 (15,1)	81/1067 (7,6)	1,98 [1,54; 2,55] <,0001[2]	2,16 [1,63; 2,86] <,0001[3]	7,5 [4,8; 10,1] <,0001[3]
Unbekannt	1/10 (10,0)	1/7 (14,3)	0,70 [0,05; 9,41] 0,7879[2]	0,67 [0,03; 12,84] 1,0000[4]	-4,3 [-36,2; 27,6] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,8939)					
Weiß	126/958 (13,2)	68/944 (7,2)	1,83 [1,38; 2,42] <,0001[2]	1,95 [1,43; 2,66] <,0001[3]	5,9 [3,2; 8,7] <,0001[3]
Asiatisch	53/250 (21,2)	26/242 (10,7)	1,97 [1,28; 3,05] 0,0022[2]	2,24 [1,35; 3,71] 0,0016[3]	10,5 [4,1; 16,9] 0,0016[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Andere	9/62 (14,5)	4/64 (6,3)	2,32 [0,75; 7,15] 0,1420[2]	2,55 [0,74; 8,75] 0,1273[3]	8,3 [-2,3; 18,9] 0,1273[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,9161)					
Tamoxifen	7/114 (6,1)	4/132 (3,0)	2,03 [0,61; 6,75] 0,2498[2]	2,09 [0,60; 7,34] 0,2392[3]	3,1 [-2,2; 8,4] 0,2392[3]
Aromatase-Inhibitor	184/1169 (15,7)	94/1133 (8,3)	1,90 [1,50; 2,40] <,0001[2]	2,06 [1,59; 2,69] <,0001[3]	7,4 [4,8; 10,1] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,5065)					
ECOG-PS 0	166/1070 (15,5)	80/1020 (7,8)	1,98 [1,54; 2,55] <,0001[2]	2,16 [1,63; 2,86] <,0001[3]	7,7 [4,9; 10,4] <,0001[3]
ECOG-PS 1	25/213 (11,7)	18/245 (7,3)	1,60 [0,90; 2,85] 0,1118[2]	1,68 [0,89; 3,17] 0,1081[3]	4,4 [-1,0; 9,8] 0,1081[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: Hepatische Ereignisse aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Primärtumorgröße (p-Wert des Interaktionsterms: 0,9994)					
< 20 mm	2/141 (1,4)	0/140 (0,0)	4,96 [0,24; 102,49] 0,2996[2]	5,04 [0,24; 105,84] 0,4982[4]	1,4 [-0,5; 3,4] 0,4982[4]
≥ 20 bis < 50 mm	9/255 (3,5)	1/249 (0,4)	8,79 [1,12; 68,86] 0,0385[2]	9,07 [1,14; 72,16] 0,0204[4]	3,1 [0,7; 5,5] 0,0204[4]
≥ 50 mm	3/145 (2,1)	0/141 (0,0)	6,81 [0,35; 130,62] 0,2032[2]	6,95 [0,36; 135,80] 0,2475[4]	2,1 [-0,2; 4,4] 0,2475[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9534)					
Negativ	2/49 (4,1)	0/44 (0,0)	4,50 [0,22; 91,25] 0,3273[2]	4,68 [0,22; 100,28] 0,4960[4]	4,1 [-1,5; 9,6] 0,4960[4]
Positiv	11/477 (2,3)	1/471 (0,2)	10,86 [1,41; 83,80] 0,0221[2]	11,09 [1,43; 86,28] 0,0039[3]	2,1 [0,7; 3,5] 0,0039[3]
Unbekannt	0/4 (0,0)	0/8 (0,0)	NB	NB	NB
ECOG-PS (p-Wert des Interaktionsterms: 0,9719)					
ECOG-PS 0	13/496 (2,6)	0/480 (0,0)	26,13 [1,56; 438,34] 0,0233[2]	26,83 [1,59; 452,64] 0,0004[3]	2,6 [1,2; 4,0] 0,0004[3]
ECOG-PS 1	1/57 (1,8)	1/55 (1,8)	0,96 [0,06; 15,05] 0,9797[2]	0,96 [0,06; 15,81] 1,0000[4]	-0,1 [-5,0; 4,8] 1,0000[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: Hepatische Ereignisse aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,4151)					
< 65 Jahre	30/918 (3,3)	9/937 (1,0)	3,40 [1,62; 7,13] 0,0012[2]	3,48 [1,64; 7,38] 0,0005[3]	2,3 [1,0; 3,6] 0,0005[3]
≥ 65 Jahre	15/365 (4,1)	2/328 (0,6)	6,74 [1,55; 29,25] 0,0108[2]	6,99 [1,59; 30,78] 0,0029[3]	3,5 [1,3; 5,7] 0,0029[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,5398)					
Neoadjuvante Chemotherapie	20/430 (4,7)	3/415 (0,7)	6,43 [1,93; 21,49] 0,0025[2]	6,70 [1,98; 22,72] 0,0005[3]	3,9 [1,8; 6,1] 0,0005[3]
Adjuvante Chemotherapie	17/784 (2,2)	6/769 (0,8)	2,78 [1,10; 7,01] 0,0304[2]	2,82 [1,11; 7,19] 0,0236[3]	1,4 [0,2; 2,6] 0,0236[3]
Keine Chemotherapie	8/69 (11,6)	2/81 (2,5)	4,70 [1,03; 21,38] 0,0455[2]	5,18 [1,06; 25,28] 0,0444[4]	9,1 [0,8; 17,4] 0,0444[4]
Region (p-Wert des Interaktionsterms: 0,2414)					
Nordamerika / Europa	17/678 (2,5)	1/650 (0,2)	16,30 [2,18; 122,11] 0,0066[2]	16,69 [2,21; 125,79] 0,0002[3]	2,4 [1,1; 3,6] 0,0002[3]
Asien	14/203 (6,9)	4/201 (2,0)	3,47 [1,16; 10,35] 0,0260[2]	3,65 [1,18; 11,28] 0,0169[3]	4,9 [0,9; 8,9] 0,0169[3]
Andere	14/402 (3,5)	6/414 (1,4)	2,40 [0,93; 6,19] 0,0694[2]	2,45 [0,93; 6,45] 0,0604[3]	2,0 [-0,1; 4,2] 0,0604[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6680)					
< 20 mm	10/331 (3,0)	1/335 (0,3)	10,12 [1,30; 78,62] 0,0269[2]	10,40 [1,32; 81,75] 0,0058[3]	2,7 [0,8; 4,7] 0,0058[3]
≥ 20 bis < 50 mm	26/646 (4,0)	7/653 (1,1)	3,75 [1,64; 8,59] 0,0017[2]	3,87 [1,67; 8,98] 0,0007[3]	3,0 [1,2; 4,7] 0,0007[3]
≥ 50 mm	8/289 (2,8)	2/265 (0,8)	3,67 [0,79; 17,12] 0,0982[2]	3,74 [0,79; 17,79] 0,1095[4]	2,0 [-0,1; 4,2] 0,1095[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,3877)					
0-3	17/427 (4,0)	2/418 (0,5)	8,32 [1,93; 35,79] 0,0044[2]	8,62 [1,98; 37,57] 0,0006[3]	3,5 [1,5; 5,5] 0,0006[3]
4-9	16/549 (2,9)	4/542 (0,7)	3,95 [1,33; 11,74] 0,0135[2]	4,04 [1,34; 12,16] 0,0074[3]	2,2 [0,6; 3,8] 0,0074[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	12/307 (3,9)	5/305 (1,6)	2,38 [0,85; 6,69] 0,0986[2]	2,44 [0,85; 7,01] 0,0876[3]	2,3 [-0,3; 4,9] 0,0876[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,8517)					
IIA	2/113 (1,8)	1/114 (0,9)	2,02 [0,19; 21,94] 0,5642[2]	2,04 [0,18; 22,78] 0,6217[4]	0,9 [-2,1; 3,9] 0,6217[4]
IIB	4/151 (2,6)	1/136 (0,7)	3,60 [0,41; 31,84] 0,2490[2]	3,67 [0,41; 33,28] 0,3741[4]	1,9 [-1,0; 4,9] 0,3741[4]
IIIA	16/495 (3,2)	2/488 (0,4)	7,89 [1,82; 34,12] 0,0057[2]	8,12 [1,86; 35,49] 0,0010[3]	2,8 [1,2; 4,5] 0,0010[3]
IIIB	4/54 (7,4)	1/45 (2,2)	3,33 [0,39; 28,77] 0,2736[2]	3,52 [0,38; 32,68] 0,3728[4]	5,2 [-3,0; 13,4] 0,3728[4]
IIIC	19/468 (4,1)	6/480 (1,3)	3,25 [1,31; 8,06] 0,0111[2]	3,34 [1,32; 8,45] 0,0069[3]	2,8 [0,8; 4,9] 0,0069[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,6829)					
G1	3/91 (3,3)	0/93 (0,0)	7,15 [0,37; 136,54] 0,1910[2]	7,40 [0,38; 145,22] 0,1189[4]	3,3 [-0,4; 7,0] 0,1189[4]
G2	21/612 (3,4)	8/603 (1,3)	2,59 [1,15; 5,79] 0,0209[2]	2,64 [1,16; 6,01] 0,0163[3]	2,1 [0,4; 3,8] 0,0163[3]
G3	20/527 (3,8)	3/506 (0,6)	6,40 [1,91; 21,41] 0,0026[2]	6,61 [1,95; 22,40] 0,0005[3]	3,2 [1,4; 5,0] 0,0005[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,2670)					
Negativ	5/156 (3,2)	2/169 (1,2)	2,71 [0,53; 13,76] 0,2296[2]	2,76 [0,53; 14,46] 0,2669[4]	2,0 [-1,2; 5,2] 0,2669[4]
Positiv	40/1089 (3,7)	9/1067 (0,8)	4,35 [2,12; 8,93] <,0001[2]	4,48 [2,16; 9,28] <,0001[3]	2,8 [1,6; 4,1] <,0001[3]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,5954)					
Weiß	27/958 (2,8)	5/944 (0,5)	5,32 [2,06; 13,76] 0,0006[2]	5,45 [2,09; 14,20] 0,0001[3]	2,3 [1,1; 3,4] 0,0001[3]
Asiatisch	14/250 (5,6)	4/242 (1,7)	3,39 [1,13; 10,15] 0,0293[2]	3,53 [1,15; 10,88] 0,0197[3]	3,9 [0,7; 7,2] 0,0197[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Andere	4/62 (6,5)	2/64 (3,1)	2,06 [0,39; 10,87] 0,3924[2]	2,14 [0,38; 12,12] 0,4361[4]	3,3 [-4,1; 10,8] 0,4361[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,7200)					
ECOG-PS 0	40/1070 (3,7)	10/1020 (1,0)	3,81 [1,92; 7,58] 0,0001[2]	3,92 [1,95; 7,89] <,0001[3]	2,8 [1,5; 4,0] <,0001[3]
ECOG-PS 1	5/213 (2,3)	1/245 (0,4)	5,75 [0,68; 48,84] 0,1090[2]	5,87 [0,68; 50,61] 0,1013[4]	1,9 [-0,2; 4,1] 0,1013[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: Hepatische Ereignisse aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,5174)					
Neoadjuvante Chemotherapie	17/217 (7,8)	7/219 (3,2)	2,45 [1,04; 5,79] 0,0410[2]	2,57 [1,05; 6,34] 0,0338[3]	4,6 [0,4; 8,9] 0,0338[3]
Adjuvante Chemotherapie	36/327 (11,0)	25/312 (8,0)	1,37 [0,84; 2,23] 0,2002[2]	1,42 [0,83; 2,43] 0,1976[3]	3,0 [-1,5; 7,5] 0,1976[3]
Keine Chemotherapie	0/9 (0,0)	0/4 (0,0)	NB	NB	NB
Region (p-Wert des Interaktionsterms: 0,2475)					
Nordamerika / Europa	19/252 (7,5)	6/233 (2,6)	2,93 [1,19; 7,20] 0,0194[2]	3,09 [1,21; 7,87] 0,0135[3]	5,0 [1,1; 8,8] 0,0135[3]
Asien	25/168 (14,9)	17/166 (10,2)	1,45 [0,82; 2,59] 0,2048[2]	1,53 [0,79; 2,96] 0,2010[3]	4,6 [-2,4; 11,7] 0,2010[3]
Andere	9/133 (6,8)	9/136 (6,6)	1,02 [0,42; 2,50] 0,9609[2]	1,02 [0,39; 2,67] 0,9609[3]	0,1 [-5,8; 6,1] 0,9609[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6243)					
< 20 mm	15/141 (10,6)	8/140 (5,7)	1,86 [0,82; 4,25] 0,1401[2]	1,96 [0,80; 4,79] 0,1322[3]	4,9 [-1,5; 11,3] 0,1322[3]
≥ 20 bis < 50 mm	25/255 (9,8)	13/249 (5,2)	1,88 [0,98; 3,59] 0,0563[2]	1,97 [0,99; 3,95] 0,0514[3]	4,6 [0,0; 9,2] 0,0514[3]
≥ 50 mm	12/145 (8,3)	10/141 (7,1)	1,17 [0,52; 2,61] 0,7076[2]	1,18 [0,49; 2,83] 0,7072[3]	1,2 [-5,0; 7,4] 0,7072[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,3799)					
0-3	21/203 (10,3)	10/214 (4,7)	2,21 [1,07; 4,59] 0,0324[2]	2,35 [1,08; 5,13] 0,0273[3]	5,7 [0,6; 10,7] 0,0273[3]
4-9	19/242 (7,9)	16/231 (6,9)	1,13 [0,60; 2,15] 0,7012[2]	1,14 [0,57; 2,28] 0,7009[3]	0,9 [-3,8; 5,6] 0,7009[3]
≥ 10	13/108 (12,0)	6/90 (6,7)	1,81 [0,72; 4,56] 0,2111[2]	1,92 [0,70; 5,26] 0,2014[3]	5,4 [-2,6; 13,4] 0,2014[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9149)					
IIA	8/59 (13,6)	5/62 (8,1)	1,68 [0,58; 4,85] 0,3362[2]	1,79 [0,55; 5,82] 0,3292[3]	5,5 [-5,6; 16,6] 0,3292[3]
IIB	5/53 (9,4)	3/69 (4,3)	2,17 [0,54; 8,68] 0,2733[2]	2,29 [0,52; 10,06] 0,2921[4]	5,1 [-4,1; 14,3] 0,2921[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	20/236 (8,5)	14/214 (6,5)	1,30 [0,67; 2,50] 0,4404[2]	1,32 [0,65; 2,69] 0,4385[3]	1,9 [-2,9; 6,8] 0,4385[3]
IIIB	1/18 (5,6)	1/15 (6,7)	0,83 [0,06; 12,22] 0,8942[2]	0,82 [0,05; 14,39] 1,0000[4]	-1,1 [-17,6; 15,4] 1,0000[4]
IIIC	18/186 (9,7)	9/174 (5,2)	1,87 [0,86; 4,05] 0,1122[2]	1,96 [0,86; 4,50] 0,1049[3]	4,5 [-0,9; 9,9] 0,1049[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,6629)					
G1	8/47 (17,0)	0/41 (0,0)	14,88 [0,88; 250,04] 0,0608[2]	17,86 [1,00; 319,85] 0,0064[4]	17,0 [6,3; 27,8] 0,0064[4]
G2	13/244 (5,3)	12/234 (5,1)	1,04 [0,48; 2,23] 0,9219[2]	1,04 [0,47; 2,33] 0,9219[3]	0,2 [-3,8; 4,2] 0,9219[3]
G3	25/233 (10,7)	17/226 (7,5)	1,43 [0,79; 2,57] 0,2367[2]	1,48 [0,78; 2,82] 0,2334[3]	3,2 [-2,0; 8,5] 0,2334[3]
GX	7/29 (24,1)	3/33 (9,1)	2,66 [0,76; 9,33] 0,1279[2]	3,18 [0,74; 13,70] 0,1672[4]	15,0 [-3,4; 33,5] 0,1672[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,0868)					
Negativ	7/49 (14,3)	1/44 (2,3)	6,29 [0,80; 49,09] 0,0796[2]	7,17 [0,84; 60,79] 0,0617[4]	12,0 [1,3; 22,8] 0,0617[4]
Positiv	45/477 (9,4)	31/471 (6,6)	1,43 [0,92; 2,22] 0,1083[2]	1,48 [0,92; 2,38] 0,1059[3]	2,9 [-0,6; 6,3] 0,1059[3]
Unbekannt	0/4 (0,0)	0/8 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,8980)					
Weiß	22/323 (6,8)	12/324 (3,7)	1,84 [0,93; 3,65] 0,0819[2]	1,90 [0,92; 3,91] 0,0765[3]	3,1 [-0,3; 6,5] 0,0765[3]
Asiatisch	28/199 (14,1)	17/180 (9,4)	1,49 [0,84; 2,63] 0,1689[2]	1,57 [0,83; 2,98] 0,1644[3]	4,6 [-1,8; 11,1] 0,1644[3]
Andere	3/19 (15,8)	2/21 (9,5)	1,66 [0,31; 8,88] 0,5549[2]	1,78 [0,26; 12,01] 0,6544[4]	6,3 [-14,4; 26,9] 0,6544[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,5945)					
ECOG-PS 0	50/496 (10,1)	31/480 (6,5)	1,56 [1,02; 2,40] 0,0425[2]	1,62 [1,02; 2,59] 0,0403[3]	3,6 [0,2; 7,1] 0,0403[3]
ECOG-PS 1	3/57 (5,3)	1/55 (1,8)	2,89 [0,31; 26,99] 0,3508[2]	3,00 [0,30; 29,76] 0,6184[4]	3,4 [-3,3; 10,2] 0,6184[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko					

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: Hepatische Ereignisse aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,8000)					
< 65 Jahre	138/918 (15,0)	75/937 (8,0)	1,88 [1,44; 2,45] <,0001[2]	2,03 [1,51; 2,74] <,0001[3]	7,0 [4,1; 9,9] <,0001[3]
≥ 65 Jahre	45/365 (12,3)	20/328 (6,1)	2,02 [1,22; 3,35] 0,0063[2]	2,17 [1,25; 3,75] 0,0050[3]	6,2 [2,0; 10,5] 0,0050[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,7419)					
Neoadjuvante Chemotherapie	71/430 (16,5)	32/415 (7,7)	2,14 [1,44; 3,18] 0,0002[2]	2,37 [1,52; 3,68] <,0001[3]	8,8 [4,5; 13,1] <,0001[3]
Adjuvante Chemotherapie	104/784 (13,3)	58/769 (7,5)	1,76 [1,30; 2,39] 0,0003[2]	1,87 [1,34; 2,63] 0,0002[3]	5,7 [2,7; 8,7] 0,0002[3]
Keine Chemotherapie	8/69 (11,6)	5/81 (6,2)	1,88 [0,64; 5,48] 0,2483[2]	1,99 [0,62; 6,40] 0,2395[3]	5,4 [-3,8; 14,6] 0,2395[3]
Region (p-Wert des Interaktionsterms: 0,5900)					
Nordamerika / Europa	69/678 (10,2)	32/650 (4,9)	2,07 [1,38; 3,10] 0,0004[2]	2,19 [1,42; 3,38] 0,0003[3]	5,3 [2,4; 8,1] 0,0003[3]
Asien	52/203 (25,6)	24/201 (11,9)	2,15 [1,38; 3,34] 0,0007[2]	2,54 [1,49; 4,32] 0,0004[3]	13,7 [6,2; 21,2] 0,0004[3]
Andere	62/402 (15,4)	39/414 (9,4)	1,64 [1,12; 2,39] 0,0102[2]	1,75 [1,14; 2,69] 0,0092[3]	6,0 [1,5; 10,5] 0,0092[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6990)					
< 20 mm	47/331 (14,2)	28/335 (8,4)	1,70 [1,09; 2,64] 0,0189[2]	1,81 [1,11; 2,98] 0,0171[3]	5,8 [1,1; 10,6] 0,0171[3]
≥ 20 bis < 50 mm	94/646 (14,6)	50/653 (7,7)	1,90 [1,37; 2,63] 0,0001[2]	2,05 [1,43; 2,95] <,0001[3]	6,9 [3,5; 10,3] <,0001[3]
≥ 50 mm	38/289 (13,1)	15/265 (5,7)	2,32 [1,31; 4,12] 0,0040[2]	2,52 [1,35; 4,70] 0,0028[3]	7,5 [2,7; 12,3] 0,0028[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,4272)					
0-3	59/427 (13,8)	26/418 (6,2)	2,22 [1,43; 3,45] 0,0004[2]	2,42 [1,49; 3,92] 0,0002[3]	7,6 [3,6; 11,6] 0,0002[3]
4-9	84/549 (15,3)	42/542 (7,7)	1,97 [1,39; 2,80] 0,0001[2]	2,15 [1,45; 3,18] <,0001[3]	7,6 [3,8; 11,3] <,0001[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	40/307 (13,0)	27/305 (8,9)	1,47 [0,93; 2,34] 0,1009[2]	1,54 [0,92; 2,58] 0,0980[3]	4,2 [-0,8; 9,1] 0,0980[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9259)					
IIA	19/113 (16,8)	10/114 (8,8)	1,92 [0,93; 3,94] 0,0766[2]	2,10 [0,93; 4,75] 0,0695[3]	8,0 [-0,6; 16,7] 0,0695[3]
IIB	15/151 (9,9)	9/136 (6,6)	1,50 [0,68; 3,32] 0,3155[2]	1,56 [0,66; 3,68] 0,3109[3]	3,3 [-3,0; 9,7] 0,3109[3]
IIIA	79/495 (16,0)	37/488 (7,6)	2,10 [1,45; 3,05] <,0001[2]	2,31 [1,53; 3,50] <,0001[3]	8,4 [4,4; 12,4] <,0001[3]
IIIB	8/54 (14,8)	3/45 (6,7)	2,22 [0,63; 7,89] 0,2166[2]	2,43 [0,61; 9,79] 0,1990[3]	8,1 [-3,8; 20,1] 0,1990[3]
IIIC	61/468 (13,0)	36/480 (7,5)	1,74 [1,17; 2,57] 0,0057[2]	1,85 [1,20; 2,85] 0,0049[3]	5,5 [1,7; 9,4] 0,0049[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,3276)					
G1	13/91 (14,3)	3/93 (3,2)	4,43 [1,31; 15,03] 0,0170[2]	5,00 [1,37; 18,19] 0,0078[3]	11,1 [3,0; 19,1] 0,0078[3]
G2	78/612 (12,7)	48/603 (8,0)	1,60 [1,14; 2,25] 0,0069[2]	1,69 [1,16; 2,47] 0,0062[3]	4,8 [1,4; 8,2] 0,0062[3]
G3	82/527 (15,6)	36/506 (7,1)	2,19 [1,51; 3,17] <,0001[2]	2,41 [1,59; 3,63] <,0001[3]	8,4 [4,6; 12,3] <,0001[3]
GX	10/51 (19,6)	7/59 (11,9)	1,65 [0,68; 4,03] 0,2687[2]	1,81 [0,63; 5,17] 0,2625[3]	7,7 [-5,9; 21,4] 0,2625[3]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,6943)					
Negativ	24/156 (15,4)	15/169 (8,9)	1,73 [0,94; 3,18] 0,0759[2]	1,87 [0,94; 3,71] 0,0712[3]	6,5 [-0,6; 13,6] 0,0712[3]
Positiv	157/1089 (14,4)	78/1067 (7,3)	1,97 [1,52; 2,55] <,0001[2]	2,14 [1,60; 2,84] <,0001[3]	7,1 [4,5; 9,7] <,0001[3]
Unbekannt	1/10 (10,0)	1/7 (14,3)	0,70 [0,05; 9,41] 0,7879[2]	0,67 [0,03; 12,84] 1,0000[4]	-4,3 [-36,2; 27,6] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,9208)					
Weiß	121/958 (12,6)	66/944 (7,0)	1,81 [1,36; 2,40] <,0001[2]	1,92 [1,40; 2,63] <,0001[3]	5,6 [3,0; 8,3] <,0001[3]
Asiatisch	52/250 (20,8)	25/242 (10,3)	2,01 [1,29; 3,14] 0,0020[2]	2,28 [1,36; 3,81] 0,0014[3]	10,5 [4,1; 16,8] 0,0014[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Andere	7/62 (11,3)	4/64 (6,3)	1,81 [0,56; 5,87] 0,3251[2]	1,91 [0,53; 6,88] 0,3163[3]	5,0 [-4,8; 14,9] 0,3163[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,9010)					
Tamoxifen	7/114 (6,1)	4/132 (3,0)	2,03 [0,61; 6,75] 0,2498[2]	2,09 [0,60; 7,34] 0,2392[3]	3,1 [-2,2; 8,4] 0,2392[3]
Aromatase-Inhibitor	176/1169 (15,1)	91/1133 (8,0)	1,87 [1,48; 2,38] <,0001[2]	2,03 [1,55; 2,65] <,0001[3]	7,0 [4,4; 9,6] <,0001[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,4430)					
ECOG-PS 0	159/1070 (14,9)	77/1020 (7,5)	1,97 [1,52; 2,55] <,0001[2]	2,14 [1,60; 2,85] <,0001[3]	7,3 [4,6; 10,0] <,0001[3]
ECOG-PS 1	24/213 (11,3)	18/245 (7,3)	1,53 [0,86; 2,75] 0,1504[2]	1,60 [0,84; 3,04] 0,1470[3]	3,9 [-1,4; 9,3] 0,1470[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis: Venöse Thromboembolie (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9949)					
Neoadjuvante Chemotherapie	14/430 (3,3)	4/415 (1,0)	3,38 [1,12; 10,18] 0,0305[2]	3,46 [1,13; 10,59] 0,0211[3]	2,3 [0,4; 4,2] 0,0211[3]
Adjuvante Chemotherapie	16/784 (2,0)	5/769 (0,7)	3,14 [1,16; 8,53] 0,0249[2]	3,18 [1,16; 8,73] 0,0177[3]	1,4 [0,2; 2,5] 0,0177[3]
Keine Chemotherapie	3/69 (4,3)	0/81 (0,0)	8,20 [0,43; 156,04] 0,1615[2]	8,58 [0,44; 169,04] 0,0950[4]	4,3 [-0,5; 9,2] 0,0950[4]
Region (p-Wert des Interaktionsterms: 0,9691)					
Nordamerika / Europa	21/678 (3,1)	7/650 (1,1)	2,88 [1,23; 6,72] 0,0147[2]	2,94 [1,24; 6,95] 0,0104[3]	2,0 [0,5; 3,5] 0,0104[3]
Asien	5/203 (2,5)	0/201 (0,0)	10,89 [0,61; 195,70] 0,1052[2]	11,17 [0,61; 203,28] 0,0610[4]	2,5 [0,3; 4,6] 0,0610[4]
Andere	7/402 (1,7)	2/414 (0,5)	3,60 [0,75; 17,25] 0,1084[2]	3,65 [0,75; 17,68] 0,1028[4]	1,3 [-0,2; 2,7] 0,1028[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,6911)					
< 20 mm	8/331 (2,4)	3/335 (0,9)	2,70 [0,72; 10,08] 0,1399[2]	2,74 [0,72; 10,42] 0,1235[3]	1,5 [-0,4; 3,5] 0,1235[3]
≥ 20 bis < 50 mm	19/646 (2,9)	4/653 (0,6)	4,80 [1,64; 14,04] 0,0041[2]	4,92 [1,66; 14,53] 0,0015[3]	2,3 [0,9; 3,8] 0,0015[3]
≥ 50 mm	5/289 (1,7)	2/265 (0,8)	2,29 [0,45; 11,72] 0,3189[2]	2,32 [0,45; 12,04] 0,4533[4]	1,0 [-0,9; 2,8] 0,4533[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,6442)					
0-3	13/427 (3,0)	2/418 (0,5)	6,36 [1,44; 28,02] 0,0144[2]	6,53 [1,46; 29,12] 0,0047[3]	2,6 [0,8; 4,3] 0,0047[3]
4-9	12/549 (2,2)	4/542 (0,7)	2,96 [0,96; 9,13] 0,0586[2]	3,01 [0,96; 9,38] 0,0467[3]	1,4 [0,0; 2,9] 0,0467[3]
≥ 10	8/307 (2,6)	3/305 (1,0)	2,65 [0,71; 9,89] 0,1472[2]	2,69 [0,71; 10,25] 0,1310[3]	1,6 [-0,5; 3,7] 0,1310[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,9971)					
IIA	4/113 (3,5)	1/114 (0,9)	4,04 [0,46; 35,55] 0,2089[2]	4,15 [0,46; 37,69] 0,2125[4]	2,7 [-1,2; 6,5] 0,2125[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	5/151 (3,3)	0/136 (0,0)	9,91 [0,55; 177,65] 0,1192[2]	10,25 [0,56; 187,10] 0,0620[4]	3,3 [0,5; 6,2] 0,0620[4]
IIIA	13/495 (2,6)	4/488 (0,8)	3,20 [1,05; 9,76] 0,0404[2]	3,26 [1,06; 10,08] 0,0298[3]	1,8 [0,2; 3,4] 0,0298[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	10/468 (2,1)	4/480 (0,8)	2,56 [0,81; 8,12] 0,1093[2]	2,60 [0,81; 8,34] 0,0962[3]	1,3 [-0,2; 2,8] 0,0962[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,5724)					
G1	1/91 (1,1)	1/93 (1,1)	1,02 [0,06; 16,09] 0,9877[2]	1,02 [0,06; 16,59] 1,0000[4]	0,0 [-3,0; 3,0] 1,0000[4]
G2	16/612 (2,6)	6/603 (1,0)	2,63 [1,04; 6,67] 0,0421[2]	2,67 [1,04; 6,87] 0,0343[3]	1,6 [0,1; 3,1] 0,0343[3]
G3	15/527 (2,8)	2/506 (0,4)	7,20 [1,66; 31,33] 0,0085[2]	7,38 [1,68; 32,45] 0,0020[3]	2,5 [0,9; 4,0] 0,0020[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9607)					
Negativ	7/156 (4,5)	0/169 (0,0)	16,24 [0,94; 282,05] 0,0556[2]	17,01 [0,96; 300,29] 0,0055[4]	4,5 [1,2; 7,7] 0,0055[4]
Positiv	25/1089 (2,3)	8/1067 (0,7)	3,06 [1,39; 6,76] 0,0056[2]	3,11 [1,40; 6,93] 0,0035[3]	1,5 [0,5; 2,6] 0,0035[3]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,2765)					
Weiß	25/958 (2,6)	6/944 (0,6)	4,11 [1,69; 9,96] 0,0018[2]	4,19 [1,71; 10,26] 0,0007[3]	2,0 [0,8; 3,1] 0,0007[3]
Asiatisch	7/250 (2,8)	0/242 (0,0)	14,52 [0,83; 252,88] 0,0664[2]	14,94 [0,85; 263,00] 0,0150[4]	2,8 [0,8; 4,8] 0,0150[4]
Andere	1/62 (1,6)	2/64 (3,1)	0,52 [0,05; 5,55] 0,5852[2]	0,51 [0,04; 5,75] 1,0000[4]	-1,5 [-6,8; 3,8] 1,0000[4]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,6446)					
Tamoxifen	5/114 (4,4)	1/132 (0,8)	5,79 [0,69; 48,83] 0,1065[2]	6,01 [0,69; 52,21] 0,0988[4]	3,6 [-0,4; 7,7] 0,0988[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Aromatase-Inhibitor	28/1169 (2,4)	8/1133 (0,7)	3,39 [1,55; 7,41] 0,0022[2]	3,45 [1,57; 7,60] 0,0011[3]	1,7 [0,7; 2,7] 0,0011[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,9008)					
ECOG-PS 0	24/1070 (2,2)	6/1020 (0,6)	3,81 [1,57; 9,29] 0,0032[2]	3,88 [1,58; 9,53] 0,0015[3]	1,7 [0,7; 2,7] 0,0015[3]
ECOG-PS 1	9/213 (4,2)	3/245 (1,2)	3,45 [0,95; 12,58] 0,0606[2]	3,56 [0,95; 13,32] 0,0449[3]	3,0 [-0,0; 6,0] 0,0449[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: Venöse Thromboembolie aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9619)					
Neoadjuvante Chemotherapie	5/430 (1,2)	0/415 (0,0)	10,62 [0,59; 191,41] 0,1093[2]	10,74 [0,59; 194,87] 0,0620[4]	1,2 [0,1; 2,2] 0,0620[4]
Adjuvante Chemotherapie	7/784 (0,9)	4/769 (0,5)	1,72 [0,50; 5,84] 0,3871[2]	1,72 [0,50; 5,91] 0,3812[3]	0,4 [-0,5; 1,2] 0,3812[3]
Keine Chemotherapie	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (p-Wert des Interaktionsterms: 0,3044)					
Nordamerika / Europa	10/678 (1,5)	2/650 (0,3)	4,79 [1,05; 21,79] 0,0425[2]	4,85 [1,06; 22,22] 0,0246[3]	1,2 [0,2; 2,2] 0,0246[3]
Asien	3/203 (1,5)	0/201 (0,0)	6,93 [0,36; 133,33] 0,1994[2]	7,03 [0,36; 137,07] 0,2482[4]	1,5 [-0,2; 3,1] 0,2482[4]
Andere	1/402 (0,2)	2/414 (0,5)	0,51 [0,05; 5,66] 0,5873[2]	0,51 [0,05; 5,69] 1,0000[4]	-0,2 [-1,1; 0,6] 1,0000[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,7048)					
< 20 mm	3/331 (0,9)	0/335 (0,0)	7,08 [0,37; 136,62] 0,1947[2]	7,15 [0,37; 138,95] 0,1222[4]	0,9 [-0,1; 1,9] 0,1222[4]
≥ 20 bis < 50 mm	10/646 (1,5)	3/653 (0,5)	3,37 [0,93; 12,19] 0,0640[2]	3,41 [0,93; 12,44] 0,0487[3]	1,1 [0,0; 2,2] 0,0487[3]
≥ 50 mm	1/289 (0,3)	1/265 (0,4)	0,92 [0,06; 14,59] 0,9510[2]	0,92 [0,06; 14,73] 1,0000[4]	-0,0 [-1,0; 1,0] 1,0000[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9632)					
Negativ	3/156 (1,9)	0/169 (0,0)	7,58 [0,39; 145,58] 0,1792[2]	7,73 [0,40; 150,85] 0,1095[4]	1,9 [-0,2; 4,1] 0,1095[4]
Positiv	11/1089 (1,0)	3/1067 (0,3)	3,59 [1,01; 12,84] 0,0491[2]	3,62 [1,01; 13,01] 0,0351[3]	0,7 [0,1; 1,4] 0,0351[3]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,9816)					
Weiß	9/958 (0,9)	4/944 (0,4)	2,22 [0,69; 7,17] 0,1839[2]	2,23 [0,68; 7,26] 0,1723[3]	0,5 [-0,2; 1,3] 0,1723[3]
Asiatisch	5/250 (2,0)	0/242 (0,0)	10,65 [0,59; 191,56] 0,1086[2]	10,87 [0,60; 197,57] 0,0614[4]	2,0 [0,3; 3,7] 0,0614[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Andere	0/62 (0,0)	0/64 (0,0)	NB	NB	NB
ECOG-PS (p-Wert des Interaktionsterms: 0,9713)					
ECOG-PS 0	9/1070 (0,8)	4/1020 (0,4)	2,14 [0,66; 6,94] 0,2029[2]	2,15 [0,66; 7,02] 0,1919[3]	0,4 [-0,2; 1,1] 0,1919[3]
ECOG-PS 1	5/213 (2,3)	0/245 (0,0)	12,64 [0,70; 227,35] 0,0852[2]	12,95 [0,71; 235,61] 0,0212[4]	2,3 [0,3; 4,4] 0,0212[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: Venöse Thromboembolie aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9749)					
Neoadjuvante Chemotherapie	10/430 (2,3)	4/415 (1,0)	2,41 [0,76; 7,63] 0,1339[2]	2,45 [0,76; 7,86] 0,1211[3]	1,4 [-0,3; 3,1] 0,1211[3]
Adjuvante Chemotherapie	9/784 (1,1)	3/769 (0,4)	2,94 [0,80; 10,83] 0,1044[2]	2,97 [0,80; 10,99] 0,0881[3]	0,8 [-0,1; 1,6] 0,0881[3]
Keine Chemotherapie	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (p-Wert des Interaktionsterms: 0,6148)					
Nordamerika / Europa	12/678 (1,8)	6/650 (0,9)	1,92 [0,72; 5,08] 0,1902[2]	1,93 [0,72; 5,18] 0,1822[3]	0,8 [-0,4; 2,1] 0,1822[3]
Asien	3/203 (1,5)	0/201 (0,0)	6,93 [0,36; 133,33] 0,1994[2]	7,03 [0,36; 137,07] 0,2482[4]	1,5 [-0,2; 3,1] 0,2482[4]
Andere	6/402 (1,5)	1/414 (0,2)	6,18 [0,75; 51,10] 0,0911[2]	6,26 [0,75; 52,21] 0,0655[4]	1,3 [-0,0; 2,5] 0,0655[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,8389)					
< 20 mm	6/331 (1,8)	3/335 (0,9)	2,02 [0,51; 8,03] 0,3157[2]	2,04 [0,51; 8,24] 0,3379[4]	0,9 [-0,8; 2,7] 0,3379[4]
≥ 20 bis < 50 mm	10/646 (1,5)	3/653 (0,5)	3,37 [0,93; 12,19] 0,0640[2]	3,41 [0,93; 12,44] 0,0487[3]	1,1 [0,0; 2,2] 0,0487[3]
≥ 50 mm	4/289 (1,4)	1/265 (0,4)	3,67 [0,41; 32,61] 0,2437[2]	3,71 [0,41; 33,36] 0,3751[4]	1,0 [-0,5; 2,5] 0,3751[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,9686)					
0-3	7/427 (1,6)	2/418 (0,5)	3,43 [0,72; 16,40] 0,1232[2]	3,47 [0,72; 16,79] 0,1776[4]	1,2 [-0,2; 2,5] 0,1776[4]
4-9	8/549 (1,5)	3/542 (0,6)	2,63 [0,70; 9,87] 0,1511[2]	2,66 [0,70; 10,07] 0,1352[3]	0,9 [-0,3; 2,1] 0,1352[3]
≥ 10	6/307 (2,0)	2/305 (0,7)	2,98 [0,61; 14,65] 0,1789[2]	3,02 [0,60; 15,08] 0,2858[4]	1,3 [-0,5; 3,1] 0,2858[4]
Tumorstadium (p-Wert des Interaktionsterms: 0,9997)					
IIA	2/113 (1,8)	1/114 (0,9)	2,02 [0,19; 21,94] 0,5642[2]	2,04 [0,18; 22,78] 0,6217[4]	0,9 [-2,1; 3,9] 0,6217[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	2/151 (1,3)	0/136 (0,0)	4,51 [0,22; 93,05] 0,3297[2]	4,57 [0,22; 95,94] 0,4996[4]	1,3 [-0,5; 3,1] 0,4996[4]
IIIA	8/495 (1,6)	3/488 (0,6)	2,63 [0,70; 9,85] 0,1515[2]	2,66 [0,70; 10,07] 0,1356[3]	1,0 [-0,3; 2,3] 0,1356[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	8/468 (1,7)	3/480 (0,6)	2,74 [0,73; 10,25] 0,1354[2]	2,77 [0,73; 10,49] 0,1191[3]	1,1 [-0,3; 2,5] 0,1191[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,9022)					
G1	1/91 (1,1)	1/93 (1,1)	1,02 [0,06; 16,09] 0,9877[2]	1,02 [0,06; 16,59] 1,0000[4]	0,0 [-3,0; 3,0] 1,0000[4]
G2	12/612 (2,0)	4/603 (0,7)	2,96 [0,96; 9,11] 0,0592[2]	3,00 [0,96; 9,34] 0,0473[3]	1,3 [0,0; 2,6] 0,0473[3]
G3	7/527 (1,3)	2/506 (0,4)	3,36 [0,70; 16,10] 0,1294[2]	3,39 [0,70; 16,41] 0,1786[4]	0,9 [-0,2; 2,1] 0,1786[4]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9617)					
Negativ	5/156 (3,2)	0/169 (0,0)	11,91 [0,66; 213,66] 0,0926[2]	12,31 [0,67; 224,42] 0,0246[4]	3,2 [0,4; 6,0] 0,0246[4]
Positiv	15/1089 (1,4)	7/1067 (0,7)	2,10 [0,86; 5,13] 0,1036[2]	2,11 [0,86; 5,21] 0,0956[3]	0,7 [-0,1; 1,6] 0,0956[3]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,2909)					
Weiß	17/958 (1,8)	4/944 (0,4)	4,19 [1,41; 12,40] 0,0097[2]	4,25 [1,42; 12,66] 0,0048[3]	1,4 [0,4; 2,3] 0,0048[3]
Asiatisch	3/250 (1,2)	0/242 (0,0)	6,78 [0,35; 130,51] 0,2048[2]	6,86 [0,35; 133,48] 0,2487[4]	1,2 [-0,1; 2,5] 0,2487[4]
Andere	1/62 (1,6)	2/64 (3,1)	0,52 [0,05; 5,55] 0,5852[2]	0,51 [0,04; 5,75] 1,0000[4]	-1,5 [-6,8; 3,8] 1,0000[4]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,6651)					
Tamoxifen	4/114 (3,5)	1/132 (0,8)	4,63 [0,53; 40,85] 0,1675[2]	4,76 [0,52; 43,25] 0,1855[4]	2,8 [-0,9; 6,4] 0,1855[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Aromatase-Inhibitor	17/1169 (1,5)	6/1133 (0,5)	2,75 [1,09; 6,94] 0,0327[2]	2,77 [1,09; 7,06] 0,0257[3]	0,9 [0,1; 1,7] 0,0257[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,4518)					
ECOG-PS 0	16/1070 (1,5)	4/1020 (0,4)	3,81 [1,28; 11,37] 0,0163[2]	3,86 [1,28; 11,57] 0,0096[3]	1,1 [0,3; 1,9] 0,0096[3]
ECOG-PS 1	5/213 (2,3)	3/245 (1,2)	1,92 [0,46; 7,93] 0,3689[2]	1,94 [0,46; 8,21] 0,4813[4]	1,1 [-1,3; 3,6] 0,4813[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Schwerwiegendes unerwünschtes Ereignis: Venöse Thromboembolie aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Region (p-Wert des Interaktionsterms: 0,9981)					
Nordamerika / Europa	9/678 (1,3)	3/650 (0,5)	2,88 [0,78; 10,58] 0,1118[2]	2,90 [0,78; 10,76] 0,0955[3]	0,9 [-0,1; 1,9] 0,0955[3]
Asien	2/203 (1,0)	0/201 (0,0)	4,95 [0,24; 102,48] 0,3008[2]	5,00 [0,24; 104,80] 0,4988[4]	1,0 [-0,4; 2,3] 0,4988[4]
Andere	3/402 (0,7)	1/414 (0,2)	3,09 [0,32; 29,58] 0,3277[2]	3,11 [0,32; 29,98] 0,3669[4]	0,5 [-0,5; 1,5] 0,3669[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,8487)					
< 20 mm	4/331 (1,2)	1/335 (0,3)	4,05 [0,45; 36,03] 0,2100[2]	4,09 [0,45; 36,75] 0,2145[4]	0,9 [-0,4; 2,2] 0,2145[4]
≥ 20 bis < 50 mm	8/646 (1,2)	2/653 (0,3)	4,04 [0,86; 18,97] 0,0765[2]	4,08 [0,86; 19,29] 0,0631[4]	0,9 [-0,0; 1,9] 0,0631[4]
≥ 50 mm	2/289 (0,7)	1/265 (0,4)	1,83 [0,17; 20,11] 0,6196[2]	1,84 [0,17; 20,41] 1,0000[4]	0,3 [-0,9; 1,5] 1,0000[4]
Tumorgrading (p-Wert des Interaktionsterms: 0,8741)					
G1	1/91 (1,1)	1/93 (1,1)	1,02 [0,06; 16,09] 0,9877[2]	1,02 [0,06; 16,59] 1,0000[4]	0,0 [-3,0; 3,0] 1,0000[4]
G2	7/612 (1,1)	3/603 (0,5)	2,30 [0,60; 8,85] 0,2261[2]	2,31 [0,60; 8,99] 0,3419[4]	0,6 [-0,4; 1,7] 0,3419[4]
G3	6/527 (1,1)	0/506 (0,0)	12,48 [0,71; 221,01] 0,0851[2]	12,63 [0,71; 224,71] 0,0310[4]	1,1 [0,2; 2,0] 0,0310[4]
GX	0/51 (0,0)	0/59 (0,0)	NB	NB	NB
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9644)					
Negativ	2/156 (1,3)	0/169 (0,0)	5,41 [0,26; 111,90] 0,2744[2]	5,49 [0,26; 115,15] 0,2296[4]	1,3 [-0,5; 3,0] 0,2296[4]
Positiv	12/1089 (1,1)	3/1067 (0,3)	3,92 [1,11; 13,85] 0,0339[2]	3,95 [1,11; 14,04] 0,0219[3]	0,8 [0,1; 1,5] 0,0219[3]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,9997)					
Weiß	10/958 (1,0)	3/944 (0,3)	3,28 [0,91; 11,90] 0,0701[2]	3,31 [0,91; 12,06] 0,0547[3]	0,7 [-0,0; 1,5] 0,0547[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Asiatisch	3/250 (1,2)	0/242 (0,0)	6,78 [0,35; 130,51] 0,2048[2]	6,86 [0,35; 133,48] 0,2487[4]	1,2 [-0,1; 2,5] 0,2487[4]
Andere	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,7144)					
ECOG-PS 0	12/1070 (1,1)	3/1020 (0,3)	3,81 [1,08; 13,47] 0,0377[2]	3,84 [1,08; 13,67] 0,0251[3]	0,8 [0,1; 1,5] 0,0251[3]
ECOG-PS 1	2/213 (0,9)	1/245 (0,4)	2,30 [0,21; 25,19] 0,4951[2]	2,31 [0,21; 25,69] 0,5998[4]	0,5 [-1,0; 2,1] 0,5998[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis: ILD/Pneumonitis (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9980)					
Neoadjuvante Chemotherapie	5/217 (2,3)	3/219 (1,4)	1,68 [0,41; 6,95] 0,4726[2]	1,70 [0,40; 7,19] 0,5023[4]	0,9 [-1,6; 3,5] 0,5023[4]
Adjuvante Chemotherapie	10/327 (3,1)	6/312 (1,9)	1,59 [0,58; 4,32] 0,3633[2]	1,61 [0,58; 4,48] 0,3587[3]	1,1 [-1,3; 3,5] 0,3587[3]
Keine Chemotherapie	0/9 (0,0)	0/4 (0,0)	NB	NB	NB
Region (p-Wert des Interaktionsterms: 0,3145)					
Nordamerika / Europa	6/252 (2,4)	1/233 (0,4)	5,55 [0,67; 45,74] 0,1114[2]	5,66 [0,68; 47,36] 0,1243[4]	2,0 [-0,1; 4,0] 0,1243[4]
Asien	8/168 (4,8)	6/166 (3,6)	1,32 [0,47; 3,71] 0,6021[2]	1,33 [0,45; 3,93] 0,6008[3]	1,1 [-3,1; 5,4] 0,6008[3]
Andere	1/133 (0,8)	2/136 (1,5)	0,51 [0,05; 5,57] 0,5820[2]	0,51 [0,05; 5,67] 1,0000[4]	-0,7 [-3,2; 1,8] 1,0000[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,7302)					
< 20 mm	2/141 (1,4)	1/140 (0,7)	1,99 [0,18; 21,65] 0,5736[2]	2,00 [0,18; 22,31] 1,0000[4]	0,7 [-1,7; 3,1] 1,0000[4]
≥ 20 bis < 50 mm	8/255 (3,1)	4/249 (1,6)	1,95 [0,60; 6,40] 0,2693[2]	1,98 [0,59; 6,67] 0,2597[3]	1,5 [-1,1; 4,2] 0,2597[3]
≥ 50 mm	4/145 (2,8)	4/141 (2,8)	0,97 [0,25; 3,81] 0,9680[2]	0,97 [0,24; 3,96] 1,0000[4]	-0,1 [-3,9; 3,7] 1,0000[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,5816)					
0-3	2/203 (1,0)	3/214 (1,4)	0,70 [0,12; 4,16] 0,6976[2]	0,70 [0,12; 4,23] 1,0000[4]	-0,4 [-2,5; 1,7] 1,0000[4]
4-9	11/242 (4,5)	5/231 (2,2)	2,10 [0,74; 5,95] 0,1627[2]	2,15 [0,74; 6,29] 0,1522[3]	2,4 [-0,8; 5,6] 0,1522[3]
≥ 10	2/108 (1,9)	1/90 (1,1)	1,67 [0,15; 18,08] 0,6745[2]	1,68 [0,15; 18,83] 1,0000[4]	0,7 [-2,6; 4,1] 1,0000[4]
Tumorstadium (p-Wert des Interaktionsterms: 0,9671)					
IIA	0/59 (0,0)	0/62 (0,0)	NB	NB	NB
IIB	0/53 (0,0)	1/69 (1,4)	0,43 [0,02; 10,40] 0,6051[2]	0,43 [0,02; 10,69] 1,0000[4]	-1,4 [-4,3; 1,4] 1,0000[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	10/236 (4,2)	4/214 (1,9)	2,27 [0,72; 7,12] 0,1611[2]	2,32 [0,72; 7,52] 0,1485[3]	2,4 [-0,8; 5,5] 0,1485[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NB	NB	NB
IIIC	5/186 (2,7)	4/174 (2,3)	1,17 [0,32; 4,28] 0,8133[2]	1,17 [0,31; 4,45] 1,0000[4]	0,4 [-2,8; 3,6] 1,0000[4]
Tumorgrading (p-Wert des Interaktionsterms: 0,8907)					
G1	1/47 (2,1)	0/41 (0,0)	2,63 [0,11; 62,73] 0,5512[2]	2,68 [0,11; 67,54] 1,0000[4]	2,1 [-2,0; 6,3] 1,0000[4]
G2	8/244 (3,3)	6/234 (2,6)	1,28 [0,45; 3,63] 0,6442[2]	1,29 [0,44; 3,77] 0,6432[3]	0,7 [-2,3; 3,7] 0,6432[3]
G3	3/233 (1,3)	2/226 (0,9)	1,45 [0,25; 8,63] 0,6797[2]	1,46 [0,24; 8,83] 1,0000[4]	0,4 [-1,5; 2,3] 1,0000[4]
GX	3/29 (10,3)	1/33 (3,0)	3,41 [0,38; 31,04] 0,2757[2]	3,69 [0,36; 37,63] 0,3321[4]	7,3 [-5,2; 19,8] 0,3321[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9997)					
Negativ	0/49 (0,0)	0/44 (0,0)	NB	NB	NB
Positiv	13/477 (2,7)	9/471 (1,9)	1,43 [0,62; 3,30] 0,4076[2]	1,44 [0,61; 3,40] 0,4049[3]	0,8 [-1,1; 2,7] 0,4049[3]
Unbekannt	0/4 (0,0)	0/8 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,7463)					
Weiß	7/323 (2,2)	3/324 (0,9)	2,34 [0,61; 8,97] 0,2148[2]	2,37 [0,61; 9,25] 0,2226[4]	1,2 [-0,7; 3,1] 0,2226[4]
Asiatisch	8/199 (4,0)	6/180 (3,3)	1,21 [0,43; 3,41] 0,7238[2]	1,21 [0,41; 3,57] 0,7234[3]	0,7 [-3,1; 4,5] 0,7234[3]
Andere	0/19 (0,0)	0/21 (0,0)	NB	NB	NB
ECOG-PS (p-Wert des Interaktionsterms: 0,5670)					
ECOG-PS 0	13/496 (2,6)	7/480 (1,5)	1,80 [0,72; 4,47] 0,2068[2]	1,82 [0,72; 4,60] 0,1999[3]	1,2 [-0,6; 2,9] 0,1999[3]
ECOG-PS 1	2/57 (3,5)	2/55 (3,6)	0,96 [0,14; 6,61] 0,9710[2]	0,96 [0,13; 7,09] 1,0000[4]	-0,1 [-7,0; 6,7] 1,0000[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; ILD: Interstitial Lung Disease; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko					

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Tabelle: Subgruppen - Unerwünschtes Ereignis: ILD/Pneumonitis (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,5516)					
< 65 Jahre	22/918 (2,4)	13/937 (1,4)	1,73 [0,88; 3,41] 0,1149[2]	1,75 [0,87; 3,49] 0,1102[3]	1,0 [-0,2; 2,2] 0,1102[3]
≥ 65 Jahre	9/365 (2,5)	3/328 (0,9)	2,70 [0,74; 9,87] 0,1343[2]	2,74 [0,74; 10,20] 0,1181[3]	1,6 [-0,3; 3,4] 0,1181[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,4108)					
Neoadjuvante Chemotherapie	12/430 (2,8)	9/415 (2,2)	1,29 [0,55; 3,02] 0,5626[2]	1,30 [0,54; 3,11] 0,5615[3]	0,6 [-1,5; 2,7] 0,5615[3]
Adjuvante Chemotherapie	18/784 (2,3)	6/769 (0,8)	2,94 [1,17; 7,37] 0,0213[2]	2,99 [1,18; 7,57] 0,0155[3]	1,5 [0,3; 2,7] 0,0155[3]
Keine Chemotherapie	1/69 (1,4)	1/81 (1,2)	1,17 [0,07; 18,42] 0,9091[2]	1,18 [0,07; 19,17] 1,0000[4]	0,2 [-3,5; 3,9] 1,0000[4]
Region (p-Wert des Interaktionsterms: 0,7972)					
Nordamerika / Europa	17/678 (2,5)	7/650 (1,1)	2,33 [0,97; 5,58] 0,0579[2]	2,36 [0,97; 5,73] 0,0504[3]	1,4 [0,0; 2,8] 0,0504[3]
Asien	9/203 (4,4)	6/201 (3,0)	1,49 [0,54; 4,10] 0,4447[2]	1,51 [0,53; 4,32] 0,4414[3]	1,4 [-2,2; 5,1] 0,4414[3]
Andere	5/402 (1,2)	3/414 (0,7)	1,72 [0,41; 7,13] 0,4574[2]	1,73 [0,41; 7,27] 0,4998[4]	0,5 [-0,8; 1,9] 0,4998[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3687)					
< 20 mm	8/331 (2,4)	2/335 (0,6)	4,05 [0,87; 18,92] 0,0755[2]	4,12 [0,87; 19,57] 0,0621[4]	1,8 [-0,0; 3,7] 0,0621[4]
≥ 20 bis < 50 mm	17/646 (2,6)	9/653 (1,4)	1,91 [0,86; 4,25] 0,1133[2]	1,93 [0,86; 4,37] 0,1068[3]	1,3 [-0,3; 2,8] 0,1068[3]
≥ 50 mm	4/289 (1,4)	4/265 (1,5)	0,92 [0,23; 3,63] 0,9017[2]	0,92 [0,23; 3,70] 1,0000[4]	-0,1 [-2,1; 1,9] 1,0000[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7833)					
0-3	12/427 (2,8)	6/418 (1,4)	1,96 [0,74; 5,17] 0,1749[2]	1,99 [0,74; 5,34] 0,1664[3]	1,4 [-0,6; 3,3] 0,1664[3]
4-9	7/549 (1,3)	5/542 (0,9)	1,38 [0,44; 4,33] 0,5784[2]	1,39 [0,44; 4,40] 0,5767[3]	0,4 [-0,9; 1,6] 0,5767[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	12/307 (3,9)	5/305 (1,6)	2,38 [0,85; 6,69] 0,0986[2]	2,44 [0,85; 7,01] 0,0876[3]	2,3 [-0,3; 4,9] 0,0876[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,8609)					
IIA	5/113 (4,4)	1/114 (0,9)	5,04 [0,60; 42,50] 0,1367[2]	5,23 [0,60; 45,51] 0,1192[4]	3,5 [-0,6; 7,7] 0,1192[4]
IIB	4/151 (2,6)	3/136 (2,2)	1,20 [0,27; 5,27] 0,8083[2]	1,21 [0,27; 5,49] 1,0000[4]	0,4 [-3,1; 4,0] 1,0000[4]
IIIA	6/495 (1,2)	4/488 (0,8)	1,48 [0,42; 5,21] 0,5425[2]	1,48 [0,42; 5,29] 0,7527[4]	0,4 [-0,9; 1,6] 0,7527[4]
IIIB	0/54 (0,0)	0/45 (0,0)	NB	NB	NB
IIIC	15/468 (3,2)	8/480 (1,7)	1,92 [0,82; 4,49] 0,1309[2]	1,95 [0,82; 4,65] 0,1238[3]	1,5 [-0,4; 3,5] 0,1238[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,9823)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	12/612 (2,0)	8/603 (1,3)	1,48 [0,61; 3,59] 0,3883[2]	1,49 [0,60; 3,67] 0,3851[3]	0,6 [-0,8; 2,1] 0,3851[3]
G3	14/527 (2,7)	7/506 (1,4)	1,92 [0,78; 4,72] 0,1549[2]	1,95 [0,78; 4,86] 0,1472[3]	1,3 [-0,4; 3,0] 0,1472[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,3967)					
Negativ	4/156 (2,6)	2/169 (1,2)	2,17 [0,40; 11,66] 0,3680[2]	2,20 [0,40; 12,17] 0,4323[4]	1,4 [-1,6; 4,3] 0,4323[4]
Positiv	27/1089 (2,5)	14/1067 (1,3)	1,89 [1,00; 3,58] 0,0513[2]	1,91 [1,00; 3,67] 0,0473[3]	1,2 [0,0; 2,3] 0,0473[3]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,7134)					
Weiß	19/958 (2,0)	8/944 (0,8)	2,34 [1,03; 5,32] 0,0424[2]	2,37 [1,03; 5,43] 0,0363[3]	1,1 [0,1; 2,2] 0,0363[3]
Asiatisch	10/250 (4,0)	7/242 (2,9)	1,38 [0,54; 3,57] 0,5035[2]	1,40 [0,52; 3,74] 0,5013[3]	1,1 [-2,1; 4,3] 0,5013[3]
Andere	2/62 (3,2)	0/64 (0,0)	5,16 [0,25; 105,34] 0,2864[2]	5,33 [0,25; 113,30] 0,2401[4]	3,2 [-1,2; 7,6] 0,2401[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,2474)					
Tamoxifen	3/114 (2,6)	4/132 (3,0)	0,87 [0,20; 3,80] 0,8514[2]	0,86 [0,19; 3,95] 1,0000[4]	-0,4 [-4,5; 3,7] 1,0000[4]
Aromatase-Inhibitor	28/1169 (2,4)	12/1133 (1,1)	2,26 [1,16; 4,43] 0,0172[2]	2,29 [1,16; 4,53] 0,0142[3]	1,3 [0,3; 2,4] 0,0142[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,2843)					
ECOG-PS 0	25/1070 (2,3)	10/1020 (1,0)	2,38 [1,15; 4,94] 0,0194[2]	2,42 [1,15; 5,06] 0,0157[3]	1,4 [0,3; 2,4] 0,0157[3]
ECOG-PS 1	6/213 (2,8)	6/245 (2,4)	1,15 [0,38; 3,51] 0,8059[2]	1,15 [0,37; 3,63] 0,8058[3]	0,4 [-2,6; 3,3] 0,8058[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; ILD: Interstitial Lung Disease; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: ILD/Pneumonitis aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9980)					
Neoadjuvante Chemotherapie	5/217 (2,3)	3/219 (1,4)	1,68 [0,41; 6,95] 0,4726[2]	1,70 [0,40; 7,19] 0,5023[4]	0,9 [-1,6; 3,5] 0,5023[4]
Adjuvante Chemotherapie	10/327 (3,1)	6/312 (1,9)	1,59 [0,58; 4,32] 0,3633[2]	1,61 [0,58; 4,48] 0,3587[3]	1,1 [-1,3; 3,5] 0,3587[3]
Keine Chemotherapie	0/9 (0,0)	0/4 (0,0)	NB	NB	NB
Region (p-Wert des Interaktionsterms: 0,3145)					
Nordamerika / Europa	6/252 (2,4)	1/233 (0,4)	5,55 [0,67; 45,74] 0,1114[2]	5,66 [0,68; 47,36] 0,1243[4]	2,0 [-0,1; 4,0] 0,1243[4]
Asien	8/168 (4,8)	6/166 (3,6)	1,32 [0,47; 3,71] 0,6021[2]	1,33 [0,45; 3,93] 0,6008[3]	1,1 [-3,1; 5,4] 0,6008[3]
Andere	1/133 (0,8)	2/136 (1,5)	0,51 [0,05; 5,57] 0,5820[2]	0,51 [0,05; 5,67] 1,0000[4]	-0,7 [-3,2; 1,8] 1,0000[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,7302)					
< 20 mm	2/141 (1,4)	1/140 (0,7)	1,99 [0,18; 21,65] 0,5736[2]	2,00 [0,18; 22,31] 1,0000[4]	0,7 [-1,7; 3,1] 1,0000[4]
≥ 20 bis < 50 mm	8/255 (3,1)	4/249 (1,6)	1,95 [0,60; 6,40] 0,2693[2]	1,98 [0,59; 6,67] 0,2597[3]	1,5 [-1,1; 4,2] 0,2597[3]
≥ 50 mm	4/145 (2,8)	4/141 (2,8)	0,97 [0,25; 3,81] 0,9680[2]	0,97 [0,24; 3,96] 1,0000[4]	-0,1 [-3,9; 3,7] 1,0000[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,5816)					
0-3	2/203 (1,0)	3/214 (1,4)	0,70 [0,12; 4,16] 0,6976[2]	0,70 [0,12; 4,23] 1,0000[4]	-0,4 [-2,5; 1,7] 1,0000[4]
4-9	11/242 (4,5)	5/231 (2,2)	2,10 [0,74; 5,95] 0,1627[2]	2,15 [0,74; 6,29] 0,1522[3]	2,4 [-0,8; 5,6] 0,1522[3]
≥ 10	2/108 (1,9)	1/90 (1,1)	1,67 [0,15; 18,08] 0,6745[2]	1,68 [0,15; 18,83] 1,0000[4]	0,7 [-2,6; 4,1] 1,0000[4]
Tumorstadium (p-Wert des Interaktionsterms: 0,9671)					
IIA	0/59 (0,0)	0/62 (0,0)	NB	NB	NB
IIB	0/53 (0,0)	1/69 (1,4)	0,43 [0,02; 10,40] 0,6051[2]	0,43 [0,02; 10,69] 1,0000[4]	-1,4 [-4,3; 1,4] 1,0000[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIIA	10/236 (4,2)	4/214 (1,9)	2,27 [0,72; 7,12] 0,1611[2]	2,32 [0,72; 7,52] 0,1485[3]	2,4 [-0,8; 5,5] 0,1485[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NB	NB	NB
IIIC	5/186 (2,7)	4/174 (2,3)	1,17 [0,32; 4,28] 0,8133[2]	1,17 [0,31; 4,45] 1,0000[4]	0,4 [-2,8; 3,6] 1,0000[4]
Tumorgrading (p-Wert des Interaktionsterms: 0,8907)					
G1	1/47 (2,1)	0/41 (0,0)	2,63 [0,11; 62,73] 0,5512[2]	2,68 [0,11; 67,54] 1,0000[4]	2,1 [-2,0; 6,3] 1,0000[4]
G2	8/244 (3,3)	6/234 (2,6)	1,28 [0,45; 3,63] 0,6442[2]	1,29 [0,44; 3,77] 0,6432[3]	0,7 [-2,3; 3,7] 0,6432[3]
G3	3/233 (1,3)	2/226 (0,9)	1,45 [0,25; 8,63] 0,6797[2]	1,46 [0,24; 8,83] 1,0000[4]	0,4 [-1,5; 2,3] 1,0000[4]
GX	3/29 (10,3)	1/33 (3,0)	3,41 [0,38; 31,04] 0,2757[2]	3,69 [0,36; 37,63] 0,3321[4]	7,3 [-5,2; 19,8] 0,3321[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9997)					
Negativ	0/49 (0,0)	0/44 (0,0)	NB	NB	NB
Positiv	13/477 (2,7)	9/471 (1,9)	1,43 [0,62; 3,30] 0,4076[2]	1,44 [0,61; 3,40] 0,4049[3]	0,8 [-1,1; 2,7] 0,4049[3]
Unbekannt	0/4 (0,0)	0/8 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,7463)					
Weiß	7/323 (2,2)	3/324 (0,9)	2,34 [0,61; 8,97] 0,2148[2]	2,37 [0,61; 9,25] 0,2226[4]	1,2 [-0,7; 3,1] 0,2226[4]
Asiatisch	8/199 (4,0)	6/180 (3,3)	1,21 [0,43; 3,41] 0,7238[2]	1,21 [0,41; 3,57] 0,7234[3]	0,7 [-3,1; 4,5] 0,7234[3]
Andere	0/19 (0,0)	0/21 (0,0)	NB	NB	NB
ECOG-PS (p-Wert des Interaktionsterms: 0,5670)					
ECOG-PS 0	13/496 (2,6)	7/480 (1,5)	1,80 [0,72; 4,47] 0,2068[2]	1,82 [0,72; 4,60] 0,1999[3]	1,2 [-0,6; 2,9] 0,1999[3]
ECOG-PS 1	2/57 (3,5)	2/55 (3,6)	0,96 [0,14; 6,61] 0,9710[2]	0,96 [0,13; 7,09] 1,0000[4]	-0,1 [-7,0; 6,7] 1,0000[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; ILD: Interstitial Lung Disease; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko					

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: ILD/Pneumonitis aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,4716)					
< 65 Jahre	20/918 (2,2)	13/937 (1,4)	1,57 [0,79; 3,14] 0,2014[2]	1,58 [0,78; 3,20] 0,1974[3]	0,8 [-0,4; 2,0] 0,1974[3]
≥ 65 Jahre	9/365 (2,5)	3/328 (0,9)	2,70 [0,74; 9,87] 0,1343[2]	2,74 [0,74; 10,20] 0,1181[3]	1,6 [-0,3; 3,4] 0,1181[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,5243)					
Neoadjuvante Chemotherapie	12/430 (2,8)	9/415 (2,2)	1,29 [0,55; 3,02] 0,5626[2]	1,30 [0,54; 3,11] 0,5615[3]	0,6 [-1,5; 2,7] 0,5615[3]
Adjuvante Chemotherapie	16/784 (2,0)	6/769 (0,8)	2,62 [1,03; 6,65] 0,0434[2]	2,65 [1,03; 6,81] 0,0356[3]	1,3 [0,1; 2,4] 0,0356[3]
Keine Chemotherapie	1/69 (1,4)	1/81 (1,2)	1,17 [0,07; 18,42] 0,9091[2]	1,18 [0,07; 19,17] 1,0000[4]	0,2 [-3,5; 3,9] 1,0000[4]
Region (p-Wert des Interaktionsterms: 0,7979)					
Nordamerika / Europa	16/678 (2,4)	7/650 (1,1)	2,19 [0,91; 5,29] 0,0812[2]	2,22 [0,91; 5,43] 0,0732[3]	1,3 [-0,1; 2,7] 0,0732[3]
Asien	9/203 (4,4)	6/201 (3,0)	1,49 [0,54; 4,10] 0,4447[2]	1,51 [0,53; 4,32] 0,4414[3]	1,4 [-2,2; 5,1] 0,4414[3]
Andere	4/402 (1,0)	3/414 (0,7)	1,37 [0,31; 6,10] 0,6767[2]	1,38 [0,31; 6,19] 0,7217[4]	0,3 [-1,0; 1,5] 0,7217[4]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3700)					
< 20 mm	8/331 (2,4)	2/335 (0,6)	4,05 [0,87; 18,92] 0,0755[2]	4,12 [0,87; 19,57] 0,0621[4]	1,8 [-0,0; 3,7] 0,0621[4]
≥ 20 bis < 50 mm	15/646 (2,3)	9/653 (1,4)	1,68 [0,74; 3,82] 0,2121[2]	1,70 [0,74; 3,92] 0,2066[3]	0,9 [-0,5; 2,4] 0,2066[3]
≥ 50 mm	4/289 (1,4)	4/265 (1,5)	0,92 [0,23; 3,63] 0,9017[2]	0,92 [0,23; 3,70] 1,0000[4]	-0,1 [-2,1; 1,9] 1,0000[4]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7687)					
0-3	10/427 (2,3)	6/418 (1,4)	1,63 [0,60; 4,45] 0,3388[2]	1,65 [0,59; 4,57] 0,3337[3]	0,9 [-0,9; 2,7] 0,3337[3]
4-9	7/549 (1,3)	5/542 (0,9)	1,38 [0,44; 4,33] 0,5784[2]	1,39 [0,44; 4,40] 0,5767[3]	0,4 [-0,9; 1,6] 0,5767[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	12/307 (3,9)	5/305 (1,6)	2,38 [0,85; 6,69] 0,0986[2]	2,44 [0,85; 7,01] 0,0876[3]	2,3 [-0,3; 4,9] 0,0876[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,6536)					
IIA	5/113 (4,4)	1/114 (0,9)	5,04 [0,60; 42,50] 0,1367[2]	5,23 [0,60; 45,51] 0,1192[4]	3,5 [-0,6; 7,7] 0,1192[4]
IIB	2/151 (1,3)	3/136 (2,2)	0,60 [0,10; 3,54] 0,5731[2]	0,60 [0,10; 3,62] 0,6704[4]	-0,9 [-4,0; 2,2] 0,6704[4]
IIIA	6/495 (1,2)	4/488 (0,8)	1,48 [0,42; 5,21] 0,5425[2]	1,48 [0,42; 5,29] 0,7527[4]	0,4 [-0,9; 1,6] 0,7527[4]
IIIB	0/54 (0,0)	0/45 (0,0)	NB	NB	NB
IIIC	15/468 (3,2)	8/480 (1,7)	1,92 [0,82; 4,49] 0,1309[2]	1,95 [0,82; 4,65] 0,1238[3]	1,5 [-0,4; 3,5] 0,1238[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,9985)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	12/612 (2,0)	8/603 (1,3)	1,48 [0,61; 3,59] 0,3883[2]	1,49 [0,60; 3,67] 0,3851[3]	0,6 [-0,8; 2,1] 0,3851[3]
G3	12/527 (2,3)	7/506 (1,4)	1,65 [0,65; 4,15] 0,2906[2]	1,66 [0,65; 4,25] 0,2853[3]	0,9 [-0,7; 2,5] 0,2853[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,3974)					
Negativ	4/156 (2,6)	2/169 (1,2)	2,17 [0,40; 11,66] 0,3680[2]	2,20 [0,40; 12,17] 0,4323[4]	1,4 [-1,6; 4,3] 0,4323[4]
Positiv	25/1089 (2,3)	14/1067 (1,3)	1,75 [0,91; 3,35] 0,0910[2]	1,77 [0,91; 3,42] 0,0866[3]	1,0 [-0,1; 2,1] 0,0866[3]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB
Ethnizität (p-Wert des Interaktionsterms: 0,6748)					
Weiß	18/958 (1,9)	8/944 (0,8)	2,22 [0,97; 5,07] 0,0595[2]	2,24 [0,97; 5,18] 0,0527[3]	1,0 [-0,0; 2,1] 0,0527[3]
Asiatisch	9/250 (3,6)	7/242 (2,9)	1,24 [0,47; 3,29] 0,6590[2]	1,25 [0,46; 3,42] 0,6583[3]	0,7 [-2,4; 3,8] 0,6583[3]
Andere	2/62 (3,2)	0/64 (0,0)	5,16 [0,25; 105,34] 0,2864[2]	5,33 [0,25; 113,30] 0,2401[4]	3,2 [-1,2; 7,6] 0,2401[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,2869)					
Tamoxifen	3/114 (2,6)	4/132 (3,0)	0,87 [0,20; 3,80] 0,8514[2]	0,86 [0,19; 3,95] 1,0000[4]	-0,4 [-4,5; 3,7] 1,0000[4]
Aromatase-Inhibitor	26/1169 (2,2)	12/1133 (1,1)	2,10 [1,06; 4,14] 0,0323[2]	2,12 [1,07; 4,23] 0,0283[3]	1,2 [0,1; 2,2] 0,0283[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,3448)					
ECOG-PS 0	23/1070 (2,1)	10/1020 (1,0)	2,19 [1,05; 4,58] 0,0369[2]	2,22 [1,05; 4,68] 0,0321[3]	1,2 [0,1; 2,2] 0,0321[3]
ECOG-PS 1	6/213 (2,8)	6/245 (2,4)	1,15 [0,38; 3,51] 0,8059[2]	1,15 [0,37; 3,63] 0,8058[3]	0,4 [-2,6; 3,3] 0,8058[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; ILD: Interstitial Lung Disease; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko

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Tabelle: Subgruppen - Unerwünschtes Ereignis: Erkrankungen der Nieren und Harnwege (SOC) (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9979)					
Neoadjuvante Chemotherapie	15/217 (6,9)	11/219 (5,0)	1,38 [0,65; 2,93] 0,4071[2]	1,40 [0,63; 3,13] 0,4048[3]	1,9 [-2,6; 6,3] 0,4048[3]
Adjuvante Chemotherapie	21/327 (6,4)	15/312 (4,8)	1,34 [0,70; 2,54] 0,3784[2]	1,36 [0,69; 2,69] 0,3763[3]	1,6 [-1,9; 5,2] 0,3763[3]
Keine Chemotherapie	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (p-Wert des Interaktionsterms: 0,3970)					
Nordamerika / Europa	20/252 (7,9)	10/233 (4,3)	1,85 [0,88; 3,87] 0,1025[2]	1,92 [0,88; 4,20] 0,0960[3]	3,6 [-0,6; 7,9] 0,0960[3]
Asien	12/168 (7,1)	9/166 (5,4)	1,32 [0,57; 3,04] 0,5186[2]	1,34 [0,55; 3,27] 0,5170[3]	1,7 [-3,5; 6,9] 0,5170[3]
Andere	5/133 (3,8)	7/136 (5,1)	0,73 [0,24; 2,24] 0,5833[2]	0,72 [0,22; 2,33] 0,5815[3]	-1,4 [-6,3; 3,5] 0,5815[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3367)					
< 20 mm	13/141 (9,2)	6/140 (4,3)	2,15 [0,84; 5,50] 0,1097[2]	2,27 [0,84; 6,15] 0,0995[3]	4,9 [-0,9; 10,8] 0,0995[3]
≥ 20 bis < 50 mm	14/255 (5,5)	15/249 (6,0)	0,91 [0,45; 1,85] 0,7970[2]	0,91 [0,43; 1,92] 0,7969[3]	-0,5 [-4,6; 3,5] 0,7969[3]
≥ 50 mm	8/145 (5,5)	5/141 (3,5)	1,56 [0,52; 4,64] 0,4280[2]	1,59 [0,51; 4,98] 0,4237[3]	2,0 [-2,8; 6,8] 0,4237[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7948)					
0-3	17/203 (8,4)	11/214 (5,1)	1,63 [0,78; 3,39] 0,1923[2]	1,69 [0,77; 3,69] 0,1872[3]	3,2 [-1,6; 8,1] 0,1872[3]
4-9	13/242 (5,4)	11/231 (4,8)	1,13 [0,52; 2,47] 0,7627[2]	1,14 [0,50; 2,59] 0,7625[3]	0,6 [-3,3; 4,6] 0,7625[3]
≥ 10	7/108 (6,5)	4/90 (4,4)	1,46 [0,44; 4,82] 0,5364[2]	1,49 [0,42; 5,26] 0,5332[3]	2,0 [-4,3; 8,3] 0,5332[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,4540)					
IIA	7/59 (11,9)	3/62 (4,8)	2,45 [0,67; 9,04] 0,1779[2]	2,65 [0,65; 10,77] 0,1978[4]	7,0 [-2,8; 16,9] 0,1978[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	1/53 (1,9)	5/69 (7,2)	0,26 [0,03; 2,16] 0,2128[2]	0,25 [0,03; 2,17] 0,2317[4]	-5,4 [-12,5; 1,8] 0,2317[4]
IIIA	19/236 (8,1)	10/214 (4,7)	1,72 [0,82; 3,62] 0,1513[2]	1,79 [0,81; 3,93] 0,1450[3]	3,4 [-1,1; 7,9] 0,1450[3]
IIIB	1/18 (5,6)	1/15 (6,7)	0,83 [0,06; 12,22] 0,8942[2]	0,82 [0,05; 14,39] 1,0000[4]	-1,1 [-17,6; 15,4] 1,0000[4]
IIIC	9/186 (4,8)	7/174 (4,0)	1,20 [0,46; 3,16] 0,7079[2]	1,21 [0,44; 3,33] 0,7074[3]	0,8 [-3,4; 5,1] 0,7074[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,8940)					
G1	6/47 (12,8)	3/41 (7,3)	1,74 [0,47; 6,54] 0,4090[2]	1,85 [0,43; 7,94] 0,4942[4]	5,4 [-7,0; 17,9] 0,4942[4]
G2	14/244 (5,7)	12/234 (5,1)	1,12 [0,53; 2,37] 0,7691[2]	1,13 [0,51; 2,49] 0,7690[3]	0,6 [-3,5; 4,7] 0,7690[3]
G3	15/233 (6,4)	10/226 (4,4)	1,45 [0,67; 3,17] 0,3454[2]	1,49 [0,65; 3,38] 0,3421[3]	2,0 [-2,1; 6,2] 0,3421[3]
GX	2/29 (6,9)	1/33 (3,0)	2,28 [0,22; 23,82] 0,4924[2]	2,37 [0,20; 27,59] 0,5951[4]	3,9 [-7,1; 14,8] 0,5951[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9325)					
Negativ	4/49 (8,2)	0/44 (0,0)	8,10 [0,45; 146,31] 0,1565[2]	8,80 [0,46; 168,31] 0,1191[4]	8,2 [0,5; 15,8] 0,1191[4]
Positiv	32/477 (6,7)	23/471 (4,9)	1,37 [0,82; 2,31] 0,2317[2]	1,40 [0,81; 2,43] 0,2293[3]	1,8 [-1,1; 4,8] 0,2293[3]
Unbekannt	0/4 (0,0)	3/8 (37,5)	0,26 [0,02; 4,04] 0,3338[2]	0,17 [0,01; 4,35] 0,4909[4]	-37,5 [-71,0; -4,0] 0,4909[4]
Ethnizität (p-Wert des Interaktionsterms: 0,9941)					
Weiß	20/323 (6,2)	15/324 (4,6)	1,34 [0,70; 2,57] 0,3817[2]	1,36 [0,68; 2,71] 0,3797[3]	1,6 [-1,9; 5,0] 0,3797[3]
Asiatisch	14/199 (7,0)	10/180 (5,6)	1,27 [0,58; 2,78] 0,5560[2]	1,29 [0,56; 2,97] 0,5548[3]	1,5 [-3,4; 6,4] 0,5548[3]
Andere	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,1790)					
ECOG-PS 0	33/496 (6,7)	20/480 (4,2)	1,60 [0,93; 2,74] 0,0900[2]	1,64 [0,93; 2,90] 0,0866[3]	2,5 [-0,3; 5,3] 0,0866[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 1	4/57 (7,0)	6/55 (10,9)	0,64 [0,19; 2,16] 0,4747[2]	0,62 [0,16; 2,32] 0,5239[4]	-3,9 [-14,5; 6,7] 0,5239[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Tabelle: Subgruppen - Unerwünschtes Ereignis: Erkrankungen der Nieren und Harnwege (SOC) (jeglicher Schweregrad) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,8217)					
< 65 Jahre	63/918 (6,9)	47/937 (5,0)	1,37 [0,95; 1,97] 0,0938[2]	1,40 [0,95; 2,06] 0,0922[3]	1,8 [-0,3; 4,0] 0,0922[3]
≥ 65 Jahre	36/365 (9,9)	22/328 (6,7)	1,47 [0,88; 2,45] 0,1376[2]	1,52 [0,88; 2,65] 0,1342[3]	3,2 [-0,9; 7,2] 0,1342[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,3188)					
Neoadjuvante Chemotherapie	29/430 (6,7)	16/415 (3,9)	1,75 [0,96; 3,17] 0,0656[2]	1,80 [0,96; 3,37] 0,0615[3]	2,9 [-0,1; 5,9] 0,0615[3]
Adjuvante Chemotherapie	61/784 (7,8)	49/769 (6,4)	1,22 [0,85; 1,75] 0,2803[2]	1,24 [0,84; 1,83] 0,2793[3]	1,4 [-1,1; 4,0] 0,2793[3]
Keine Chemotherapie	9/69 (13,0)	4/81 (4,9)	2,64 [0,85; 8,20] 0,0930[2]	2,89 [0,85; 9,83] 0,0787[3]	8,1 [-1,1; 17,3] 0,0787[3]
Region (p-Wert des Interaktionsterms: 0,7167)					
Nordamerika / Europa	63/678 (9,3)	43/650 (6,6)	1,40 [0,97; 2,04] 0,0738[2]	1,45 [0,97; 2,17] 0,0720[3]	2,7 [-0,2; 5,6] 0,0720[3]
Asien	12/203 (5,9)	11/201 (5,5)	1,08 [0,49; 2,39] 0,8491[2]	1,09 [0,47; 2,52] 0,8491[3]	0,4 [-4,1; 5,0] 0,8491[3]
Andere	24/402 (6,0)	15/414 (3,6)	1,65 [0,88; 3,09] 0,1205[2]	1,69 [0,87; 3,27] 0,1161[3]	2,3 [-0,6; 5,3] 0,1161[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,1325)					
< 20 mm	29/331 (8,8)	15/335 (4,5)	1,96 [1,07; 3,58] 0,0295[2]	2,05 [1,08; 3,90] 0,0261[3]	4,3 [0,5; 8,0] 0,0261[3]
≥ 20 bis < 50 mm	46/646 (7,1)	44/653 (6,7)	1,06 [0,71; 1,57] 0,7860[2]	1,06 [0,69; 1,63] 0,7860[3]	0,4 [-2,4; 3,1] 0,7860[3]
≥ 50 mm	22/289 (7,6)	10/265 (3,8)	2,02 [0,97; 4,18] 0,0591[2]	2,10 [0,98; 4,52] 0,0530[3]	3,8 [0,0; 7,7] 0,0530[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,7713)					
0-3	31/427 (7,3)	25/418 (6,0)	1,21 [0,73; 2,02] 0,4558[2]	1,23 [0,71; 2,12] 0,4549[3]	1,3 [-2,1; 4,6] 0,4549[3]
4-9	45/549 (8,2)	29/542 (5,4)	1,53 [0,98; 2,41] 0,0640[2]	1,58 [0,97; 2,56] 0,0616[3]	2,8 [-0,1; 5,8] 0,0616[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	23/307 (7,5)	15/305 (4,9)	1,52 [0,81; 2,86] 0,1910[2]	1,57 [0,80; 3,06] 0,1871[3]	2,6 [-1,2; 6,4] 0,1871[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,3374)					
IIA	11/113 (9,7)	5/114 (4,4)	2,22 [0,80; 6,18] 0,1272[2]	2,35 [0,79; 7,00] 0,1155[3]	5,3 [-1,3; 12,0] 0,1155[3]
IIB	10/151 (6,6)	9/136 (6,6)	1,00 [0,42; 2,39] 0,9987[2]	1,00 [0,39; 2,54] 0,9987[3]	0,0 [-5,8; 5,8] 0,9987[3]
IIIA	38/495 (7,7)	25/488 (5,1)	1,50 [0,92; 2,44] 0,1050[2]	1,54 [0,91; 2,59] 0,1021[3]	2,6 [-0,5; 5,6] 0,1021[3]
IIIB	1/54 (1,9)	4/45 (8,9)	0,21 [0,02; 1,80] 0,1537[2]	0,19 [0,02; 1,80] 0,1738[4]	-7,0 [-16,1; 2,0] 0,1738[4]
IIIC	39/468 (8,3)	26/480 (5,4)	1,54 [0,95; 2,49] 0,0783[2]	1,59 [0,95; 2,65] 0,0756[3]	2,9 [-0,3; 6,1] 0,0756[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,9962)					
G1	6/91 (6,6)	4/93 (4,3)	1,53 [0,45; 5,25] 0,4966[2]	1,57 [0,43; 5,76] 0,5339[4]	2,3 [-4,3; 8,8] 0,5339[4]
G2	44/612 (7,2)	31/603 (5,1)	1,40 [0,90; 2,18] 0,1402[2]	1,43 [0,89; 2,30] 0,1379[3]	2,0 [-0,7; 4,7] 0,1379[3]
G3	47/527 (8,9)	32/506 (6,3)	1,41 [0,92; 2,17] 0,1191[2]	1,45 [0,91; 2,31] 0,1168[3]	2,6 [-0,6; 5,8] 0,1168[3]
GX	2/51 (3,9)	2/59 (3,4)	1,16 [0,17; 7,92] 0,8820[2]	1,16 [0,16; 8,57] 1,0000[4]	0,5 [-6,5; 7,6] 1,0000[4]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,7175)					
Tamoxifen	6/114 (5,3)	6/132 (4,5)	1,16 [0,38; 3,49] 0,7946[2]	1,17 [0,37; 3,72] 0,7944[3]	0,7 [-4,7; 6,1] 0,7944[3]
Aromatase-Inhibitor	93/1169 (8,0)	63/1133 (5,6)	1,43 [1,05; 1,95] 0,0232[2]	1,47 [1,05; 2,04] 0,0223[3]	2,4 [0,3; 4,4] 0,0223[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,4340)					
ECOG-PS 0	80/1070 (7,5)	57/1020 (5,6)	1,34 [0,96; 1,86] 0,0826[2]	1,37 [0,96; 1,94] 0,0812[3]	1,9 [-0,2; 4,0] 0,0812[3]
ECOG-PS 1	19/213 (8,9)	12/245 (4,9)	1,82 [0,91; 3,66] 0,0928[2]	1,90 [0,90; 4,02] 0,0874[3]	4,0 [-0,7; 8,7] 0,0874[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test. Abkürzungen: ARR: Absolute Risikoreduktion; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class					

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad ≥ 3: Erkrankungen der Nieren und Harnwege (SOC) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Region (p-Wert des Interaktionsterms: 0,2983)					
Nordamerika / Europa	10/678 (1,5)	1/650 (0,2)	9,59 [1,23; 74,68] 0,0309[2]	9,72 [1,24; 76,11] 0,0079[3]	1,3 [0,4; 2,3] 0,0079[3]
Asien	1/203 (0,5)	1/201 (0,5)	0,99 [0,06; 15,72] 0,9944[2]	0,99 [0,06; 15,94] 1,0000[4]	-0,0 [-1,4; 1,4] 1,0000[4]
Andere	1/402 (0,2)	1/414 (0,2)	1,03 [0,06; 16,41] 0,9834[2]	1,03 [0,06; 16,52] 1,0000[4]	0,0 [-0,7; 0,7] 1,0000[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9998)					
Negativ	0/156 (0,0)	0/169 (0,0)	NB	NB	NB
Positiv	12/1089 (1,1)	3/1067 (0,3)	3,92 [1,11; 13,85] 0,0339[2]	3,95 [1,11; 14,04] 0,0219[3]	0,8 [0,1; 1,5] 0,0219[3]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB
ECOG-PS (p-Wert des Interaktionsterms: 0,9722)					
ECOG-PS 0	8/1070 (0,7)	3/1020 (0,3)	2,54 [0,68; 9,56] 0,1673[2]	2,55 [0,68; 9,65] 0,1520[3]	0,5 [-0,2; 1,1] 0,1520[3]
ECOG-PS 1	4/213 (1,9)	0/245 (0,0)	10,35 [0,56; 191,06] 0,1163[2]	10,55 [0,56; 197,03] 0,0461[4]	1,9 [0,1; 3,7] 0,0461[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: Erkrankungen der Nieren und Harnwege (SOC) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Prämenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,9877)					
Neoadjuvante Chemotherapie	15/217 (6,9)	11/219 (5,0)	1,38 [0,65; 2,93] 0,4071[2]	1,40 [0,63; 3,13] 0,4048[3]	1,9 [-2,6; 6,3] 0,4048[3]
Adjuvante Chemotherapie	20/327 (6,1)	15/312 (4,8)	1,27 [0,66; 2,44] 0,4688[2]	1,29 [0,65; 2,57] 0,4674[3]	1,3 [-2,2; 4,8] 0,4674[3]
Keine Chemotherapie	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (p-Wert des Interaktionsterms: 0,4425)					
Nordamerika / Europa	19/252 (7,5)	10/233 (4,3)	1,76 [0,83; 3,70] 0,1381[2]	1,82 [0,83; 4,00] 0,1318[3]	3,2 [-0,9; 7,4] 0,1318[3]
Asien	12/168 (7,1)	9/166 (5,4)	1,32 [0,57; 3,04] 0,5186[2]	1,34 [0,55; 3,27] 0,5170[3]	1,7 [-3,5; 6,9] 0,5170[3]
Andere	5/133 (3,8)	7/136 (5,1)	0,73 [0,24; 2,24] 0,5833[2]	0,72 [0,22; 2,33] 0,5815[3]	-1,4 [-6,3; 3,5] 0,5815[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,3553)					
< 20 mm	13/141 (9,2)	6/140 (4,3)	2,15 [0,84; 5,50] 0,1097[2]	2,27 [0,84; 6,15] 0,0995[3]	4,9 [-0,9; 10,8] 0,0995[3]
≥ 20 bis < 50 mm	14/255 (5,5)	15/249 (6,0)	0,91 [0,45; 1,85] 0,7970[2]	0,91 [0,43; 1,92] 0,7969[3]	-0,5 [-4,6; 3,5] 0,7969[3]
≥ 50 mm	7/145 (4,8)	5/141 (3,5)	1,36 [0,44; 4,19] 0,5906[2]	1,38 [0,43; 4,45] 0,5889[3]	1,3 [-3,4; 5,9] 0,5889[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8475)					
0-3	16/203 (7,9)	11/214 (5,1)	1,53 [0,73; 3,22] 0,2597[2]	1,58 [0,71; 3,49] 0,2555[3]	2,7 [-2,0; 7,5] 0,2555[3]
4-9	13/242 (5,4)	11/231 (4,8)	1,13 [0,52; 2,47] 0,7627[2]	1,14 [0,50; 2,59] 0,7625[3]	0,6 [-3,3; 4,6] 0,7625[3]
≥ 10	7/108 (6,5)	4/90 (4,4)	1,46 [0,44; 4,82] 0,5364[2]	1,49 [0,42; 5,26] 0,5332[3]	2,0 [-4,3; 8,3] 0,5332[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,4733)					
IIA	7/59 (11,9)	3/62 (4,8)	2,45 [0,67; 9,04] 0,1779[2]	2,65 [0,65; 10,77] 0,1978[4]	7,0 [-2,8; 16,9] 0,1978[4]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
IIB	1/53 (1,9)	5/69 (7,2)	0,26 [0,03; 2,16] 0,2128[2]	0,25 [0,03; 2,17] 0,2317[4]	-5,4 [-12,5; 1,8] 0,2317[4]
IIIA	18/236 (7,6)	10/214 (4,7)	1,63 [0,77; 3,46] 0,2008[2]	1,68 [0,76; 3,73] 0,1951[3]	3,0 [-1,5; 7,4] 0,1951[3]
IIIB	1/18 (5,6)	1/15 (6,7)	0,83 [0,06; 12,22] 0,8942[2]	0,82 [0,05; 14,39] 1,0000[4]	-1,1 [-17,6; 15,4] 1,0000[4]
IIIC	9/186 (4,8)	7/174 (4,0)	1,20 [0,46; 3,16] 0,7079[2]	1,21 [0,44; 3,33] 0,7074[3]	0,8 [-3,4; 5,1] 0,7074[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,9033)					
G1	6/47 (12,8)	3/41 (7,3)	1,74 [0,47; 6,54] 0,4090[2]	1,85 [0,43; 7,94] 0,4942[4]	5,4 [-7,0; 17,9] 0,4942[4]
G2	14/244 (5,7)	12/234 (5,1)	1,12 [0,53; 2,37] 0,7691[2]	1,13 [0,51; 2,49] 0,7690[3]	0,6 [-3,5; 4,7] 0,7690[3]
G3	14/233 (6,0)	10/226 (4,4)	1,36 [0,62; 2,99] 0,4481[2]	1,38 [0,60; 3,18] 0,4460[3]	1,6 [-2,5; 5,6] 0,4460[3]
GX	2/29 (6,9)	1/33 (3,0)	2,28 [0,22; 23,82] 0,4924[2]	2,37 [0,20; 27,59] 0,5951[4]	3,9 [-7,1; 14,8] 0,5951[4]
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9325)					
Negativ	4/49 (8,2)	0/44 (0,0)	8,10 [0,45; 146,31] 0,1565[2]	8,80 [0,46; 168,31] 0,1191[4]	8,2 [0,5; 15,8] 0,1191[4]
Positiv	31/477 (6,5)	23/471 (4,9)	1,33 [0,79; 2,25] 0,2851[2]	1,35 [0,78; 2,36] 0,2832[3]	1,6 [-1,3; 4,6] 0,2832[3]
Unbekannt	0/4 (0,0)	3/8 (37,5)	0,26 [0,02; 4,04] 0,3338[2]	0,17 [0,01; 4,35] 0,4909[4]	-37,5 [-71,0; -4,0] 0,4909[4]
Ethnizität (p-Wert des Interaktionsterms: 0,9996)					
Weiß	19/323 (5,9)	15/324 (4,6)	1,27 [0,66; 2,46] 0,4764[2]	1,29 [0,64; 2,58] 0,4752[3]	1,3 [-2,2; 4,7] 0,4752[3]
Asiatisch	14/199 (7,0)	10/180 (5,6)	1,27 [0,58; 2,78] 0,5560[2]	1,29 [0,56; 2,97] 0,5548[3]	1,5 [-3,4; 6,4] 0,5548[3]
Andere	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (p-Wert des Interaktionsterms: 0,1946)					
ECOG-PS 0	32/496 (6,5)	20/480 (4,2)	1,55 [0,90; 2,67] 0,1155[2]	1,59 [0,89; 2,81] 0,1121[3]	2,3 [-0,5; 5,1] 0,1121[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 1	4/57 (7,0)	6/55 (10,9)	0,64 [0,19; 2,16] 0,4747[2]	0,62 [0,16; 2,32] 0,5239[4]	-3,9 [-14,5; 6,7] 0,5239[4]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Tabelle: Subgruppen - Unerwünschtes Ereignis CTCAE Grad < 3: Erkrankungen der Nieren und Harnwege (SOC) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Alter (p-Wert des Interaktionsterms: 0,7563)					
< 65 Jahre	61/918 (6,6)	46/937 (4,9)	1,35 [0,93; 1,96] 0,1105[2]	1,38 [0,93; 2,04] 0,1089[3]	1,7 [-0,4; 3,9] 0,1089[3]
≥ 65 Jahre	35/365 (9,6)	21/328 (6,4)	1,50 [0,89; 2,52] 0,1279[2]	1,55 [0,88; 2,72] 0,1243[3]	3,2 [-0,8; 7,2] 0,1243[3]
Vorherige Chemotherapie (p-Wert des Interaktionsterms: 0,3765)					
Neoadjuvante Chemotherapie	28/430 (6,5)	14/415 (3,4)	1,93 [1,03; 3,61] 0,0399[2]	2,00 [1,03; 3,85] 0,0359[3]	3,1 [0,2; 6,0] 0,0359[3]
Adjuvante Chemotherapie	61/784 (7,8)	49/769 (6,4)	1,22 [0,85; 1,75] 0,2803[2]	1,24 [0,84; 1,83] 0,2793[3]	1,4 [-1,1; 4,0] 0,2793[3]
Keine Chemotherapie	7/69 (10,1)	4/81 (4,9)	2,05 [0,63; 6,72] 0,2340[2]	2,17 [0,61; 7,76] 0,2228[3]	5,2 [-3,3; 13,8] 0,2228[3]
Region (p-Wert des Interaktionsterms: 0,6315)					
Nordamerika / Europa	60/678 (8,8)	42/650 (6,5)	1,37 [0,94; 2,00] 0,1042[2]	1,41 [0,93; 2,12] 0,1023[3]	2,4 [-0,5; 5,2] 0,1023[3]
Asien	12/203 (5,9)	11/201 (5,5)	1,08 [0,49; 2,39] 0,8491[2]	1,09 [0,47; 2,52] 0,8491[3]	0,4 [-4,1; 5,0] 0,8491[3]
Andere	24/402 (6,0)	14/414 (3,4)	1,77 [0,93; 3,36] 0,0840[2]	1,81 [0,92; 3,56] 0,0794[3]	2,6 [-0,3; 5,5] 0,0794[3]
Primärtumorgröße (p-Wert des Interaktionsterms: 0,0707)					
< 20 mm	29/331 (8,8)	14/335 (4,2)	2,10 [1,13; 3,90] 0,0192[2]	2,20 [1,14; 4,25] 0,0161[3]	4,6 [0,9; 8,3] 0,0161[3]
≥ 20 bis < 50 mm	44/646 (6,8)	44/653 (6,7)	1,01 [0,68; 1,51] 0,9582[2]	1,01 [0,66; 1,56] 0,9582[3]	0,1 [-2,7; 2,8] 0,9582[3]
≥ 50 mm	21/289 (7,3)	9/265 (3,4)	2,14 [1,00; 4,59] 0,0507[2]	2,23 [1,00; 4,96] 0,0444[3]	3,9 [0,2; 7,6] 0,0444[3]
Anzahl betr. Lymphknoten (p-Wert des Interaktionsterms: 0,8320)					
0-3	29/427 (6,8)	23/418 (5,5)	1,23 [0,73; 2,10] 0,4366[2]	1,25 [0,71; 2,20] 0,4356[3]	1,3 [-1,9; 4,5] 0,4356[3]
4-9	44/549 (8,0)	29/542 (5,4)	1,50 [0,95; 2,36] 0,0808[2]	1,54 [0,95; 2,50] 0,0783[3]	2,7 [-0,3; 5,6] 0,0783[3]

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
≥ 10	23/307 (7,5)	15/305 (4,9)	1,52 [0,81; 2,86] 0,1910[2]	1,57 [0,80; 3,06] 0,1871[3]	2,6 [-1,2; 6,4] 0,1871[3]
Tumorstadium (p-Wert des Interaktionsterms: 0,2331)					
IIA	11/113 (9,7)	4/114 (3,5)	2,77 [0,91; 8,46] 0,0727[2]	2,97 [0,92; 9,61] 0,0590[3]	6,2 [-0,2; 12,7] 0,0590[3]
IIB	9/151 (6,0)	9/136 (6,6)	0,90 [0,37; 2,20] 0,8187[2]	0,89 [0,34; 2,32] 0,8186[3]	-0,7 [-6,3; 5,0] 0,8186[3]
IIIA	38/495 (7,7)	24/488 (4,9)	1,56 [0,95; 2,56] 0,0782[2]	1,61 [0,95; 2,72] 0,0752[3]	2,8 [-0,3; 5,8] 0,0752[3]
IIIB	1/54 (1,9)	4/45 (8,9)	0,21 [0,02; 1,80] 0,1537[2]	0,19 [0,02; 1,80] 0,1738[4]	-7,0 [-16,1; 2,0] 0,1738[4]
IIIC	37/468 (7,9)	26/480 (5,4)	1,46 [0,90; 2,37] 0,1266[2]	1,50 [0,89; 2,52] 0,1239[3]	2,5 [-0,7; 5,7] 0,1239[3]
Tumorgrading (p-Wert des Interaktionsterms: 0,9961)					
G1	6/91 (6,6)	4/93 (4,3)	1,53 [0,45; 5,25] 0,4966[2]	1,57 [0,43; 5,76] 0,5339[4]	2,3 [-4,3; 8,8] 0,5339[4]
G2	43/612 (7,0)	30/603 (5,0)	1,41 [0,90; 2,22] 0,1349[2]	1,44 [0,89; 2,33] 0,1325[3]	2,1 [-0,6; 4,7] 0,1325[3]
G3	45/527 (8,5)	31/506 (6,1)	1,39 [0,90; 2,17] 0,1400[2]	1,43 [0,89; 2,30] 0,1376[3]	2,4 [-0,8; 5,6] 0,1376[3]
GX	2/51 (3,9)	2/59 (3,4)	1,16 [0,17; 7,92] 0,8820[2]	1,16 [0,16; 8,57] 1,0000[4]	0,5 [-6,5; 7,6] 1,0000[4]
Ethnizität (p-Wert des Interaktionsterms: 0,0610)					
Weiß	78/958 (8,1)	46/944 (4,9)	1,67 [1,17; 2,38] 0,0044[2]	1,73 [1,19; 2,52] 0,0039[3]	3,3 [1,1; 5,5] 0,0039[3]
Asiatisch	12/250 (4,8)	12/242 (5,0)	0,97 [0,44; 2,11] 0,9349[2]	0,97 [0,43; 2,20] 0,9349[3]	-0,2 [-4,0; 3,6] 0,9349[3]
Andere	4/62 (6,5)	9/64 (14,1)	0,46 [0,15; 1,41] 0,1746[2]	0,42 [0,12; 1,45] 0,1603[3]	-7,6 [-18,1; 2,9] 0,1603[3]
Endokrine Therapie zu Beginn (p-Wert des Interaktionsterms: 0,7185)					
Tamoxifen	6/114 (5,3)	6/132 (4,5)	1,16 [0,38; 3,49] 0,7946[2]	1,17 [0,37; 3,72] 0,7944[3]	0,7 [-4,7; 6,1] 0,7944[3]
Aromatase-Inhibitor	90/1169 (7,7)	61/1133 (5,4)	1,43 [1,04; 1,96] 0,0259[2]	1,47 [1,05; 2,05] 0,0249[3]	2,3 [0,3; 4,3] 0,0249[3]
ECOG-PS (p-Wert des Interaktionsterms: 0,4319)					

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
ECOG-PS 0	77/1070 (7,2)	55/1020 (5,4)	1,33 [0,95; 1,87] 0,0915[2]	1,36 [0,95; 1,94] 0,0901[3]	1,8 [-0,3; 3,9] 0,0901[3]
ECOG-PS 1	19/213 (8,9)	12/245 (4,9)	1,82 [0,91; 3,66] 0,0928[2]	1,90 [0,90; 4,02] 0,0874[3]	4,0 [-0,7; 8,7] 0,0874[3]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; KI: Konfidenzintervall; mm: Millimeter; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Tabelle: Subgruppen - Schwerwiegendes unerwünschtes Ereignis: Erkrankungen der Nieren und Harnwege (SOC) aus RCT mit dem zu bewertenden Arzneimittel - Cohort 1 Population - Safety - Postmenopausale Patientinnen

Subgruppe	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Progesteronrezeptorstatus (p-Wert des Interaktionsterms: 0,9655)					
Negativ	1/156 (0,6)	0/169 (0,0)	3,25 [0,13; 79,16] 0,4696[2]	3,27 [0,13; 80,87] 0,4800[4]	0,6 [-0,6; 1,9] 0,4800[4]
Positiv	7/1089 (0,6)	3/1067 (0,3)	2,29 [0,59; 8,82] 0,2299[2]	2,29 [0,59; 8,90] 0,3429[4]	0,4 [-0,2; 0,9] 0,3429[4]
Unbekannt	0/10 (0,0)	0/7 (0,0)	NB	NB	NB

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Anastrozol, Letrozol; Anastrozol oder Exemestan in Sequenz nach Tamoxifen; 2: p-Wert basierend auf Z-Test; 3: p-Wert basierend auf Chi^2-Test; 4: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NB: Nicht berechnet; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

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Anhang 4-G2.8.3: Häufige unerwünschte Ereignisse nach SOC und PT - Subgruppenanalysen

Tabelle 4-131 (Anhang): Ergebnis des Interaktionsterms der Subgruppenanalysen der häufigen unerwünschten Ereignisse für Studie MONARCH-E

Table: Interaction term results of the subgroup analysis for adverse events according SOC/PT - from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Endpoint	Subgroup										
	Age group	ECOG PS	First endocrine therapy	Number of positive lymph nodes	Prior chemo-therapy	Progesterone receptor status	Race	Region	Tumor grade	Primary tumor size	Tumor stage
Adverse events according PT - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											
Abdominal distension	NE	0,9798	NE	NE	0,9670	0,9940	0,9996	0,9993	NE	NE	0,8905
Abdominal pain	NE	0,8491	NE	0,5248	0,1382	0,9877	**0,0491**	0,0758	0,9130	0,6108	0,8128
Abdominal pain upper	NE	0,9658	NE	0,9630	0,7024	**<,0001**	0,0556	0,1970	0,8482	0,4292	0,4507
Alopecia	NE	0,1204	NE	0,3360	0,9783	0,9409	0,8096	0,6774	0,2373	0,5830	0,5322
Anaemia	NE	0,9768	NE	0,1655	0,6725	0,1446	0,7455	0,6095	0,2215	0,8752	**0,0253**
Arthralgia	NE	0,4672	NE	0,8910	0,5860	0,0955	0,1109	0,5813	0,3486	0,3539	0,9359
Aspartate aminotransferase increased	NE	0,9705	NE	0,6085	0,5018	0,0899	0,8432	0,3999	0,7241	0,7847	0,9155
Asthenia	NE	0,6844	NE	0,5155	0,6529	0,9854	0,9063	0,1989	0,3845	0,1353	0,8774
Blood creatinine increased	NE	0,9808	NE	0,9992	0,9442	0,9974	0,9770	0,9996	0,9999	0,9992	0,9997
Cellulitis	NE	0,4060	NE	NE	0,8326	0,9619	0,9371	0,9922	0,9991	0,9995	0,7159
Chills	NE	0,9804	NE	NE	NE	0,9997	NE	0,8881	NE	NE	NE
Constipation	NE	0,6189	NE	0,8683	0,9847	**<,0001**	**0,0423**	**0,0283**	0,0916	0,1682	0,8557
Cough	NE	**0,0027**	NE	0,4054	0,8481	**0,0009**	0,7781	0,4479	0,8980	0,3874	0,5701
Decreased appetite	NE	**0,0227**	NE	0,7979	0,4143	0,9562	0,8992	0,7978	0,5045	0,5204	0,3706
Diarrhoea	NE	**0,0282**	NE	0,9068	0,8118	0,4113	0,4635	0,0851	0,8698	0,1289	0,8542
Dry eye	NE	0,7213	NE	0,3971	0,4080	0,9971	0,5229	0,7523	0,6946	0,2160	0,9955
Dry mouth	NE	0,9804	NE	NE	0,8670	0,6071	0,9996	0,9992	NE	NE	NE
Dry skin	NE	0,4791	NE	0,4831	0,9551	0,9353	0,4927	0,8325	0,9782	0,9751	0,8025
Dysgeusia	NE	0,9831	NE	NE	NE	0,9563	NE	NE	NE	NE	NE
Dyspepsia	NE	0,7158	NE	0,9994	0,1235	0,9327	0,1464	0,1226	0,9368	0,7935	0,8547
Dyspnoea	NE	0,8060	NE	0,8810	0,7242	0,9957	0,7179	0,9246	0,2983	0,6947	0,7258
Eczema	NE	**<,0001**	NE	0,9846	0,4900	0,9432	0,9999	0,9997	0,6716	0,4567	NE

	Subgroup										
Endpoint	**Age group**	**ECOG PS**	**First endocrine therapy**	**Number of positive lymph nodes**	**Prior chemo-therapy**	**Progesterone receptor status**	**Race**	**Region**	**Tumor grade**	**Primary tumor size**	**Tumor stage**
Erythema	NE	0,9809	NE	NE	NE	0,9594	0,9350	0,9703	NE	NE	NE
Fatigue	NE	0,3975	NE	0,6169	0,1161	0,3299	0,5512	0,6015	0,4514	0,0947	**0,0300**
Gamma-glutamyltransferase increased	NE	**<,0001**	NE	NE	0,7009	0,9594	0,8554	NE	0,9914	0,5718	NE
Gastritis	NE	0,7965	NE	0,5688	0,7520	0,5473	0,9517	0,7870	0,9994	NE	0,9494
Haemorrhoids	NE	0,9798	NE	0,9855	0,9873	0,9412	0,4547	0,5303	0,9907	0,0878	0,8607
Hot flush	NE	0,4543	NE	0,2448	0,7851	0,2079	0,0947	0,2559	0,1877	0,1833	0,6900
Hypokalaemia	NE	0,9821	NE	NE	0,9883	0,9563	NE	NE	NE	NE	0,9998
Influenza like illness	NE	0,7007	NE	0,2439	0,5620	0,4900	0,9849	0,2956	0,9838	0,3921	0,5501
Lacrimation increased	NE	0,9842	NE	0,9993	0,9850	0,9580	0,9996	0,9996	1,0000	0,9771	0,9997
Leukopenia	NE	0,6313	NE	0,6316	0,7016	0,9562	0,3673	0,9902	0,9555	0,4019	1,0000
Lymphocyte count decreased	NE	0,8289	NE	0,7853	0,9402	0,3528	0,2334	**0,0446**	0,8879	0,8185	0,9848
Lymphoedema	NE	0,0894	NE	0,3014	0,6625	0,7095	0,9559	0,8660	0,3860	0,0787	0,5401
Lymphopenia	NE	0,9790	NE	0,9313	0,9611	0,9619	0,9714	0,6494	0,8725	0,9214	0,9811
Malaise	NE	0,1420	NE	0,9787	0,8598	0,9998	0,3227	0,1126	0,8506	0,6044	0,8795
Mucosal inflammation	NE	0,9724	NE	0,9617	NE	0,9594	0,9996	0,9993	NE	NE	NE
Nail disorder	NE	**<,0001**	NE	0,9776	0,9244	0,9997	0,9995	0,9993	NE	NE	NE
Nasopharyngitis	NE	0,4049	NE	0,9268	0,7639	0,5473	0,9972	0,3166	0,7605	0,5648	0,9323
Nausea	NE	0,3179	NE	0,4831	0,9482	0,8780	0,7545	0,4178	0,9358	0,1240	0,3359
Neutropenia	NE	0,2405	NE	0,9668	0,2858	**0,0242**	0,3029	0,6866	0,7779	0,4940	0,8437
Neutrophil count decreased	NE	0,9784	NE	0,2673	0,6707	0,5801	0,7787	0,8008	**0,0390**	0,5636	0,8927
Oedema	NE	0,9811	NE	NE	NE	0,9997	NE	NE	NE	NE	NE
Oedema peripheral	NE	0,2917	NE	0,1243	0,9319	0,1759	0,8403	0,5001	0,9690	0,4774	0,2749
Onychoclasis	NE	0,9753	NE	NE	0,9976	0,9940	0,9996	0,3770	0,4976	NE	NE
Platelet count decreased	NE	0,4583	NE	0,6807	0,9456	0,9980	0,8096	0,2752	0,9725	0,1075	0,9906
Pruritus	NE	0,8851	NE	0,8148	0,5778	0,9155	0,9956	0,7526	0,6828	0,7703	0,6290
Pyrexia	NE	0,0951	NE	0,3926	0,5748	0,9994	0,9003	0,8856	0,4590	0,5263	0,3413

Endpoint	Subgroup										
	Age group	**ECOG PS**	**First endocrine therapy**	**Number of positive lymph nodes**	**Prior chemo-therapy**	**Progesterone receptor status**	**Race**	**Region**	**Tumor grade**	**Primary tumor size**	**Tumor stage**
Rash	NE	0,8251	NE	0,8516	0,9934	0,7298	0,4729	0,1369	0,9804	0,0810	0,6844
Rectal haemorrhage	NE	0,1878	NE	NE	0,9923	0,9594	0,9948	0,2096	NE	NE	NE
Sinusitis	NE	0,9802	NE	0,8854	0,9868	0,9801	0,9996	0,9992	0,4869	0,6085	0,5066
Stomatitis	NE	0,9784	NE	0,8027	0,9990	0,9555	0,4480	0,5940	0,9300	0,5018	0,4156
Thrombocytopenia	NE	0,8846	NE	0,8715	0,8467	0,9619	0,9893	0,7644	0,6785	0,4543	NE
Urinary tract infection	NE	0,0935	NE	0,5575	0,9612	0,9397	0,6285	0,2984	0,9959	0,7343	0,3954
Vaginal discharge	NE	0,9786	NE	0,8479	0,9239	0,9997	0,6845	0,5853	0,9605	0,8961	0,9910
Vomiting	NE	0,8083	NE	**0,0287**	0,1272	0,8165	0,9929	0,8501	0,9784	0,1516	0,4620
White blood cell count decreased	NE	0,1001	NE	0,4429	0,4586	0,0627	0,5899	0,7872	0,2374	0,5552	0,5575
Adverse events according SOC - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											
Blood and lymphatic system disorders	NE	0,9174	NE	0,2441	0,8420	**0,0045**	0,4109	0,1738	0,5726	0,3519	0,1017
Endocrine disorders	NE	0,9751	NE	0,3656	0,8061	0,5333	0,9647	0,2235	**<,0001**	0,9196	0,3145
Eye disorders	NE	0,7157	NE	0,8203	0,8043	0,9177	0,8332	0,6762	0,5998	0,4691	0,9390
Gastrointestinal disorders	NE	0,9278	NE	0,9970	0,3349	0,3404	0,8771	0,3671	0,3314	0,1652	NE
General disorders and administration site conditions	NE	**0,0278**	NE	0,3084	0,0592	0,0511	0,7128	0,8582	0,1889	0,2312	0,5465
Hepatobiliary disorders	NE	0,8106	NE	0,4629	0,9958	0,7513	0,9793	0,5573	0,3642	0,5113	0,6950
Infections and infestations	NE	**0,0139**	NE	0,8869	0,2874	**0,0462**	0,9035	0,8912	0,2818	0,4491	0,5545
Investigations	NE	0,3031	NE	0,3526	0,8707	0,5200	0,7612	**0,0332**	0,7902	0,8962	0,9113
Metabolism and nutrition disorders	NE	0,6748	NE	0,1337	0,0769	0,9507	0,2510	0,2885	0,8342	0,8120	0,2322
Nervous system disorders	NE	**0,0323**	NE	0,2698	0,0949	0,4907	**0,0255**	**0,0246**	0,7272	0,1426	0,5172
Respiratory, thoracic and mediastinal disorders	NE	**0,0103**	NE	0,3293	0,7341	0,9988	0,7851	0,3830	0,5464	0,8109	0,5088
Skin and subcutaneous tissue disorders	NE	0,6750	NE	0,9321	0,6052	0,7396	0,3934	0,8553	0,7140	0,3600	0,8156

Endpoint	Subgroup										
	Age group	ECOG PS	First endocrine therapy	Number of positive lymph nodes	Prior chemo-therapy	Progesterone receptor status	Race	Region	Tumor grade	Primary tumor size	Tumor stage
Adverse events with CTCAE Grade ≥ 3 according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											
Alanine aminotransferase increased	NE	0,9725	NE	NE	NE	0,9563	NE	NE	NE	NE	NE
Aspartate aminotransferase increased	NE	**<,0001**	NE	NE	NE	NE	NE	NE	NE	NE	NE
Diarrhoea	NE	**<,0001**	NE	0,9318	0,9380	0,9940	0,5692	0,7188	0,2012	0,9829	0,9038
Leukopenia	NE	**<,0001**	NE	NE	NE	0,9933	0,9998	**<,0001**	NE	NE	NE
Lymphocyte count decreased	NE	**<,0001**	NE	**<,0001**	0,9959	0,9933	**<,0001**	**<,0001**	1,0000	NE	0,9999
Neutropenia	NE	0,1163	NE	0,5028	0,8872	0,2850	0,3055	0,6076	0,9163	0,1417	0,9836
Neutrophil count decreased	NE	0,9801	NE	0,6515	0,2748	0,1534	0,9121	0,7296	0,7170	0,3257	0,9494
White blood cell count decreased	NE	0,4508	NE	0,9814	0,8768	0,9594	0,9590	0,9973	0,8083	0,3551	0,7443
Adverse events with CTCAE Grade ≥ 3 according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											
Blood and lymphatic system disorders	NE	0,2068	NE	0,9861	0,9971	0,1369	0,7498	0,6315	0,9994	0,3662	0,8954
Gastrointestinal disorders	NE	0,9824	NE	0,8679	0,9363	0,9974	0,2390	0,9347	0,0954	0,5923	0,6143
Investigations	NE	0,1475	NE	0,1489	0,1827	**0,0444**	0,7848	0,9734	0,8831	0,2803	0,5558

Data cut-off: 01.04.2021
The table shows p-values of the interaction term of subgroup factor and treatment group from logistic regression model: event = treatment, subgroup, treatment*subgroup. Only endpoints with z-test p-value < 0.05 for relative risk in the main analysis are included.
NE: not evaluable/not calculated. If fewer than 10 patients with an event occur in a subgroup category, an interaction test is not performed.
Abbreviations: CTCAE: common terminology criteria for adverse events; PT: preferred term; SOC: system organ class

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Table: Interaction term results of the subgroup analysis for adverse events according SOC/PT - from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Endpoint	Subgroup										
	Age group	ECOG PS	First endocrine therapy	Number of positive lymph nodes	Prior chemo-therapy	Progesterone receptor status	Race	Region	Tumor grade	Primary tumor size	Tumor stage
Adverse events according PT - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											
Abdominal discomfort	0,4101	0,1764	0,8962	NE	**<,0001**	0,3409	0,9775	0,9969	**<,0001**	0,1589	0,8927
Abdominal distension	0,7056	0,4519	0,6692	0,0841	0,8295	0,0923	0,5197	0,7559	0,1696	0,5660	0,4242
Abdominal pain	0,4775	0,9243	0,2404	0,5987	0,8985	**<,0001**	0,9326	0,5579	0,8687	0,1821	0,7154
Abdominal pain upper	0,8348	0,7607	0,1812	0,4068	0,2252	0,9897	0,9724	0,0798	0,9479	0,7465	0,3332
Alanine aminotransferase increased	0,9613	0,5029	0,8311	0,3330	0,4526	0,6561	0,4562	0,7377	0,1844	0,6663	0,2640
Alopecia	0,1687	0,4488	**<,0001**	0,0807	0,3063	**<,0001**	0,3910	0,2818	0,6432	0,1434	0,5863
Anaemia	0,7805	0,2908	0,2710	0,4475	0,9879	**<,0001**	0,5404	0,4307	0,4531	0,5305	0,2523
Anxiety	**0,0263**	0,2279	0,2712	0,1826	0,3875	**<,0001**	0,4117	0,8946	**<,0001**	0,9615	0,5776
Arthralgia	0,8378	0,8189	0,2251	0,2518	0,6036	0,5287	0,8957	0,6246	0,3115	0,9627	0,7009
Aspartate aminotransferase increased	0,4422	0,5767	0,9366	0,3742	0,2142	0,5847	0,5585	0,2779	0,3003	0,7758	0,9862
Asthenia	0,6560	0,9292	0,8285	0,7790	0,3679	**<,0001**	0,7165	0,6671	0,7545	0,4653	0,8844
Back pain	0,3744	0,2712	0,9621	0,0759	0,5424	0,7751	0,8277	0,5280	0,4754	0,9178	0,1132
Blood alkaline phosphatase increased	0,6780	**0,0215**	0,4349	0,5525	0,8456	0,1109	0,6760	0,4545	0,2890	0,4252	0,9768
Blood creatinine increased	0,6228	0,9820	**<,0001**	0,7590	0,5189	**<,0001**	0,5195	0,2558	0,9980	0,5337	0,4006
COVID-19	0,6590	0,9713	0,9043	0,5870	**<,0001**	0,3329	0,9997	0,4042	0,1709	0,8550	0,9999
Cataract	0,9722	0,5707	0,0973	0,4346	0,3553	**<,0001**	0,5949	0,4461	0,1052	0,6176	0,7025
Constipation	**0,0028**	0,2201	0,3238	0,1021	0,2479	**<,0001**	0,4480	0,9983	0,7654	0,0950	0,3606
Cough	0,7150	**0,0212**	0,6757	0,8212	0,2592	**<,0001**	0,7773	0,5782	0,7189	0,3757	0,2321
Decreased appetite	0,1201	0,4689	0,7194	0,2485	0,7552	**<,0001**	0,1277	0,5603	0,7199	0,1662	**0,0253**
Deep vein thrombosis	**<,0001**	0,2788	**<,0001**	NE	0,9414	0,9633	0,2489	0,9082	0,1851	0,9557	0,9876

	Subgroup										
Endpoint	**Age group**	**ECOG PS**	**First endocrine therapy**	**Number of positive lymph nodes**	**Prior chemo-therapy**	**Progesterone receptor status**	**Race**	**Region**	**Tumor grade**	**Primary tumor size**	**Tumor stage**
Dehydration	**<,0001**	0,9744	**<,0001**	0,8228	0,8265	0,2718	0,9997	0,9107	0,8956	0,4459	0,9797
Dermatitis	0,8656	0,2503	0,1876	0,5961	0,8056	0,9998	0,5724	0,2454	0,7866	0,3117	0,9001
Diarrhoea	**0,0005**	0,5859	0,4084	0,8134	0,7383	**<,0001**	0,0559	**0,0042**	0,4291	0,5685	0,5363
Dizziness	0,6982	0,8928	0,3393	0,6027	0,3818	**0,0068**	0,8703	0,6374	0,9316	0,3180	0,7475
Dry eye	0,5416	**0,0477**	0,6239	0,5065	0,9903	0,2708	0,9645	0,6950	0,4793	0,8818	0,5145
Dry mouth	0,3571	0,4836	0,6272	0,3501	0,7135	0,9617	0,5650	0,4059	0,3477	0,1323	0,7485
Dry skin	0,5096	0,3671	0,6427	**0,0379**	0,7986	0,1223	0,5616	0,4602	0,2911	0,4309	0,1576
Dysgeusia	0,4205	0,9734	**0,0159**	0,4673	0,9678	0,9978	0,7622	0,8841	0,9943	0,8644	1,0000
Dyspepsia	**0,0126**	0,2615	0,5134	0,9577	0,1107	**<,0001**	**0,0175**	**0,0198**	0,8732	0,1472	0,8584
Dyspnoea	0,7226	0,6578	0,5208	0,5236	0,6254	**<,0001**	0,2524	0,0884	0,5210	0,2347	0,7923
Epistaxis	**<,0001**	0,9729	**<,0001**	0,6671	0,9889	0,2732	0,3165	0,3978	0,6201	0,9937	NE
Fatigue	0,5699	0,1324	0,2998	0,9661	0,3293	0,6413	0,3825	0,1480	0,9718	0,5116	0,1648
Flatulence	0,1023	0,3879	0,9142	0,1580	0,7405	0,9644	0,9996	0,9925	0,6636	0,7549	0,5290
Gamma-glutamyltransferase increased	0,9341	0,8163	**<,0001**	0,7644	0,7491	0,9971	0,9865	0,6060	0,7561	0,9625	0,7794
Gastrointestinal pain	**<,0001**	**<,0001**	**<,0001**	NE	**<,0001**	0,9699	1,0000	NE	NE	**<,0001**	NE
Gastrooesophageal reflux disease	0,3983	0,4624	0,8107	0,1006	0,3354	0,9086	0,8672	0,1226	0,6776	0,3282	0,4008
Haemorrhoids	0,5596	0,2066	**<,0001**	0,5855	0,9169	0,2672	0,8087	0,7326	0,6993	0,5100	0,8784
Headache	0,2661	0,6451	0,9465	0,8346	0,9698	**<,0001**	0,9915	0,6320	0,2567	0,5729	0,9185
Hot flush	0,3646	0,9781	0,2847	0,7879	0,2670	**<,0001**	0,6711	0,2477	0,7045	0,8597	0,6090
Hypokalaemia	0,8384	0,9570	0,7323	0,9112	0,6420	0,1698	0,8956	0,9637	0,8408	0,8428	0,2335
Hyponatraemia	**<,0001**	0,2067	**<,0001**	0,3719	0,3720	0,9644	0,6303	0,9048	0,4813	0,6007	0,4081
Hypotension	0,9063	0,4539	0,7695	0,9576	0,9365	0,2224	0,9909	0,2009	0,3621	0,5031	0,8994
Joint stiffness	0,6952	0,9915	0,1280	0,1750	0,9989	0,6179	0,7789	0,2017	0,6173	0,3220	0,8119
Lacrimation increased	0,1329	0,9048	0,6601	0,9973	0,6993	0,9587	0,9997	0,9706	0,3816	0,7061	0,7214
Leukopenia	0,6569	0,1962	**<,0001**	0,8811	0,9362	0,3113	0,8110	0,2306	0,6185	0,5714	0,9605

Endpoint	Subgroup										
	Age group	ECOG PS	First endocrine therapy	Number of positive lymph nodes	Prior chemo-therapy	Progesterone receptor status	Race	Region	Tumor grade	Primary tumor size	Tumor stage
Lymphocyte count decreased	0,7497	0,0962	0,1327	0,9597	0,9516	**<,0001**	0,9068	0,6806	0,4692	0,8490	0,8842
Lymphoedema	0,1911	0,8379	**0,0049**	0,2562	0,4143	**<,0001**	0,2852	0,1143	0,3179	0,4732	0,5239
Lymphopenia	0,4393	0,3230	**<,0001**	0,6951	0,0877	**<,0001**	0,9599	0,9887	0,9978	0,8140	0,7160
Malaise	0,5649	0,8139	0,3664	0,7563	0,8834	0,9617	0,7589	0,6898	0,6842	0,4421	0,9387
Mucosal inflammation	0,6623	0,8942	**<,0001**	0,8516	0,2715	0,1007	0,9883	0,9722	0,8846	0,3821	0,9885
Muscle spasms	0,1602	0,1489	0,2670	0,8654	0,9956	**<,0001**	0,5606	0,8144	0,7573	0,1377	0,1162
Nail disorder	**<,0001**	0,0957	**<,0001**	0,9643	0,9813	0,9634	0,9993	0,4542	0,9999	0,9210	0,5712
Nausea	0,8363	0,2930	0,5206	0,0789	0,4923	0,9310	0,4204	0,2860	0,1426	0,9731	0,2689
Neutropenia	0,4891	0,2859	0,4820	0,7528	0,9880	**<,0001**	0,3960	**0,0081**	0,1753	0,9199	0,6048
Neutrophil count decreased	0,1769	0,8172	0,1084	0,5321	0,3434	**<,0001**	0,7209	0,5243	0,2095	0,1695	0,8583
Oedema peripheral	0,6710	0,6512	0,7681	0,9450	0,5552	**<,0001**	0,8260	0,7172	0,5440	0,5834	0,7053
Onychoclasis	0,6190	0,3196	0,3153	0,8058	0,9941	0,9644	0,9853	0,9780	0,9991	0,8909	0,9556
Oral herpes	0,6291	0,9331	0,5297	0,6521	0,9995	0,9624	0,9576	**<,0001**	**<,0001**	0,7506	NE
Oropharyngeal pain	0,1609	0,2456	**<,0001**	0,5920	0,6185	0,1352	0,5494	0,2567	0,9304	0,8828	0,9953
Osteoporosis	0,5273	0,3258	0,9512	0,4533	0,8709	0,2959	0,9976	0,6236	0,5696	0,6596	0,2917
Palpitations	0,3716	0,9592	**<,0001**	0,9506	0,7696	0,6594	0,4467	0,5773	0,9992	0,6042	0,9421
Paronychia	0,8273	0,9731	**<,0001**	NE	0,9667	0,5742	0,9735	0,9933	NE	NE	NE
Platelet count decreased	0,8800	0,6406	0,4626	0,4736	0,9964	**<,0001**	0,2783	0,1250	0,5950	0,1521	0,4729
Pneumonitis	**<,0001**	**<,0001**	**<,0001**	NE	0,7206	0,3906	0,7754	0,7872	0,9956	0,5329	NE
Pruritus	0,6434	**0,0111**	0,5912	0,4927	0,1008	**<,0001**	0,0513	0,2287	0,2640	0,1486	0,2233
Pyrexia	0,9528	0,1677	0,5072	0,0873	0,6865	**<,0001**	0,8847	0,7952	0,3366	0,3841	0,0737
Rash	0,5596	0,5844	0,9424	0,5879	0,1762	0,2676	0,6837	0,8358	0,7125	0,3994	0,8983
Rash maculo-papular	**<,0001**	0,9393	**<,0001**	0,9624	0,8911	0,9645	0,9997	0,9994	0,9858	0,8964	0,8611
Seroma	0,6291	0,7046	**<,0001**	NE	0,3491	**<,0001**	0,9909	0,7171	**0,0010**	NE	0,7481
Stomatitis	0,6398	0,4494	0,3273	0,2777	0,7122	0,9385	0,8247	0,9298	0,5414	0,3252	0,9979
Taste disorder	0,7790	0,5158	0,2947	0,8195	0,9719	0,2089	0,9867	0,9756	0,5164	0,9210	1,0000
Thrombocytopenia	0,1114	0,4661	**<,0001**	0,3433	0,9420	0,5670	0,1625	0,5748	0,9985	0,6587	0,9665

Endpoint	Subgroup										
	Age group	**ECOG PS**	**First endocrine therapy**	**Number of positive lymph nodes**	**Prior chemo-therapy**	**Progesterone receptor status**	**Race**	**Region**	**Tumor grade**	**Primary tumor size**	**Tumor stage**
Urinary tract infection	0,8305	0,5396	0,1254	0,8497	0,1169	**<,0001**	0,7814	0,6684	0,7026	0,9052	0,6657
Viral infection	0,2124	0,9757	**<,0001**	NE	0,9831	0,9634	0,9853	0,9779	0,5758	NE	NE
Vision blurred	0,1757	0,7858	0,9962	0,9363	0,7750	0,2114	0,9531	0,5694	0,7477	0,2515	0,5698
Vitamin B12 deficiency	0,0712	0,8913	**<,0001**	NE	**<,0001**	0,5736	0,9844	0,5269	0,8821	0,8845	1,0000
Vomiting	0,5712	0,0929	0,3704	**0,0194**	0,9722	**<,0001**	0,3578	0,0774	0,7829	0,7189	0,0560
Weight decreased	0,9699	0,5729	0,7136	0,9276	0,6748	0,8297	0,6838	0,8340	0,3963	0,2082	0,8894
White blood cell count decreased	0,2645	0,3787	0,3940	0,9900	0,6387	**<,0001**	0,7497	0,7683	0,7645	0,6750	0,6965
Adverse events according SOC - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											
Blood and lymphatic system disorders	0,1441	0,2584	**0,0170**	0,6660	0,9719	**0,0474**	**0,0398**	**0,0041**	0,5781	0,6928	0,4628
Cardiac disorders	0,6036	0,6612	0,2000	**0,0194**	0,9337	0,0548	0,3400	0,6679	0,8844	0,0856	0,7704
Eye disorders	0,8501	0,3495	0,3008	0,7961	0,6986	**<,0001**	0,2669	0,2854	0,3885	0,6996	0,4508
Gastrointestinal disorders	0,0813	0,1328	0,8958	0,3183	0,6865	0,5174	0,1825	**0,0011**	0,0652	0,0667	0,1063
General disorders and administration site conditions	0,8971	0,8743	0,3668	0,6074	0,6830	0,6939	0,6870	**0,0361**	0,0849	0,8944	0,4042
Infections and infestations	0,3729	0,6788	0,9764	0,9843	0,4327	0,6511	0,0990	0,0832	0,7092	0,2290	0,8578
Investigations	0,2239	0,4161	0,3096	0,2999	0,8181	0,8237	0,1113	**0,0368**	0,9526	0,4580	0,4600
Metabolism and nutrition disorders	0,4166	0,9135	0,3232	0,2235	0,4378	0,8137	0,2756	**0,0054**	0,2085	**0,0345**	0,1890
Musculoskeletal and connective tissue disorders	0,0795	0,8779	0,2030	0,1501	0,9046	0,5538	0,8598	0,9094	0,4852	0,8529	0,2938
Nervous system disorders	0,4778	0,3231	0,3437	0,9121	0,3863	0,2257	0,9466	0,3340	0,1438	0,7760	0,8015
Renal and urinary disorders	0,8217	0,4340	0,7175	0,7713	0,3188	**0,0001**	**0,0348**	0,7167	0,9962	0,1325	0,3374
Reproductive system and breast disorders	0,2682	0,2184	0,8616	0,8417	0,9435	0,3366	0,6838	0,8749	0,2693	0,9378	0,6333
Respiratory, thoracic and mediastinal disorders	0,3445	0,0500	0,5055	0,6749	0,6611	**<,0001**	0,8144	0,7407	0,4042	0,9353	0,7141

Endpoint	Subgroup										
	Age group	ECOG PS	First endocrine therapy	Number of positive lymph nodes	Prior chemo-therapy	Progesterone receptor status	Race	Region	Tumor grade	Primary tumor size	Tumor stage
Skin and subcutaneous tissue disorders	0,0788	0,4863	0,5269	0,7840	0,1090	0,4762	0,1023	**0,0149**	0,2329	0,7933	0,9836
Serious adverse events according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											
Gastrointestinal disorders	**0,0457**	0,1449	**<,0001**	0,2714	0,9576	**<,0001**	0,8628	0,5645	0,2748	0,9402	0,9730
Infections and infestations	0,4685	0,6051	**<,0001**	0,8691	0,1971	**0,0119**	0,7666	0,1281	**0,0362**	**0,0286**	0,1905
Vascular disorders	0,7527	0,4071	0,5759	NE	0,7223	0,5572	0,9997	0,9319	0,8553	0,3049	0,7369
Adverse events with CTCAE Grade ≥ 3 according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											
Alanine aminotransferase increased	0,5420	0,9736	**<,0001**	0,6165	0,2629	0,4403	0,6527	0,7023	0,9346	0,9677	0,9397
Anaemia	0,7391	0,9709	**<,0001**	0,6517	0,8958	0,6514	0,9997	0,6800	0,9559	0,9159	0,9915
Aspartate aminotransferase increased	0,8660	0,6687	**<,0001**	0,7711	0,2497	0,3666	0,1049	0,8121	0,7857	0,9031	0,9710
Diarrhoea	0,6734	0,9752	**<,0001**	0,9946	0,9540	**<,0001**	0,9998	0,9994	**<,0001**	0,7882	0,9968
Fatigue	0,9301	0,9742	**<,0001**	0,9979	0,8086	0,9606	0,9864	0,9995	1,0000	0,9993	0,9981
Gamma-glutamyltransferase increased	**<,0001**	0,8802	**<,0001**	0,2469	0,8567	0,9644	0,9285	0,9490	0,8954	0,0941	NE
Hypokalaemia	0,9572	0,9780	**<,0001**	0,3597	0,6716	0,9576	0,9882	0,5783	0,9069	0,9874	0,8990
Leukopenia	0,5851	0,5427	**<,0001**	0,9830	0,9717	0,9595	0,9997	0,9992	0,9991	0,9996	0,9999
Lymphocyte count decreased	0,9109	0,9727	**<,0001**	0,8190	0,8981	**<,0001**	0,6885	0,5944	0,9020	0,9875	0,9166
Lymphopenia	**<,0001**	**<,0001**	**<,0001**	0,9992	0,9355	0,9994	0,9998	0,9994	0,9999	0,9990	1,0000
Neutropenia	0,8935	0,9073	**<,0001**	0,9079	0,8443	0,9274	0,9997	0,9781	**<,0001**	0,9260	0,5961
Neutrophil count decreased	0,1737	0,9753	**<,0001**	0,9644	0,9600	0,9965	0,8953	0,9563	0,8649	0,4542	0,9974
Platelet count decreased	NE	**<,0001**	**<,0001**	NE	NE	0,9724	NE	NE	NE	NE	NE
White blood cell count decreased	0,1282	0,9748	**<,0001**	0,5108	0,9438	0,9999	0,8718	0,9734	0,6983	0,9636	1,0000
Adverse events with CTCAE Grade ≥ 3 according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm											

Endpoint	Subgroup										
	Age group	**ECOG PS**	**First endocrine therapy**	**Number of positive lymph nodes**	**Prior chemo-therapy**	**Progesterone receptor status**	**Race**	**Region**	**Tumor grade**	**Primary tumor size**	**Tumor stage**
Blood and lymphatic system disorders	0,5066	0,8503	**<,0001**	0,4720	0,8030	0,7451	0,9505	0,9090	**<,0001**	0,2477	0,9467
Gastrointestinal disorders	0,2058	0,7578	**<,0001**	0,4932	0,7029	**<,0001**	0,9913	0,3038	0,2055	0,8657	0,8896
General disorders and administration site conditions	0,7471	0,2387	0,4912	0,6983	0,4961	**0,0442**	0,9844	0,4844	0,9168	0,6858	0,4385
Infections and infestations	0,5500	0,7656	**<,0001**	0,8242	0,2967	**0,0371**	0,6629	0,1715	0,1246	0,0751	0,6341
Investigations	0,1773	0,9379	0,8074	0,0897	0,3053	**<,0001**	0,5921	0,3436	0,6727	0,8394	0,7337
Metabolism and nutrition disorders	0,7852	0,2656	0,8024	0,6392	0,2503	0,0916	0,2878	0,3325	0,6269	0,3553	0,3366
Respiratory, thoracic and mediastinal disorders	0,2635	0,1224	**<,0001**	0,8880	0,8206	0,4887	0,6138	0,7592	0,8373	0,4954	0,9138

Data cut-off: 01.04.2021
The table shows p-values of the interaction term of subgroup factor and treatment group from logistic regression model: event = treatment, subgroup, treatment*subgroup. Only endpoints with z-test p-value < 0.05 for relative risk in the main analysis are included.
NE: not evaluable/not calculated. If fewer than 10 patients with an event occur in a subgroup category, an interaction test is not performed.
Abbreviations: CTCAE: common terminology criteria for adverse events; PT: preferred term; SOC: system organ class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_interact_bp_aesocpt.sas
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Tabelle 4-132 (Anhang): Häufige unerwünschte Ereignisse nach SOC und PT - interagierende Subgruppen (prämenopausale Patientinnen)

Table: Interacting subgroups - adverse events according PT Abdominal pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Race (Interaction p-value: 0,0491)					
White	89/323 (27,6)	22/324 (6,8)	4,06 [2,61; 6,30] <,0001[2]	5,22 [3,18; 8,58] <,0001[3]	20,8 [15,2; 26,4] <,0001[3]
Asian	39/199 (19,6)	1/180 (0,6)	35,28 [4,90; 254,14] 0,0004[2]	43,63 [5,93; 321,22] <,0001[3]	19,0 [13,4; 24,7] <,0001[3]
Other	5/19 (26,3)	3/21 (14,3)	1,84 [0,51; 6,69] 0,3532[2]	2,14 [0,44; 10,54] 0,4420[4]	12,0 [-12,8; 36,9] 0,4420[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Abdominal pain upper from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	11/49 (22,4)	1/44 (2,3)	9,88 [1,33; 73,44] 0,0253[2]	12,45 [1,53; 100,95] 0,0038[3]	20,2 [7,7; 32,7] 0,0038[3]
Positive	56/477 (11,7)	21/471 (4,5)	2,63 [1,62; 4,28] <,0001[2]	2,85 [1,70; 4,79] <,0001[3]	7,3 [3,8; 10,7] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Anaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,0253)					
IIA	7/59 (11,9)	3/62 (4,8)	2,45 [0,67; 9,04] 0,1779[2]	2,65 [0,65; 10,77] 0,1978[4]	7,0 [-2,8; 16,9] 0,1978[4]
IIB	7/53 (13,2)	8/69 (11,6)	1,14 [0,44; 2,94] 0,7879[2]	1,16 [0,39; 3,43] 0,7879[3]	1,6 [-10,2; 13,5] 0,7879[3]
IIIA	42/236 (17,8)	9/214 (4,2)	4,23 [2,11; 8,49] <,0001[2]	4,93 [2,34; 10,40] <,0001[3]	13,6 [8,0; 19,2] <,0001[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	43/186 (23,1)	3/174 (1,7)	13,41 [4,24; 42,43] <,0001[2]	17,14 [5,21; 56,41] <,0001[3]	21,4 [15,0; 27,8] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Constipation from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0283)					
North America / Europe	49/252 (19,4)	20/233 (8,6)	2,27 [1,39; 3,69] 0,0010[2]	2,57 [1,48; 4,48] 0,0006[3]	10,9 [4,8; 16,9] 0,0006[3]
Asia	15/168 (8,9)	18/166 (10,8)	0,82 [0,43; 1,58] 0,5584[2]	0,81 [0,39; 1,66] 0,5576[3]	-1,9 [-8,3; 4,5] 0,5576[3]
Other	14/133 (10,5)	5/136 (3,7)	2,86 [1,06; 7,73] 0,0378[2]	3,08 [1,08; 8,82] 0,0284[3]	6,8 [0,8; 12,9] 0,0284[3]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	10/49 (20,4)	6/44 (13,6)	1,50 [0,59; 3,78] 0,3938[2]	1,62 [0,54; 4,91] 0,3876[3]	6,8 [-8,4; 21,9] 0,3876[3]
Positive	62/477 (13,0)	37/471 (7,9)	1,65 [1,12; 2,44] 0,0107[2]	1,75 [1,14; 2,69] 0,0096[3]	5,1 [1,3; 9,0] 0,0096[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,0423)					
White	53/323 (16,4)	21/324 (6,5)	2,53 [1,56; 4,10] 0,0002[2]	2,83 [1,66; 4,82] <,0001[3]	9,9 [5,1; 14,8] <,0001[3]
Asian	19/199 (9,5)	18/180 (10,0)	0,95 [0,52; 1,76] 0,8822[2]	0,95 [0,48; 1,87] 0,8822[3]	-0,5 [-6,4; 5,5] 0,8822[3]
Other	3/19 (15,8)	1/21 (4,8)	3,32 [0,38; 29,23] 0,2804[2]	3,75 [0,36; 39,59] 0,3306[4]	11,0 [-7,7; 29,8] 0,3306[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according PT Cough from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0009)					
Negative	5/49 (10,2)	4/44 (9,1)	1,12 [0,32; 3,92] 0,8563[2]	1,14 [0,29; 4,53] 1,0000[4]	1,1 [-10,9; 13,1] 1,0000[4]
Positive	54/477 (11,3)	22/471 (4,7)	2,42 [1,50; 3,91] 0,0003[2]	2,61 [1,56; 4,35] 0,0002[3]	6,6 [3,2; 10,1] 0,0002[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,0027)					
ECOG-PS 0	61/496 (12,3)	19/480 (4,0)	3,11 [1,89; 5,12] <,0001[2]	3,40 [2,00; 5,79] <,0001[3]	8,3 [5,0; 11,7] <,0001[3]
ECOG-PS 1	5/57 (8,8)	9/55 (16,4)	0,54 [0,19; 1,50] 0,2348[2]	0,49 [0,15; 1,57] 0,2246[3]	-7,6 [-19,8; 4,6] 0,2246[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Decreased appetite from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: 0,0227)					
ECOG-PS 0	48/496 (9,7)	5/480 (1,0)	9,29 [3,73; 23,14] <,0001[2]	10,18 [4,02; 25,80] <,0001[3]	8,6 [5,9; 11,4] <,0001[3]
ECOG-PS 1	1/57 (1,8)	2/55 (3,6)	0,48 [0,05; 5,17] 0,5470[2]	0,47 [0,04; 5,37] 0,6149[4]	-1,9 [-7,9; 4,1] 0,6149[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Diarrhoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: 0,0282)					
ECOG-PS 0	407/496 (82,1)	25/480 (5,2)	15,75 [10,73; 23,13] <,0001[2]	83,23 [52,37; 132,28] <,0001[3]	76,8 [72,9; 80,8] <,0001[3]
ECOG-PS 1	37/57 (64,9)	6/55 (10,9)	5,95 [2,73; 12,97] <,0001[2]	15,11 [5,52; 41,37] <,0001[3]	54,0 [39,1; 68,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Eczema from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	5/496 (1,0)	14/480 (2,9)	0,35 [0,13; 0,95] 0,0399[2]	0,34 [0,12; 0,95] 0,0310[3]	-1,9 [-3,7; -0,2] 0,0310[3]
ECOG-PS 1	0/57 (0,0)	0/55 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi²-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Fatigue from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,0300)					
IIA	18/59 (30,5)	18/62 (29,0)	1,05 [0,61; 1,82] 0,8591[2]	1,07 [0,49; 2,34] 0,8591[3]	1,5 [-14,8; 17,8] 0,8591[3]
IIB	14/53 (26,4)	4/69 (5,8)	4,56 [1,59; 13,05] 0,0047[2]	5,83 [1,79; 18,98] 0,0015[3]	20,6 [7,5; 33,7] 0,0015[3]
IIIA	65/236 (27,5)	26/214 (12,1)	2,27 [1,50; 3,43] 0,0001[2]	2,75 [1,67; 4,53] <,0001[3]	15,4 [8,2; 22,6] <,0001[3]
IIIB	4/18 (22,2)	3/15 (20,0)	1,11 [0,29; 4,21] 0,8767[2]	1,14 [0,21; 6,16] 1,0000[4]	2,2 [-25,7; 30,1] 1,0000[4]
IIIC	45/186 (24,2)	14/174 (8,0)	3,01 [1,71; 5,28] 0,0001[2]	3,65 [1,92; 6,92] <,0001[3]	16,1 [8,8; 23,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Gamma-glutamyltransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	15/496 (3,0)	5/480 (1,0)	2,90 [1,06; 7,93] 0,0375[2]	2,96 [1,07; 8,22] 0,0288[3]	2,0 [0,2; 3,7] 0,0288[3]
ECOG-PS 1	0/57 (0,0)	0/55 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Tabl: Interacting subgroups - adverse events according PT Lymphocyte count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0446)					
North America / Europe	17/252 (6,7)	3/233 (1,3)	5,24 [1,56; 17,65] 0,0075[2]	5,55 [1,60; 19,18] 0,0025[3]	5,5 [2,0; 8,9] 0,0025[3]
Asia	26/168 (15,5)	3/166 (1,8)	8,56 [2,64; 27,75] 0,0003[2]	9,95 [2,95; 33,57] <,0001[3]	13,7 [7,8; 19,5] <,0001[3]
Other	14/133 (10,5)	9/136 (6,6)	1,59 [0,71; 3,55] 0,2570[2]	1,66 [0,69; 3,98] 0,2517[3]	3,9 [-2,8; 10,6] 0,2517[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Nail disorder from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	15/496 (3,0)	2/480 (0,4)	7,26 [1,67; 31,57] 0,0082[2]	7,45 [1,70; 32,77] 0,0019[3]	2,6 [1,0; 4,2] 0,0019[3]
ECOG-PS 1	0/57 (0,0)	0/55 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi²-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Neutropenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0242)					
Negative	12/49 (24,5)	1/44 (2,3)	10,78 [1,46; 79,54] 0,0198[2]	13,95 [1,73; 112,39] 0,0020[3]	22,2 [9,4; 35,0] 0,0020[3]
Positive	91/477 (19,1)	16/471 (3,4)	5,62 [3,35; 9,41] <,0001[2]	6,70 [3,87; 11,60] <,0001[3]	15,7 [11,8; 19,6] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Neutrophil count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor grade (Interaction p-value: 0,0390)					
G1	16/47 (34,0)	1/41 (2,4)	13,96 [1,93; 100,73] 0,0089[2]	20,65 [2,59; 164,27] 0,0002[3]	31,6 [17,3; 45,9] 0,0002[3]
G2	49/244 (20,1)	4/234 (1,7)	11,75 [4,31; 32,04] <,0001[2]	14,45 [5,12; 40,75] <,0001[3]	18,4 [13,1; 23,7] <,0001[3]
G3	59/233 (25,3)	9/226 (4,0)	6,36 [3,23; 12,51] <,0001[2]	8,18 [3,94; 16,95] <,0001[3]	21,3 [15,2; 27,5] <,0001[3]
GX	14/29 (48,3)	7/33 (21,2)	2,28 [1,07; 4,86] 0,0334[2]	3,47 [1,15; 10,50] 0,0247[3]	27,1 [4,1; 50,0] 0,0247[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Vomiting from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Number of positive lymph nodes (Interaction p-value: 0,0287)					
0-3	36/203 (17,7)	3/214 (1,4)	12,65 [3,96; 40,44] <,0001[2]	15,16 [4,59; 50,10] <,0001[3]	16,3 [10,8; 21,8] <,0001[3]
4-9	29/242 (12,0)	11/231 (4,8)	2,52 [1,29; 4,92] 0,0070[2]	2,72 [1,33; 5,59] 0,0048[3]	7,2 [2,3; 12,1] 0,0048[3]
≥ 10	17/108 (15,7)	1/90 (1,1)	14,17 [1,92; 104,40] 0,0093[2]	16,63 [2,17; 127,59] 0,0004[3]	14,6 [7,4; 21,8] 0,0004[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according SOC Blood and lymphatic system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0045)					
Negative	20/49 (40,8)	4/44 (9,1)	4,49 [1,66; 12,12] 0,0030[2]	6,90 [2,13; 22,33] 0,0005[3]	31,7 [15,6; 47,9] 0,0005[3]
Positive	161/477 (33,8)	50/471 (10,6)	3,18 [2,38; 4,25] <,0001[2]	4,29 [3,03; 6,08] <,0001[3]	23,1 [18,1; 28,2] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Endocrine disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor grade (Interaction p-value: <,0001)					
G1	0/47 (0,0)	0/41 (0,0)	NE	NE	NE
G2	2/244 (0,8)	12/234 (5,1)	0,16 [0,04; 0,71] 0,0156[2]	0,15 [0,03; 0,69] 0,0052[3]	-4,3 [-7,4; -1,3] 0,0052[3]
G3	5/233 (2,1)	8/226 (3,5)	0,61 [0,20; 1,83] 0,3735[2]	0,60 [0,19; 1,85] 0,3681[3]	-1,4 [-4,4; 1,7] 0,3681[3]
GX	1/29 (3,4)	0/33 (0,0)	3,40 [0,14; 80,36] 0,4482[2]	3,53 [0,14; 89,98] 0,4677[4]	3,4 [-3,2; 10,1] 0,4677[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt_sub.sas
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Table: Interacting subgroups - adverse events according SOC General disorders and administration site conditions from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: 0,0278)					
ECOG-PS 0	282/496 (56,9)	142/480 (29,6)	1,92 [1,64; 2,25] <,0001[2]	3,14 [2,41; 4,09] <,0001[3]	27,3 [21,3; 33,2] <,0001[3]
ECOG-PS 1	28/57 (49,1)	23/55 (41,8)	1,17 [0,78; 1,77] 0,4400[2]	1,34 [0,64; 2,83] 0,4377[3]	7,3 [-11,1; 25,7] 0,4377[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt_sub.sas
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Table: Interacting subgroups - adverse events according SOC Infections and infestations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0462)					
Negative	21/49 (42,9)	23/44 (52,3)	0,82 [0,53; 1,26] 0,3645[2]	0,68 [0,30; 1,55] 0,3639[3]	-9,4 [-29,7; 10,8] 0,3639[3]
Positive	262/477 (54,9)	185/471 (39,3)	1,40 [1,22; 1,61] <,0001[2]	1,88 [1,46; 2,44] <,0001[3]	15,6 [9,4; 21,9] <,0001[3]
Unknown	2/4 (50,0)	5/8 (62,5)	0,80 [0,26; 2,45] 0,6955[2]	0,60 [0,05; 6,79] 1,0000[4]	-12,5 [-71,9; 46,9] 1,0000[4]
ECOG-PS (Interaction p-value: 0,0139)					
ECOG-PS 0	277/496 (55,8)	195/480 (40,6)	1,37 [1,20; 1,57] <,0001[2]	1,85 [1,43; 2,38] <,0001[3]	15,2 [9,0; 21,4] <,0001[3]
ECOG-PS 1	22/57 (38,6)	27/55 (49,1)	0,79 [0,51; 1,20] 0,2661[2]	0,65 [0,31; 1,38] 0,2630[3]	-10,5 [-28,8; 7,8] 0,2630[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Investigations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0332)					
North America / Europe	106/252 (42,1)	30/233 (12,9)	3,27 [2,27; 4,70] <,0001[2]	4,91 [3,11; 7,76] <,0001[3]	29,2 [21,7; 36,6] <,0001[3]
Asia	115/168 (68,5)	40/166 (24,1)	2,84 [2,13; 3,79] <,0001[2]	6,83 [4,22; 11,07] <,0001[3]	44,4 [34,8; 53,9] <,0001[3]
Other	47/133 (35,3)	29/136 (21,3)	1,66 [1,11; 2,46] 0,0125[2]	2,02 [1,17; 3,47] 0,0107[3]	14,0 [3,4; 24,7] 0,0107[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Nervous system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0246)					
North America / Europe	91/252 (36,1)	81/233 (34,8)	1,04 [0,82; 1,32] 0,7568[2]	1,06 [0,73; 1,54] 0,7567[3]	1,3 [-7,2; 9,9] 0,7567[3]
Asia	73/168 (43,5)	40/166 (24,1)	1,80 [1,31; 2,48] 0,0003[2]	2,42 [1,51; 3,87] 0,0002[3]	19,4 [9,4; 29,3] 0,0002[3]
Other	35/133 (26,3)	31/136 (22,8)	1,15 [0,76; 1,76] 0,5028[2]	1,21 [0,69; 2,11] 0,5021[3]	3,5 [-6,8; 13,8] 0,5021[3]
Race (Interaction p-value: 0,0255)					
White	106/323 (32,8)	97/324 (29,9)	1,10 [0,87; 1,38] 0,4304[2]	1,14 [0,82; 1,59] 0,4300[3]	2,9 [-4,3; 10,0] 0,4300[3]
Asian	80/199 (40,2)	41/180 (22,8)	1,76 [1,28; 2,43] 0,0005[2]	2,28 [1,45; 3,57] 0,0003[3]	17,4 [8,3; 26,6] 0,0003[3]
Other	6/19 (31,6)	9/21 (42,9)	0,74 [0,32; 1,68] 0,4686[2]	0,62 [0,17; 2,25] 0,4619[3]	-11,3 [-41,0; 18,5] 0,4619[3]
ECOG-PS (Interaction p-value: 0,0323)					
ECOG-PS 0	182/496 (36,7)	130/480 (27,1)	1,35 [1,12; 1,63] 0,0014[2]	1,56 [1,19; 2,05] 0,0013[3]	9,6 [3,8; 15,4] 0,0013[3]
ECOG-PS 1	17/57 (29,8)	22/55 (40,0)	0,75 [0,45; 1,25] 0,2622[2]	0,64 [0,29; 1,39] 0,2585[3]	-10,2 [-27,7; 7,4] 0,2585[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Respiratory, thoracic and mediastinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: 0,0103)					
ECOG-PS 0	142/496 (28,6)	59/480 (12,3)	2,33 [1,77; 3,07] <,0001[2]	2,86 [2,05; 4,00] <,0001[3]	16,3 [11,4; 21,3] <,0001[3]
ECOG-PS 1	15/57 (26,3)	15/55 (27,3)	0,96 [0,52; 1,78] 0,9090[2]	0,95 [0,41; 2,20] 0,9090[3]	-1,0 [-17,4; 15,5] 0,9090[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Aspartate aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	10/496 (2,0)	0/480 (0,0)	20,32 [1,19; 345,87] 0,0373[2]	20,74 [1,21; 354,94] 0,0019[4]	2,0 [0,8; 3,3] 0,0019[4]
ECOG-PS 1	0/57 (0,0)	1/55 (1,8)	0,32 [0,01; 7,74] 0,4846[2]	0,32 [0,01; 7,92] 0,4911[4]	-1,8 [-5,3; 1,7] 0,4911[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Diarrhoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	30/496 (6,0)	2/480 (0,4)	14,52 [3,49; 60,41] 0,0002[2]	15,39 [3,66; 64,75] <,0001[3]	5,6 [3,5; 7,8] <,0001[3]
ECOG-PS 1	0/57 (0,0)	0/55 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi²-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t272_bp_aesocpt_premp_safc1_1.rtf
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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Leukopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: <,0001)					
North America / Europe	1/252 (0,4)	0/233 (0,0)	2,77 [0,11; 67,78] 0,5314[2]	2,79 [0,11; 68,71] 1,0000[4]	0,4 [-0,4; 1,2] 1,0000[4]
Asia	2/168 (1,2)	0/166 (0,0)	4,94 [0,24; 102,14] 0,3012[2]	5,00 [0,24; 104,94] 0,4985[4]	1,2 [-0,4; 2,8] 0,4985[4]
Other	11/133 (8,3)	0/136 (0,0)	23,51 [1,40; 395,06] 0,0283[2]	25,63 [1,49; 439,49] 0,0006[3]	8,3 [3,6; 13,0] 0,0006[3]
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	13/496 (2,6)	0/480 (0,0)	26,13 [1,56; 438,34] 0,0233[2]	26,83 [1,59; 452,64] 0,0004[3]	2,6 [1,2; 4,0] 0,0004[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Lymphocyte count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: <,0001)					
North America / Europe	11/252 (4,4)	0/233 (0,0)	21,27 [1,26; 358,98] 0,0340[2]	22,24 [1,30; 379,53] 0,0013[3]	4,4 [1,8; 6,9] 0,0013[3]
Asia	11/168 (6,5)	0/166 (0,0)	22,73 [1,35; 382,58] 0,0301[2]	24,31 [1,42; 416,07] 0,0008[3]	6,5 [2,8; 10,3] 0,0008[3]
Other	2/133 (1,5)	0/136 (0,0)	5,11 [0,25; 105,49] 0,2908[2]	5,19 [0,25; 109,13] 0,2435[4]	1,5 [-0,6; 3,6] 0,2435[4]
Number of positive lymph nodes (Interaction p-value: <,0001)					
0-3	11/203 (5,4)	0/214 (0,0)	24,24 [1,44; 408,69] 0,0270[2]	25,63 [1,50; 437,82] 0,0006[3]	5,4 [2,3; 8,5] 0,0006[3]
4-9	13/242 (5,4)	0/231 (0,0)	25,78 [1,54; 431,14] 0,0238[2]	27,24 [1,61; 460,85] 0,0004[3]	5,4 [2,5; 8,2] 0,0004[3]
≥ 10	0/108 (0,0)	0/90 (0,0)	NE	NE	NE
Race (Interaction p-value: <,0001)					
White	13/323 (4,0)	0/324 (0,0)	27,08 [1,62; 453,68] 0,0218[2]	28,22 [1,67; 476,70] 0,0003[3]	4,0 [1,9; 6,2] 0,0003[3]
Asian	11/199 (5,5)	0/180 (0,0)	20,82 [1,24; 350,71] 0,0351[2]	22,02 [1,29; 376,49] 0,0014[3]	5,5 [2,4; 8,7] 0,0014[3]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	21/496 (4,2)	0/480 (0,0)	41,62 [2,53; 685,07] 0,0091[2]	43,45 [2,62; 719,37] <,0001[3]	4,2 [2,5; 6,0] <,0001[3]
ECOG-PS 1	3/57 (5,3)	0/55 (0,0)	6,76 [0,36; 127,89] 0,2028[2]	7,13 [0,36; 141,28] 0,2435[4]	5,3 [-0,5; 11,1] 0,2435[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi²-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Investigations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0444)					
Negative	10/49 (20,4)	1/44 (2,3)	8,98 [1,20; 67,35] 0,0328[2]	11,03 [1,35; 90,11] 0,0069[3]	18,1 [6,0; 30,2] 0,0069[3]
Positive	88/477 (18,4)	8/471 (1,7)	10,86 [5,33; 22,15] <,0001[2]	13,09 [6,27; 27,34] <,0001[3]	16,8 [13,1; 20,4] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Tabelle 4-133 (Anhang): Häufige unerwünschte Ereignisse nach SOC und PT - interagierende Subgruppen (postmenopausale Patientinnen)

Table: Interacting subgroups - adverse events according PT Abdominal discomfort from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: <,0001)					
Neoadjuvant chemotherapy	7/430 (1,6)	4/415 (1,0)	1,69 [0,50; 5,73] 0,4002[2]	1,70 [0,49; 5,85] 0,3946[3]	0,7 [-0,9; 2,2] 0,3946[3]
Adjuvant chemotherapy	12/784 (1,5)	3/769 (0,4)	3,92 [1,11; 13,85] 0,0336[2]	3,97 [1,12; 14,12] 0,0216[3]	1,1 [0,2; 2,1] 0,0216[3]
No chemotherapy	0/69 (0,0)	0/81 (0,0)	NE	NE	NE
Tumor grade (Interaction p-value: <,0001)					
G1	0/91 (0,0)	0/93 (0,0)	NE	NE	NE
G2	8/612 (1,3)	4/603 (0,7)	1,97 [0,60; 6,51] 0,2659[2]	1,98 [0,59; 6,62] 0,2565[3]	0,6 [-0,5; 1,8] 0,2565[3]
G3	11/527 (2,1)	3/506 (0,6)	3,52 [0,99; 12,55] 0,0522[2]	3,57 [0,99; 12,89] 0,0378[3]	1,5 [0,1; 2,9] 0,0378[3]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Abdominal pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	36/156 (23,1)	8/169 (4,7)	4,88 [2,34; 10,16] <,0001[2]	6,04 [2,71; 13,46] <,0001[3]	18,3 [11,0; 25,7] <,0001[3]
Positive	256/1089 (23,5)	51/1067 (4,8)	4,92 [3,69; 6,56] <,0001[2]	6,12 [4,47; 8,38] <,0001[3]	18,7 [15,9; 21,6] <,0001[3]
Unknown	4/10 (40,0)	0/7 (0,0)	6,55 [0,41; 105,10] 0,1847[2]	10,38 [0,47; 231,63] 0,1029[4]	40,0 [9,6; 70,4] 0,1029[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according PT Alopecia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	19/156 (12,2)	8/169 (4,7)	2,57 [1,16; 5,71] 0,0201[2]	2,79 [1,18; 6,58] 0,0151[3]	7,4 [1,4; 13,5] 0,0151[3]
Positive	124/1089 (11,4)	25/1067 (2,3)	4,86 [3,19; 7,41] <,0001[2]	5,36 [3,45; 8,30] <,0001[3]	9,0 [7,0; 11,1] <,0001[3]
Unknown	2/10 (20,0)	0/7 (0,0)	3,64 [0,20; 65,86] 0,3824[2]	4,41 [0,18; 107,28] 0,4853[4]	20,0 [-4,8; 44,8] 0,4853[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	8/114 (7,0)	0/132 (0,0)	19,66 [1,15; 336,92] 0,0399[2]	21,15 [1,21; 370,63] 0,0019[4]	7,0 [2,3; 11,7] 0,0019[4]
Aromatase inhibitor	142/1169 (12,1)	34/1133 (3,0)	4,05 [2,81; 5,83] <,0001[2]	4,47 [3,04; 6,56] <,0001[3]	9,1 [7,0; 11,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Anaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	41/156 (26,3)	6/169 (3,6)	7,40 [3,23; 16,95] <,0001[2]	9,69 [3,98; 23,57] <,0001[3]	22,7 [15,3; 30,2] <,0001[3]
Positive	284/1089 (26,1)	39/1067 (3,7)	7,13 [5,16; 9,86] <,0001[2]	9,30 [6,57; 13,16] <,0001[3]	22,4 [19,6; 25,3] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Anxiety from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0263)					
< 65 years	31/918 (3,4)	37/937 (3,9)	0,86 [0,54; 1,37] 0,5128[2]	0,85 [0,52; 1,38] 0,5123[3]	-0,6 [-2,3; 1,1] 0,5123[3]
≥ 65 years	5/365 (1,4)	18/328 (5,5)	0,25 [0,09; 0,66] 0,0055[2]	0,24 [0,09; 0,65] 0,0025[3]	-4,1 [-6,9; -1,4] 0,0025[3]
Tumor grade (Interaction p-value: <,0001)					
G1	2/91 (2,2)	5/93 (5,4)	0,41 [0,08; 2,05] 0,2774[2]	0,40 [0,07; 2,09] 0,4442[4]	-3,2 [-8,7; 2,3] 0,4442[4]
G2	17/612 (2,8)	37/603 (6,1)	0,45 [0,26; 0,80] 0,0058[2]	0,44 [0,24; 0,79] 0,0045[3]	-3,4 [-5,7; -1,0] 0,0045[3]
G3	17/527 (3,2)	13/506 (2,6)	1,26 [0,62; 2,56] 0,5308[2]	1,26 [0,61; 2,63] 0,5298[3]	0,7 [-1,4; 2,7] 0,5298[3]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	5/156 (3,2)	7/169 (4,1)	0,77 [0,25; 2,39] 0,6556[2]	0,77 [0,24; 2,47] 0,6545[3]	-0,9 [-5,0; 3,1] 0,6545[3]
Positive	29/1089 (2,7)	48/1067 (4,5)	0,59 [0,38; 0,93] 0,0234[2]	0,58 [0,36; 0,93] 0,0217[3]	-1,8 [-3,4; -0,3] 0,0217[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Asthenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	18/156 (11,5)	15/169 (8,9)	1,30 [0,68; 2,49] 0,4287[2]	1,34 [0,65; 2,76] 0,4272[3]	2,7 [-3,9; 9,3] 0,4272[3]
Positive	128/1089 (11,8)	50/1067 (4,7)	2,51 [1,83; 3,44] <,0001[2]	2,71 [1,93; 3,80] <,0001[3]	7,1 [4,8; 9,4] <,0001[3]
Unknown	0/10 (0,0)	1/7 (14,3)	0,24 [0,01; 5,21] 0,3654[2]	0,21 [0,01; 5,86] 0,4118[4]	-14,3 [-40,2; 11,6] 0,4118[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according PT Blood alkaline phosphatase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: 0,0215)					
ECOG-PS 0	43/1070 (4,0)	35/1020 (3,4)	1,17 [0,76; 1,81] 0,4794[2]	1,18 [0,75; 1,86] 0,4789[3]	0,6 [-1,0; 2,2] 0,4789[3]
ECOG-PS 1	16/213 (7,5)	4/245 (1,6)	4,60 [1,56; 13,55] 0,0056[2]	4,89 [1,61; 14,87] 0,0021[3]	5,9 [2,0; 9,8] 0,0021[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Blood creatinine increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	23/156 (14,7)	1/169 (0,6)	24,92 [3,41; 182,33] 0,0015[2]	29,05 [3,87; 217,92] <,0001[3]	14,2 [8,5; 19,8] <,0001[3]
Positive	118/1089 (10,8)	13/1067 (1,2)	8,89 [5,05; 15,67] <,0001[2]	9,85 [5,52; 17,59] <,0001[3]	9,6 [7,7; 11,6] <,0001[3]
Unknown	4/10 (40,0)	0/7 (0,0)	6,55 [0,41; 105,10] 0,1847[2]	10,38 [0,47; 231,63] 0,1029[4]	40,0 [9,6; 70,4] 0,1029[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	8/114 (7,0)	0/132 (0,0)	19,66 [1,15; 336,92] 0,0399[2]	21,15 [1,21; 370,63] 0,0019[4]	7,0 [2,3; 11,7] 0,0019[4]
Aromatase inhibitor	142/1169 (12,1)	14/1133 (1,2)	9,83 [5,71; 16,92] <,0001[2]	11,05 [6,34; 19,26] <,0001[3]	10,9 [8,9; 12,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT COVID-19 from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: <,0001)					
Neoadjuvant chemotherapy	11/430 (2,6)	2/415 (0,5)	5,31 [1,18; 23,80] 0,0292[2]	5,42 [1,19; 24,61] 0,0142[3]	2,1 [0,4; 3,7] 0,0142[3]
Adjuvant chemotherapy	22/784 (2,8)	6/769 (0,8)	3,60 [1,47; 8,82] 0,0052[2]	3,67 [1,48; 9,11] 0,0027[3]	2,0 [0,7; 3,3] 0,0027[3]
No chemotherapy	0/69 (0,0)	0/81 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Cataract from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	3/156 (1,9)	1/169 (0,6)	3,25 [0,34; 30,92] 0,3051[2]	3,29 [0,34; 32,00] 0,3537[4]	1,3 [-1,1; 3,8] 0,3537[4]
Positive	21/1089 (1,9)	10/1067 (0,9)	2,06 [0,97; 4,35] 0,0588[2]	2,08 [0,97; 4,43] 0,0532[3]	1,0 [-0,0; 2,0] 0,0532[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Constipation from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0028)					
< 65 years	110/918 (12,0)	39/937 (4,2)	2,88 [2,02; 4,10] <,0001[2]	3,13 [2,15; 4,57] <,0001[3]	7,8 [5,4; 10,3] <,0001[3]
≥ 65 years	42/365 (11,5)	31/328 (9,5)	1,22 [0,78; 1,89] 0,3801[2]	1,25 [0,76; 2,03] 0,3788[3]	2,1 [-2,5; 6,6] 0,3788[3]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	23/156 (14,7)	10/169 (5,9)	2,49 [1,23; 5,07] 0,0117[2]	2,75 [1,26; 5,98] 0,0085[3]	8,8 [2,2; 15,4] 0,0085[3]
Positive	118/1089 (10,8)	59/1067 (5,5)	1,96 [1,45; 2,65] <,0001[2]	2,08 [1,50; 2,87] <,0001[3]	5,3 [3,0; 7,6] <,0001[3]
Unknown	3/10 (30,0)	0/7 (0,0)	5,09 [0,30; 85,39] 0,2580[2]	7,00 [0,31; 160,32] 0,2279[4]	30,0 [1,6; 58,4] 0,2279[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Cough from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	23/156 (14,7)	13/169 (7,7)	1,92 [1,01; 3,65] 0,0478[2]	2,08 [1,01; 4,26] 0,0430[3]	7,1 [0,2; 13,9] 0,0430[3]
Positive	156/1089 (14,3)	95/1067 (8,9)	1,61 [1,26; 2,05] 0,0001[2]	1,71 [1,31; 2,24] <,0001[3]	5,4 [2,7; 8,1] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
ECOG-PS (Interaction p-value: 0,0212)					
ECOG-PS 0	139/1070 (13,0)	92/1020 (9,0)	1,44 [1,12; 1,85] 0,0041[2]	1,51 [1,14; 1,99] 0,0038[3]	4,0 [1,3; 6,6] 0,0038[3]
ECOG-PS 1	46/213 (21,6)	19/245 (7,8)	2,78 [1,69; 4,60] <,0001[2]	3,28 [1,85; 5,80] <,0001[3]	13,8 [7,4; 20,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Decreased appetite from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,0253)					
IIA	8/113 (7,1)	7/114 (6,1)	1,15 [0,43; 3,07] 0,7760[2]	1,16 [0,41; 3,33] 0,7758[3]	0,9 [-5,5; 7,4] 0,7758[3]
IIB	18/151 (11,9)	2/136 (1,5)	8,11 [1,92; 34,29] 0,0045[2]	9,07 [2,06; 39,85] 0,0005[3]	10,4 [4,9; 16,0] 0,0005[3]
IIIA	69/495 (13,9)	11/488 (2,3)	6,18 [3,31; 11,54] <,0001[2]	7,02 [3,67; 13,45] <,0001[3]	11,7 [8,4; 15,0] <,0001[3]
IIIB	5/54 (9,3)	3/45 (6,7)	1,39 [0,35; 5,50] 0,6397[2]	1,43 [0,32; 6,34] 0,7248[4]	2,6 [-8,0; 13,2] 0,7248[4]
IIIC	62/468 (13,2)	18/480 (3,8)	3,53 [2,12; 5,88] <,0001[2]	3,92 [2,28; 6,74] <,0001[3]	9,5 [6,0; 13,0] <,0001[3]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	25/156 (16,0)	5/169 (3,0)	5,42 [2,13; 13,80] 0,0004[2]	6,26 [2,33; 16,80] <,0001[3]	13,1 [6,8; 19,4] <,0001[3]
Positive	133/1089 (12,2)	34/1067 (3,2)	3,83 [2,66; 5,53] <,0001[2]	4,23 [2,87; 6,22] <,0001[3]	9,0 [6,8; 11,2] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Deep vein thrombosis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	12/918 (1,3)	3/937 (0,3)	4,08 [1,16; 14,42] 0,0289[2]	4,12 [1,16; 14,66] 0,0176[3]	1,0 [0,2; 1,8] 0,0176[3]
≥ 65 years	9/365 (2,5)	0/328 (0,0)	17,08 [1,00; 292,30] 0,0502[2]	17,51 [1,01; 301,99] 0,0041[4]	2,5 [0,9; 4,1] 0,0041[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	3/114 (2,6)	0/132 (0,0)	8,10 [0,42; 155,09] 0,1651[2]	8,32 [0,43; 162,77] 0,0981[4]	2,6 [-0,3; 5,6] 0,0981[4]
Aromatase inhibitor	18/1169 (1,5)	3/1133 (0,3)	5,82 [1,72; 19,69] 0,0047[2]	5,89 [1,73; 20,05] 0,0013[3]	1,3 [0,5; 2,0] 0,0013[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Dehydration from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	11/918 (1,2)	3/937 (0,3)	3,74 [1,05; 13,37] 0,0422[2]	3,78 [1,05; 13,58] 0,0289[3]	0,9 [0,1; 1,7] 0,0289[3]
≥ 65 years	15/365 (4,1)	0/328 (0,0)	27,87 [1,67; 463,88] 0,0204[2]	29,05 [1,73; 487,53] 0,0002[3]	4,1 [2,1; 6,1] 0,0002[3]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	0/114 (0,0)	0/132 (0,0)	NE	NE	NE
Aromatase inhibitor	26/1169 (2,2)	3/1133 (0,3)	8,40 [2,55; 27,67] 0,0005[2]	8,57 [2,59; 28,39] <,0001[3]	2,0 [1,1; 2,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Diarrhoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0005)					
< 65 years	768/918 (83,7)	67/937 (7,2)	11,70 [9,27; 14,76] <,0001[2]	66,48 [49,06; 90,10] <,0001[3]	76,5 [73,6; 79,4] <,0001[3]
≥ 65 years	291/365 (79,7)	43/328 (13,1)	6,08 [4,58; 8,07] <,0001[2]	26,06 [17,30; 39,27] <,0001[3]	66,6 [61,1; 72,1] <,0001[3]
Region (Interaction p-value: 0,0042)					
North America / Europe	585/678 (86,3)	76/650 (11,7)	7,38 [5,96; 9,13] <,0001[2]	47,51 [34,35; 65,70] <,0001[3]	74,6 [71,0; 78,2] <,0001[3]
Asia	176/203 (86,7)	10/201 (5,0)	17,43 [9,50; 31,96] <,0001[2]	124,50 [58,58; 264,60] <,0001[3]	81,7 [76,2; 87,3] <,0001[3]
Other	298/402 (74,1)	24/414 (5,8)	12,79 [8,64; 18,94] <,0001[2]	46,56 [29,14; 74,41] <,0001[3]	68,3 [63,5; 73,2] <,0001[3]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	125/156 (80,1)	15/169 (8,9)	9,03 [5,53; 14,73] <,0001[2]	41,40 [21,40; 80,10] <,0001[3]	71,3 [63,7; 78,8] <,0001[3]
Positive	901/1089 (82,7)	92/1067 (8,6)	9,60 [7,88; 11,69] <,0001[2]	50,79 [38,95; 66,22] <,0001[3]	74,1 [71,3; 76,9] <,0001[3]
Unknown	8/10 (80,0)	0/7 (0,0)	12,36 [0,83; 184,49] 0,0682[2]	51,00 [2,10; 1240,17] 0,0023[4]	80,0 [55,2; 100,0] 0,0023[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Dizziness from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0068)					
Negative	18/156 (11,5)	11/169 (6,5)	1,77 [0,86; 3,63] 0,1180[2]	1,87 [0,86; 4,10] 0,1121[3]	5,0 [-1,2; 11,3] 0,1121[3]
Positive	118/1089 (10,8)	70/1067 (6,6)	1,65 [1,24; 2,19] 0,0005[2]	1,73 [1,27; 2,36] 0,0004[3]	4,3 [1,9; 6,6] 0,0004[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Dry eye from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: 0,0477)					
ECOG-PS 0	33/1070 (3,1)	6/1020 (0,6)	5,24 [2,21; 12,46] 0,0002[2]	5,38 [2,24; 12,89] <,0001[3]	2,5 [1,4; 3,6] <,0001[3]
ECOG-PS 1	5/213 (2,3)	5/245 (2,0)	1,15 [0,34; 3,92] 0,8229[2]	1,15 [0,33; 4,04] 1,0000[4]	0,3 [-2,4; 3,0] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Dry skin from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Number of positive lymph nodes (Interaction p-value: 0,0379)					
0-3	13/427 (3,0)	13/418 (3,1)	0,98 [0,46; 2,09] 0,9560[2]	0,98 [0,45; 2,14] 0,9560[3]	-0,1 [-2,4; 2,3] 0,9560[3]
4-9	27/549 (4,9)	6/542 (1,1)	4,44 [1,85; 10,67] 0,0009[2]	4,62 [1,89; 11,28] 0,0002[3]	3,8 [1,8; 5,8] 0,0002[3]
≥ 10	11/307 (3,6)	6/305 (2,0)	1,82 [0,68; 4,86] 0,2314[2]	1,85 [0,68; 5,07] 0,2239[3]	1,6 [-1,0; 4,2] 0,2239[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt_sub.sas
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Table: Interacting subgroups - adverse events according PT Dysgeusia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: 0,0159)					
Tamoxifen	2/114 (1,8)	2/132 (1,5)	1,16 [0,17; 8,09] 0,8825[2]	1,16 [0,16; 8,37] 1,0000[4]	0,2 [-2,9; 3,4] 1,0000[4]
Aromatase inhibitor	58/1169 (5,0)	3/1133 (0,3)	18,74 [5,89; 59,63] <,0001[2]	19,66 [6,14; 62,94] <,0001[3]	4,7 [3,4; 6,0] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Dyspepsia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0126)					
< 65 years	75/918 (8,2)	18/937 (1,9)	4,25 [2,56; 7,06] <,0001[2]	4,54 [2,69; 7,66] <,0001[3]	6,2 [4,3; 8,2] <,0001[3]
≥ 65 years	21/365 (5,8)	13/328 (4,0)	1,45 [0,74; 2,85] 0,2795[2]	1,48 [0,73; 3,00] 0,2760[3]	1,8 [-1,4; 5,0] 0,2760[3]
Region (Interaction p-value: 0,0198)					
North America / Europe	69/678 (10,2)	17/650 (2,6)	3,89 [2,31; 6,54] <,0001[2]	4,22 [2,45; 7,26] <,0001[3]	7,6 [5,0; 10,1] <,0001[3]
Asia	10/203 (4,9)	10/201 (5,0)	0,99 [0,42; 2,33] 0,9819[2]	0,99 [0,40; 2,43] 0,9819[3]	-0,0 [-4,3; 4,2] 0,9819[3]
Other	17/402 (4,2)	4/414 (1,0)	4,38 [1,49; 12,90] 0,0074[2]	4,53 [1,51; 13,57] 0,0033[3]	3,3 [1,1; 5,4] 0,0033[3]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	12/156 (7,7)	8/169 (4,7)	1,63 [0,68; 3,87] 0,2728[2]	1,68 [0,67; 4,22] 0,2675[3]	3,0 [-2,3; 8,2] 0,2675[3]
Positive	80/1089 (7,3)	22/1067 (2,1)	3,56 [2,24; 5,67] <,0001[2]	3,77 [2,33; 6,08] <,0001[3]	5,3 [3,5; 7,1] <,0001[3]
Unknown	2/10 (20,0)	0/7 (0,0)	3,64 [0,20; 65,86] 0,3824[2]	4,41 [0,18; 107,28] 0,4853[4]	20,0 [-4,8; 44,8] 0,4853[4]
Race (Interaction p-value: 0,0175)					
White	82/958 (8,6)	20/944 (2,1)	4,04 [2,50; 6,53] <,0001[2]	4,32 [2,63; 7,11] <,0001[3]	6,4 [4,4; 8,4] <,0001[3]
Asian	10/250 (4,0)	10/242 (4,1)	0,97 [0,41; 2,28] 0,9408[2]	0,97 [0,40; 2,37] 0,9408[3]	-0,1 [-3,6; 3,4] 0,9408[3]
Other	3/62 (4,8)	1/64 (1,6)	3,10 [0,33; 28,97] 0,3218[2]	3,20 [0,32; 31,66] 0,3610[4]	3,3 [-2,9; 9,4] 0,3610[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Tabl: Interacting subgroups - adverse events according PT Dyspnoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	13/156 (8,3)	8/169 (4,7)	1,76 [0,75; 4,13] 0,1940[2]	1,83 [0,74; 4,54] 0,1873[3]	3,6 [-1,8; 9,0] 0,1873[3]
Positive	75/1089 (6,9)	41/1067 (3,8)	1,79 [1,24; 2,60] 0,0021[2]	1,85 [1,25; 2,73] 0,0017[3]	3,0 [1,1; 4,9] 0,0017[3]
Unknown	3/10 (30,0)	0/7 (0,0)	5,09 [0,30; 85,39] 0,2580[2]	7,00 [0,31; 160,32] 0,2279[4]	30,0 [1,6; 58,4] 0,2279[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Epistaxis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	15/918 (1,6)	3/937 (0,3)	5,10 [1,48; 17,57] 0,0098[2]	5,17 [1,49; 17,92] 0,0039[3]	1,3 [0,4; 2,2] 0,0039[3]
≥ 65 years	8/365 (2,2)	0/328 (0,0)	15,28 [0,89; 263,73] 0,0606[2]	15,62 [0,90; 271,70] 0,0081[4]	2,2 [0,7; 3,7] 0,0081[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	3/114 (2,6)	0/132 (0,0)	8,10 [0,42; 155,09] 0,1651[2]	8,32 [0,43; 162,77] 0,0981[4]	2,6 [-0,3; 5,6] 0,0981[4]
Aromatase inhibitor	20/1169 (1,7)	3/1133 (0,3)	6,46 [1,93; 21,68] 0,0025[2]	6,56 [1,94; 22,13] 0,0005[3]	1,4 [0,6; 2,2] 0,0005[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according PT Gamma-glutamyltransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	41/1169 (3,5)	16/1133 (1,4)	2,48 [1,40; 4,40] 0,0018[2]	2,54 [1,42; 4,55] 0,0012[3]	2,1 [0,8; 3,4] 0,0012[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Gastrointestinal pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	12/918 (1,3)	0/937 (0,0)	25,52 [1,51; 430,34] 0,0246[2]	25,85 [1,53; 437,32] 0,0004[3]	1,3 [0,6; 2,0] 0,0004[3]
≥ 65 years	5/365 (1,4)	0/328 (0,0)	9,89 [0,55; 178,14] 0,1204[2]	10,02 [0,55; 181,97] 0,0634[4]	1,4 [0,2; 2,6] 0,0634[4]
Prior treatment (Interaction p-value: <,0001)					
Neoadjuvant chemotherapy	4/430 (0,9)	0/415 (0,0)	8,69 [0,47; 160,84] 0,1466[2]	8,77 [0,47; 163,36] 0,1243[4]	0,9 [0,0; 1,8] 0,1243[4]
Adjuvant chemotherapy	10/784 (1,3)	0/769 (0,0)	20,60 [1,21; 350,91] 0,0365[2]	20,86 [1,22; 356,68] 0,0019[4]	1,3 [0,5; 2,1] 0,0019[4]
No chemotherapy	3/69 (4,3)	0/81 (0,0)	8,20 [0,43; 156,04] 0,1615[2]	8,58 [0,44; 169,04] 0,0950[4]	4,3 [-0,5; 9,2] 0,0950[4]
Primary tumor size (Interaction p-value: <,0001)					
< 20 mm	1/331 (0,3)	0/335 (0,0)	3,04 [0,12; 74,26] 0,4960[2]	3,05 [0,12; 75,03] 0,4970[4]	0,3 [-0,3; 0,9] 0,4970[4]
≥ 20 but < 50 mm	11/646 (1,7)	0/653 (0,0)	23,25 [1,37; 393,70] 0,0293[2]	23,65 [1,39; 402,20] 0,0008[3]	1,7 [0,7; 2,7] 0,0008[3]
≥ 50 mm	5/289 (1,7)	0/265 (0,0)	10,09 [0,56; 181,60] 0,1170[2]	10,27 [0,56; 186,54] 0,0625[4]	1,7 [0,2; 3,2] 0,0625[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	16/1169 (1,4)	0/1133 (0,0)	31,98 [1,92; 532,49] 0,0157[2]	32,43 [1,94; 541,15] <,0001[3]	1,4 [0,7; 2,0] <,0001[3]
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	16/1070 (1,5)	0/1020 (0,0)	31,46 [1,89; 523,68] 0,0162[2]	31,94 [1,91; 533,01] <,0001[3]	1,5 [0,8; 2,2] <,0001[3]
ECOG-PS 1	1/213 (0,5)	0/245 (0,0)	3,45 [0,14; 84,21] 0,4476[2]	3,47 [0,14; 85,53] 0,4651[4]	0,5 [-0,4; 1,4] 0,4651[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Haemorrhoids from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	0/114 (0,0)	0/132 (0,0)	NE	NE	NE
Aromatase inhibitor	27/1169 (2,3)	14/1133 (1,2)	1,87 [0,99; 3,55] 0,0555[2]	1,89 [0,99; 3,62] 0,0514[3]	1,1 [-0,0; 2,1] 0,0514[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Headache from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	25/156 (16,0)	20/169 (11,8)	1,35 [0,78; 2,34] 0,2767[2]	1,42 [0,75; 2,68] 0,2744[3]	4,2 [-3,3; 11,7] 0,2744[3]
Positive	188/1089 (17,3)	126/1067 (11,8)	1,46 [1,19; 1,80] 0,0004[2]	1,56 [1,22; 1,99] 0,0003[3]	5,5 [2,5; 8,4] 0,0003[3]
Unknown	3/10 (30,0)	0/7 (0,0)	5,09 [0,30; 85,39] 0,2580[2]	7,00 [0,31; 160,32] 0,2279[4]	30,0 [1,6; 58,4] 0,2279[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Hot flush from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	19/156 (12,2)	31/169 (18,3)	0,66 [0,39; 1,13] 0,1285[2]	0,62 [0,33; 1,15] 0,1239[3]	-6,2 [-13,9; 1,6] 0,1239[3]
Positive	118/1089 (10,8)	178/1067 (16,7)	0,65 [0,52; 0,81] <,0001[2]	0,61 [0,47; 0,78] <,0001[3]	-5,8 [-8,7; -2,9] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according PT Hyponatraemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	12/918 (1,3)	8/937 (0,9)	1,53 [0,63; 3,73] 0,3482[2]	1,54 [0,63; 3,78] 0,3445[3]	0,5 [-0,5; 1,4] 0,3445[3]
≥ 65 years	7/365 (1,9)	0/328 (0,0)	13,48 [0,77; 235,17] 0,0745[2]	13,74 [0,78; 241,60] 0,0161[4]	1,9 [0,5; 3,3] 0,0161[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	18/1169 (1,5)	8/1133 (0,7)	2,18 [0,95; 5,00] 0,0652[2]	2,20 [0,95; 5,08] 0,0584[3]	0,8 [-0,0; 1,7] 0,0584[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Leukopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	22/114 (19,3)	0/132 (0,0)	52,04 [3,19; 848,42] 0,0055[2]	64,46 [3,86; 1076,02] <,0001[3]	19,3 [12,1; 26,5] <,0001[3]
Aromatase inhibitor	164/1169 (14,0)	25/1133 (2,2)	6,36 [4,21; 9,61] <,0001[2]	7,23 [4,71; 11,11] <,0001[3]	11,8 [9,7; 14,0] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Lymphocyte count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	13/156 (8,3)	5/169 (3,0)	2,82 [1,03; 7,72] 0,0441[2]	2,98 [1,04; 8,57] 0,0343[3]	5,4 [0,3; 10,4] 0,0343[3]
Positive	94/1089 (8,6)	22/1067 (2,1)	4,19 [2,65; 6,61] <,0001[2]	4,49 [2,80; 7,20] <,0001[3]	6,6 [4,7; 8,4] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Lymphoedema from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	22/156 (14,1)	15/169 (8,9)	1,59 [0,86; 2,95] 0,1427[2]	1,69 [0,84; 3,38] 0,1383[3]	5,2 [-1,7; 12,2] 0,1383[3]
Positive	125/1089 (11,5)	84/1067 (7,9)	1,46 [1,12; 1,90] 0,0050[2]	1,52 [1,13; 2,03] 0,0047[3]	3,6 [1,1; 6,1] 0,0047[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: 0,0049)					
Tamoxifen	6/114 (5,3)	16/132 (12,1)	0,43 [0,18; 1,07] 0,0706[2]	0,40 [0,15; 1,07] 0,0602[3]	-6,9 [-13,8; 0,1] 0,0602[3]
Aromatase inhibitor	147/1169 (12,6)	85/1133 (7,5)	1,68 [1,30; 2,16] <,0001[2]	1,77 [1,34; 2,35] <,0001[3]	5,1 [2,6; 7,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Lymphopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	6/156 (3,8)	2/169 (1,2)	3,25 [0,67; 15,86] 0,1451[2]	3,34 [0,66; 16,80] 0,1598[4]	2,7 [-0,8; 6,1] 0,1598[4]
Positive	62/1089 (5,7)	6/1067 (0,6)	10,12 [4,40; 23,31] <,0001[2]	10,68 [4,60; 24,79] <,0001[3]	5,1 [3,7; 6,6] <,0001[3]
Unknown	0/10 (0,0)	1/7 (14,3)	0,24 [0,01; 5,21] 0,3654[2]	0,21 [0,01; 5,86] 0,4118[4]	-14,3 [-40,2; 11,6] 0,4118[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	6/114 (5,3)	0/132 (0,0)	15,03 [0,86; 264,00] 0,0638[2]	15,88 [0,88; 284,97] 0,0092[4]	5,3 [1,2; 9,4] 0,0092[4]
Aromatase inhibitor	62/1169 (5,3)	9/1133 (0,8)	6,68 [3,33; 13,37] <,0001[2]	6,99 [3,46; 14,14] <,0001[3]	4,5 [3,1; 5,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Mucosal inflammation from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	5/114 (4,4)	0/132 (0,0)	12,72 [0,71; 227,60] 0,0839[2]	13,31 [0,73; 243,39] 0,0204[4]	4,4 [0,6; 8,1] 0,0204[4]
Aromatase inhibitor	32/1169 (2,7)	9/1133 (0,8)	3,45 [1,65; 7,19] 0,0010[2]	3,51 [1,67; 7,40] 0,0004[3]	1,9 [0,9; 3,0] 0,0004[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Muscle spasms from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	12/156 (7,7)	2/169 (1,2)	6,50 [1,48; 28,58] 0,0132[2]	6,96 [1,53; 31,61] 0,0039[3]	6,5 [2,0; 11,0] 0,0039[3]
Positive	57/1089 (5,2)	44/1067 (4,1)	1,27 [0,86; 1,86] 0,2238[2]	1,28 [0,86; 1,92] 0,2225[3]	1,1 [-0,7; 2,9] 0,2225[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Tabl: Interacting subgroups - adverse events according PT Nail disorder from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	16/918 (1,7)	2/937 (0,2)	8,17 [1,88; 35,41] 0,0050[2]	8,29 [1,90; 36,17] 0,0008[3]	1,5 [0,6; 2,4] 0,0008[3]
≥ 65 years	7/365 (1,9)	0/328 (0,0)	13,48 [0,77; 235,17] 0,0745[2]	13,74 [0,78; 241,60] 0,0161[4]	1,9 [0,5; 3,3] 0,0161[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	2/114 (1,8)	0/132 (0,0)	5,78 [0,28; 119,22] 0,2557[2]	5,89 [0,28; 123,94] 0,2137[4]	1,8 [-0,7; 4,2] 0,2137[4]
Aromatase inhibitor	21/1169 (1,8)	2/1133 (0,2)	10,18 [2,39; 43,30] 0,0017[2]	10,34 [2,42; 44,22] <,0001[3]	1,6 [0,8; 2,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Neutropenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0081)					
North America / Europe	146/678 (21,5)	6/650 (0,9)	23,33 [10,39; 52,40] <,0001[2]	29,46 [12,92; 67,18] <,0001[3]	20,6 [17,4; 23,8] <,0001[3]
Asia	23/203 (11,3)	1/201 (0,5)	22,77 [3,10; 167,03] 0,0021[2]	25,56 [3,42; 191,15] <,0001[3]	10,8 [6,4; 15,3] <,0001[3]
Other	126/402 (31,3)	22/414 (5,3)	5,90 [3,83; 9,08] <,0001[2]	8,13 [5,04; 13,12] <,0001[3]	26,0 [21,0; 31,1] <,0001[3]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	38/156 (24,4)	3/169 (1,8)	13,72 [4,32; 43,56] <,0001[2]	17,82 [5,37; 59,09] <,0001[3]	22,6 [15,6; 29,6] <,0001[3]
Positive	255/1089 (23,4)	26/1067 (2,4)	9,61 [6,48; 14,26] <,0001[2]	12,24 [8,09; 18,51] <,0001[3]	21,0 [18,3; 23,7] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Neutrophil count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	37/156 (23,7)	4/169 (2,4)	10,02 [3,66; 27,47] <,0001[2]	12,83 [4,45; 36,95] <,0001[3]	21,4 [14,3; 28,4] <,0001[3]
Positive	232/1089 (21,3)	17/1067 (1,6)	13,37 [8,23; 21,72] <,0001[2]	16,72 [10,13; 27,59] <,0001[3]	19,7 [17,2; 22,3] <,0001[3]
Unknown	4/10 (40,0)	0/7 (0,0)	6,55 [0,41; 105,10] 0,1847[2]	10,38 [0,47; 231,63] 0,1029[4]	40,0 [9,6; 70,4] 0,1029[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according PT Oedema peripheral from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	15/156 (9,6)	10/169 (5,9)	1,63 [0,75; 3,51] 0,2165[2]	1,69 [0,74; 3,89] 0,2113[3]	3,7 [-2,1; 9,5] 0,2113[3]
Positive	76/1089 (7,0)	38/1067 (3,6)	1,96 [1,34; 2,87] 0,0005[2]	2,03 [1,36; 3,03] 0,0004[3]	3,4 [1,5; 5,3] 0,0004[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according PT Oral herpes from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: <,0001)					
North America / Europe	13/678 (1,9)	3/650 (0,5)	4,15 [1,19; 14,51] 0,0256[2]	4,22 [1,20; 14,86] 0,0151[3]	1,5 [0,3; 2,6] 0,0151[3]
Asia	3/203 (1,5)	1/201 (0,5)	2,97 [0,31; 28,32] 0,3440[2]	3,00 [0,31; 29,09] 0,6232[4]	1,0 [-0,9; 2,9] 0,6232[4]
Other	0/402 (0,0)	1/414 (0,2)	0,34 [0,01; 8,40] 0,5122[2]	0,34 [0,01; 8,43] 1,0000[4]	-0,2 [-0,7; 0,2] 1,0000[4]
Tumor grade (Interaction p-value: <,0001)					
G1	1/91 (1,1)	0/93 (0,0)	3,07 [0,13; 74,28] 0,4910[2]	3,10 [0,12; 77,08] 0,4946[4]	1,1 [-1,0; 3,2] 0,4946[4]
G2	8/612 (1,3)	3/603 (0,5)	2,63 [0,70; 9,86] 0,1521[2]	2,65 [0,70; 10,03] 0,1363[3]	0,8 [-0,3; 1,9] 0,1363[3]
G3	7/527 (1,3)	2/506 (0,4)	3,36 [0,70; 16,10] 0,1294[2]	3,39 [0,70; 16,41] 0,1786[4]	0,9 [-0,2; 2,1] 0,1786[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Oropharyngeal pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	5/114 (4,4)	0/132 (0,0)	12,72 [0,71; 227,60] 0,0839[2]	13,31 [0,73; 243,39] 0,0204[4]	4,4 [0,6; 8,1] 0,0204[4]
Aromatase inhibitor	44/1169 (3,8)	31/1133 (2,7)	1,38 [0,88; 2,16] 0,1669[2]	1,39 [0,87; 2,22] 0,1649[3]	1,0 [-0,4; 2,5] 0,1649[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Palpitations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	2/114 (1,8)	0/132 (0,0)	5,78 [0,28; 119,22] 0,2557[2]	5,89 [0,28; 123,94] 0,2137[4]	1,8 [-0,7; 4,2] 0,2137[4]
Aromatase inhibitor	25/1169 (2,1)	12/1133 (1,1)	2,02 [1,02; 4,00] 0,0439[2]	2,04 [1,02; 4,08] 0,0395[3]	1,1 [0,1; 2,1] 0,0395[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Paronychia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	0/114 (0,0)	1/132 (0,8)	0,39 [0,02; 9,37] 0,5582[2]	0,38 [0,02; 9,49] 1,0000[4]	-0,8 [-2,2; 0,7] 1,0000[4]
Aromatase inhibitor	15/1169 (1,3)	3/1133 (0,3)	4,85 [1,41; 16,69] 0,0124[2]	4,90 [1,41; 16,96] 0,0055[3]	1,0 [0,3; 1,7] 0,0055[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Platelet count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	9/156 (5,8)	1/169 (0,6)	9,75 [1,25; 76,08] 0,0298[2]	10,29 [1,29; 82,15] 0,0082[4]	5,2 [1,3; 9,0] 0,0082[4]
Positive	103/1089 (9,5)	8/1067 (0,7)	12,61 [6,17; 25,77] <,0001[2]	13,83 [6,70; 28,54] <,0001[3]	8,7 [6,9; 10,5] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Pneumonitis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	11/918 (1,2)	3/937 (0,3)	3,74 [1,05; 13,37] 0,0422[2]	3,78 [1,05; 13,58] 0,0289[3]	0,9 [0,1; 1,7] 0,0289[3]
≥ 65 years	7/365 (1,9)	0/328 (0,0)	13,48 [0,77; 235,17] 0,0745[2]	13,74 [0,78; 241,60] 0,0161[4]	1,9 [0,5; 3,3] 0,0161[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	17/1169 (1,5)	3/1133 (0,3)	5,49 [1,61; 18,69] 0,0064[2]	5,56 [1,62; 19,02] 0,0021[3]	1,2 [0,4; 1,9] 0,0021[3]
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	13/1070 (1,2)	0/1020 (0,0)	25,74 [1,53; 432,42] 0,0240[2]	26,06 [1,55; 438,87] 0,0004[3]	1,2 [0,6; 1,9] 0,0004[3]
ECOG-PS 1	5/213 (2,3)	3/245 (1,2)	1,92 [0,46; 7,93] 0,3689[2]	1,94 [0,46; 8,21] 0,4813[4]	1,1 [-1,3; 3,6] 0,4813[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Pruritus from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	11/156 (7,1)	12/169 (7,1)	0,99 [0,45; 2,19] 0,9862[2]	0,99 [0,42; 2,32] 0,9862[3]	-0,0 [-5,6; 5,5] 0,9862[3]
Positive	93/1089 (8,5)	45/1067 (4,2)	2,02 [1,43; 2,86] <,0001[2]	2,12 [1,47; 3,06] <,0001[3]	4,3 [2,3; 6,4] <,0001[3]
Unknown	3/10 (30,0)	0/7 (0,0)	5,09 [0,30; 85,39] 0,2580[2]	7,00 [0,31; 160,32] 0,2279[4]	30,0 [1,6; 58,4] 0,2279[4]
ECOG-PS (Interaction p-value: 0,0111)					
ECOG-PS 0	79/1070 (7,4)	51/1020 (5,0)	1,48 [1,05; 2,08] 0,0253[2]	1,51 [1,05; 2,18] 0,0241[3]	2,4 [0,3; 4,4] 0,0241[3]
ECOG-PS 1	28/213 (13,1)	7/245 (2,9)	4,60 [2,05; 10,32] 0,0002[2]	5,15 [2,20; 12,04] <,0001[3]	10,3 [5,3; 15,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Pyrexia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	14/156 (9,0)	7/169 (4,1)	2,17 [0,90; 5,23] 0,0853[2]	2,28 [0,90; 5,81] 0,0767[3]	4,8 [-0,6; 10,2] 0,0767[3]
Positive	82/1089 (7,5)	35/1067 (3,3)	2,30 [1,56; 3,38] <,0001[2]	2,40 [1,60; 3,60] <,0001[3]	4,2 [2,4; 6,1] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Rash maculo-papular from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	17/918 (1,9)	3/937 (0,3)	5,78 [1,70; 19,67] 0,0049[2]	5,87 [1,72; 20,11] 0,0014[3]	1,5 [0,6; 2,5] 0,0014[3]
≥ 65 years	5/365 (1,4)	0/328 (0,0)	9,89 [0,55; 178,14] 0,1204[2]	10,02 [0,55; 181,97] 0,0634[4]	1,4 [0,2; 2,6] 0,0634[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	2/114 (1,8)	0/132 (0,0)	5,78 [0,28; 119,22] 0,2557[2]	5,89 [0,28; 123,94] 0,2137[4]	1,8 [-0,7; 4,2] 0,2137[4]
Aromatase inhibitor	20/1169 (1,7)	3/1133 (0,3)	6,46 [1,93; 21,68] 0,0025[2]	6,56 [1,94; 22,13] 0,0005[3]	1,4 [0,6; 2,2] 0,0005[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Seroma from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor grade (Interaction p-value: 0,0010)					
G1	3/91 (3,3)	0/93 (0,0)	7,15 [0,37; 136,54] 0,1910[2]	7,40 [0,38; 145,22] 0,1189[4]	3,3 [-0,4; 7,0] 0,1189[4]
G2	8/612 (1,3)	4/603 (0,7)	1,97 [0,60; 6,51] 0,2659[2]	1,98 [0,59; 6,62] 0,2565[3]	0,6 [-0,5; 1,8] 0,2565[3]
G3	5/527 (0,9)	1/506 (0,2)	4,80 [0,56; 40,95] 0,1515[2]	4,84 [0,56; 41,55] 0,2180[4]	0,8 [-0,2; 1,7] 0,2180[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	2/156 (1,3)	1/169 (0,6)	2,17 [0,20; 23,66] 0,5261[2]	2,18 [0,20; 24,30] 0,6093[4]	0,7 [-1,4; 2,8] 0,6093[4]
Positive	13/1089 (1,2)	4/1067 (0,4)	3,18 [1,04; 9,73] 0,0422[2]	3,21 [1,04; 9,88] 0,0316[3]	0,8 [0,1; 1,6] 0,0316[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	0/114 (0,0)	0/132 (0,0)	NE	NE	NE
Aromatase inhibitor	16/1169 (1,4)	5/1133 (0,4)	3,10 [1,14; 8,44] 0,0267[2]	3,13 [1,14; 8,57] 0,0193[3]	0,9 [0,2; 1,7] 0,0193[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Thrombocytopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	5/114 (4,4)	0/132 (0,0)	12,72 [0,71; 227,60] 0,0839[2]	13,31 [0,73; 243,39] 0,0204[4]	4,4 [0,6; 8,1] 0,0204[4]
Aromatase inhibitor	81/1169 (6,9)	9/1133 (0,8)	8,72 [4,40; 17,28] <,0001[2]	9,30 [4,65; 18,61] <,0001[3]	6,1 [4,6; 7,7] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Urinary tract infection from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	13/156 (8,3)	7/169 (4,1)	2,01 [0,82; 4,91] 0,1248[2]	2,10 [0,82; 5,42] 0,1162[3]	4,2 [-1,1; 9,5] 0,1162[3]
Positive	101/1089 (9,3)	60/1067 (5,6)	1,65 [1,21; 2,24] 0,0015[2]	1,72 [1,23; 2,39] 0,0013[3]	3,7 [1,4; 5,9] 0,0013[3]
Unknown	2/10 (20,0)	0/7 (0,0)	3,64 [0,20; 65,86] 0,3824[2]	4,41 [0,18; 107,28] 0,4853[4]	20,0 [-4,8; 44,8] 0,4853[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Viral infection from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	3/114 (2,6)	0/132 (0,0)	8,10 [0,42; 155,09] 0,1651[2]	8,32 [0,43; 162,77] 0,0981[4]	2,6 [-0,3; 5,6] 0,0981[4]
Aromatase inhibitor	12/1169 (1,0)	2/1133 (0,2)	5,82 [1,30; 25,92] 0,0210[2]	5,87 [1,31; 26,26] 0,0087[3]	0,8 [0,2; 1,5] 0,0087[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Vitamin B12 deficiency from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: <,0001)					
Neoadjuvant chemotherapy	5/430 (1,2)	1/415 (0,2)	4,83 [0,57; 41,13] 0,1500[2]	4,87 [0,57; 41,87] 0,2175[4]	0,9 [-0,2; 2,0] 0,2175[4]
Adjuvant chemotherapy	11/784 (1,4)	3/769 (0,4)	3,60 [1,01; 12,84] 0,0487[2]	3,63 [1,01; 13,07] 0,0347[3]	1,0 [0,1; 1,9] 0,0347[3]
No chemotherapy	0/69 (0,0)	0/81 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	2/114 (1,8)	0/132 (0,0)	5,78 [0,28; 119,22] 0,2557[2]	5,89 [0,28; 123,94] 0,2137[4]	1,8 [-0,7; 4,2] 0,2137[4]
Aromatase inhibitor	14/1169 (1,2)	4/1133 (0,4)	3,39 [1,12; 10,27] 0,0307[2]	3,42 [1,12; 10,43] 0,0215[3]	0,8 [0,1; 1,6] 0,0215[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT Vomiting from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Number of positive lymph nodes (Interaction p-value: 0,0194)					
0-3	74/427 (17,3)	17/418 (4,1)	4,26 [2,56; 7,09] <,0001[2]	4,94 [2,86; 8,54] <,0001[3]	13,3 [9,2; 17,3] <,0001[3]
4-9	86/549 (15,7)	30/542 (5,5)	2,83 [1,90; 4,21] <,0001[2]	3,17 [2,05; 4,89] <,0001[3]	10,1 [6,5; 13,7] <,0001[3]
≥ 10	62/307 (20,2)	6/305 (2,0)	10,27 [4,51; 23,38] <,0001[2]	12,61 [5,36; 29,65] <,0001[3]	18,2 [13,5; 23,0] <,0001[3]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	28/156 (17,9)	12/169 (7,1)	2,53 [1,33; 4,80] 0,0045[2]	2,86 [1,40; 5,85] 0,0029[3]	10,8 [3,7; 18,0] 0,0029[3]
Positive	184/1089 (16,9)	41/1067 (3,8)	4,40 [3,17; 6,10] <,0001[2]	5,09 [3,59; 7,22] <,0001[3]	13,1 [10,5; 15,6] <,0001[3]
Unknown	3/10 (30,0)	0/7 (0,0)	5,09 [0,30; 85,39] 0,2580[2]	7,00 [0,31; 160,32] 0,2279[4]	30,0 [1,6; 58,4] 0,2279[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events according PT White blood cell count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	32/156 (20,5)	11/169 (6,5)	3,15 [1,65; 6,03] 0,0005[2]	3,71 [1,80; 7,65] 0,0002[3]	14,0 [6,7; 21,4] 0,0002[3]
Positive	246/1089 (22,6)	39/1067 (3,7)	6,18 [4,46; 8,57] <,0001[2]	7,69 [5,42; 10,91] <,0001[3]	18,9 [16,2; 21,7] <,0001[3]
Unknown	2/10 (20,0)	0/7 (0,0)	3,64 [0,20; 65,86] 0,3824[2]	4,41 [0,18; 107,28] 0,4853[4]	20,0 [-4,8; 44,8] 0,4853[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according SOC Blood and lymphatic system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0041)					
North America / Europe	268/678 (39,5)	42/650 (6,5)	6,12 [4,50; 8,32] <,0001[2]	9,46 [6,68; 13,41] <,0001[3]	33,1 [28,9; 37,2] <,0001[3]
Asia	97/203 (47,8)	10/201 (5,0)	9,60 [5,16; 17,87] <,0001[2]	17,48 [8,74; 34,95] <,0001[3]	42,8 [35,3; 50,3] <,0001[3]
Other	222/402 (55,2)	61/414 (14,7)	3,75 [2,93; 4,80] <,0001[2]	7,14 [5,10; 9,98] <,0001[3]	40,5 [34,5; 46,4] <,0001[3]
Progesterone receptor status (Interaction p-value: 0,0474)					
Negative	73/156 (46,8)	13/169 (7,7)	6,08 [3,52; 10,53] <,0001[2]	10,55 [5,52; 20,16] <,0001[3]	39,1 [30,3; 47,9] <,0001[3]
Positive	509/1089 (46,7)	97/1067 (9,1)	5,14 [4,21; 6,28] <,0001[2]	8,78 [6,90; 11,16] <,0001[3]	37,6 [34,2; 41,1] <,0001[3]
Unknown	1/10 (10,0)	2/7 (28,6)	0,35 [0,04; 3,15] 0,3491[2]	0,28 [0,02; 3,88] 0,5368[4]	-18,6 [-56,9; 19,7] 0,5368[4]
Race (Interaction p-value: 0,0398)					
White	431/958 (45,0)	90/944 (9,5)	4,72 [3,83; 5,81] <,0001[2]	7,76 [6,03; 9,98] <,0001[3]	35,5 [31,8; 39,1] <,0001[3]
Asian	116/250 (46,4)	12/242 (5,0)	9,36 [5,31; 16,50] <,0001[2]	16,59 [8,82; 31,20] <,0001[3]	41,4 [34,7; 48,2] <,0001[3]
Other	33/62 (53,2)	10/64 (15,6)	3,41 [1,84; 6,30] <,0001[2]	6,14 [2,66; 14,22] <,0001[3]	37,6 [22,3; 52,9] <,0001[3]
First endocrine therapy (Interaction p-value: 0,0170)					
Tamoxifen	50/114 (43,9)	3/132 (2,3)	19,30 [6,19; 60,21] <,0001[2]	33,59 [10,09; 111,87] <,0001[3]	41,6 [32,1; 51,0] <,0001[3]
Aromatase inhibitor	537/1169 (45,9)	110/1133 (9,7)	4,73 [3,92; 5,71] <,0001[2]	7,90 [6,29; 9,92] <,0001[3]	36,2 [32,9; 39,6] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Cardiac disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Number of positive lymph nodes (Interaction p-value: 0,0194)					
0-3	39/427 (9,1)	13/418 (3,1)	2,94 [1,59; 5,42] 0,0006[2]	3,13 [1,65; 5,96] 0,0003[3]	6,0 [2,8; 9,2] 0,0003[3]
4-9	30/549 (5,5)	31/542 (5,7)	0,96 [0,59; 1,56] 0,8545[2]	0,95 [0,57; 1,60] 0,8545[3]	-0,3 [-3,0; 2,5] 0,8545[3]
≥ 10	21/307 (6,8)	14/305 (4,6)	1,49 [0,77; 2,88] 0,2343[2]	1,53 [0,76; 3,06] 0,2307[3]	2,3 [-1,4; 5,9] 0,2307[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Eye disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	29/156 (18,6)	9/169 (5,3)	3,49 [1,71; 7,14] 0,0006[2]	4,06 [1,85; 8,88] 0,0002[3]	13,3 [6,3; 20,2] 0,0002[3]
Positive	162/1089 (14,9)	56/1067 (5,2)	2,83 [2,12; 3,80] <,0001[2]	3,15 [2,30; 4,33] <,0001[3]	9,6 [7,1; 12,1] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Gastrointestinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0011)					
North America / Europe	630/678 (92,9)	251/650 (38,6)	2,41 [2,18; 2,66] <,0001[2]	20,86 [14,95; 29,12] <,0001[3]	54,3 [50,1; 58,5] <,0001[3]
Asia	191/203 (94,1)	61/201 (30,3)	3,10 [2,51; 3,83] <,0001[2]	36,53 [18,95; 70,41] <,0001[3]	63,7 [56,6; 70,9] <,0001[3]
Other	321/402 (79,9)	96/414 (23,2)	3,44 [2,87; 4,13] <,0001[2]	13,13 [9,40; 18,33] <,0001[3]	56,7 [51,0; 62,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according SOC General disorders and administration site conditions from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0361)					
North America / Europe	444/678 (65,5)	272/650 (41,8)	1,56 [1,41; 1,74] <,0001[2]	2,64 [2,11; 3,29] <,0001[3]	23,6 [18,4; 28,9] <,0001[3]
Asia	90/203 (44,3)	46/201 (22,9)	1,94 [1,44; 2,61] <,0001[2]	2,68 [1,75; 4,13] <,0001[3]	21,4 [12,5; 30,4] <,0001[3]
Other	179/402 (44,5)	88/414 (21,3)	2,09 [1,69; 2,60] <,0001[2]	2,97 [2,19; 4,04] <,0001[3]	23,3 [17,0; 29,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt_sub.sas
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Table: Interacting subgroups - adverse events according SOC Investigations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0368)					
North America / Europe	301/678 (44,4)	117/650 (18,0)	2,47 [2,05; 2,97] <,0001[2]	3,64 [2,83; 4,67] <,0001[3]	26,4 [21,6; 31,2] <,0001[3]
Asia	155/203 (76,4)	62/201 (30,8)	2,48 [1,99; 3,09] <,0001[2]	7,24 [4,66; 11,25] <,0001[3]	45,5 [36,9; 54,2] <,0001[3]
Other	165/402 (41,0)	96/414 (23,2)	1,77 [1,43; 2,19] <,0001[2]	2,31 [1,70; 3,12] <,0001[3]	17,9 [11,6; 24,2] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt_sub.sas
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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events according SOC Metabolism and nutrition disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0054)					
North America / Europe	197/678 (29,1)	99/650 (15,2)	1,91 [1,54; 2,37] <,0001[2]	2,28 [1,74; 2,99] <,0001[3]	13,8 [9,4; 18,2] <,0001[3]
Asia	54/203 (26,6)	18/201 (9,0)	2,97 [1,81; 4,88] <,0001[2]	3,68 [2,07; 6,55] <,0001[3]	17,6 [10,4; 24,9] <,0001[3]
Other	107/402 (26,6)	85/414 (20,5)	1,30 [1,01; 1,66] 0,0414[2]	1,40 [1,01; 1,94] 0,0405[3]	6,1 [0,3; 11,9] 0,0405[3]
Primary tumor size (Interaction p-value: 0,0345)					
< 20 mm	80/331 (24,2)	61/335 (18,2)	1,33 [0,99; 1,79] 0,0612[2]	1,43 [0,98; 2,08] 0,0598[3]	6,0 [-0,2; 12,2] 0,0598[3]
≥ 20 but < 50 mm	176/646 (27,2)	99/653 (15,2)	1,80 [1,44; 2,24] <,0001[2]	2,10 [1,59; 2,76] <,0001[3]	12,1 [7,7; 16,5] <,0001[3]
≥ 50 mm	97/289 (33,6)	37/265 (14,0)	2,40 [1,71; 3,38] <,0001[2]	3,11 [2,04; 4,76] <,0001[3]	19,6 [12,7; 26,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi²-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Renal and urinary disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0001)					
Negative	12/156 (7,7)	11/169 (6,5)	1,18 [0,54; 2,60] 0,6780[2]	1,20 [0,51; 2,80] 0,6777[3]	1,2 [-4,4; 6,8] 0,6777[3]
Positive	85/1089 (7,8)	58/1067 (5,4)	1,44 [1,04; 1,98] 0,0281[2]	1,47 [1,04; 2,08] 0,0271[3]	2,4 [0,3; 4,5] 0,0271[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,0348)					
White	81/958 (8,5)	47/944 (5,0)	1,70 [1,20; 2,40] 0,0029[2]	1,76 [1,22; 2,56] 0,0025[3]	3,5 [1,2; 5,7] 0,0025[3]
Asian	12/250 (4,8)	12/242 (5,0)	0,97 [0,44; 2,11] 0,9349[2]	0,97 [0,43; 2,20] 0,9349[3]	-0,2 [-4,0; 3,6] 0,9349[3]
Other	4/62 (6,5)	10/64 (15,6)	0,41 [0,14; 1,25] 0,1169[2]	0,37 [0,11; 1,26] 0,1014[3]	-9,2 [-20,0; 1,6] 0,1014[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Respiratory, thoracic and mediastinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	48/156 (30,8)	34/169 (20,1)	1,53 [1,04; 2,24] 0,0291[2]	1,76 [1,06; 2,93] 0,0272[3]	10,7 [1,2; 20,1] 0,0272[3]
Positive	314/1089 (28,8)	207/1067 (19,4)	1,49 [1,27; 1,73] <,0001[2]	1,68 [1,38; 2,06] <,0001[3]	9,4 [5,8; 13,0] <,0001[3]
Unknown	3/10 (30,0)	0/7 (0,0)	5,09 [0,30; 85,39] 0,2580[2]	7,00 [0,31; 160,32] 0,2279[4]	30,0 [1,6; 58,4] 0,2279[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events according SOC Skin and subcutaneous tissue disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,0149)					
North America / Europe	296/678 (43,7)	174/650 (26,8)	1,63 [1,40; 1,90] <,0001[2]	2,12 [1,68; 2,67] <,0001[3]	16,9 [11,8; 21,9] <,0001[3]
Asia	90/203 (44,3)	58/201 (28,9)	1,54 [1,18; 2,01] 0,0016[2]	1,96 [1,30; 2,96] 0,0012[3]	15,5 [6,2; 24,7] 0,0012[3]
Other	120/402 (29,9)	47/414 (11,4)	2,63 [1,93; 3,58] <,0001[2]	3,32 [2,29; 4,82] <,0001[3]	18,5 [13,1; 23,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - serious adverse events according SOC Gastrointestinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0457)					
< 65 years	24/918 (2,6)	7/937 (0,7)	3,50 [1,52; 8,08] 0,0034[2]	3,57 [1,53; 8,32] 0,0017[3]	1,9 [0,7; 3,0] 0,0017[3]
≥ 65 years	7/365 (1,9)	7/328 (2,1)	0,90 [0,32; 2,53] 0,8399[2]	0,90 [0,31; 2,58] 0,8398[3]	-0,2 [-2,3; 1,9] 0,8398[3]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	3/156 (1,9)	3/169 (1,8)	1,08 [0,22; 5,29] 0,9212[2]	1,08 [0,22; 5,46] 1,0000[4]	0,1 [-2,8; 3,1] 1,0000[4]
Positive	26/1089 (2,4)	11/1067 (1,0)	2,32 [1,15; 4,66] 0,0187[2]	2,35 [1,15; 4,78] 0,0153[3]	1,4 [0,3; 2,4] 0,0153[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	4/114 (3,5)	0/132 (0,0)	10,41 [0,57; 191,27] 0,1147[2]	10,79 [0,57; 202,64] 0,0448[4]	3,5 [0,1; 6,9] 0,0448[4]
Aromatase inhibitor	27/1169 (2,3)	14/1133 (1,2)	1,87 [0,99; 3,55] 0,0555[2]	1,89 [0,99; 3,62] 0,0514[3]	1,1 [-0,0; 2,1] 0,0514[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - serious adverse events according SOC Infections and infestations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Primary tumor size (Interaction p-value: 0,0286)					
< 20 mm	17/331 (5,1)	4/335 (1,2)	4,30 [1,46; 12,65] 0,0080[2]	4,48 [1,49; 13,46] 0,0036[3]	3,9 [1,3; 6,6] 0,0036[3]
≥ 20 but < 50 mm	30/646 (4,6)	25/653 (3,8)	1,21 [0,72; 2,04] 0,4663[2]	1,22 [0,71; 2,10] 0,4655[3]	0,8 [-1,4; 3,0] 0,4655[3]
≥ 50 mm	21/289 (7,3)	5/265 (1,9)	3,85 [1,47; 10,07] 0,0060[2]	4,07 [1,51; 10,97] 0,0028[3]	5,4 [2,0; 8,8] 0,0028[3]
Tumor grade (Interaction p-value: 0,0362)					
G1	4/91 (4,4)	5/93 (5,4)	0,82 [0,23; 2,95] 0,7583[2]	0,81 [0,21; 3,11] 1,0000[4]	-1,0 [-7,2; 5,2] 1,0000[4]
G2	37/612 (6,0)	9/603 (1,5)	4,05 [1,97; 8,32] 0,0001[2]	4,25 [2,03; 8,88] <,0001[3]	4,6 [2,4; 6,7] <,0001[3]
G3	22/527 (4,2)	18/506 (3,6)	1,17 [0,64; 2,16] 0,6077[2]	1,18 [0,63; 2,23] 0,6072[3]	0,6 [-1,7; 3,0] 0,6072[3]
GX	5/51 (9,8)	2/59 (3,4)	2,89 [0,59; 14,27] 0,1923[2]	3,10 [0,57; 16,71] 0,2463[4]	6,4 [-3,0; 15,8] 0,2463[4]
Progesterone receptor status (Interaction p-value: 0,0119)					
Negative	7/156 (4,5)	7/169 (4,1)	1,08 [0,39; 3,02] 0,8783[2]	1,09 [0,37; 3,17] 0,8783[3]	0,3 [-4,1; 4,8] 0,8783[3]
Positive	60/1089 (5,5)	26/1067 (2,4)	2,26 [1,44; 3,55] 0,0004[2]	2,33 [1,46; 3,73] 0,0003[3]	3,1 [1,4; 4,7] 0,0003[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	5/114 (4,4)	0/132 (0,0)	12,72 [0,71; 227,60] 0,0839[2]	13,31 [0,73; 243,39] 0,0204[4]	4,4 [0,6; 8,1] 0,0204[4]
Aromatase inhibitor	64/1169 (5,5)	34/1133 (3,0)	1,82 [1,21; 2,74] 0,0039[2]	1,87 [1,22; 2,86] 0,0033[3]	2,5 [0,8; 4,1] 0,0033[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Alanine aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	34/1169 (2,9)	6/1133 (0,5)	5,49 [2,31; 13,03] 0,0001[2]	5,63 [2,35; 13,45] <,0001[3]	2,4 [1,3; 3,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Anaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	0/114 (0,0)	0/132 (0,0)	NE	NE	NE
Aromatase inhibitor	38/1169 (3,3)	5/1133 (0,4)	7,37 [2,91; 18,65] <,0001[2]	7,58 [2,97; 19,33] <,0001[3]	2,8 [1,7; 3,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Aspartate aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	21/1169 (1,8)	4/1133 (0,4)	5,09 [1,75; 14,78] 0,0028[2]	5,16 [1,77; 15,09] 0,0008[3]	1,4 [0,6; 2,3] 0,0008[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Diarrhoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor grade (Interaction p-value: <,0001)					
G1	8/91 (8,8)	0/93 (0,0)	17,37 [1,02; 296,59] 0,0486[2]	19,04 [1,08; 334,86] 0,0030[4]	8,8 [3,0; 14,6] 0,0030[4]
G2	52/612 (8,5)	1/603 (0,2)	51,24 [7,11; 369,43] <,0001[2]	55,90 [7,70; 405,71] <,0001[3]	8,3 [6,1; 10,6] <,0001[3]
G3	63/527 (12,0)	1/506 (0,2)	60,49 [8,42; 434,48] <,0001[2]	68,57 [9,47; 496,35] <,0001[3]	11,8 [9,0; 14,6] <,0001[3]
GX	2/51 (3,9)	0/59 (0,0)	5,77 [0,28; 117,46] 0,2544[2]	6,01 [0,28; 128,14] 0,2127[4]	3,9 [-1,4; 9,2] 0,2127[4]
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	19/156 (12,2)	1/169 (0,6)	20,58 [2,79; 151,95] 0,0030[2]	23,30 [3,08; 176,25] <,0001[3]	11,6 [6,3; 16,8] <,0001[3]
Positive	102/1089 (9,4)	1/1067 (0,1)	99,94 [13,97; 715,01] <,0001[2]	110,16 [15,34; 791,10] <,0001[3]	9,3 [7,5; 11,0] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	7/114 (6,1)	0/132 (0,0)	17,35 [1,00; 300,45] 0,0499[2]	18,49 [1,04; 327,38] 0,0041[4]	6,1 [1,7; 10,5] 0,0041[4]
Aromatase inhibitor	118/1169 (10,1)	2/1133 (0,2)	57,18 [14,17; 230,78] <,0001[2]	63,49 [15,65; 257,50] <,0001[3]	9,9 [8,2; 11,7] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Fatigue from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	2/114 (1,8)	0/132 (0,0)	5,78 [0,28; 119,22] 0,2557[2]	5,89 [0,28; 123,94] 0,2137[4]	1,8 [-0,7; 4,2] 0,2137[4]
Aromatase inhibitor	32/1169 (2,7)	2/1133 (0,2)	15,51 [3,73; 64,56] 0,0002[2]	15,92 [3,81; 66,57] <,0001[3]	2,6 [1,6; 3,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Gamma-glutamyltransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	14/918 (1,5)	5/937 (0,5)	2,86 [1,03; 7,90] 0,0430[2]	2,89 [1,04; 8,05] 0,0340[3]	1,0 [0,1; 1,9] 0,0340[3]
≥ 65 years	6/365 (1,6)	0/328 (0,0)	11,69 [0,66; 206,64] 0,0935[2]	11,88 [0,67; 211,69] 0,0319[4]	1,6 [0,3; 2,9] 0,0319[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	0/114 (0,0)	0/132 (0,0)	NE	NE	NE
Aromatase inhibitor	20/1169 (1,7)	5/1133 (0,4)	3,88 [1,46; 10,29] 0,0065[2]	3,93 [1,47; 10,50] 0,0033[3]	1,3 [0,4; 2,1] 0,0033[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Hypokalaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	17/1169 (1,5)	5/1133 (0,4)	3,30 [1,22; 8,90] 0,0187[2]	3,33 [1,22; 9,05] 0,0125[3]	1,0 [0,2; 1,8] 0,0125[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Leukopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	4/114 (3,5)	0/132 (0,0)	10,41 [0,57; 191,27] 0,1147[2]	10,79 [0,57; 202,64] 0,0448[4]	3,5 [0,1; 6,9] 0,0448[4]
Aromatase inhibitor	43/1169 (3,7)	2/1133 (0,2)	20,84 [5,06; 85,81] <,0001[2]	21,60 [5,22; 89,36] <,0001[3]	3,5 [2,4; 4,6] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Lymphocyte count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	5/156 (3,2)	1/169 (0,6)	5,42 [0,64; 45,85] 0,1211[2]	5,56 [0,64; 48,15] 0,1086[4]	2,6 [-0,4; 5,6] 0,1086[4]
Positive	34/1089 (3,1)	4/1067 (0,4)	8,33 [2,97; 23,39] <,0001[2]	8,56 [3,03; 24,22] <,0001[3]	2,7 [1,7; 3,8] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	0/114 (0,0)	1/132 (0,8)	0,39 [0,02; 9,37] 0,5582[2]	0,38 [0,02; 9,49] 1,0000[4]	-0,8 [-2,2; 0,7] 1,0000[4]
Aromatase inhibitor	42/1169 (3,6)	4/1133 (0,4)	10,18 [3,66; 28,29] <,0001[2]	10,52 [3,76; 29,43] <,0001[3]	3,2 [2,1; 4,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Lymphopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: <,0001)					
< 65 years	12/918 (1,3)	0/937 (0,0)	25,52 [1,51; 430,34] 0,0246[2]	25,85 [1,53; 437,32] 0,0004[3]	1,3 [0,6; 2,0] 0,0004[3]
≥ 65 years	10/365 (2,7)	1/328 (0,3)	8,99 [1,16; 69,82] 0,0358[2]	9,21 [1,17; 72,35] 0,0105[3]	2,4 [0,7; 4,2] 0,0105[3]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	21/1169 (1,8)	1/1133 (0,1)	20,35 [2,74; 151,06] 0,0032[2]	20,71 [2,78; 154,20] <,0001[3]	1,7 [0,9; 2,5] <,0001[3]
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	17/1070 (1,6)	0/1020 (0,0)	33,37 [2,01; 554,11] 0,0144[2]	33,90 [2,04; 564,51] <,0001[3]	1,6 [0,8; 2,3] <,0001[3]
ECOG-PS 1	5/213 (2,3)	1/245 (0,4)	5,75 [0,68; 48,84] 0,1090[2]	5,87 [0,68; 50,61] 0,1013[4]	1,9 [-0,2; 4,1] 0,1013[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Neutropenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor grade (Interaction p-value: <,0001)					
G1	5/91 (5,5)	0/93 (0,0)	11,24 [0,63; 200,37] 0,0997[2]	11,89 [0,65; 218,22] 0,0280[4]	5,5 [0,8; 10,2] 0,0280[4]
G2	64/612 (10,5)	3/603 (0,5)	21,02 [6,64; 66,54] <,0001[2]	23,36 [7,30; 74,78] <,0001[3]	10,0 [7,5; 12,4] <,0001[3]
G3	65/527 (12,3)	1/506 (0,2)	62,41 [8,69; 448,06] <,0001[2]	71,05 [9,82; 514,09] <,0001[3]	12,1 [9,3; 15,0] <,0001[3]
GX	5/51 (9,8)	0/59 (0,0)	12,69 [0,72; 224,11] 0,0828[2]	14,08 [0,76; 261,07] 0,0192[4]	9,8 [1,6; 18,0] 0,0192[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	13/114 (11,4)	0/132 (0,0)	31,23 [1,88; 519,50] 0,0164[2]	35,25 [2,07; 599,95] <,0001[3]	11,4 [5,6; 17,2] <,0001[3]
Aromatase inhibitor	126/1169 (10,8)	4/1133 (0,4)	30,53 [11,32; 82,33] <,0001[2]	34,10 [12,56; 92,59] <,0001[3]	10,4 [8,6; 12,2] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Neutrophil count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	7/114 (6,1)	0/132 (0,0)	17,35 [1,00; 300,45] 0,0499[2]	18,49 [1,04; 327,38] 0,0041[4]	6,1 [1,7; 10,5] 0,0041[4]
Aromatase inhibitor	121/1169 (10,4)	3/1133 (0,3)	39,09 [12,47; 122,55] <,0001[2]	43,49 [13,79; 137,16] <,0001[3]	10,1 [8,3; 11,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT Platelet count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	1/114 (0,9)	0/132 (0,0)	3,47 [0,14; 84,34] 0,4448[2]	3,50 [0,14; 86,82] 0,4634[4]	0,9 [-0,8; 2,6] 0,4634[4]
Aromatase inhibitor	12/1169 (1,0)	0/1133 (0,0)	24,23 [1,44; 408,77] 0,0270[2]	24,48 [1,45; 413,98] 0,0006[3]	1,0 [0,4; 1,6] 0,0006[3]
ECOG-PS (Interaction p-value: <,0001)					
ECOG-PS 0	11/1070 (1,0)	0/1020 (0,0)	21,93 [1,29; 371,60] 0,0325[2]	22,15 [1,30; 376,42] 0,0012[3]	1,0 [0,4; 1,6] 0,0012[3]
ECOG-PS 1	2/213 (0,9)	0/245 (0,0)	5,75 [0,28; 119,06] 0,2581[2]	5,80 [0,28; 121,56] 0,2157[4]	0,9 [-0,4; 2,2] 0,2157[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according PT White blood cell count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	5/114 (4,4)	0/132 (0,0)	12,72 [0,71; 227,60] 0,0839[2]	13,31 [0,73; 243,39] 0,0204[4]	4,4 [0,6; 8,1] 0,0204[4]
Aromatase inhibitor	93/1169 (8,0)	3/1133 (0,3)	30,05 [9,54; 94,58] <,0001[2]	32,56 [10,28; 103,10] <,0001[3]	7,7 [6,1; 9,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Blood and lymphatic system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor grade (Interaction p-value: <,0001)					
G1	13/91 (14,3)	0/93 (0,0)	27,59 [1,66; 457,30] 0,0206[2]	32,16 [1,88; 549,64] 0,0002[3]	14,3 [7,1; 21,5] 0,0002[3]
G2	105/612 (17,2)	9/603 (1,5)	11,50 [5,87; 22,50] <,0001[2]	13,67 [6,85; 27,28] <,0001[3]	15,7 [12,5; 18,8] <,0001[3]
G3	82/527 (15,6)	4/506 (0,8)	19,68 [7,27; 53,30] <,0001[2]	23,13 [8,41; 63,60] <,0001[3]	14,8 [11,6; 18,0] <,0001[3]
GX	9/51 (17,6)	0/59 (0,0)	21,92 [1,31; 367,60] 0,0318[2]	26,60 [1,51; 469,58] 0,0007[4]	17,6 [7,2; 28,1] 0,0007[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	17/114 (14,9)	0/132 (0,0)	40,48 [2,46; 665,67] 0,0096[2]	47,56 [2,83; 800,58] <,0001[3]	14,9 [8,4; 21,5] <,0001[3]
Aromatase inhibitor	192/1169 (16,4)	13/1133 (1,1)	14,31 [8,21; 24,95] <,0001[2]	16,93 [9,59; 29,88] <,0001[3]	15,3 [13,1; 17,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi²-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Gastrointestinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	21/156 (13,5)	5/169 (3,0)	4,55 [1,76; 11,77] 0,0018[2]	5,10 [1,87; 13,89] 0,0005[3]	10,5 [4,6; 16,4] 0,0005[3]
Positive	121/1089 (11,1)	13/1067 (1,2)	9,12 [5,18; 16,06] <,0001[2]	10,13 [5,68; 18,08] <,0001[3]	9,9 [7,9; 11,9] <,0001[3]
Unknown	2/10 (20,0)	0/7 (0,0)	3,64 [0,20; 65,86] 0,3824[2]	4,41 [0,18; 107,28] 0,4853[4]	20,0 [-4,8; 44,8] 0,4853[4]
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	8/114 (7,0)	0/132 (0,0)	19,66 [1,15; 336,92] 0,0399[2]	21,15 [1,21; 370,63] 0,0019[4]	7,0 [2,3; 11,7] 0,0019[4]
Aromatase inhibitor	140/1169 (12,0)	18/1133 (1,6)	7,54 [4,65; 12,23] <,0001[2]	8,43 [5,12; 13,87] <,0001[3]	10,4 [8,4; 12,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according SOC General disorders and administration site conditions from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0442)					
Negative	9/156 (5,8)	1/169 (0,6)	9,75 [1,25; 76,08] 0,0298[2]	10,29 [1,29; 82,15] 0,0082[4]	5,2 [1,3; 9,0] 0,0082[4]
Positive	44/1089 (4,0)	6/1067 (0,6)	7,19 [3,07; 16,79] <,0001[2]	7,45 [3,16; 17,55] <,0001[3]	3,5 [2,2; 4,7] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Infections and infestations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,0371)					
Negative	6/156 (3,8)	7/169 (4,1)	0,93 [0,32; 2,70] 0,8919[2]	0,93 [0,30; 2,82] 0,8918[3]	-0,3 [-4,6; 4,0] 0,8918[3]
Positive	61/1089 (5,6)	28/1067 (2,6)	2,13 [1,38; 3,31] 0,0007[2]	2,20 [1,40; 3,47] 0,0005[3]	3,0 [1,3; 4,6] 0,0005[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	7/114 (6,1)	0/132 (0,0)	17,35 [1,00; 300,45] 0,0499[2]	18,49 [1,04; 327,38] 0,0041[4]	6,1 [1,7; 10,5] 0,0041[4]
Aromatase inhibitor	62/1169 (5,3)	36/1133 (3,2)	1,67 [1,12; 2,50] 0,0126[2]	1,71 [1,12; 2,60] 0,0115[3]	2,1 [0,5; 3,8] 0,0115[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Investigations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: <,0001)					
Negative	31/156 (19,9)	4/169 (2,4)	8,40 [3,03; 23,24] <,0001[2]	10,23 [3,52; 29,73] <,0001[3]	17,5 [10,8; 24,2] <,0001[3]
Positive	210/1089 (19,3)	24/1067 (2,2)	8,57 [5,67; 12,97] <,0001[2]	10,38 [6,74; 15,99] <,0001[3]	17,0 [14,5; 19,5] <,0001[3]
Unknown	2/10 (20,0)	0/7 (0,0)	3,64 [0,20; 65,86] 0,3824[2]	4,41 [0,18; 107,28] 0,4853[4]	20,0 [-4,8; 44,8] 0,4853[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Interacting subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Respiratory, thoracic and mediastinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
First endocrine therapy (Interaction p-value: <,0001)					
Tamoxifen	2/114 (1,8)	0/132 (0,0)	5,78 [0,28; 119,22] 0,2557[2]	5,89 [0,28; 123,94] 0,2137[4]	1,8 [-0,7; 4,2] 0,2137[4]
Aromatase inhibitor	21/1169 (1,8)	10/1133 (0,9)	2,04 [0,96; 4,30] 0,0628[2]	2,05 [0,96; 4,38] 0,0572[3]	0,9 [-0,0; 1,8] 0,0572[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Tabelle 4-134 (Anhang): Häufige unerwünschte Ereignisse nach SOC und PT - nicht-interagierende Subgruppen (prämenopausale Patientinnen)

Table: Subgroups - adverse events according PT Abdominal distension from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9670)					
Neoadjuvant chemotherapy	6/217 (2,8)	1/219 (0,5)	6,06 [0,74; 49,88] 0,0941[2]	6,20 [0,74; 51,93] 0,0672[4]	2,3 [-0,0; 4,7] 0,0672[4]
Adjuvant chemotherapy	9/327 (2,8)	2/312 (0,6)	4,29 [0,94; 19,72] 0,0610[2]	4,39 [0,94; 20,47] 0,0403[3]	2,1 [0,1; 4,1] 0,0403[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,9993)					
North America / Europe	10/252 (4,0)	3/233 (1,3)	3,08 [0,86; 11,06] 0,0843[2]	3,17 [0,86; 11,66] 0,0678[3]	2,7 [-0,1; 5,5] 0,0678[3]
Asia	3/168 (1,8)	0/166 (0,0)	6,92 [0,36; 132,88] 0,1996[2]	7,04 [0,36; 137,40] 0,2478[4]	1,8 [-0,2; 3,8] 0,2478[4]
Other	2/133 (1,5)	0/136 (0,0)	5,11 [0,25; 105,49] 0,2908[2]	5,19 [0,25; 109,13] 0,2435[4]	1,5 [-0,6; 3,6] 0,2435[4]
Tumor stage (Interaction p-value: 0,8905)					
IIA	1/59 (1,7)	1/62 (1,6)	1,05 [0,07; 16,42] 0,9718[2]	1,05 [0,06; 17,21] 1,0000[4]	0,1 [-4,5; 4,6] 1,0000[4]
IIB	1/53 (1,9)	0/69 (0,0)	3,89 [0,16; 93,60] 0,4027[2]	3,97 [0,16; 99,46] 0,4344[4]	1,9 [-1,8; 5,5] 0,4344[4]
IIIA	5/236 (2,1)	0/214 (0,0)	9,98 [0,56; 179,40] 0,1186[2]	10,19 [0,56; 185,42] 0,0626[4]	2,1 [0,3; 4,0] 0,0626[4]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	8/186 (4,3)	2/174 (1,1)	3,74 [0,81; 17,38] 0,0921[2]	3,87 [0,81; 18,46] 0,1064[4]	3,2 [-0,2; 6,5] 0,1064[4]
Progesterone receptor status (Interaction p-value: 0,9940)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	11/477 (2,3)	3/471 (0,6)	3,62 [1,02; 12,90] 0,0471[2]	3,68 [1,02; 13,28] 0,0332[3]	1,7 [0,1; 3,2] 0,0332[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,9996)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
White	10/323 (3,1)	3/324 (0,9)	3,34 [0,93; 12,04] 0,0648[2]	3,42 [0,93; 12,54] 0,0492[3]	2,2 [0,0; 4,3] 0,0492[3]
Asian	4/199 (2,0)	0/180 (0,0)	8,15 [0,44; 150,24] 0,1584[2]	8,31 [0,44; 155,42] 0,1249[4]	2,0 [0,1; 4,0] 0,1249[4]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9798)					
ECOG-PS 0	13/496 (2,6)	3/480 (0,6)	4,19 [1,20; 14,62] 0,0245[2]	4,28 [1,21; 15,11] 0,0141[3]	2,0 [0,4; 3,6] 0,0141[3]
ECOG-PS 1	2/57 (3,5)	0/55 (0,0)	4,83 [0,24; 98,34] 0,3060[2]	5,00 [0,23; 106,54] 0,4957[4]	3,5 [-1,3; 8,3] 0,4957[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Abdominal pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,1382)					
Neoadjuvant chemotherapy	55/217 (25,3)	9/219 (4,1)	6,17 [3,13; 12,17] <,0001[2]	7,92 [3,80; 16,50] <,0001[3]	21,2 [14,9; 27,6] <,0001[3]
Adjuvant chemotherapy	80/327 (24,5)	16/312 (5,1)	4,77 [2,85; 7,98] <,0001[2]	5,99 [3,41; 10,52] <,0001[3]	19,3 [14,1; 24,6] <,0001[3]
No chemotherapy	1/9 (11,1)	1/4 (25,0)	0,44 [0,04; 5,46] 0,5264[2]	0,38 [0,02; 8,10] 1,0000[4]	-13,9 [-61,0; 33,3] 1,0000[4]
Region (Interaction p-value: 0,0758)					
North America / Europe	76/252 (30,2)	20/233 (8,6)	3,51 [2,22; 5,56] <,0001[2]	4,60 [2,70; 7,82] <,0001[3]	21,6 [14,9; 28,3] <,0001[3]
Asia	36/168 (21,4)	1/166 (0,6)	35,57 [4,93; 256,45] 0,0004[2]	45,00 [6,09; 332,55] <,0001[3]	20,8 [14,5; 27,1] <,0001[3]
Other	24/133 (18,0)	5/136 (3,7)	4,91 [1,93; 12,48] 0,0008[2]	5,77 [2,13; 15,63] 0,0001[3]	14,4 [7,1; 21,6] 0,0001[3]
Primary tumor size (Interaction p-value: 0,6108)					
< 20 mm	36/141 (25,5)	8/140 (5,7)	4,47 [2,15; 9,27] <,0001[2]	5,66 [2,52; 12,69] <,0001[3]	19,8 [11,7; 28,0] <,0001[3]
≥ 20 but < 50 mm	61/255 (23,9)	9/249 (3,6)	6,62 [3,36; 13,03] <,0001[2]	8,38 [4,06; 17,31] <,0001[3]	20,3 [14,6; 26,0] <,0001[3]
≥ 50 mm	39/145 (26,9)	9/141 (6,4)	4,21 [2,12; 8,37] <,0001[2]	5,40 [2,50; 11,64] <,0001[3]	20,5 [12,2; 28,8] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,5248)					
0-3	48/203 (23,6)	10/214 (4,7)	5,06 [2,63; 9,73] <,0001[2]	6,32 [3,10; 12,88] <,0001[3]	19,0 [12,5; 25,5] <,0001[3]
4-9	59/242 (24,4)	9/231 (3,9)	6,26 [3,18; 12,32] <,0001[2]	7,95 [3,84; 16,47] <,0001[3]	20,5 [14,5; 26,4] <,0001[3]
≥ 10	29/108 (26,9)	7/90 (7,8)	3,45 [1,59; 7,51] 0,0018[2]	4,35 [1,80; 10,50] 0,0005[3]	19,1 [9,1; 29,1] 0,0005[3]
Tumor stage (Interaction p-value: 0,8128)					
IIA	13/59 (22,0)	2/62 (3,2)	6,83 [1,61; 28,99] 0,0092[2]	8,48 [1,82; 39,45] 0,0017[3]	18,8 [7,4; 30,3] 0,0017[3]
IIB	8/53 (15,1)	3/69 (4,3)	3,47 [0,97; 12,46] 0,0562[2]	3,91 [0,98; 15,55] 0,0557[4]	10,7 [-0,0; 21,5] 0,0557[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	55/236 (23,3)	8/214 (3,7)	6,23 [3,04; 12,78] <,0001[2]	7,82 [3,63; 16,87] <,0001[3]	19,6 [13,6; 25,5] <,0001[3]
IIIB	7/18 (38,9)	0/15 (0,0)	12,63 [0,78; 204,50] 0,0742[2]	20,22 [1,04; 391,17] 0,0090[4]	38,9 [16,4; 61,4] 0,0090[4]
IIIC	53/186 (28,5)	13/174 (7,5)	3,81 [2,16; 6,75] <,0001[2]	4,94 [2,58; 9,44] <,0001[3]	21,0 [13,5; 28,6] <,0001[3]
Tumor grade (Interaction p-value: 0,9130)					
G1	8/47 (17,0)	2/41 (4,9)	3,49 [0,78; 15,51] 0,1006[2]	4,00 [0,80; 20,05] 0,0974[4]	12,1 [-0,5; 24,7] 0,0974[4]
G2	70/244 (28,7)	12/234 (5,1)	5,59 [3,11; 10,05] <,0001[2]	7,44 [3,91; 14,17] <,0001[3]	23,6 [17,2; 29,9] <,0001[3]
G3	52/233 (22,3)	11/226 (4,9)	4,59 [2,46; 8,56] <,0001[2]	5,62 [2,85; 11,08] <,0001[3]	17,5 [11,4; 23,5] <,0001[3]
GX	6/29 (20,7)	1/33 (3,0)	6,83 [0,87; 53,43] 0,0672[2]	8,35 [0,94; 74,12] 0,0437[4]	17,7 [1,8; 33,5] 0,0437[4]
Progesterone receptor status (Interaction p-value: 0,9877)					
Negative	17/49 (34,7)	3/44 (6,8)	5,09 [1,60; 16,20] 0,0059[2]	7,26 [1,96; 26,95] 0,0011[3]	27,9 [12,6; 43,1] 0,0011[3]
Positive	104/477 (21,8)	20/471 (4,2)	5,13 [3,24; 8,14] <,0001[2]	6,29 [3,82; 10,34] <,0001[3]	17,6 [13,4; 21,7] <,0001[3]
Unknown	3/4 (75,0)	1/8 (12,5)	6,00 [0,88; 40,87] 0,0672[2]	21,00 [0,96; 458,84] 0,0667[4]	62,5 [14,3; 100,0] 0,0667[4]
ECOG-PS (Interaction p-value: 0,8491)					
ECOG-PS 0	124/496 (25,0)	24/480 (5,0)	5,00 [3,29; 7,60] <,0001[2]	6,33 [4,01; 10,01] <,0001[3]	20,0 [15,7; 24,3] <,0001[3]
ECOG-PS 1	12/57 (21,1)	2/55 (3,6)	5,79 [1,36; 24,69] 0,0176[2]	7,07 [1,50; 33,25] 0,0053[3]	17,4 [5,7; 29,1] 0,0053[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Abdominal pain upper from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7024)					
Neoadjuvant chemotherapy	27/217 (12,4)	7/219 (3,2)	3,89 [1,73; 8,75] 0,0010[2]	4,30 [1,83; 10,11] 0,0003[3]	9,2 [4,3; 14,2] 0,0003[3]
Adjuvant chemotherapy	40/327 (12,2)	15/312 (4,8)	2,54 [1,43; 4,51] 0,0014[2]	2,76 [1,49; 5,11] 0,0008[3]	7,4 [3,2; 11,7] 0,0008[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,1970)					
North America / Europe	37/252 (14,7)	7/233 (3,0)	4,89 [2,22; 10,75] <,0001[2]	5,56 [2,42; 12,73] <,0001[3]	11,7 [6,8; 16,6] <,0001[3]
Asia	14/168 (8,3)	8/166 (4,8)	1,73 [0,75; 4,01] 0,2023[2]	1,80 [0,73; 4,40] 0,1955[3]	3,5 [-1,8; 8,8] 0,1955[3]
Other	17/133 (12,8)	7/136 (5,1)	2,48 [1,06; 5,79] 0,0353[2]	2,70 [1,08; 6,74] 0,0281[3]	7,6 [0,9; 14,4] 0,0281[3]
Primary tumor size (Interaction p-value: 0,4292)					
< 20 mm	21/141 (14,9)	7/140 (5,0)	2,98 [1,31; 6,78] 0,0093[2]	3,33 [1,37; 8,10] 0,0056[3]	9,9 [3,0; 16,8] 0,0056[3]
≥ 20 but < 50 mm	29/255 (11,4)	12/249 (4,8)	2,36 [1,23; 4,52] 0,0096[2]	2,53 [1,26; 5,09] 0,0071[3]	6,6 [1,8; 11,3] 0,0071[3]
≥ 50 mm	18/145 (12,4)	3/141 (2,1)	5,83 [1,76; 19,37] 0,0040[2]	6,52 [1,88; 22,66] 0,0009[3]	10,3 [4,4; 16,2] 0,0009[3]
Number of positive lymph nodes (Interaction p-value: 0,9630)					
0-3	25/203 (12,3)	10/214 (4,7)	2,64 [1,30; 5,35] 0,0073[2]	2,87 [1,34; 6,13] 0,0049[3]	7,6 [2,3; 13,0] 0,0049[3]
4-9	29/242 (12,0)	12/231 (5,2)	2,31 [1,21; 4,41] 0,0115[2]	2,48 [1,24; 5,00] 0,0087[3]	6,8 [1,8; 11,8] 0,0087[3]
≥ 10	14/108 (13,0)	0/90 (0,0)	24,21 [1,46; 400,31] 0,0260[2]	27,77 [1,63; 472,45] 0,0004[3]	13,0 [6,6; 19,3] 0,0004[3]
Tumor stage (Interaction p-value: 0,4507)					
IIA	8/59 (13,6)	4/62 (6,5)	2,10 [0,67; 6,61] 0,2040[2]	2,27 [0,65; 8,00] 0,1910[3]	7,1 [-3,6; 17,8] 0,1910[3]
IIB	5/53 (9,4)	4/69 (5,8)	1,63 [0,46; 5,77] 0,4506[2]	1,69 [0,43; 6,64] 0,4999[4]	3,6 [-6,0; 13,2] 0,4999[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	29/236 (12,3)	9/214 (4,2)	2,92 [1,42; 6,03] 0,0037[2]	3,19 [1,47; 6,91] 0,0021[3]	8,1 [3,1; 13,1] 0,0021[3]
IIIB	1/18 (5,6)	1/15 (6,7)	0,83 [0,06; 12,22] 0,8942[2]	0,82 [0,05; 14,39] 1,0000[4]	-1,1 [-17,6; 15,4] 1,0000[4]
IIIC	25/186 (13,4)	4/174 (2,3)	5,85 [2,08; 16,46] 0,0008[2]	6,60 [2,25; 19,38] 0,0001[3]	11,1 [5,8; 16,5] 0,0001[3]
Tumor grade (Interaction p-value: 0,8482)					
G1	7/47 (14,9)	1/41 (2,4)	6,11 [0,78; 47,58] 0,0841[2]	7,00 [0,82; 59,53] 0,0629[4]	12,5 [1,2; 23,7] 0,0629[4]
G2	25/244 (10,2)	8/234 (3,4)	3,00 [1,38; 6,51] 0,0055[2]	3,22 [1,42; 7,30] 0,0032[3]	6,8 [2,4; 11,3] 0,0032[3]
G3	32/233 (13,7)	12/226 (5,3)	2,59 [1,37; 4,89] 0,0035[2]	2,84 [1,42; 5,67] 0,0022[3]	8,4 [3,1; 13,7] 0,0022[3]
GX	4/29 (13,8)	1/33 (3,0)	4,55 [0,54; 38,45] 0,1639[2]	5,12 [0,54; 48,72] 0,1762[4]	10,8 [-3,1; 24,6] 0,1762[4]
Race (Interaction p-value: 0,0556)					
White	46/323 (14,2)	10/324 (3,1)	4,61 [2,37; 8,98] <,0001[2]	5,21 [2,58; 10,53] <,0001[3]	11,2 [6,9; 15,4] <,0001[3]
Asian	14/199 (7,0)	9/180 (5,0)	1,41 [0,62; 3,17] 0,4102[2]	1,44 [0,61; 3,41] 0,4073[3]	2,0 [-2,7; 6,8] 0,4073[3]
Other	7/19 (36,8)	1/21 (4,8)	7,74 [1,05; 57,24] 0,0451[2]	11,67 [1,27; 106,79] 0,0174[4]	32,1 [8,6; 55,6] 0,0174[4]
ECOG-PS (Interaction p-value: 0,9658)					
ECOG-PS 0	62/496 (12,5)	20/480 (4,2)	3,00 [1,84; 4,89] <,0001[2]	3,29 [1,95; 5,53] <,0001[3]	8,3 [4,9; 11,7] <,0001[3]
ECOG-PS 1	6/57 (10,5)	2/55 (3,6)	2,89 [0,61; 13,73] 0,1809[2]	3,12 [0,60; 16,17] 0,2716[4]	6,9 [-2,5; 16,3] 0,2716[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Alopecia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9783)					
Neoadjuvant chemotherapy	18/217 (8,3)	5/219 (2,3)	3,63 [1,37; 9,61] 0,0093[2]	3,87 [1,41; 10,62] 0,0050[3]	6,0 [1,8; 10,2] 0,0050[3]
Adjuvant chemotherapy	22/327 (6,7)	5/312 (1,6)	4,20 [1,61; 10,95] 0,0034[2]	4,43 [1,66; 11,85] 0,0013[3]	5,1 [2,1; 8,2] 0,0013[3]
No chemotherapy	3/9 (33,3)	0/4 (0,0)	3,50 [0,22; 55,40] 0,3740[2]	4,85 [0,20; 118,61] 0,4965[4]	33,3 [2,5; 64,1] 0,4965[4]
Region (Interaction p-value: 0,6774)					
North America / Europe	22/252 (8,7)	8/233 (3,4)	2,54 [1,15; 5,60] 0,0205[2]	2,69 [1,17; 6,17] 0,0156[3]	5,3 [1,1; 9,5] 0,0156[3]
Asia	11/168 (6,5)	2/166 (1,2)	5,43 [1,22; 24,14] 0,0261[2]	5,75 [1,25; 26,33] 0,0116[3]	5,3 [1,3; 9,4] 0,0116[3]
Other	10/133 (7,5)	0/136 (0,0)	21,47 [1,27; 362,74] 0,0335[2]	23,21 [1,35; 400,24] 0,0007[4]	7,5 [3,0; 12,0] 0,0007[4]
Primary tumor size (Interaction p-value: 0,5830)					
< 20 mm	11/141 (7,8)	4/140 (2,9)	2,73 [0,89; 8,37] 0,0788[2]	2,88 [0,89; 9,26] 0,0653[3]	4,9 [-0,3; 10,2] 0,0653[3]
≥ 20 but < 50 mm	20/255 (7,8)	3/249 (1,2)	6,51 [1,96; 21,63] 0,0022[2]	6,98 [2,05; 23,79] 0,0004[3]	6,6 [3,1; 10,2] 0,0004[3]
≥ 50 mm	12/145 (8,3)	3/141 (2,1)	3,89 [1,12; 13,49] 0,0323[2]	4,15 [1,15; 15,04] 0,0197[3]	6,1 [1,1; 11,2] 0,0197[3]
Number of positive lymph nodes (Interaction p-value: 0,3360)					
0-3	19/203 (9,4)	3/214 (1,4)	6,68 [2,01; 22,22] 0,0020[2]	7,26 [2,12; 24,94] 0,0003[3]	8,0 [3,7; 12,3] 0,0003[3]
4-9	16/242 (6,6)	7/231 (3,0)	2,18 [0,91; 5,21] 0,0787[2]	2,27 [0,91; 5,61] 0,0703[3]	3,6 [-0,3; 7,4] 0,0703[3]
≥ 10	8/108 (7,4)	0/90 (0,0)	14,19 [0,83; 242,57] 0,0670[2]	15,31 [0,87; 268,99] 0,0085[4]	7,4 [2,5; 12,3] 0,0085[4]
Tumor stage (Interaction p-value: 0,5322)					
IIA	4/59 (6,8)	0/62 (0,0)	9,45 [0,52; 171,79] 0,1291[2]	10,14 [0,53; 192,49] 0,0536[4]	6,8 [0,4; 13,2] 0,0536[4]
IIB	6/53 (11,3)	0/69 (0,0)	16,85 [0,97; 292,63] 0,0525[2]	19,02 [1,05; 345,69] 0,0057[4]	11,3 [2,8; 19,9] 0,0057[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	16/236 (6,8)	8/214 (3,7)	1,81 [0,79; 4,15] 0,1589[2]	1,87 [0,78; 4,47] 0,1516[3]	3,0 [-1,1; 7,1] 0,1516[3]
IIIB	3/18 (16,7)	1/15 (6,7)	2,50 [0,29; 21,61] 0,4051[2]	2,80 [0,26; 30,18] 0,6074[4]	10,0 [-11,3; 31,3] 0,6074[4]
IIIC	14/186 (7,5)	1/174 (0,6)	13,10 [1,74; 98,55] 0,0125[2]	14,08 [1,83; 108,26] 0,0010[3]	7,0 [3,0; 10,9] 0,0010[3]
Tumor grade (Interaction p-value: 0,2373)					
G1	3/47 (6,4)	3/41 (7,3)	0,87 [0,19; 4,09] 0,8624[2]	0,86 [0,16; 4,53] 1,0000[4]	-0,9 [-11,5; 9,7] 1,0000[4]
G2	20/244 (8,2)	3/234 (1,3)	6,39 [1,93; 21,23] 0,0024[2]	6,88 [2,01; 23,46] 0,0004[3]	6,9 [3,2; 10,6] 0,0004[3]
G3	18/233 (7,7)	4/226 (1,8)	4,36 [1,50; 12,70] 0,0068[2]	4,65 [1,55; 13,95] 0,0028[3]	6,0 [2,1; 9,8] 0,0028[3]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,9409)					
Negative	1/49 (2,0)	1/44 (2,3)	0,90 [0,06; 13,93] 0,9387[2]	0,90 [0,05; 14,76] 1,0000[4]	-0,2 [-6,2; 5,7] 1,0000[4]
Positive	39/477 (8,2)	8/471 (1,7)	4,81 [2,27; 10,19] <,0001[2]	5,15 [2,38; 11,15] <,0001[3]	6,5 [3,8; 9,2] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8096)					
White	27/323 (8,4)	8/324 (2,5)	3,39 [1,56; 7,34] 0,0020[2]	3,60 [1,61; 8,06] 0,0009[3]	5,9 [2,4; 9,3] 0,0009[3]
Asian	13/199 (6,5)	2/180 (1,1)	5,88 [1,35; 25,70] 0,0186[2]	6,22 [1,38; 27,96] 0,0069[3]	5,4 [1,7; 9,2] 0,0069[3]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,1204)					
ECOG-PS 0	41/496 (8,3)	8/480 (1,7)	4,96 [2,35; 10,47] <,0001[2]	5,32 [2,47; 11,46] <,0001[3]	6,6 [3,9; 9,3] <,0001[3]
ECOG-PS 1	2/57 (3,5)	2/55 (3,6)	0,96 [0,14; 6,61] 0,9710[2]	0,96 [0,13; 7,09] 1,0000[4]	-0,1 [-7,0; 6,7] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Anaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,6725)					
Neoadjuvant chemotherapy	34/217 (15,7)	6/219 (2,7)	5,72 [2,45; 13,34] <,0001[2]	6,60 [2,71; 16,06] <,0001[3]	12,9 [7,6; 18,2] <,0001[3]
Adjuvant chemotherapy	65/327 (19,9)	17/312 (5,4)	3,65 [2,19; 6,08] <,0001[2]	4,31 [2,46; 7,53] <,0001[3]	14,4 [9,4; 19,4] <,0001[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,6095)					
North America / Europe	33/252 (13,1)	9/233 (3,9)	3,39 [1,66; 6,93] 0,0008[2]	3,75 [1,75; 8,02] 0,0003[3]	9,2 [4,4; 14,1] 0,0003[3]
Asia	31/168 (18,5)	5/166 (3,0)	6,13 [2,44; 15,37] 0,0001[2]	7,29 [2,76; 19,25] <,0001[3]	15,4 [9,0; 21,9] <,0001[3]
Other	37/133 (27,8)	9/136 (6,6)	4,20 [2,11; 8,37] <,0001[2]	5,44 [2,51; 11,81] <,0001[3]	21,2 [12,5; 29,9] <,0001[3]
Primary tumor size (Interaction p-value: 0,8752)					
< 20 mm	21/141 (14,9)	6/140 (4,3)	3,48 [1,45; 8,35] 0,0054[2]	3,91 [1,53; 10,01] 0,0026[3]	10,6 [3,8; 17,4] 0,0026[3]
≥ 20 but < 50 mm	49/255 (19,2)	12/249 (4,8)	3,99 [2,17; 7,31] <,0001[2]	4,70 [2,43; 9,07] <,0001[3]	14,4 [8,9; 19,9] <,0001[3]
≥ 50 mm	25/145 (17,2)	5/141 (3,5)	4,86 [1,91; 12,34] 0,0009[2]	5,67 [2,10; 15,27] 0,0002[3]	13,7 [6,8; 20,6] 0,0002[3]
Number of positive lymph nodes (Interaction p-value: 0,1655)					
0-3	28/203 (13,8)	11/214 (5,1)	2,68 [1,37; 5,25] 0,0039[2]	2,95 [1,43; 6,10] 0,0024[3]	8,7 [3,1; 14,2] 0,0024[3]
4-9	45/242 (18,6)	10/231 (4,3)	4,30 [2,22; 8,32] <,0001[2]	5,05 [2,48; 10,28] <,0001[3]	14,3 [8,7; 19,8] <,0001[3]
≥ 10	28/108 (25,9)	2/90 (2,2)	11,67 [2,86; 47,64] 0,0006[2]	15,40 [3,55; 66,72] <,0001[3]	23,7 [14,9; 32,5] <,0001[3]
Tumor grade (Interaction p-value: 0,2215)					
G1	8/47 (17,0)	1/41 (2,4)	6,98 [0,91; 53,47] 0,0615[2]	8,21 [0,98; 68,71] 0,0334[4]	14,6 [2,8; 26,3] 0,0334[4]
G2	44/244 (18,0)	5/234 (2,1)	8,44 [3,41; 20,91] <,0001[2]	10,08 [3,92; 25,90] <,0001[3]	15,9 [10,7; 21,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G3	41/233 (17,6)	14/226 (6,2)	2,84 [1,59; 5,07] 0,0004[2]	3,23 [1,71; 6,12] 0,0002[3]	11,4 [5,6; 17,2] 0,0002[3]
GX	8/29 (27,6)	3/33 (9,1)	3,03 [0,89; 10,38] 0,0768[2]	3,81 [0,90; 16,07] 0,0572[3]	18,5 [-0,5; 37,5] 0,0572[3]
Progesterone receptor status (Interaction p-value: 0,1446)					
Negative	9/49 (18,4)	3/44 (6,8)	2,69 [0,78; 9,32] 0,1177[2]	3,08 [0,78; 12,19] 0,0972[3]	11,5 [-1,6; 24,7] 0,0972[3]
Positive	90/477 (18,9)	19/471 (4,0)	4,68 [2,90; 7,55] <,0001[2]	5,53 [3,31; 9,24] <,0001[3]	14,8 [10,9; 18,8] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,7455)					
White	59/323 (18,3)	17/324 (5,2)	3,48 [2,08; 5,84] <,0001[2]	4,04 [2,30; 7,09] <,0001[3]	13,0 [8,2; 17,9] <,0001[3]
Asian	34/199 (17,1)	6/180 (3,3)	5,13 [2,20; 11,92] 0,0001[2]	5,98 [2,45; 14,60] <,0001[3]	13,8 [7,9; 19,6] <,0001[3]
Other	7/19 (36,8)	0/21 (0,0)	16,50 [1,01; 270,78] 0,0496[2]	25,80 [1,36; 491,15] 0,0027[4]	36,8 [15,2; 58,5] 0,0027[4]
ECOG-PS (Interaction p-value: 0,9768)					
ECOG-PS 0	91/496 (18,3)	23/480 (4,8)	3,83 [2,47; 5,94] <,0001[2]	4,46 [2,77; 7,19] <,0001[3]	13,6 [9,6; 17,5] <,0001[3]
ECOG-PS 1	10/57 (17,5)	0/55 (0,0)	20,28 [1,22; 337,85] 0,0360[2]	24,54 [1,40; 429,89] 0,0013[4]	17,5 [7,7; 27,4] 0,0013[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Arthralgia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,5860)					
Neoadjuvant chemotherapy	46/217 (21,2)	55/219 (25,1)	0,84 [0,60; 1,19] 0,3337[2]	0,80 [0,51; 1,25] 0,3325[3]	-3,9 [-11,8; 4,0] 0,3325[3]
Adjuvant chemotherapy	60/327 (18,3)	86/312 (27,6)	0,67 [0,50; 0,89] 0,0061[2]	0,59 [0,41; 0,86] 0,0055[3]	-9,2 [-15,7; -2,7] 0,0055[3]
No chemotherapy	0/9 (0,0)	1/4 (25,0)	0,17 [0,01; 3,40] 0,2441[2]	0,12 [0,00; 3,78] 0,3077[4]	-25,0 [-67,4; 17,4] 0,3077[4]
Region (Interaction p-value: 0,5813)					
North America / Europe	66/252 (26,2)	78/233 (33,5)	0,78 [0,59; 1,03] 0,0804[2]	0,71 [0,48; 1,04] 0,0793[3]	-7,3 [-15,4; 0,8] 0,0793[3]
Asia	25/168 (14,9)	37/166 (22,3)	0,67 [0,42; 1,06] 0,0851[2]	0,61 [0,35; 1,07] 0,0817[3]	-7,4 [-15,7; 0,9] 0,0817[3]
Other	15/133 (11,3)	27/136 (19,9)	0,57 [0,32; 1,02] 0,0578[2]	0,51 [0,26; 1,02] 0,0527[3]	-8,6 [-17,2; 0,0] 0,0527[3]
Primary tumor size (Interaction p-value: 0,3539)					
< 20 mm	28/141 (19,9)	43/140 (30,7)	0,65 [0,43; 0,98] 0,0392[2]	0,56 [0,32; 0,97] 0,0363[3]	-10,9 [-20,9; -0,8] 0,0363[3]
≥ 20 but < 50 mm	48/255 (18,8)	69/249 (27,7)	0,68 [0,49; 0,94] 0,0195[2]	0,60 [0,40; 0,92] 0,0181[3]	-8,9 [-16,2; -1,5] 0,0181[3]
≥ 50 mm	30/145 (20,7)	30/141 (21,3)	0,97 [0,62; 1,52] 0,9030[2]	0,97 [0,55; 1,71] 0,9030[3]	-0,6 [-10,0; 8,9] 0,9030[3]
Number of positive lymph nodes (Interaction p-value: 0,8910)					
0-3	44/203 (21,7)	60/214 (28,0)	0,77 [0,55; 1,08] 0,1359[2]	0,71 [0,45; 1,11] 0,1334[3]	-6,4 [-14,6; 1,9] 0,1334[3]
4-9	46/242 (19,0)	62/231 (26,8)	0,71 [0,51; 0,99] 0,0442[2]	0,64 [0,41; 0,99] 0,0425[3]	-7,8 [-15,4; -0,3] 0,0425[3]
≥ 10	16/108 (14,8)	20/90 (22,2)	0,67 [0,37; 1,21] 0,1816[2]	0,61 [0,29; 1,26] 0,1784[3]	-7,4 [-18,3; 3,5] 0,1784[3]
Tumor stage (Interaction p-value: 0,9359)					
IIA	13/59 (22,0)	22/62 (35,5)	0,62 [0,35; 1,12] 0,1108[2]	0,51 [0,23; 1,15] 0,1029[3]	-13,4 [-29,4; 2,5] 0,1029[3]
IIB	10/53 (18,9)	19/69 (27,5)	0,69 [0,35; 1,35] 0,2737[2]	0,61 [0,26; 1,46] 0,2649[3]	-8,7 [-23,6; 6,2] 0,2649[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	44/236 (18,6)	56/214 (26,2)	0,71 [0,50; 1,01] 0,0568[2]	0,65 [0,41; 1,01] 0,0552[3]	-7,5 [-15,2; 0,2] 0,0552[3]
IIIB	2/18 (11,1)	3/15 (20,0)	0,56 [0,11; 2,90] 0,4858[2]	0,50 [0,07; 3,48] 0,6390[4]	-8,9 [-33,8; 16,0] 0,6390[4]
IIIC	37/186 (19,9)	42/174 (24,1)	0,82 [0,56; 1,22] 0,3317[2]	0,78 [0,47; 1,29] 0,3307[3]	-4,2 [-12,8; 4,3] 0,3307[3]
Tumor grade (Interaction p-value: 0,3486)					
G1	6/47 (12,8)	14/41 (34,1)	0,37 [0,16; 0,88] 0,0249[2]	0,28 [0,10; 0,83] 0,0170[3]	-21,4 [-38,8; -4,0] 0,0170[3]
G2	57/244 (23,4)	65/234 (27,8)	0,84 [0,62; 1,14] 0,2691[2]	0,79 [0,52; 1,20] 0,2682[3]	-4,4 [-12,2; 3,4] 0,2682[3]
G3	40/233 (17,2)	57/226 (25,2)	0,68 [0,47; 0,98] 0,0365[2]	0,61 [0,39; 0,97] 0,0346[3]	-8,1 [-15,5; -0,6] 0,0346[3]
GX	3/29 (10,3)	5/33 (15,2)	0,68 [0,18; 2,61] 0,5772[2]	0,65 [0,14; 2,98] 0,7126[4]	-4,8 [-21,3; 11,7] 0,7126[4]
Progesterone receptor status (Interaction p-value: 0,0955)					
Negative	12/49 (24,5)	6/44 (13,6)	1,80 [0,74; 4,38] 0,1980[2]	2,05 [0,70; 6,05] 0,1859[3]	10,9 [-4,9; 26,6] 0,1859[3]
Positive	83/477 (17,4)	127/471 (27,0)	0,65 [0,50; 0,82] 0,0005[2]	0,57 [0,42; 0,78] 0,0004[3]	-9,6 [-14,8; -4,3] 0,0004[3]
Unknown	0/4 (0,0)	2/8 (25,0)	0,36 [0,02; 6,12] 0,4796[2]	0,29 [0,01; 7,57] 0,5152[4]	-25,0 [-55,0; 5,0] 0,5152[4]
Race (Interaction p-value: 0,1109)					
White	67/323 (20,7)	99/324 (30,6)	0,68 [0,52; 0,89] 0,0048[2]	0,59 [0,42; 0,85] 0,0043[3]	-9,8 [-16,5; -3,1] 0,0043[3]
Asian	29/199 (14,6)	40/180 (22,2)	0,66 [0,43; 1,01] 0,0564[2]	0,60 [0,35; 1,01] 0,0540[3]	-7,6 [-15,5; 0,2] 0,0540[3]
Other	6/19 (31,6)	2/21 (9,5)	3,32 [0,76; 14,49] 0,1112[2]	4,38 [0,76; 25,20] 0,1202[4]	22,1 [-2,3; 46,4] 0,1202[4]
ECOG-PS (Interaction p-value: 0,4672)					
ECOG-PS 0	96/496 (19,4)	125/480 (26,0)	0,74 [0,59; 0,94] 0,0131[2]	0,68 [0,50; 0,92] 0,0126[3]	-6,7 [-11,9; -1,4] 0,0126[3]
ECOG-PS 1	10/57 (17,5)	17/55 (30,9)	0,57 [0,29; 1,13] 0,1065[2]	0,48 [0,20; 1,16] 0,0983[3]	-13,4 [-29,1; 2,3] 0,0983[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Aspartate aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,5018)					
Neoadjuvant chemotherapy	15/217 (6,9)	5/219 (2,3)	3,03 [1,12; 8,19] 0,0290[2]	3,18 [1,13; 8,90] 0,0209[3]	4,6 [0,7; 8,5] 0,0209[3]
Adjuvant chemotherapy	27/327 (8,3)	17/312 (5,4)	1,52 [0,84; 2,72] 0,1649[2]	1,56 [0,83; 2,93] 0,1611[3]	2,8 [-1,1; 6,7] 0,1611[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,3999)					
North America / Europe	14/252 (5,6)	4/233 (1,7)	3,24 [1,08; 9,69] 0,0359[2]	3,37 [1,09; 10,38] 0,0255[3]	3,8 [0,6; 7,1] 0,0255[3]
Asia	20/168 (11,9)	11/166 (6,6)	1,80 [0,89; 3,63] 0,1028[2]	1,90 [0,88; 4,11] 0,0965[3]	5,3 [-0,9; 11,5] 0,0965[3]
Other	8/133 (6,0)	7/136 (5,1)	1,17 [0,44; 3,13] 0,7567[2]	1,18 [0,42; 3,35] 0,7564[3]	0,9 [-4,6; 6,4] 0,7564[3]
Primary tumor size (Interaction p-value: 0,7847)					
< 20 mm	13/141 (9,2)	5/140 (3,6)	2,58 [0,95; 7,05] 0,0643[2]	2,74 [0,95; 7,91] 0,0532[3]	5,6 [-0,0; 11,3] 0,0532[3]
≥ 20 but < 50 mm	19/255 (7,5)	11/249 (4,4)	1,69 [0,82; 3,47] 0,1557[2]	1,74 [0,81; 3,74] 0,1502[3]	3,0 [-1,1; 7,1] 0,1502[3]
≥ 50 mm	9/145 (6,2)	5/141 (3,5)	1,75 [0,60; 5,09] 0,3044[2]	1,80 [0,59; 5,51] 0,2971[3]	2,7 [-2,3; 7,6] 0,2971[3]
Number of positive lymph nodes (Interaction p-value: 0,6085)					
0-3	15/203 (7,4)	6/214 (2,8)	2,64 [1,04; 6,66] 0,0405[2]	2,77 [1,05; 7,28] 0,0323[3]	4,6 [0,4; 8,8] 0,0323[3]
4-9	17/242 (7,0)	10/231 (4,3)	1,62 [0,76; 3,47] 0,2119[2]	1,67 [0,75; 3,73] 0,2065[3]	2,7 [-1,5; 6,8] 0,2065[3]
≥ 10	10/108 (9,3)	6/90 (6,7)	1,39 [0,53; 3,67] 0,5080[2]	1,43 [0,50; 4,10] 0,5051[3]	2,6 [-4,9; 10,1] 0,5051[3]
Tumor stage (Interaction p-value: 0,9155)					
IIA	7/59 (11,9)	3/62 (4,8)	2,45 [0,67; 9,04] 0,1779[2]	2,65 [0,65; 10,77] 0,1978[4]	7,0 [-2,8; 16,9] 0,1978[4]
IIB	4/53 (7,5)	2/69 (2,9)	2,60 [0,50; 13,68] 0,2583[2]	2,73 [0,48; 15,53] 0,4016[4]	4,6 [-3,5; 12,8] 0,4016[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	15/236 (6,4)	10/214 (4,7)	1,36 [0,62; 2,96] 0,4387[2]	1,38 [0,61; 3,15] 0,4363[3]	1,7 [-2,5; 5,9] 0,4363[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	15/186 (8,1)	7/174 (4,0)	2,00 [0,84; 4,80] 0,1184[2]	2,09 [0,83; 5,26] 0,1096[3]	4,0 [-0,8; 8,9] 0,1096[3]
Tumor grade (Interaction p-value: 0,7241)					
G1	6/47 (12,8)	0/41 (0,0)	11,38 [0,66; 195,96] 0,0941[2]	13,00 [0,71; 238,27] 0,0281[4]	12,8 [3,2; 22,3] 0,0281[4]
G2	11/244 (4,5)	6/234 (2,6)	1,76 [0,66; 4,68] 0,2583[2]	1,79 [0,65; 4,93] 0,2513[3]	1,9 [-1,4; 5,2] 0,2513[3]
G3	19/233 (8,2)	14/226 (6,2)	1,32 [0,68; 2,56] 0,4183[2]	1,34 [0,66; 2,75] 0,4164[3]	2,0 [-2,8; 6,7] 0,4164[3]
GX	6/29 (20,7)	2/33 (6,1)	3,41 [0,75; 15,62] 0,1135[2]	4,04 [0,75; 21,89] 0,1314[4]	14,6 [-2,2; 31,5] 0,1314[4]
Progesterone receptor status (Interaction p-value: 0,0899)					
Negative	7/49 (14,3)	1/44 (2,3)	6,29 [0,80; 49,09] 0,0796[2]	7,17 [0,84; 60,79] 0,0617[4]	12,0 [1,3; 22,8] 0,0617[4]
Positive	34/477 (7,1)	21/471 (4,5)	1,60 [0,94; 2,71] 0,0821[2]	1,64 [0,94; 2,88] 0,0788[3]	2,7 [-0,3; 5,6] 0,0788[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8432)					
White	18/323 (5,6)	9/324 (2,8)	2,01 [0,91; 4,40] 0,0822[2]	2,07 [0,91; 4,67] 0,0755[3]	2,8 [-0,3; 5,9] 0,0755[3]
Asian	21/199 (10,6)	11/180 (6,1)	1,73 [0,86; 3,48] 0,1267[2]	1,81 [0,85; 3,87] 0,1204[3]	4,4 [-1,1; 10,0] 0,1204[3]
Other	3/19 (15,8)	1/21 (4,8)	3,32 [0,38; 29,23] 0,2804[2]	3,75 [0,36; 39,59] 0,3306[4]	11,0 [-7,7; 29,8] 0,3306[4]
ECOG-PS (Interaction p-value: 0,9705)					
ECOG-PS 0	40/496 (8,1)	21/480 (4,4)	1,84 [1,10; 3,08] 0,0195[2]	1,92 [1,11; 3,30] 0,0173[3]	3,7 [0,7; 6,7] 0,0173[3]
ECOG-PS 1	2/57 (3,5)	1/55 (1,8)	1,93 [0,18; 20,68] 0,5869[2]	1,96 [0,17; 22,30] 1,0000[4]	1,7 [-4,2; 7,6] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Asthenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,6529)					
Neoadjuvant chemotherapy	20/217 (9,2)	10/219 (4,6)	2,02 [0,97; 4,21] 0,0613[2]	2,12 [0,97; 4,65] 0,0551[3]	4,7 [-0,1; 9,4] 0,0551[3]
Adjuvant chemotherapy	37/327 (11,3)	11/312 (3,5)	3,21 [1,67; 6,18] 0,0005[2]	3,49 [1,75; 6,98] 0,0002[3]	7,8 [3,8; 11,8] 0,0002[3]
No chemotherapy	0/9 (0,0)	1/4 (25,0)	0,17 [0,01; 3,40] 0,2441[2]	0,12 [0,00; 3,78] 0,3077[4]	-25,0 [-67,4; 17,4] 0,3077[4]
Region (Interaction p-value: 0,1989)					
North America / Europe	38/252 (15,1)	19/233 (8,2)	1,85 [1,10; 3,11] 0,0208[2]	2,00 [1,12; 3,58] 0,0180[3]	6,9 [1,3; 12,6] 0,0180[3]
Asia	1/168 (0,6)	0/166 (0,0)	2,96 [0,12; 72,25] 0,5048[2]	2,98 [0,12; 73,73] 1,0000[4]	0,6 [-0,6; 1,8] 1,0000[4]
Other	18/133 (13,5)	3/136 (2,2)	6,14 [1,85; 20,34] 0,0030[2]	6,94 [1,99; 24,16] 0,0005[3]	11,3 [5,0; 17,6] 0,0005[3]
Primary tumor size (Interaction p-value: 0,1353)					
< 20 mm	19/141 (13,5)	4/140 (2,9)	4,72 [1,65; 13,51] 0,0039[2]	5,30 [1,75; 16,00] 0,0012[3]	10,6 [4,3; 16,9] 0,0012[3]
≥ 20 but < 50 mm	30/255 (11,8)	11/249 (4,4)	2,66 [1,36; 5,20] 0,0041[2]	2,88 [1,41; 5,89] 0,0026[3]	7,3 [2,6; 12,1] 0,0026[3]
≥ 50 mm	8/145 (5,5)	7/141 (5,0)	1,11 [0,41; 2,98] 0,8341[2]	1,12 [0,39; 3,17] 0,8340[3]	0,6 [-4,6; 5,7] 0,8340[3]
Number of positive lymph nodes (Interaction p-value: 0,5155)					
0-3	22/203 (10,8)	10/214 (4,7)	2,32 [1,13; 4,78] 0,0225[2]	2,48 [1,14; 5,38] 0,0181[3]	6,2 [1,0; 11,3] 0,0181[3]
4-9	22/242 (9,1)	10/231 (4,3)	2,10 [1,02; 4,34] 0,0450[2]	2,21 [1,02; 4,78] 0,0393[3]	4,8 [0,3; 9,2] 0,0393[3]
≥ 10	13/108 (12,0)	2/90 (2,2)	5,42 [1,26; 23,37] 0,0235[2]	6,02 [1,32; 27,44] 0,0094[3]	9,8 [3,0; 16,7] 0,0094[3]
Tumor stage (Interaction p-value: 0,8774)					
IIA	8/59 (13,6)	3/62 (4,8)	2,80 [0,78; 10,06] 0,1141[2]	3,08 [0,78; 12,25] 0,0953[3]	8,7 [-1,5; 19,0] 0,0953[3]
IIB	5/53 (9,4)	3/69 (4,3)	2,17 [0,54; 8,68] 0,2733[2]	2,29 [0,52; 10,06] 0,2921[4]	5,1 [-4,1; 14,3] 0,2921[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	23/236 (9,7)	6/214 (2,8)	3,48 [1,44; 8,37] 0,0055[2]	3,74 [1,49; 9,38] 0,0027[3]	6,9 [2,6; 11,3] 0,0027[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	20/186 (10,8)	10/174 (5,7)	1,87 [0,90; 3,88] 0,0928[2]	1,98 [0,90; 4,35] 0,0859[3]	5,0 [-0,6; 10,6] 0,0859[3]
Tumor grade (Interaction p-value: 0,3845)					
G1	6/47 (12,8)	2/41 (4,9)	2,62 [0,56; 12,26] 0,2222[2]	2,85 [0,54; 15,00] 0,2755[4]	7,9 [-3,7; 19,5] 0,2755[4]
G2	22/244 (9,0)	13/234 (5,6)	1,62 [0,84; 3,15] 0,1515[2]	1,68 [0,83; 3,43] 0,1465[3]	3,5 [-1,2; 8,1] 0,1465[3]
G3	26/233 (11,2)	6/226 (2,7)	4,20 [1,76; 10,02] 0,0012[2]	4,61 [1,86; 11,42] 0,0003[3]	8,5 [4,0; 13,1] 0,0003[3]
GX	3/29 (10,3)	1/33 (3,0)	3,41 [0,38; 31,04] 0,2757[2]	3,69 [0,36; 37,63] 0,3321[4]	7,3 [-5,2; 19,8] 0,3321[4]
Progesterone receptor status (Interaction p-value: 0,9854)					
Negative	7/49 (14,3)	0/44 (0,0)	13,50 [0,79; 229,74] 0,0719[2]	15,71 [0,87; 283,57] 0,0131[4]	14,3 [4,5; 24,1] 0,0131[4]
Positive	48/477 (10,1)	22/471 (4,7)	2,15 [1,32; 3,51] 0,0021[2]	2,28 [1,36; 3,85] 0,0015[3]	5,4 [2,1; 8,7] 0,0015[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9063)					
White	48/323 (14,9)	20/324 (6,2)	2,41 [1,46; 3,96] 0,0005[2]	2,65 [1,54; 4,58] 0,0003[3]	8,7 [4,0; 13,4] 0,0003[3]
Asian	4/199 (2,0)	1/180 (0,6)	3,62 [0,41; 32,07] 0,2481[2]	3,67 [0,41; 33,16] 0,3749[4]	1,5 [-0,8; 3,7] 0,3749[4]
Other	3/19 (15,8)	1/21 (4,8)	3,32 [0,38; 29,23] 0,2804[2]	3,75 [0,36; 39,59] 0,3306[4]	11,0 [-7,7; 29,8] 0,3306[4]
ECOG-PS (Interaction p-value: 0,6844)					
ECOG-PS 0	50/496 (10,1)	20/480 (4,2)	2,42 [1,46; 4,00] 0,0006[2]	2,58 [1,51; 4,40] 0,0003[3]	5,9 [2,7; 9,1] 0,0003[3]
ECOG-PS 1	7/57 (12,3)	2/55 (3,6)	3,38 [0,73; 15,55] 0,1183[2]	3,71 [0,74; 18,71] 0,1624[4]	8,6 [-1,2; 18,5] 0,1624[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Blood creatinine increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9442)					
Neoadjuvant chemotherapy	21/217 (9,7)	0/219 (0,0)	43,39 [2,65; 711,89] 0,0083[2]	48,03 [2,89; 798,19] <,0001[3]	9,7 [5,7; 13,6] <,0001[3]
Adjuvant chemotherapy	29/327 (8,9)	2/312 (0,6)	13,83 [3,33; 57,49] 0,0003[2]	15,08 [3,57; 63,77] <,0001[3]	8,2 [5,0; 11,4] <,0001[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,9996)					
North America / Europe	23/252 (9,1)	1/233 (0,4)	21,27 [2,89; 156,22] 0,0027[2]	23,30 [3,12; 173,98] <,0001[3]	8,7 [5,0; 12,4] <,0001[3]
Asia	22/168 (13,1)	1/166 (0,6)	21,74 [2,96; 159,42] 0,0025[2]	24,86 [3,31; 186,74] <,0001[3]	12,5 [7,3; 17,7] <,0001[3]
Other	6/133 (4,5)	0/136 (0,0)	13,29 [0,76; 233,61] 0,0769[2]	13,92 [0,78; 249,56] 0,0138[4]	4,5 [1,0; 8,0] 0,0138[4]
Primary tumor size (Interaction p-value: 0,9992)					
< 20 mm	18/141 (12,8)	0/140 (0,0)	36,74 [2,24; 603,76] 0,0116[2]	42,09 [2,51; 705,77] <,0001[3]	12,8 [7,3; 18,3] <,0001[3]
≥ 20 but < 50 mm	18/255 (7,1)	2/249 (0,8)	8,79 [2,06; 37,48] 0,0033[2]	9,38 [2,15; 40,86] 0,0003[3]	6,3 [2,9; 9,6] 0,0003[3]
≥ 50 mm	13/145 (9,0)	0/141 (0,0)	26,26 [1,58; 437,58] 0,0228[2]	28,83 [1,70; 489,88] 0,0003[3]	9,0 [4,3; 13,6] 0,0003[3]
Number of positive lymph nodes (Interaction p-value: 0,9992)					
0-3	24/203 (11,8)	0/214 (0,0)	51,64 [3,16; 843,64] 0,0056[2]	58,55 [3,54; 969,63] <,0001[3]	11,8 [7,4; 16,3] <,0001[3]
4-9	21/242 (8,7)	2/231 (0,9)	10,02 [2,38; 42,27] 0,0017[2]	10,88 [2,52; 46,95] <,0001[3]	7,8 [4,1; 11,6] <,0001[3]
≥ 10	6/108 (5,6)	0/90 (0,0)	10,85 [0,62; 190,07] 0,1026[2]	11,48 [0,64; 206,59] 0,0327[4]	5,6 [1,2; 9,9] 0,0327[4]
Tumor stage (Interaction p-value: 0,9997)					
IIA	7/59 (11,9)	0/62 (0,0)	15,75 [0,92; 269,79] 0,0572[2]	17,86 [1,00; 320,07] 0,0054[4]	11,9 [3,6; 20,1] 0,0054[4]
IIB	5/53 (9,4)	0/69 (0,0)	14,26 [0,81; 252,30] 0,0699[2]	15,76 [0,85; 291,74] 0,0138[4]	9,4 [1,6; 17,3] 0,0138[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	21/236 (8,9)	1/214 (0,5)	19,04 [2,58; 140,36] 0,0038[2]	20,80 [2,77; 156,05] <,0001[3]	8,4 [4,7; 12,2] <,0001[3]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	15/186 (8,1)	1/174 (0,6)	14,03 [1,87; 105,11] 0,0101[2]	15,18 [1,98; 116,15] 0,0006[3]	7,5 [3,4; 11,6] 0,0006[3]
Tumor grade (Interaction p-value: 0,9999)					
G1	1/47 (2,1)	0/41 (0,0)	2,63 [0,11; 62,73] 0,5512[2]	2,68 [0,11; 67,54] 1,0000[4]	2,1 [-2,0; 6,3] 1,0000[4]
G2	23/244 (9,4)	1/234 (0,4)	22,06 [3,00; 162,02] 0,0024[2]	24,25 [3,25; 181,08] <,0001[3]	9,0 [5,2; 12,8] <,0001[3]
G3	21/233 (9,0)	1/226 (0,4)	20,37 [2,76; 150,17] 0,0031[2]	22,29 [2,97; 167,15] <,0001[3]	8,6 [4,8; 12,3] <,0001[3]
GX	6/29 (20,7)	0/33 (0,0)	14,73 [0,87; 250,72] 0,0628[2]	18,53 [1,00; 345,12] 0,0077[4]	20,7 [5,9; 35,4] 0,0077[4]
Progesterone receptor status (Interaction p-value: 0,9974)					
Negative	4/49 (8,2)	0/44 (0,0)	8,10 [0,45; 146,31] 0,1565[2]	8,80 [0,46; 168,31] 0,1191[4]	8,2 [0,5; 15,8] 0,1191[4]
Positive	41/477 (8,6)	2/471 (0,4)	20,24 [4,92; 83,21] <,0001[2]	22,05 [5,30; 91,71] <,0001[3]	8,2 [5,6; 10,8] <,0001[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,9770)					
White	27/323 (8,4)	1/324 (0,3)	27,08 [3,70; 198,13] 0,0012[2]	29,46 [3,98; 218,17] <,0001[3]	8,1 [5,0; 11,1] <,0001[3]
Asian	22/199 (11,1)	1/180 (0,6)	19,90 [2,71; 146,14] 0,0033[2]	22,25 [2,97; 166,84] <,0001[3]	10,5 [6,0; 15,0] <,0001[3]
Other	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (Interaction p-value: 0,9808)					
ECOG-PS 0	45/496 (9,1)	2/480 (0,4)	21,77 [5,31; 89,26] <,0001[2]	23,85 [5,75; 98,88] <,0001[3]	8,7 [6,1; 11,2] <,0001[3]
ECOG-PS 1	6/57 (10,5)	0/55 (0,0)	12,55 [0,72; 217,62] 0,0822[2]	14,01 [0,77; 254,95] 0,0273[4]	10,5 [2,6; 18,5] 0,0273[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Cellulitis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8326)					
Neoadjuvant chemotherapy	6/217 (2,8)	3/219 (1,4)	2,02 [0,51; 7,97] 0,3161[2]	2,05 [0,51; 8,29] 0,3369[4]	1,4 [-1,3; 4,1] 0,3369[4]
Adjuvant chemotherapy	8/327 (2,4)	2/312 (0,6)	3,82 [0,82; 17,83] 0,0886[2]	3,89 [0,82; 18,45] 0,1076[4]	1,8 [-0,1; 3,7] 0,1076[4]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,9922)					
North America / Europe	5/252 (2,0)	2/233 (0,9)	2,31 [0,45; 11,80] 0,3137[2]	2,34 [0,45; 12,17] 0,4523[4]	1,1 [-1,0; 3,2] 0,4523[4]
Asia	8/168 (4,8)	3/166 (1,8)	2,63 [0,71; 9,76] 0,1470[2]	2,72 [0,71; 10,42] 0,1303[3]	3,0 [-0,9; 6,8] 0,1303[3]
Other	2/133 (1,5)	0/136 (0,0)	5,11 [0,25; 105,49] 0,2908[2]	5,19 [0,25; 109,13] 0,2435[4]	1,5 [-0,6; 3,6] 0,2435[4]
Primary tumor size (Interaction p-value: 0,9995)					
< 20 mm	0/141 (0,0)	2/140 (1,4)	0,20 [0,01; 4,10] 0,2953[2]	0,20 [0,01; 4,11] 0,2473[4]	-1,4 [-3,4; 0,5] 0,2473[4]
≥ 20 but < 50 mm	10/255 (3,9)	2/249 (0,8)	4,88 [1,08; 22,06] 0,0393[2]	5,04 [1,09; 23,24] 0,0217[3]	3,1 [0,5; 5,7] 0,0217[3]
≥ 50 mm	5/145 (3,4)	1/141 (0,7)	4,86 [0,58; 41,10] 0,1465[2]	5,00 [0,58; 43,35] 0,2141[4]	2,7 [-0,5; 6,0] 0,2141[4]
Tumor stage (Interaction p-value: 0,7159)					
IIA	0/59 (0,0)	1/62 (1,6)	0,35 [0,01; 8,42] 0,5177[2]	0,34 [0,01; 8,63] 1,0000[4]	-1,6 [-4,7; 1,5] 1,0000[4]
IIB	1/53 (1,9)	0/69 (0,0)	3,89 [0,16; 93,60] 0,4027[2]	3,97 [0,16; 99,46] 0,4344[4]	1,9 [-1,8; 5,5] 0,4344[4]
IIIA	9/236 (3,8)	1/214 (0,5)	8,16 [1,04; 63,88] 0,0455[2]	8,44 [1,06; 67,22] 0,0216[4]	3,3 [0,7; 6,0] 0,0216[4]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	4/186 (2,2)	3/174 (1,7)	1,25 [0,28; 5,49] 0,7702[2]	1,25 [0,28; 5,68] 1,0000[4]	0,4 [-2,4; 3,3] 1,0000[4]
Tumor grade (Interaction p-value: 0,9991)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	0/47 (0,0)	1/41 (2,4)	0,29 [0,01; 6,97] 0,4467[2]	0,28 [0,01; 7,17] 0,4659[4]	-2,4 [-7,2; 2,3] 0,4659[4]
G2	9/244 (3,7)	4/234 (1,7)	2,16 [0,67; 6,91] 0,1953[2]	2,20 [0,67; 7,25] 0,1836[3]	2,0 [-0,9; 4,9] 0,1836[3]
G3	5/233 (2,1)	0/226 (0,0)	10,67 [0,59; 191,87] 0,1083[2]	10,90 [0,60; 198,34] 0,0613[4]	2,1 [0,3; 4,0] 0,0613[4]
GX	1/29 (3,4)	0/33 (0,0)	3,40 [0,14; 80,36] 0,4482[2]	3,53 [0,14; 89,98] 0,4677[4]	3,4 [-3,2; 10,1] 0,4677[4]
Progesterone receptor status (Interaction p-value: 0,9619)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	13/477 (2,7)	5/471 (1,1)	2,57 [0,92; 7,14] 0,0710[2]	2,61 [0,92; 7,38] 0,0606[3]	1,7 [-0,1; 3,4] 0,0606[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9371)					
White	7/323 (2,2)	2/324 (0,6)	3,51 [0,73; 16,77] 0,1155[2]	3,57 [0,74; 17,30] 0,1067[4]	1,5 [-0,3; 3,4] 0,1067[4]
Asian	8/199 (4,0)	3/180 (1,7)	2,41 [0,65; 8,95] 0,1882[2]	2,47 [0,65; 9,46] 0,1729[3]	2,4 [-1,0; 5,7] 0,1729[3]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,4060)					
ECOG-PS 0	14/496 (2,8)	4/480 (0,8)	3,39 [1,12; 10,22] 0,0303[2]	3,46 [1,13; 10,58] 0,0209[3]	2,0 [0,3; 3,7] 0,0209[3]
ECOG-PS 1	1/57 (1,8)	1/55 (1,8)	0,96 [0,06; 15,05] 0,9797[2]	0,96 [0,06; 15,81] 1,0000[4]	-0,1 [-5,0; 4,8] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Chills from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,8881)					
North America / Europe	9/252 (3,6)	1/233 (0,4)	8,32 [1,06; 65,18] 0,0436[2]	8,59 [1,08; 68,35] 0,0212[4]	3,1 [0,7; 5,6] 0,0212[4]
Asia	4/168 (2,4)	1/166 (0,6)	3,95 [0,45; 34,99] 0,2168[2]	4,02 [0,45; 36,39] 0,3713[4]	1,8 [-0,8; 4,4] 0,3713[4]
Other	1/133 (0,8)	0/136 (0,0)	3,07 [0,13; 74,63] 0,4913[2]	3,09 [0,12; 76,54] 0,4944[4]	0,8 [-0,7; 2,2] 0,4944[4]
Progesterone receptor status (Interaction p-value: 0,9997)					
Negative	0/49 (0,0)	0/44 (0,0)	NE	NE	NE
Positive	13/477 (2,7)	2/471 (0,4)	6,42 [1,46; 28,29] 0,0140[2]	6,57 [1,47; 29,28] 0,0045[3]	2,3 [0,7; 3,9] 0,0045[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9804)					
ECOG-PS 0	12/496 (2,4)	2/480 (0,4)	5,81 [1,31; 25,81] 0,0208[2]	5,93 [1,32; 26,62] 0,0085[3]	2,0 [0,5; 3,5] 0,0085[3]
ECOG-PS 1	2/57 (3,5)	0/55 (0,0)	4,83 [0,24; 98,34] 0,3060[2]	5,00 [0,23; 106,54] 0,4957[4]	3,5 [-1,3; 8,3] 0,4957[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Constipation from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9847)					
Neoadjuvant chemotherapy	33/217 (15,2)	19/219 (8,7)	1,75 [1,03; 2,98] 0,0388[2]	1,89 [1,04; 3,44] 0,0354[3]	6,5 [0,5; 12,6] 0,0354[3]
Adjuvant chemotherapy	45/327 (13,8)	23/312 (7,4)	1,87 [1,16; 3,01] 0,0105[2]	2,01 [1,18; 3,40] 0,0088[3]	6,4 [1,7; 11,1] 0,0088[3]
No chemotherapy	0/9 (0,0)	1/4 (25,0)	0,17 [0,01; 3,40] 0,2441[2]	0,12 [0,00; 3,78] 0,3077[4]	-25,0 [-67,4; 17,4] 0,3077[4]
Primary tumor size (Interaction p-value: 0,1682)					
< 20 mm	17/141 (12,1)	12/140 (8,6)	1,41 [0,70; 2,84] 0,3401[2]	1,46 [0,67; 3,19] 0,3369[3]	3,5 [-3,6; 10,6] 0,3369[3]
≥ 20 but < 50 mm	35/255 (13,7)	23/249 (9,2)	1,49 [0,90; 2,44] 0,1178[2]	1,56 [0,89; 2,73] 0,1144[3]	4,5 [-1,1; 10,0] 0,1144[3]
≥ 50 mm	25/145 (17,2)	7/141 (5,0)	3,47 [1,55; 7,77] 0,0024[2]	3,99 [1,66; 9,55] 0,0010[3]	12,3 [5,2; 19,4] 0,0010[3]
Number of positive lymph nodes (Interaction p-value: 0,8683)					
0-3	32/203 (15,8)	21/214 (9,8)	1,61 [0,96; 2,69] 0,0717[2]	1,72 [0,96; 3,10] 0,0682[3]	6,0 [-0,5; 12,4] 0,0682[3]
4-9	31/242 (12,8)	16/231 (6,9)	1,85 [1,04; 3,29] 0,0363[2]	1,97 [1,05; 3,72] 0,0325[3]	5,9 [0,5; 11,2] 0,0325[3]
≥ 10	15/108 (13,9)	6/90 (6,7)	2,08 [0,84; 5,15] 0,1117[2]	2,26 [0,84; 6,09] 0,1003[3]	7,2 [-1,1; 15,5] 0,1003[3]
Tumor stage (Interaction p-value: 0,8557)					
IIA	5/59 (8,5)	4/62 (6,5)	1,31 [0,37; 4,66] 0,6727[2]	1,34 [0,34; 5,26] 0,7393[4]	2,0 [-7,4; 11,4] 0,7393[4]
IIB	9/53 (17,0)	10/69 (14,5)	1,17 [0,51; 2,68] 0,7070[2]	1,21 [0,45; 3,22] 0,7071[3]	2,5 [-10,6; 15,6] 0,7071[3]
IIIA	33/236 (14,0)	16/214 (7,5)	1,87 [1,06; 3,30] 0,0307[2]	2,01 [1,07; 3,77] 0,0269[3]	6,5 [0,8; 12,2] 0,0269[3]
IIIB	3/18 (16,7)	0/15 (0,0)	5,89 [0,33; 105,81] 0,2285[2]	7,00 [0,33; 147,17] 0,2330[4]	16,7 [-0,5; 33,9] 0,2330[4]
IIIC	28/186 (15,1)	13/174 (7,5)	2,01 [1,08; 3,76] 0,0279[2]	2,19 [1,10; 4,39] 0,0236[3]	7,6 [1,1; 14,0] 0,0236[3]
Tumor grade (Interaction p-value: 0,0916)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	8/47 (17,0)	1/41 (2,4)	6,98 [0,91; 53,47] 0,0615[2]	8,21 [0,98; 68,71] 0,0334[4]	14,6 [2,8; 26,3] 0,0334[4]
G2	38/244 (15,6)	14/234 (6,0)	2,60 [1,45; 4,68] 0,0014[2]	2,90 [1,53; 5,51] 0,0008[3]	9,6 [4,1; 15,1] 0,0008[3]
G3	29/233 (12,4)	25/226 (11,1)	1,13 [0,68; 1,86] 0,6457[2]	1,14 [0,65; 2,02] 0,6453[3]	1,4 [-4,5; 7,3] 0,6453[3]
GX	3/29 (10,3)	2/33 (6,1)	1,71 [0,31; 9,52] 0,5419[2]	1,79 [0,28; 11,53] 0,6577[4]	4,3 [-9,5; 18,0] 0,6577[4]
ECOG-PS (Interaction p-value: 0,6189)					
ECOG-PS 0	71/496 (14,3)	38/480 (7,9)	1,81 [1,24; 2,63] 0,0019[2]	1,94 [1,28; 2,95] 0,0015[3]	6,4 [2,5; 10,3] 0,0015[3]
ECOG-PS 1	7/57 (12,3)	5/55 (9,1)	1,35 [0,46; 4,00] 0,5873[2]	1,40 [0,42; 4,71] 0,5853[3]	3,2 [-8,2; 14,6] 0,5853[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Cough from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8481)					
Neoadjuvant chemotherapy	31/217 (14,3)	12/219 (5,5)	2,61 [1,38; 4,94] 0,0033[2]	2,88 [1,43; 5,76] 0,0020[3]	8,8 [3,3; 14,4] 0,0020[3]
Adjuvant chemotherapy	34/327 (10,4)	16/312 (5,1)	2,03 [1,14; 3,60] 0,0157[2]	2,15 [1,16; 3,97] 0,0132[3]	5,3 [1,2; 9,4] 0,0132[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,4479)					
North America / Europe	32/252 (12,7)	16/233 (6,9)	1,85 [1,04; 3,28] 0,0355[2]	1,97 [1,05; 3,70] 0,0317[3]	5,8 [0,6; 11,1] 0,0317[3]
Asia	21/168 (12,5)	9/166 (5,4)	2,31 [1,09; 4,88] 0,0292[2]	2,49 [1,11; 5,62] 0,0237[3]	7,1 [1,0; 13,2] 0,0237[3]
Other	13/133 (9,8)	3/136 (2,2)	4,43 [1,29; 15,20] 0,0179[2]	4,80 [1,34; 17,26] 0,0087[3]	7,6 [2,0; 13,2] 0,0087[3]
Primary tumor size (Interaction p-value: 0,3874)					
< 20 mm	13/141 (9,2)	9/140 (6,4)	1,43 [0,63; 3,25] 0,3870[2]	1,48 [0,61; 3,58] 0,3838[3]	2,8 [-3,5; 9,1] 0,3838[3]
≥ 20 but < 50 mm	31/255 (12,2)	10/249 (4,0)	3,03 [1,52; 6,04] 0,0017[2]	3,31 [1,58; 6,90] 0,0008[3]	8,1 [3,4; 12,8] 0,0008[3]
≥ 50 mm	19/145 (13,1)	9/141 (6,4)	2,05 [0,96; 4,38] 0,0631[2]	2,21 [0,96; 5,07] 0,0559[3]	6,7 [-0,1; 13,5] 0,0559[3]
Number of positive lymph nodes (Interaction p-value: 0,4054)					
0-3	28/203 (13,8)	12/214 (5,6)	2,46 [1,29; 4,70] 0,0065[2]	2,69 [1,33; 5,46] 0,0046[3]	8,2 [2,5; 13,8] 0,0046[3]
4-9	23/242 (9,5)	13/231 (5,6)	1,69 [0,88; 3,25] 0,1173[2]	1,76 [0,87; 3,57] 0,1120[3]	3,9 [-0,9; 8,6] 0,1120[3]
≥ 10	15/108 (13,9)	3/90 (3,3)	4,17 [1,25; 13,94] 0,0205[2]	4,68 [1,31; 16,72] 0,0101[3]	10,6 [3,1; 18,1] 0,0101[3]
Tumor stage (Interaction p-value: 0,5701)					
IIA	5/59 (8,5)	4/62 (6,5)	1,31 [0,37; 4,66] 0,6727[2]	1,34 [0,34; 5,26] 0,7393[4]	2,0 [-7,4; 11,4] 0,7393[4]
IIB	4/53 (7,5)	5/69 (7,2)	1,04 [0,29; 3,69] 0,9498[2]	1,04 [0,27; 4,10] 1,0000[4]	0,3 [-9,1; 9,7] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	30/236 (12,7)	11/214 (5,1)	2,47 [1,27; 4,81] 0,0077[2]	2,69 [1,31; 5,51] 0,0053[3]	7,6 [2,4; 12,7] 0,0053[3]
IIIB	3/18 (16,7)	1/15 (6,7)	2,50 [0,29; 21,61] 0,4051[2]	2,80 [0,26; 30,18] 0,6074[4]	10,0 [-11,3; 31,3] 0,6074[4]
IIIC	24/186 (12,9)	7/174 (4,0)	3,21 [1,42; 7,25] 0,0051[2]	3,53 [1,48; 8,43] 0,0027[3]	8,9 [3,2; 14,5] 0,0027[3]
Tumor grade (Interaction p-value: 0,8980)					
G1	6/47 (12,8)	3/41 (7,3)	1,74 [0,47; 6,54] 0,4090[2]	1,85 [0,43; 7,94] 0,4942[4]	5,4 [-7,0; 17,9] 0,4942[4]
G2	27/244 (11,1)	11/234 (4,7)	2,35 [1,20; 4,64] 0,0133[2]	2,52 [1,22; 5,21] 0,0101[3]	6,4 [1,6; 11,1] 0,0101[3]
G3	29/233 (12,4)	13/226 (5,8)	2,16 [1,15; 4,05] 0,0160[2]	2,33 [1,18; 4,61] 0,0129[3]	6,7 [1,5; 11,9] 0,0129[3]
GX	4/29 (13,8)	1/33 (3,0)	4,55 [0,54; 38,45] 0,1639[2]	5,12 [0,54; 48,72] 0,1762[4]	10,8 [-3,1; 24,6] 0,1762[4]
Race (Interaction p-value: 0,7781)					
White	35/323 (10,8)	17/324 (5,2)	2,07 [1,18; 3,61] 0,0109[2]	2,19 [1,20; 4,00] 0,0089[3]	5,6 [1,4; 9,8] 0,0089[3]
Asian	26/199 (13,1)	10/180 (5,6)	2,35 [1,17; 4,74] 0,0168[2]	2,55 [1,20; 5,46] 0,0128[3]	7,5 [1,8; 13,3] 0,0128[3]
Other	4/19 (21,1)	1/21 (4,8)	4,42 [0,54; 36,16] 0,1657[2]	5,33 [0,54; 52,73] 0,1723[4]	16,3 [-4,2; 36,8] 0,1723[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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06JAN2022 / 04:51

Table: Subgroups - adverse events according PT Decreased appetite from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,4143)					
Neoadjuvant chemotherapy	20/217 (9,2)	1/219 (0,5)	20,18 [2,73; 149,08] 0,0032[2]	22,13 [2,94; 166,44] <,0001[3]	8,8 [4,8; 12,7] <,0001[3]
Adjuvant chemotherapy	29/327 (8,9)	6/312 (1,9)	4,61 [1,94; 10,96] 0,0005[2]	4,96 [2,03; 12,13] 0,0001[3]	6,9 [3,5; 10,4] 0,0001[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,7978)					
North America / Europe	23/252 (9,1)	4/233 (1,7)	5,32 [1,87; 15,14] 0,0018[2]	5,75 [1,96; 16,89] 0,0004[3]	7,4 [3,5; 11,3] 0,0004[3]
Asia	15/168 (8,9)	2/166 (1,2)	7,41 [1,72; 31,90] 0,0072[2]	8,04 [1,81; 35,73] 0,0013[3]	7,7 [3,1; 12,3] 0,0013[3]
Other	11/133 (8,3)	1/136 (0,7)	11,25 [1,47; 85,91] 0,0196[2]	12,17 [1,55; 95,67] 0,0028[3]	7,5 [2,6; 12,4] 0,0028[3]
Primary tumor size (Interaction p-value: 0,5204)					
< 20 mm	10/141 (7,1)	2/140 (1,4)	4,96 [1,11; 22,25] 0,0363[2]	5,27 [1,13; 24,49] 0,0189[3]	5,7 [1,0; 10,3] 0,0189[3]
≥ 20 but < 50 mm	20/255 (7,8)	4/249 (1,6)	4,88 [1,69; 14,08] 0,0033[2]	5,21 [1,76; 15,48] 0,0010[3]	6,2 [2,6; 9,9] 0,0010[3]
≥ 50 mm	18/145 (12,4)	1/141 (0,7)	17,50 [2,37; 129,37] 0,0050[2]	19,84 [2,61; 150,77] <,0001[3]	11,7 [6,2; 17,2] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,7979)					
0-3	14/203 (6,9)	5/214 (2,3)	2,95 [1,08; 8,05] 0,0344[2]	3,10 [1,09; 8,76] 0,0256[3]	4,6 [0,5; 8,6] 0,0256[3]
4-9	22/242 (9,1)	0/231 (0,0)	42,96 [2,62; 704,15] 0,0084[2]	47,24 [2,85; 783,56] <,0001[3]	9,1 [5,5; 12,7] <,0001[3]
≥ 10	13/108 (12,0)	2/90 (2,2)	5,42 [1,26; 23,37] 0,0235[2]	6,02 [1,32; 27,44] 0,0094[3]	9,8 [3,0; 16,7] 0,0094[3]
Tumor stage (Interaction p-value: 0,3706)					
IIA	3/59 (5,1)	1/62 (1,6)	3,15 [0,34; 29,46] 0,3140[2]	3,27 [0,33; 32,34] 0,3565[4]	3,5 [-3,0; 9,9] 0,3565[4]
IIB	4/53 (7,5)	4/69 (5,8)	1,30 [0,34; 4,97] 0,6994[2]	1,33 [0,32; 5,57] 0,7266[4]	1,8 [-7,2; 10,7] 0,7266[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	16/236 (6,8)	0/214 (0,0)	29,94 [1,81; 495,97] 0,0176[2]	32,10 [1,91; 538,44] 0,0001[3]	6,8 [3,6; 10,0] 0,0001[3]
IIIB	4/18 (22,2)	0/15 (0,0)	7,58 [0,44; 130,38] 0,1629[2]	9,62 [0,48; 194,83] 0,1081[4]	22,2 [3,0; 41,4] 0,1081[4]
IIIC	22/186 (11,8)	2/174 (1,1)	10,29 [2,46; 43,12] 0,0014[2]	11,54 [2,67; 49,84] <,0001[3]	10,7 [5,8; 15,6] <,0001[3]
Tumor grade (Interaction p-value: 0,5045)					
G1	1/47 (2,1)	0/41 (0,0)	2,63 [0,11; 62,73] 0,5512[2]	2,68 [0,11; 67,54] 1,0000[4]	2,1 [-2,0; 6,3] 1,0000[4]
G2	28/244 (11,5)	2/234 (0,9)	13,43 [3,23; 55,73] 0,0003[2]	15,04 [3,54; 63,88] <,0001[3]	10,6 [6,5; 14,8] <,0001[3]
G3	18/233 (7,7)	5/226 (2,2)	3,49 [1,32; 9,25] 0,0118[2]	3,70 [1,35; 10,14] 0,0068[3]	5,5 [1,6; 9,4] 0,0068[3]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,9562)					
Negative	5/49 (10,2)	0/44 (0,0)	9,90 [0,56; 174,07] 0,1170[2]	11,00 [0,59; 204,92] 0,0576[4]	10,2 [1,7; 18,7] 0,0576[4]
Positive	40/477 (8,4)	6/471 (1,3)	6,58 [2,82; 15,38] <,0001[2]	7,09 [2,98; 16,90] <,0001[3]	7,1 [4,4; 9,8] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8992)					
White	28/323 (8,7)	4/324 (1,2)	7,02 [2,49; 19,79] 0,0002[2]	7,59 [2,63; 21,91] <,0001[3]	7,4 [4,1; 10,7] <,0001[3]
Asian	16/199 (8,0)	3/180 (1,7)	4,82 [1,43; 16,28] 0,0112[2]	5,16 [1,48; 18,01] 0,0045[3]	6,4 [2,2; 10,6] 0,0045[3]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Diarrhoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8118)					
Neoadjuvant chemotherapy	174/217 (80,2)	11/219 (5,0)	15,96 [8,94; 28,50] <,0001[2]	76,52 [38,30; 152,88] <,0001[3]	75,2 [69,1; 81,2] <,0001[3]
Adjuvant chemotherapy	264/327 (80,7)	20/312 (6,4)	12,59 [8,22; 19,31] <,0001[2]	61,18 [36,02; 103,93] <,0001[3]	74,3 [69,3; 79,4] <,0001[3]
No chemotherapy	6/9 (66,7)	0/4 (0,0)	6,50 [0,45; 93,73] 0,1692[2]	16,71 [0,68; 409,09] 0,0699[4]	66,7 [35,9; 97,5] 0,0699[4]
Region (Interaction p-value: 0,0851)					
North America / Europe	208/252 (82,5)	20/233 (8,6)	9,62 [6,30; 14,68] <,0001[2]	50,35 [28,70; 88,32] <,0001[3]	74,0 [68,0; 79,9] <,0001[3]
Asia	152/168 (90,5)	8/166 (4,8)	18,77 [9,53; 36,98] <,0001[2]	187,63 [78,02; 451,18] <,0001[3]	85,7 [80,2; 91,2] <,0001[3]
Other	84/133 (63,2)	3/136 (2,2)	28,63 [9,28; 88,33] <,0001[2]	76,00 [22,95; 251,65] <,0001[3]	61,0 [52,4; 69,5] <,0001[3]
Primary tumor size (Interaction p-value: 0,1289)					
< 20 mm	115/141 (81,6)	8/140 (5,7)	14,27 [7,25; 28,10] <,0001[2]	72,98 [31,79; 167,52] <,0001[3]	75,8 [68,4; 83,3] <,0001[3]
≥ 20 but < 50 mm	198/255 (77,6)	19/249 (7,6)	10,18 [6,57; 15,75] <,0001[2]	42,05 [24,19; 73,09] <,0001[3]	70,0 [63,9; 76,1] <,0001[3]
≥ 50 mm	123/145 (84,8)	4/141 (2,8)	29,90 [11,35; 78,76] <,0001[2]	191,49 [64,20; 571,15] <,0001[3]	82,0 [75,5; 88,4] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9068)					
0-3	164/203 (80,8)	12/214 (5,6)	14,41 [8,28; 25,07] <,0001[2]	70,79 [35,90; 139,59] <,0001[3]	75,2 [68,9; 81,4] <,0001[3]
4-9	195/242 (80,6)	13/231 (5,6)	14,32 [8,41; 24,37] <,0001[2]	69,57 [36,54; 132,46] <,0001[3]	75,0 [69,1; 80,8] <,0001[3]
≥ 10	85/108 (78,7)	6/90 (6,7)	11,81 [5,42; 25,73] <,0001[2]	51,74 [20,06; 133,48] <,0001[3]	72,0 [62,8; 81,3] <,0001[3]
Tumor stage (Interaction p-value: 0,8542)					
IIA	47/59 (79,7)	5/62 (8,1)	9,88 [4,22; 23,12] <,0001[2]	44,65 [14,68; 135,82] <,0001[3]	71,6 [59,3; 83,9] <,0001[3]
IIB	40/53 (75,5)	5/69 (7,2)	10,42 [4,42; 24,56] <,0001[2]	39,38 [13,05; 118,85] <,0001[3]	68,2 [55,1; 81,3] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	191/236 (80,9)	11/214 (5,1)	15,74 [8,83; 28,09] <,0001[2]	78,33 [39,36; 155,89] <,0001[3]	75,8 [70,0; 81,6] <,0001[3]
IIIB	15/18 (83,3)	1/15 (6,7)	12,50 [1,86; 83,97] 0,0094[2]	70,00 [6,49; 754,44] <,0001[3]	76,7 [55,3; 98,0] <,0001[3]
IIIC	150/186 (80,6)	9/174 (5,2)	15,59 [8,22; 29,57] <,0001[2]	76,39 [35,61; 163,86] <,0001[3]	75,5 [68,9; 82,0] <,0001[3]
Tumor grade (Interaction p-value: 0,8698)					
G1	38/47 (80,9)	2/41 (4,9)	16,57 [4,26; 64,50] <,0001[2]	82,33 [16,69; 406,16] <,0001[3]	76,0 [62,9; 89,0] <,0001[3]
G2	204/244 (83,6)	16/234 (6,8)	12,23 [7,59; 19,69] <,0001[2]	69,49 [37,74; 127,94] <,0001[3]	76,8 [71,1; 82,4] <,0001[3]
G3	183/233 (78,5)	11/226 (4,9)	16,14 [9,03; 28,83] <,0001[2]	71,54 [36,17; 141,46] <,0001[3]	73,7 [67,7; 79,6] <,0001[3]
GX	19/29 (65,5)	2/33 (6,1)	10,81 [2,75; 42,50] 0,0007[2]	29,45 [5,82; 149,12] <,0001[3]	59,5 [40,3; 78,6] <,0001[3]
Progesterone receptor status (Interaction p-value: 0,4113)					
Negative	40/49 (81,6)	3/44 (6,8)	11,97 [3,98; 35,98] <,0001[2]	60,74 [15,32; 240,80] <,0001[3]	74,8 [61,7; 88,0] <,0001[3]
Positive	385/477 (80,7)	24/471 (5,1)	15,84 [10,70; 23,45] <,0001[2]	77,94 [48,74; 124,64] <,0001[3]	75,6 [71,6; 79,7] <,0001[3]
Unknown	2/4 (50,0)	1/8 (12,5)	4,00 [0,50; 31,98] 0,1912[2]	7,00 [0,40; 123,35] 0,2364[4]	37,5 [-16,6; 91,6] 0,2364[4]
Race (Interaction p-value: 0,4635)					
White	246/323 (76,2)	21/324 (6,5)	11,75 [7,74; 17,85] <,0001[2]	46,10 [27,65; 76,84] <,0001[3]	69,7 [64,3; 75,0] <,0001[3]
Asian	171/199 (85,9)	8/180 (4,4)	19,33 [9,80; 38,15] <,0001[2]	131,30 [58,19; 296,26] <,0001[3]	81,5 [75,8; 87,2] <,0001[3]
Other	15/19 (78,9)	1/21 (4,8)	16,58 [2,41; 113,85] 0,0043[2]	75,00 [7,59; 741,57] <,0001[3]	74,2 [53,7; 94,7] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dry eye from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,4080)					
Neoadjuvant chemotherapy	8/217 (3,7)	5/219 (2,3)	1,61 [0,54; 4,86] 0,3939[2]	1,64 [0,53; 5,09] 0,3889[3]	1,4 [-1,8; 4,6] 0,3889[3]
Adjuvant chemotherapy	12/327 (3,7)	2/312 (0,6)	5,72 [1,29; 25,37] 0,0216[2]	5,90 [1,31; 26,60] 0,0089[3]	3,0 [0,8; 5,3] 0,0089[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,7523)					
North America / Europe	11/252 (4,4)	3/233 (1,3)	3,39 [0,96; 12,00] 0,0584[2]	3,50 [0,96; 12,70] 0,0431[3]	3,1 [0,2; 6,0] 0,0431[3]
Asia	7/168 (4,2)	4/166 (2,4)	1,73 [0,52; 5,80] 0,3749[2]	1,76 [0,51; 6,13] 0,3683[3]	1,8 [-2,1; 5,6] 0,3683[3]
Other	3/133 (2,3)	0/136 (0,0)	7,16 [0,37; 137,23] 0,1916[2]	7,32 [0,37; 143,13] 0,1195[4]	2,3 [-0,3; 4,8] 0,1195[4]
Primary tumor size (Interaction p-value: 0,2160)					
< 20 mm	5/141 (3,5)	4/140 (2,9)	1,24 [0,34; 4,53] 0,7435[2]	1,25 [0,33; 4,76] 1,0000[4]	0,7 [-3,4; 4,8] 1,0000[4]
≥ 20 but < 50 mm	11/255 (4,3)	1/249 (0,4)	10,74 [1,40; 82,58] 0,0225[2]	11,18 [1,43; 87,26] 0,0040[3]	3,9 [1,3; 6,5] 0,0040[3]
≥ 50 mm	5/145 (3,4)	2/141 (1,4)	2,43 [0,48; 12,33] 0,2835[2]	2,48 [0,47; 13,01] 0,4476[4]	2,0 [-1,5; 5,6] 0,4476[4]
Number of positive lymph nodes (Interaction p-value: 0,3971)					
0-3	8/203 (3,9)	4/214 (1,9)	2,11 [0,64; 6,89] 0,2172[2]	2,15 [0,64; 7,27] 0,2059[3]	2,1 [-1,2; 5,3] 0,2059[3]
4-9	12/242 (5,0)	2/231 (0,9)	5,73 [1,30; 25,31] 0,0213[2]	5,97 [1,32; 26,99] 0,0087[3]	4,1 [1,1; 7,1] 0,0087[3]
≥ 10	1/108 (0,9)	1/90 (1,1)	0,83 [0,05; 13,14] 0,8969[2]	0,83 [0,05; 13,49] 1,0000[4]	-0,2 [-3,0; 2,6] 1,0000[4]
Tumor stage (Interaction p-value: 0,9955)					
IIA	1/59 (1,7)	2/62 (3,2)	0,53 [0,05; 5,64] 0,5952[2]	0,52 [0,05; 5,86] 1,0000[4]	-1,5 [-7,0; 4,0] 1,0000[4]
IIB	3/53 (5,7)	0/69 (0,0)	9,07 [0,48; 171,96] 0,1417[2]	9,63 [0,49; 190,67] 0,0793[4]	5,7 [-0,6; 11,9] 0,0793[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	13/236 (5,5)	0/214 (0,0)	24,49 [1,46; 409,54] 0,0260[2]	25,91 [1,53; 438,61] 0,0005[3]	5,5 [2,6; 8,4] 0,0005[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	4/186 (2,2)	5/174 (2,9)	0,75 [0,20; 2,74] 0,6617[2]	0,74 [0,20; 2,81] 0,7438[4]	-0,7 [-4,0; 2,5] 0,7438[4]
Tumor grade (Interaction p-value: 0,6946)					
G1	1/47 (2,1)	0/41 (0,0)	2,63 [0,11; 62,73] 0,5512[2]	2,68 [0,11; 67,54] 1,0000[4]	2,1 [-2,0; 6,3] 1,0000[4]
G2	11/244 (4,5)	2/234 (0,9)	5,27 [1,18; 23,54] 0,0294[2]	5,48 [1,20; 24,98] 0,0141[3]	3,7 [0,8; 6,5] 0,0141[3]
G3	8/233 (3,4)	4/226 (1,8)	1,94 [0,59; 6,35] 0,2736[2]	1,97 [0,59; 6,65] 0,2641[3]	1,7 [-1,2; 4,6] 0,2641[3]
GX	1/29 (3,4)	1/33 (3,0)	1,14 [0,07; 17,39] 0,9260[2]	1,14 [0,07; 19,13] 1,0000[4]	0,4 [-8,4; 9,3] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,9971)					
Negative	3/49 (6,1)	1/44 (2,3)	2,69 [0,29; 24,96] 0,3830[2]	2,80 [0,28; 28,00] 0,6190[4]	3,8 [-4,2; 11,9] 0,6190[4]
Positive	15/477 (3,1)	6/471 (1,3)	2,47 [0,97; 6,31] 0,0590[2]	2,52 [0,97; 6,54] 0,0504[3]	1,9 [0,0; 3,7] 0,0504[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,5229)					
White	13/323 (4,0)	3/324 (0,9)	4,35 [1,25; 15,11] 0,0208[2]	4,49 [1,27; 15,90] 0,0112[3]	3,1 [0,7; 5,5] 0,0112[3]
Asian	7/199 (3,5)	4/180 (2,2)	1,58 [0,47; 5,32] 0,4576[2]	1,60 [0,46; 5,57] 0,4532[3]	1,3 [-2,0; 4,6] 0,4532[3]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,7213)					
ECOG-PS 0	19/496 (3,8)	6/480 (1,3)	3,06 [1,23; 7,61] 0,0158[2]	3,15 [1,25; 7,95] 0,0107[3]	2,6 [0,6; 4,5] 0,0107[3]
ECOG-PS 1	2/57 (3,5)	1/55 (1,8)	1,93 [0,18; 20,68] 0,5869[2]	1,96 [0,17; 22,30] 1,0000[4]	1,7 [-4,2; 7,6] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Dry mouth from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8670)					
Neoadjuvant chemotherapy	5/217 (2,3)	1/219 (0,5)	5,05 [0,59; 42,84] 0,1380[2]	5,14 [0,60; 44,38] 0,1211[4]	1,8 [-0,3; 4,0] 0,1211[4]
Adjuvant chemotherapy	8/327 (2,4)	3/312 (1,0)	2,54 [0,68; 9,50] 0,1648[2]	2,58 [0,68; 9,83] 0,1491[3]	1,5 [-0,5; 3,5] 0,1491[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,9992)					
North America / Europe	7/252 (2,8)	4/233 (1,7)	1,62 [0,48; 5,46] 0,4378[2]	1,64 [0,47; 5,66] 0,4330[3]	1,1 [-1,6; 3,7] 0,4330[3]
Asia	2/168 (1,2)	0/166 (0,0)	4,94 [0,24; 102,14] 0,3012[2]	5,00 [0,24; 104,94] 0,4985[4]	1,2 [-0,4; 2,8] 0,4985[4]
Other	4/133 (3,0)	0/136 (0,0)	9,20 [0,50; 169,25] 0,1352[2]	9,49 [0,51; 177,95] 0,0584[4]	3,0 [0,1; 5,9] 0,0584[4]
Progesterone receptor status (Interaction p-value: 0,6071)					
Negative	2/49 (4,1)	1/44 (2,3)	1,80 [0,17; 19,13] 0,6276[2]	1,83 [0,16; 20,91] 1,0000[4]	1,8 [-5,3; 8,9] 1,0000[4]
Positive	9/477 (1,9)	1/471 (0,2)	8,89 [1,13; 69,87] 0,0379[2]	9,04 [1,14; 71,62] 0,0209[4]	1,7 [0,4; 3,0] 0,0209[4]
Unknown	0/4 (0,0)	1/8 (12,5)	0,60 [0,03; 12,15] 0,7393[2]	0,56 [0,02; 16,77] 1,0000[4]	-12,5 [-35,4; 10,4] 1,0000[4]
Race (Interaction p-value: 0,9996)					
White	10/323 (3,1)	4/324 (1,2)	2,51 [0,79; 7,91] 0,1169[2]	2,56 [0,79; 8,23] 0,1037[3]	1,9 [-0,4; 4,1] 0,1037[3]
Asian	3/199 (1,5)	0/180 (0,0)	6,34 [0,33; 121,81] 0,2210[2]	6,43 [0,33; 125,34] 0,2499[4]	1,5 [-0,2; 3,2] 0,2499[4]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9804)					
ECOG-PS 0	12/496 (2,4)	4/480 (0,8)	2,90 [0,94; 8,94] 0,0632[2]	2,95 [0,94; 9,21] 0,0511[3]	1,6 [0,0; 3,2] 0,0511[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Dry skin from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9551)					
Neoadjuvant chemotherapy	14/217 (6,5)	7/219 (3,2)	2,02 [0,83; 4,90] 0,1210[2]	2,09 [0,83; 5,28] 0,1125[3]	3,3 [-0,8; 7,3] 0,1125[3]
Adjuvant chemotherapy	14/327 (4,3)	8/312 (2,6)	1,67 [0,71; 3,92] 0,2398[2]	1,70 [0,70; 4,11] 0,2340[3]	1,7 [-1,1; 4,5] 0,2340[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,8325)					
North America / Europe	12/252 (4,8)	7/233 (3,0)	1,59 [0,63; 3,96] 0,3238[2]	1,61 [0,62; 4,17] 0,3189[3]	1,8 [-1,7; 5,2] 0,3189[3]
Asia	14/168 (8,3)	6/166 (3,6)	2,31 [0,91; 5,86] 0,0790[2]	2,42 [0,91; 6,47] 0,0692[3]	4,7 [-0,3; 9,8] 0,0692[3]
Other	3/133 (2,3)	2/136 (1,5)	1,53 [0,26; 9,03] 0,6363[2]	1,55 [0,25; 9,40] 0,6817[4]	0,8 [-2,4; 4,0] 0,6817[4]
Primary tumor size (Interaction p-value: 0,9751)					
< 20 mm	7/141 (5,0)	3/140 (2,1)	2,32 [0,61; 8,78] 0,2164[2]	2,39 [0,60; 9,42] 0,3349[4]	2,8 [-1,5; 7,1] 0,3349[4]
≥ 20 but < 50 mm	12/255 (4,7)	6/249 (2,4)	1,95 [0,74; 5,12] 0,1737[2]	2,00 [0,74; 5,41] 0,1649[3]	2,3 [-0,9; 5,5] 0,1649[3]
≥ 50 mm	10/145 (6,9)	5/141 (3,5)	1,94 [0,68; 5,55] 0,2136[2]	2,01 [0,67; 6,05] 0,2038[3]	3,4 [-1,8; 8,5] 0,2038[3]
Number of positive lymph nodes (Interaction p-value: 0,4831)					
0-3	10/203 (4,9)	6/214 (2,8)	1,76 [0,65; 4,75] 0,2663[2]	1,80 [0,64; 5,04] 0,2594[3]	2,1 [-1,6; 5,8] 0,2594[3]
4-9	16/242 (6,6)	6/231 (2,6)	2,55 [1,01; 6,39] 0,0467[2]	2,65 [1,02; 6,91] 0,0382[3]	4,0 [0,3; 7,8] 0,0382[3]
≥ 10	3/108 (2,8)	3/90 (3,3)	0,83 [0,17; 4,03] 0,8206[2]	0,83 [0,16; 4,21] 1,0000[4]	-0,6 [-5,4; 4,3] 1,0000[4]
Tumor stage (Interaction p-value: 0,8025)					
IIA	3/59 (5,1)	2/62 (3,2)	1,58 [0,27; 9,10] 0,6110[2]	1,61 [0,26; 9,98] 0,6745[4]	1,9 [-5,3; 9,0] 0,6745[4]
IIB	2/53 (3,8)	3/69 (4,3)	0,87 [0,15; 5,01] 0,8742[2]	0,86 [0,14; 5,36] 1,0000[4]	-0,6 [-7,6; 6,5] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	15/236 (6,4)	5/214 (2,3)	2,72 [1,01; 7,36] 0,0487[2]	2,84 [1,01; 7,94] 0,0388[3]	4,0 [0,3; 7,7] 0,0388[3]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	7/186 (3,8)	5/174 (2,9)	1,31 [0,42; 4,05] 0,6395[2]	1,32 [0,41; 4,24] 0,6383[3]	0,9 [-2,8; 4,6] 0,6383[3]
Tumor grade (Interaction p-value: 0,9782)					
G1	5/47 (10,6)	0/41 (0,0)	9,63 [0,55; 168,96] 0,1214[2]	10,74 [0,58; 200,45] 0,0583[4]	10,6 [1,8; 19,5] 0,0583[4]
G2	13/244 (5,3)	7/234 (3,0)	1,78 [0,72; 4,39] 0,2094[2]	1,82 [0,72; 4,66] 0,2022[3]	2,3 [-1,2; 5,9] 0,2022[3]
G3	10/233 (4,3)	7/226 (3,1)	1,39 [0,54; 3,58] 0,5003[2]	1,40 [0,52; 3,75] 0,4981[3]	1,2 [-2,3; 4,6] 0,4981[3]
GX	1/29 (3,4)	1/33 (3,0)	1,14 [0,07; 17,39] 0,9260[2]	1,14 [0,07; 19,13] 1,0000[4]	0,4 [-8,4; 9,3] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,9353)					
Negative	4/49 (8,2)	0/44 (0,0)	8,10 [0,45; 146,31] 0,1565[2]	8,80 [0,46; 168,31] 0,1191[4]	8,2 [0,5; 15,8] 0,1191[4]
Positive	24/477 (5,0)	14/471 (3,0)	1,69 [0,89; 3,23] 0,1107[2]	1,73 [0,88; 3,39] 0,1061[3]	2,1 [-0,4; 4,5] 0,1061[3]
Unknown	0/4 (0,0)	1/8 (12,5)	0,60 [0,03; 12,15] 0,7393[2]	0,56 [0,02; 16,77] 1,0000[4]	-12,5 [-35,4; 10,4] 1,0000[4]
Race (Interaction p-value: 0,4927)					
White	8/323 (2,5)	8/324 (2,5)	1,00 [0,38; 2,64] 0,9950[2]	1,00 [0,37; 2,71] 0,9950[3]	0,0 [-2,4; 2,4] 0,9950[3]
Asian	15/199 (7,5)	6/180 (3,3)	2,26 [0,90; 5,70] 0,0838[2]	2,36 [0,90; 6,23] 0,0740[3]	4,2 [-0,3; 8,7] 0,0740[3]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,4791)					
ECOG-PS 0	27/496 (5,4)	13/480 (2,7)	2,01 [1,05; 3,85] 0,0352[2]	2,07 [1,05; 4,06] 0,0312[3]	2,7 [0,3; 5,2] 0,0312[3]
ECOG-PS 1	2/57 (3,5)	2/55 (3,6)	0,96 [0,14; 6,61] 0,9710[2]	0,96 [0,13; 7,09] 1,0000[4]	-0,1 [-7,0; 6,7] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Dysgeusia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,9563)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	13/477 (2,7)	1/471 (0,2)	12,84 [1,69; 97,73] 0,0137[2]	13,17 [1,72; 101,07] 0,0013[3]	2,5 [1,0; 4,0] 0,0013[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9831)					
ECOG-PS 0	14/496 (2,8)	1/480 (0,2)	13,55 [1,79; 102,63] 0,0116[2]	13,91 [1,82; 106,22] 0,0009[3]	2,6 [1,1; 4,1] 0,0009[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dyspepsia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,1235)					
Neoadjuvant chemotherapy	30/217 (13,8)	5/219 (2,3)	6,06 [2,39; 15,32] 0,0001[2]	6,87 [2,61; 18,06] <,0001[3]	11,5 [6,5; 16,5] <,0001[3]
Adjuvant chemotherapy	24/327 (7,3)	8/312 (2,6)	2,86 [1,31; 6,28] 0,0086[2]	3,01 [1,33; 6,81] 0,0057[3]	4,8 [1,4; 8,1] 0,0057[3]
No chemotherapy	1/9 (11,1)	1/4 (25,0)	0,44 [0,04; 5,46] 0,5264[2]	0,38 [0,02; 8,10] 1,0000[4]	-13,9 [-61,0; 33,3] 1,0000[4]
Region (Interaction p-value: 0,1226)					
North America / Europe	18/252 (7,1)	8/233 (3,4)	2,08 [0,92; 4,69] 0,0776[2]	2,16 [0,92; 5,08] 0,0700[3]	3,7 [-0,2; 7,7] 0,0700[3]
Asia	28/168 (16,7)	3/166 (1,8)	9,22 [2,86; 29,75] 0,0002[2]	10,87 [3,23; 36,51] <,0001[3]	14,9 [8,9; 20,8] <,0001[3]
Other	9/133 (6,8)	3/136 (2,2)	3,07 [0,85; 11,08] 0,0872[2]	3,22 [0,85; 12,16] 0,0700[3]	4,6 [-0,4; 9,5] 0,0700[3]
Primary tumor size (Interaction p-value: 0,7935)					
< 20 mm	19/141 (13,5)	4/140 (2,9)	4,72 [1,65; 13,51] 0,0039[2]	5,30 [1,75; 16,00] 0,0012[3]	10,6 [4,3; 16,9] 0,0012[3]
≥ 20 but < 50 mm	21/255 (8,2)	5/249 (2,0)	4,10 [1,57; 10,71] 0,0039[2]	4,38 [1,62; 11,81] 0,0016[3]	6,2 [2,4; 10,0] 0,0016[3]
≥ 50 mm	15/145 (10,3)	5/141 (3,5)	2,92 [1,09; 7,81] 0,0332[2]	3,14 [1,11; 8,88] 0,0242[3]	6,8 [1,0; 12,6] 0,0242[3]
Number of positive lymph nodes (Interaction p-value: 0,9994)					
0-3	22/203 (10,8)	6/214 (2,8)	3,87 [1,60; 9,34] 0,0027[2]	4,21 [1,67; 10,62] 0,0011[3]	8,0 [3,2; 12,8] 0,0011[3]
4-9	24/242 (9,9)	6/231 (2,6)	3,82 [1,59; 9,17] 0,0027[2]	4,13 [1,66; 10,30] 0,0011[3]	7,3 [3,0; 11,6] 0,0011[3]
≥ 10	9/108 (8,3)	2/90 (2,2)	3,75 [0,83; 16,91] 0,0855[2]	4,00 [0,84; 19,01] 0,0616[3]	6,1 [0,1; 12,1] 0,0616[3]
Tumor stage (Interaction p-value: 0,8547)					
IIA	6/59 (10,2)	1/62 (1,6)	6,31 [0,78; 50,81] 0,0837[2]	6,91 [0,81; 59,21] 0,0574[4]	8,6 [0,2; 16,9] 0,0574[4]
IIB	5/53 (9,4)	3/69 (4,3)	2,17 [0,54; 8,68] 0,2733[2]	2,29 [0,52; 10,06] 0,2921[4]	5,1 [-4,1; 14,3] 0,2921[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	27/236 (11,4)	5/214 (2,3)	4,90 [1,92; 12,49] 0,0009[2]	5,40 [2,04; 14,29] 0,0002[3]	9,1 [4,6; 13,6] 0,0002[3]
IIIB	3/18 (16,7)	1/15 (6,7)	2,50 [0,29; 21,61] 0,4051[2]	2,80 [0,26; 30,18] 0,6074[4]	10,0 [-11,3; 31,3] 0,6074[4]
IIIC	14/186 (7,5)	4/174 (2,3)	3,27 [1,10; 9,76] 0,0332[2]	3,46 [1,12; 10,72] 0,0229[3]	5,2 [0,8; 9,6] 0,0229[3]
Tumor grade (Interaction p-value: 0,9368)					
G1	2/47 (4,3)	1/41 (2,4)	1,74 [0,16; 18,55] 0,6444[2]	1,78 [0,16; 20,35] 1,0000[4]	1,8 [-5,6; 9,3] 1,0000[4]
G2	25/244 (10,2)	6/234 (2,6)	4,00 [1,67; 9,56] 0,0019[2]	4,34 [1,75; 10,78] 0,0007[3]	7,7 [3,4; 12,0] 0,0007[3]
G3	26/233 (11,2)	7/226 (3,1)	3,60 [1,60; 8,13] 0,0020[2]	3,93 [1,67; 9,25] 0,0008[3]	8,1 [3,4; 12,7] 0,0008[3]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,9327)					
Negative	11/49 (22,4)	0/44 (0,0)	20,70 [1,26; 341,30] 0,0341[2]	26,58 [1,52; 466,11] 0,0008[3]	22,4 [10,8; 34,1] 0,0008[3]
Positive	43/477 (9,0)	13/471 (2,8)	3,27 [1,78; 5,99] 0,0001[2]	3,49 [1,85; 6,58] <,0001[3]	6,3 [3,3; 9,2] <,0001[3]
Unknown	0/4 (0,0)	1/8 (12,5)	0,60 [0,03; 12,15] 0,7393[2]	0,56 [0,02; 16,77] 1,0000[4]	-12,5 [-35,4; 10,4] 1,0000[4]
Race (Interaction p-value: 0,1464)					
White	25/323 (7,7)	10/324 (3,1)	2,51 [1,22; 5,14] 0,0120[2]	2,63 [1,24; 5,58] 0,0089[3]	4,7 [1,2; 8,1] 0,0089[3]
Asian	29/199 (14,6)	3/180 (1,7)	8,74 [2,71; 28,21] 0,0003[2]	10,06 [3,01; 33,66] <,0001[3]	12,9 [7,7; 18,2] <,0001[3]
Other	1/19 (5,3)	1/21 (4,8)	1,11 [0,07; 16,47] 0,9421[2]	1,11 [0,06; 19,09] 1,0000[4]	0,5 [-13,1; 14,1] 1,0000[4]
ECOG-PS (Interaction p-value: 0,7158)					
ECOG-PS 0	49/496 (9,9)	12/480 (2,5)	3,95 [2,13; 7,34] <,0001[2]	4,28 [2,24; 8,14] <,0001[3]	7,4 [4,4; 10,4] <,0001[3]
ECOG-PS 1	6/57 (10,5)	2/55 (3,6)	2,89 [0,61; 13,73] 0,1809[2]	3,12 [0,60; 16,17] 0,2716[4]	6,9 [-2,5; 16,3] 0,2716[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Dyspnoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7242)					
Neoadjuvant chemotherapy	13/217 (6,0)	3/219 (1,4)	4,37 [1,26; 15,13] 0,0198[2]	4,59 [1,29; 16,34] 0,0103[3]	4,6 [1,1; 8,1] 0,0103[3]
Adjuvant chemotherapy	20/327 (6,1)	8/312 (2,6)	2,39 [1,07; 5,34] 0,0343[2]	2,48 [1,07; 5,71] 0,0283[3]	3,6 [0,4; 6,7] 0,0283[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,9246)					
North America / Europe	27/252 (10,7)	8/233 (3,4)	3,12 [1,45; 6,73] 0,0037[2]	3,38 [1,50; 7,59] 0,0020[3]	7,3 [2,8; 11,8] 0,0020[3]
Asia	2/168 (1,2)	1/166 (0,6)	1,98 [0,18; 21,59] 0,5766[2]	1,99 [0,18; 22,14] 1,0000[4]	0,6 [-1,4; 2,6] 1,0000[4]
Other	5/133 (3,8)	2/136 (1,5)	2,56 [0,50; 12,95] 0,2568[2]	2,62 [0,50; 13,73] 0,2781[4]	2,3 [-1,5; 6,1] 0,2781[4]
Primary tumor size (Interaction p-value: 0,6947)					
< 20 mm	9/141 (6,4)	4/140 (2,9)	2,23 [0,70; 7,09] 0,1723[2]	2,32 [0,70; 7,71] 0,1595[3]	3,5 [-1,4; 8,4] 0,1595[3]
≥ 20 but < 50 mm	14/255 (5,5)	3/249 (1,2)	4,56 [1,33; 15,66] 0,0161[2]	4,76 [1,35; 16,79] 0,0077[3]	4,3 [1,2; 7,4] 0,0077[3]
≥ 50 mm	11/145 (7,6)	4/141 (2,8)	2,67 [0,87; 8,20] 0,0854[2]	2,81 [0,87; 9,05] 0,0717[3]	4,7 [-0,4; 9,9] 0,0717[3]
Number of positive lymph nodes (Interaction p-value: 0,8810)					
0-3	16/203 (7,9)	5/214 (2,3)	3,37 [1,26; 9,04] 0,0156[2]	3,58 [1,29; 9,95] 0,0096[3]	5,5 [1,3; 9,8] 0,0096[3]
4-9	13/242 (5,4)	4/231 (1,7)	3,10 [1,03; 9,38] 0,0448[2]	3,22 [1,03; 10,03] 0,0335[3]	3,6 [0,3; 6,9] 0,0335[3]
≥ 10	5/108 (4,6)	2/90 (2,2)	2,08 [0,41; 10,48] 0,3733[2]	2,14 [0,40; 11,28] 0,4586[4]	2,4 [-2,6; 7,4] 0,4586[4]
Tumor stage (Interaction p-value: 0,7258)					
IIA	4/59 (6,8)	2/62 (3,2)	2,10 [0,40; 11,05] 0,3804[2]	2,18 [0,38; 12,39] 0,4318[4]	3,6 [-4,2; 11,3] 0,4318[4]
IIB	2/53 (3,8)	2/69 (2,9)	1,30 [0,19; 8,94] 0,7884[2]	1,31 [0,18; 9,64] 1,0000[4]	0,9 [-5,6; 7,4] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	14/236 (5,9)	2/214 (0,9)	6,35 [1,46; 27,61] 0,0137[2]	6,68 [1,50; 29,76] 0,0042[3]	5,0 [1,7; 8,3] 0,0042[3]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	12/186 (6,5)	5/174 (2,9)	2,25 [0,81; 6,24] 0,1211[2]	2,33 [0,80; 6,76] 0,1097[3]	3,6 [-0,7; 7,9] 0,1097[3]
Tumor grade (Interaction p-value: 0,2983)					
G1	5/47 (10,6)	1/41 (2,4)	4,36 [0,53; 35,82] 0,1704[2]	4,76 [0,53; 42,56] 0,2092[4]	8,2 [-1,8; 18,2] 0,2092[4]
G2	13/244 (5,3)	5/234 (2,1)	2,49 [0,90; 6,89] 0,0779[2]	2,58 [0,90; 7,35] 0,0669[3]	3,2 [-0,2; 6,6] 0,0669[3]
G3	16/233 (6,9)	5/226 (2,2)	3,10 [1,16; 8,33] 0,0246[2]	3,26 [1,17; 9,05] 0,0170[3]	4,7 [0,9; 8,4] 0,0170[3]
GX	0/29 (0,0)	0/33 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9957)					
Negative	2/49 (4,1)	0/44 (0,0)	4,50 [0,22; 91,25] 0,3273[2]	4,68 [0,22; 100,28] 0,4960[4]	4,1 [-1,5; 9,6] 0,4960[4]
Positive	29/477 (6,1)	11/471 (2,3)	2,60 [1,32; 5,15] 0,0060[2]	2,71 [1,34; 5,48] 0,0041[3]	3,7 [1,2; 6,3] 0,0041[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,7179)					
White	24/323 (7,4)	8/324 (2,5)	3,01 [1,37; 6,60] 0,0060[2]	3,17 [1,40; 7,17] 0,0036[3]	5,0 [1,6; 8,3] 0,0036[3]
Asian	5/199 (2,5)	1/180 (0,6)	4,52 [0,53; 38,35] 0,1664[2]	4,61 [0,53; 39,87] 0,2186[4]	2,0 [-0,5; 4,4] 0,2186[4]
Other	1/19 (5,3)	1/21 (4,8)	1,11 [0,07; 16,47] 0,9421[2]	1,11 [0,06; 19,09] 1,0000[4]	0,5 [-13,1; 14,1] 1,0000[4]
ECOG-PS (Interaction p-value: 0,8060)					
ECOG-PS 0	30/496 (6,0)	10/480 (2,1)	2,90 [1,44; 5,87] 0,0030[2]	3,03 [1,46; 6,26] 0,0018[3]	4,0 [1,5; 6,4] 0,0018[3]
ECOG-PS 1	4/57 (7,0)	1/55 (1,8)	3,86 [0,45; 33,46] 0,2203[2]	4,08 [0,44; 37,67] 0,3640[4]	5,2 [-2,3; 12,7] 0,3640[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Eczema from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,4900)					
Neoadjuvant chemotherapy	1/217 (0,5)	7/219 (3,2)	0,14 [0,02; 1,16] 0,0689[2]	0,14 [0,02; 1,15] 0,0678[4]	-2,7 [-5,2; -0,2] 0,0678[4]
Adjuvant chemotherapy	4/327 (1,2)	6/312 (1,9)	0,64 [0,18; 2,23] 0,4801[2]	0,63 [0,18; 2,26] 0,5372[4]	-0,7 [-2,6; 1,2] 0,5372[4]
No chemotherapy	0/9 (0,0)	1/4 (25,0)	0,17 [0,01; 3,40] 0,2441[2]	0,12 [0,00; 3,78] 0,3077[4]	-25,0 [-67,4; 17,4] 0,3077[4]
Region (Interaction p-value: 0,9997)					
North America / Europe	2/252 (0,8)	5/233 (2,1)	0,37 [0,07; 1,89] 0,2317[2]	0,36 [0,07; 1,90] 0,2689[4]	-1,4 [-3,5; 0,8] 0,2689[4]
Asia	3/168 (1,8)	8/166 (4,8)	0,37 [0,10; 1,37] 0,1373[2]	0,36 [0,09; 1,38] 0,1204[3]	-3,0 [-6,9; 0,8] 0,1204[3]
Other	0/133 (0,0)	1/136 (0,7)	0,34 [0,01; 8,29] 0,5086[2]	0,34 [0,01; 8,38] 1,0000[4]	-0,7 [-2,2; 0,7] 1,0000[4]
Primary tumor size (Interaction p-value: 0,4567)					
< 20 mm	2/141 (1,4)	3/140 (2,1)	0,66 [0,11; 3,90] 0,6485[2]	0,66 [0,11; 3,99] 0,6841[4]	-0,7 [-3,8; 2,4] 0,6841[4]
≥ 20 but < 50 mm	2/255 (0,8)	10/249 (4,0)	0,20 [0,04; 0,88] 0,0338[2]	0,19 [0,04; 0,87] 0,0173[3]	-3,2 [-5,9; -0,6] 0,0173[3]
≥ 50 mm	1/145 (0,7)	1/141 (0,7)	0,97 [0,06; 15,40] 0,9842[2]	0,97 [0,06; 15,70] 1,0000[4]	-0,0 [-2,0; 1,9] 1,0000[4]
Number of positive lymph nodes (Interaction p-value: 0,9846)					
0-3	3/203 (1,5)	8/214 (3,7)	0,40 [0,11; 1,47] 0,1659[2]	0,39 [0,10; 1,48] 0,1500[3]	-2,3 [-5,3; 0,8] 0,1500[3]
4-9	2/242 (0,8)	4/231 (1,7)	0,48 [0,09; 2,58] 0,3904[2]	0,47 [0,09; 2,61] 0,4402[4]	-0,9 [-2,9; 1,1] 0,4402[4]
≥ 10	0/108 (0,0)	2/90 (2,2)	0,17 [0,01; 3,43] 0,2459[2]	0,16 [0,01; 3,44] 0,2054[4]	-2,2 [-5,3; 0,8] 0,2054[4]
Tumor grade (Interaction p-value: 0,6716)					
G1	0/47 (0,0)	0/41 (0,0)	NE	NE	NE
G2	2/244 (0,8)	5/234 (2,1)	0,38 [0,08; 1,96] 0,2493[2]	0,38 [0,07; 1,97] 0,2762[4]	-1,3 [-3,5; 0,9] 0,2762[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G3	3/233 (1,3)	9/226 (4,0)	0,32 [0,09; 1,18] 0,0872[2]	0,31 [0,08; 1,18] 0,0705[3]	-2,7 [-5,6; 0,2] 0,0705[3]
GX	0/29 (0,0)	0/33 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9432)					
Negative	1/49 (2,0)	1/44 (2,3)	0,90 [0,06; 13,93] 0,9387[2]	0,90 [0,05; 14,76] 1,0000[4]	-0,2 [-6,2; 5,7] 1,0000[4]
Positive	4/477 (0,8)	13/471 (2,8)	0,30 [0,10; 0,93] 0,0360[2]	0,30 [0,10; 0,92] 0,0258[3]	-1,9 [-3,6; -0,2] 0,0258[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9999)					
White	2/323 (0,6)	6/324 (1,9)	0,33 [0,07; 1,64] 0,1777[2]	0,33 [0,07; 1,65] 0,2860[4]	-1,2 [-2,9; 0,5] 0,2860[4]
Asian	3/199 (1,5)	8/180 (4,4)	0,34 [0,09; 1,26] 0,1061[2]	0,33 [0,09; 1,26] 0,0890[3]	-2,9 [-6,4; 0,5] 0,0890[3]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t222_bp_aesocpt_premp_safc1_2.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Subgroups - adverse events according PT Erythema from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,9703)					
North America / Europe	9/252 (3,6)	2/233 (0,9)	4,16 [0,91; 19,06] 0,0663[2]	4,28 [0,91; 20,01] 0,0450[3]	2,7 [0,1; 5,3] 0,0450[3]
Asia	3/168 (1,8)	1/166 (0,6)	2,96 [0,31; 28,21] 0,3445[2]	3,00 [0,31; 29,14] 0,6228[4]	1,2 [-1,1; 3,5] 0,6228[4]
Other	1/133 (0,8)	0/136 (0,0)	3,07 [0,13; 74,63] 0,4913[2]	3,09 [0,12; 76,54] 0,4944[4]	0,8 [-0,7; 2,2] 0,4944[4]
Progesterone receptor status (Interaction p-value: 0,9594)					
Negative	2/49 (4,1)	0/44 (0,0)	4,50 [0,22; 91,25] 0,3273[2]	4,68 [0,22; 100,28] 0,4960[4]	4,1 [-1,5; 9,6] 0,4960[4]
Positive	11/477 (2,3)	3/471 (0,6)	3,62 [1,02; 12,90] 0,0471[2]	3,68 [1,02; 13,28] 0,0332[3]	1,7 [0,1; 3,2] 0,0332[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9350)					
White	9/323 (2,8)	2/324 (0,6)	4,51 [0,98; 20,73] 0,0526[2]	4,61 [0,99; 21,53] 0,0328[3]	2,2 [0,2; 4,2] 0,0328[3]
Asian	3/199 (1,5)	1/180 (0,6)	2,71 [0,28; 25,85] 0,3854[2]	2,74 [0,28; 26,58] 0,6249[4]	1,0 [-1,1; 3,0] 0,6249[4]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9809)					
ECOG-PS 0	12/496 (2,4)	3/480 (0,6)	3,87 [1,10; 13,63] 0,0351[2]	3,94 [1,11; 14,06] 0,0227[3]	1,8 [0,3; 3,3] 0,0227[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Fatigue from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,1161)					
Neoadjuvant chemotherapy	70/217 (32,3)	29/219 (13,2)	2,44 [1,65; 3,60] <,0001[2]	3,12 [1,92; 5,06] <,0001[3]	19,0 [11,3; 26,7] <,0001[3]
Adjuvant chemotherapy	74/327 (22,6)	34/312 (10,9)	2,08 [1,43; 3,02] 0,0001[2]	2,39 [1,54; 3,71] <,0001[3]	11,7 [6,0; 17,4] <,0001[3]
No chemotherapy	2/9 (22,2)	2/4 (50,0)	0,44 [0,09; 2,13] 0,3103[2]	0,29 [0,02; 3,52] 0,5301[4]	-27,8 [-83,8; 28,2] 0,5301[4]
Region (Interaction p-value: 0,6015)					
North America / Europe	98/252 (38,9)	40/233 (17,2)	2,27 [1,64; 3,12] <,0001[2]	3,07 [2,01; 4,69] <,0001[3]	21,7 [14,0; 29,4] <,0001[3]
Asia	28/168 (16,7)	12/166 (7,2)	2,31 [1,21; 4,38] 0,0107[2]	2,57 [1,26; 5,24] 0,0079[3]	9,4 [2,6; 16,3] 0,0079[3]
Other	20/133 (15,0)	13/136 (9,6)	1,57 [0,82; 3,03] 0,1759[2]	1,67 [0,80; 3,52] 0,1709[3]	5,5 [-2,4; 13,3] 0,1709[3]
Primary tumor size (Interaction p-value: 0,0947)					
< 20 mm	39/141 (27,7)	25/140 (17,9)	1,55 [0,99; 2,42] 0,0536[2]	1,76 [1,00; 3,11] 0,0501[3]	9,8 [0,1; 19,5] 0,0501[3]
≥ 20 but < 50 mm	72/255 (28,2)	23/249 (9,2)	3,06 [1,98; 4,73] <,0001[2]	3,87 [2,33; 6,43] <,0001[3]	19,0 [12,4; 25,6] <,0001[3]
≥ 50 mm	34/145 (23,4)	17/141 (12,1)	1,94 [1,14; 3,32] 0,0146[2]	2,23 [1,18; 4,22] 0,0119[3]	11,4 [2,6; 20,1] 0,0119[3]
Number of positive lymph nodes (Interaction p-value: 0,6169)					
0-3	54/203 (26,6)	30/214 (14,0)	1,90 [1,27; 2,84] 0,0018[2]	2,22 [1,35; 3,65] 0,0014[3]	12,6 [4,9; 20,2] 0,0014[3]
4-9	69/242 (28,5)	26/231 (11,3)	2,53 [1,68; 3,83] <,0001[2]	3,14 [1,92; 5,16] <,0001[3]	17,3 [10,3; 24,3] <,0001[3]
≥ 10	23/108 (21,3)	9/90 (10,0)	2,13 [1,04; 4,37] 0,0391[2]	2,44 [1,06; 5,58] 0,0315[3]	11,3 [1,4; 21,2] 0,0315[3]
Tumor grade (Interaction p-value: 0,4514)					
G1	11/47 (23,4)	1/41 (2,4)	9,60 [1,29; 71,17] 0,0270[2]	12,22 [1,50; 99,42] 0,0043[3]	21,0 [8,0; 34,0] 0,0043[3]
G2	76/244 (31,1)	33/234 (14,1)	2,21 [1,53; 3,19] <,0001[2]	2,76 [1,74; 4,35] <,0001[3]	17,0 [9,7; 24,4] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G3	56/233 (24,0)	29/226 (12,8)	1,87 [1,24; 2,82] 0,0027[2]	2,15 [1,31; 3,52] 0,0020[3]	11,2 [4,2; 18,2] 0,0020[3]
GX	3/29 (10,3)	2/33 (6,1)	1,71 [0,31; 9,52] 0,5419[2]	1,79 [0,28; 11,53] 0,6577[4]	4,3 [-9,5; 18,0] 0,6577[4]
Progesterone receptor status (Interaction p-value: 0,3299)					
Negative	21/49 (42,9)	5/44 (11,4)	3,77 [1,55; 9,15] 0,0033[2]	5,85 [1,97; 17,39] 0,0007[3]	31,5 [14,8; 48,2] 0,0007[3]
Positive	109/477 (22,9)	52/471 (11,0)	2,07 [1,53; 2,81] <,0001[2]	2,39 [1,67; 3,42] <,0001[3]	11,8 [7,1; 16,5] <,0001[3]
Unknown	3/4 (75,0)	4/8 (50,0)	1,50 [0,61; 3,67] 0,3744[2]	3,00 [0,21; 42,62] 0,5758[4]	25,0 [-29,8; 79,8] 0,5758[4]
Race (Interaction p-value: 0,5512)					
White	107/323 (33,1)	48/324 (14,8)	2,24 [1,65; 3,03] <,0001[2]	2,85 [1,94; 4,18] <,0001[3]	18,3 [11,9; 24,7] <,0001[3]
Asian	30/199 (15,1)	12/180 (6,7)	2,26 [1,19; 4,28] 0,0122[2]	2,49 [1,23; 5,02] 0,0092[3]	8,4 [2,2; 14,6] 0,0092[3]
Other	4/19 (21,1)	4/21 (19,0)	1,11 [0,32; 3,82] 0,8742[2]	1,13 [0,24; 5,34] 1,0000[4]	2,0 [-22,9; 26,9] 1,0000[4]
ECOG-PS (Interaction p-value: 0,3975)					
ECOG-PS 0	135/496 (27,2)	58/480 (12,1)	2,25 [1,70; 2,98] <,0001[2]	2,72 [1,94; 3,82] <,0001[3]	15,1 [10,3; 20,0] <,0001[3]
ECOG-PS 1	11/57 (19,3)	7/55 (12,7)	1,52 [0,63; 3,63] 0,3496[2]	1,64 [0,59; 4,59] 0,3439[3]	6,6 [-6,9; 20,1] 0,3439[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi²-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Gamma-glutamyltransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7009)					
Neoadjuvant chemotherapy	6/217 (2,8)	1/219 (0,5)	6,06 [0,74; 49,88] 0,0941[2]	6,20 [0,74; 51,93] 0,0672[4]	2,3 [-0,0; 4,7] 0,0672[4]
Adjuvant chemotherapy	9/327 (2,8)	4/312 (1,3)	2,15 [0,67; 6,90] 0,1997[2]	2,18 [0,66; 7,15] 0,1882[3]	1,5 [-0,7; 3,6] 0,1882[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Primary tumor size (Interaction p-value: 0,5718)					
< 20 mm	2/141 (1,4)	1/140 (0,7)	1,99 [0,18; 21,65] 0,5736[2]	2,00 [0,18; 22,31] 1,0000[4]	0,7 [-1,7; 3,1] 1,0000[4]
≥ 20 but < 50 mm	10/255 (3,9)	2/249 (0,8)	4,88 [1,08; 22,06] 0,0393[2]	5,04 [1,09; 23,24] 0,0217[3]	3,1 [0,5; 5,7] 0,0217[3]
≥ 50 mm	3/145 (2,1)	2/141 (1,4)	1,46 [0,25; 8,60] 0,6767[2]	1,47 [0,24; 8,92] 1,0000[4]	0,7 [-2,4; 3,7] 1,0000[4]
Tumor grade (Interaction p-value: 0,9914)					
G1	2/47 (4,3)	0/41 (0,0)	4,38 [0,22; 88,58] 0,3362[2]	4,56 [0,21; 97,79] 0,4966[4]	4,3 [-1,5; 10,0] 0,4966[4]
G2	8/244 (3,3)	4/234 (1,7)	1,92 [0,59; 6,28] 0,2821[2]	1,95 [0,58; 6,56] 0,2729[3]	1,6 [-1,2; 4,4] 0,2729[3]
G3	3/233 (1,3)	1/226 (0,4)	2,91 [0,30; 27,77] 0,3534[2]	2,93 [0,30; 28,42] 0,6235[4]	0,8 [-0,8; 2,5] 0,6235[4]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,9594)					
Negative	2/49 (4,1)	0/44 (0,0)	4,50 [0,22; 91,25] 0,3273[2]	4,68 [0,22; 100,28] 0,4960[4]	4,1 [-1,5; 9,6] 0,4960[4]
Positive	13/477 (2,7)	5/471 (1,1)	2,57 [0,92; 7,14] 0,0710[2]	2,61 [0,92; 7,38] 0,0606[3]	1,7 [-0,1; 3,4] 0,0606[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8554)					
White	8/323 (2,5)	2/324 (0,6)	4,01 [0,86; 18,75] 0,0774[2]	4,09 [0,86; 19,40] 0,0632[4]	1,9 [-0,0; 3,8] 0,0632[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Asian	5/199 (2,5)	2/180 (1,1)	2,26 [0,44; 11,51] 0,3258[2]	2,29 [0,44; 11,97] 0,4529[4]	1,4 [-1,3; 4,1] 0,4529[4]
Other	2/19 (10,5)	1/21 (4,8)	2,21 [0,22; 22,47] 0,5026[2]	2,35 [0,20; 28,27] 0,5962[4]	5,8 [-10,8; 22,3] 0,5962[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt_sub.sas
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Table: Subgroups - adverse events according PT Gastritis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7520)					
Neoadjuvant chemotherapy	8/217 (3,7)	2/219 (0,9)	4,04 [0,87; 18,79] 0,0754[2]	4,15 [0,87; 19,79] 0,0615[4]	2,8 [-0,0; 5,6] 0,0615[4]
Adjuvant chemotherapy	8/327 (2,4)	4/312 (1,3)	1,91 [0,58; 6,27] 0,2873[2]	1,93 [0,58; 6,48] 0,2784[3]	1,2 [-0,9; 3,3] 0,2784[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,7870)					
North America / Europe	4/252 (1,6)	1/233 (0,4)	3,70 [0,42; 32,85] 0,2405[2]	3,74 [0,42; 33,72] 0,3743[4]	1,2 [-0,6; 2,9] 0,3743[4]
Asia	9/168 (5,4)	3/166 (1,8)	2,96 [0,82; 10,76] 0,0985[2]	3,08 [0,82; 11,57] 0,0813[3]	3,5 [-0,4; 7,5] 0,0813[3]
Other	3/133 (2,3)	2/136 (1,5)	1,53 [0,26; 9,03] 0,6363[2]	1,55 [0,25; 9,40] 0,6817[4]	0,8 [-2,4; 4,0] 0,6817[4]
Number of positive lymph nodes (Interaction p-value: 0,5688)					
0-3	3/203 (1,5)	3/214 (1,4)	1,05 [0,22; 5,16] 0,9481[2]	1,06 [0,21; 5,29] 1,0000[4]	0,1 [-2,2; 2,4] 1,0000[4]
4-9	10/242 (4,1)	3/231 (1,3)	3,18 [0,89; 11,42] 0,0758[2]	3,28 [0,89; 12,06] 0,0595[3]	2,8 [-0,1; 5,7] 0,0595[3]
≥ 10	3/108 (2,8)	0/90 (0,0)	5,84 [0,31; 111,67] 0,2408[2]	6,00 [0,31; 117,80] 0,2524[4]	2,8 [-0,3; 5,9] 0,2524[4]
Tumor stage (Interaction p-value: 0,9494)					
IIA	2/59 (3,4)	0/62 (0,0)	5,25 [0,26; 107,12] 0,2812[2]	5,43 [0,26; 115,61] 0,2357[4]	3,4 [-1,2; 8,0] 0,2357[4]
IIB	1/53 (1,9)	1/69 (1,4)	1,30 [0,08; 20,34] 0,8508[2]	1,31 [0,08; 21,40] 1,0000[4]	0,4 [-4,2; 5,1] 1,0000[4]
IIIA	8/236 (3,4)	4/214 (1,9)	1,81 [0,55; 5,94] 0,3252[2]	1,84 [0,55; 6,21] 0,3173[3]	1,5 [-1,4; 4,5] 0,3173[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	5/186 (2,7)	1/174 (0,6)	4,68 [0,55; 39,64] 0,1571[2]	4,78 [0,55; 41,32] 0,2164[4]	2,1 [-0,5; 4,7] 0,2164[4]
Tumor grade (Interaction p-value: 0,9994)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	0/47 (0,0)	1/41 (2,4)	0,29 [0,01; 6,97] 0,4467[2]	0,28 [0,01; 7,17] 0,4659[4]	-2,4 [-7,2; 2,3] 0,4659[4]
G2	8/244 (3,3)	3/234 (1,3)	2,56 [0,69; 9,52] 0,1616[2]	2,61 [0,68; 9,96] 0,1456[3]	2,0 [-0,7; 4,7] 0,1456[3]
G3	6/233 (2,6)	2/226 (0,9)	2,91 [0,59; 14,27] 0,1879[2]	2,96 [0,59; 14,82] 0,2852[4]	1,7 [-0,7; 4,1] 0,2852[4]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,5473)					
Negative	1/49 (2,0)	2/44 (4,5)	0,45 [0,04; 4,78] 0,5070[2]	0,44 [0,04; 5,00] 0,6013[4]	-2,5 [-9,8; 4,8] 0,6013[4]
Positive	15/477 (3,1)	4/471 (0,8)	3,70 [1,24; 11,07] 0,0192[2]	3,79 [1,25; 11,51] 0,0117[3]	2,3 [0,5; 4,1] 0,0117[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9517)					
White	6/323 (1,9)	3/324 (0,9)	2,01 [0,51; 7,95] 0,3218[2]	2,03 [0,50; 8,17] 0,3399[4]	0,9 [-0,9; 2,7] 0,3399[4]
Asian	9/199 (4,5)	3/180 (1,7)	2,71 [0,75; 9,87] 0,1296[2]	2,79 [0,74; 10,49] 0,1128[3]	2,9 [-0,6; 6,3] 0,1128[3]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,7965)					
ECOG-PS 0	14/496 (2,8)	5/480 (1,0)	2,71 [0,98; 7,46] 0,0539[2]	2,76 [0,99; 7,72] 0,0441[3]	1,8 [0,1; 3,5] 0,0441[3]
ECOG-PS 1	2/57 (3,5)	1/55 (1,8)	1,93 [0,18; 20,68] 0,5869[2]	1,96 [0,17; 22,30] 1,0000[4]	1,7 [-4,2; 7,6] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Haemorrhoids from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9873)					
Neoadjuvant chemotherapy	8/217 (3,7)	4/219 (1,8)	2,02 [0,62; 6,60] 0,2456[2]	2,06 [0,61; 6,94] 0,2352[3]	1,9 [-1,2; 4,9] 0,2352[3]
Adjuvant chemotherapy	12/327 (3,7)	5/312 (1,6)	2,29 [0,82; 6,42] 0,1155[2]	2,34 [0,81; 6,72] 0,1046[3]	2,1 [-0,4; 4,5] 0,1046[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,5303)					
North America / Europe	15/252 (6,0)	5/233 (2,1)	2,77 [1,02; 7,51] 0,0448[2]	2,89 [1,03; 8,07] 0,0352[3]	3,8 [0,3; 7,3] 0,0352[3]
Asia	3/168 (1,8)	3/166 (1,8)	0,99 [0,20; 4,83] 0,9882[2]	0,99 [0,20; 4,97] 1,0000[4]	-0,0 [-2,9; 2,8] 1,0000[4]
Other	3/133 (2,3)	1/136 (0,7)	3,07 [0,32; 29,12] 0,3290[2]	3,12 [0,32; 30,34] 0,3667[4]	1,5 [-1,4; 4,4] 0,3667[4]
Primary tumor size (Interaction p-value: 0,0878)					
< 20 mm	9/141 (6,4)	1/140 (0,7)	8,94 [1,15; 69,60] 0,0365[2]	9,48 [1,18; 75,84] 0,0193[4]	5,7 [1,4; 9,9] 0,0193[4]
≥ 20 but < 50 mm	10/255 (3,9)	4/249 (1,6)	2,44 [0,78; 7,68] 0,1270[2]	2,50 [0,77; 8,08] 0,1138[3]	2,3 [-0,5; 5,2] 0,1138[3]
≥ 50 mm	2/145 (1,4)	4/141 (2,8)	0,49 [0,09; 2,61] 0,4006[2]	0,48 [0,09; 2,66] 0,4425[4]	-1,5 [-4,8; 1,9] 0,4425[4]
Number of positive lymph nodes (Interaction p-value: 0,9855)					
0-3	8/203 (3,9)	4/214 (1,9)	2,11 [0,64; 6,89] 0,2172[2]	2,15 [0,64; 7,27] 0,2059[3]	2,1 [-1,2; 5,3] 0,2059[3]
4-9	10/242 (4,1)	4/231 (1,7)	2,39 [0,76; 7,50] 0,1367[2]	2,45 [0,76; 7,91] 0,1236[3]	2,4 [-0,6; 5,4] 0,1236[3]
≥ 10	3/108 (2,8)	1/90 (1,1)	2,50 [0,26; 23,62] 0,4239[2]	2,54 [0,26; 24,88] 0,6275[4]	1,7 [-2,1; 5,4] 0,6275[4]
Tumor stage (Interaction p-value: 0,8607)					
IIA	4/59 (6,8)	0/62 (0,0)	9,45 [0,52; 171,79] 0,1291[2]	10,14 [0,53; 192,49] 0,0536[4]	6,8 [0,4; 13,2] 0,0536[4]
IIB	1/53 (1,9)	2/69 (2,9)	0,65 [0,06; 6,99] 0,7230[2]	0,64 [0,06; 7,30] 1,0000[4]	-1,0 [-6,4; 4,4] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	9/236 (3,8)	5/214 (2,3)	1,63 [0,56; 4,79] 0,3728[2]	1,66 [0,55; 5,02] 0,3674[3]	1,5 [-1,7; 4,6] 0,3674[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	7/186 (3,8)	2/174 (1,1)	3,27 [0,69; 15,55] 0,1356[2]	3,36 [0,69; 16,42] 0,1764[4]	2,6 [-0,5; 5,8] 0,1764[4]
Tumor grade (Interaction p-value: 0,9907)					
G1	4/47 (8,5)	0/41 (0,0)	7,88 [0,44; 142,02] 0,1620[2]	8,59 [0,45; 164,46] 0,1199[4]	8,5 [0,5; 16,5] 0,1199[4]
G2	7/244 (2,9)	2/234 (0,9)	3,36 [0,70; 15,99] 0,1285[2]	3,43 [0,70; 16,66] 0,1764[4]	2,0 [-0,4; 4,4] 0,1764[4]
G3	10/233 (4,3)	4/226 (1,8)	2,42 [0,77; 7,62] 0,1295[2]	2,49 [0,77; 8,05] 0,1162[3]	2,5 [-0,6; 5,6] 0,1162[3]
GX	0/29 (0,0)	3/33 (9,1)	0,16 [0,01; 3,01] 0,2220[2]	0,15 [0,01; 2,98] 0,2409[4]	-9,1 [-18,9; 0,7] 0,2409[4]
Progesterone receptor status (Interaction p-value: 0,9412)					
Negative	1/49 (2,0)	1/44 (2,3)	0,90 [0,06; 13,93] 0,9387[2]	0,90 [0,05; 14,76] 1,0000[4]	-0,2 [-6,2; 5,7] 1,0000[4]
Positive	20/477 (4,2)	8/471 (1,7)	2,47 [1,10; 5,55] 0,0288[2]	2,53 [1,10; 5,81] 0,0233[3]	2,5 [0,4; 4,6] 0,0233[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,4547)					
White	15/323 (4,6)	5/324 (1,5)	3,01 [1,11; 8,18] 0,0309[2]	3,11 [1,12; 8,65] 0,0227[3]	3,1 [0,4; 5,8] 0,0227[3]
Asian	3/199 (1,5)	3/180 (1,7)	0,90 [0,18; 4,42] 0,9014[2]	0,90 [0,18; 4,53] 1,0000[4]	-0,2 [-2,7; 2,4] 1,0000[4]
Other	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (Interaction p-value: 0,9798)					
ECOG-PS 0	20/496 (4,0)	9/480 (1,9)	2,15 [0,99; 4,68] 0,0533[2]	2,20 [0,99; 4,88] 0,0472[3]	2,2 [0,0; 4,3] 0,0472[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Hot flush from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7851)					
Neoadjuvant chemotherapy	39/217 (18,0)	50/219 (22,8)	0,79 [0,54; 1,14] 0,2102[2]	0,74 [0,46; 1,18] 0,2082[3]	-4,9 [-12,4; 2,7] 0,2082[3]
Adjuvant chemotherapy	57/327 (17,4)	71/312 (22,8)	0,77 [0,56; 1,05] 0,0942[2]	0,72 [0,49; 1,06] 0,0927[3]	-5,3 [-11,5; 0,9] 0,0927[3]
No chemotherapy	2/9 (22,2)	2/4 (50,0)	0,44 [0,09; 2,13] 0,3103[2]	0,29 [0,02; 3,52] 0,5301[4]	-27,8 [-83,8; 28,2] 0,5301[4]
Region (Interaction p-value: 0,2559)					
North America / Europe	64/252 (25,4)	87/233 (37,3)	0,68 [0,52; 0,89] 0,0050[2]	0,57 [0,39; 0,84] 0,0045[3]	-11,9 [-20,2; -3,7] 0,0045[3]
Asia	24/168 (14,3)	21/166 (12,7)	1,13 [0,65; 1,95] 0,6620[2]	1,15 [0,61; 2,16] 0,6617[3]	1,6 [-5,7; 9,0] 0,6617[3]
Other	10/133 (7,5)	15/136 (11,0)	0,68 [0,32; 1,46] 0,3254[2]	0,66 [0,28; 1,52] 0,3214[3]	-3,5 [-10,4; 3,4] 0,3214[3]
Primary tumor size (Interaction p-value: 0,1833)					
< 20 mm	28/141 (19,9)	36/140 (25,7)	0,77 [0,50; 1,19] 0,2443[2]	0,72 [0,41; 1,25] 0,2419[3]	-5,9 [-15,6; 3,9] 0,2419[3]
≥ 20 but < 50 mm	45/255 (17,6)	47/249 (18,9)	0,93 [0,65; 1,35] 0,7212[2]	0,92 [0,59; 1,45] 0,7211[3]	-1,2 [-8,0; 5,5] 0,7211[3]
≥ 50 mm	22/145 (15,2)	40/141 (28,4)	0,53 [0,34; 0,85] 0,0084[2]	0,45 [0,25; 0,81] 0,0068[3]	-13,2 [-22,7; -3,7] 0,0068[3]
Number of positive lymph nodes (Interaction p-value: 0,2448)					
0-3	40/203 (19,7)	50/214 (23,4)	0,84 [0,58; 1,22] 0,3652[2]	0,80 [0,50; 1,29] 0,3638[3]	-3,7 [-11,5; 4,2] 0,3638[3]
4-9	39/242 (16,1)	59/231 (25,5)	0,63 [0,44; 0,91] 0,0127[2]	0,56 [0,36; 0,88] 0,0115[3]	-9,4 [-16,7; -2,1] 0,0115[3]
≥ 10	19/108 (17,6)	14/90 (15,6)	1,13 [0,60; 2,13] 0,7023[2]	1,16 [0,54; 2,47] 0,7017[3]	2,0 [-8,3; 12,4] 0,7017[3]
Tumor stage (Interaction p-value: 0,6900)					
IIA	10/59 (16,9)	15/62 (24,2)	0,70 [0,34; 1,43] 0,3302[2]	0,64 [0,26; 1,56] 0,3252[3]	-7,2 [-21,6; 7,1] 0,3252[3]
IIB	12/53 (22,6)	16/69 (23,2)	0,98 [0,51; 1,88] 0,9433[2]	0,97 [0,41; 2,27] 0,9432[3]	-0,5 [-15,6; 14,5] 0,9432[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	35/236 (14,8)	49/214 (22,9)	0,65 [0,44; 0,96] 0,0300[2]	0,59 [0,36; 0,95] 0,0283[3]	-8,1 [-15,3; -0,8] 0,0283[3]
IIIB	5/18 (27,8)	3/15 (20,0)	1,39 [0,40; 4,88] 0,6084[2]	1,54 [0,30; 7,87] 0,6992[4]	7,8 [-21,2; 36,7] 0,6992[4]
IIIC	35/186 (18,8)	40/174 (23,0)	0,82 [0,55; 1,23] 0,3311[2]	0,78 [0,47; 1,29] 0,3301[3]	-4,2 [-12,6; 4,2] 0,3301[3]
Tumor grade (Interaction p-value: 0,1877)					
G1	11/47 (23,4)	10/41 (24,4)	0,96 [0,45; 2,03] 0,9138[2]	0,95 [0,35; 2,53] 0,9138[3]	-1,0 [-18,9; 16,9] 0,9138[3]
G2	38/244 (15,6)	62/234 (26,5)	0,59 [0,41; 0,84] 0,0040[2]	0,51 [0,33; 0,80] 0,0033[3]	-10,9 [-18,2; -3,7] 0,0033[3]
G3	44/233 (18,9)	48/226 (21,2)	0,89 [0,62; 1,28] 0,5290[2]	0,86 [0,55; 1,36] 0,5287[3]	-2,4 [-9,7; 5,0] 0,5287[3]
GX	5/29 (17,2)	3/33 (9,1)	1,90 [0,50; 7,25] 0,3498[2]	2,08 [0,45; 9,61] 0,4561[4]	8,2 [-8,7; 25,0] 0,4561[4]
Progesterone receptor status (Interaction p-value: 0,2079)					
Negative	10/49 (20,4)	5/44 (11,4)	1,80 [0,67; 4,85] 0,2480[2]	2,00 [0,63; 6,39] 0,2364[3]	9,0 [-5,6; 23,7] 0,2364[3]
Positive	82/477 (17,2)	114/471 (24,2)	0,71 [0,55; 0,92] 0,0082[2]	0,65 [0,47; 0,89] 0,0077[3]	-7,0 [-12,2; -1,9] 0,0077[3]
Unknown	0/4 (0,0)	2/8 (25,0)	0,36 [0,02; 6,12] 0,4796[2]	0,29 [0,01; 7,57] 0,5152[4]	-25,0 [-55,0; 5,0] 0,5152[4]
Race (Interaction p-value: 0,0947)					
White	64/323 (19,8)	94/324 (29,0)	0,68 [0,52; 0,90] 0,0071[2]	0,60 [0,42; 0,87] 0,0065[3]	-9,2 [-15,8; -2,6] 0,0065[3]
Asian	28/199 (14,1)	22/180 (12,2)	1,15 [0,68; 1,94] 0,5961[2]	1,18 [0,65; 2,14] 0,5955[3]	1,8 [-5,0; 8,6] 0,5955[3]
Other	3/19 (15,8)	1/21 (4,8)	3,32 [0,38; 29,23] 0,2804[2]	3,75 [0,36; 39,59] 0,3306[4]	11,0 [-7,7; 29,8] 0,3306[4]
ECOG-PS (Interaction p-value: 0,4543)					
ECOG-PS 0	91/496 (18,3)	117/480 (24,4)	0,75 [0,59; 0,96] 0,0222[2]	0,70 [0,51; 0,95] 0,0215[3]	-6,0 [-11,2; -0,9] 0,0215[3]
ECOG-PS 1	7/57 (12,3)	6/55 (10,9)	1,13 [0,40; 3,14] 0,8209[2]	1,14 [0,36; 3,65] 0,8208[3]	1,4 [-10,5; 13,2] 0,8208[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Hypokalaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9883)					
Neoadjuvant chemotherapy	10/217 (4,6)	0/219 (0,0)	21,19 [1,25; 359,42] 0,0345[2]	22,21 [1,29; 381,50] 0,0008[4]	4,6 [1,8; 7,4] 0,0008[4]
Adjuvant chemotherapy	8/327 (2,4)	1/312 (0,3)	7,63 [0,96; 60,68] 0,0547[2]	7,80 [0,97; 62,72] 0,0382[4]	2,1 [0,3; 3,9] 0,0382[4]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Tumor stage (Interaction p-value: 0,9998)					
IIA	1/59 (1,7)	0/62 (0,0)	3,15 [0,13; 75,82] 0,4796[2]	3,21 [0,13; 80,25] 0,4876[4]	1,7 [-1,6; 5,0] 0,4876[4]
IIB	0/53 (0,0)	1/69 (1,4)	0,43 [0,02; 10,40] 0,6051[2]	0,43 [0,02; 10,69] 1,0000[4]	-1,4 [-4,3; 1,4] 1,0000[4]
IIIA	7/236 (3,0)	0/214 (0,0)	13,61 [0,78; 236,84] 0,0733[2]	14,02 [0,80; 246,96] 0,0157[4]	3,0 [0,8; 5,1] 0,0157[4]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	10/186 (5,4)	0/174 (0,0)	19,65 [1,16; 332,86] 0,0391[2]	20,76 [1,21; 357,05] 0,0018[4]	5,4 [2,1; 8,6] 0,0018[4]
Progesterone receptor status (Interaction p-value: 0,9563)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	16/477 (3,4)	1/471 (0,2)	15,80 [2,10; 118,65] 0,0073[2]	16,31 [2,15; 123,51] 0,0003[3]	3,1 [1,5; 4,8] 0,0003[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9821)					
ECOG-PS 0	16/496 (3,2)	1/480 (0,2)	15,48 [2,06; 116,30] 0,0077[2]	15,97 [2,11; 120,87] 0,0003[3]	3,0 [1,4; 4,6] 0,0003[3]
ECOG-PS 1	2/57 (3,5)	0/55 (0,0)	4,83 [0,24; 98,34] 0,3060[2]	5,00 [0,23; 106,54] 0,4957[4]	3,5 [-1,3; 8,3] 0,4957[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Tabl: Subgroups - adverse events according PT Influenza like illness from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,5620)					
Neoadjuvant chemotherapy	17/217 (7,8)	7/219 (3,2)	2,45 [1,04; 5,79] 0,0410[2]	2,57 [1,05; 6,34] 0,0338[3]	4,6 [0,4; 8,9] 0,0338[3]
Adjuvant chemotherapy	23/327 (7,0)	16/312 (5,1)	1,37 [0,74; 2,55] 0,3170[2]	1,40 [0,73; 2,70] 0,3145[3]	1,9 [-1,8; 5,6] 0,3145[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,2956)					
North America / Europe	20/252 (7,9)	9/233 (3,9)	2,05 [0,95; 4,42] 0,0655[2]	2,15 [0,96; 4,81] 0,0587[3]	4,1 [-0,1; 8,2] 0,0587[3]
Asia	16/168 (9,5)	8/166 (4,8)	1,98 [0,87; 4,49] 0,1040[2]	2,08 [0,86; 5,00] 0,0960[3]	4,7 [-0,8; 10,2] 0,0960[3]
Other	4/133 (3,0)	6/136 (4,4)	0,68 [0,20; 2,36] 0,5455[2]	0,67 [0,19; 2,44] 0,7494[4]	-1,4 [-5,9; 3,1] 0,7494[4]
Primary tumor size (Interaction p-value: 0,3921)					
< 20 mm	7/141 (5,0)	7/140 (5,0)	0,99 [0,36; 2,76] 0,9891[2]	0,99 [0,34; 2,91] 0,9891[3]	-0,0 [-5,1; 5,1] 0,9891[3]
≥ 20 but < 50 mm	18/255 (7,1)	7/249 (2,8)	2,51 [1,07; 5,91] 0,0349[2]	2,63 [1,08; 6,40] 0,0281[3]	4,2 [0,5; 8,0] 0,0281[3]
≥ 50 mm	15/145 (10,3)	9/141 (6,4)	1,62 [0,73; 3,58] 0,2328[2]	1,69 [0,72; 4,00] 0,2270[3]	4,0 [-2,4; 10,4] 0,2270[3]
Number of positive lymph nodes (Interaction p-value: 0,2439)					
0-3	16/203 (7,9)	12/214 (5,6)	1,41 [0,68; 2,90] 0,3563[2]	1,44 [0,66; 3,12] 0,3537[3]	2,3 [-2,5; 7,1] 0,3537[3]
4-9	14/242 (5,8)	10/231 (4,3)	1,34 [0,61; 2,95] 0,4726[2]	1,36 [0,59; 3,12] 0,4707[3]	1,5 [-2,5; 5,4] 0,4707[3]
≥ 10	10/108 (9,3)	1/90 (1,1)	8,33 [1,09; 63,86] 0,0413[2]	9,08 [1,14; 72,37] 0,0127[3]	8,1 [2,3; 14,0] 0,0127[3]
Tumor stage (Interaction p-value: 0,5501)					
IIA	3/59 (5,1)	2/62 (3,2)	1,58 [0,27; 9,10] 0,6110[2]	1,61 [0,26; 9,98] 0,6745[4]	1,9 [-5,3; 9,0] 0,6745[4]
IIB	5/53 (9,4)	1/69 (1,4)	6,51 [0,78; 54,07] 0,0829[2]	7,08 [0,80; 62,57] 0,0843[4]	8,0 [-0,4; 16,3] 0,0843[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	16/236 (6,8)	7/214 (3,3)	2,07 [0,87; 4,94] 0,1001[2]	2,15 [0,87; 5,33] 0,0914[3]	3,5 [-0,5; 7,5] 0,0914[3]
IIIB	2/18 (11,1)	1/15 (6,7)	1,67 [0,17; 16,63] 0,6634[2]	1,75 [0,14; 21,43] 1,0000[4]	4,4 [-14,8; 23,7] 1,0000[4]
IIIC	14/186 (7,5)	12/174 (6,9)	1,09 [0,52; 2,29] 0,8175[2]	1,10 [0,49; 2,45] 0,8174[3]	0,6 [-4,7; 6,0] 0,8174[3]
Tumor grade (Interaction p-value: 0,9838)					
G1	4/47 (8,5)	2/41 (4,9)	1,74 [0,34; 9,04] 0,5072[2]	1,81 [0,31; 10,46] 0,6810[4]	3,6 [-6,7; 14,0] 0,6810[4]
G2	18/244 (7,4)	11/234 (4,7)	1,57 [0,76; 3,25] 0,2253[2]	1,61 [0,75; 3,50] 0,2205[3]	2,7 [-1,6; 6,9] 0,2205[3]
G3	17/233 (7,3)	9/226 (4,0)	1,83 [0,83; 4,02] 0,1316[2]	1,90 [0,83; 4,35] 0,1247[3]	3,3 [-0,9; 7,5] 0,1247[3]
GX	1/29 (3,4)	1/33 (3,0)	1,14 [0,07; 17,39] 0,9260[2]	1,14 [0,07; 19,13] 1,0000[4]	0,4 [-8,4; 9,3] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,4900)					
Negative	7/49 (14,3)	4/44 (9,1)	1,57 [0,49; 5,01] 0,4447[2]	1,67 [0,45; 6,13] 0,4386[3]	5,2 [-7,8; 18,2] 0,4386[3]
Positive	33/477 (6,9)	19/471 (4,0)	1,71 [0,99; 2,97] 0,0545[2]	1,77 [0,99; 3,16] 0,0512[3]	2,9 [-0,0; 5,8] 0,0512[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9849)					
White	23/323 (7,1)	14/324 (4,3)	1,65 [0,86; 3,14] 0,1298[2]	1,70 [0,86; 3,36] 0,1252[3]	2,8 [-0,8; 6,4] 0,1252[3]
Asian	16/199 (8,0)	8/180 (4,4)	1,81 [0,79; 4,13] 0,1587[2]	1,88 [0,78; 4,50] 0,1512[3]	3,6 [-1,2; 8,4] 0,1512[3]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,7007)					
ECOG-PS 0	36/496 (7,3)	20/480 (4,2)	1,74 [1,02; 2,97] 0,0409[2]	1,80 [1,03; 3,16] 0,0379[3]	3,1 [0,2; 6,0] 0,0379[3]
ECOG-PS 1	4/57 (7,0)	3/55 (5,5)	1,29 [0,30; 5,49] 0,7335[2]	1,31 [0,28; 6,13] 1,0000[4]	1,6 [-7,4; 10,5] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Lacrimation increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9850)					
Neoadjuvant chemotherapy	14/217 (6,5)	0/219 (0,0)	29,27 [1,76; 487,55] 0,0186[2]	31,28 [1,85; 527,75] 0,0001[3]	6,5 [3,2; 9,7] 0,0001[3]
Adjuvant chemotherapy	14/327 (4,3)	1/312 (0,3)	13,36 [1,77; 100,98] 0,0120[2]	13,91 [1,82; 106,43] 0,0009[3]	4,0 [1,7; 6,2] 0,0009[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,9996)					
North America / Europe	17/252 (6,7)	0/233 (0,0)	32,37 [1,96; 535,27] 0,0151[2]	34,70 [2,07; 580,43] <,0001[3]	6,7 [3,6; 9,8] <,0001[3]
Asia	5/168 (3,0)	0/166 (0,0)	10,87 [0,61; 195,03] 0,1053[2]	11,20 [0,61; 204,21] 0,0607[4]	3,0 [0,4; 5,5] 0,0607[4]
Other	6/133 (4,5)	1/136 (0,7)	6,14 [0,75; 50,28] 0,0910[2]	6,38 [0,76; 53,71] 0,0644[4]	3,8 [-0,0; 7,6] 0,0644[4]
Primary tumor size (Interaction p-value: 0,9771)					
< 20 mm	8/141 (5,7)	1/140 (0,7)	7,94 [1,01; 62,68] 0,0493[2]	8,36 [1,03; 67,76] 0,0361[4]	5,0 [0,9; 9,0] 0,0361[4]
≥ 20 but < 50 mm	10/255 (3,9)	0/249 (0,0)	20,51 [1,21; 348,10] 0,0365[2]	21,34 [1,24; 366,20] 0,0018[4]	3,9 [1,5; 6,3] 0,0018[4]
≥ 50 mm	8/145 (5,5)	0/141 (0,0)	16,53 [0,96; 283,79] 0,0531[2]	17,49 [1,00; 306,03] 0,0071[4]	5,5 [1,8; 9,2] 0,0071[4]
Number of positive lymph nodes (Interaction p-value: 0,9993)					
0-3	11/203 (5,4)	0/214 (0,0)	24,24 [1,44; 408,69] 0,0270[2]	25,63 [1,50; 437,82] 0,0006[3]	5,4 [2,3; 8,5] 0,0006[3]
4-9	11/242 (4,5)	1/231 (0,4)	10,50 [1,37; 80,68] 0,0238[2]	10,95 [1,40; 85,52] 0,0045[3]	4,1 [1,4; 6,9] 0,0045[3]
≥ 10	6/108 (5,6)	0/90 (0,0)	10,85 [0,62; 190,07] 0,1026[2]	11,48 [0,64; 206,59] 0,0327[4]	5,6 [1,2; 9,9] 0,0327[4]
Tumor stage (Interaction p-value: 0,9997)					
IIA	4/59 (6,8)	0/62 (0,0)	9,45 [0,52; 171,79] 0,1291[2]	10,14 [0,53; 192,49] 0,0536[4]	6,8 [0,4; 13,2] 0,0536[4]
IIB	0/53 (0,0)	0/69 (0,0)	NE	NE	NE

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	9/236 (3,8)	1/214 (0,5)	8,16 [1,04; 63,88] 0,0455[2]	8,44 [1,06; 67,22] 0,0216[4]	3,3 [0,7; 6,0] 0,0216[4]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	13/186 (7,0)	0/174 (0,0)	25,27 [1,51; 421,85] 0,0245[2]	27,16 [1,60; 460,39] 0,0004[3]	7,0 [3,3; 10,7] 0,0004[3]
Tumor grade (Interaction p-value: 1,0000)					
G1	3/47 (6,4)	0/41 (0,0)	6,13 [0,33; 115,18] 0,2260[2]	6,53 [0,33; 130,23] 0,2449[4]	6,4 [-0,6; 13,4] 0,2449[4]
G2	10/244 (4,1)	0/234 (0,0)	20,14 [1,19; 341,80] 0,0376[2]	21,00 [1,22; 360,44] 0,0018[4]	4,1 [1,6; 6,6] 0,0018[4]
G3	13/233 (5,6)	1/226 (0,4)	12,61 [1,66; 95,60] 0,0142[2]	13,30 [1,72; 102,50] 0,0014[3]	5,1 [2,1; 8,2] 0,0014[3]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,9580)					
Negative	3/49 (6,1)	0/44 (0,0)	6,30 [0,33; 118,66] 0,2191[2]	6,70 [0,34; 133,42] 0,2440[4]	6,1 [-0,6; 12,8] 0,2440[4]
Positive	25/477 (5,2)	1/471 (0,2)	24,69 [3,36; 181,44] 0,0016[2]	26,00 [3,51; 192,65] <,0001[3]	5,0 [3,0; 7,1] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9996)					
White	19/323 (5,9)	1/324 (0,3)	19,06 [2,57; 141,53] 0,0040[2]	20,19 [2,69; 151,72] <,0001[3]	5,6 [2,9; 8,2] <,0001[3]
Asian	6/199 (3,0)	0/180 (0,0)	11,77 [0,67; 207,38] 0,0922[2]	12,13 [0,68; 216,80] 0,0312[4]	3,0 [0,6; 5,4] 0,0312[4]
Other	3/19 (15,8)	0/21 (0,0)	7,70 [0,42; 140,03] 0,1678[2]	9,12 [0,44; 189,13] 0,0981[4]	15,8 [-0,6; 32,2] 0,0981[4]
ECOG-PS (Interaction p-value: 0,9842)					
ECOG-PS 0	27/496 (5,4)	1/480 (0,2)	26,13 [3,56; 191,53] 0,0013[2]	27,58 [3,73; 203,76] <,0001[3]	5,2 [3,2; 7,3] <,0001[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Leukopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7016)					
Neoadjuvant chemotherapy	17/217 (7,8)	4/219 (1,8)	4,29 [1,47; 12,54] 0,0078[2]	4,57 [1,51; 13,81] 0,0034[3]	6,0 [2,0; 10,0] 0,0034[3]
Adjuvant chemotherapy	34/327 (10,4)	4/312 (1,3)	8,11 [2,91; 22,59] <,0001[2]	8,94 [3,13; 25,49] <,0001[3]	9,1 [5,6; 12,7] <,0001[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,9902)					
North America / Europe	13/252 (5,2)	2/233 (0,9)	6,01 [1,37; 26,35] 0,0174[2]	6,28 [1,40; 28,15] 0,0063[3]	4,3 [1,3; 7,3] 0,0063[3]
Asia	7/168 (4,2)	1/166 (0,6)	6,92 [0,86; 55,60] 0,0690[2]	7,17 [0,87; 58,97] 0,0671[4]	3,6 [0,3; 6,8] 0,0671[4]
Other	33/133 (24,8)	5/136 (3,7)	6,75 [2,72; 16,76] <,0001[2]	8,65 [3,26; 22,94] <,0001[3]	21,1 [13,1; 29,1] <,0001[3]
Primary tumor size (Interaction p-value: 0,4019)					
< 20 mm	14/141 (9,9)	4/140 (2,9)	3,48 [1,17; 10,30] 0,0246[2]	3,75 [1,20; 11,69] 0,0155[3]	7,1 [1,4; 12,7] 0,0155[3]
≥ 20 but < 50 mm	23/255 (9,0)	2/249 (0,8)	11,23 [2,68; 47,13] 0,0010[2]	12,24 [2,85; 52,51] <,0001[3]	8,2 [4,5; 11,9] <,0001[3]
≥ 50 mm	16/145 (11,0)	2/141 (1,4)	7,78 [1,82; 33,22] 0,0056[2]	8,62 [1,94; 38,22] 0,0008[3]	9,6 [4,2; 15,1] 0,0008[3]
Number of positive lymph nodes (Interaction p-value: 0,6316)					
0-3	16/203 (7,9)	4/214 (1,9)	4,22 [1,43; 12,40] 0,0089[2]	4,49 [1,48; 13,67] 0,0041[3]	6,0 [1,9; 10,1] 0,0041[3]
4-9	21/242 (8,7)	2/231 (0,9)	10,02 [2,38; 42,27] 0,0017[2]	10,88 [2,52; 46,95] <,0001[3]	7,8 [4,1; 11,6] <,0001[3]
≥ 10	16/108 (14,8)	2/90 (2,2)	6,67 [1,57; 28,23] 0,0100[2]	7,65 [1,71; 34,25] 0,0021[3]	12,6 [5,2; 20,0] 0,0021[3]
Tumor stage (Interaction p-value: 1,0000)					
IIA	5/59 (8,5)	1/62 (1,6)	5,25 [0,63; 43,65] 0,1246[2]	5,65 [0,64; 49,87] 0,1085[4]	6,9 [-0,9; 14,6] 0,1085[4]
IIB	2/53 (3,8)	0/69 (0,0)	6,48 [0,32; 132,22] 0,2245[2]	6,75 [0,32; 143,57] 0,1867[4]	3,8 [-1,4; 8,9] 0,1867[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	19/236 (8,1)	3/214 (1,4)	5,74 [1,72; 19,13] 0,0044[2]	6,16 [1,80; 21,12] 0,0011[3]	6,6 [2,8; 10,5] 0,0011[3]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	25/186 (13,4)	4/174 (2,3)	5,85 [2,08; 16,46] 0,0008[2]	6,60 [2,25; 19,38] 0,0001[3]	11,1 [5,8; 16,5] 0,0001[3]
Tumor grade (Interaction p-value: 0,9555)					
G1	5/47 (10,6)	0/41 (0,0)	9,63 [0,55; 168,96] 0,1214[2]	10,74 [0,58; 200,45] 0,0583[4]	10,6 [1,8; 19,5] 0,0583[4]
G2	28/244 (11,5)	4/234 (1,7)	6,71 [2,39; 18,84] 0,0003[2]	7,45 [2,57; 21,60] <,0001[3]	9,8 [5,4; 14,1] <,0001[3]
G3	18/233 (7,7)	4/226 (1,8)	4,36 [1,50; 12,70] 0,0068[2]	4,65 [1,55; 13,95] 0,0028[3]	6,0 [2,1; 9,8] 0,0028[3]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,9562)					
Negative	5/49 (10,2)	0/44 (0,0)	9,90 [0,56; 174,07] 0,1170[2]	11,00 [0,59; 204,92] 0,0576[4]	10,2 [1,7; 18,7] 0,0576[4]
Positive	48/477 (10,1)	8/471 (1,7)	5,92 [2,83; 12,39] <,0001[2]	6,48 [3,03; 13,85] <,0001[3]	8,4 [5,4; 11,3] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,3673)					
White	40/323 (12,4)	5/324 (1,5)	8,02 [3,21; 20,07] <,0001[2]	9,02 [3,51; 23,16] <,0001[3]	10,8 [7,0; 14,7] <,0001[3]
Asian	9/199 (4,5)	1/180 (0,6)	8,14 [1,04; 63,62] 0,0456[2]	8,48 [1,06; 67,60] 0,0214[4]	4,0 [0,9; 7,1] 0,0214[4]
Other	4/19 (21,1)	2/21 (9,5)	2,21 [0,46; 10,73] 0,3251[2]	2,53 [0,41; 15,75] 0,3976[4]	11,5 [-10,7; 33,7] 0,3976[4]
ECOG-PS (Interaction p-value: 0,6313)					
ECOG-PS 0	49/496 (9,9)	7/480 (1,5)	6,77 [3,10; 14,81] <,0001[2]	7,41 [3,32; 16,53] <,0001[3]	8,4 [5,6; 11,3] <,0001[3]
ECOG-PS 1	4/57 (7,0)	1/55 (1,8)	3,86 [0,45; 33,46] 0,2203[2]	4,08 [0,44; 37,67] 0,3640[4]	5,2 [-2,3; 12,7] 0,3640[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Lymphocyte count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9402)					
Neoadjuvant chemotherapy	19/217 (8,8)	6/219 (2,7)	3,20 [1,30; 7,85] 0,0113[2]	3,41 [1,33; 8,70] 0,0069[3]	6,0 [1,7; 10,4] 0,0069[3]
Adjuvant chemotherapy	37/327 (11,3)	9/312 (2,9)	3,92 [1,93; 7,99] 0,0002[2]	4,30 [2,04; 9,06] <,0001[3]	8,4 [4,5; 12,3] <,0001[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Primary tumor size (Interaction p-value: 0,8185)					
< 20 mm	13/141 (9,2)	3/140 (2,1)	4,30 [1,25; 14,77] 0,0204[2]	4,64 [1,29; 16,65] 0,0105[3]	7,1 [1,7; 12,4] 0,0105[3]
≥ 20 but < 50 mm	24/255 (9,4)	8/249 (3,2)	2,93 [1,34; 6,40] 0,0070[2]	3,13 [1,38; 7,11] 0,0043[3]	6,2 [2,0; 10,4] 0,0043[3]
≥ 50 mm	17/145 (11,7)	4/141 (2,8)	4,13 [1,43; 11,98] 0,0090[2]	4,55 [1,49; 13,88] 0,0040[3]	8,9 [3,0; 14,8] 0,0040[3]
Number of positive lymph nodes (Interaction p-value: 0,7853)					
0-3	22/203 (10,8)	5/214 (2,3)	4,64 [1,79; 12,02] 0,0016[2]	5,08 [1,89; 13,69] 0,0004[3]	8,5 [3,8; 13,2] 0,0004[3]
4-9	29/242 (12,0)	8/231 (3,5)	3,46 [1,62; 7,41] 0,0014[2]	3,80 [1,70; 8,49] 0,0006[3]	8,5 [3,8; 13,2] 0,0006[3]
≥ 10	6/108 (5,6)	2/90 (2,2)	2,50 [0,52; 12,08] 0,2544[2]	2,59 [0,51; 13,15] 0,2956[4]	3,3 [-2,0; 8,6] 0,2956[4]
Tumor stage (Interaction p-value: 0,9848)					
IIA	7/59 (11,9)	0/62 (0,0)	15,75 [0,92; 269,79] 0,0572[2]	17,86 [1,00; 320,07] 0,0054[4]	11,9 [3,6; 20,1] 0,0054[4]
IIB	7/53 (13,2)	4/69 (5,8)	2,28 [0,70; 7,38] 0,1696[2]	2,47 [0,68; 8,94] 0,2063[4]	7,4 [-3,2; 18,1] 0,2063[4]
IIIA	31/236 (13,1)	8/214 (3,7)	3,51 [1,65; 7,48] 0,0011[2]	3,89 [1,75; 8,67] 0,0004[3]	9,4 [4,4; 14,4] 0,0004[3]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	10/186 (5,4)	3/174 (1,7)	3,12 [0,87; 11,14] 0,0801[2]	3,24 [0,88; 11,97] 0,0634[3]	3,7 [-0,1; 7,4] 0,0634[3]
Tumor grade (Interaction p-value: 0,8879)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	6/47 (12,8)	0/41 (0,0)	11,38 [0,66; 195,96] 0,0941[2]	13,00 [0,71; 238,27] 0,0281[4]	12,8 [3,2; 22,3] 0,0281[4]
G2	28/244 (11,5)	8/234 (3,4)	3,36 [1,56; 7,21] 0,0019[2]	3,66 [1,63; 8,21] 0,0008[3]	8,1 [3,4; 12,7] 0,0008[3]
G3	17/233 (7,3)	6/226 (2,7)	2,75 [1,10; 6,84] 0,0299[2]	2,89 [1,12; 7,46] 0,0227[3]	4,6 [0,7; 8,6] 0,0227[3]
GX	6/29 (20,7)	1/33 (3,0)	6,83 [0,87; 53,43] 0,0672[2]	8,35 [0,94; 74,12] 0,0437[4]	17,7 [1,8; 33,5] 0,0437[4]
Progesterone receptor status (Interaction p-value: 0,3528)					
Negative	5/49 (10,2)	2/44 (4,5)	2,24 [0,46; 10,99] 0,3184[2]	2,39 [0,44; 12,98] 0,4398[4]	5,7 [-4,8; 16,1] 0,4398[4]
Positive	48/477 (10,1)	12/471 (2,5)	3,95 [2,13; 7,34] <,0001[2]	4,28 [2,24; 8,17] <,0001[3]	7,5 [4,5; 10,6] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,2334)					
White	29/323 (9,0)	12/324 (3,7)	2,42 [1,26; 4,67] 0,0080[2]	2,56 [1,28; 5,12] 0,0059[3]	5,3 [1,5; 9,0] 0,0059[3]
Asian	26/199 (13,1)	3/180 (1,7)	7,84 [2,41; 25,46] 0,0006[2]	8,87 [2,64; 29,83] <,0001[3]	11,4 [6,4; 16,4] <,0001[3]
Other	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (Interaction p-value: 0,8289)					
ECOG-PS 0	54/496 (10,9)	14/480 (2,9)	3,73 [2,10; 6,63] <,0001[2]	4,07 [2,23; 7,42] <,0001[3]	8,0 [4,8; 11,1] <,0001[3]
ECOG-PS 1	3/57 (5,3)	1/55 (1,8)	2,89 [0,31; 26,99] 0,3508[2]	3,00 [0,30; 29,76] 0,6184[4]	3,4 [-3,3; 10,2] 0,6184[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Lymphoedema from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,6625)					
Neoadjuvant chemotherapy	31/217 (14,3)	18/219 (8,2)	1,74 [1,00; 3,01] 0,0487[2]	1,86 [1,01; 3,44] 0,0449[3]	6,1 [0,2; 12,0] 0,0449[3]
Adjuvant chemotherapy	45/327 (13,8)	34/312 (10,9)	1,26 [0,83; 1,92] 0,2733[2]	1,30 [0,81; 2,10] 0,2716[3]	2,9 [-2,2; 8,0] 0,2716[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,8660)					
North America / Europe	34/252 (13,5)	24/233 (10,3)	1,31 [0,80; 2,14] 0,2815[2]	1,36 [0,78; 2,37] 0,2791[3]	3,2 [-2,6; 8,9] 0,2791[3]
Asia	30/168 (17,9)	19/166 (11,4)	1,56 [0,92; 2,66] 0,1020[2]	1,68 [0,90; 3,13] 0,0978[3]	6,4 [-1,1; 14,0] 0,0978[3]
Other	14/133 (10,5)	9/136 (6,6)	1,59 [0,71; 3,55] 0,2570[2]	1,66 [0,69; 3,98] 0,2517[3]	3,9 [-2,8; 10,6] 0,2517[3]
Primary tumor size (Interaction p-value: 0,0787)					
< 20 mm	17/141 (12,1)	18/140 (12,9)	0,94 [0,50; 1,74] 0,8390[2]	0,93 [0,46; 1,89] 0,8390[3]	-0,8 [-8,5; 6,9] 0,8390[3]
≥ 20 but < 50 mm	37/255 (14,5)	26/249 (10,4)	1,39 [0,87; 2,22] 0,1702[2]	1,46 [0,85; 2,49] 0,1674[3]	4,1 [-1,7; 9,8] 0,1674[3]
≥ 50 mm	22/145 (15,2)	7/141 (5,0)	3,06 [1,35; 6,93] 0,0075[2]	3,42 [1,41; 8,30] 0,0042[3]	10,2 [3,4; 17,1] 0,0042[3]
Number of positive lymph nodes (Interaction p-value: 0,3014)					
0-3	21/203 (10,3)	19/214 (8,9)	1,17 [0,65; 2,10] 0,6117[2]	1,18 [0,62; 2,27] 0,6113[3]	1,5 [-4,2; 7,1] 0,6113[3]
4-9	36/242 (14,9)	26/231 (11,3)	1,32 [0,83; 2,12] 0,2459[2]	1,38 [0,80; 2,37] 0,2435[3]	3,6 [-2,4; 9,7] 0,2435[3]
≥ 10	21/108 (19,4)	7/90 (7,8)	2,50 [1,11; 5,61] 0,0263[2]	2,86 [1,16; 7,09] 0,0190[3]	11,7 [2,4; 21,0] 0,0190[3]
Tumor stage (Interaction p-value: 0,5401)					
IIA	6/59 (10,2)	8/62 (12,9)	0,79 [0,29; 2,14] 0,6396[2]	0,76 [0,25; 2,35] 0,6384[3]	-2,7 [-14,1; 8,6] 0,6384[3]
IIB	6/53 (11,3)	7/69 (10,1)	1,12 [0,40; 3,13] 0,8347[2]	1,13 [0,36; 3,59] 0,8347[3]	1,2 [-9,9; 12,3] 0,8347[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	33/236 (14,0)	22/214 (10,3)	1,36 [0,82; 2,26] 0,2341[2]	1,42 [0,80; 2,52] 0,2311[3]	3,7 [-2,3; 9,7] 0,2311[3]
IIIB	3/18 (16,7)	1/15 (6,7)	2,50 [0,29; 21,61] 0,4051[2]	2,80 [0,26; 30,18] 0,6074[4]	10,0 [-11,3; 31,3] 0,6074[4]
IIIC	30/186 (16,1)	14/174 (8,0)	2,00 [1,10; 3,65] 0,0230[2]	2,20 [1,12; 4,30] 0,0193[3]	8,1 [1,4; 14,7] 0,0193[3]
Tumor grade (Interaction p-value: 0,3860)					
G1	11/47 (23,4)	4/41 (9,8)	2,40 [0,83; 6,96] 0,1073[2]	2,83 [0,82; 9,70] 0,0894[3]	13,6 [-1,5; 28,8] 0,0894[3]
G2	38/244 (15,6)	21/234 (9,0)	1,74 [1,05; 2,87] 0,0313[2]	1,87 [1,06; 3,30] 0,0283[3]	6,6 [0,8; 12,4] 0,0283[3]
G3	27/233 (11,6)	25/226 (11,1)	1,05 [0,63; 1,75] 0,8589[2]	1,05 [0,59; 1,88] 0,8589[3]	0,5 [-5,3; 6,3] 0,8589[3]
GX	2/29 (6,9)	1/33 (3,0)	2,28 [0,22; 23,82] 0,4924[2]	2,37 [0,20; 27,59] 0,5951[4]	3,9 [-7,1; 14,8] 0,5951[4]
Progesterone receptor status (Interaction p-value: 0,7095)					
Negative	6/49 (12,2)	2/44 (4,5)	2,69 [0,57; 12,66] 0,2095[2]	2,93 [0,56; 15,35] 0,2731[4]	7,7 [-3,4; 18,8] 0,2731[4]
Positive	67/477 (14,0)	48/471 (10,2)	1,38 [0,97; 1,95] 0,0708[2]	1,44 [0,97; 2,14] 0,0691[3]	3,9 [-0,3; 8,0] 0,0691[3]
Unknown	0/4 (0,0)	1/8 (12,5)	0,60 [0,03; 12,15] 0,7393[2]	0,56 [0,02; 16,77] 1,0000[4]	-12,5 [-35,4; 10,4] 1,0000[4]
Race (Interaction p-value: 0,9559)					
White	45/323 (13,9)	29/324 (9,0)	1,56 [1,00; 2,42] 0,0490[2]	1,65 [1,00; 2,70] 0,0465[3]	5,0 [0,1; 9,9] 0,0465[3]
Asian	31/199 (15,6)	20/180 (11,1)	1,40 [0,83; 2,37] 0,2069[2]	1,48 [0,81; 2,70] 0,2032[3]	4,5 [-2,3; 11,3] 0,2032[3]
Other	0/19 (0,0)	2/21 (9,5)	0,22 [0,01; 4,31] 0,3186[2]	0,20 [0,01; 4,44] 0,4885[4]	-9,5 [-22,1; 3,0] 0,4885[4]
ECOG-PS (Interaction p-value: 0,0894)					
ECOG-PS 0	74/496 (14,9)	45/480 (9,4)	1,59 [1,12; 2,26] 0,0090[2]	1,70 [1,14; 2,51] 0,0081[3]	5,5 [1,5; 9,6] 0,0081[3]
ECOG-PS 1	4/57 (7,0)	7/55 (12,7)	0,55 [0,17; 1,78] 0,3192[2]	0,52 [0,14; 1,88] 0,3101[3]	-5,7 [-16,7; 5,3] 0,3101[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Lymphopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9611)					
Neoadjuvant chemotherapy	8/217 (3,7)	3/219 (1,4)	2,69 [0,72; 10,01] 0,1396[2]	2,76 [0,72; 10,53] 0,1230[3]	2,3 [-0,6; 5,3] 0,1230[3]
Adjuvant chemotherapy	11/327 (3,4)	3/312 (1,0)	3,50 [0,99; 12,42] 0,0527[2]	3,59 [0,99; 12,98] 0,0381[3]	2,4 [0,2; 4,6] 0,0381[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,6494)					
North America / Europe	8/252 (3,2)	4/233 (1,7)	1,85 [0,56; 6,06] 0,3100[2]	1,88 [0,56; 6,32] 0,3018[3]	1,5 [-1,3; 4,2] 0,3018[3]
Asia	2/168 (1,2)	0/166 (0,0)	4,94 [0,24; 102,14] 0,3012[2]	5,00 [0,24; 104,94] 0,4985[4]	1,2 [-0,4; 2,8] 0,4985[4]
Other	9/133 (6,8)	2/136 (1,5)	4,60 [1,01; 20,90] 0,0481[2]	4,86 [1,03; 22,95] 0,0283[3]	5,3 [0,6; 10,0] 0,0283[3]
Primary tumor size (Interaction p-value: 0,9214)					
< 20 mm	5/141 (3,5)	2/140 (1,4)	2,48 [0,49; 12,58] 0,2723[2]	2,54 [0,48; 13,30] 0,4472[4]	2,1 [-1,5; 5,7] 0,4472[4]
≥ 20 but < 50 mm	8/255 (3,1)	2/249 (0,8)	3,91 [0,84; 18,21] 0,0828[2]	4,00 [0,84; 19,03] 0,1061[4]	2,3 [-0,1; 4,7] 0,1061[4]
≥ 50 mm	6/145 (4,1)	2/141 (1,4)	2,92 [0,60; 14,21] 0,1851[2]	3,00 [0,60; 15,12] 0,2825[4]	2,7 [-1,1; 6,5] 0,2825[4]
Number of positive lymph nodes (Interaction p-value: 0,9313)					
0-3	5/203 (2,5)	3/214 (1,4)	1,76 [0,43; 7,26] 0,4361[2]	1,78 [0,42; 7,53] 0,4934[4]	1,1 [-1,6; 3,7] 0,4934[4]
4-9	8/242 (3,3)	3/231 (1,3)	2,55 [0,68; 9,48] 0,1636[2]	2,60 [0,68; 9,92] 0,1477[3]	2,0 [-0,7; 4,7] 0,1477[3]
≥ 10	6/108 (5,6)	0/90 (0,0)	10,85 [0,62; 190,07] 0,1026[2]	11,48 [0,64; 206,59] 0,0327[4]	5,6 [1,2; 9,9] 0,0327[4]
Tumor stage (Interaction p-value: 0,9811)					
IIA	1/59 (1,7)	1/62 (1,6)	1,05 [0,07; 16,42] 0,9718[2]	1,05 [0,06; 17,21] 1,0000[4]	0,1 [-4,5; 4,6] 1,0000[4]
IIB	0/53 (0,0)	0/69 (0,0)	NE	NE	NE

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	5/236 (2,1)	4/214 (1,9)	1,13 [0,31; 4,17] 0,8504[2]	1,14 [0,30; 4,29] 1,0000[4]	0,2 [-2,3; 2,8] 1,0000[4]
IIIB	3/18 (16,7)	1/15 (6,7)	2,50 [0,29; 21,61] 0,4051[2]	2,80 [0,26; 30,18] 0,6074[4]	10,0 [-11,3; 31,3] 0,6074[4]
IIIC	10/186 (5,4)	0/174 (0,0)	19,65 [1,16; 332,86] 0,0391[2]	20,76 [1,21; 357,05] 0,0018[4]	5,4 [2,1; 8,6] 0,0018[4]
Tumor grade (Interaction p-value: 0,8725)					
G1	2/47 (4,3)	0/41 (0,0)	4,38 [0,22; 88,58] 0,3362[2]	4,56 [0,21; 97,79] 0,4966[4]	4,3 [-1,5; 10,0] 0,4966[4]
G2	7/244 (2,9)	4/234 (1,7)	1,68 [0,50; 5,66] 0,4037[2]	1,70 [0,49; 5,88] 0,3980[3]	1,2 [-1,5; 3,8] 0,3980[3]
G3	8/233 (3,4)	2/226 (0,9)	3,88 [0,83; 18,07] 0,0842[2]	3,98 [0,84; 18,96] 0,1059[4]	2,5 [-0,1; 5,2] 0,1059[4]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,9619)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	18/477 (3,8)	6/471 (1,3)	2,96 [1,19; 7,40] 0,0200[2]	3,04 [1,20; 7,73] 0,0143[3]	2,5 [0,5; 4,5] 0,0143[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9714)					
White	15/323 (4,6)	5/324 (1,5)	3,01 [1,11; 8,18] 0,0309[2]	3,11 [1,12; 8,65] 0,0227[3]	3,1 [0,4; 5,8] 0,0227[3]
Asian	2/199 (1,0)	0/180 (0,0)	4,53 [0,22; 93,63] 0,3288[2]	4,57 [0,22; 95,82] 0,4999[4]	1,0 [-0,4; 2,4] 0,4999[4]
Other	2/19 (10,5)	1/21 (4,8)	2,21 [0,22; 22,47] 0,5026[2]	2,35 [0,20; 28,27] 0,5962[4]	5,8 [-10,8; 22,3] 0,5962[4]
ECOG-PS (Interaction p-value: 0,9790)					
ECOG-PS 0	17/496 (3,4)	6/480 (1,3)	2,74 [1,09; 6,90] 0,0321[2]	2,80 [1,10; 7,17] 0,0250[3]	2,2 [0,3; 4,1] 0,0250[3]
ECOG-PS 1	2/57 (3,5)	0/55 (0,0)	4,83 [0,24; 98,34] 0,3060[2]	5,00 [0,23; 106,54] 0,4957[4]	3,5 [-1,3; 8,3] 0,4957[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Malaise from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8598)					
Neoadjuvant chemotherapy	10/217 (4,6)	5/219 (2,3)	2,02 [0,70; 5,81] 0,1928[2]	2,07 [0,69; 6,15] 0,1829[3]	2,3 [-1,1; 5,7] 0,1829[3]
Adjuvant chemotherapy	13/327 (4,0)	4/312 (1,3)	3,10 [1,02; 9,41] 0,0457[2]	3,19 [1,03; 9,88] 0,0344[3]	2,7 [0,2; 5,2] 0,0344[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,1126)					
North America / Europe	4/252 (1,6)	5/233 (2,1)	0,74 [0,20; 2,72] 0,6501[2]	0,74 [0,20; 2,77] 0,7436[4]	-0,6 [-3,0; 1,9] 0,7436[4]
Asia	18/168 (10,7)	4/166 (2,4)	4,45 [1,54; 12,86] 0,0059[2]	4,86 [1,61; 14,69] 0,0022[3]	8,3 [3,1; 13,5] 0,0022[3]
Other	2/133 (1,5)	0/136 (0,0)	5,11 [0,25; 105,49] 0,2908[2]	5,19 [0,25; 109,13] 0,2435[4]	1,5 [-0,6; 3,6] 0,2435[4]
Primary tumor size (Interaction p-value: 0,6044)					
< 20 mm	6/141 (4,3)	4/140 (2,9)	1,49 [0,43; 5,16] 0,5300[2]	1,51 [0,42; 5,48] 0,7494[4]	1,4 [-2,9; 5,7] 0,7494[4]
≥ 20 but < 50 mm	11/255 (4,3)	3/249 (1,2)	3,58 [1,01; 12,68] 0,0481[2]	3,70 [1,02; 13,41] 0,0337[3]	3,1 [0,3; 5,9] 0,0337[3]
≥ 50 mm	6/145 (4,1)	2/141 (1,4)	2,92 [0,60; 14,21] 0,1851[2]	3,00 [0,60; 15,12] 0,2825[4]	2,7 [-1,1; 6,5] 0,2825[4]
Number of positive lymph nodes (Interaction p-value: 0,9787)					
0-3	8/203 (3,9)	4/214 (1,9)	2,11 [0,64; 6,89] 0,2172[2]	2,15 [0,64; 7,27] 0,2059[3]	2,1 [-1,2; 5,3] 0,2059[3]
4-9	13/242 (5,4)	5/231 (2,2)	2,48 [0,90; 6,85] 0,0794[2]	2,57 [0,90; 7,32] 0,0684[3]	3,2 [-0,2; 6,6] 0,0684[3]
≥ 10	3/108 (2,8)	0/90 (0,0)	5,84 [0,31; 111,67] 0,2408[2]	6,00 [0,31; 117,80] 0,2524[4]	2,8 [-0,3; 5,9] 0,2524[4]
Tumor stage (Interaction p-value: 0,8795)					
IIA	3/59 (5,1)	1/62 (1,6)	3,15 [0,34; 29,46] 0,3140[2]	3,27 [0,33; 32,34] 0,3565[4]	3,5 [-3,0; 9,9] 0,3565[4]
IIB	2/53 (3,8)	1/69 (1,4)	2,60 [0,24; 27,95] 0,4294[2]	2,67 [0,24; 30,22] 0,5789[4]	2,3 [-3,5; 8,2] 0,5789[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	12/236 (5,1)	3/214 (1,4)	3,63 [1,04; 12,68] 0,0436[2]	3,77 [1,05; 13,54] 0,0297[3]	3,7 [0,5; 6,9] 0,0297[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	6/186 (3,2)	4/174 (2,3)	1,40 [0,40; 4,89] 0,5947[2]	1,42 [0,39; 5,11] 0,7518[4]	0,9 [-2,5; 4,3] 0,7518[4]
Tumor grade (Interaction p-value: 0,8506)					
G1	4/47 (8,5)	0/41 (0,0)	7,88 [0,44; 142,02] 0,1620[2]	8,59 [0,45; 164,46] 0,1199[4]	8,5 [0,5; 16,5] 0,1199[4]
G2	6/244 (2,5)	5/234 (2,1)	1,15 [0,36; 3,72] 0,8145[2]	1,15 [0,35; 3,84] 0,8143[3]	0,3 [-2,4; 3,0] 0,8143[3]
G3	10/233 (4,3)	4/226 (1,8)	2,42 [0,77; 7,62] 0,1295[2]	2,49 [0,77; 8,05] 0,1162[3]	2,5 [-0,6; 5,6] 0,1162[3]
GX	4/29 (13,8)	0/33 (0,0)	10,20 [0,57; 181,74] 0,1140[2]	11,82 [0,61; 229,73] 0,0426[4]	13,8 [1,2; 26,3] 0,0426[4]
Progesterone receptor status (Interaction p-value: 0,9998)					
Negative	0/49 (0,0)	0/44 (0,0)	NE	NE	NE
Positive	24/477 (5,0)	9/471 (1,9)	2,63 [1,24; 5,60] 0,0120[2]	2,72 [1,25; 5,91] 0,0088[3]	3,1 [0,8; 5,4] 0,0088[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,3227)					
White	6/323 (1,9)	5/324 (1,5)	1,20 [0,37; 3,90] 0,7575[2]	1,21 [0,36; 4,00] 0,7571[3]	0,3 [-1,7; 2,3] 0,7571[3]
Asian	18/199 (9,0)	4/180 (2,2)	4,07 [1,40; 11,80] 0,0097[2]	4,38 [1,45; 13,19] 0,0046[3]	6,8 [2,3; 11,4] 0,0046[3]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,1420)					
ECOG-PS 0	23/496 (4,6)	7/480 (1,5)	3,18 [1,38; 7,34] 0,0067[2]	3,29 [1,40; 7,73] 0,0040[3]	3,2 [1,0; 5,3] 0,0040[3]
ECOG-PS 1	1/57 (1,8)	2/55 (3,6)	0,48 [0,05; 5,17] 0,5470[2]	0,47 [0,04; 5,37] 0,6149[4]	-1,9 [-7,9; 4,1] 0,6149[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Mucosal inflammation from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Region (Interaction p-value: 0,9993)					
North America / Europe	8/252 (3,2)	3/233 (1,3)	2,47 [0,66; 9,18] 0,1786[2]	2,51 [0,66; 9,59] 0,1631[3]	1,9 [-0,7; 4,5] 0,1631[3]
Asia	3/168 (1,8)	0/166 (0,0)	6,92 [0,36; 132,88] 0,1996[2]	7,04 [0,36; 137,40] 0,2478[4]	1,8 [-0,2; 3,8] 0,2478[4]
Other	1/133 (0,8)	0/136 (0,0)	3,07 [0,13; 74,63] 0,4913[2]	3,09 [0,12; 76,54] 0,4944[4]	0,8 [-0,7; 2,2] 0,4944[4]
Number of positive lymph nodes (Interaction p-value: 0,9617)					
0-3	8/203 (3,9)	2/214 (0,9)	4,22 [0,91; 19,62] 0,0666[2]	4,35 [0,91; 20,73] 0,0565[4]	3,0 [0,0; 6,0] 0,0565[4]
4-9	3/242 (1,2)	1/231 (0,4)	2,86 [0,30; 27,33] 0,3607[2]	2,89 [0,30; 27,96] 0,6238[4]	0,8 [-0,8; 2,4] 0,6238[4]
≥ 10	1/108 (0,9)	0/90 (0,0)	2,50 [0,10; 60,74] 0,5725[2]	2,53 [0,10; 62,76] 1,0000[4]	0,9 [-0,9; 2,7] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,9594)					
Negative	2/49 (4,1)	0/44 (0,0)	4,50 [0,22; 91,25] 0,3273[2]	4,68 [0,22; 100,28] 0,4960[4]	4,1 [-1,5; 9,6] 0,4960[4]
Positive	10/477 (2,1)	3/471 (0,6)	3,29 [0,91; 11,88] 0,0690[2]	3,34 [0,91; 12,22] 0,0534[3]	1,5 [-0,0; 2,9] 0,0534[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9996)					
White	8/323 (2,5)	3/324 (0,9)	2,67 [0,72; 9,99] 0,1434[2]	2,72 [0,71; 10,34] 0,1271[3]	1,6 [-0,4; 3,5] 0,1271[3]
Asian	4/199 (2,0)	0/180 (0,0)	8,15 [0,44; 150,24] 0,1584[2]	8,31 [0,44; 155,42] 0,1249[4]	2,0 [0,1; 4,0] 0,1249[4]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9724)					
ECOG-PS 0	12/496 (2,4)	1/480 (0,2)	11,61 [1,52; 88,97] 0,0183[2]	11,88 [1,54; 91,69] 0,0026[3]	2,2 [0,8; 3,6] 0,0026[3]
ECOG-PS 1	0/57 (0,0)	2/55 (3,6)	0,19 [0,01; 3,93] 0,2849[2]	0,19 [0,01; 3,97] 0,2389[4]	-3,6 [-8,6; 1,3] 0,2389[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Nail disorder from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9244)					
Neoadjuvant chemotherapy	10/217 (4,6)	2/219 (0,9)	5,05 [1,12; 22,76] 0,0352[2]	5,24 [1,13; 24,21] 0,0184[3]	3,7 [0,6; 6,8] 0,0184[3]
Adjuvant chemotherapy	5/327 (1,5)	0/312 (0,0)	10,50 [0,58; 189,05] 0,1109[2]	10,66 [0,59; 193,57] 0,0619[4]	1,5 [0,2; 2,9] 0,0619[4]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,9993)					
North America / Europe	8/252 (3,2)	2/233 (0,9)	3,70 [0,79; 17,24] 0,0958[2]	3,79 [0,80; 18,02] 0,1084[4]	2,3 [-0,2; 4,8] 0,1084[4]
Asia	6/168 (3,6)	0/166 (0,0)	12,85 [0,73; 226,22] 0,0811[2]	13,32 [0,74; 238,37] 0,0299[4]	3,6 [0,8; 6,4] 0,0299[4]
Other	1/133 (0,8)	0/136 (0,0)	3,07 [0,13; 74,63] 0,4913[2]	3,09 [0,12; 76,54] 0,4944[4]	0,8 [-0,7; 2,2] 0,4944[4]
Number of positive lymph nodes (Interaction p-value: 0,9776)					
0-3	4/203 (2,0)	2/214 (0,9)	2,11 [0,39; 11,39] 0,3860[2]	2,13 [0,39; 11,76] 0,4386[4]	1,0 [-1,3; 3,3] 0,4386[4]
4-9	10/242 (4,1)	0/231 (0,0)	20,05 [1,18; 340,20] 0,0379[2]	20,91 [1,22; 358,91] 0,0018[4]	4,1 [1,6; 6,6] 0,0018[4]
≥ 10	1/108 (0,9)	0/90 (0,0)	2,50 [0,10; 60,74] 0,5725[2]	2,53 [0,10; 62,76] 1,0000[4]	0,9 [-0,9; 2,7] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,9997)					
Negative	0/49 (0,0)	0/44 (0,0)	NE	NE	NE
Positive	15/477 (3,1)	2/471 (0,4)	7,41 [1,70; 32,21] 0,0076[2]	7,61 [1,73; 33,48] 0,0016[3]	2,7 [1,0; 4,4] 0,0016[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9995)					
White	8/323 (2,5)	2/324 (0,6)	4,01 [0,86; 18,75] 0,0774[2]	4,09 [0,86; 19,40] 0,0632[4]	1,9 [-0,0; 3,8] 0,0632[4]
Asian	7/199 (3,5)	0/180 (0,0)	13,58 [0,78; 236,01] 0,0734[2]	14,06 [0,80; 248,04] 0,0156[4]	3,5 [1,0; 6,1] 0,0156[4]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Nasopharyngitis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7639)					
Neoadjuvant chemotherapy	34/217 (15,7)	26/219 (11,9)	1,32 [0,82; 2,12] 0,2522[2]	1,38 [0,80; 2,39] 0,2500[3]	3,8 [-2,7; 10,3] 0,2500[3]
Adjuvant chemotherapy	46/327 (14,1)	26/312 (8,3)	1,69 [1,07; 2,66] 0,0242[2]	1,80 [1,08; 2,99] 0,0219[3]	5,7 [0,9; 10,6] 0,0219[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,3166)					
North America / Europe	31/252 (12,3)	21/233 (9,0)	1,36 [0,81; 2,31] 0,2451[2]	1,42 [0,79; 2,54] 0,2422[3]	3,3 [-2,2; 8,8] 0,2422[3]
Asia	44/168 (26,2)	30/166 (18,1)	1,45 [0,96; 2,19] 0,0772[2]	1,61 [0,95; 2,72] 0,0741[3]	8,1 [-0,7; 17,0] 0,0741[3]
Other	7/133 (5,3)	1/136 (0,7)	7,16 [0,89; 57,39] 0,0639[2]	7,50 [0,91; 61,82] 0,0347[4]	4,5 [0,5; 8,6] 0,0347[4]
Primary tumor size (Interaction p-value: 0,5648)					
< 20 mm	21/141 (14,9)	12/140 (8,6)	1,74 [0,89; 3,39] 0,1058[2]	1,87 [0,88; 3,96] 0,0998[3]	6,3 [-1,2; 13,8] 0,0998[3]
≥ 20 but < 50 mm	33/255 (12,9)	26/249 (10,4)	1,24 [0,76; 2,01] 0,3842[2]	1,27 [0,74; 2,20] 0,3829[3]	2,5 [-3,1; 8,1] 0,3829[3]
≥ 50 mm	26/145 (17,9)	14/141 (9,9)	1,81 [0,98; 3,31] 0,0563[2]	1,98 [0,99; 3,98] 0,0511[3]	8,0 [0,0; 16,0] 0,0511[3]
Number of positive lymph nodes (Interaction p-value: 0,9268)					
0-3	28/203 (13,8)	21/214 (9,8)	1,41 [0,83; 2,39] 0,2099[2]	1,47 [0,81; 2,68] 0,2071[3]	4,0 [-2,2; 10,2] 0,2071[3]
4-9	39/242 (16,1)	23/231 (10,0)	1,62 [1,00; 2,62] 0,0506[2]	1,74 [1,00; 3,01] 0,0473[3]	6,2 [0,1; 12,2] 0,0473[3]
≥ 10	15/108 (13,9)	8/90 (8,9)	1,56 [0,69; 3,52] 0,2809[2]	1,65 [0,67; 4,10] 0,2742[3]	5,0 [-3,8; 13,8] 0,2742[3]
Tumor stage (Interaction p-value: 0,9323)					
IIA	10/59 (16,9)	6/62 (9,7)	1,75 [0,68; 4,52] 0,2462[2]	1,90 [0,65; 5,62] 0,2379[3]	7,3 [-4,8; 19,3] 0,2379[3]
IIB	9/53 (17,0)	7/69 (10,1)	1,67 [0,67; 4,20] 0,2728[2]	1,81 [0,63; 5,23] 0,2675[3]	6,8 [-5,5; 19,2] 0,2675[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	32/236 (13,6)	21/214 (9,8)	1,38 [0,82; 2,32] 0,2215[2]	1,44 [0,80; 2,59] 0,2182[3]	3,7 [-2,2; 9,7] 0,2182[3]
IIIB	4/18 (22,2)	1/15 (6,7)	3,33 [0,42; 26,72] 0,2569[2]	4,00 [0,40; 40,42] 0,3457[4]	15,6 [-7,4; 38,5] 0,3457[4]
IIIC	26/186 (14,0)	17/174 (9,8)	1,43 [0,80; 2,54] 0,2224[2]	1,50 [0,78; 2,87] 0,2186[3]	4,2 [-2,4; 10,9] 0,2186[3]
Tumor grade (Interaction p-value: 0,7605)					
G1	11/47 (23,4)	4/41 (9,8)	2,40 [0,83; 6,96] 0,1073[2]	2,83 [0,82; 9,70] 0,0894[3]	13,6 [-1,5; 28,8] 0,0894[3]
G2	32/244 (13,1)	20/234 (8,5)	1,53 [0,90; 2,60] 0,1127[2]	1,62 [0,90; 2,91] 0,1089[3]	4,6 [-1,0; 10,1] 0,1089[3]
G3	31/233 (13,3)	19/226 (8,4)	1,58 [0,92; 2,72] 0,0963[2]	1,67 [0,91; 3,06] 0,0922[3]	4,9 [-0,8; 10,6] 0,0922[3]
GX	8/29 (27,6)	8/33 (24,2)	1,14 [0,49; 2,65] 0,7640[2]	1,19 [0,38; 3,72] 0,7640[3]	3,3 [-18,5; 25,2] 0,7640[3]
Progesterone receptor status (Interaction p-value: 0,5473)					
Negative	5/49 (10,2)	5/44 (11,4)	0,90 [0,28; 2,90] 0,8570[2]	0,89 [0,24; 3,29] 1,0000[4]	-1,2 [-13,8; 11,5] 1,0000[4]
Positive	75/477 (15,7)	44/471 (9,3)	1,68 [1,19; 2,39] 0,0035[2]	1,81 [1,22; 2,69] 0,0030[3]	6,4 [2,2; 10,6] 0,0030[3]
Unknown	1/4 (25,0)	2/8 (25,0)	1,00 [0,13; 8,00] 1,0000[2]	1,00 [0,06; 15,99] 1,0000[4]	0,0 [-52,0; 52,0] 1,0000[4]
Race (Interaction p-value: 0,9972)					
White	31/323 (9,6)	22/324 (6,8)	1,41 [0,84; 2,39] 0,1957[2]	1,46 [0,82; 2,58] 0,1929[3]	2,8 [-1,4; 7,0] 0,1929[3]
Asian	48/199 (24,1)	30/180 (16,7)	1,45 [0,96; 2,18] 0,0766[2]	1,59 [0,96; 2,64] 0,0731[3]	7,5 [-0,6; 15,5] 0,0731[3]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,4049)					
ECOG-PS 0	76/496 (15,3)	50/480 (10,4)	1,47 [1,05; 2,05] 0,0236[2]	1,56 [1,06; 2,28] 0,0223[3]	4,9 [0,7; 9,1] 0,0223[3]
ECOG-PS 1	6/57 (10,5)	2/55 (3,6)	2,89 [0,61; 13,73] 0,1809[2]	3,12 [0,60; 16,17] 0,2716[4]	6,9 [-2,5; 16,3] 0,2716[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Nausea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9482)					
Neoadjuvant chemotherapy	66/217 (30,4)	19/219 (8,7)	3,51 [2,18; 5,63] <,0001[2]	4,60 [2,65; 7,99] <,0001[3]	21,7 [14,6; 28,9] <,0001[3]
Adjuvant chemotherapy	86/327 (26,3)	21/312 (6,7)	3,91 [2,49; 6,14] <,0001[2]	4,94 [2,98; 8,21] <,0001[3]	19,6 [14,0; 25,1] <,0001[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,4178)					
North America / Europe	71/252 (28,2)	22/233 (9,4)	2,98 [1,91; 4,65] <,0001[2]	3,76 [2,24; 6,31] <,0001[3]	18,7 [12,0; 25,4] <,0001[3]
Asia	49/168 (29,2)	11/166 (6,6)	4,40 [2,37; 8,16] <,0001[2]	5,80 [2,89; 11,64] <,0001[3]	22,5 [14,7; 30,4] <,0001[3]
Other	34/133 (25,6)	7/136 (5,1)	4,97 [2,28; 10,81] <,0001[2]	6,33 [2,69; 14,88] <,0001[3]	20,4 [12,1; 28,7] <,0001[3]
Primary tumor size (Interaction p-value: 0,1240)					
< 20 mm	38/141 (27,0)	11/140 (7,9)	3,43 [1,83; 6,43] 0,0001[2]	4,33 [2,11; 8,88] <,0001[3]	19,1 [10,5; 27,7] <,0001[3]
≥ 20 but < 50 mm	61/255 (23,9)	22/249 (8,8)	2,71 [1,72; 4,27] <,0001[2]	3,24 [1,92; 5,48] <,0001[3]	15,1 [8,8; 21,4] <,0001[3]
≥ 50 mm	49/145 (33,8)	7/141 (5,0)	6,81 [3,19; 14,52] <,0001[2]	9,77 [4,24; 22,50] <,0001[3]	28,8 [20,3; 37,3] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,4831)					
0-3	64/203 (31,5)	17/214 (7,9)	3,97 [2,41; 6,54] <,0001[2]	5,34 [3,00; 9,50] <,0001[3]	23,6 [16,2; 30,9] <,0001[3]
4-9	57/242 (23,6)	18/231 (7,8)	3,02 [1,84; 4,98] <,0001[2]	3,65 [2,07; 6,42] <,0001[3]	15,8 [9,4; 22,1] <,0001[3]
≥ 10	33/108 (30,6)	5/90 (5,6)	5,50 [2,24; 13,50] 0,0002[2]	7,48 [2,78; 20,14] <,0001[3]	25,0 [15,1; 34,9] <,0001[3]
Tumor stage (Interaction p-value: 0,3359)					
IIA	13/59 (22,0)	6/62 (9,7)	2,28 [0,93; 5,60] 0,0729[2]	2,64 [0,93; 7,48] 0,0618[3]	12,4 [-0,5; 25,2] 0,0618[3]
IIB	15/53 (28,3)	7/69 (10,1)	2,79 [1,23; 6,35] 0,0145[2]	3,50 [1,31; 9,35] 0,0097[3]	18,2 [4,1; 32,2] 0,0097[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	57/236 (24,2)	13/214 (6,1)	3,98 [2,24; 7,05] <,0001[2]	4,92 [2,61; 9,29] <,0001[3]	18,1 [11,7; 24,4] <,0001[3]
IIIB	6/18 (33,3)	3/15 (20,0)	1,67 [0,50; 5,56] 0,4059[2]	2,00 [0,40; 9,91] 0,4585[4]	13,3 [-16,4; 43,1] 0,4585[4]
IIIC	62/186 (33,3)	11/174 (6,3)	5,27 [2,87; 9,68] <,0001[2]	7,41 [3,74; 14,66] <,0001[3]	27,0 [19,3; 34,7] <,0001[3]
Tumor grade (Interaction p-value: 0,9358)					
G1	11/47 (23,4)	3/41 (7,3)	3,20 [0,96; 10,68] 0,0588[2]	3,87 [1,00; 15,01] 0,0396[3]	16,1 [1,6; 30,6] 0,0396[3]
G2	67/244 (27,5)	16/234 (6,8)	4,02 [2,40; 6,72] <,0001[2]	5,16 [2,89; 9,21] <,0001[3]	20,6 [14,2; 27,1] <,0001[3]
G3	69/233 (29,6)	18/226 (8,0)	3,72 [2,29; 6,04] <,0001[2]	4,86 [2,78; 8,49] <,0001[3]	21,6 [14,8; 28,5] <,0001[3]
GX	7/29 (24,1)	3/33 (9,1)	2,66 [0,76; 9,33] 0,1279[2]	3,18 [0,74; 13,70] 0,1672[4]	15,0 [-3,4; 33,5] 0,1672[4]
Progesterone receptor status (Interaction p-value: 0,8780)					
Negative	21/49 (42,9)	5/44 (11,4)	3,77 [1,55; 9,15] 0,0033[2]	5,85 [1,97; 17,39] 0,0007[3]	31,5 [14,8; 48,2] 0,0007[3]
Positive	125/477 (26,2)	32/471 (6,8)	3,86 [2,67; 5,57] <,0001[2]	4,87 [3,22; 7,36] <,0001[3]	19,4 [14,9; 24,0] <,0001[3]
Unknown	1/4 (25,0)	1/8 (12,5)	2,00 [0,16; 24,33] 0,5866[2]	2,33 [0,11; 50,98] 1,0000[4]	12,5 [-35,7; 60,7] 1,0000[4]
Race (Interaction p-value: 0,7545)					
White	91/323 (28,2)	25/324 (7,7)	3,65 [2,41; 5,53] <,0001[2]	4,69 [2,92; 7,54] <,0001[3]	20,5 [14,8; 26,2] <,0001[3]
Asian	54/199 (27,1)	12/180 (6,7)	4,07 [2,25; 7,36] <,0001[2]	5,21 [2,68; 10,13] <,0001[3]	20,5 [13,3; 27,6] <,0001[3]
Other	7/19 (36,8)	1/21 (4,8)	7,74 [1,05; 57,24] 0,0451[2]	11,67 [1,27; 106,79] 0,0174[4]	32,1 [8,6; 55,6] 0,0174[4]
ECOG-PS (Interaction p-value: 0,3179)					
ECOG-PS 0	142/496 (28,6)	35/480 (7,3)	3,93 [2,77; 5,56] <,0001[2]	5,10 [3,43; 7,57] <,0001[3]	21,3 [16,7; 25,9] <,0001[3]
ECOG-PS 1	12/57 (21,1)	5/55 (9,1)	2,32 [0,87; 6,14] 0,0915[2]	2,67 [0,87; 8,16] 0,0778[3]	12,0 [-1,1; 25,0] 0,0778[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Neutropenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,2858)					
Neoadjuvant chemotherapy	38/217 (17,5)	10/219 (4,6)	3,84 [1,96; 7,50] <,0001[2]	4,44 [2,15; 9,16] <,0001[3]	12,9 [7,2; 18,7] <,0001[3]
Adjuvant chemotherapy	64/327 (19,6)	7/312 (2,2)	8,72 [4,06; 18,74] <,0001[2]	10,60 [4,78; 23,54] <,0001[3]	17,3 [12,7; 21,9] <,0001[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,6866)					
North America / Europe	46/252 (18,3)	7/233 (3,0)	6,08 [2,80; 13,19] <,0001[2]	7,21 [3,18; 16,32] <,0001[3]	15,2 [10,0; 20,5] <,0001[3]
Asia	16/168 (9,5)	4/166 (2,4)	3,95 [1,35; 11,57] 0,0122[2]	4,26 [1,39; 13,04] 0,0061[3]	7,1 [2,1; 12,1] 0,0061[3]
Other	42/133 (31,6)	6/136 (4,4)	7,16 [3,15; 16,27] <,0001[2]	10,00 [4,08; 24,51] <,0001[3]	27,2 [18,5; 35,8] <,0001[3]
Primary tumor size (Interaction p-value: 0,4940)					
< 20 mm	29/141 (20,6)	6/140 (4,3)	4,80 [2,06; 11,20] 0,0003[2]	5,78 [2,32; 14,43] <,0001[3]	16,3 [8,8; 23,7] <,0001[3]
≥ 20 but < 50 mm	41/255 (16,1)	8/249 (3,2)	5,00 [2,39; 10,46] <,0001[2]	5,77 [2,65; 12,59] <,0001[3]	12,9 [7,9; 17,9] <,0001[3]
≥ 50 mm	33/145 (22,8)	3/141 (2,1)	10,70 [3,36; 34,09] <,0001[2]	13,55 [4,05; 45,36] <,0001[3]	20,6 [13,4; 27,9] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9668)					
0-3	35/203 (17,2)	6/214 (2,8)	6,15 [2,64; 14,31] <,0001[2]	7,22 [2,97; 17,58] <,0001[3]	14,4 [8,8; 20,1] <,0001[3]
4-9	44/242 (18,2)	7/231 (3,0)	6,00 [2,76; 13,05] <,0001[2]	7,11 [3,13; 16,15] <,0001[3]	15,2 [9,8; 20,5] <,0001[3]
≥ 10	25/108 (23,1)	4/90 (4,4)	5,21 [1,88; 14,41] 0,0015[2]	6,48 [2,16; 19,41] 0,0002[3]	18,7 [9,7; 27,7] 0,0002[3]
Tumor stage (Interaction p-value: 0,8437)					
IIA	9/59 (15,3)	2/62 (3,2)	4,73 [1,07; 20,98] 0,0410[2]	5,40 [1,12; 26,15] 0,0214[3]	12,0 [1,9; 22,2] 0,0214[3]
IIB	6/53 (11,3)	2/69 (2,9)	3,91 [0,82; 18,58] 0,0869[2]	4,28 [0,83; 22,12] 0,0766[4]	8,4 [-1,0; 17,8] 0,0766[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	37/236 (15,7)	4/214 (1,9)	8,39 [3,04; 23,14] <,0001[2]	9,76 [3,42; 27,88] <,0001[3]	13,8 [8,8; 18,8] <,0001[3]
IIIB	3/18 (16,7)	1/15 (6,7)	2,50 [0,29; 21,61] 0,4051[2]	2,80 [0,26; 30,18] 0,6074[4]	10,0 [-11,3; 31,3] 0,6074[4]
IIIC	49/186 (26,3)	8/174 (4,6)	5,73 [2,79; 11,75] <,0001[2]	7,42 [3,40; 16,20] <,0001[3]	21,7 [14,7; 28,8] <,0001[3]
Tumor grade (Interaction p-value: 0,7779)					
G1	5/47 (10,6)	0/41 (0,0)	9,63 [0,55; 168,96] 0,1214[2]	10,74 [0,58; 200,45] 0,0583[4]	10,6 [1,8; 19,5] 0,0583[4]
G2	50/244 (20,5)	11/234 (4,7)	4,36 [2,33; 8,17] <,0001[2]	5,22 [2,65; 10,32] <,0001[3]	15,8 [10,0; 21,5] <,0001[3]
G3	47/233 (20,2)	6/226 (2,7)	7,60 [3,31; 17,42] <,0001[2]	9,27 [3,87; 22,16] <,0001[3]	17,5 [12,0; 23,1] <,0001[3]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Race (Interaction p-value: 0,3029)					
White	80/323 (24,8)	11/324 (3,4)	7,30 [3,96; 13,44] <,0001[2]	9,37 [4,88; 17,98] <,0001[3]	21,4 [16,3; 26,5] <,0001[3]
Asian	18/199 (9,0)	4/180 (2,2)	4,07 [1,40; 11,80] 0,0097[2]	4,38 [1,45; 13,19] 0,0046[3]	6,8 [2,3; 11,4] 0,0046[3]
Other	4/19 (21,1)	2/21 (9,5)	2,21 [0,46; 10,73] 0,3251[2]	2,53 [0,41; 15,75] 0,3976[4]	11,5 [-10,7; 33,7] 0,3976[4]
ECOG-PS (Interaction p-value: 0,2405)					
ECOG-PS 0	95/496 (19,2)	14/480 (2,9)	6,57 [3,80; 11,35] <,0001[2]	7,89 [4,43; 14,04] <,0001[3]	16,2 [12,5; 20,0] <,0001[3]
ECOG-PS 1	9/57 (15,8)	3/55 (5,5)	2,89 [0,83; 10,13] 0,0964[2]	3,25 [0,83; 12,72] 0,0771[3]	10,3 [-0,9; 21,5] 0,0771[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Neutrophil count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,6707)					
Neoadjuvant chemotherapy	47/217 (21,7)	10/219 (4,6)	4,74 [2,46; 9,14] <,0001[2]	5,78 [2,84; 11,78] <,0001[3]	17,1 [11,0; 23,2] <,0001[3]
Adjuvant chemotherapy	89/327 (27,2)	12/312 (3,8)	7,08 [3,95; 12,67] <,0001[2]	9,35 [5,00; 17,49] <,0001[3]	23,4 [18,1; 28,6] <,0001[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,8008)					
North America / Europe	35/252 (13,9)	4/233 (1,7)	8,09 [2,92; 22,41] <,0001[2]	9,23 [3,23; 26,41] <,0001[3]	12,2 [7,6; 16,8] <,0001[3]
Asia	84/168 (50,0)	15/166 (9,0)	5,53 [3,34; 9,18] <,0001[2]	10,07 [5,47; 18,54] <,0001[3]	41,0 [32,2; 49,7] <,0001[3]
Other	19/133 (14,3)	3/136 (2,2)	6,48 [1,96; 21,37] 0,0022[2]	7,39 [2,13; 25,61] 0,0003[3]	12,1 [5,6; 18,5] 0,0003[3]
Primary tumor size (Interaction p-value: 0,5636)					
< 20 mm	29/141 (20,6)	3/140 (2,1)	9,60 [2,99; 30,78] 0,0001[2]	11,82 [3,51; 39,84] <,0001[3]	18,4 [11,3; 25,5] <,0001[3]
≥ 20 but < 50 mm	67/255 (26,3)	13/249 (5,2)	5,03 [2,85; 8,88] <,0001[2]	6,47 [3,47; 12,08] <,0001[3]	21,1 [15,0; 27,1] <,0001[3]
≥ 50 mm	37/145 (25,5)	5/141 (3,5)	7,20 [2,91; 17,78] <,0001[2]	9,32 [3,54; 24,52] <,0001[3]	22,0 [14,2; 29,7] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,2673)					
0-3	50/203 (24,6)	5/214 (2,3)	10,54 [4,29; 25,90] <,0001[2]	13,66 [5,32; 35,06] <,0001[3]	22,3 [16,0; 28,6] <,0001[3]
4-9	65/242 (26,9)	14/231 (6,1)	4,43 [2,56; 7,67] <,0001[2]	5,69 [3,09; 10,48] <,0001[3]	20,8 [14,4; 27,2] <,0001[3]
≥ 10	23/108 (21,3)	3/90 (3,3)	6,39 [1,98; 20,59] 0,0019[2]	7,85 [2,27; 27,11] 0,0002[3]	18,0 [9,4; 26,5] 0,0002[3]
Tumor stage (Interaction p-value: 0,8927)					
IIA	11/59 (18,6)	3/62 (4,8)	3,85 [1,13; 13,13] 0,0310[2]	4,51 [1,19; 17,08] 0,0176[3]	13,8 [2,5; 25,1] 0,0176[3]
IIB	16/53 (30,2)	2/69 (2,9)	10,42 [2,50; 43,34] 0,0013[2]	14,49 [3,16; 66,49] <,0001[3]	27,3 [14,3; 40,3] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	74/236 (31,4)	12/214 (5,6)	5,59 [3,13; 10,00] <,0001[2]	7,69 [4,04; 14,64] <,0001[3]	25,7 [19,1; 32,4] <,0001[3]
IIIB	3/18 (16,7)	0/15 (0,0)	5,89 [0,33; 105,81] 0,2285[2]	7,00 [0,33; 147,17] 0,2330[4]	16,7 [-0,5; 33,9] 0,2330[4]
IIIC	33/186 (17,7)	5/174 (2,9)	6,17 [2,47; 15,46] 0,0001[2]	7,29 [2,78; 19,15] <,0001[3]	14,9 [8,8; 20,9] <,0001[3]
Progesterone receptor status (Interaction p-value: 0,5801)					
Negative	11/49 (22,4)	3/44 (6,8)	3,29 [0,98; 11,04] 0,0536[2]	3,96 [1,02; 15,27] 0,0353[3]	15,6 [1,8; 29,5] 0,0353[3]
Positive	120/477 (25,2)	18/471 (3,8)	6,58 [4,08; 10,63] <,0001[2]	8,46 [5,06; 14,15] <,0001[3]	21,3 [17,1; 25,6] <,0001[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,7787)					
White	50/323 (15,5)	7/324 (2,2)	7,16 [3,30; 15,56] <,0001[2]	8,29 [3,70; 18,59] <,0001[3]	13,3 [9,1; 17,6] <,0001[3]
Asian	85/199 (42,7)	15/180 (8,3)	5,13 [3,08; 8,54] <,0001[2]	8,20 [4,51; 14,92] <,0001[3]	34,4 [26,4; 42,4] <,0001[3]
Other	3/19 (15,8)	0/21 (0,0)	7,70 [0,42; 140,03] 0,1678[2]	9,12 [0,44; 189,13] 0,0981[4]	15,8 [-0,6; 32,2] 0,0981[4]
ECOG-PS (Interaction p-value: 0,9784)					
ECOG-PS 0	132/496 (26,6)	22/480 (4,6)	5,81 [3,76; 8,96] <,0001[2]	7,55 [4,71; 12,10] <,0001[3]	22,0 [17,7; 26,3] <,0001[3]
ECOG-PS 1	6/57 (10,5)	0/55 (0,0)	12,55 [0,72; 217,62] 0,0822[2]	14,01 [0,77; 254,95] 0,0273[4]	10,5 [2,6; 18,5] 0,0273[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Oedema from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,9997)					
Negative	0/49 (0,0)	0/44 (0,0)	NE	NE	NE
Positive	10/477 (2,1)	2/471 (0,4)	4,94 [1,09; 22,41] 0,0386[2]	5,02 [1,09; 23,04] 0,0213[3]	1,7 [0,3; 3,1] 0,0213[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9811)					
ECOG-PS 0	9/496 (1,8)	2/480 (0,4)	4,35 [0,95; 20,05] 0,0590[2]	4,42 [0,95; 20,55] 0,0386[3]	1,4 [0,1; 2,7] 0,0386[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Oedema peripheral from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9319)					
Neoadjuvant chemotherapy	21/217 (9,7)	10/219 (4,6)	2,12 [1,02; 4,39] 0,0435[2]	2,24 [1,03; 4,87] 0,0379[3]	5,1 [0,3; 9,9] 0,0379[3]
Adjuvant chemotherapy	22/327 (6,7)	12/312 (3,8)	1,75 [0,88; 3,47] 0,1102[2]	1,80 [0,88; 3,71] 0,1047[3]	2,9 [-0,6; 6,3] 0,1047[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,5001)					
North America / Europe	22/252 (8,7)	11/233 (4,7)	1,85 [0,92; 3,73] 0,0859[2]	1,93 [0,91; 4,07] 0,0798[3]	4,0 [-0,4; 8,4] 0,0798[3]
Asia	9/168 (5,4)	7/166 (4,2)	1,27 [0,48; 3,33] 0,6266[2]	1,29 [0,47; 3,54] 0,6256[3]	1,1 [-3,4; 5,7] 0,6256[3]
Other	12/133 (9,0)	4/136 (2,9)	3,07 [1,01; 9,27] 0,0470[2]	3,27 [1,03; 10,42] 0,0350[3]	6,1 [0,4; 11,7] 0,0350[3]
Primary tumor size (Interaction p-value: 0,4774)					
< 20 mm	17/141 (12,1)	7/140 (5,0)	2,41 [1,03; 5,63] 0,0421[2]	2,60 [1,04; 6,49] 0,0343[3]	7,1 [0,6; 13,5] 0,0343[3]
≥ 20 but < 50 mm	17/255 (6,7)	12/249 (4,8)	1,38 [0,67; 2,84] 0,3758[2]	1,41 [0,66; 3,02] 0,3732[3]	1,8 [-2,2; 5,9] 0,3732[3]
≥ 50 mm	9/145 (6,2)	3/141 (2,1)	2,92 [0,81; 10,55] 0,1027[2]	3,04 [0,81; 11,49] 0,0854[3]	4,1 [-0,5; 8,7] 0,0854[3]
Number of positive lymph nodes (Interaction p-value: 0,1243)					
0-3	9/203 (4,4)	10/214 (4,7)	0,95 [0,39; 2,29] 0,9067[2]	0,95 [0,38; 2,38] 0,9067[3]	-0,2 [-4,2; 3,8] 0,9067[3]
4-9	25/242 (10,3)	11/231 (4,8)	2,17 [1,09; 4,31] 0,0269[2]	2,30 [1,11; 4,80] 0,0224[3]	5,6 [0,9; 10,3] 0,0224[3]
≥ 10	9/108 (8,3)	1/90 (1,1)	7,50 [0,97; 58,08] 0,0537[2]	8,09 [1,01; 65,14] 0,0233[4]	7,2 [1,6; 12,9] 0,0233[4]
Tumor stage (Interaction p-value: 0,2749)					
IIA	5/59 (8,5)	5/62 (8,1)	1,05 [0,32; 3,44] 0,9347[2]	1,06 [0,29; 3,85] 1,0000[4]	0,4 [-9,4; 10,2] 1,0000[4]
IIB	1/53 (1,9)	4/69 (5,8)	0,33 [0,04; 2,83] 0,3088[2]	0,31 [0,03; 2,88] 0,3866[4]	-3,9 [-10,5; 2,7] 0,3866[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	17/236 (7,2)	8/214 (3,7)	1,93 [0,85; 4,37] 0,1168[2]	2,00 [0,84; 4,73] 0,1090[3]	3,5 [-0,7; 7,6] 0,1090[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	19/186 (10,2)	5/174 (2,9)	3,55 [1,36; 9,31] 0,0099[2]	3,85 [1,40; 10,54] 0,0053[3]	7,3 [2,3; 12,4] 0,0053[3]
Tumor grade (Interaction p-value: 0,9690)					
G1	4/47 (8,5)	2/41 (4,9)	1,74 [0,34; 9,04] 0,5072[2]	1,81 [0,31; 10,46] 0,6810[4]	3,6 [-6,7; 14,0] 0,6810[4]
G2	20/244 (8,2)	9/234 (3,8)	2,13 [0,99; 4,58] 0,0529[2]	2,23 [0,99; 5,01] 0,0464[3]	4,4 [0,1; 8,6] 0,0464[3]
G3	17/233 (7,3)	10/226 (4,4)	1,65 [0,77; 3,52] 0,1968[2]	1,70 [0,76; 3,80] 0,1912[3]	2,9 [-1,4; 7,2] 0,1912[3]
GX	2/29 (6,9)	1/33 (3,0)	2,28 [0,22; 23,82] 0,4924[2]	2,37 [0,20; 27,59] 0,5951[4]	3,9 [-7,1; 14,8] 0,5951[4]
Progesterone receptor status (Interaction p-value: 0,1759)					
Negative	5/49 (10,2)	1/44 (2,3)	4,49 [0,55; 36,96] 0,1626[2]	4,89 [0,55; 43,56] 0,2075[4]	7,9 [-1,6; 17,5] 0,2075[4]
Positive	37/477 (7,8)	20/471 (4,2)	1,83 [1,08; 3,10] 0,0255[2]	1,90 [1,08; 3,32] 0,0230[3]	3,5 [0,5; 6,5] 0,0230[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8403)					
White	24/323 (7,4)	12/324 (3,7)	2,01 [1,02; 3,94] 0,0434[2]	2,09 [1,03; 4,25] 0,0387[3]	3,7 [0,2; 7,2] 0,0387[3]
Asian	11/199 (5,5)	7/180 (3,9)	1,42 [0,56; 3,59] 0,4567[2]	1,45 [0,55; 3,81] 0,4538[3]	1,6 [-2,6; 5,9] 0,4538[3]
Other	4/19 (21,1)	0/21 (0,0)	9,90 [0,57; 172,58] 0,1159[2]	12,48 [0,63; 249,21] 0,0424[4]	21,1 [2,7; 39,4] 0,0424[4]
ECOG-PS (Interaction p-value: 0,2917)					
ECOG-PS 0	39/496 (7,9)	18/480 (3,8)	2,10 [1,22; 3,61] 0,0077[2]	2,19 [1,23; 3,89] 0,0062[3]	4,1 [1,2; 7,0] 0,0062[3]
ECOG-PS 1	4/57 (7,0)	4/55 (7,3)	0,96 [0,25; 3,67] 0,9582[2]	0,96 [0,23; 4,05] 1,0000[4]	-0,3 [-9,8; 9,3] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Onychoclasis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9976)					
Neoadjuvant chemotherapy	7/217 (3,2)	0/219 (0,0)	15,14 [0,87; 263,42] 0,0623[2]	15,64 [0,89; 275,58] 0,0072[4]	3,2 [0,9; 5,6] 0,0072[4]
Adjuvant chemotherapy	7/327 (2,1)	4/312 (1,3)	1,67 [0,49; 5,65] 0,4096[2]	1,68 [0,49; 5,81] 0,4042[3]	0,9 [-1,1; 2,9] 0,4042[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,3770)					
North America / Europe	13/252 (5,2)	3/233 (1,3)	4,01 [1,16; 13,88] 0,0286[2]	4,17 [1,17; 14,83] 0,0171[3]	3,9 [0,8; 7,0] 0,0171[3]
Asia	0/168 (0,0)	0/166 (0,0)	NE	NE	NE
Other	1/133 (0,8)	1/136 (0,7)	1,02 [0,06; 16,18] 0,9874[2]	1,02 [0,06; 16,52] 1,0000[4]	0,0 [-2,0; 2,1] 1,0000[4]
Tumor grade (Interaction p-value: 0,4976)					
G1	2/47 (4,3)	2/41 (4,9)	0,87 [0,13; 5,92] 0,8888[2]	0,87 [0,12; 6,44] 1,0000[4]	-0,6 [-9,4; 8,1] 1,0000[4]
G2	8/244 (3,3)	2/234 (0,9)	3,84 [0,82; 17,88] 0,0869[2]	3,93 [0,83; 18,71] 0,1065[4]	2,4 [-0,1; 5,0] 0,1065[4]
G3	4/233 (1,7)	0/226 (0,0)	8,73 [0,47; 161,24] 0,1453[2]	8,88 [0,48; 165,93] 0,1235[4]	1,7 [0,0; 3,4] 0,1235[4]
GX	0/29 (0,0)	0/33 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9940)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	9/477 (1,9)	4/471 (0,8)	2,22 [0,69; 7,16] 0,1815[2]	2,25 [0,69; 7,34] 0,1696[3]	1,0 [-0,4; 2,5] 0,1696[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,9996)					
White	11/323 (3,4)	4/324 (1,2)	2,76 [0,89; 8,57] 0,0795[2]	2,82 [0,89; 8,95] 0,0665[3]	2,2 [-0,1; 4,5] 0,0665[3]
Asian	1/199 (0,5)	0/180 (0,0)	2,72 [0,11; 66,23] 0,5400[2]	2,73 [0,11; 67,39] 1,0000[4]	0,5 [-0,5; 1,5] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,9753)					
ECOG-PS 0	14/496 (2,8)	3/480 (0,6)	4,52 [1,31; 15,62] 0,0172[2]	4,62 [1,32; 16,17] 0,0087[3]	2,2 [0,6; 3,8] 0,0087[3]
ECOG-PS 1	0/57 (0,0)	1/55 (1,8)	0,32 [0,01; 7,74] 0,4846[2]	0,32 [0,01; 7,92] 0,4911[4]	-1,8 [-5,3; 1,7] 0,4911[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Platelet count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9456)					
Neoadjuvant chemotherapy	11/217 (5,1)	2/219 (0,9)	5,55 [1,24; 24,75] 0,0246[2]	5,79 [1,27; 26,45] 0,0107[3]	4,2 [1,0; 7,3] 0,0107[3]
Adjuvant chemotherapy	26/327 (8,0)	6/312 (1,9)	4,13 [1,73; 9,91] 0,0015[2]	4,41 [1,79; 10,86] 0,0005[3]	6,0 [2,7; 9,3] 0,0005[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,2752)					
North America / Europe	11/252 (4,4)	1/233 (0,4)	10,17 [1,32; 78,17] 0,0258[2]	10,59 [1,36; 82,67] 0,0053[3]	3,9 [1,3; 6,6] 0,0053[3]
Asia	19/168 (11,3)	3/166 (1,8)	6,26 [1,89; 20,75] 0,0027[2]	6,93 [2,01; 23,89] 0,0005[3]	9,5 [4,3; 14,7] 0,0005[3]
Other	8/133 (6,0)	4/136 (2,9)	2,05 [0,63; 6,63] 0,2332[2]	2,11 [0,62; 7,19] 0,2221[3]	3,1 [-1,9; 8,0] 0,2221[3]
Primary tumor size (Interaction p-value: 0,1075)					
< 20 mm	6/141 (4,3)	2/140 (1,4)	2,98 [0,61; 14,51] 0,1766[2]	3,07 [0,61; 15,46] 0,2820[4]	2,8 [-1,0; 6,7] 0,2820[4]
≥ 20 but < 50 mm	23/255 (9,0)	2/249 (0,8)	11,23 [2,68; 47,13] 0,0010[2]	12,24 [2,85; 52,51] <,0001[3]	8,2 [4,5; 11,9] <,0001[3]
≥ 50 mm	6/145 (4,1)	4/141 (2,8)	1,46 [0,42; 5,06] 0,5519[2]	1,48 [0,41; 5,35] 0,7497[4]	1,3 [-2,9; 5,5] 0,7497[4]
Number of positive lymph nodes (Interaction p-value: 0,6807)					
0-3	14/203 (6,9)	2/214 (0,9)	7,38 [1,70; 32,07] 0,0077[2]	7,85 [1,76; 35,00] 0,0015[3]	6,0 [2,2; 9,7] 0,0015[3]
4-9	17/242 (7,0)	4/231 (1,7)	4,06 [1,39; 11,88] 0,0106[2]	4,29 [1,42; 12,94] 0,0052[3]	5,3 [1,7; 8,9] 0,0052[3]
≥ 10	7/108 (6,5)	2/90 (2,2)	2,92 [0,62; 13,69] 0,1749[2]	3,05 [0,62; 15,06] 0,1862[4]	4,3 [-1,3; 9,8] 0,1862[4]
Tumor stage (Interaction p-value: 0,9906)					
IIA	2/59 (3,4)	1/62 (1,6)	2,10 [0,20; 22,57] 0,5397[2]	2,14 [0,19; 24,25] 0,6126[4]	1,8 [-3,8; 7,4] 0,6126[4]
IIB	7/53 (13,2)	0/69 (0,0)	19,44 [1,14; 333,01] 0,0406[2]	22,42 [1,25; 402,07] 0,0023[4]	13,2 [4,1; 22,3] 0,0023[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	18/236 (7,6)	4/214 (1,9)	4,08 [1,40; 11,87] 0,0098[2]	4,33 [1,44; 13,02] 0,0047[3]	5,8 [1,9; 9,6] 0,0047[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	10/186 (5,4)	3/174 (1,7)	3,12 [0,87; 11,14] 0,0801[2]	3,24 [0,88; 11,97] 0,0634[3]	3,7 [-0,1; 7,4] 0,0634[3]
Tumor grade (Interaction p-value: 0,9725)					
G1	1/47 (2,1)	0/41 (0,0)	2,63 [0,11; 62,73] 0,5512[2]	2,68 [0,11; 67,54] 1,0000[4]	2,1 [-2,0; 6,3] 1,0000[4]
G2	16/244 (6,6)	3/234 (1,3)	5,11 [1,51; 17,32] 0,0087[2]	5,40 [1,55; 18,80] 0,0032[3]	5,3 [1,9; 8,7] 0,0032[3]
G3	18/233 (7,7)	5/226 (2,2)	3,49 [1,32; 9,25] 0,0118[2]	3,70 [1,35; 10,14] 0,0068[3]	5,5 [1,6; 9,4] 0,0068[3]
GX	3/29 (10,3)	0/33 (0,0)	7,93 [0,43; 147,42] 0,1648[2]	8,85 [0,44; 178,93] 0,0966[4]	10,3 [-0,7; 21,4] 0,0966[4]
Progesterone receptor status (Interaction p-value: 0,9980)					
Negative	5/49 (10,2)	0/44 (0,0)	9,90 [0,56; 174,07] 0,1170[2]	11,00 [0,59; 204,92] 0,0576[4]	10,2 [1,7; 18,7] 0,0576[4]
Positive	30/477 (6,3)	8/471 (1,7)	3,70 [1,72; 7,99] 0,0009[2]	3,88 [1,76; 8,56] 0,0003[3]	4,6 [2,1; 7,1] 0,0003[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,8096)					
White	18/323 (5,6)	5/324 (1,5)	3,61 [1,36; 9,61] 0,0101[2]	3,77 [1,38; 10,27] 0,0056[3]	4,0 [1,2; 6,9] 0,0056[3]
Asian	20/199 (10,1)	3/180 (1,7)	6,03 [1,82; 19,95] 0,0033[2]	6,59 [1,92; 22,58] 0,0006[3]	8,4 [3,8; 13,0] 0,0006[3]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,4583)					
ECOG-PS 0	36/496 (7,3)	7/480 (1,5)	4,98 [2,24; 11,07] <,0001[2]	5,29 [2,33; 12,00] <,0001[3]	5,8 [3,3; 8,3] <,0001[3]
ECOG-PS 1	2/57 (3,5)	1/55 (1,8)	1,93 [0,18; 20,68] 0,5869[2]	1,96 [0,17; 22,30] 1,0000[4]	1,7 [-4,2; 7,6] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Pruritus from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,5778)					
Neoadjuvant chemotherapy	24/217 (11,1)	7/219 (3,2)	3,46 [1,52; 7,86] 0,0030[2]	3,77 [1,59; 8,94] 0,0014[3]	7,9 [3,1; 12,6] 0,0014[3]
Adjuvant chemotherapy	27/327 (8,3)	13/312 (4,2)	1,98 [1,04; 3,77] 0,0372[2]	2,07 [1,05; 4,09] 0,0329[3]	4,1 [0,4; 7,8] 0,0329[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,7526)					
North America / Europe	19/252 (7,5)	7/233 (3,0)	2,51 [1,07; 5,86] 0,0335[2]	2,63 [1,09; 6,38] 0,0267[3]	4,5 [0,6; 8,5] 0,0267[3]
Asia	24/168 (14,3)	11/166 (6,6)	2,16 [1,09; 4,26] 0,0270[2]	2,35 [1,11; 4,97] 0,0223[3]	7,7 [1,2; 14,2] 0,0223[3]
Other	8/133 (6,0)	2/136 (1,5)	4,09 [0,88; 18,91] 0,0713[2]	4,29 [0,89; 20,58] 0,0583[4]	4,5 [0,0; 9,1] 0,0583[4]
Primary tumor size (Interaction p-value: 0,7703)					
< 20 mm	16/141 (11,3)	5/140 (3,6)	3,18 [1,20; 8,44] 0,0203[2]	3,46 [1,23; 9,71] 0,0132[3]	7,8 [1,7; 13,8] 0,0132[3]
≥ 20 but < 50 mm	22/255 (8,6)	8/249 (3,2)	2,69 [1,22; 5,92] 0,0143[2]	2,84 [1,24; 6,52] 0,0102[3]	5,4 [1,3; 9,5] 0,0102[3]
≥ 50 mm	12/145 (8,3)	6/141 (4,3)	1,94 [0,75; 5,04] 0,1709[2]	2,03 [0,74; 5,57] 0,1616[3]	4,0 [-1,6; 9,6] 0,1616[3]
Number of positive lymph nodes (Interaction p-value: 0,8148)					
0-3	19/203 (9,4)	8/214 (3,7)	2,50 [1,12; 5,59] 0,0252[2]	2,66 [1,14; 6,22] 0,0197[3]	5,6 [0,9; 10,4] 0,0197[3]
4-9	26/242 (10,7)	9/231 (3,9)	2,76 [1,32; 5,76] 0,0069[2]	2,97 [1,36; 6,48] 0,0045[3]	6,8 [2,2; 11,5] 0,0045[3]
≥ 10	6/108 (5,6)	3/90 (3,3)	1,67 [0,43; 6,48] 0,4608[2]	1,71 [0,41; 7,02] 0,5145[4]	2,2 [-3,5; 7,9] 0,5145[4]
Tumor stage (Interaction p-value: 0,6290)					
IIA	5/59 (8,5)	1/62 (1,6)	5,25 [0,63; 43,65] 0,1246[2]	5,65 [0,64; 49,87] 0,1085[4]	6,9 [-0,9; 14,6] 0,1085[4]
IIB	6/53 (11,3)	1/69 (1,4)	7,81 [0,97; 62,93] 0,0535[2]	8,68 [1,01; 74,48] 0,0421[4]	9,9 [0,9; 18,9] 0,0421[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	26/236 (11,0)	10/214 (4,7)	2,36 [1,16; 4,77] 0,0172[2]	2,53 [1,19; 5,37] 0,0132[3]	6,3 [1,4; 11,2] 0,0132[3]
IIIB	2/18 (11,1)	1/15 (6,7)	1,67 [0,17; 16,63] 0,6634[2]	1,75 [0,14; 21,43] 1,0000[4]	4,4 [-14,8; 23,7] 1,0000[4]
IIIC	12/186 (6,5)	7/174 (4,0)	1,60 [0,65; 3,98] 0,3085[2]	1,65 [0,63; 4,28] 0,3031[3]	2,4 [-2,2; 7,0] 0,3031[3]
Tumor grade (Interaction p-value: 0,6828)					
G1	6/47 (12,8)	0/41 (0,0)	11,38 [0,66; 195,96] 0,0941[2]	13,00 [0,71; 238,27] 0,0281[4]	12,8 [3,2; 22,3] 0,0281[4]
G2	17/244 (7,0)	9/234 (3,8)	1,81 [0,82; 3,98] 0,1394[2]	1,87 [0,82; 4,29] 0,1326[3]	3,1 [-0,9; 7,2] 0,1326[3]
G3	23/233 (9,9)	7/226 (3,1)	3,19 [1,40; 7,28] 0,0060[2]	3,43 [1,44; 8,15] 0,0033[3]	6,8 [2,3; 11,2] 0,0033[3]
GX	5/29 (17,2)	4/33 (12,1)	1,42 [0,42; 4,80] 0,5702[2]	1,51 [0,36; 6,26] 0,7221[4]	5,1 [-12,6; 22,8] 0,7221[4]
Progesterone receptor status (Interaction p-value: 0,9155)					
Negative	2/49 (4,1)	2/44 (4,5)	0,90 [0,13; 6,11] 0,9124[2]	0,89 [0,12; 6,63] 1,0000[4]	-0,5 [-8,7; 7,8] 1,0000[4]
Positive	48/477 (10,1)	18/471 (3,8)	2,63 [1,56; 4,46] 0,0003[2]	2,82 [1,61; 4,92] 0,0002[3]	6,2 [3,0; 9,4] 0,0002[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9956)					
White	19/323 (5,9)	9/324 (2,8)	2,12 [0,97; 4,61] 0,0587[2]	2,19 [0,97; 4,91] 0,0523[3]	3,1 [-0,0; 6,2] 0,0523[3]
Asian	27/199 (13,6)	11/180 (6,1)	2,22 [1,13; 4,35] 0,0199[2]	2,41 [1,16; 5,02] 0,0158[3]	7,5 [1,6; 13,4] 0,0158[3]
Other	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (Interaction p-value: 0,8851)					
ECOG-PS 0	48/496 (9,7)	19/480 (4,0)	2,44 [1,46; 4,10] 0,0007[2]	2,60 [1,50; 4,49] 0,0004[3]	5,7 [2,6; 8,9] 0,0004[3]
ECOG-PS 1	3/57 (5,3)	1/55 (1,8)	2,89 [0,31; 26,99] 0,3508[2]	3,00 [0,30; 29,76] 0,6184[4]	3,4 [-3,3; 10,2] 0,6184[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Pyrexia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,5748)					
Neoadjuvant chemotherapy	28/217 (12,9)	10/219 (4,6)	2,83 [1,41; 5,67] 0,0035[2]	3,10 [1,46; 6,54] 0,0020[3]	8,3 [3,1; 13,6] 0,0020[3]
Adjuvant chemotherapy	27/327 (8,3)	15/312 (4,8)	1,72 [0,93; 3,17] 0,0832[2]	1,78 [0,93; 3,42] 0,0786[3]	3,4 [-0,4; 7,3] 0,0786[3]
No chemotherapy	3/9 (33,3)	0/4 (0,0)	3,50 [0,22; 55,40] 0,3740[2]	4,85 [0,20; 118,61] 0,4965[4]	33,3 [2,5; 64,1] 0,4965[4]
Region (Interaction p-value: 0,8856)					
North America / Europe	22/252 (8,7)	8/233 (3,4)	2,54 [1,15; 5,60] 0,0205[2]	2,69 [1,17; 6,17] 0,0156[3]	5,3 [1,1; 9,5] 0,0156[3]
Asia	22/168 (13,1)	11/166 (6,6)	1,98 [0,99; 3,94] 0,0534[2]	2,12 [0,99; 4,53] 0,0476[3]	6,5 [0,1; 12,8] 0,0476[3]
Other	14/133 (10,5)	6/136 (4,4)	2,39 [0,95; 6,02] 0,0657[2]	2,55 [0,95; 6,85] 0,0560[3]	6,1 [-0,1; 12,4] 0,0560[3]
Primary tumor size (Interaction p-value: 0,5263)					
< 20 mm	12/141 (8,5)	8/140 (5,7)	1,49 [0,63; 3,53] 0,3659[2]	1,53 [0,61; 3,88] 0,3620[3]	2,8 [-3,2; 8,8] 0,3620[3]
≥ 20 but < 50 mm	28/255 (11,0)	11/249 (4,4)	2,49 [1,27; 4,88] 0,0082[2]	2,67 [1,30; 5,49] 0,0058[3]	6,6 [2,0; 11,2] 0,0058[3]
≥ 50 mm	18/145 (12,4)	6/141 (4,3)	2,92 [1,19; 7,14] 0,0190[2]	3,19 [1,23; 8,29] 0,0129[3]	8,2 [1,8; 14,5] 0,0129[3]
Number of positive lymph nodes (Interaction p-value: 0,3926)					
0-3	16/203 (7,9)	6/214 (2,8)	2,81 [1,12; 7,04] 0,0274[2]	2,97 [1,14; 7,74] 0,0204[3]	5,1 [0,8; 9,4] 0,0204[3]
4-9	31/242 (12,8)	17/231 (7,4)	1,74 [0,99; 3,06] 0,0538[2]	1,85 [0,99; 3,44] 0,0497[3]	5,5 [0,1; 10,8] 0,0497[3]
≥ 10	11/108 (10,2)	2/90 (2,2)	4,58 [1,04; 20,14] 0,0438[2]	4,99 [1,08; 23,14] 0,0243[3]	8,0 [1,5; 14,4] 0,0243[3]
Tumor stage (Interaction p-value: 0,3413)					
IIA	6/59 (10,2)	1/62 (1,6)	6,31 [0,78; 50,81] 0,0837[2]	6,91 [0,81; 59,21] 0,0574[4]	8,6 [0,2; 16,9] 0,0574[4]
IIB	2/53 (3,8)	2/69 (2,9)	1,30 [0,19; 8,94] 0,7884[2]	1,31 [0,18; 9,64] 1,0000[4]	0,9 [-5,6; 7,4] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	27/236 (11,4)	17/214 (7,9)	1,44 [0,81; 2,57] 0,2161[2]	1,50 [0,79; 2,83] 0,2123[3]	3,5 [-1,9; 8,9] 0,2123[3]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	21/186 (11,3)	5/174 (2,9)	3,93 [1,51; 10,19] 0,0049[2]	4,30 [1,58; 11,68] 0,0020[3]	8,4 [3,2; 13,6] 0,0020[3]
Tumor grade (Interaction p-value: 0,4590)					
G1	9/47 (19,1)	0/41 (0,0)	16,63 [1,00; 277,11] 0,0502[2]	20,48 [1,15; 363,91] 0,0030[4]	19,1 [7,9; 30,4] 0,0030[4]
G2	25/244 (10,2)	17/234 (7,3)	1,41 [0,78; 2,54] 0,2530[2]	1,46 [0,77; 2,77] 0,2498[3]	3,0 [-2,1; 8,0] 0,2498[3]
G3	19/233 (8,2)	7/226 (3,1)	2,63 [1,13; 6,14] 0,0251[2]	2,78 [1,14; 6,74] 0,0191[3]	5,1 [0,9; 9,2] 0,0191[3]
GX	5/29 (17,2)	1/33 (3,0)	5,69 [0,70; 45,92] 0,1027[2]	6,67 [0,73; 60,85] 0,0895[4]	14,2 [-0,7; 29,2] 0,0895[4]
Progesterone receptor status (Interaction p-value: 0,9994)					
Negative	5/49 (10,2)	0/44 (0,0)	9,90 [0,56; 174,07] 0,1170[2]	11,00 [0,59; 204,92] 0,0576[4]	10,2 [1,7; 18,7] 0,0576[4]
Positive	52/477 (10,9)	25/471 (5,3)	2,05 [1,30; 3,25] 0,0022[2]	2,18 [1,33; 3,58] 0,0016[3]	5,6 [2,1; 9,0] 0,0016[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,9003)					
White	28/323 (8,7)	12/324 (3,7)	2,34 [1,21; 4,52] 0,0114[2]	2,47 [1,23; 4,94] 0,0087[3]	5,0 [1,3; 8,7] 0,0087[3]
Asian	25/199 (12,6)	12/180 (6,7)	1,88 [0,98; 3,64] 0,0592[2]	2,01 [0,98; 4,13] 0,0535[3]	5,9 [0,0; 11,8] 0,0535[3]
Other	2/19 (10,5)	1/21 (4,8)	2,21 [0,22; 22,47] 0,5026[2]	2,35 [0,20; 28,27] 0,5962[4]	5,8 [-10,8; 22,3] 0,5962[4]
ECOG-PS (Interaction p-value: 0,0951)					
ECOG-PS 0	52/496 (10,5)	19/480 (4,0)	2,65 [1,59; 4,41] 0,0002[2]	2,84 [1,65; 4,88] <,0001[3]	6,5 [3,3; 9,7] <,0001[3]
ECOG-PS 1	6/57 (10,5)	6/55 (10,9)	0,96 [0,33; 2,81] 0,9478[2]	0,96 [0,29; 3,18] 0,9478[3]	-0,4 [-11,8; 11,1] 0,9478[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Rash from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9934)					
Neoadjuvant chemotherapy	14/217 (6,5)	6/219 (2,7)	2,35 [0,92; 6,01] 0,0734[2]	2,45 [0,92; 6,49] 0,0640[3]	3,7 [-0,2; 7,6] 0,0640[3]
Adjuvant chemotherapy	29/327 (8,9)	11/312 (3,5)	2,52 [1,28; 4,95] 0,0075[2]	2,66 [1,31; 5,43] 0,0053[3]	5,3 [1,6; 9,0] 0,0053[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,1369)					
North America / Europe	21/252 (8,3)	4/233 (1,7)	4,85 [1,69; 13,93] 0,0033[2]	5,20 [1,76; 15,40] 0,0010[3]	6,6 [2,8; 10,4] 0,0010[3]
Asia	18/168 (10,7)	12/166 (7,2)	1,48 [0,74; 2,98] 0,2694[2]	1,54 [0,72; 3,31] 0,2653[3]	3,5 [-2,6; 9,6] 0,2653[3]
Other	5/133 (3,8)	1/136 (0,7)	5,11 [0,61; 43,18] 0,1339[2]	5,27 [0,61; 45,75] 0,1174[4]	3,0 [-0,5; 6,6] 0,1174[4]
Primary tumor size (Interaction p-value: 0,0810)					
< 20 mm	14/141 (9,9)	2/140 (1,4)	6,95 [1,61; 30,02] 0,0094[2]	7,61 [1,70; 34,13] 0,0021[3]	8,5 [3,2; 13,8] 0,0021[3]
≥ 20 but < 50 mm	17/255 (6,7)	12/249 (4,8)	1,38 [0,67; 2,84] 0,3758[2]	1,41 [0,66; 3,02] 0,3732[3]	1,8 [-2,2; 5,9] 0,3732[3]
≥ 50 mm	13/145 (9,0)	3/141 (2,1)	4,21 [1,23; 14,47] 0,0223[2]	4,53 [1,26; 16,26] 0,0119[3]	6,8 [1,6; 12,1] 0,0119[3]
Number of positive lymph nodes (Interaction p-value: 0,8516)					
0-3	15/203 (7,4)	7/214 (3,3)	2,26 [0,94; 5,43] 0,0684[2]	2,36 [0,94; 5,91] 0,0601[3]	4,1 [-0,2; 8,4] 0,0601[3]
4-9	19/242 (7,9)	6/231 (2,6)	3,02 [1,23; 7,43] 0,0160[2]	3,20 [1,25; 8,15] 0,0107[3]	5,3 [1,3; 9,2] 0,0107[3]
≥ 10	10/108 (9,3)	4/90 (4,4)	2,08 [0,68; 6,42] 0,2011[2]	2,19 [0,66; 7,25] 0,1882[3]	4,8 [-2,1; 11,7] 0,1882[3]
Tumor stage (Interaction p-value: 0,6844)					
IIA	5/59 (8,5)	1/62 (1,6)	5,25 [0,63; 43,65] 0,1246[2]	5,65 [0,64; 49,87] 0,1085[4]	6,9 [-0,9; 14,6] 0,1085[4]
IIB	4/53 (7,5)	4/69 (5,8)	1,30 [0,34; 4,97] 0,6994[2]	1,33 [0,32; 5,57] 0,7266[4]	1,8 [-7,2; 10,7] 0,7266[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	17/236 (7,2)	4/214 (1,9)	3,85 [1,32; 11,27] 0,0138[2]	4,08 [1,35; 12,31] 0,0074[3]	5,3 [1,6; 9,1] 0,0074[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	17/186 (9,1)	8/174 (4,6)	1,99 [0,88; 4,49] 0,0983[2]	2,09 [0,88; 4,97] 0,0902[3]	4,5 [-0,6; 9,7] 0,0902[3]
Tumor grade (Interaction p-value: 0,9804)					
G1	6/47 (12,8)	0/41 (0,0)	11,38 [0,66; 195,96] 0,0941[2]	13,00 [0,71; 238,27] 0,0281[4]	12,8 [3,2; 22,3] 0,0281[4]
G2	16/244 (6,6)	9/234 (3,8)	1,70 [0,77; 3,78] 0,1894[2]	1,75 [0,76; 4,05] 0,1832[3]	2,7 [-1,3; 6,7] 0,1832[3]
G3	18/233 (7,7)	8/226 (3,5)	2,18 [0,97; 4,92] 0,0597[2]	2,28 [0,97; 5,36] 0,0525[3]	4,2 [-0,0; 8,4] 0,0525[3]
GX	4/29 (13,8)	0/33 (0,0)	10,20 [0,57; 181,74] 0,1140[2]	11,82 [0,61; 229,73] 0,0426[4]	13,8 [1,2; 26,3] 0,0426[4]
Progesterone receptor status (Interaction p-value: 0,7298)					
Negative	1/49 (2,0)	1/44 (2,3)	0,90 [0,06; 13,93] 0,9387[2]	0,90 [0,05; 14,76] 1,0000[4]	-0,2 [-6,2; 5,7] 1,0000[4]
Positive	41/477 (8,6)	15/471 (3,2)	2,70 [1,51; 4,81] 0,0008[2]	2,86 [1,56; 5,24] 0,0004[3]	5,4 [2,4; 8,4] 0,0004[3]
Unknown	1/4 (25,0)	1/8 (12,5)	2,00 [0,16; 24,33] 0,5866[2]	2,33 [0,11; 50,98] 1,0000[4]	12,5 [-35,7; 60,7] 1,0000[4]
Race (Interaction p-value: 0,4729)					
White	21/323 (6,5)	6/324 (1,9)	3,51 [1,44; 8,58] 0,0059[2]	3,69 [1,47; 9,26] 0,0031[3]	4,6 [1,6; 7,7] 0,0031[3]
Asian	21/199 (10,6)	11/180 (6,1)	1,73 [0,86; 3,48] 0,1267[2]	1,81 [0,85; 3,87] 0,1204[3]	4,4 [-1,1; 10,0] 0,1204[3]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,8251)					
ECOG-PS 0	42/496 (8,5)	16/480 (3,3)	2,54 [1,45; 4,46] 0,0011[2]	2,68 [1,49; 4,84] 0,0007[3]	5,1 [2,2; 8,1] 0,0007[3]
ECOG-PS 1	2/57 (3,5)	1/55 (1,8)	1,93 [0,18; 20,68] 0,5869[2]	1,96 [0,17; 22,30] 1,0000[4]	1,7 [-4,2; 7,6] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Rectal haemorrhage from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9923)					
Neoadjuvant chemotherapy	3/217 (1,4)	0/219 (0,0)	7,06 [0,37; 135,95] 0,1951[2]	7,16 [0,37; 139,51] 0,1224[4]	1,4 [-0,2; 2,9] 0,1224[4]
Adjuvant chemotherapy	8/327 (2,4)	2/312 (0,6)	3,82 [0,82; 17,83] 0,0886[2]	3,89 [0,82; 18,45] 0,1076[4]	1,8 [-0,1; 3,7] 0,1076[4]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,2096)					
North America / Europe	10/252 (4,0)	1/233 (0,4)	9,25 [1,19; 71,67] 0,0333[2]	9,59 [1,22; 75,48] 0,0089[3]	3,5 [1,0; 6,1] 0,0089[3]
Asia	0/168 (0,0)	0/166 (0,0)	NE	NE	NE
Other	1/133 (0,8)	1/136 (0,7)	1,02 [0,06; 16,18] 0,9874[2]	1,02 [0,06; 16,52] 1,0000[4]	0,0 [-2,0; 2,1] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,9594)					
Negative	2/49 (4,1)	0/44 (0,0)	4,50 [0,22; 91,25] 0,3273[2]	4,68 [0,22; 100,28] 0,4960[4]	4,1 [-1,5; 9,6] 0,4960[4]
Positive	8/477 (1,7)	2/471 (0,4)	3,95 [0,84; 18,50] 0,0813[2]	4,00 [0,84; 18,94] 0,1076[4]	1,3 [-0,0; 2,5] 0,1076[4]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9948)					
White	10/323 (3,1)	1/324 (0,3)	10,03 [1,29; 77,91] 0,0275[2]	10,32 [1,31; 81,09] 0,0061[3]	2,8 [0,8; 4,8] 0,0061[3]
Asian	0/199 (0,0)	0/180 (0,0)	NE	NE	NE
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,1878)					
ECOG-PS 0	10/496 (2,0)	1/480 (0,2)	9,68 [1,24; 75,31] 0,0301[2]	9,86 [1,26; 77,29] 0,0075[3]	1,8 [0,5; 3,1] 0,0075[3]
ECOG-PS 1	1/57 (1,8)	1/55 (1,8)	0,96 [0,06; 15,05] 0,9797[2]	0,96 [0,06; 15,81] 1,0000[4]	-0,1 [-5,0; 4,8] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Sinusitis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9868)					
Neoadjuvant chemotherapy	9/217 (4,1)	3/219 (1,4)	3,03 [0,83; 11,03] 0,0931[2]	3,12 [0,83; 11,67] 0,0763[3]	2,8 [-0,3; 5,8] 0,0763[3]
Adjuvant chemotherapy	11/327 (3,4)	4/312 (1,3)	2,62 [0,84; 8,15] 0,0954[2]	2,68 [0,84; 8,51] 0,0823[3]	2,1 [-0,2; 4,4] 0,0823[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,9992)					
North America / Europe	11/252 (4,4)	7/233 (3,0)	1,45 [0,57; 3,69] 0,4314[2]	1,47 [0,56; 3,87] 0,4283[3]	1,4 [-2,0; 4,7] 0,4283[3]
Asia	1/168 (0,6)	0/166 (0,0)	2,96 [0,12; 72,25] 0,5048[2]	2,98 [0,12; 73,73] 1,0000[4]	0,6 [-0,6; 1,8] 1,0000[4]
Other	8/133 (6,0)	0/136 (0,0)	17,38 [1,01; 298,14] 0,0489[2]	18,49 [1,06; 323,66] 0,0032[4]	6,0 [2,0; 10,1] 0,0032[4]
Primary tumor size (Interaction p-value: 0,6085)					
< 20 mm	4/141 (2,8)	4/140 (2,9)	0,99 [0,25; 3,89] 0,9919[2]	0,99 [0,24; 4,05] 1,0000[4]	-0,0 [-3,9; 3,9] 1,0000[4]
≥ 20 but < 50 mm	8/255 (3,1)	3/249 (1,2)	2,60 [0,70; 9,70] 0,1539[2]	2,66 [0,70; 10,13] 0,1377[3]	1,9 [-0,6; 4,5] 0,1377[3]
≥ 50 mm	8/145 (5,5)	0/141 (0,0)	16,53 [0,96; 283,79] 0,0531[2]	17,49 [1,00; 306,03] 0,0071[4]	5,5 [1,8; 9,2] 0,0071[4]
Number of positive lymph nodes (Interaction p-value: 0,8854)					
0-3	9/203 (4,4)	4/214 (1,9)	2,37 [0,74; 7,58] 0,1452[2]	2,44 [0,74; 8,04] 0,1321[3]	2,6 [-0,8; 5,9] 0,1321[3]
4-9	8/242 (3,3)	2/231 (0,9)	3,82 [0,82; 17,79] 0,0880[2]	3,91 [0,82; 18,63] 0,1066[4]	2,4 [-0,1; 5,0] 0,1066[4]
≥ 10	3/108 (2,8)	1/90 (1,1)	2,50 [0,26; 23,62] 0,4239[2]	2,54 [0,26; 24,88] 0,6275[4]	1,7 [-2,1; 5,4] 0,6275[4]
Tumor stage (Interaction p-value: 0,5066)					
IIA	1/59 (1,7)	2/62 (3,2)	0,53 [0,05; 5,64] 0,5952[2]	0,52 [0,05; 5,86] 1,0000[4]	-1,5 [-7,0; 4,0] 1,0000[4]
IIB	2/53 (3,8)	2/69 (2,9)	1,30 [0,19; 8,94] 0,7884[2]	1,31 [0,18; 9,64] 1,0000[4]	0,9 [-5,6; 7,4] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	9/236 (3,8)	2/214 (0,9)	4,08 [0,89; 18,67] 0,0700[2]	4,20 [0,90; 19,67] 0,0483[3]	2,9 [0,1; 5,6] 0,0483[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	7/186 (3,8)	1/174 (0,6)	6,55 [0,81; 52,68] 0,0773[2]	6,77 [0,82; 55,56] 0,0685[4]	3,2 [0,2; 6,1] 0,0685[4]
Tumor grade (Interaction p-value: 0,4869)					
G1	5/47 (10,6)	1/41 (2,4)	4,36 [0,53; 35,82] 0,1704[2]	4,76 [0,53; 42,56] 0,2092[4]	8,2 [-1,8; 18,2] 0,2092[4]
G2	6/244 (2,5)	3/234 (1,3)	1,92 [0,49; 7,58] 0,3529[2]	1,94 [0,48; 7,85] 0,5045[4]	1,2 [-1,2; 3,6] 0,5045[4]
G3	9/233 (3,9)	3/226 (1,3)	2,91 [0,80; 10,61] 0,1056[2]	2,99 [0,80; 11,18] 0,0888[3]	2,5 [-0,4; 5,4] 0,0888[3]
GX	0/29 (0,0)	0/33 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9801)					
Negative	0/49 (0,0)	0/44 (0,0)	NE	NE	NE
Positive	19/477 (4,0)	6/471 (1,3)	3,13 [1,26; 7,76] 0,0140[2]	3,22 [1,27; 8,12] 0,0092[3]	2,7 [0,7; 4,7] 0,0092[3]
Unknown	0/4 (0,0)	1/8 (12,5)	0,60 [0,03; 12,15] 0,7393[2]	0,56 [0,02; 16,77] 1,0000[4]	-12,5 [-35,4; 10,4] 1,0000[4]
Race (Interaction p-value: 0,9996)					
White	18/323 (5,6)	7/324 (2,2)	2,58 [1,09; 6,09] 0,0307[2]	2,67 [1,10; 6,49] 0,0243[3]	3,4 [0,5; 6,4] 0,0243[3]
Asian	1/199 (0,5)	0/180 (0,0)	2,72 [0,11; 66,23] 0,5400[2]	2,73 [0,11; 67,39] 1,0000[4]	0,5 [-0,5; 1,5] 1,0000[4]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,9802)					
ECOG-PS 0	19/496 (3,8)	7/480 (1,5)	2,63 [1,11; 6,19] 0,0273[2]	2,69 [1,12; 6,46] 0,0214[3]	2,4 [0,4; 4,4] 0,0214[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Stomatitis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9990)					
Neoadjuvant chemotherapy	20/217 (9,2)	5/219 (2,3)	4,04 [1,54; 10,56] 0,0045[2]	4,35 [1,60; 11,80] 0,0018[3]	6,9 [2,6; 11,3] 0,0018[3]
Adjuvant chemotherapy	26/327 (8,0)	6/312 (1,9)	4,13 [1,73; 9,91] 0,0015[2]	4,41 [1,79; 10,86] 0,0005[3]	6,0 [2,7; 9,3] 0,0005[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,5940)					
North America / Europe	21/252 (8,3)	3/233 (1,3)	6,47 [1,96; 21,41] 0,0022[2]	6,97 [2,05; 23,69] 0,0004[3]	7,0 [3,3; 10,8] 0,0004[3]
Asia	25/168 (14,9)	8/166 (4,8)	3,09 [1,43; 6,65] 0,0039[2]	3,45 [1,51; 7,90] 0,0021[3]	10,1 [3,8; 16,4] 0,0021[3]
Other	2/133 (1,5)	0/136 (0,0)	5,11 [0,25; 105,49] 0,2908[2]	5,19 [0,25; 109,13] 0,2435[4]	1,5 [-0,6; 3,6] 0,2435[4]
Primary tumor size (Interaction p-value: 0,5018)					
< 20 mm	13/141 (9,2)	3/140 (2,1)	4,30 [1,25; 14,77] 0,0204[2]	4,64 [1,29; 16,65] 0,0105[3]	7,1 [1,7; 12,4] 0,0105[3]
≥ 20 but < 50 mm	25/255 (9,8)	4/249 (1,6)	6,10 [2,16; 17,28] 0,0007[2]	6,66 [2,28; 19,42] <,0001[3]	8,2 [4,2; 12,2] <,0001[3]
≥ 50 mm	10/145 (6,9)	4/141 (2,8)	2,43 [0,78; 7,57] 0,1254[2]	2,54 [0,78; 8,29] 0,1117[3]	4,1 [-0,9; 9,0] 0,1117[3]
Number of positive lymph nodes (Interaction p-value: 0,8027)					
0-3	17/203 (8,4)	5/214 (2,3)	3,58 [1,35; 9,54] 0,0106[2]	3,82 [1,38; 10,56] 0,0058[3]	6,0 [1,7; 10,4] 0,0058[3]
4-9	23/242 (9,5)	4/231 (1,7)	5,49 [1,93; 15,63] 0,0014[2]	5,96 [2,03; 17,51] 0,0003[3]	7,8 [3,7; 11,8] 0,0003[3]
≥ 10	8/108 (7,4)	2/90 (2,2)	3,33 [0,73; 15,30] 0,1215[2]	3,52 [0,73; 17,02] 0,1150[4]	5,2 [-0,6; 11,0] 0,1150[4]
Tumor stage (Interaction p-value: 0,4156)					
IIA	6/59 (10,2)	2/62 (3,2)	3,15 [0,66; 15,00] 0,1492[2]	3,40 [0,66; 17,55] 0,1567[4]	6,9 [-1,9; 15,8] 0,1567[4]
IIB	2/53 (3,8)	2/69 (2,9)	1,30 [0,19; 8,94] 0,7884[2]	1,31 [0,18; 9,64] 1,0000[4]	0,9 [-5,6; 7,4] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	26/236 (11,0)	3/214 (1,4)	7,86 [2,41; 25,59] 0,0006[2]	8,71 [2,60; 29,21] <,0001[3]	9,6 [5,3; 13,9] <,0001[3]
IIIB	1/18 (5,6)	1/15 (6,7)	0,83 [0,06; 12,22] 0,8942[2]	0,82 [0,05; 14,39] 1,0000[4]	-1,1 [-17,6; 15,4] 1,0000[4]
IIIC	13/186 (7,0)	3/174 (1,7)	4,05 [1,18; 13,98] 0,0267[2]	4,28 [1,20; 15,30] 0,0154[3]	5,3 [1,1; 9,4] 0,0154[3]
Tumor grade (Interaction p-value: 0,9300)					
G1	8/47 (17,0)	2/41 (4,9)	3,49 [0,78; 15,51] 0,1006[2]	4,00 [0,80; 20,05] 0,0974[4]	12,1 [-0,5; 24,7] 0,0974[4]
G2	21/244 (8,6)	4/234 (1,7)	5,03 [1,75; 14,45] 0,0027[2]	5,41 [1,83; 16,02] 0,0007[3]	6,9 [3,0; 10,8] 0,0007[3]
G3	16/233 (6,9)	5/226 (2,2)	3,10 [1,16; 8,33] 0,0246[2]	3,26 [1,17; 9,05] 0,0170[3]	4,7 [0,9; 8,4] 0,0170[3]
GX	3/29 (10,3)	0/33 (0,0)	7,93 [0,43; 147,42] 0,1648[2]	8,85 [0,44; 178,93] 0,0966[4]	10,3 [-0,7; 21,4] 0,0966[4]
Progesterone receptor status (Interaction p-value: 0,9555)					
Negative	6/49 (12,2)	0/44 (0,0)	11,70 [0,68; 201,88] 0,0905[2]	13,30 [0,73; 243,31] 0,0276[4]	12,2 [3,1; 21,4] 0,0276[4]
Positive	41/477 (8,6)	11/471 (2,3)	3,68 [1,92; 7,07] <,0001[2]	3,93 [2,00; 7,75] <,0001[3]	6,3 [3,4; 9,1] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,4480)					
White	17/323 (5,3)	2/324 (0,6)	8,53 [1,99; 36,61] 0,0039[2]	8,94 [2,05; 39,04] 0,0005[3]	4,6 [2,1; 7,2] 0,0005[3]
Asian	26/199 (13,1)	8/180 (4,4)	2,94 [1,37; 6,33] 0,0058[2]	3,23 [1,42; 7,34] 0,0034[3]	8,6 [3,1; 14,2] 0,0034[3]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9784)					
ECOG-PS 0	44/496 (8,9)	11/480 (2,3)	3,87 [2,02; 7,41] <,0001[2]	4,15 [2,12; 8,14] <,0001[3]	6,6 [3,7; 9,4] <,0001[3]
ECOG-PS 1	4/57 (7,0)	0/55 (0,0)	8,69 [0,48; 157,70] 0,1437[2]	9,34 [0,49; 177,63] 0,1185[4]	7,0 [0,4; 13,6] 0,1185[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Thrombocytopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8467)					
Neoadjuvant chemotherapy	5/217 (2,3)	3/219 (1,4)	1,68 [0,41; 6,95] 0,4726[2]	1,70 [0,40; 7,19] 0,5023[4]	0,9 [-1,6; 3,5] 0,5023[4]
Adjuvant chemotherapy	12/327 (3,7)	4/312 (1,3)	2,86 [0,93; 8,78] 0,0659[2]	2,93 [0,94; 9,19] 0,0535[3]	2,4 [-0,0; 4,8] 0,0535[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,7644)					
North America / Europe	6/252 (2,4)	4/233 (1,7)	1,39 [0,40; 4,85] 0,6088[2]	1,40 [0,39; 5,01] 0,7533[4]	0,7 [-1,9; 3,2] 0,7533[4]
Asia	4/168 (2,4)	0/166 (0,0)	8,89 [0,48; 163,89] 0,1416[2]	9,11 [0,49; 170,54] 0,1228[4]	2,4 [0,1; 4,7] 0,1228[4]
Other	8/133 (6,0)	3/136 (2,2)	2,73 [0,74; 10,06] 0,1320[2]	2,84 [0,74; 10,94] 0,1147[3]	3,8 [-0,9; 8,5] 0,1147[3]
Primary tumor size (Interaction p-value: 0,4543)					
< 20 mm	4/141 (2,8)	3/140 (2,1)	1,32 [0,30; 5,81] 0,7100[2]	1,33 [0,29; 6,07] 1,0000[4]	0,7 [-2,9; 4,3] 1,0000[4]
≥ 20 but < 50 mm	7/255 (2,7)	3/249 (1,2)	2,28 [0,60; 8,71] 0,2288[2]	2,31 [0,59; 9,05] 0,3392[4]	1,5 [-0,9; 4,0] 0,3392[4]
≥ 50 mm	7/145 (4,8)	1/141 (0,7)	6,81 [0,85; 54,62] 0,0711[2]	7,10 [0,86; 58,48] 0,0667[4]	4,1 [0,4; 7,9] 0,0667[4]
Number of positive lymph nodes (Interaction p-value: 0,8715)					
0-3	9/203 (4,4)	3/214 (1,4)	3,16 [0,87; 11,52] 0,0808[2]	3,26 [0,87; 12,23] 0,0642[3]	3,0 [-0,2; 6,3] 0,0642[3]
4-9	6/242 (2,5)	3/231 (1,3)	1,91 [0,48; 7,54] 0,3564[2]	1,93 [0,48; 7,82] 0,5047[4]	1,2 [-1,3; 3,6] 0,5047[4]
≥ 10	3/108 (2,8)	1/90 (1,1)	2,50 [0,26; 23,62] 0,4239[2]	2,54 [0,26; 24,88] 0,6275[4]	1,7 [-2,1; 5,4] 0,6275[4]
Tumor grade (Interaction p-value: 0,6785)					
G1	2/47 (4,3)	0/41 (0,0)	4,38 [0,22; 88,58] 0,3362[2]	4,56 [0,21; 97,79] 0,4966[4]	4,3 [-1,5; 10,0] 0,4966[4]
G2	6/244 (2,5)	5/234 (2,1)	1,15 [0,36; 3,72] 0,8145[2]	1,15 [0,35; 3,84] 0,8143[3]	0,3 [-2,4; 3,0] 0,8143[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G3	8/233 (3,4)	2/226 (0,9)	3,88 [0,83; 18,07] 0,0842[2]	3,98 [0,84; 18,96] 0,1059[4]	2,5 [-0,1; 5,2] 0,1059[4]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,9619)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	17/477 (3,6)	7/471 (1,5)	2,40 [1,00; 5,73] 0,0490[2]	2,45 [1,01; 5,96] 0,0417[3]	2,1 [0,1; 4,1] 0,0417[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9893)					
White	11/323 (3,4)	6/324 (1,9)	1,84 [0,69; 4,91] 0,2243[2]	1,87 [0,68; 5,11] 0,2167[3]	1,6 [-0,9; 4,0] 0,2167[3]
Asian	5/199 (2,5)	0/180 (0,0)	9,96 [0,55; 178,78] 0,1189[2]	10,21 [0,56; 185,92] 0,0624[4]	2,5 [0,3; 4,7] 0,0624[4]
Other	2/19 (10,5)	1/21 (4,8)	2,21 [0,22; 22,47] 0,5026[2]	2,35 [0,20; 28,27] 0,5962[4]	5,8 [-10,8; 22,3] 0,5962[4]
ECOG-PS (Interaction p-value: 0,8846)					
ECOG-PS 0	15/496 (3,0)	6/480 (1,3)	2,42 [0,95; 6,18] 0,0650[2]	2,46 [0,95; 6,40] 0,0562[3]	1,8 [-0,0; 3,6] 0,0562[3]
ECOG-PS 1	3/57 (5,3)	1/55 (1,8)	2,89 [0,31; 26,99] 0,3508[2]	3,00 [0,30; 29,76] 0,6184[4]	3,4 [-3,3; 10,2] 0,6184[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Urinary tract infection from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9612)					
Neoadjuvant chemotherapy	17/217 (7,8)	9/219 (4,1)	1,91 [0,87; 4,18] 0,1076[2]	1,98 [0,86; 4,55] 0,1006[3]	3,7 [-0,7; 8,2] 0,1006[3]
Adjuvant chemotherapy	30/327 (9,2)	13/312 (4,2)	2,20 [1,17; 4,14] 0,0144[2]	2,32 [1,19; 4,54] 0,0115[3]	5,0 [1,2; 8,8] 0,0115[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,2984)					
North America / Europe	34/252 (13,5)	11/233 (4,7)	2,86 [1,48; 5,51] 0,0017[2]	3,15 [1,56; 6,37] 0,0009[3]	8,8 [3,8; 13,8] 0,0009[3]
Asia	3/168 (1,8)	2/166 (1,2)	1,48 [0,25; 8,76] 0,6642[2]	1,49 [0,25; 9,04] 1,0000[4]	0,6 [-2,0; 3,2] 1,0000[4]
Other	11/133 (8,3)	9/136 (6,6)	1,25 [0,54; 2,92] 0,6063[2]	1,27 [0,51; 3,18] 0,6054[3]	1,7 [-4,6; 7,9] 0,6054[3]
Primary tumor size (Interaction p-value: 0,7343)					
< 20 mm	17/141 (12,1)	6/140 (4,3)	2,81 [1,14; 6,93] 0,0244[2]	3,06 [1,17; 8,01] 0,0175[3]	7,8 [1,4; 14,1] 0,0175[3]
≥ 20 but < 50 mm	17/255 (6,7)	9/249 (3,6)	1,84 [0,84; 4,06] 0,1283[2]	1,90 [0,83; 4,36] 0,1214[3]	3,1 [-0,8; 6,9] 0,1214[3]
≥ 50 mm	13/145 (9,0)	7/141 (5,0)	1,81 [0,74; 4,39] 0,1926[2]	1,89 [0,73; 4,87] 0,1847[3]	4,0 [-1,9; 9,9] 0,1847[3]
Number of positive lymph nodes (Interaction p-value: 0,5575)					
0-3	14/203 (6,9)	10/214 (4,7)	1,48 [0,67; 3,25] 0,3332[2]	1,51 [0,66; 3,48] 0,3298[3]	2,2 [-2,3; 6,7] 0,3298[3]
4-9	22/242 (9,1)	8/231 (3,5)	2,63 [1,19; 5,78] 0,0165[2]	2,79 [1,22; 6,39] 0,0121[3]	5,6 [1,3; 9,9] 0,0121[3]
≥ 10	12/108 (11,1)	4/90 (4,4)	2,50 [0,84; 7,48] 0,1014[2]	2,69 [0,84; 8,65] 0,0866[3]	6,7 [-0,6; 14,0] 0,0866[3]
Tumor stage (Interaction p-value: 0,3954)					
IIA	6/59 (10,2)	2/62 (3,2)	3,15 [0,66; 15,00] 0,1492[2]	3,40 [0,66; 17,55] 0,1567[4]	6,9 [-1,9; 15,8] 0,1567[4]
IIB	1/53 (1,9)	3/69 (4,3)	0,43 [0,05; 4,05] 0,4641[2]	0,42 [0,04; 4,19] 0,6319[4]	-2,5 [-8,5; 3,6] 0,6319[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	16/236 (6,8)	9/214 (4,2)	1,61 [0,73; 3,57] 0,2394[2]	1,66 [0,72; 3,83] 0,2339[3]	2,6 [-1,6; 6,8] 0,2339[3]
IIIB	1/18 (5,6)	1/15 (6,7)	0,83 [0,06; 12,22] 0,8942[2]	0,82 [0,05; 14,39] 1,0000[4]	-1,1 [-17,6; 15,4] 1,0000[4]
IIIC	24/186 (12,9)	7/174 (4,0)	3,21 [1,42; 7,25] 0,0051[2]	3,53 [1,48; 8,43] 0,0027[3]	8,9 [3,2; 14,5] 0,0027[3]
Tumor grade (Interaction p-value: 0,9959)					
G1	4/47 (8,5)	0/41 (0,0)	7,88 [0,44; 142,02] 0,1620[2]	8,59 [0,45; 164,46] 0,1199[4]	8,5 [0,5; 16,5] 0,1199[4]
G2	23/244 (9,4)	12/234 (5,1)	1,84 [0,94; 3,61] 0,0769[2]	1,93 [0,93; 3,96] 0,0714[3]	4,3 [-0,3; 8,9] 0,0714[3]
G3	19/233 (8,2)	9/226 (4,0)	2,05 [0,95; 4,43] 0,0687[2]	2,14 [0,95; 4,84] 0,0619[3]	4,2 [-0,2; 8,5] 0,0619[3]
GX	2/29 (6,9)	1/33 (3,0)	2,28 [0,22; 23,82] 0,4924[2]	2,37 [0,20; 27,59] 0,5951[4]	3,9 [-7,1; 14,8] 0,5951[4]
Progesterone receptor status (Interaction p-value: 0,9397)					
Negative	1/49 (2,0)	1/44 (2,3)	0,90 [0,06; 13,93] 0,9387[2]	0,90 [0,05; 14,76] 1,0000[4]	-0,2 [-6,2; 5,7] 1,0000[4]
Positive	44/477 (9,2)	21/471 (4,5)	2,07 [1,25; 3,42] 0,0047[2]	2,18 [1,27; 3,72] 0,0037[3]	4,8 [1,6; 8,0] 0,0037[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,6285)					
White	35/323 (10,8)	18/324 (5,6)	1,95 [1,13; 3,37] 0,0167[2]	2,07 [1,14; 3,73] 0,0143[3]	5,3 [1,1; 9,5] 0,0143[3]
Asian	5/199 (2,5)	2/180 (1,1)	2,26 [0,44; 11,51] 0,3258[2]	2,29 [0,44; 11,97] 0,4529[4]	1,4 [-1,3; 4,1] 0,4529[4]
Other	5/19 (26,3)	1/21 (4,8)	5,53 [0,71; 43,16] 0,1031[2]	7,14 [0,75; 67,98] 0,0848[4]	21,6 [-0,2; 43,3] 0,0848[4]
ECOG-PS (Interaction p-value: 0,0935)					
ECOG-PS 0	44/496 (8,9)	17/480 (3,5)	2,50 [1,45; 4,32] 0,0010[2]	2,65 [1,49; 4,71] 0,0006[3]	5,3 [2,3; 8,3] 0,0006[3]
ECOG-PS 1	4/57 (7,0)	5/55 (9,1)	0,77 [0,22; 2,73] 0,6875[2]	0,75 [0,19; 2,97] 0,7401[4]	-2,1 [-12,2; 8,0] 0,7401[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Vaginal discharge from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9239)					
Neoadjuvant chemotherapy	2/217 (0,9)	8/219 (3,7)	0,25 [0,05; 1,17] 0,0793[2]	0,25 [0,05; 1,17] 0,1054[4]	-2,7 [-5,5; 0,1] 0,1054[4]
Adjuvant chemotherapy	5/327 (1,5)	13/312 (4,2)	0,37 [0,13; 1,02] 0,0540[2]	0,36 [0,13; 1,01] 0,0440[3]	-2,6 [-5,2; -0,1] 0,0440[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,5853)					
North America / Europe	4/252 (1,6)	7/233 (3,0)	0,53 [0,16; 1,78] 0,3036[2]	0,52 [0,15; 1,80] 0,2950[3]	-1,4 [-4,1; 1,3] 0,2950[3]
Asia	2/168 (1,2)	10/166 (6,0)	0,20 [0,04; 0,89] 0,0345[2]	0,19 [0,04; 0,87] 0,0176[3]	-4,8 [-8,8; -0,9] 0,0176[3]
Other	1/133 (0,8)	4/136 (2,9)	0,26 [0,03; 2,26] 0,2197[2]	0,25 [0,03; 2,27] 0,3705[4]	-2,2 [-5,4; 1,0] 0,3705[4]
Primary tumor size (Interaction p-value: 0,8961)					
< 20 mm	3/141 (2,1)	8/140 (5,7)	0,37 [0,10; 1,37] 0,1382[2]	0,36 [0,09; 1,38] 0,1211[3]	-3,6 [-8,1; 0,9] 0,1211[3]
≥ 20 but < 50 mm	2/255 (0,8)	8/249 (3,2)	0,24 [0,05; 1,14] 0,0726[2]	0,24 [0,05; 1,13] 0,0601[4]	-2,4 [-4,9; 0,0] 0,0601[4]
≥ 50 mm	2/145 (1,4)	5/141 (3,5)	0,39 [0,08; 1,97] 0,2543[2]	0,38 [0,07; 1,99] 0,2771[4]	-2,2 [-5,8; 1,4] 0,2771[4]
Number of positive lymph nodes (Interaction p-value: 0,8479)					
0-3	3/203 (1,5)	11/214 (5,1)	0,29 [0,08; 1,02] 0,0529[2]	0,28 [0,08; 1,01] 0,0380[3]	-3,7 [-7,1; -0,3] 0,0380[3]
4-9	4/242 (1,7)	8/231 (3,5)	0,48 [0,15; 1,56] 0,2218[2]	0,47 [0,14; 1,58] 0,2107[3]	-1,8 [-4,7; 1,0] 0,2107[3]
≥ 10	0/108 (0,0)	2/90 (2,2)	0,17 [0,01; 3,43] 0,2459[2]	0,16 [0,01; 3,44] 0,2054[4]	-2,2 [-5,3; 0,8] 0,2054[4]
Tumor stage (Interaction p-value: 0,9910)					
IIA	2/59 (3,4)	5/62 (8,1)	0,42 [0,08; 2,08] 0,2886[2]	0,40 [0,07; 2,15] 0,4402[4]	-4,7 [-12,9; 3,5] 0,4402[4]
IIB	1/53 (1,9)	4/69 (5,8)	0,33 [0,04; 2,83] 0,3088[2]	0,31 [0,03; 2,88] 0,3866[4]	-3,9 [-10,5; 2,7] 0,3866[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	4/236 (1,7)	6/214 (2,8)	0,60 [0,17; 2,11] 0,4306[2]	0,60 [0,17; 2,15] 0,5288[4]	-1,1 [-3,9; 1,6] 0,5288[4]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	0/186 (0,0)	6/174 (3,4)	0,07 [0,00; 1,27] 0,0723[2]	0,07 [0,00; 1,24] 0,0122[4]	-3,4 [-6,2; -0,7] 0,0122[4]
Tumor grade (Interaction p-value: 0,9605)					
G1	0/47 (0,0)	1/41 (2,4)	0,29 [0,01; 6,97] 0,4467[2]	0,28 [0,01; 7,17] 0,4659[4]	-2,4 [-7,2; 2,3] 0,4659[4]
G2	6/244 (2,5)	8/234 (3,4)	0,72 [0,25; 2,04] 0,5358[2]	0,71 [0,24; 2,08] 0,5339[3]	-1,0 [-4,0; 2,1] 0,5339[3]
G3	1/233 (0,4)	12/226 (5,3)	0,08 [0,01; 0,62] 0,0152[2]	0,08 [0,01; 0,60] 0,0016[3]	-4,9 [-7,9; -1,8] 0,0016[3]
GX	0/29 (0,0)	0/33 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9997)					
Negative	0/49 (0,0)	0/44 (0,0)	NE	NE	NE
Positive	5/477 (1,0)	21/471 (4,5)	0,24 [0,09; 0,62] 0,0033[2]	0,23 [0,08; 0,61] 0,0013[3]	-3,4 [-5,5; -1,3] 0,0013[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,6845)					
White	5/323 (1,5)	11/324 (3,4)	0,46 [0,16; 1,30] 0,1411[2]	0,45 [0,15; 1,30] 0,1304[3]	-1,8 [-4,2; 0,5] 0,1304[3]
Asian	2/199 (1,0)	9/180 (5,0)	0,20 [0,04; 0,92] 0,0384[2]	0,19 [0,04; 0,91] 0,0207[3]	-4,0 [-7,5; -0,5] 0,0207[3]
Other	0/19 (0,0)	1/21 (4,8)	0,37 [0,02; 8,50] 0,5315[2]	0,35 [0,01; 9,13] 1,0000[4]	-4,8 [-13,9; 4,3] 1,0000[4]
ECOG-PS (Interaction p-value: 0,9786)					
ECOG-PS 0	7/496 (1,4)	19/480 (4,0)	0,36 [0,15; 0,84] 0,0184[2]	0,35 [0,14; 0,83] 0,0135[3]	-2,5 [-4,6; -0,5] 0,0135[3]
ECOG-PS 1	0/57 (0,0)	2/55 (3,6)	0,19 [0,01; 3,93] 0,2849[2]	0,19 [0,01; 3,97] 0,2389[4]	-3,6 [-8,6; 1,3] 0,2389[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Vomiting from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,1272)					
Neoadjuvant chemotherapy	38/217 (17,5)	3/219 (1,4)	12,78 [4,01; 40,79] <,0001[2]	15,28 [4,64; 50,34] <,0001[3]	16,1 [10,9; 21,4] <,0001[3]
Adjuvant chemotherapy	41/327 (12,5)	12/312 (3,8)	3,26 [1,75; 6,09] 0,0002[2]	3,58 [1,85; 6,96] <,0001[3]	8,7 [4,5; 12,9] <,0001[3]
No chemotherapy	3/9 (33,3)	0/4 (0,0)	3,50 [0,22; 55,40] 0,3740[2]	4,85 [0,20; 118,61] 0,4965[4]	33,3 [2,5; 64,1] 0,4965[4]
Region (Interaction p-value: 0,8501)					
North America / Europe	46/252 (18,3)	7/233 (3,0)	6,08 [2,80; 13,19] <,0001[2]	7,21 [3,18; 16,32] <,0001[3]	15,2 [10,0; 20,5] <,0001[3]
Asia	17/168 (10,1)	4/166 (2,4)	4,20 [1,44; 12,22] 0,0084[2]	4,56 [1,50; 13,86] 0,0037[3]	7,7 [2,6; 12,8] 0,0037[3]
Other	19/133 (14,3)	4/136 (2,9)	4,86 [1,70; 13,90] 0,0032[2]	5,50 [1,82; 16,64] 0,0009[3]	11,3 [4,8; 17,9] 0,0009[3]
Primary tumor size (Interaction p-value: 0,1516)					
< 20 mm	19/141 (13,5)	4/140 (2,9)	4,72 [1,65; 13,51] 0,0039[2]	5,30 [1,75; 16,00] 0,0012[3]	10,6 [4,3; 16,9] 0,0012[3]
≥ 20 but < 50 mm	34/255 (13,3)	10/249 (4,0)	3,32 [1,68; 6,57] 0,0006[2]	3,68 [1,77; 7,62] 0,0002[3]	9,3 [4,5; 14,1] 0,0002[3]
≥ 50 mm	27/145 (18,6)	1/141 (0,7)	26,26 [3,62; 190,62] 0,0012[2]	32,03 [4,29; 239,30] <,0001[3]	17,9 [11,4; 24,4] <,0001[3]
Tumor stage (Interaction p-value: 0,4620)					
IIA	9/59 (15,3)	3/62 (4,8)	3,15 [0,90; 11,08] 0,0734[2]	3,54 [0,91; 13,79] 0,0554[3]	10,4 [-0,2; 21,0] 0,0554[3]
IIB	10/53 (18,9)	0/69 (0,0)	27,22 [1,63; 454,31] 0,0214[2]	33,55 [1,92; 587,17] 0,0001[4]	18,9 [8,3; 29,4] 0,0001[4]
IIIA	31/236 (13,1)	9/214 (4,2)	3,12 [1,52; 6,41] 0,0019[2]	3,44 [1,60; 7,42] 0,0009[3]	8,9 [3,9; 14,0] 0,0009[3]
IIIB	3/18 (16,7)	1/15 (6,7)	2,50 [0,29; 21,61] 0,4051[2]	2,80 [0,26; 30,18] 0,6074[4]	10,0 [-11,3; 31,3] 0,6074[4]
IIIC	29/186 (15,6)	2/174 (1,1)	13,56 [3,29; 56,00] 0,0003[2]	15,89 [3,73; 67,66] <,0001[3]	14,4 [9,0; 19,9] <,0001[3]
Tumor grade (Interaction p-value: 0,9784)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	6/47 (12,8)	1/41 (2,4)	5,23 [0,66; 41,69] 0,1180[2]	5,85 [0,67; 50,83] 0,1161[4]	10,3 [-0,3; 21,0] 0,1161[4]
G2	36/244 (14,8)	6/234 (2,6)	5,75 [2,47; 13,40] <,0001[2]	6,58 [2,72; 15,93] <,0001[3]	12,2 [7,3; 17,1] <,0001[3]
G3	37/233 (15,9)	7/226 (3,1)	5,13 [2,33; 11,26] <,0001[2]	5,91 [2,57; 13,55] <,0001[3]	12,8 [7,6; 18,0] <,0001[3]
GX	3/29 (10,3)	1/33 (3,0)	3,41 [0,38; 31,04] 0,2757[2]	3,69 [0,36; 37,63] 0,3321[4]	7,3 [-5,2; 19,8] 0,3321[4]
Progesterone receptor status (Interaction p-value: 0,8165)					
Negative	11/49 (22,4)	1/44 (2,3)	9,88 [1,33; 73,44] 0,0253[2]	12,45 [1,53; 100,95] 0,0038[3]	20,2 [7,7; 32,7] 0,0038[3]
Positive	66/477 (13,8)	13/471 (2,8)	5,01 [2,80; 8,96] <,0001[2]	5,66 [3,08; 10,41] <,0001[3]	11,1 [7,6; 14,5] <,0001[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,9929)					
White	56/323 (17,3)	11/324 (3,4)	5,11 [2,73; 9,57] <,0001[2]	5,97 [3,06; 11,62] <,0001[3]	13,9 [9,4; 18,5] <,0001[3]
Asian	21/199 (10,6)	4/180 (2,2)	4,75 [1,66; 13,57] 0,0036[2]	5,19 [1,75; 15,43] 0,0011[3]	8,3 [3,5; 13,1] 0,0011[3]
Other	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (Interaction p-value: 0,8083)					
ECOG-PS 0	75/496 (15,1)	14/480 (2,9)	5,18 [2,97; 9,05] <,0001[2]	5,93 [3,30; 10,65] <,0001[3]	12,2 [8,7; 15,7] <,0001[3]
ECOG-PS 1	7/57 (12,3)	1/55 (1,8)	6,75 [0,86; 53,12] 0,0695[2]	7,56 [0,90; 63,64] 0,0609[4]	10,5 [1,2; 19,7] 0,0609[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT White blood cell count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,4586)					
Neoadjuvant chemotherapy	49/217 (22,6)	15/219 (6,8)	3,30 [1,91; 5,70] <,0001[2]	3,97 [2,15; 7,32] <,0001[3]	15,7 [9,2; 22,2] <,0001[3]
Adjuvant chemotherapy	89/327 (27,2)	16/312 (5,1)	5,31 [3,19; 8,83] <,0001[2]	6,92 [3,96; 12,10] <,0001[3]	22,1 [16,7; 27,5] <,0001[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,7872)					
North America / Europe	41/252 (16,3)	7/233 (3,0)	5,42 [2,48; 11,83] <,0001[2]	6,27 [2,75; 14,29] <,0001[3]	13,3 [8,2; 18,3] <,0001[3]
Asia	72/168 (42,9)	18/166 (10,8)	3,95 [2,47; 6,32] <,0001[2]	6,17 [3,46; 10,98] <,0001[3]	32,0 [23,2; 40,9] <,0001[3]
Other	27/133 (20,3)	6/136 (4,4)	4,60 [1,96; 10,78] 0,0004[2]	5,52 [2,20; 13,86] <,0001[3]	15,9 [8,2; 23,5] <,0001[3]
Primary tumor size (Interaction p-value: 0,5552)					
< 20 mm	32/141 (22,7)	6/140 (4,3)	5,30 [2,29; 12,27] 0,0001[2]	6,56 [2,64; 16,25] <,0001[3]	18,4 [10,7; 26,1] <,0001[3]
≥ 20 but < 50 mm	70/255 (27,5)	14/249 (5,6)	4,88 [2,83; 8,43] <,0001[2]	6,35 [3,47; 11,63] <,0001[3]	21,8 [15,6; 28,0] <,0001[3]
≥ 50 mm	33/145 (22,8)	10/141 (7,1)	3,21 [1,64; 6,26] 0,0006[2]	3,86 [1,82; 8,18] 0,0002[3]	15,7 [7,6; 23,7] 0,0002[3]
Number of positive lymph nodes (Interaction p-value: 0,4429)					
0-3	48/203 (23,6)	8/214 (3,7)	6,33 [3,07; 13,04] <,0001[2]	7,97 [3,67; 17,34] <,0001[3]	19,9 [13,5; 26,3] <,0001[3]
4-9	64/242 (26,4)	17/231 (7,4)	3,59 [2,17; 5,95] <,0001[2]	4,53 [2,56; 8,01] <,0001[3]	19,1 [12,6; 25,6] <,0001[3]
≥ 10	28/108 (25,9)	6/90 (6,7)	3,89 [1,69; 8,97] 0,0015[2]	4,90 [1,93; 12,46] 0,0003[3]	19,3 [9,5; 29,0] 0,0003[3]
Tumor stage (Interaction p-value: 0,5575)					
IIA	11/59 (18,6)	3/62 (4,8)	3,85 [1,13; 13,13] 0,0310[2]	4,51 [1,19; 17,08] 0,0176[3]	13,8 [2,5; 25,1] 0,0176[3]
IIB	17/53 (32,1)	1/69 (1,4)	22,13 [3,04; 161,06] 0,0022[2]	32,11 [4,11; 251,15] <,0001[3]	30,6 [17,7; 43,5] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	70/236 (29,7)	17/214 (7,9)	3,73 [2,27; 6,14] <,0001[2]	4,89 [2,77; 8,63] <,0001[3]	21,7 [14,9; 28,6] <,0001[3]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	39/186 (21,0)	10/174 (5,7)	3,65 [1,88; 7,08] 0,0001[2]	4,35 [2,10; 9,02] <,0001[3]	15,2 [8,4; 22,0] <,0001[3]
Tumor grade (Interaction p-value: 0,2374)					
G1	19/47 (40,4)	1/41 (2,4)	16,57 [2,32; 118,47] 0,0051[2]	27,14 [3,43; 214,69] <,0001[3]	38,0 [23,2; 52,8] <,0001[3]
G2	53/244 (21,7)	13/234 (5,6)	3,91 [2,19; 6,98] <,0001[2]	4,72 [2,50; 8,92] <,0001[3]	16,2 [10,2; 22,1] <,0001[3]
G3	52/233 (22,3)	9/226 (4,0)	5,60 [2,83; 11,10] <,0001[2]	6,93 [3,32; 14,44] <,0001[3]	18,3 [12,4; 24,3] <,0001[3]
GX	16/29 (55,2)	7/33 (21,2)	2,60 [1,25; 5,42] 0,0108[2]	4,57 [1,51; 13,87] 0,0057[3]	34,0 [11,1; 56,8] 0,0057[3]
Progesterone receptor status (Interaction p-value: 0,0627)					
Negative	8/49 (16,3)	1/44 (2,3)	7,18 [0,94; 55,17] 0,0580[2]	8,39 [1,00; 70,07] 0,0325[4]	14,1 [2,8; 25,3] 0,0325[4]
Positive	126/477 (26,4)	29/471 (6,2)	4,29 [2,92; 6,29] <,0001[2]	5,47 [3,57; 8,39] <,0001[3]	20,3 [15,7; 24,8] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,5899)					
White	61/323 (18,9)	12/324 (3,7)	5,10 [2,80; 9,29] <,0001[2]	6,05 [3,19; 11,48] <,0001[3]	15,2 [10,4; 19,9] <,0001[3]
Asian	72/199 (36,2)	19/180 (10,6)	3,43 [2,16; 5,45] <,0001[2]	4,80 [2,75; 8,38] <,0001[3]	25,6 [17,6; 33,7] <,0001[3]
Other	6/19 (31,6)	0/21 (0,0)	14,30 [0,86; 237,99] 0,0637[2]	20,70 [1,08; 397,89] 0,0071[4]	31,6 [10,7; 52,5] 0,0071[4]
ECOG-PS (Interaction p-value: 0,1001)					
ECOG-PS 0	133/496 (26,8)	27/480 (5,6)	4,77 [3,21; 7,07] <,0001[2]	6,15 [3,97; 9,51] <,0001[3]	21,2 [16,8; 25,6] <,0001[3]
ECOG-PS 1	7/57 (12,3)	4/55 (7,3)	1,69 [0,52; 5,45] 0,3807[2]	1,79 [0,49; 6,48] 0,3733[3]	5,0 [-5,9; 15,9] 0,3733[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according SOC Blood and lymphatic system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8420)					
Neoadjuvant chemotherapy	66/217 (30,4)	23/219 (10,5)	2,90 [1,87; 4,48] <,0001[2]	3,72 [2,21; 6,26] <,0001[3]	19,9 [12,6; 27,3] <,0001[3]
Adjuvant chemotherapy	115/327 (35,2)	32/312 (10,3)	3,43 [2,39; 4,91] <,0001[2]	4,75 [3,09; 7,30] <,0001[3]	24,9 [18,7; 31,1] <,0001[3]
No chemotherapy	3/9 (33,3)	0/4 (0,0)	3,50 [0,22; 55,40] 0,3740[2]	4,85 [0,20; 118,61] 0,4965[4]	33,3 [2,5; 64,1] 0,4965[4]
Region (Interaction p-value: 0,1738)					
North America / Europe	68/252 (27,0)	24/233 (10,3)	2,62 [1,70; 4,03] <,0001[2]	3,22 [1,94; 5,34] <,0001[3]	16,7 [10,0; 23,4] <,0001[3]
Asia	47/168 (28,0)	8/166 (4,8)	5,81 [2,83; 11,91] <,0001[2]	7,67 [3,50; 16,84] <,0001[3]	23,2 [15,6; 30,7] <,0001[3]
Other	69/133 (51,9)	23/136 (16,9)	3,07 [2,04; 4,61] <,0001[2]	5,30 [3,02; 9,30] <,0001[3]	35,0 [24,4; 45,5] <,0001[3]
Primary tumor size (Interaction p-value: 0,3519)					
< 20 mm	45/141 (31,9)	19/140 (13,6)	2,35 [1,45; 3,81] 0,0005[2]	2,99 [1,64; 5,44] 0,0002[3]	18,3 [8,8; 27,9] 0,0002[3]
≥ 20 but < 50 mm	85/255 (33,3)	24/249 (9,6)	3,46 [2,28; 5,25] <,0001[2]	4,69 [2,86; 7,69] <,0001[3]	23,7 [16,8; 30,5] <,0001[3]
≥ 50 mm	48/145 (33,1)	12/141 (8,5)	3,89 [2,16; 7,01] <,0001[2]	5,32 [2,68; 10,56] <,0001[3]	24,6 [15,7; 33,5] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,2441)					
0-3	59/203 (29,1)	25/214 (11,7)	2,49 [1,62; 3,81] <,0001[2]	3,10 [1,85; 5,19] <,0001[3]	17,4 [9,8; 25,0] <,0001[3]
4-9	78/242 (32,2)	22/231 (9,5)	3,38 [2,19; 5,24] <,0001[2]	4,52 [2,70; 7,57] <,0001[3]	22,7 [15,7; 29,7] <,0001[3]
≥ 10	47/108 (43,5)	8/90 (8,9)	4,90 [2,44; 9,81] <,0001[2]	7,90 [3,48; 17,92] <,0001[3]	34,6 [23,6; 45,7] <,0001[3]
Tumor stage (Interaction p-value: 0,1017)					
IIA	17/59 (28,8)	9/62 (14,5)	1,98 [0,96; 4,10] 0,0638[2]	2,38 [0,97; 5,88] 0,0556[3]	14,3 [-0,2; 28,8] 0,0556[3]
IIB	14/53 (26,4)	11/69 (15,9)	1,66 [0,82; 3,35] 0,1597[2]	1,89 [0,78; 4,60] 0,1554[3]	10,5 [-4,2; 25,2] 0,1554[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	68/236 (28,8)	19/214 (8,9)	3,25 [2,02; 5,21] <,0001[2]	4,15 [2,40; 7,19] <,0001[3]	19,9 [13,0; 26,9] <,0001[3]
IIIB	5/18 (27,8)	1/15 (6,7)	4,17 [0,54; 31,88] 0,1692[2]	5,38 [0,55; 52,43] 0,1861[4]	21,1 [-3,1; 45,3] 0,1861[4]
IIIC	79/186 (42,5)	15/174 (8,6)	4,93 [2,95; 8,22] <,0001[2]	7,83 [4,28; 14,32] <,0001[3]	33,9 [25,6; 42,1] <,0001[3]
Tumor grade (Interaction p-value: 0,5726)					
G1	12/47 (25,5)	1/41 (2,4)	10,47 [1,42; 77,08] 0,0211[2]	13,71 [1,70; 110,86] 0,0023[3]	23,1 [9,8; 36,4] 0,0023[3]
G2	83/244 (34,0)	24/234 (10,3)	3,32 [2,18; 5,03] <,0001[2]	4,51 [2,74; 7,43] <,0001[3]	23,8 [16,7; 30,9] <,0001[3]
G3	78/233 (33,5)	27/226 (11,9)	2,80 [1,88; 4,17] <,0001[2]	3,71 [2,28; 6,03] <,0001[3]	21,5 [14,1; 28,9] <,0001[3]
GX	11/29 (37,9)	3/33 (9,1)	4,17 [1,29; 13,51] 0,0172[2]	6,11 [1,50; 24,88] 0,0067[3]	28,8 [8,6; 49,0] 0,0067[3]
Race (Interaction p-value: 0,4109)					
White	119/323 (36,8)	41/324 (12,7)	2,91 [2,11; 4,01] <,0001[2]	4,03 [2,70; 5,99] <,0001[3]	24,2 [17,8; 30,6] <,0001[3]
Asian	52/199 (26,1)	10/180 (5,6)	4,70 [2,47; 8,97] <,0001[2]	6,01 [2,95; 12,25] <,0001[3]	20,6 [13,6; 27,5] <,0001[3]
Other	10/19 (52,6)	4/21 (19,0)	2,76 [1,04; 7,36] 0,0420[2]	4,72 [1,15; 19,41] 0,0262[3]	33,6 [5,5; 61,6] 0,0262[3]
ECOG-PS (Interaction p-value: 0,9174)					
ECOG-PS 0	168/496 (33,9)	50/480 (10,4)	3,25 [2,43; 4,34] <,0001[2]	4,40 [3,11; 6,23] <,0001[3]	23,5 [18,5; 28,4] <,0001[3]
ECOG-PS 1	16/57 (28,1)	5/55 (9,1)	3,09 [1,21; 7,85] 0,0179[2]	3,90 [1,32; 11,56] 0,0101[3]	19,0 [5,1; 32,9] 0,0101[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Endocrine disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8061)					
Neoadjuvant chemotherapy	3/217 (1,4)	10/219 (4,6)	0,30 [0,08; 1,09] 0,0666[2]	0,29 [0,08; 1,08] 0,0507[3]	-3,2 [-6,4; -0,0] 0,0507[3]
Adjuvant chemotherapy	5/327 (1,5)	9/312 (2,9)	0,53 [0,18; 1,56] 0,2503[2]	0,52 [0,17; 1,58] 0,2420[3]	-1,4 [-3,6; 0,9] 0,2420[3]
No chemotherapy	0/9 (0,0)	1/4 (25,0)	0,17 [0,01; 3,40] 0,2441[2]	0,12 [0,00; 3,78] 0,3077[4]	-25,0 [-67,4; 17,4] 0,3077[4]
Region (Interaction p-value: 0,2235)					
North America / Europe	3/252 (1,2)	12/233 (5,2)	0,23 [0,07; 0,81] 0,0219[2]	0,22 [0,06; 0,80] 0,0118[3]	-4,0 [-7,1; -0,8] 0,0118[3]
Asia	2/168 (1,2)	6/166 (3,6)	0,33 [0,07; 1,61] 0,1699[2]	0,32 [0,06; 1,62] 0,1725[4]	-2,4 [-5,7; 0,9] 0,1725[4]
Other	3/133 (2,3)	2/136 (1,5)	1,53 [0,26; 9,03] 0,6363[2]	1,55 [0,25; 9,40] 0,6817[4]	0,8 [-2,4; 4,0] 0,6817[4]
Primary tumor size (Interaction p-value: 0,9196)					
< 20 mm	3/141 (2,1)	7/140 (5,0)	0,43 [0,11; 1,61] 0,2087[2]	0,41 [0,10; 1,63] 0,2173[4]	-2,9 [-7,2; 1,5] 0,2173[4]
≥ 20 but < 50 mm	5/255 (2,0)	8/249 (3,2)	0,61 [0,20; 1,84] 0,3805[2]	0,60 [0,19; 1,87] 0,3753[3]	-1,3 [-4,0; 1,5] 0,3753[3]
≥ 50 mm	0/145 (0,0)	5/141 (3,5)	0,09 [0,00; 1,58] 0,0995[2]	0,09 [0,00; 1,56] 0,0281[4]	-3,5 [-6,6; -0,5] 0,0281[4]
Number of positive lymph nodes (Interaction p-value: 0,3656)					
0-3	4/203 (2,0)	5/214 (2,3)	0,84 [0,23; 3,10] 0,7974[2]	0,84 [0,22; 3,17] 1,0000[4]	-0,4 [-3,2; 2,4] 1,0000[4]
4-9	3/242 (1,2)	12/231 (5,2)	0,24 [0,07; 0,83] 0,0249[2]	0,23 [0,06; 0,82] 0,0141[3]	-4,0 [-7,1; -0,8] 0,0141[3]
≥ 10	1/108 (0,9)	3/90 (3,3)	0,28 [0,03; 2,62] 0,2636[2]	0,27 [0,03; 2,65] 0,3317[4]	-2,4 [-6,5; 1,7] 0,3317[4]
Tumor stage (Interaction p-value: 0,3145)					
IIA	3/59 (5,1)	2/62 (3,2)	1,58 [0,27; 9,10] 0,6110[2]	1,61 [0,26; 9,98] 0,6745[4]	1,9 [-5,3; 9,0] 0,6745[4]
IIB	0/53 (0,0)	1/69 (1,4)	0,43 [0,02; 10,40] 0,6051[2]	0,43 [0,02; 10,69] 1,0000[4]	-1,4 [-4,3; 1,4] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	1/236 (0,4)	11/214 (5,1)	0,08 [0,01; 0,63] 0,0164[2]	0,08 [0,01; 0,61] 0,0019[3]	-4,7 [-7,8; -1,6] 0,0019[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	4/186 (2,2)	6/174 (3,4)	0,62 [0,18; 2,17] 0,4584[2]	0,62 [0,17; 2,22] 0,5316[4]	-1,3 [-4,7; 2,1] 0,5316[4]
Progesterone receptor status (Interaction p-value: 0,5333)					
Negative	1/49 (2,0)	2/44 (4,5)	0,45 [0,04; 4,78] 0,5070[2]	0,44 [0,04; 5,00] 0,6013[4]	-2,5 [-9,8; 4,8] 0,6013[4]
Positive	7/477 (1,5)	18/471 (3,8)	0,38 [0,16; 0,91] 0,0299[2]	0,37 [0,16; 0,91] 0,0237[3]	-2,4 [-4,4; -0,3] 0,0237[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9647)					
White	5/323 (1,5)	14/324 (4,3)	0,36 [0,13; 0,98] 0,0462[2]	0,35 [0,12; 0,98] 0,0367[3]	-2,8 [-5,4; -0,2] 0,0367[3]
Asian	3/199 (1,5)	6/180 (3,3)	0,45 [0,11; 1,78] 0,2567[2]	0,44 [0,11; 1,80] 0,3185[4]	-1,8 [-4,9; 1,3] 0,3185[4]
Other	0/19 (0,0)	0/21 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9751)					
ECOG-PS 0	6/496 (1,2)	20/480 (4,2)	0,29 [0,12; 0,72] 0,0073[2]	0,28 [0,11; 0,71] 0,0041[3]	-3,0 [-5,0; -0,9] 0,0041[3]
ECOG-PS 1	2/57 (3,5)	0/55 (0,0)	4,83 [0,24; 98,34] 0,3060[2]	5,00 [0,23; 106,54] 0,4957[4]	3,5 [-1,3; 8,3] 0,4957[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Eye disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8043)					
Neoadjuvant chemotherapy	30/217 (13,8)	15/219 (6,8)	2,02 [1,12; 3,64] 0,0198[2]	2,18 [1,14; 4,18] 0,0167[3]	7,0 [1,3; 12,7] 0,0167[3]
Adjuvant chemotherapy	47/327 (14,4)	17/312 (5,4)	2,64 [1,55; 4,49] 0,0004[2]	2,91 [1,63; 5,19] 0,0002[3]	8,9 [4,4; 13,5] 0,0002[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,6762)					
North America / Europe	42/252 (16,7)	14/233 (6,0)	2,77 [1,56; 4,94] 0,0005[2]	3,13 [1,66; 5,90] 0,0002[3]	10,7 [5,1; 16,2] 0,0002[3]
Asia	24/168 (14,3)	11/166 (6,6)	2,16 [1,09; 4,26] 0,0270[2]	2,35 [1,11; 4,97] 0,0223[3]	7,7 [1,2; 14,2] 0,0223[3]
Other	12/133 (9,0)	7/136 (5,1)	1,75 [0,71; 4,32] 0,2221[2]	1,83 [0,70; 4,80] 0,2148[3]	3,9 [-2,2; 10,0] 0,2148[3]
Primary tumor size (Interaction p-value: 0,4691)					
< 20 mm	20/141 (14,2)	12/140 (8,6)	1,65 [0,84; 3,25] 0,1444[2]	1,76 [0,83; 3,76] 0,1386[3]	5,6 [-1,8; 13,0] 0,1386[3]
≥ 20 but < 50 mm	36/255 (14,1)	12/249 (4,8)	2,93 [1,56; 5,50] 0,0008[2]	3,25 [1,65; 6,40] 0,0004[3]	9,3 [4,3; 14,3] 0,0004[3]
≥ 50 mm	18/145 (12,4)	7/141 (5,0)	2,50 [1,08; 5,80] 0,0328[2]	2,71 [1,10; 6,71] 0,0257[3]	7,4 [1,0; 13,9] 0,0257[3]
Number of positive lymph nodes (Interaction p-value: 0,8203)					
0-3	27/203 (13,3)	14/214 (6,5)	2,03 [1,10; 3,77] 0,0240[2]	2,19 [1,11; 4,31] 0,0205[3]	6,8 [1,0; 12,5] 0,0205[3]
4-9	39/242 (16,1)	14/231 (6,1)	2,66 [1,48; 4,77] 0,0010[2]	2,98 [1,57; 5,65] 0,0005[3]	10,1 [4,5; 15,6] 0,0005[3]
≥ 10	12/108 (11,1)	4/90 (4,4)	2,50 [0,84; 7,48] 0,1014[2]	2,69 [0,84; 8,65] 0,0866[3]	6,7 [-0,6; 14,0] 0,0866[3]
Tumor stage (Interaction p-value: 0,9390)					
IIA	9/59 (15,3)	5/62 (8,1)	1,89 [0,67; 5,32] 0,2267[2]	2,05 [0,65; 6,53] 0,2165[3]	7,2 [-4,2; 18,6] 0,2165[3]
IIB	4/53 (7,5)	3/69 (4,3)	1,74 [0,41; 7,43] 0,4571[2]	1,80 [0,38; 8,39] 0,4665[4]	3,2 [-5,4; 11,8] 0,4665[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	37/236 (15,7)	12/214 (5,6)	2,80 [1,50; 5,22] 0,0012[2]	3,13 [1,59; 6,18] 0,0006[3]	10,1 [4,5; 15,6] 0,0006[3]
IIIB	2/18 (11,1)	0/15 (0,0)	4,21 [0,22; 81,47] 0,3416[2]	4,70 [0,21; 105,79] 0,4886[4]	11,1 [-3,4; 25,6] 0,4886[4]
IIIC	26/186 (14,0)	12/174 (6,9)	2,03 [1,06; 3,89] 0,0337[2]	2,19 [1,07; 4,50] 0,0289[3]	7,1 [0,8; 13,3] 0,0289[3]
Tumor grade (Interaction p-value: 0,5998)					
G1	8/47 (17,0)	0/41 (0,0)	14,88 [0,88; 250,04] 0,0608[2]	17,86 [1,00; 319,85] 0,0064[4]	17,0 [6,3; 27,8] 0,0064[4]
G2	32/244 (13,1)	10/234 (4,3)	3,07 [1,54; 6,10] 0,0014[2]	3,38 [1,62; 7,05] 0,0006[3]	8,8 [3,9; 13,8] 0,0006[3]
G3	34/233 (14,6)	19/226 (8,4)	1,74 [1,02; 2,95] 0,0417[2]	1,86 [1,03; 3,37] 0,0382[3]	6,2 [0,4; 12,0] 0,0382[3]
GX	4/29 (13,8)	3/33 (9,1)	1,52 [0,37; 6,22] 0,5626[2]	1,60 [0,33; 7,83] 0,6960[4]	4,7 [-11,2; 20,6] 0,6960[4]
Progesterone receptor status (Interaction p-value: 0,9177)					
Negative	9/49 (18,4)	3/44 (6,8)	2,69 [0,78; 9,32] 0,1177[2]	3,08 [0,78; 12,19] 0,0972[3]	11,5 [-1,6; 24,7] 0,0972[3]
Positive	60/477 (12,6)	29/471 (6,2)	2,04 [1,34; 3,12] 0,0010[2]	2,19 [1,38; 3,48] 0,0007[3]	6,4 [2,7; 10,1] 0,0007[3]
Unknown	2/4 (50,0)	0/8 (0,0)	9,00 [0,53; 152,93] 0,1284[2]	17,00 [0,60; 483,50] 0,0909[4]	50,0 [1,0; 99,0] 0,0909[4]
Race (Interaction p-value: 0,8332)					
White	43/323 (13,3)	19/324 (5,9)	2,27 [1,35; 3,81] 0,0019[2]	2,47 [1,40; 4,33] 0,0013[3]	7,4 [2,9; 12,0] 0,0013[3]
Asian	29/199 (14,6)	11/180 (6,1)	2,38 [1,23; 4,63] 0,0103[2]	2,62 [1,27; 5,42] 0,0074[3]	8,5 [2,4; 14,5] 0,0074[3]
Other	4/19 (21,1)	1/21 (4,8)	4,42 [0,54; 36,16] 0,1657[2]	5,33 [0,54; 52,73] 0,1723[4]	16,3 [-4,2; 36,8] 0,1723[4]
ECOG-PS (Interaction p-value: 0,7157)					
ECOG-PS 0	70/496 (14,1)	28/480 (5,8)	2,42 [1,59; 3,68] <,0001[2]	2,65 [1,68; 4,19] <,0001[3]	8,3 [4,6; 12,0] <,0001[3]
ECOG-PS 1	8/57 (14,0)	4/55 (7,3)	1,93 [0,62; 6,04] 0,2590[2]	2,08 [0,59; 7,36] 0,2474[3]	6,8 [-4,6; 18,1] 0,2474[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events according SOC Gastrointestinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,3349)					
Neoadjuvant chemotherapy	195/217 (89,9)	76/219 (34,7)	2,59 [2,15; 3,12] <,0001[2]	16,68 [9,90; 28,09] <,0001[3]	55,2 [47,7; 62,6] <,0001[3]
Adjuvant chemotherapy	295/327 (90,2)	99/312 (31,7)	2,84 [2,41; 3,36] <,0001[2]	19,83 [12,83; 30,67] <,0001[3]	58,5 [52,4; 64,6] <,0001[3]
No chemotherapy	6/9 (66,7)	2/4 (50,0)	1,33 [0,45; 3,94] 0,6028[2]	2,00 [0,18; 22,06] 1,0000[4]	16,7 [-41,2; 74,5] 1,0000[4]
Region (Interaction p-value: 0,3671)					
North America / Europe	228/252 (90,5)	82/233 (35,2)	2,57 [2,15; 3,07] <,0001[2]	17,49 [10,62; 28,82] <,0001[3]	55,3 [48,2; 62,4] <,0001[3]
Asia	162/168 (96,4)	62/166 (37,3)	2,58 [2,12; 3,15] <,0001[2]	45,29 [18,91; 108,47] <,0001[3]	59,1 [51,2; 67,0] <,0001[3]
Other	106/133 (79,7)	33/136 (24,3)	3,28 [2,41; 4,47] <,0001[2]	12,25 [6,89; 21,81] <,0001[3]	55,4 [45,5; 65,4] <,0001[3]
Primary tumor size (Interaction p-value: 0,1652)					
< 20 mm	126/141 (89,4)	49/140 (35,0)	2,55 [2,02; 3,22] <,0001[2]	15,60 [8,24; 29,53] <,0001[3]	54,4 [45,0; 63,8] <,0001[3]
≥ 20 but < 50 mm	224/255 (87,8)	88/249 (35,3)	2,49 [2,09; 2,96] <,0001[2]	13,22 [8,37; 20,87] <,0001[3]	52,5 [45,3; 59,7] <,0001[3]
≥ 50 mm	135/145 (93,1)	39/141 (27,7)	3,37 [2,57; 4,41] <,0001[2]	35,31 [16,83; 74,06] <,0001[3]	65,4 [57,0; 73,9] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9970)					
0-3	186/203 (91,6)	72/214 (33,6)	2,72 [2,25; 3,30] <,0001[2]	21,58 [12,18; 38,23] <,0001[3]	58,0 [50,6; 65,4] <,0001[3]
4-9	218/242 (90,1)	77/231 (33,3)	2,70 [2,24; 3,26] <,0001[2]	18,17 [10,99; 30,03] <,0001[3]	56,7 [49,6; 63,9] <,0001[3]
≥ 10	92/108 (85,2)	28/90 (31,1)	2,74 [1,99; 3,76] <,0001[2]	12,73 [6,36; 25,47] <,0001[3]	54,1 [42,4; 65,8] <,0001[3]
Tumor grade (Interaction p-value: 0,3314)					
G1	42/47 (89,4)	13/41 (31,7)	2,82 [1,78; 4,46] <,0001[2]	18,09 [5,80; 56,39] <,0001[3]	57,7 [40,9; 74,4] <,0001[3]
G2	220/244 (90,2)	72/234 (30,8)	2,93 [2,41; 3,57] <,0001[2]	20,63 [12,45; 34,16] <,0001[3]	59,4 [52,4; 66,4] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G3	211/233 (90,6)	77/226 (34,1)	2,66 [2,21; 3,20] <,0001[2]	18,56 [11,05; 31,16] <,0001[3]	56,5 [49,3; 63,7] <,0001[3]
GX	23/29 (79,3)	14/33 (42,4)	1,87 [1,21; 2,90] 0,0052[2]	5,20 [1,68; 16,15] 0,0031[3]	36,9 [14,5; 59,3] 0,0031[3]
Progesterone receptor status (Interaction p-value: 0,3404)					
Negative	46/49 (93,9)	17/44 (38,6)	2,43 [1,66; 3,55] <,0001[2]	24,35 [6,53; 90,81] <,0001[3]	55,2 [39,4; 71,1] <,0001[3]
Positive	426/477 (89,3)	151/471 (32,1)	2,79 [2,43; 3,19] <,0001[2]	17,70 [12,49; 25,09] <,0001[3]	57,2 [52,2; 62,3] <,0001[3]
Unknown	3/4 (75,0)	4/8 (50,0)	1,50 [0,61; 3,67] 0,3744[2]	3,00 [0,21; 42,62] 0,5758[4]	25,0 [-29,8; 79,8] 0,5758[4]
Race (Interaction p-value: 0,8771)					
White	283/323 (87,6)	103/324 (31,8)	2,76 [2,34; 3,25] <,0001[2]	15,18 [10,12; 22,77] <,0001[3]	55,8 [49,6; 62,0] <,0001[3]
Asian	184/199 (92,5)	63/180 (35,0)	2,64 [2,16; 3,24] <,0001[2]	22,78 [12,39; 41,88] <,0001[3]	57,5 [49,6; 65,3] <,0001[3]
Other	17/19 (89,5)	6/21 (28,6)	3,13 [1,57; 6,27] 0,0013[2]	21,25 [3,71; 121,61] <,0001[3]	60,9 [37,2; 84,6] <,0001[3]
ECOG-PS (Interaction p-value: 0,9278)					
ECOG-PS 0	453/496 (91,3)	162/480 (33,8)	2,71 [2,38; 3,08] <,0001[2]	20,68 [14,35; 29,80] <,0001[3]	57,6 [52,7; 62,5] <,0001[3]
ECOG-PS 1	43/57 (75,4)	15/55 (27,3)	2,77 [1,75; 4,37] <,0001[2]	8,19 [3,51; 19,09] <,0001[3]	48,2 [31,9; 64,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi²-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC General disorders and administration site conditions from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,0592)					
Neoadjuvant chemotherapy	130/217 (59,9)	71/219 (32,4)	1,85 [1,48; 2,30] <,0001[2]	3,11 [2,10; 4,61] <,0001[3]	27,5 [18,5; 36,5] <,0001[3]
Adjuvant chemotherapy	176/327 (53,8)	91/312 (29,2)	1,85 [1,51; 2,25] <,0001[2]	2,83 [2,04; 3,93] <,0001[3]	24,7 [17,3; 32,0] <,0001[3]
No chemotherapy	4/9 (44,4)	3/4 (75,0)	0,59 [0,24; 1,49] 0,2670[2]	0,27 [0,02; 3,65] 0,5594[4]	-30,6 [-84,0; 22,9] 0,5594[4]
Region (Interaction p-value: 0,8582)					
North America / Europe	176/252 (69,8)	88/233 (37,8)	1,85 [1,54; 2,22] <,0001[2]	3,82 [2,62; 5,57] <,0001[3]	32,1 [23,7; 40,5] <,0001[3]
Asia	80/168 (47,6)	47/166 (28,3)	1,68 [1,26; 2,25] 0,0004[2]	2,30 [1,46; 3,62] 0,0003[3]	19,3 [9,1; 29,5] 0,0003[3]
Other	54/133 (40,6)	30/136 (22,1)	1,84 [1,26; 2,68] 0,0015[2]	2,42 [1,42; 4,12] 0,0010[3]	18,5 [7,7; 29,4] 0,0010[3]
Primary tumor size (Interaction p-value: 0,2312)					
< 20 mm	82/141 (58,2)	52/140 (37,1)	1,57 [1,21; 2,02] 0,0006[2]	2,35 [1,46; 3,80] 0,0004[3]	21,0 [9,6; 32,4] 0,0004[3]
≥ 20 but < 50 mm	148/255 (58,0)	69/249 (27,7)	2,09 [1,67; 2,63] <,0001[2]	3,61 [2,49; 5,24] <,0001[3]	30,3 [22,1; 38,5] <,0001[3]
≥ 50 mm	78/145 (53,8)	44/141 (31,2)	1,72 [1,29; 2,30] 0,0002[2]	2,57 [1,58; 4,16] 0,0001[3]	22,6 [11,4; 33,7] 0,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,3084)					
0-3	115/203 (56,7)	75/214 (35,0)	1,62 [1,30; 2,01] <,0001[2]	2,42 [1,63; 3,59] <,0001[3]	21,6 [12,3; 30,9] <,0001[3]
4-9	143/242 (59,1)	71/231 (30,7)	1,92 [1,54; 2,40] <,0001[2]	3,26 [2,23; 4,76] <,0001[3]	28,4 [19,8; 36,9] <,0001[3]
≥ 10	52/108 (48,1)	19/90 (21,1)	2,28 [1,46; 3,56] 0,0003[2]	3,47 [1,85; 6,52] <,0001[3]	27,0 [14,4; 39,7] <,0001[3]
Tumor stage (Interaction p-value: 0,5465)					
IIA	37/59 (62,7)	28/62 (45,2)	1,39 [0,99; 1,95] 0,0566[2]	2,04 [0,99; 4,23] 0,0529[3]	17,6 [0,1; 35,0] 0,0529[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIB	28/53 (52,8)	21/69 (30,4)	1,74 [1,12; 2,69] 0,0136[2]	2,56 [1,22; 5,39] 0,0124[3]	22,4 [5,1; 39,7] 0,0124[3]
IIIA	133/236 (56,4)	63/214 (29,4)	1,91 [1,51; 2,42] <,0001[2]	3,09 [2,09; 4,57] <,0001[3]	26,9 [18,1; 35,7] <,0001[3]
IIIB	11/18 (61,1)	4/15 (26,7)	2,29 [0,92; 5,73] 0,0762[2]	4,32 [0,98; 19,09] 0,0479[3]	34,4 [2,7; 66,2] 0,0479[3]
IIIC	101/186 (54,3)	49/174 (28,2)	1,93 [1,47; 2,53] <,0001[2]	3,03 [1,95; 4,70] <,0001[3]	26,1 [16,3; 35,9] <,0001[3]
Tumor grade (Interaction p-value: 0,1889)					
G1	28/47 (59,6)	8/41 (19,5)	3,05 [1,57; 5,94] 0,0010[2]	6,08 [2,31; 16,00] 0,0001[3]	40,1 [21,5; 58,6] 0,0001[3]
G2	136/244 (55,7)	83/234 (35,5)	1,57 [1,28; 1,93] <,0001[2]	2,29 [1,59; 3,31] <,0001[3]	20,3 [11,5; 29,0] <,0001[3]
G3	130/233 (55,8)	66/226 (29,2)	1,91 [1,51; 2,41] <,0001[2]	3,06 [2,08; 4,50] <,0001[3]	26,6 [17,9; 35,3] <,0001[3]
GX	16/29 (55,2)	8/33 (24,2)	2,28 [1,15; 4,52] 0,0189[2]	3,85 [1,30; 11,34] 0,0126[3]	30,9 [7,7; 54,2] 0,0126[3]
Progesterone receptor status (Interaction p-value: 0,0511)					
Negative	34/49 (69,4)	12/44 (27,3)	2,54 [1,52; 4,27] 0,0004[2]	6,04 [2,46; 14,86] <,0001[3]	42,1 [23,7; 60,5] <,0001[3]
Positive	256/477 (53,7)	142/471 (30,1)	1,78 [1,52; 2,09] <,0001[2]	2,68 [2,06; 3,50] <,0001[3]	23,5 [17,4; 29,6] <,0001[3]
Unknown	4/4 (100,0)	5/8 (62,5)	1,47 [0,81; 2,68] 0,2041[2]	5,73 [0,23; 142,55] 0,4909[4]	37,5 [4,0; 71,0] 0,4909[4]
Race (Interaction p-value: 0,7128)					
White	196/323 (60,7)	105/324 (32,4)	1,87 [1,56; 2,24] <,0001[2]	3,22 [2,33; 4,44] <,0001[3]	28,3 [20,9; 35,6] <,0001[3]
Asian	93/199 (46,7)	49/180 (27,2)	1,72 [1,30; 2,27] 0,0002[2]	2,35 [1,53; 3,61] <,0001[3]	19,5 [10,0; 29,0] <,0001[3]
Other	11/19 (57,9)	5/21 (23,8)	2,43 [1,03; 5,72] 0,0419[2]	4,40 [1,13; 17,07] 0,0280[3]	34,1 [5,4; 62,8] 0,0280[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Hepatobiliary disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9958)					
Neoadjuvant chemotherapy	11/217 (5,1)	6/219 (2,7)	1,85 [0,70; 4,91] 0,2170[2]	1,90 [0,69; 5,22] 0,2090[3]	2,3 [-1,3; 6,0] 0,2090[3]
Adjuvant chemotherapy	22/327 (6,7)	12/312 (3,8)	1,75 [0,88; 3,47] 0,1102[2]	1,80 [0,88; 3,71] 0,1047[3]	2,9 [-0,6; 6,3] 0,1047[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,5573)					
North America / Europe	8/252 (3,2)	2/233 (0,9)	3,70 [0,79; 17,24] 0,0958[2]	3,79 [0,80; 18,02] 0,1084[4]	2,3 [-0,2; 4,8] 0,1084[4]
Asia	11/168 (6,5)	6/166 (3,6)	1,81 [0,69; 4,78] 0,2306[2]	1,87 [0,67; 5,18] 0,2227[3]	2,9 [-1,8; 7,6] 0,2227[3]
Other	14/133 (10,5)	10/136 (7,4)	1,43 [0,66; 3,11] 0,3645[2]	1,48 [0,63; 3,47] 0,3613[3]	3,2 [-3,6; 10,0] 0,3613[3]
Primary tumor size (Interaction p-value: 0,5113)					
< 20 mm	9/141 (6,4)	3/140 (2,1)	2,98 [0,82; 10,77] 0,0961[2]	3,11 [0,82; 11,75] 0,0788[3]	4,2 [-0,5; 8,9] 0,0788[3]
≥ 20 but < 50 mm	14/255 (5,5)	6/249 (2,4)	2,28 [0,89; 5,83] 0,0861[2]	2,35 [0,89; 6,22] 0,0765[3]	3,1 [-0,3; 6,5] 0,0765[3]
≥ 50 mm	9/145 (6,2)	7/141 (5,0)	1,25 [0,48; 3,27] 0,6485[2]	1,27 [0,46; 3,50] 0,6476[3]	1,2 [-4,1; 6,6] 0,6476[3]
Number of positive lymph nodes (Interaction p-value: 0,4629)					
0-3	9/203 (4,4)	6/214 (2,8)	1,58 [0,57; 4,36] 0,3762[2]	1,61 [0,56; 4,60] 0,3717[3]	1,6 [-2,0; 5,2] 0,3717[3]
4-9	18/242 (7,4)	7/231 (3,0)	2,45 [1,04; 5,77] 0,0394[2]	2,57 [1,05; 6,28] 0,0322[3]	4,4 [0,4; 8,4] 0,0322[3]
≥ 10	6/108 (5,6)	5/90 (5,6)	1,00 [0,32; 3,17] 1,0000[2]	1,00 [0,29; 3,39] 1,0000[3]	0,0 [-6,4; 6,4] 1,0000[3]
Tumor stage (Interaction p-value: 0,6950)					
IIA	4/59 (6,8)	3/62 (4,8)	1,40 [0,33; 6,00] 0,6493[2]	1,43 [0,31; 6,68] 0,7128[4]	1,9 [-6,4; 10,3] 0,7128[4]
IIB	1/53 (1,9)	2/69 (2,9)	0,65 [0,06; 6,99] 0,7230[2]	0,64 [0,06; 7,30] 1,0000[4]	-1,0 [-6,4; 4,4] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	18/236 (7,6)	6/214 (2,8)	2,72 [1,10; 6,73] 0,0302[2]	2,86 [1,11; 7,35] 0,0230[3]	4,8 [0,8; 8,9] 0,0230[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	9/186 (4,8)	7/174 (4,0)	1,20 [0,46; 3,16] 0,7079[2]	1,21 [0,44; 3,33] 0,7074[3]	0,8 [-3,4; 5,1] 0,7074[3]
Tumor grade (Interaction p-value: 0,3642)					
G1	4/47 (8,5)	2/41 (4,9)	1,74 [0,34; 9,04] 0,5072[2]	1,81 [0,31; 10,46] 0,6810[4]	3,6 [-6,7; 14,0] 0,6810[4]
G2	15/244 (6,1)	4/234 (1,7)	3,60 [1,21; 10,68] 0,0212[2]	3,77 [1,23; 11,52] 0,0130[3]	4,4 [1,0; 7,9] 0,0130[3]
G3	13/233 (5,6)	10/226 (4,4)	1,26 [0,56; 2,82] 0,5718[2]	1,28 [0,55; 2,97] 0,5708[3]	1,2 [-2,8; 5,1] 0,5708[3]
GX	1/29 (3,4)	2/33 (6,1)	0,57 [0,05; 5,95] 0,6378[2]	0,55 [0,05; 6,44] 1,0000[4]	-2,6 [-13,1; 7,9] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,7513)					
Negative	3/49 (6,1)	2/44 (4,5)	1,35 [0,24; 7,69] 0,7376[2]	1,37 [0,22; 8,60] 1,0000[4]	1,6 [-7,5; 10,7] 1,0000[4]
Positive	29/477 (6,1)	16/471 (3,4)	1,79 [0,99; 3,25] 0,0560[2]	1,84 [0,99; 3,44] 0,0521[3]	2,7 [-0,0; 5,4] 0,0521[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9793)					
White	19/323 (5,9)	11/324 (3,4)	1,73 [0,84; 3,58] 0,1381[2]	1,78 [0,83; 3,80] 0,1325[3]	2,5 [-0,7; 5,7] 0,1325[3]
Asian	13/199 (6,5)	6/180 (3,3)	1,96 [0,76; 5,05] 0,1634[2]	2,03 [0,75; 5,45] 0,1541[3]	3,2 [-1,1; 7,5] 0,1541[3]
Other	0/19 (0,0)	1/21 (4,8)	0,37 [0,02; 8,50] 0,5315[2]	0,35 [0,01; 9,13] 1,0000[4]	-4,8 [-13,9; 4,3] 1,0000[4]
ECOG-PS (Interaction p-value: 0,8106)					
ECOG-PS 0	30/496 (6,0)	16/480 (3,3)	1,81 [1,00; 3,29] 0,0492[2]	1,87 [1,00; 3,47] 0,0454[3]	2,7 [0,1; 5,4] 0,0454[3]
ECOG-PS 1	3/57 (5,3)	2/55 (3,6)	1,45 [0,25; 8,33] 0,6789[2]	1,47 [0,24; 9,17] 1,0000[4]	1,6 [-6,0; 9,2] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events according SOC Infections and infestations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,2874)					
Neoadjuvant chemotherapy	108/217 (49,8)	94/219 (42,9)	1,16 [0,95; 1,42] 0,1529[2]	1,32 [0,90; 1,92] 0,1517[3]	6,8 [-2,5; 16,2] 0,1517[3]
Adjuvant chemotherapy	185/327 (56,6)	127/312 (40,7)	1,39 [1,18; 1,64] <,0001[2]	1,90 [1,39; 2,60] <,0001[3]	15,9 [8,2; 23,5] <,0001[3]
No chemotherapy	6/9 (66,7)	1/4 (25,0)	2,67 [0,46; 15,49] 0,2745[2]	6,00 [0,42; 85,25] 0,2657[4]	41,7 [-10,8; 94,1] 0,2657[4]
Region (Interaction p-value: 0,8912)					
North America / Europe	136/252 (54,0)	100/233 (42,9)	1,26 [1,04; 1,52] 0,0163[2]	1,56 [1,09; 2,23] 0,0150[3]	11,0 [2,2; 19,9] 0,0150[3]
Asia	101/168 (60,1)	75/166 (45,2)	1,33 [1,08; 1,64] 0,0071[2]	1,83 [1,18; 2,82] 0,0063[3]	14,9 [4,3; 25,5] 0,0063[3]
Other	62/133 (46,6)	47/136 (34,6)	1,35 [1,01; 1,81] 0,0462[2]	1,65 [1,01; 2,70] 0,0440[3]	12,1 [0,4; 23,7] 0,0440[3]
Primary tumor size (Interaction p-value: 0,4491)					
< 20 mm	83/141 (58,9)	58/140 (41,4)	1,42 [1,12; 1,81] 0,0042[2]	2,02 [1,26; 3,25] 0,0035[3]	17,4 [5,9; 28,9] 0,0035[3]
≥ 20 but < 50 mm	128/255 (50,2)	104/249 (41,8)	1,20 [0,99; 1,45] 0,0592[2]	1,41 [0,99; 2,00] 0,0577[3]	8,4 [-0,2; 17,1] 0,0577[3]
≥ 50 mm	83/145 (57,2)	57/141 (40,4)	1,42 [1,11; 1,81] 0,0054[2]	1,97 [1,23; 3,16] 0,0045[3]	16,8 [5,4; 28,2] 0,0045[3]
Number of positive lymph nodes (Interaction p-value: 0,8869)					
0-3	108/203 (53,2)	91/214 (42,5)	1,25 [1,02; 1,53] 0,0299[2]	1,54 [1,04; 2,26] 0,0291[3]	10,7 [1,1; 20,2] 0,0291[3]
4-9	128/242 (52,9)	92/231 (39,8)	1,33 [1,09; 1,62] 0,0050[2]	1,70 [1,18; 2,44] 0,0044[3]	13,1 [4,2; 22,0] 0,0044[3]
≥ 10	63/108 (58,3)	39/90 (43,3)	1,35 [1,01; 1,79] 0,0409[2]	1,83 [1,04; 3,22] 0,0355[3]	15,0 [1,2; 28,8] 0,0355[3]
Tumor stage (Interaction p-value: 0,5545)					
IIA	33/59 (55,9)	22/62 (35,5)	1,58 [1,05; 2,36] 0,0276[2]	2,31 [1,11; 4,79] 0,0239[3]	20,4 [3,1; 37,8] 0,0239[3]
IIB	27/53 (50,9)	34/69 (49,3)	1,03 [0,72; 1,48] 0,8548[2]	1,07 [0,52; 2,19] 0,8551[3]	1,7 [-16,2; 19,6] 0,8551[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	121/236 (51,3)	87/214 (40,7)	1,26 [1,03; 1,55] 0,0259[2]	1,54 [1,06; 2,23] 0,0241[3]	10,6 [1,5; 19,8] 0,0241[3]
IIIB	10/18 (55,6)	5/15 (33,3)	1,67 [0,73; 3,81] 0,2257[2]	2,50 [0,60; 10,34] 0,2018[3]	22,2 [-10,9; 55,3] 0,2018[3]
IIIC	107/186 (57,5)	74/174 (42,5)	1,35 [1,09; 1,67] 0,0053[2]	1,83 [1,20; 2,78] 0,0045[3]	15,0 [4,8; 25,2] 0,0045[3]
Tumor grade (Interaction p-value: 0,2818)					
G1	28/47 (59,6)	15/41 (36,6)	1,63 [1,02; 2,60] 0,0406[2]	2,55 [1,08; 6,05] 0,0314[3]	23,0 [2,6; 43,3] 0,0314[3]
G2	130/244 (53,3)	95/234 (40,6)	1,31 [1,08; 1,59] 0,0062[2]	1,67 [1,16; 2,40] 0,0055[3]	12,7 [3,8; 21,6] 0,0055[3]
G3	124/233 (53,2)	90/226 (39,8)	1,34 [1,09; 1,63] 0,0046[2]	1,72 [1,19; 2,49] 0,0040[3]	13,4 [4,4; 22,4] 0,0040[3]
GX	17/29 (58,6)	21/33 (63,6)	0,92 [0,62; 1,37] 0,6875[2]	0,81 [0,29; 2,25] 0,6858[3]	-5,0 [-29,3; 19,3] 0,6858[3]
Race (Interaction p-value: 0,9035)					
White	169/323 (52,3)	133/324 (41,0)	1,27 [1,08; 1,51] 0,0044[2]	1,58 [1,15; 2,15] 0,0041[3]	11,3 [3,6; 18,9] 0,0041[3]
Asian	113/199 (56,8)	76/180 (42,2)	1,34 [1,09; 1,66] 0,0056[2]	1,80 [1,20; 2,70] 0,0046[3]	14,6 [4,6; 24,5] 0,0046[3]
Other	11/19 (57,9)	10/21 (47,6)	1,22 [0,67; 2,19] 0,5164[2]	1,51 [0,43; 5,28] 0,5158[3]	10,3 [-20,5; 41,1] 0,5158[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Investigations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8707)					
Neoadjuvant chemotherapy	96/217 (44,2)	40/219 (18,3)	2,42 [1,76; 3,33] <,0001[2]	3,55 [2,30; 5,49] <,0001[3]	26,0 [17,6; 34,3] <,0001[3]
Adjuvant chemotherapy	167/327 (51,1)	59/312 (18,9)	2,70 [2,10; 3,48] <,0001[2]	4,48 [3,13; 6,39] <,0001[3]	32,2 [25,2; 39,1] <,0001[3]
No chemotherapy	5/9 (55,6)	0/4 (0,0)	5,50 [0,37; 80,92] 0,2140[2]	11,00 [0,46; 263,53] 0,1049[4]	55,6 [23,1; 88,0] 0,1049[4]
Primary tumor size (Interaction p-value: 0,8962)					
< 20 mm	65/141 (46,1)	24/140 (17,1)	2,69 [1,79; 4,03] <,0001[2]	4,13 [2,38; 7,17] <,0001[3]	29,0 [18,6; 39,3] <,0001[3]
≥ 20 but < 50 mm	129/255 (50,6)	46/249 (18,5)	2,74 [2,05; 3,65] <,0001[2]	4,52 [3,02; 6,76] <,0001[3]	32,1 [24,3; 39,9] <,0001[3]
≥ 50 mm	68/145 (46,9)	27/141 (19,1)	2,45 [1,67; 3,58] <,0001[2]	3,73 [2,19; 6,34] <,0001[3]	27,7 [17,3; 38,1] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,3526)					
0-3	102/203 (50,2)	34/214 (15,9)	3,16 [2,26; 4,43] <,0001[2]	5,35 [3,38; 8,45] <,0001[3]	34,4 [25,9; 42,8] <,0001[3]
4-9	112/242 (46,3)	45/231 (19,5)	2,38 [1,77; 3,19] <,0001[2]	3,56 [2,36; 5,38] <,0001[3]	26,8 [18,7; 34,9] <,0001[3]
≥ 10	54/108 (50,0)	20/90 (22,2)	2,25 [1,46; 3,46] 0,0002[2]	3,50 [1,88; 6,53] <,0001[3]	27,8 [15,0; 40,5] <,0001[3]
Tumor stage (Interaction p-value: 0,9113)					
IIA	25/59 (42,4)	10/62 (16,1)	2,63 [1,38; 4,99] 0,0031[2]	3,82 [1,63; 8,96] 0,0015[3]	26,2 [10,7; 41,8] 0,0015[3]
IIB	31/53 (58,5)	12/69 (17,4)	3,36 [1,92; 5,90] <,0001[2]	6,69 [2,92; 15,32] <,0001[3]	41,1 [25,1; 57,1] <,0001[3]
IIIA	119/236 (50,4)	44/214 (20,6)	2,45 [1,83; 3,28] <,0001[2]	3,93 [2,59; 5,97] <,0001[3]	29,9 [21,5; 38,2] <,0001[3]
IIIB	7/18 (38,9)	2/15 (13,3)	2,92 [0,71; 12,00] 0,1379[2]	4,14 [0,71; 24,16] 0,1336[4]	25,6 [-2,8; 53,9] 0,1336[4]
IIIC	85/186 (45,7)	31/174 (17,8)	2,57 [1,80; 3,66] <,0001[2]	3,88 [2,39; 6,30] <,0001[3]	27,9 [18,7; 37,0] <,0001[3]
Tumor grade (Interaction p-value: 0,7902)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	28/47 (59,6)	8/41 (19,5)	3,05 [1,57; 5,94] 0,0010[2]	6,08 [2,31; 16,00] 0,0001[3]	40,1 [21,5; 58,6] 0,0001[3]
G2	111/244 (45,5)	45/234 (19,2)	2,37 [1,76; 3,18] <,0001[2]	3,51 [2,32; 5,29] <,0001[3]	26,3 [18,2; 34,3] <,0001[3]
G3	108/233 (46,4)	36/226 (15,9)	2,91 [2,09; 4,05] <,0001[2]	4,56 [2,94; 7,08] <,0001[3]	30,4 [22,4; 38,4] <,0001[3]
GX	21/29 (72,4)	9/33 (27,3)	2,66 [1,46; 4,84] 0,0014[2]	7,00 [2,29; 21,41] 0,0004[3]	45,1 [22,9; 67,4] 0,0004[3]
Progesterone receptor status (Interaction p-value: 0,5200)					
Negative	23/49 (46,9)	5/44 (11,4)	4,13 [1,72; 9,93] 0,0015[2]	6,90 [2,33; 20,46] 0,0002[3]	35,6 [18,7; 52,4] 0,0002[3]
Positive	230/477 (48,2)	93/471 (19,7)	2,44 [1,99; 3,00] <,0001[2]	3,78 [2,83; 5,05] <,0001[3]	28,5 [22,7; 34,2] <,0001[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,7612)					
White	138/323 (42,7)	54/324 (16,7)	2,56 [1,95; 3,37] <,0001[2]	3,73 [2,59; 5,38] <,0001[3]	26,1 [19,3; 32,8] <,0001[3]
Asian	121/199 (60,8)	42/180 (23,3)	2,61 [1,96; 3,47] <,0001[2]	5,10 [3,26; 7,97] <,0001[3]	37,5 [28,3; 46,6] <,0001[3]
Other	8/19 (42,1)	2/21 (9,5)	4,42 [1,07; 18,29] 0,0402[2]	6,91 [1,24; 38,52] 0,0281[4]	32,6 [7,1; 58,1] 0,0281[4]
ECOG-PS (Interaction p-value: 0,3031)					
ECOG-PS 0	251/496 (50,6)	90/480 (18,8)	2,70 [2,20; 3,31] <,0001[2]	4,44 [3,33; 5,93] <,0001[3]	31,9 [26,2; 37,5] <,0001[3]
ECOG-PS 1	17/57 (29,8)	9/55 (16,4)	1,82 [0,89; 3,74] 0,1013[2]	2,17 [0,87; 5,41] 0,0916[3]	13,5 [-1,9; 28,8] 0,0916[3]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Metabolism and nutrition disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,0769)					
Neoadjuvant chemotherapy	44/217 (20,3)	15/219 (6,8)	2,96 [1,70; 5,16] 0,0001[2]	3,46 [1,86; 6,43] <,0001[3]	13,4 [7,1; 19,7] <,0001[3]
Adjuvant chemotherapy	69/327 (21,1)	36/312 (11,5)	1,83 [1,26; 2,65] 0,0015[2]	2,05 [1,32; 3,17] 0,0011[3]	9,6 [3,9; 15,2] 0,0011[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,2885)					
North America / Europe	47/252 (18,7)	21/233 (9,0)	2,07 [1,28; 3,35] 0,0031[2]	2,31 [1,34; 4,01] 0,0023[3]	9,6 [3,6; 15,7] 0,0023[3]
Asia	31/168 (18,5)	9/166 (5,4)	3,40 [1,67; 6,93] 0,0007[2]	3,95 [1,82; 8,58] 0,0002[3]	13,0 [6,2; 19,8] 0,0002[3]
Other	35/133 (26,3)	21/136 (15,4)	1,70 [1,05; 2,77] 0,0313[2]	1,96 [1,07; 3,58] 0,0281[3]	10,9 [1,2; 20,5] 0,0281[3]
Primary tumor size (Interaction p-value: 0,8120)					
< 20 mm	26/141 (18,4)	11/140 (7,9)	2,35 [1,21; 4,56] 0,0119[2]	2,65 [1,25; 5,60] 0,0087[3]	10,6 [2,8; 18,4] 0,0087[3]
≥ 20 but < 50 mm	50/255 (19,6)	25/249 (10,0)	1,95 [1,25; 3,05] 0,0034[2]	2,19 [1,30; 3,66] 0,0025[3]	9,6 [3,4; 15,7] 0,0025[3]
≥ 50 mm	35/145 (24,1)	14/141 (9,9)	2,43 [1,37; 4,32] 0,0025[2]	2,89 [1,48; 5,64] 0,0014[3]	14,2 [5,7; 22,7] 0,0014[3]
Number of positive lymph nodes (Interaction p-value: 0,1337)					
0-3	32/203 (15,8)	16/214 (7,5)	2,11 [1,19; 3,72] 0,0101[2]	2,32 [1,23; 4,37] 0,0080[3]	8,3 [2,2; 14,4] 0,0080[3]
4-9	58/242 (24,0)	20/231 (8,7)	2,77 [1,72; 4,45] <,0001[2]	3,33 [1,93; 5,74] <,0001[3]	15,3 [8,8; 21,8] <,0001[3]
≥ 10	23/108 (21,3)	15/90 (16,7)	1,28 [0,71; 2,30] 0,4133[2]	1,35 [0,66; 2,78] 0,4101[3]	4,6 [-6,3; 15,5] 0,4101[3]
Tumor stage (Interaction p-value: 0,2322)					
IIA	10/59 (16,9)	2/62 (3,2)	5,25 [1,20; 22,98] 0,0276[2]	6,12 [1,28; 29,26] 0,0116[3]	13,7 [3,2; 24,3] 0,0116[3]
IIB	6/53 (11,3)	9/69 (13,0)	0,87 [0,33; 2,29] 0,7745[2]	0,85 [0,28; 2,56] 0,7739[3]	-1,7 [-13,4; 9,9] 0,7739[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	53/236 (22,5)	19/214 (8,9)	2,53 [1,55; 4,13] 0,0002[2]	2,97 [1,70; 5,21] <,0001[3]	13,6 [7,0; 20,1] <,0001[3]
IIIB	4/18 (22,2)	0/15 (0,0)	7,58 [0,44; 130,38] 0,1629[2]	9,62 [0,48; 194,83] 0,1081[4]	22,2 [3,0; 41,4] 0,1081[4]
IIIC	40/186 (21,5)	21/174 (12,1)	1,78 [1,10; 2,90] 0,0198[2]	2,00 [1,12; 3,55] 0,0171[3]	9,4 [1,8; 17,1] 0,0171[3]
Tumor grade (Interaction p-value: 0,8342)					
G1	9/47 (19,1)	5/41 (12,2)	1,57 [0,57; 4,31] 0,3812[2]	1,71 [0,52; 5,57] 0,3736[3]	7,0 [-8,1; 22,0] 0,3736[3]
G2	55/244 (22,5)	24/234 (10,3)	2,20 [1,41; 3,43] 0,0005[2]	2,55 [1,52; 4,28] 0,0003[3]	12,3 [5,8; 18,8] 0,0003[3]
G3	45/233 (19,3)	21/226 (9,3)	2,08 [1,28; 3,37] 0,0031[2]	2,34 [1,34; 4,07] 0,0022[3]	10,0 [3,7; 16,3] 0,0022[3]
GX	4/29 (13,8)	1/33 (3,0)	4,55 [0,54; 38,45] 0,1639[2]	5,12 [0,54; 48,72] 0,1762[4]	10,8 [-3,1; 24,6] 0,1762[4]
Progesterone receptor status (Interaction p-value: 0,9507)					
Negative	6/49 (12,2)	3/44 (6,8)	1,80 [0,48; 6,76] 0,3864[2]	1,91 [0,45; 8,13] 0,4916[4]	5,4 [-6,4; 17,2] 0,4916[4]
Positive	102/477 (21,4)	45/471 (9,6)	2,24 [1,61; 3,10] <,0001[2]	2,57 [1,77; 3,75] <,0001[3]	11,8 [7,3; 16,4] <,0001[3]
Unknown	0/4 (0,0)	2/8 (25,0)	0,36 [0,02; 6,12] 0,4796[2]	0,29 [0,01; 7,57] 0,5152[4]	-25,0 [-55,0; 5,0] 0,5152[4]
Race (Interaction p-value: 0,2510)					
White	67/323 (20,7)	35/324 (10,8)	1,92 [1,31; 2,80] 0,0007[2]	2,16 [1,39; 3,36] 0,0005[3]	9,9 [4,4; 15,5] 0,0005[3]
Asian	34/199 (17,1)	10/180 (5,6)	3,08 [1,56; 6,04] 0,0011[2]	3,50 [1,68; 7,32] 0,0005[3]	11,5 [5,3; 17,7] 0,0005[3]
Other	5/19 (26,3)	5/21 (23,8)	1,11 [0,38; 3,23] 0,8550[2]	1,14 [0,27; 4,79] 1,0000[4]	2,5 [-24,4; 29,4] 1,0000[4]
ECOG-PS (Interaction p-value: 0,6748)					
ECOG-PS 0	104/496 (21,0)	46/480 (9,6)	2,19 [1,58; 3,02] <,0001[2]	2,50 [1,72; 3,63] <,0001[3]	11,4 [6,9; 15,8] <,0001[3]
ECOG-PS 1	9/57 (15,8)	5/55 (9,1)	1,74 [0,62; 4,86] 0,2928[2]	1,88 [0,59; 6,00] 0,2839[3]	6,7 [-5,4; 18,8] 0,2839[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events according SOC Nervous system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,0949)					
Neoadjuvant chemotherapy	71/217 (32,7)	71/219 (32,4)	1,01 [0,77; 1,32] 0,9469[2]	1,01 [0,68; 1,51] 0,9469[3]	0,3 [-8,5; 9,1] 0,9469[3]
Adjuvant chemotherapy	122/327 (37,3)	80/312 (25,6)	1,46 [1,15; 1,84] 0,0018[2]	1,73 [1,23; 2,42] 0,0015[3]	11,7 [4,5; 18,8] 0,0015[3]
No chemotherapy	6/9 (66,7)	1/4 (25,0)	2,67 [0,46; 15,49] 0,2745[2]	6,00 [0,42; 85,25] 0,2657[4]	41,7 [-10,8; 94,1] 0,2657[4]
Primary tumor size (Interaction p-value: 0,1426)					
< 20 mm	50/141 (35,5)	44/140 (31,4)	1,13 [0,81; 1,57] 0,4745[2]	1,20 [0,73; 1,97] 0,4738[3]	4,0 [-7,0; 15,1] 0,4738[3]
≥ 20 but < 50 mm	91/255 (35,7)	78/249 (31,3)	1,14 [0,89; 1,46] 0,3009[2]	1,22 [0,84; 1,76] 0,2998[3]	4,4 [-3,9; 12,6] 0,2998[3]
≥ 50 mm	54/145 (37,2)	30/141 (21,3)	1,75 [1,20; 2,56] 0,0040[2]	2,20 [1,30; 3,71] 0,0030[3]	16,0 [5,6; 26,3] 0,0030[3]
Number of positive lymph nodes (Interaction p-value: 0,2698)					
0-3	71/203 (35,0)	68/214 (31,8)	1,10 [0,84; 1,44] 0,4886[2]	1,15 [0,77; 1,74] 0,4884[3]	3,2 [-5,9; 12,3] 0,4884[3]
4-9	84/242 (34,7)	62/231 (26,8)	1,29 [0,98; 1,70] 0,0660[2]	1,45 [0,98; 2,15] 0,0640[3]	7,9 [-0,4; 16,2] 0,0640[3]
≥ 10	44/108 (40,7)	22/90 (24,4)	1,67 [1,09; 2,56] 0,0195[2]	2,13 [1,15; 3,93] 0,0154[3]	16,3 [3,5; 29,1] 0,0154[3]
Tumor stage (Interaction p-value: 0,5172)					
IIA	21/59 (35,6)	20/62 (32,3)	1,10 [0,67; 1,82] 0,6986[2]	1,16 [0,55; 2,47] 0,6984[3]	3,3 [-13,5; 20,2] 0,6984[3]
IIB	18/53 (34,0)	25/69 (36,2)	0,94 [0,57; 1,53] 0,7953[2]	0,91 [0,43; 1,92] 0,7948[3]	-2,3 [-19,3; 14,8] 0,7948[3]
IIIA	84/236 (35,6)	54/214 (25,2)	1,41 [1,06; 1,88] 0,0190[2]	1,64 [1,09; 2,46] 0,0173[3]	10,4 [1,9; 18,8] 0,0173[3]
IIIB	5/18 (27,8)	5/15 (33,3)	0,83 [0,30; 2,34] 0,7294[2]	0,77 [0,17; 3,41] 1,0000[4]	-5,6 [-37,1; 26,0] 1,0000[4]
IIIC	71/186 (38,2)	48/174 (27,6)	1,38 [1,02; 1,87] 0,0352[2]	1,62 [1,04; 2,53] 0,0329[3]	10,6 [1,0; 20,2] 0,0329[3]
Tumor grade (Interaction p-value: 0,7272)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	24/47 (51,1)	13/41 (31,7)	1,61 [0,95; 2,73] 0,0776[2]	2,25 [0,94; 5,37] 0,0665[3]	19,4 [-0,8; 39,5] 0,0665[3]
G2	78/244 (32,0)	65/234 (27,8)	1,15 [0,87; 1,52] 0,3185[2]	1,22 [0,82; 1,81] 0,3173[3]	4,2 [-4,0; 12,4] 0,3173[3]
G3	91/233 (39,1)	68/226 (30,1)	1,30 [1,01; 1,68] 0,0453[2]	1,49 [1,01; 2,19] 0,0435[3]	9,0 [0,3; 17,6] 0,0435[3]
GX	6/29 (20,7)	5/33 (15,2)	1,37 [0,47; 4,01] 0,5707[2]	1,46 [0,39; 5,41] 0,5690[3]	5,5 [-13,6; 24,7] 0,5690[3]
Progesterone receptor status (Interaction p-value: 0,4907)					
Negative	21/49 (42,9)	11/44 (25,0)	1,71 [0,94; 3,14] 0,0810[2]	2,25 [0,93; 5,46] 0,0703[3]	17,9 [-1,0; 36,7] 0,0703[3]
Positive	166/477 (34,8)	134/471 (28,5)	1,22 [1,01; 1,48] 0,0363[2]	1,34 [1,02; 1,77] 0,0355[3]	6,4 [0,4; 12,3] 0,0355[3]
Unknown	2/4 (50,0)	2/8 (25,0)	2,00 [0,42; 9,42] 0,3806[2]	3,00 [0,24; 37,67] 0,5475[4]	25,0 [-32,5; 82,5] 0,5475[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Respiratory, thoracic and mediastinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7341)					
Neoadjuvant chemotherapy	62/217 (28,6)	27/219 (12,3)	2,32 [1,54; 3,50] <,0001[2]	2,84 [1,73; 4,69] <,0001[3]	16,2 [8,8; 23,7] <,0001[3]
Adjuvant chemotherapy	91/327 (27,8)	46/312 (14,7)	1,89 [1,37; 2,60] <,0001[2]	2,23 [1,50; 3,31] <,0001[3]	13,1 [6,8; 19,3] <,0001[3]
No chemotherapy	4/9 (44,4)	1/4 (25,0)	1,78 [0,28; 11,28] 0,5417[2]	2,40 [0,18; 32,88] 1,0000[4]	19,4 [-34,0; 72,9] 1,0000[4]
Region (Interaction p-value: 0,3830)					
North America / Europe	82/252 (32,5)	32/233 (13,7)	2,37 [1,64; 3,42] <,0001[2]	3,03 [1,92; 4,78] <,0001[3]	18,8 [11,5; 26,1] <,0001[3]
Asia	54/168 (32,1)	27/166 (16,3)	1,98 [1,31; 2,98] 0,0011[2]	2,44 [1,44; 4,12] 0,0007[3]	15,9 [6,9; 24,9] 0,0007[3]
Other	21/133 (15,8)	15/136 (11,0)	1,43 [0,77; 2,66] 0,2552[2]	1,51 [0,74; 3,08] 0,2516[3]	4,8 [-3,4; 12,9] 0,2516[3]
Primary tumor size (Interaction p-value: 0,8109)					
< 20 mm	37/141 (26,2)	19/140 (13,6)	1,93 [1,17; 3,19] 0,0099[2]	2,27 [1,23; 4,18] 0,0079[3]	12,7 [3,5; 21,9] 0,0079[3]
≥ 20 but < 50 mm	74/255 (29,0)	33/249 (13,3)	2,19 [1,51; 3,17] <,0001[2]	2,68 [1,70; 4,22] <,0001[3]	15,8 [8,8; 22,7] <,0001[3]
≥ 50 mm	41/145 (28,3)	22/141 (15,6)	1,81 [1,14; 2,88] 0,0119[2]	2,13 [1,19; 3,81] 0,0097[3]	12,7 [3,2; 22,1] 0,0097[3]
Number of positive lymph nodes (Interaction p-value: 0,3293)					
0-3	57/203 (28,1)	28/214 (13,1)	2,15 [1,42; 3,23] 0,0003[2]	2,59 [1,57; 4,28] 0,0001[3]	15,0 [7,3; 22,7] 0,0001[3]
4-9	67/242 (27,7)	37/231 (16,0)	1,73 [1,21; 2,47] 0,0028[2]	2,01 [1,28; 3,15] 0,0022[3]	11,7 [4,3; 19,0] 0,0022[3]
≥ 10	33/108 (30,6)	9/90 (10,0)	3,06 [1,55; 6,04] 0,0013[2]	3,96 [1,78; 8,82] 0,0004[3]	20,6 [9,9; 31,2] 0,0004[3]
Tumor stage (Interaction p-value: 0,5088)					
IIA	15/59 (25,4)	6/62 (9,7)	2,63 [1,09; 6,32] 0,0309[2]	3,18 [1,14; 8,88] 0,0223[3]	15,7 [2,4; 29,1] 0,0223[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIB	9/53 (17,0)	10/69 (14,5)	1,17 [0,51; 2,68] 0,7070[2]	1,21 [0,45; 3,22] 0,7071[3]	2,5 [-10,6; 15,6] 0,7071[3]
IIIA	70/236 (29,7)	33/214 (15,4)	1,92 [1,33; 2,79] 0,0005[2]	2,31 [1,45; 3,68] 0,0003[3]	14,2 [6,7; 21,8] 0,0003[3]
IIIB	7/18 (38,9)	1/15 (6,7)	5,83 [0,81; 42,25] 0,0809[2]	8,91 [0,95; 83,62] 0,0463[4]	32,2 [6,4; 58,0] 0,0463[4]
IIIC	56/186 (30,1)	24/174 (13,8)	2,18 [1,42; 3,36] 0,0004[2]	2,69 [1,58; 4,59] 0,0002[3]	16,3 [8,0; 24,7] 0,0002[3]
Tumor grade (Interaction p-value: 0,5464)					
G1	15/47 (31,9)	4/41 (9,8)	3,27 [1,18; 9,07] 0,0228[2]	4,34 [1,31; 14,40] 0,0117[3]	22,2 [6,0; 38,3] 0,0117[3]
G2	66/244 (27,0)	37/234 (15,8)	1,71 [1,19; 2,45] 0,0035[2]	1,97 [1,26; 3,10] 0,0028[3]	11,2 [4,0; 18,5] 0,0028[3]
G3	67/233 (28,8)	29/226 (12,8)	2,24 [1,51; 3,33] <,0001[2]	2,74 [1,69; 4,44] <,0001[3]	15,9 [8,7; 23,2] <,0001[3]
GX	9/29 (31,0)	4/33 (12,1)	2,56 [0,88; 7,44] 0,0842[2]	3,26 [0,88; 12,07] 0,0679[3]	18,9 [-1,3; 39,1] 0,0679[3]
Progesterone receptor status (Interaction p-value: 0,9988)					
Negative	13/49 (26,5)	6/44 (13,6)	1,95 [0,81; 4,68] 0,1371[2]	2,29 [0,78; 6,66] 0,1236[3]	12,9 [-3,1; 28,9] 0,1236[3]
Positive	131/477 (27,5)	65/471 (13,8)	1,99 [1,52; 2,60] <,0001[2]	2,36 [1,70; 3,29] <,0001[3]	13,7 [8,6; 18,7] <,0001[3]
Unknown	1/4 (25,0)	1/8 (12,5)	2,00 [0,16; 24,33] 0,5866[2]	2,33 [0,11; 50,98] 1,0000[4]	12,5 [-35,7; 60,7] 1,0000[4]
Race (Interaction p-value: 0,7851)					
White	84/323 (26,0)	43/324 (13,3)	1,96 [1,40; 2,74] <,0001[2]	2,30 [1,53; 3,45] <,0001[3]	12,7 [6,7; 18,8] <,0001[3]
Asian	60/199 (30,2)	28/180 (15,6)	1,94 [1,30; 2,89] 0,0012[2]	2,34 [1,42; 3,88] 0,0008[3]	14,6 [6,3; 22,9] 0,0008[3]
Other	6/19 (31,6)	2/21 (9,5)	3,32 [0,76; 14,49] 0,1112[2]	4,38 [0,76; 25,20] 0,1202[4]	22,1 [-2,3; 46,4] 0,1202[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Skin and subcutaneous tissue disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,6052)					
Neoadjuvant chemotherapy	88/217 (40,6)	40/219 (18,3)	2,22 [1,61; 3,07] <,0001[2]	3,05 [1,97; 4,73] <,0001[3]	22,3 [14,0; 30,6] <,0001[3]
Adjuvant chemotherapy	126/327 (38,5)	66/312 (21,2)	1,82 [1,41; 2,35] <,0001[2]	2,34 [1,64; 3,32] <,0001[3]	17,4 [10,4; 24,3] <,0001[3]
No chemotherapy	6/9 (66,7)	1/4 (25,0)	2,67 [0,46; 15,49] 0,2745[2]	6,00 [0,42; 85,25] 0,2657[4]	41,7 [-10,8; 94,1] 0,2657[4]
Region (Interaction p-value: 0,8553)					
North America / Europe	113/252 (44,8)	53/233 (22,7)	1,97 [1,50; 2,59] <,0001[2]	2,76 [1,86; 4,10] <,0001[3]	22,1 [13,9; 30,3] <,0001[3]
Asia	80/168 (47,6)	42/166 (25,3)	1,88 [1,39; 2,56] <,0001[2]	2,68 [1,69; 4,26] <,0001[3]	22,3 [12,3; 32,4] <,0001[3]
Other	27/133 (20,3)	12/136 (8,8)	2,30 [1,22; 4,35] 0,0103[2]	2,63 [1,27; 5,45] 0,0075[3]	11,5 [3,1; 19,8] 0,0075[3]
Primary tumor size (Interaction p-value: 0,3600)					
< 20 mm	55/141 (39,0)	23/140 (16,4)	2,37 [1,55; 3,64] <,0001[2]	3,25 [1,86; 5,70] <,0001[3]	22,6 [12,5; 32,7] <,0001[3]
≥ 20 but < 50 mm	97/255 (38,0)	46/249 (18,5)	2,06 [1,52; 2,79] <,0001[2]	2,71 [1,80; 4,07] <,0001[3]	19,6 [11,9; 27,2] <,0001[3]
≥ 50 mm	62/145 (42,8)	37/141 (26,2)	1,63 [1,17; 2,28] 0,0043[2]	2,10 [1,27; 3,46] 0,0033[3]	16,5 [5,7; 27,4] 0,0033[3]
Number of positive lymph nodes (Interaction p-value: 0,9321)					
0-3	84/203 (41,4)	45/214 (21,0)	1,97 [1,45; 2,67] <,0001[2]	2,65 [1,72; 4,08] <,0001[3]	20,4 [11,7; 29,1] <,0001[3]
4-9	99/242 (40,9)	48/231 (20,8)	1,97 [1,47; 2,64] <,0001[2]	2,64 [1,75; 3,97] <,0001[3]	20,1 [12,0; 28,2] <,0001[3]
≥ 10	37/108 (34,3)	14/90 (15,6)	2,20 [1,27; 3,81] 0,0047[2]	2,83 [1,41; 5,67] 0,0027[3]	18,7 [7,0; 30,4] 0,0027[3]
Tumor stage (Interaction p-value: 0,8156)					
IIA	22/59 (37,3)	9/62 (14,5)	2,57 [1,29; 5,11] 0,0073[2]	3,50 [1,45; 8,46] 0,0041[3]	22,8 [7,6; 37,9] 0,0041[3]
IIB	22/53 (41,5)	16/69 (23,2)	1,79 [1,05; 3,06] 0,0330[2]	2,35 [1,08; 5,14] 0,0303[3]	18,3 [1,7; 34,9] 0,0303[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	96/236 (40,7)	43/214 (20,1)	2,02 [1,49; 2,76] <,0001[2]	2,73 [1,79; 4,16] <,0001[3]	20,6 [12,3; 28,8] <,0001[3]
IIIB	8/18 (44,4)	2/15 (13,3)	3,33 [0,83; 13,38] 0,0895[2]	5,20 [0,90; 30,08] 0,0696[4]	31,1 [2,4; 59,8] 0,0696[4]
IIIC	71/186 (38,2)	37/174 (21,3)	1,80 [1,28; 2,52] 0,0007[2]	2,29 [1,43; 3,65] 0,0005[3]	16,9 [7,6; 26,2] 0,0005[3]
Tumor grade (Interaction p-value: 0,7140)					
G1	21/47 (44,7)	7/41 (17,1)	2,62 [1,24; 5,52] 0,0115[2]	3,92 [1,45; 10,62] 0,0055[3]	27,6 [9,3; 45,9] 0,0055[3]
G2	101/244 (41,4)	47/234 (20,1)	2,06 [1,53; 2,77] <,0001[2]	2,81 [1,87; 4,23] <,0001[3]	21,3 [13,3; 29,3] <,0001[3]
G3	88/233 (37,8)	45/226 (19,9)	1,90 [1,39; 2,58] <,0001[2]	2,44 [1,60; 3,72] <,0001[3]	17,9 [9,7; 26,0] <,0001[3]
GX	10/29 (34,5)	8/33 (24,2)	1,42 [0,65; 3,12] 0,3787[2]	1,64 [0,54; 4,96] 0,3754[3]	10,2 [-12,4; 32,9] 0,3754[3]
Progesterone receptor status (Interaction p-value: 0,7396)					
Negative	13/49 (26,5)	7/44 (15,9)	1,67 [0,73; 3,80] 0,2237[2]	1,91 [0,68; 5,33] 0,2132[3]	10,6 [-5,8; 27,0] 0,2132[3]
Positive	196/477 (41,1)	98/471 (20,8)	1,97 [1,61; 2,43] <,0001[2]	2,65 [1,99; 3,54] <,0001[3]	20,3 [14,5; 26,0] <,0001[3]
Unknown	2/4 (50,0)	1/8 (12,5)	4,00 [0,50; 31,98] 0,1912[2]	7,00 [0,40; 123,35] 0,2364[4]	37,5 [-16,6; 91,6] 0,2364[4]
Race (Interaction p-value: 0,3934)					
White	112/323 (34,7)	61/324 (18,8)	1,84 [1,40; 2,42] <,0001[2]	2,29 [1,60; 3,28] <,0001[3]	15,8 [9,1; 22,6] <,0001[3]
Asian	90/199 (45,2)	42/180 (23,3)	1,94 [1,43; 2,63] <,0001[2]	2,71 [1,74; 4,23] <,0001[3]	21,9 [12,6; 31,2] <,0001[3]
Other	9/19 (47,4)	2/21 (9,5)	4,97 [1,23; 20,19] 0,0248[2]	8,55 [1,54; 47,41] 0,0074[3]	37,8 [12,1; 63,6] 0,0074[3]
ECOG-PS (Interaction p-value: 0,6750)					
ECOG-PS 0	203/496 (40,9)	100/480 (20,8)	1,96 [1,60; 2,41] <,0001[2]	2,63 [1,98; 3,50] <,0001[3]	20,1 [14,4; 25,7] <,0001[3]
ECOG-PS 1	17/57 (29,8)	7/55 (12,7)	2,34 [1,05; 5,21] 0,0366[2]	2,91 [1,10; 7,73] 0,0275[3]	17,1 [2,3; 31,9] 0,0275[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Alanine aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,9563)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	9/477 (1,9)	1/471 (0,2)	8,89 [1,13; 69,87] 0,0379[2]	9,04 [1,14; 71,62] 0,0209[4]	1,7 [0,4; 3,0] 0,0209[4]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9725)					
ECOG-PS 0	10/496 (2,0)	0/480 (0,0)	20,32 [1,19; 345,87] 0,0373[2]	20,74 [1,21; 354,94] 0,0019[4]	2,0 [0,8; 3,3] 0,0019[4]
ECOG-PS 1	1/57 (1,8)	1/55 (1,8)	0,96 [0,06; 15,05] 0,9797[2]	0,96 [0,06; 15,81] 1,0000[4]	-0,1 [-5,0; 4,8] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Diarrhoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9380)					
Neoadjuvant chemotherapy	10/217 (4,6)	0/219 (0,0)	21,19 [1,25; 359,42] 0,0345[2]	22,21 [1,29; 381,50] 0,0008[4]	4,6 [1,8; 7,4] 0,0008[4]
Adjuvant chemotherapy	18/327 (5,5)	2/312 (0,6)	8,59 [2,01; 36,70] 0,0037[2]	9,03 [2,08; 39,24] 0,0004[3]	4,9 [2,2; 7,5] 0,0004[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,7188)					
North America / Europe	18/252 (7,1)	1/233 (0,4)	16,64 [2,24; 123,69] 0,0060[2]	17,85 [2,36; 134,78] 0,0001[3]	6,7 [3,4; 10,0] 0,0001[3]
Asia	5/168 (3,0)	1/166 (0,6)	4,94 [0,58; 41,84] 0,1428[2]	5,06 [0,58; 43,80] 0,2146[4]	2,4 [-0,5; 5,2] 0,2146[4]
Other	7/133 (5,3)	0/136 (0,0)	15,34 [0,88; 265,86] 0,0607[2]	16,19 [0,92; 286,30] 0,0067[4]	5,3 [1,5; 9,1] 0,0067[4]
Primary tumor size (Interaction p-value: 0,9829)					
< 20 mm	9/141 (6,4)	1/140 (0,7)	8,94 [1,15; 69,60] 0,0365[2]	9,48 [1,18; 75,84] 0,0193[4]	5,7 [1,4; 9,9] 0,0193[4]
≥ 20 but < 50 mm	13/255 (5,1)	0/249 (0,0)	26,37 [1,58; 441,16] 0,0228[2]	27,78 [1,64; 469,89] 0,0003[3]	5,1 [2,4; 7,8] 0,0003[3]
≥ 50 mm	7/145 (4,8)	1/141 (0,7)	6,81 [0,85; 54,62] 0,0711[2]	7,10 [0,86; 58,48] 0,0667[4]	4,1 [0,4; 7,9] 0,0667[4]
Number of positive lymph nodes (Interaction p-value: 0,9318)					
0-3	11/203 (5,4)	1/214 (0,5)	11,60 [1,51; 89,01] 0,0184[2]	12,20 [1,56; 95,40] 0,0025[3]	5,0 [1,7; 8,2] 0,0025[3]
4-9	11/242 (4,5)	0/231 (0,0)	21,96 [1,30; 370,51] 0,0321[2]	23,00 [1,35; 392,59] 0,0010[3]	4,5 [1,9; 7,2] 0,0010[3]
≥ 10	8/108 (7,4)	1/90 (1,1)	6,67 [0,85; 52,30] 0,0711[2]	7,12 [0,87; 58,05] 0,0417[4]	6,3 [0,9; 11,7] 0,0417[4]
Tumor stage (Interaction p-value: 0,9038)					
IIA	4/59 (6,8)	1/62 (1,6)	4,20 [0,48; 36,53] 0,1930[2]	4,44 [0,48; 40,90] 0,1997[4]	5,2 [-2,0; 12,3] 0,1997[4]
IIB	2/53 (3,8)	0/69 (0,0)	6,48 [0,32; 132,22] 0,2245[2]	6,75 [0,32; 143,57] 0,1867[4]	3,8 [-1,4; 8,9] 0,1867[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	9/236 (3,8)	0/214 (0,0)	17,24 [1,01; 294,37] 0,0493[2]	17,91 [1,04; 309,68] 0,0039[4]	3,8 [1,4; 6,3] 0,0039[4]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	14/186 (7,5)	1/174 (0,6)	13,10 [1,74; 98,55] 0,0125[2]	14,08 [1,83; 108,26] 0,0010[3]	7,0 [3,0; 10,9] 0,0010[3]
Tumor grade (Interaction p-value: 0,2012)					
G1	0/47 (0,0)	0/41 (0,0)	NE	NE	NE
G2	14/244 (5,7)	1/234 (0,4)	13,43 [1,78; 101,29] 0,0118[2]	14,18 [1,85; 108,74] 0,0009[3]	5,3 [2,3; 8,3] 0,0009[3]
G3	16/233 (6,9)	1/226 (0,4)	15,52 [2,08; 116,06] 0,0076[2]	16,59 [2,18; 126,17] 0,0003[3]	6,4 [3,1; 9,8] 0,0003[3]
GX	0/29 (0,0)	0/33 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9940)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	27/477 (5,7)	1/471 (0,2)	26,66 [3,64; 195,40] 0,0012[2]	28,20 [3,82; 208,39] <,0001[3]	5,4 [3,3; 7,6] <,0001[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,5692)					
White	22/323 (6,8)	1/324 (0,3)	22,07 [2,99; 162,75] 0,0024[2]	23,61 [3,16; 176,22] <,0001[3]	6,5 [3,7; 9,3] <,0001[3]
Asian	5/199 (2,5)	1/180 (0,6)	4,52 [0,53; 38,35] 0,1664[2]	4,61 [0,53; 39,87] 0,2186[4]	2,0 [-0,5; 4,4] 0,2186[4]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Leukopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,9933)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	13/477 (2,7)	0/471 (0,0)	26,66 [1,59; 447,20] 0,0225[2]	27,41 [1,62; 462,37] 0,0003[3]	2,7 [1,3; 4,2] 0,0003[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9998)					
White	10/323 (3,1)	0/324 (0,0)	21,06 [1,24; 357,98] 0,0350[2]	21,74 [1,27; 372,52] 0,0009[4]	3,1 [1,2; 5,0] 0,0009[4]
Asian	3/199 (1,5)	0/180 (0,0)	6,34 [0,33; 121,81] 0,2210[2]	6,43 [0,33; 125,34] 0,2499[4]	1,5 [-0,2; 3,2] 0,2499[4]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Lymphocyte count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9959)					
Neoadjuvant chemotherapy	9/217 (4,1)	0/219 (0,0)	19,17 [1,12; 327,41] 0,0413[2]	20,00 [1,16; 345,84] 0,0017[4]	4,1 [1,5; 6,8] 0,0017[4]
Adjuvant chemotherapy	14/327 (4,3)	0/312 (0,0)	27,67 [1,66; 461,93] 0,0208[2]	28,91 [1,72; 486,70] 0,0002[3]	4,3 [2,1; 6,5] 0,0002[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Tumor stage (Interaction p-value: 0,9999)					
IIA	5/59 (8,5)	0/62 (0,0)	11,55 [0,65; 204,40] 0,0951[2]	12,61 [0,68; 233,37] 0,0252[4]	8,5 [1,4; 15,6] 0,0252[4]
IIB	3/53 (5,7)	0/69 (0,0)	9,07 [0,48; 171,96] 0,1417[2]	9,63 [0,49; 190,67] 0,0793[4]	5,7 [-0,6; 11,9] 0,0793[4]
IIIA	15/236 (6,4)	0/214 (0,0)	28,12 [1,69; 467,16] 0,0200[2]	30,02 [1,79; 504,86] 0,0002[3]	6,4 [3,2; 9,5] 0,0002[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	0/186 (0,0)	0/174 (0,0)	NE	NE	NE
Tumor grade (Interaction p-value: 1,0000)					
G1	3/47 (6,4)	0/41 (0,0)	6,13 [0,33; 115,18] 0,2260[2]	6,53 [0,33; 130,23] 0,2449[4]	6,4 [-0,6; 13,4] 0,2449[4]
G2	10/244 (4,1)	0/234 (0,0)	20,14 [1,19; 341,80] 0,0376[2]	21,00 [1,22; 360,44] 0,0018[4]	4,1 [1,6; 6,6] 0,0018[4]
G3	7/233 (3,0)	0/226 (0,0)	14,55 [0,84; 253,30] 0,0662[2]	15,00 [0,85; 264,19] 0,0150[4]	3,0 [0,8; 5,2] 0,0150[4]
GX	4/29 (13,8)	0/33 (0,0)	10,20 [0,57; 181,74] 0,1140[2]	11,82 [0,61; 229,73] 0,0426[4]	13,8 [1,2; 26,3] 0,0426[4]
Progesterone receptor status (Interaction p-value: 0,9933)					
Negative	1/49 (2,0)	0/44 (0,0)	2,70 [0,11; 64,61] 0,5398[2]	2,75 [0,11; 69,33] 1,0000[4]	2,0 [-1,9; 6,0] 1,0000[4]
Positive	20/477 (4,2)	0/471 (0,0)	40,49 [2,46; 667,45] 0,0096[2]	42,25 [2,55; 700,69] <,0001[3]	4,2 [2,4; 6,0] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi²-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Neutropenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8872)					
Neoadjuvant chemotherapy	23/217 (10,6)	4/219 (1,8)	5,80 [2,04; 16,50] 0,0010[2]	6,37 [2,17; 18,75] 0,0001[3]	8,8 [4,3; 13,2] 0,0001[3]
Adjuvant chemotherapy	19/327 (5,8)	2/312 (0,6)	9,06 [2,13; 38,59] 0,0029[2]	9,56 [2,21; 41,40] 0,0002[3]	5,2 [2,5; 7,9] 0,0002[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,6076)					
North America / Europe	18/252 (7,1)	3/233 (1,3)	5,55 [1,66; 18,59] 0,0055[2]	5,90 [1,71; 20,29] 0,0015[3]	5,9 [2,4; 9,3] 0,0015[3]
Asia	9/168 (5,4)	2/166 (1,2)	4,45 [0,98; 20,27] 0,0539[2]	4,64 [0,99; 21,82] 0,0335[3]	4,2 [0,4; 7,9] 0,0335[3]
Other	15/133 (11,3)	1/136 (0,7)	15,34 [2,05; 114,48] 0,0078[2]	17,16 [2,23; 131,88] 0,0003[3]	10,5 [5,0; 16,1] 0,0003[3]
Primary tumor size (Interaction p-value: 0,1417)					
< 20 mm	10/141 (7,1)	4/140 (2,9)	2,48 [0,80; 7,73] 0,1166[2]	2,60 [0,79; 8,48] 0,1028[3]	4,2 [-0,8; 9,3] 0,1028[3]
≥ 20 but < 50 mm	19/255 (7,5)	1/249 (0,4)	18,55 [2,50; 137,54] 0,0043[2]	19,97 [2,65; 150,33] <,0001[3]	7,0 [3,7; 10,4] <,0001[3]
≥ 50 mm	13/145 (9,0)	1/141 (0,7)	12,64 [1,68; 95,36] 0,0139[2]	13,79 [1,78; 106,87] 0,0012[3]	8,3 [3,4; 13,1] 0,0012[3]
Number of positive lymph nodes (Interaction p-value: 0,5028)					
0-3	18/203 (8,9)	2/214 (0,9)	9,49 [2,23; 40,37] 0,0023[2]	10,31 [2,36; 45,04] 0,0002[3]	7,9 [3,8; 12,0] 0,0002[3]
4-9	17/242 (7,0)	2/231 (0,9)	8,11 [1,90; 34,73] 0,0048[2]	8,65 [1,98; 37,88] 0,0006[3]	6,2 [2,7; 9,6] 0,0006[3]
≥ 10	7/108 (6,5)	2/90 (2,2)	2,92 [0,62; 13,69] 0,1749[2]	3,05 [0,62; 15,06] 0,1862[4]	4,3 [-1,3; 9,8] 0,1862[4]
Tumor stage (Interaction p-value: 0,9836)					
IIA	6/59 (10,2)	1/62 (1,6)	6,31 [0,78; 50,81] 0,0837[2]	6,91 [0,81; 59,21] 0,0574[4]	8,6 [0,2; 16,9] 0,0574[4]
IIB	4/53 (7,5)	1/69 (1,4)	5,21 [0,60; 45,24] 0,1347[2]	5,55 [0,60; 51,21] 0,1655[4]	6,1 [-1,6; 13,7] 0,1655[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	12/236 (5,1)	1/214 (0,5)	10,88 [1,43; 82,98] 0,0213[2]	11,41 [1,47; 88,51] 0,0035[3]	4,6 [1,7; 7,6] 0,0035[3]
IIIB	3/18 (16,7)	0/15 (0,0)	5,89 [0,33; 105,81] 0,2285[2]	7,00 [0,33; 147,17] 0,2330[4]	16,7 [-0,5; 33,9] 0,2330[4]
IIIC	17/186 (9,1)	3/174 (1,7)	5,30 [1,58; 17,77] 0,0069[2]	5,73 [1,65; 19,93] 0,0021[3]	7,4 [2,8; 12,0] 0,0021[3]
Tumor grade (Interaction p-value: 0,9163)					
G1	2/47 (4,3)	0/41 (0,0)	4,38 [0,22; 88,58] 0,3362[2]	4,56 [0,21; 97,79] 0,4966[4]	4,3 [-1,5; 10,0] 0,4966[4]
G2	20/244 (8,2)	4/234 (1,7)	4,80 [1,66; 13,82] 0,0037[2]	5,13 [1,73; 15,26] 0,0012[3]	6,5 [2,7; 10,3] 0,0012[3]
G3	19/233 (8,2)	2/226 (0,9)	9,21 [2,17; 39,11] 0,0026[2]	9,94 [2,29; 43,21] 0,0002[3]	7,3 [3,5; 11,0] 0,0002[3]
GX	1/29 (3,4)	0/33 (0,0)	3,40 [0,14; 80,36] 0,4482[2]	3,53 [0,14; 89,98] 0,4677[4]	3,4 [-3,2; 10,1] 0,4677[4]
Progesterone receptor status (Interaction p-value: 0,2850)					
Negative	4/49 (8,2)	1/44 (2,3)	3,59 [0,42; 30,93] 0,2445[2]	3,82 [0,41; 35,58] 0,3650[4]	5,9 [-3,0; 14,7] 0,3650[4]
Positive	38/477 (8,0)	5/471 (1,1)	7,50 [2,98; 18,90] <,0001[2]	8,07 [3,15; 20,68] <,0001[3]	6,9 [4,3; 9,5] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,3055)					
White	30/323 (9,3)	3/324 (0,9)	10,03 [3,09; 32,54] 0,0001[2]	10,96 [3,31; 36,28] <,0001[3]	8,4 [5,0; 11,7] <,0001[3]
Asian	10/199 (5,0)	2/180 (1,1)	4,52 [1,00; 20,37] 0,0493[2]	4,71 [1,02; 21,79] 0,0298[3]	3,9 [0,5; 7,3] 0,0298[3]
Other	1/19 (5,3)	1/21 (4,8)	1,11 [0,07; 16,47] 0,9421[2]	1,11 [0,06; 19,09] 1,0000[4]	0,5 [-13,1; 14,1] 1,0000[4]
ECOG-PS (Interaction p-value: 0,1163)					
ECOG-PS 0	38/496 (7,7)	4/480 (0,8)	9,19 [3,31; 25,56] <,0001[2]	9,87 [3,50; 27,88] <,0001[3]	6,8 [4,3; 9,3] <,0001[3]
ECOG-PS 1	4/57 (7,0)	2/55 (3,6)	1,93 [0,37; 10,11] 0,4366[2]	2,00 [0,35; 11,39] 0,6791[4]	3,4 [-4,9; 11,7] 0,6791[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Neutrophil count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,2748)					
Neoadjuvant chemotherapy	21/217 (9,7)	4/219 (1,8)	5,30 [1,85; 15,18] 0,0019[2]	5,76 [1,94; 17,07] 0,0004[3]	7,9 [3,5; 12,2] 0,0004[3]
Adjuvant chemotherapy	35/327 (10,7)	1/312 (0,3)	33,39 [4,60; 242,28] 0,0005[2]	37,28 [5,07; 273,84] <,0001[3]	10,4 [7,0; 13,8] <,0001[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,7296)					
North America / Europe	13/252 (5,2)	2/233 (0,9)	6,01 [1,37; 26,35] 0,0174[2]	6,28 [1,40; 28,15] 0,0063[3]	4,3 [1,3; 7,3] 0,0063[3]
Asia	39/168 (23,2)	3/166 (1,8)	12,85 [4,05; 40,75] <,0001[2]	16,43 [4,96; 54,36] <,0001[3]	21,4 [14,7; 28,1] <,0001[3]
Other	5/133 (3,8)	0/136 (0,0)	11,25 [0,63; 201,40] 0,1002[2]	11,68 [0,64; 213,44] 0,0284[4]	3,8 [0,5; 7,0] 0,0284[4]
Primary tumor size (Interaction p-value: 0,3257)					
< 20 mm	17/141 (12,1)	1/140 (0,7)	16,88 [2,28; 125,12] 0,0057[2]	19,06 [2,50; 145,28] 0,0001[3]	11,3 [5,8; 16,9] 0,0001[3]
≥ 20 but < 50 mm	24/255 (9,4)	1/249 (0,4)	23,44 [3,19; 171,91] 0,0019[2]	25,77 [3,46; 191,99] <,0001[3]	9,0 [5,3; 12,7] <,0001[3]
≥ 50 mm	15/145 (10,3)	3/141 (2,1)	4,86 [1,44; 16,43] 0,0109[2]	5,31 [1,50; 18,76] 0,0042[3]	8,2 [2,7; 13,7] 0,0042[3]
Number of positive lymph nodes (Interaction p-value: 0,6515)					
0-3	22/203 (10,8)	1/214 (0,5)	23,19 [3,16; 170,48] 0,0020[2]	25,89 [3,46; 193,95] <,0001[3]	10,4 [6,0; 14,7] <,0001[3]
4-9	25/242 (10,3)	3/231 (1,3)	7,95 [2,43; 25,99] 0,0006[2]	8,76 [2,61; 29,42] <,0001[3]	9,0 [4,9; 13,1] <,0001[3]
≥ 10	10/108 (9,3)	1/90 (1,1)	8,33 [1,09; 63,86] 0,0413[2]	9,08 [1,14; 72,37] 0,0127[3]	8,1 [2,3; 14,0] 0,0127[3]
Tumor stage (Interaction p-value: 0,9494)					
IIA	4/59 (6,8)	1/62 (1,6)	4,20 [0,48; 36,53] 0,1930[2]	4,44 [0,48; 40,90] 0,1997[4]	5,2 [-2,0; 12,3] 0,1997[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIB	7/53 (13,2)	0/69 (0,0)	19,44 [1,14; 333,01] 0,0406[2]	22,42 [1,25; 402,07] 0,0023[4]	13,2 [4,1; 22,3] 0,0023[4]
IIIA	27/236 (11,4)	2/214 (0,9)	12,24 [2,95; 50,87] 0,0006[2]	13,69 [3,22; 58,32] <,0001[3]	10,5 [6,2; 14,8] <,0001[3]
IIIB	3/18 (16,7)	0/15 (0,0)	5,89 [0,33; 105,81] 0,2285[2]	7,00 [0,33; 147,17] 0,2330[4]	16,7 [-0,5; 33,9] 0,2330[4]
IIIC	15/186 (8,1)	2/174 (1,1)	7,02 [1,63; 30,24] 0,0090[2]	7,54 [1,70; 33,49] 0,0020[3]	6,9 [2,7; 11,1] 0,0020[3]
Tumor grade (Interaction p-value: 0,7170)					
G1	12/47 (25,5)	0/41 (0,0)	21,88 [1,34; 358,36] 0,0306[2]	29,23 [1,67; 511,34] 0,0005[3]	25,5 [13,1; 38,0] 0,0005[3]
G2	22/244 (9,0)	2/234 (0,9)	10,55 [2,51; 44,36] 0,0013[2]	11,50 [2,67; 49,46] <,0001[3]	8,2 [4,4; 11,9] <,0001[3]
G3	21/233 (9,0)	2/226 (0,9)	10,18 [2,42; 42,93] 0,0016[2]	11,09 [2,57; 47,89] <,0001[3]	8,1 [4,3; 12,0] <,0001[3]
GX	2/29 (6,9)	1/33 (3,0)	2,28 [0,22; 23,82] 0,4924[2]	2,37 [0,20; 27,59] 0,5951[4]	3,9 [-7,1; 14,8] 0,5951[4]
Progesterone receptor status (Interaction p-value: 0,1534)					
Negative	6/49 (12,2)	1/44 (2,3)	5,39 [0,67; 43,02] 0,1121[2]	6,00 [0,69; 51,96] 0,1146[4]	10,0 [-0,2; 20,2] 0,1146[4]
Positive	50/477 (10,5)	4/471 (0,8)	12,34 [4,49; 33,90] <,0001[2]	13,67 [4,90; 38,17] <,0001[3]	9,6 [6,8; 12,5] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9121)					
White	16/323 (5,0)	2/324 (0,6)	8,02 [1,86; 34,62] 0,0052[2]	8,39 [1,91; 36,80] 0,0008[3]	4,3 [1,8; 6,9] 0,0008[3]
Asian	40/199 (20,1)	3/180 (1,7)	12,06 [3,80; 38,31] <,0001[2]	14,84 [4,50; 48,92] <,0001[3]	18,4 [12,6; 24,3] <,0001[3]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,9801)					
ECOG-PS 0	53/496 (10,7)	5/480 (1,0)	10,26 [4,14; 25,44] <,0001[2]	11,37 [4,50; 28,69] <,0001[3]	9,6 [6,8; 12,5] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	4/57 (7,0)	0/55 (0,0)	8,69 [0,48; 157,70] 0,1437[2]	9,34 [0,49; 177,63] 0,1185[4]	7,0 [0,4; 13,6] 0,1185[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT White blood cell count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8768)					
Neoadjuvant chemotherapy	20/217 (9,2)	3/219 (1,4)	6,73 [2,03; 22,31] 0,0018[2]	7,31 [2,14; 24,98] 0,0002[3]	7,8 [3,7; 12,0] 0,0002[3]
Adjuvant chemotherapy	23/327 (7,0)	2/312 (0,6)	10,97 [2,61; 46,15] 0,0011[2]	11,73 [2,74; 50,17] <,0001[3]	6,4 [3,5; 9,3] <,0001[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,9973)					
North America / Europe	16/252 (6,3)	2/233 (0,9)	7,40 [1,72; 31,82] 0,0072[2]	7,83 [1,78; 34,44] 0,0014[3]	5,5 [2,3; 8,7] 0,0014[3]
Asia	24/168 (14,3)	3/166 (1,8)	7,90 [2,43; 25,75] 0,0006[2]	9,06 [2,67; 30,70] <,0001[3]	12,5 [6,8; 18,1] <,0001[3]
Other	4/133 (3,0)	0/136 (0,0)	9,20 [0,50; 169,25] 0,1352[2]	9,49 [0,51; 177,95] 0,0584[4]	3,0 [0,1; 5,9] 0,0584[4]
Primary tumor size (Interaction p-value: 0,3551)					
< 20 mm	11/141 (7,8)	2/140 (1,4)	5,46 [1,23; 24,19] 0,0254[2]	5,84 [1,27; 26,84] 0,0110[3]	6,4 [1,5; 11,2] 0,0110[3]
≥ 20 but < 50 mm	24/255 (9,4)	1/249 (0,4)	23,44 [3,19; 171,91] 0,0019[2]	25,77 [3,46; 191,99] <,0001[3]	9,0 [5,3; 12,7] <,0001[3]
≥ 50 mm	8/145 (5,5)	2/141 (1,4)	3,89 [0,84; 18,00] 0,0823[2]	4,06 [0,85; 19,46] 0,1036[4]	4,1 [-0,1; 8,3] 0,1036[4]
Number of positive lymph nodes (Interaction p-value: 0,9814)					
0-3	17/203 (8,4)	0/214 (0,0)	36,89 [2,23; 609,39] 0,0117[2]	40,25 [2,40; 673,98] <,0001[3]	8,4 [4,6; 12,2] <,0001[3]
4-9	22/242 (9,1)	4/231 (1,7)	5,25 [1,84; 15,00] 0,0020[2]	5,68 [1,92; 16,73] 0,0004[3]	7,4 [3,4; 11,4] 0,0004[3]
≥ 10	5/108 (4,6)	1/90 (1,1)	4,17 [0,50; 35,02] 0,1889[2]	4,32 [0,50; 37,68] 0,2233[4]	3,5 [-1,0; 8,0] 0,2233[4]
Tumor stage (Interaction p-value: 0,7443)					
IIA	4/59 (6,8)	0/62 (0,0)	9,45 [0,52; 171,79] 0,1291[2]	10,14 [0,53; 192,49] 0,0536[4]	6,8 [0,4; 13,2] 0,0536[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIB	8/53 (15,1)	0/69 (0,0)	22,04 [1,30; 373,42] 0,0322[2]	25,97 [1,46; 460,99] 0,0009[4]	15,1 [5,5; 24,7] 0,0009[4]
IIIA	22/236 (9,3)	2/214 (0,9)	9,97 [2,37; 41,92] 0,0017[2]	10,90 [2,53; 46,92] <,0001[3]	8,4 [4,5; 12,3] <,0001[3]
IIIB	1/18 (5,6)	0/15 (0,0)	2,53 [0,11; 57,83] 0,5618[2]	2,66 [0,10; 70,11] 1,0000[4]	5,6 [-5,0; 16,1] 1,0000[4]
IIIC	8/186 (4,3)	3/174 (1,7)	2,49 [0,67; 9,25] 0,1716[2]	2,56 [0,67; 9,82] 0,1557[3]	2,6 [-0,9; 6,1] 0,1557[3]
Tumor grade (Interaction p-value: 0,8083)					
G1	8/47 (17,0)	0/41 (0,0)	14,88 [0,88; 250,04] 0,0608[2]	17,86 [1,00; 319,85] 0,0064[4]	17,0 [6,3; 27,8] 0,0064[4]
G2	15/244 (6,1)	3/234 (1,3)	4,80 [1,41; 16,35] 0,0122[2]	5,04 [1,44; 17,66] 0,0052[3]	4,9 [1,5; 8,2] 0,0052[3]
G3	16/233 (6,9)	1/226 (0,4)	15,52 [2,08; 116,06] 0,0076[2]	16,59 [2,18; 126,17] 0,0003[3]	6,4 [3,1; 9,8] 0,0003[3]
GX	5/29 (17,2)	1/33 (3,0)	5,69 [0,70; 45,92] 0,1027[2]	6,67 [0,73; 60,85] 0,0895[4]	14,2 [-0,7; 29,2] 0,0895[4]
Progesterone receptor status (Interaction p-value: 0,9594)					
Negative	2/49 (4,1)	0/44 (0,0)	4,50 [0,22; 91,25] 0,3273[2]	4,68 [0,22; 100,28] 0,4960[4]	4,1 [-1,5; 9,6] 0,4960[4]
Positive	38/477 (8,0)	5/471 (1,1)	7,50 [2,98; 18,90] <,0001[2]	8,07 [3,15; 20,68] <,0001[3]	6,9 [4,3; 9,5] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9590)					
White	19/323 (5,9)	2/324 (0,6)	9,53 [2,24; 40,58] 0,0023[2]	10,06 [2,32; 43,56] 0,0002[3]	5,3 [2,6; 8,0] 0,0002[3]
Asian	24/199 (12,1)	3/180 (1,7)	7,24 [2,22; 23,62] 0,0010[2]	8,09 [2,39; 27,36] <,0001[3]	10,4 [5,5; 15,3] <,0001[3]
Other	1/19 (5,3)	0/21 (0,0)	3,30 [0,14; 76,46] 0,4565[2]	3,49 [0,13; 90,86] 0,4750[4]	5,3 [-4,8; 15,3] 0,4750[4]
ECOG-PS (Interaction p-value: 0,4508)					
ECOG-PS 0	40/496 (8,1)	4/480 (0,8)	9,68 [3,49; 26,84] <,0001[2]	10,44 [3,71; 29,41] <,0001[3]	7,2 [4,7; 9,8] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	4/57 (7,0)	1/55 (1,8)	3,86 [0,45; 33,46] 0,2203[2]	4,08 [0,44; 37,67] 0,3640[4]	5,2 [-2,3; 12,7] 0,3640[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Blood and lymphatic system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9971)					
Neoadjuvant chemotherapy	31/217 (14,3)	4/219 (1,8)	7,82 [2,81; 21,78] <,0001[2]	8,96 [3,10; 25,85] <,0001[3]	12,5 [7,5; 17,4] <,0001[3]
Adjuvant chemotherapy	31/327 (9,5)	4/312 (1,3)	7,39 [2,64; 20,71] 0,0001[2]	8,06 [2,81; 23,12] <,0001[3]	8,2 [4,8; 11,6] <,0001[3]
No chemotherapy	0/9 (0,0)	0/4 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,6315)					
North America / Europe	22/252 (8,7)	4/233 (1,7)	5,09 [1,78; 14,54] 0,0024[2]	5,48 [1,86; 16,14] 0,0006[3]	7,0 [3,1; 10,9] 0,0006[3]
Asia	17/168 (10,1)	2/166 (1,2)	8,40 [1,97; 35,78] 0,0040[2]	9,23 [2,10; 40,63] 0,0004[3]	8,9 [4,1; 13,8] 0,0004[3]
Other	23/133 (17,3)	2/136 (1,5)	11,76 [2,83; 48,89] 0,0007[2]	14,01 [3,23; 60,73] <,0001[3]	15,8 [9,1; 22,6] <,0001[3]
Primary tumor size (Interaction p-value: 0,3662)					
< 20 mm	16/141 (11,3)	4/140 (2,9)	3,97 [1,36; 11,58] 0,0116[2]	4,35 [1,42; 13,37] 0,0056[3]	8,5 [2,6; 14,4] 0,0056[3]
≥ 20 but < 50 mm	28/255 (11,0)	2/249 (0,8)	13,67 [3,29; 56,78] 0,0003[2]	15,23 [3,59; 64,67] <,0001[3]	10,2 [6,2; 14,2] <,0001[3]
≥ 50 mm	18/145 (12,4)	2/141 (1,4)	8,75 [2,07; 37,03] 0,0032[2]	9,85 [2,24; 43,30] 0,0003[3]	11,0 [5,3; 16,7] 0,0003[3]
Number of positive lymph nodes (Interaction p-value: 0,9861)					
0-3	22/203 (10,8)	3/214 (1,4)	7,73 [2,35; 25,43] 0,0008[2]	8,55 [2,52; 29,03] <,0001[3]	9,4 [4,9; 14,0] <,0001[3]
4-9	24/242 (9,9)	3/231 (1,3)	7,64 [2,33; 25,02] 0,0008[2]	8,37 [2,48; 28,19] <,0001[3]	8,6 [4,6; 12,7] <,0001[3]
≥ 10	16/108 (14,8)	2/90 (2,2)	6,67 [1,57; 28,23] 0,0100[2]	7,65 [1,71; 34,25] 0,0021[3]	12,6 [5,2; 20,0] 0,0021[3]
Tumor stage (Interaction p-value: 0,8954)					
IIA	8/59 (13,6)	1/62 (1,6)	8,41 [1,08; 65,18] 0,0416[2]	9,57 [1,16; 79,07] 0,0151[4]	11,9 [2,7; 21,2] 0,0151[4]
IIB	5/53 (9,4)	2/69 (2,9)	3,25 [0,66; 16,13] 0,1484[2]	3,49 [0,65; 18,75] 0,2374[4]	6,5 [-2,3; 15,3] 0,2374[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	16/236 (6,8)	2/214 (0,9)	7,25 [1,69; 31,18] 0,0077[2]	7,71 [1,75; 33,93] 0,0016[3]	5,8 [2,4; 9,3] 0,0016[3]
IIIB	4/18 (22,2)	0/15 (0,0)	7,58 [0,44; 130,38] 0,1629[2]	9,62 [0,48; 194,83] 0,1081[4]	22,2 [3,0; 41,4] 0,1081[4]
IIIC	29/186 (15,6)	3/174 (1,7)	9,04 [2,81; 29,15] 0,0002[2]	10,53 [3,15; 35,25] <,0001[3]	13,9 [8,3; 19,4] <,0001[3]
Tumor grade (Interaction p-value: 0,9994)					
G1	5/47 (10,6)	0/41 (0,0)	9,63 [0,55; 168,96] 0,1214[2]	10,74 [0,58; 200,45] 0,0583[4]	10,6 [1,8; 19,5] 0,0583[4]
G2	29/244 (11,9)	4/234 (1,7)	6,95 [2,48; 19,47] 0,0002[2]	7,76 [2,68; 22,43] <,0001[3]	10,2 [5,8; 14,6] <,0001[3]
G3	26/233 (11,2)	4/226 (1,8)	6,30 [2,24; 17,78] 0,0005[2]	6,97 [2,39; 20,31] <,0001[3]	9,4 [5,0; 13,8] <,0001[3]
GX	2/29 (6,9)	0/33 (0,0)	5,67 [0,28; 113,41] 0,2565[2]	6,09 [0,28; 132,26] 0,2147[4]	6,9 [-2,3; 16,1] 0,2147[4]
Progesterone receptor status (Interaction p-value: 0,1369)					
Negative	6/49 (12,2)	1/44 (2,3)	5,39 [0,67; 43,02] 0,1121[2]	6,00 [0,69; 51,96] 0,1146[4]	10,0 [-0,2; 20,2] 0,1146[4]
Positive	56/477 (11,7)	7/471 (1,5)	7,90 [3,64; 17,15] <,0001[2]	8,82 [3,97; 19,56] <,0001[3]	10,3 [7,2; 13,3] <,0001[3]
Unknown	0/4 (0,0)	0/8 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,7498)					
White	39/323 (12,1)	5/324 (1,5)	7,82 [3,12; 19,60] <,0001[2]	8,76 [3,41; 22,53] <,0001[3]	10,5 [6,7; 14,3] <,0001[3]
Asian	19/199 (9,5)	2/180 (1,1)	8,59 [2,03; 36,38] 0,0035[2]	9,39 [2,16; 40,93] 0,0003[3]	8,4 [4,1; 12,8] 0,0003[3]
Other	3/19 (15,8)	1/21 (4,8)	3,32 [0,38; 29,23] 0,2804[2]	3,75 [0,36; 39,59] 0,3306[4]	11,0 [-7,7; 29,8] 0,3306[4]
ECOG-PS (Interaction p-value: 0,2068)					
ECOG-PS 0	56/496 (11,3)	6/480 (1,3)	9,03 [3,93; 20,77] <,0001[2]	10,05 [4,29; 23,57] <,0001[3]	10,0 [7,1; 13,0] <,0001[3]
ECOG-PS 1	6/57 (10,5)	2/55 (3,6)	2,89 [0,61; 13,73] 0,1809[2]	3,12 [0,60; 16,17] 0,2716[4]	6,9 [-2,5; 16,3] 0,2716[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Gastrointestinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9363)					
Neoadjuvant chemotherapy	12/217 (5,5)	0/219 (0,0)	25,23 [1,50; 423,48] 0,0249[2]	26,70 [1,57; 453,90] 0,0004[3]	5,5 [2,5; 8,6] 0,0004[3]
Adjuvant chemotherapy	26/327 (8,0)	4/312 (1,3)	6,20 [2,19; 17,57] 0,0006[2]	6,65 [2,29; 19,29] <,0001[3]	6,7 [3,5; 9,9] <,0001[3]
No chemotherapy	2/9 (22,2)	0/4 (0,0)	2,50 [0,15; 42,80] 0,5272[2]	3,00 [0,12; 77,64] 1,0000[4]	22,2 [-4,9; 49,4] 1,0000[4]
Region (Interaction p-value: 0,9347)					
North America / Europe	24/252 (9,5)	2/233 (0,9)	11,10 [2,65; 46,43] 0,0010[2]	12,16 [2,84; 52,04] <,0001[3]	8,7 [4,9; 12,5] <,0001[3]
Asia	7/168 (4,2)	1/166 (0,6)	6,92 [0,86; 55,60] 0,0690[2]	7,17 [0,87; 58,97] 0,0671[4]	3,6 [0,3; 6,8] 0,0671[4]
Other	9/133 (6,8)	1/136 (0,7)	9,20 [1,18; 71,64] 0,0340[2]	9,80 [1,22; 78,46] 0,0097[4]	6,0 [1,5; 10,5] 0,0097[4]
Primary tumor size (Interaction p-value: 0,5923)					
< 20 mm	13/141 (9,2)	1/140 (0,7)	12,91 [1,71; 97,35] 0,0131[2]	14,12 [1,82; 109,45] 0,0011[3]	8,5 [3,5; 13,5] 0,0011[3]
≥ 20 but < 50 mm	16/255 (6,3)	1/249 (0,4)	15,62 [2,09; 116,92] 0,0074[2]	16,60 [2,18; 126,17] 0,0003[3]	5,9 [2,8; 9,0] 0,0003[3]
≥ 50 mm	10/145 (6,9)	2/141 (1,4)	4,86 [1,08; 21,80] 0,0388[2]	5,15 [1,11; 23,93] 0,0209[3]	5,5 [0,9; 10,0] 0,0209[3]
Number of positive lymph nodes (Interaction p-value: 0,8679)					
0-3	15/203 (7,4)	3/214 (1,4)	5,27 [1,55; 17,94] 0,0078[2]	5,61 [1,60; 19,69] 0,0026[3]	6,0 [2,1; 9,9] 0,0026[3]
4-9	13/242 (5,4)	0/231 (0,0)	25,78 [1,54; 431,14] 0,0238[2]	27,24 [1,61; 460,85] 0,0004[3]	5,4 [2,5; 8,2] 0,0004[3]
≥ 10	12/108 (11,1)	1/90 (1,1)	10,00 [1,33; 75,44] 0,0255[2]	11,13 [1,42; 87,31] 0,0047[3]	10,0 [3,7; 16,3] 0,0047[3]
Tumor stage (Interaction p-value: 0,6143)					
IIA	4/59 (6,8)	1/62 (1,6)	4,20 [0,48; 36,53] 0,1930[2]	4,44 [0,48; 40,90] 0,1997[4]	5,2 [-2,0; 12,3] 0,1997[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIB	3/53 (5,7)	2/69 (2,9)	1,95 [0,34; 11,27] 0,4543[2]	2,01 [0,32; 12,48] 0,6517[4]	2,8 [-4,6; 10,1] 0,6517[4]
IIIA	13/236 (5,5)	0/214 (0,0)	24,49 [1,46; 409,54] 0,0260[2]	25,91 [1,53; 438,61] 0,0005[3]	5,5 [2,6; 8,4] 0,0005[3]
IIIB	0/18 (0,0)	0/15 (0,0)	NE	NE	NE
IIIC	19/186 (10,2)	1/174 (0,6)	17,77 [2,40; 131,36] 0,0048[2]	19,68 [2,61; 148,68] <,0001[3]	9,6 [5,1; 14,1] <,0001[3]
Tumor grade (Interaction p-value: 0,0954)					
G1	1/47 (2,1)	0/41 (0,0)	2,63 [0,11; 62,73] 0,5512[2]	2,68 [0,11; 67,54] 1,0000[4]	2,1 [-2,0; 6,3] 1,0000[4]
G2	20/244 (8,2)	2/234 (0,9)	9,59 [2,27; 40,58] 0,0021[2]	10,36 [2,39; 44,83] 0,0001[3]	7,3 [3,7; 11,0] 0,0001[3]
G3	19/233 (8,2)	2/226 (0,9)	9,21 [2,17; 39,11] 0,0026[2]	9,94 [2,29; 43,21] 0,0002[3]	7,3 [3,5; 11,0] 0,0002[3]
GX	0/29 (0,0)	0/33 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9974)					
Negative	4/49 (8,2)	0/44 (0,0)	8,10 [0,45; 146,31] 0,1565[2]	8,80 [0,46; 168,31] 0,1191[4]	8,2 [0,5; 15,8] 0,1191[4]
Positive	33/477 (6,9)	3/471 (0,6)	10,86 [3,35; 35,17] <,0001[2]	11,59 [3,53; 38,07] <,0001[3]	6,3 [3,9; 8,7] <,0001[3]
Unknown	1/4 (25,0)	0/8 (0,0)	5,40 [0,27; 109,35] 0,2719[2]	7,29 [0,23; 225,89] 0,3333[4]	25,0 [-17,4; 67,4] 0,3333[4]
Race (Interaction p-value: 0,2390)					
White	30/323 (9,3)	2/324 (0,6)	15,05 [3,63; 62,44] 0,0002[2]	16,48 [3,91; 69,58] <,0001[3]	8,7 [5,4; 11,9] <,0001[3]
Asian	7/199 (3,5)	1/180 (0,6)	6,33 [0,79; 50,96] 0,0828[2]	6,53 [0,80; 53,57] 0,0702[4]	3,0 [0,2; 5,7] 0,0702[4]
Other	1/19 (5,3)	1/21 (4,8)	1,11 [0,07; 16,47] 0,9421[2]	1,11 [0,06; 19,09] 1,0000[4]	0,5 [-13,1; 14,1] 1,0000[4]
ECOG-PS (Interaction p-value: 0,9824)					
ECOG-PS 0	39/496 (7,9)	4/480 (0,8)	9,44 [3,40; 26,20] <,0001[2]	10,16 [3,60; 28,65] <,0001[3]	7,0 [4,5; 9,5] <,0001[3]
ECOG-PS 1	1/57 (1,8)	0/55 (0,0)	2,90 [0,12; 69,62] 0,5121[2]	2,95 [0,12; 73,90] 1,0000[4]	1,8 [-1,7; 5,2] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Investigations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,1827)					
Neoadjuvant chemotherapy	44/217 (20,3)	7/219 (3,2)	6,34 [2,92; 13,77] <,0001[2]	7,70 [3,38; 17,53] <,0001[3]	17,1 [11,2; 22,9] <,0001[3]
Adjuvant chemotherapy	60/327 (18,3)	2/312 (0,6)	28,62 [7,06; 116,10] <,0001[2]	34,83 [8,43; 143,86] <,0001[3]	17,7 [13,4; 22,0] <,0001[3]
No chemotherapy	1/9 (11,1)	0/4 (0,0)	1,50 [0,07; 30,59] 0,7921[2]	1,59 [0,05; 47,52] 1,0000[4]	11,1 [-9,4; 31,6] 1,0000[4]
Region (Interaction p-value: 0,9734)					
North America / Europe	36/252 (14,3)	3/233 (1,3)	11,10 [3,46; 35,54] <,0001[2]	12,78 [3,88; 42,10] <,0001[3]	13,0 [8,4; 17,6] <,0001[3]
Asia	57/168 (33,9)	6/166 (3,6)	9,39 [4,16; 21,17] <,0001[2]	13,69 [5,71; 32,86] <,0001[3]	30,3 [22,6; 38,0] <,0001[3]
Other	12/133 (9,0)	0/136 (0,0)	25,56 [1,53; 427,38] 0,0241[2]	28,09 [1,65; 479,40] 0,0003[3]	9,0 [4,2; 13,9] 0,0003[3]
Primary tumor size (Interaction p-value: 0,2803)					
< 20 mm	27/141 (19,1)	3/140 (2,1)	8,94 [2,77; 28,78] 0,0002[2]	10,82 [3,20; 36,58] <,0001[3]	17,0 [10,1; 23,9] <,0001[3]
≥ 20 but < 50 mm	51/255 (20,0)	2/249 (0,8)	24,90 [6,13; 101,18] <,0001[2]	30,88 [7,43; 128,37] <,0001[3]	19,2 [14,2; 24,2] <,0001[3]
≥ 50 mm	25/145 (17,2)	4/141 (2,8)	6,08 [2,17; 17,02] 0,0006[2]	7,14 [2,41; 21,09] <,0001[3]	14,4 [7,7; 21,1] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,1489)					
0-3	42/203 (20,7)	1/214 (0,5)	44,28 [6,15; 318,71] 0,0002[2]	55,57 [7,57; 407,99] <,0001[3]	20,2 [14,6; 25,9] <,0001[3]
4-9	47/242 (19,4)	5/231 (2,2)	8,97 [3,63; 22,16] <,0001[2]	10,89 [4,25; 27,94] <,0001[3]	17,3 [11,9; 22,6] <,0001[3]
≥ 10	16/108 (14,8)	3/90 (3,3)	4,44 [1,34; 14,77] 0,0149[2]	5,04 [1,42; 17,91] 0,0063[3]	11,5 [3,8; 19,1] 0,0063[3]
Tumor stage (Interaction p-value: 0,5558)					
IIA	13/59 (22,0)	1/62 (1,6)	13,66 [1,84; 101,19] 0,0105[2]	17,24 [2,18; 136,57] 0,0004[3]	20,4 [9,4; 31,5] 0,0004[3]
IIB	15/53 (28,3)	0/69 (0,0)	40,19 [2,46; 656,68] 0,0096[2]	55,96 [3,26; 961,23] <,0001[3]	28,3 [16,2; 40,4] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	49/236 (20,8)	3/214 (1,4)	14,81 [4,69; 46,82] <,0001[2]	18,43 [5,65; 60,11] <,0001[3]	19,4 [14,0; 24,8] <,0001[3]
IIIB	4/18 (22,2)	0/15 (0,0)	7,58 [0,44; 130,38] 0,1629[2]	9,62 [0,48; 194,83] 0,1081[4]	22,2 [3,0; 41,4] 0,1081[4]
IIIC	23/186 (12,4)	5/174 (2,9)	4,30 [1,67; 11,07] 0,0025[2]	4,77 [1,77; 12,85] 0,0008[3]	9,5 [4,1; 14,8] 0,0008[3]
Tumor grade (Interaction p-value: 0,8831)					
G1	15/47 (31,9)	0/41 (0,0)	27,13 [1,67; 439,66] 0,0202[2]	39,58 [2,28; 686,62] <,0001[3]	31,9 [18,6; 45,2] <,0001[3]
G2	40/244 (16,4)	5/234 (2,1)	7,67 [3,08; 19,10] <,0001[2]	8,98 [3,48; 23,19] <,0001[3]	14,3 [9,3; 19,3] <,0001[3]
G3	43/233 (18,5)	3/226 (1,3)	13,90 [4,38; 44,17] <,0001[2]	16,82 [5,14; 55,09] <,0001[3]	17,1 [11,9; 22,3] <,0001[3]
GX	7/29 (24,1)	1/33 (3,0)	7,97 [1,04; 60,96] 0,0457[2]	10,18 [1,17; 88,68] 0,0206[4]	21,1 [4,5; 37,7] 0,0206[4]
Race (Interaction p-value: 0,7848)					
White	44/323 (13,6)	3/324 (0,9)	14,71 [4,62; 46,90] <,0001[2]	16,87 [5,18; 54,94] <,0001[3]	12,7 [8,8; 16,6] <,0001[3]
Asian	59/199 (29,6)	6/180 (3,3)	8,89 [3,94; 20,10] <,0001[2]	12,22 [5,13; 29,14] <,0001[3]	26,3 [19,4; 33,2] <,0001[3]
Other	2/19 (10,5)	0/21 (0,0)	5,50 [0,28; 107,78] 0,2615[2]	6,14 [0,28; 136,53] 0,2192[4]	10,5 [-3,3; 24,3] 0,2192[4]
ECOG-PS (Interaction p-value: 0,1475)					
ECOG-PS 0	97/496 (19,6)	7/480 (1,5)	13,41 [6,29; 28,58] <,0001[2]	16,43 [7,54; 35,78] <,0001[3]	18,1 [14,4; 21,7] <,0001[3]
ECOG-PS 1	8/57 (14,0)	2/55 (3,6)	3,86 [0,86; 17,38] 0,0785[2]	4,33 [0,88; 21,37] 0,0941[4]	10,4 [0,1; 20,7] 0,0941[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to appropriate comparator by GBA: Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Tabelle 4-135 (Anhang): Häufige unerwünschte Ereignisse nach SOC und PT - nicht-interagierende Subgruppen (postmenopausale Patientinnen)

Table: Subgroups - adverse events according PT Abdominal discomfort from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4101)					
< 65 years	18/918 (2,0)	6/937 (0,6)	3,06 [1,22; 7,68] 0,0171[2]	3,10 [1,23; 7,85] 0,0119[3]	1,3 [0,3; 2,4] 0,0119[3]
≥ 65 years	1/365 (0,3)	1/328 (0,3)	0,90 [0,06; 14,31] 0,9397[2]	0,90 [0,06; 14,42] 1,0000[4]	-0,0 [-0,8; 0,8] 1,0000[4]
Region (Interaction p-value: 0,9969)					
North America / Europe	12/678 (1,8)	5/650 (0,8)	2,30 [0,82; 6,49] 0,1155[2]	2,32 [0,81; 6,63] 0,1049[3]	1,0 [-0,2; 2,2] 0,1049[3]
Asia	5/203 (2,5)	2/201 (1,0)	2,48 [0,49; 12,61] 0,2752[2]	2,51 [0,48; 13,10] 0,4491[4]	1,5 [-1,1; 4,0] 0,4491[4]
Other	2/402 (0,5)	0/414 (0,0)	5,15 [0,25; 106,92] 0,2896[2]	5,17 [0,25; 108,12] 0,2424[4]	0,5 [-0,2; 1,2] 0,2424[4]
Primary tumor size (Interaction p-value: 0,1589)					
< 20 mm	5/331 (1,5)	3/335 (0,9)	1,69 [0,41; 7,00] 0,4715[2]	1,70 [0,40; 7,16] 0,5029[4]	0,6 [-1,0; 2,3] 0,5029[4]
≥ 20 but < 50 mm	11/646 (1,7)	1/653 (0,2)	11,12 [1,44; 85,88] 0,0209[2]	11,29 [1,45; 87,74] 0,0035[3]	1,5 [0,5; 2,6] 0,0035[3]
≥ 50 mm	3/289 (1,0)	3/265 (1,1)	0,92 [0,19; 4,50] 0,9150[2]	0,92 [0,18; 4,58] 1,0000[4]	-0,1 [-1,8; 1,6] 1,0000[4]
Tumor stage (Interaction p-value: 0,8927)					
IIA	1/113 (0,9)	0/114 (0,0)	3,03 [0,12; 73,51] 0,4963[2]	3,05 [0,12; 75,75] 0,4978[4]	0,9 [-0,8; 2,6] 0,4978[4]
IIB	4/151 (2,6)	0/136 (0,0)	8,11 [0,44; 149,30] 0,1589[2]	8,33 [0,44; 156,14] 0,1244[4]	2,6 [0,1; 5,2] 0,1244[4]
IIIA	6/495 (1,2)	1/488 (0,2)	5,92 [0,71; 48,95] 0,0992[2]	5,98 [0,72; 49,82] 0,1237[4]	1,0 [-0,0; 2,1] 0,1237[4]
IIIB	0/54 (0,0)	1/45 (2,2)	0,28 [0,01; 6,68] 0,4306[2]	0,27 [0,01; 6,85] 0,4545[4]	-2,2 [-6,5; 2,1] 0,4545[4]
IIIC	8/468 (1,7)	5/480 (1,0)	1,64 [0,54; 4,98] 0,3818[2]	1,65 [0,54; 5,09] 0,3768[3]	0,7 [-0,8; 2,2] 0,3768[3]
Progesterone receptor status (Interaction p-value: 0,3409)					
Negative	3/156 (1,9)	1/169 (0,6)	3,25 [0,34; 30,92] 0,3051[2]	3,29 [0,34; 32,00] 0,3537[4]	1,3 [-1,1; 3,8] 0,3537[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Positive	16/1089 (1,5)	6/1067 (0,6)	2,61 [1,03; 6,65] 0,0440[2]	2,64 [1,03; 6,76] 0,0362[3]	0,9 [0,1; 1,8] 0,0362[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9775)					
White	12/958 (1,3)	5/944 (0,5)	2,36 [0,84; 6,69] 0,1046[2]	2,38 [0,84; 6,79] 0,0939[3]	0,7 [-0,1; 1,6] 0,0939[3]
Asian	6/250 (2,4)	2/242 (0,8)	2,90 [0,59; 14,25] 0,1889[2]	2,95 [0,59; 14,77] 0,2856[4]	1,6 [-0,6; 3,8] 0,2856[4]
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
First endocrine therapy (Interaction p-value: 0,8962)					
Tamoxifen	2/114 (1,8)	1/132 (0,8)	2,32 [0,21; 25,21] 0,4906[2]	2,34 [0,21; 26,14] 0,5979[4]	1,0 [-1,8; 3,8] 0,5979[4]
Aromatase inhibitor	17/1169 (1,5)	6/1133 (0,5)	2,75 [1,09; 6,94] 0,0327[2]	2,77 [1,09; 7,06] 0,0257[3]	0,9 [0,1; 1,7] 0,0257[3]
ECOG-PS (Interaction p-value: 0,1764)					
ECOG-PS 0	18/1070 (1,7)	5/1020 (0,5)	3,43 [1,28; 9,21] 0,0143[2]	3,47 [1,28; 9,39] 0,0090[3]	1,2 [0,3; 2,1] 0,0090[3]
ECOG-PS 1	1/213 (0,5)	2/245 (0,8)	0,58 [0,05; 6,30] 0,6506[2]	0,57 [0,05; 6,37] 1,0000[4]	-0,3 [-1,8; 1,1] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Abdominal distension from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7056)					
< 65 years	28/918 (3,1)	9/937 (1,0)	3,18 [1,51; 6,69] 0,0024[2]	3,24 [1,52; 6,91] 0,0013[3]	2,1 [0,8; 3,4] 0,0013[3]
≥ 65 years	5/365 (1,4)	2/328 (0,6)	2,25 [0,44; 11,50] 0,3313[2]	2,26 [0,44; 11,75] 0,4555[4]	0,8 [-0,7; 2,2] 0,4555[4]
Prior treatment (Interaction p-value: 0,8295)					
Neoadjuvant chemotherapy	11/430 (2,6)	3/415 (0,7)	3,54 [0,99; 12,59] 0,0510[2]	3,61 [1,00; 13,02] 0,0367[3]	1,8 [0,1; 3,5] 0,0367[3]
Adjuvant chemotherapy	18/784 (2,3)	8/769 (1,0)	2,21 [0,97; 5,05] 0,0606[2]	2,24 [0,97; 5,17] 0,0538[3]	1,3 [-0,0; 2,5] 0,0538[3]
No chemotherapy	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (Interaction p-value: 0,7559)					
North America / Europe	20/678 (2,9)	9/650 (1,4)	2,13 [0,98; 4,64] 0,0571[2]	2,16 [0,98; 4,79] 0,0511[3]	1,6 [0,0; 3,1] 0,0511[3]
Asia	5/203 (2,5)	0/201 (0,0)	10,89 [0,61; 195,70] 0,1052[2]	11,17 [0,61; 203,28] 0,0610[4]	2,5 [0,3; 4,6] 0,0610[4]
Other	8/402 (2,0)	2/414 (0,5)	4,12 [0,88; 19,28] 0,0722[2]	4,18 [0,88; 19,82] 0,0604[4]	1,5 [-0,0; 3,0] 0,0604[4]
Primary tumor size (Interaction p-value: 0,5660)					
< 20 mm	7/331 (2,1)	4/335 (1,2)	1,77 [0,52; 5,99] 0,3581[2]	1,79 [0,52; 6,17] 0,3512[3]	0,9 [-1,0; 2,9] 0,3512[3]
≥ 20 but < 50 mm	17/646 (2,6)	4/653 (0,6)	4,30 [1,45; 12,70] 0,0084[2]	4,39 [1,47; 13,10] 0,0039[3]	2,0 [0,6; 3,4] 0,0039[3]
≥ 50 mm	9/289 (3,1)	3/265 (1,1)	2,75 [0,75; 10,05] 0,1259[2]	2,81 [0,75; 10,48] 0,1094[3]	2,0 [-0,4; 4,4] 0,1094[3]
Number of positive lymph nodes (Interaction p-value: 0,0841)					
0-3	13/427 (3,0)	6/418 (1,4)	2,12 [0,81; 5,53] 0,1239[2]	2,16 [0,81; 5,73] 0,1147[3]	1,6 [-0,4; 3,6] 0,1147[3]
4-9	16/549 (2,9)	1/542 (0,2)	15,80 [2,10; 118,69] 0,0073[2]	16,24 [2,15; 122,89] 0,0003[3]	2,7 [1,3; 4,2] 0,0003[3]
≥ 10	4/307 (1,3)	4/305 (1,3)	0,99 [0,25; 3,94] 0,9926[2]	0,99 [0,25; 4,01] 1,0000[4]	-0,0 [-1,8; 1,8] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,4242)					
IIA	2/113 (1,8)	2/114 (1,8)	1,01 [0,14; 7,04] 0,9929[2]	1,01 [0,14; 7,29] 1,0000[4]	0,0 [-3,4; 3,4] 1,0000[4]
IIB	4/151 (2,6)	3/136 (2,2)	1,20 [0,27; 5,27] 0,8083[2]	1,21 [0,27; 5,49] 1,0000[4]	0,4 [-3,1; 4,0] 1,0000[4]
IIIA	15/495 (3,0)	2/488 (0,4)	7,39 [1,70; 32,16] 0,0076[2]	7,59 [1,73; 33,39] 0,0016[3]	2,6 [1,0; 4,2] 0,0016[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	10/468 (2,1)	4/480 (0,8)	2,56 [0,81; 8,12] 0,1093[2]	2,60 [0,81; 8,34] 0,0962[3]	1,3 [-0,2; 2,8] 0,0962[3]
Tumor grade (Interaction p-value: 0,1696)					
G1	1/91 (1,1)	2/93 (2,2)	0,51 [0,05; 5,54] 0,5808[2]	0,51 [0,05; 5,67] 1,0000[4]	-1,1 [-4,7; 2,6] 1,0000[4]
G2	15/612 (2,5)	1/603 (0,2)	14,78 [1,96; 111,54] 0,0090[2]	15,13 [1,99; 114,87] 0,0005[3]	2,3 [1,0; 3,6] 0,0005[3]
G3	16/527 (3,0)	7/506 (1,4)	2,19 [0,91; 5,29] 0,0799[2]	2,23 [0,91; 5,47] 0,0719[3]	1,7 [-0,1; 3,4] 0,0719[3]
GX	1/51 (2,0)	1/59 (1,7)	1,16 [0,07; 18,03] 0,9172[2]	1,16 [0,07; 19,03] 1,0000[4]	0,3 [-4,8; 5,3] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,0923)					
Negative	8/156 (5,1)	2/169 (1,2)	4,33 [0,93; 20,09] 0,0610[2]	4,51 [0,94; 21,59] 0,0532[4]	3,9 [0,1; 7,8] 0,0532[4]
Positive	24/1089 (2,2)	9/1067 (0,8)	2,61 [1,22; 5,59] 0,0134[2]	2,65 [1,23; 5,73] 0,0101[3]	1,4 [0,3; 2,4] 0,0101[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,5197)					
White	25/958 (2,6)	7/944 (0,7)	3,52 [1,53; 8,10] 0,0031[2]	3,59 [1,54; 8,33] 0,0015[3]	1,9 [0,7; 3,0] 0,0015[3]
Asian	6/250 (2,4)	2/242 (0,8)	2,90 [0,59; 14,25] 0,1889[2]	2,95 [0,59; 14,77] 0,2856[4]	1,6 [-0,6; 3,8] 0,2856[4]
Other	2/62 (3,2)	2/64 (3,1)	1,03 [0,15; 7,10] 0,9743[2]	1,03 [0,14; 7,57] 1,0000[4]	0,1 [-6,0; 6,2] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,6692)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	4/114 (3,5)	1/132 (0,8)	4,63 [0,53; 40,85] 0,1675[2]	4,76 [0,52; 43,25] 0,1855[4]	2,8 [-0,9; 6,4] 0,1855[4]
Aromatase inhibitor	29/1169 (2,5)	10/1133 (0,9)	2,81 [1,38; 5,74] 0,0046[2]	2,86 [1,39; 5,89] 0,0030[3]	1,6 [0,6; 2,6] 0,0030[3]
ECOG-PS (Interaction p-value: 0,4519)					
ECOG-PS 0	26/1070 (2,4)	7/1020 (0,7)	3,54 [1,54; 8,12] 0,0028[2]	3,60 [1,56; 8,34] 0,0014[3]	1,7 [0,7; 2,8] 0,0014[3]
ECOG-PS 1	7/213 (3,3)	4/245 (1,6)	2,01 [0,60; 6,78] 0,2590[2]	2,05 [0,59; 7,09] 0,2489[3]	1,7 [-1,2; 4,5] 0,2489[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Abdominal pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4775)					
< 65 years	236/918 (25,7)	46/937 (4,9)	5,24 [3,87; 7,09] <,0001[2]	6,70 [4,81; 9,33] <,0001[3]	20,8 [17,7; 23,9] <,0001[3]
≥ 65 years	75/365 (20,5)	16/328 (4,9)	4,21 [2,51; 7,08] <,0001[2]	5,04 [2,87; 8,85] <,0001[3]	15,7 [10,9; 20,4] <,0001[3]
Prior treatment (Interaction p-value: 0,8985)					
Neoadjuvant chemotherapy	106/430 (24,7)	19/415 (4,6)	5,38 [3,37; 8,61] <,0001[2]	6,82 [4,10; 11,35] <,0001[3]	20,1 [15,5; 24,6] <,0001[3]
Adjuvant chemotherapy	190/784 (24,2)	39/769 (5,1)	4,78 [3,44; 6,65] <,0001[2]	5,99 [4,17; 8,59] <,0001[3]	19,2 [15,8; 22,5] <,0001[3]
No chemotherapy	15/69 (21,7)	4/81 (4,9)	4,40 [1,53; 12,64] 0,0059[2]	5,35 [1,68; 17,00] 0,0020[3]	16,8 [6,0; 27,6] 0,0020[3]
Region (Interaction p-value: 0,5579)					
North America / Europe	197/678 (29,1)	34/650 (5,2)	5,55 [3,92; 7,86] <,0001[2]	7,42 [5,06; 10,88] <,0001[3]	23,8 [20,0; 27,6] <,0001[3]
Asia	22/203 (10,8)	5/201 (2,5)	4,36 [1,68; 11,28] 0,0024[2]	4,76 [1,77; 12,85] 0,0008[3]	8,3 [3,6; 13,1] 0,0008[3]
Other	92/402 (22,9)	23/414 (5,6)	4,12 [2,66; 6,37] <,0001[2]	5,05 [3,12; 8,16] <,0001[3]	17,3 [12,7; 22,0] <,0001[3]
Primary tumor size (Interaction p-value: 0,1821)					
< 20 mm	80/331 (24,2)	18/335 (5,4)	4,50 [2,76; 7,33] <,0001[2]	5,61 [3,28; 9,61] <,0001[3]	18,8 [13,6; 24,0] <,0001[3]
≥ 20 but < 50 mm	156/646 (24,1)	25/653 (3,8)	6,31 [4,19; 9,49] <,0001[2]	8,00 [5,16; 12,40] <,0001[3]	20,3 [16,7; 23,9] <,0001[3]
≥ 50 mm	73/289 (25,3)	19/265 (7,2)	3,52 [2,19; 5,67] <,0001[2]	4,38 [2,56; 7,49] <,0001[3]	18,1 [12,2; 24,0] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,5987)					
0-3	108/427 (25,3)	24/418 (5,7)	4,41 [2,89; 6,71] <,0001[2]	5,56 [3,49; 8,86] <,0001[3]	19,6 [14,9; 24,2] <,0001[3]
4-9	136/549 (24,8)	23/542 (4,2)	5,84 [3,81; 8,94] <,0001[2]	7,43 [4,69; 11,78] <,0001[3]	20,5 [16,5; 24,5] <,0001[3]
≥ 10	67/307 (21,8)	15/305 (4,9)	4,44 [2,59; 7,59] <,0001[2]	5,40 [3,01; 9,69] <,0001[3]	16,9 [11,7; 22,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7154)					
IIA	25/113 (22,1)	4/114 (3,5)	6,31 [2,27; 17,54] 0,0004[2]	7,81 [2,62; 23,28] <,0001[3]	18,6 [10,2; 27,0] <,0001[3]
IIB	35/151 (23,2)	7/136 (5,1)	4,50 [2,07; 9,80] 0,0001[2]	5,56 [2,38; 13,00] <,0001[3]	18,0 [10,3; 25,7] <,0001[3]
IIIA	127/495 (25,7)	21/488 (4,3)	5,96 [3,82; 9,30] <,0001[2]	7,67 [4,74; 12,42] <,0001[3]	21,4 [17,1; 25,6] <,0001[3]
IIIB	14/54 (25,9)	2/45 (4,4)	5,83 [1,40; 24,32] 0,0155[2]	7,53 [1,61; 35,20] 0,0038[3]	21,5 [8,3; 34,6] 0,0038[3]
IIIC	109/468 (23,3)	28/480 (5,8)	3,99 [2,69; 5,93] <,0001[2]	4,90 [3,16; 7,59] <,0001[3]	17,5 [13,1; 21,8] <,0001[3]
Tumor grade (Interaction p-value: 0,8687)					
G1	22/91 (24,2)	5/93 (5,4)	4,50 [1,78; 11,36] 0,0015[2]	5,61 [2,02; 15,58] 0,0003[3]	18,8 [8,9; 28,7] 0,0003[3]
G2	146/612 (23,9)	27/603 (4,5)	5,33 [3,59; 7,91] <,0001[2]	6,68 [4,35; 10,26] <,0001[3]	19,4 [15,6; 23,1] <,0001[3]
G3	127/527 (24,1)	29/506 (5,7)	4,20 [2,86; 6,18] <,0001[2]	5,22 [3,42; 7,99] <,0001[3]	18,4 [14,2; 22,5] <,0001[3]
GX	16/51 (31,4)	0/59 (0,0)	38,08 [2,34; 619,24] 0,0105[2]	55,31 [3,22; 950,49] <,0001[3]	31,4 [18,6; 44,1] <,0001[3]
Race (Interaction p-value: 0,9326)					
White	256/958 (26,7)	51/944 (5,4)	4,95 [3,71; 6,59] <,0001[2]	6,39 [4,65; 8,76] <,0001[3]	21,3 [18,2; 24,5] <,0001[3]
Asian	31/250 (12,4)	6/242 (2,5)	5,00 [2,12; 11,77] 0,0002[2]	5,57 [2,28; 13,60] <,0001[3]	9,9 [5,4; 14,5] <,0001[3]
Other	20/62 (32,3)	5/64 (7,8)	4,13 [1,65; 10,32] 0,0024[2]	5,62 [1,95; 16,17] 0,0006[3]	24,4 [11,1; 37,8] 0,0006[3]
First endocrine therapy (Interaction p-value: 0,2404)					
Tamoxifen	25/114 (21,9)	3/132 (2,3)	9,65 [2,99; 31,12] 0,0001[2]	12,08 [3,54; 41,23] <,0001[3]	19,7 [11,6; 27,7] <,0001[3]
Aromatase inhibitor	286/1169 (24,5)	59/1133 (5,2)	4,70 [3,59; 6,14] <,0001[2]	5,90 [4,39; 7,91] <,0001[3]	19,3 [16,5; 22,0] <,0001[3]
ECOG-PS (Interaction p-value: 0,9243)					
ECOG-PS 0	258/1070 (24,1)	50/1020 (4,9)	4,92 [3,68; 6,58] <,0001[2]	6,16 [4,49; 8,46] <,0001[3]	19,2 [16,3; 22,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	53/213 (24,9)	12/245 (4,9)	5,08 [2,79; 9,25] <,0001[2]	6,43 [3,33; 12,42] <,0001[3]	20,0 [13,6; 26,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Abdominal pain upper from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8348)					
< 65 years	89/918 (9,7)	32/937 (3,4)	2,84 [1,92; 4,21] <,0001[2]	3,04 [2,01; 4,60] <,0001[3]	6,3 [4,0; 8,5] <,0001[3]
≥ 65 years	35/365 (9,6)	12/328 (3,7)	2,62 [1,38; 4,96] 0,0031[2]	2,79 [1,42; 5,48] 0,0019[3]	5,9 [2,3; 9,6] 0,0019[3]
Prior treatment (Interaction p-value: 0,2252)					
Neoadjuvant chemotherapy	45/430 (10,5)	10/415 (2,4)	4,34 [2,22; 8,50] <,0001[2]	4,73 [2,35; 9,53] <,0001[3]	8,1 [4,8; 11,3] <,0001[3]
Adjuvant chemotherapy	70/784 (8,9)	31/769 (4,0)	2,21 [1,47; 3,34] 0,0001[2]	2,33 [1,51; 3,61] <,0001[3]	4,9 [2,5; 7,3] <,0001[3]
No chemotherapy	9/69 (13,0)	3/81 (3,7)	3,52 [0,99; 12,50] 0,0514[2]	3,90 [1,01; 15,03] 0,0356[3]	9,3 [0,4; 18,3] 0,0356[3]
Region (Interaction p-value: 0,0798)					
North America / Europe	69/678 (10,2)	16/650 (2,5)	4,13 [2,43; 7,05] <,0001[2]	4,49 [2,58; 7,82] <,0001[3]	7,7 [5,1; 10,3] <,0001[3]
Asia	17/203 (8,4)	6/201 (3,0)	2,81 [1,13; 6,97] 0,0263[2]	2,97 [1,15; 7,70] 0,0194[3]	5,4 [0,9; 9,9] 0,0194[3]
Other	38/402 (9,5)	22/414 (5,3)	1,78 [1,07; 2,95] 0,0259[2]	1,86 [1,08; 3,21] 0,0235[3]	4,1 [0,6; 7,7] 0,0235[3]
Primary tumor size (Interaction p-value: 0,7465)					
< 20 mm	32/331 (9,7)	9/335 (2,7)	3,60 [1,75; 7,42] 0,0005[2]	3,88 [1,82; 8,26] 0,0002[3]	7,0 [3,4; 10,6] 0,0002[3]
≥ 20 but < 50 mm	53/646 (8,2)	20/653 (3,1)	2,68 [1,62; 4,43] 0,0001[2]	2,83 [1,67; 4,79] <,0001[3]	5,1 [2,6; 7,6] <,0001[3]
≥ 50 mm	39/289 (13,5)	14/265 (5,3)	2,55 [1,42; 4,60] 0,0018[2]	2,80 [1,48; 5,28] 0,0010[3]	8,2 [3,4; 13,0] 0,0010[3]
Number of positive lymph nodes (Interaction p-value: 0,4068)					
0-3	47/427 (11,0)	14/418 (3,3)	3,29 [1,84; 5,88] <,0001[2]	3,57 [1,93; 6,59] <,0001[3]	7,7 [4,2; 11,1] <,0001[3]
4-9	45/549 (8,2)	14/542 (2,6)	3,17 [1,76; 5,71] 0,0001[2]	3,37 [1,83; 6,21] <,0001[3]	5,6 [3,0; 8,3] <,0001[3]
≥ 10	32/307 (10,4)	16/305 (5,2)	1,99 [1,11; 3,54] 0,0201[2]	2,10 [1,13; 3,92] 0,0172[3]	5,2 [0,9; 9,4] 0,0172[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,3332)					
IIA	10/113 (8,8)	2/114 (1,8)	5,04 [1,13; 22,51] 0,0340[2]	5,44 [1,16; 25,40] 0,0169[3]	7,1 [1,3; 12,9] 0,0169[3]
IIB	13/151 (8,6)	6/136 (4,4)	1,95 [0,76; 4,99] 0,1629[2]	2,04 [0,75; 5,53] 0,1533[3]	4,2 [-1,5; 9,8] 0,1533[3]
IIIA	55/495 (11,1)	13/488 (2,7)	4,17 [2,31; 7,53] <,0001[2]	4,57 [2,46; 8,47] <,0001[3]	8,4 [5,3; 11,6] <,0001[3]
IIIB	3/54 (5,6)	0/45 (0,0)	5,85 [0,31; 110,43] 0,2383[2]	6,18 [0,31; 122,97] 0,2486[4]	5,6 [-0,6; 11,7] 0,2486[4]
IIIC	43/468 (9,2)	22/480 (4,6)	2,00 [1,22; 3,30] 0,0062[2]	2,11 [1,24; 3,58] 0,0050[3]	4,6 [1,4; 7,8] 0,0050[3]
Tumor grade (Interaction p-value: 0,9479)					
G1	10/91 (11,0)	5/93 (5,4)	2,04 [0,73; 5,75] 0,1753[2]	2,17 [0,71; 6,63] 0,1642[3]	5,6 [-2,3; 13,5] 0,1642[3]
G2	61/612 (10,0)	21/603 (3,5)	2,86 [1,77; 4,64] <,0001[2]	3,07 [1,84; 5,11] <,0001[3]	6,5 [3,7; 9,3] <,0001[3]
G3	45/527 (8,5)	17/506 (3,4)	2,54 [1,47; 4,38] 0,0008[2]	2,69 [1,52; 4,76] 0,0005[3]	5,2 [2,3; 8,0] 0,0005[3]
GX	8/51 (15,7)	0/59 (0,0)	19,62 [1,16; 331,69] 0,0391[2]	23,25 [1,31; 413,75] 0,0016[4]	15,7 [5,7; 25,7] 0,0016[4]
Progesterone receptor status (Interaction p-value: 0,9897)					
Negative	19/156 (12,2)	2/169 (1,2)	10,29 [2,44; 43,47] 0,0015[2]	11,58 [2,65; 50,59] <,0001[3]	11,0 [5,6; 16,4] <,0001[3]
Positive	102/1089 (9,4)	42/1067 (3,9)	2,38 [1,68; 3,37] <,0001[2]	2,52 [1,74; 3,65] <,0001[3]	5,4 [3,3; 7,5] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9724)					
White	96/958 (10,0)	35/944 (3,7)	2,70 [1,85; 3,94] <,0001[2]	2,89 [1,94; 4,31] <,0001[3]	6,3 [4,1; 8,6] <,0001[3]
Asian	18/250 (7,2)	6/242 (2,5)	2,90 [1,17; 7,19] 0,0212[2]	3,05 [1,19; 7,82] 0,0151[3]	4,7 [1,0; 8,5] 0,0151[3]
Other	9/62 (14,5)	3/64 (4,7)	3,10 [0,88; 10,91] 0,0785[2]	3,45 [0,89; 13,42] 0,0602[3]	9,8 [-0,4; 20,0] 0,0602[3]
First endocrine therapy (Interaction p-value: 0,1812)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	11/114 (9,6)	8/132 (6,1)	1,59 [0,66; 3,82] 0,2979[2]	1,66 [0,64; 4,27] 0,2931[3]	3,6 [-3,2; 10,4] 0,2931[3]
Aromatase inhibitor	113/1169 (9,7)	36/1133 (3,2)	3,04 [2,11; 4,39] <,0001[2]	3,26 [2,22; 4,79] <,0001[3]	6,5 [4,5; 8,5] <,0001[3]
ECOG-PS (Interaction p-value: 0,7607)					
ECOG-PS 0	105/1070 (9,8)	37/1020 (3,6)	2,71 [1,88; 3,90] <,0001[2]	2,89 [1,97; 4,25] <,0001[3]	6,2 [4,1; 8,3] <,0001[3]
ECOG-PS 1	19/213 (8,9)	7/245 (2,9)	3,12 [1,34; 7,28] 0,0084[2]	3,33 [1,37; 8,09] 0,0052[3]	6,1 [1,7; 10,4] 0,0052[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Alanine aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9613)					
< 65 years	118/918 (12,9)	53/937 (5,7)	2,27 [1,67; 3,10] <,0001[2]	2,46 [1,75; 3,45] <,0001[3]	7,2 [4,6; 9,8] <,0001[3]
≥ 65 years	36/365 (9,9)	14/328 (4,3)	2,31 [1,27; 4,21] 0,0061[2]	2,45 [1,30; 4,64] 0,0045[3]	5,6 [1,8; 9,4] 0,0045[3]
Prior treatment (Interaction p-value: 0,4526)					
Neoadjuvant chemotherapy	65/430 (15,1)	25/415 (6,0)	2,51 [1,61; 3,90] <,0001[2]	2,78 [1,71; 4,50] <,0001[3]	9,1 [5,0; 13,2] <,0001[3]
Adjuvant chemotherapy	81/784 (10,3)	40/769 (5,2)	1,99 [1,38; 2,86] 0,0002[2]	2,10 [1,42; 3,11] 0,0002[3]	5,1 [2,5; 7,8] 0,0002[3]
No chemotherapy	8/69 (11,6)	2/81 (2,5)	4,70 [1,03; 21,38] 0,0455[2]	5,18 [1,06; 25,28] 0,0444[4]	9,1 [0,8; 17,4] 0,0444[4]
Region (Interaction p-value: 0,7377)					
North America / Europe	52/678 (7,7)	25/650 (3,8)	1,99 [1,25; 3,17] 0,0036[2]	2,08 [1,27; 3,39] 0,0029[3]	3,8 [1,3; 6,3] 0,0029[3]
Asia	45/203 (22,2)	17/201 (8,5)	2,62 [1,55; 4,42] 0,0003[2]	3,08 [1,70; 5,60] 0,0001[3]	13,7 [6,8; 20,6] 0,0001[3]
Other	57/402 (14,2)	25/414 (6,0)	2,35 [1,50; 3,68] 0,0002[2]	2,57 [1,57; 4,20] 0,0001[3]	8,1 [4,0; 12,3] 0,0001[3]
Primary tumor size (Interaction p-value: 0,6663)					
< 20 mm	46/331 (13,9)	18/335 (5,4)	2,59 [1,53; 4,36] 0,0004[2]	2,84 [1,61; 5,02] 0,0002[3]	8,5 [4,1; 13,0] 0,0002[3]
≥ 20 but < 50 mm	72/646 (11,1)	36/653 (5,5)	2,02 [1,38; 2,97] 0,0003[2]	2,15 [1,42; 3,26] 0,0002[3]	5,6 [2,6; 8,6] 0,0002[3]
≥ 50 mm	32/289 (11,1)	11/265 (4,2)	2,67 [1,37; 5,18] 0,0038[2]	2,88 [1,42; 5,83] 0,0024[3]	6,9 [2,6; 11,3] 0,0024[3]
Number of positive lymph nodes (Interaction p-value: 0,3330)					
0-3	52/427 (12,2)	20/418 (4,8)	2,55 [1,55; 4,19] 0,0002[2]	2,76 [1,62; 4,71] 0,0001[3]	7,4 [3,7; 11,1] 0,0001[3]
4-9	70/549 (12,8)	27/542 (5,0)	2,56 [1,67; 3,93] <,0001[2]	2,79 [1,76; 4,42] <,0001[3]	7,8 [4,4; 11,1] <,0001[3]
≥ 10	32/307 (10,4)	20/305 (6,6)	1,59 [0,93; 2,72] 0,0900[2]	1,66 [0,93; 2,97] 0,0863[3]	3,9 [-0,5; 8,3] 0,0863[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,2640)					
IIA	19/113 (16,8)	7/114 (6,1)	2,74 [1,20; 6,26] 0,0169[2]	3,09 [1,24; 7,67] 0,0116[3]	10,7 [2,5; 18,9] 0,0116[3]
IIB	12/151 (7,9)	10/136 (7,4)	1,08 [0,48; 2,42] 0,8503[2]	1,09 [0,45; 2,60] 0,8502[3]	0,6 [-5,6; 6,7] 0,8502[3]
IIIA	65/495 (13,1)	24/488 (4,9)	2,67 [1,70; 4,19] <,0001[2]	2,92 [1,80; 4,75] <,0001[3]	8,2 [4,7; 11,8] <,0001[3]
IIIB	8/54 (14,8)	1/45 (2,2)	6,67 [0,87; 51,32] 0,0685[2]	7,65 [0,92; 63,72] 0,0374[4]	12,6 [2,2; 23,0] 0,0374[4]
IIIC	49/468 (10,5)	25/480 (5,2)	2,01 [1,26; 3,20] 0,0032[2]	2,13 [1,29; 3,51] 0,0025[3]	5,3 [1,8; 8,7] 0,0025[3]
Tumor grade (Interaction p-value: 0,1844)					
G1	7/91 (7,7)	1/93 (1,1)	7,15 [0,90; 56,99] 0,0631[2]	7,67 [0,92; 63,62] 0,0336[4]	6,6 [0,8; 12,5] 0,0336[4]
G2	67/612 (10,9)	36/603 (6,0)	1,83 [1,24; 2,71] 0,0023[2]	1,94 [1,27; 2,95] 0,0018[3]	5,0 [1,9; 8,1] 0,0018[3]
G3	70/527 (13,3)	28/506 (5,5)	2,40 [1,58; 3,66] <,0001[2]	2,61 [1,66; 4,13] <,0001[3]	7,7 [4,2; 11,3] <,0001[3]
GX	10/51 (19,6)	1/59 (1,7)	11,57 [1,53; 87,31] 0,0176[2]	14,15 [1,74; 114,85] 0,0018[3]	17,9 [6,5; 29,3] 0,0018[3]
Progesterone receptor status (Interaction p-value: 0,6561)					
Negative	18/156 (11,5)	9/169 (5,3)	2,17 [1,00; 4,68] 0,0491[2]	2,32 [1,01; 5,33] 0,0426[3]	6,2 [0,2; 12,3] 0,0426[3]
Positive	134/1089 (12,3)	56/1067 (5,2)	2,34 [1,74; 3,17] <,0001[2]	2,53 [1,83; 3,50] <,0001[3]	7,1 [4,7; 9,4] <,0001[3]
Unknown	1/10 (10,0)	1/7 (14,3)	0,70 [0,05; 9,41] 0,7879[2]	0,67 [0,03; 12,84] 1,0000[4]	-4,3 [-36,2; 27,6] 1,0000[4]
Race (Interaction p-value: 0,4562)					
White	100/958 (10,4)	48/944 (5,1)	2,05 [1,47; 2,86] <,0001[2]	2,18 [1,52; 3,11] <,0001[3]	5,4 [3,0; 7,7] <,0001[3]
Asian	45/250 (18,0)	18/242 (7,4)	2,42 [1,44; 4,06] 0,0008[2]	2,73 [1,53; 4,87] 0,0005[3]	10,6 [4,8; 16,4] 0,0005[3]
Other	7/62 (11,3)	1/64 (1,6)	7,23 [0,92; 57,03] 0,0606[2]	8,02 [0,96; 67,22] 0,0313[4]	9,7 [1,3; 18,2] 0,0313[4]
First endocrine therapy (Interaction p-value: 0,8311)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	5/114 (4,4)	3/132 (2,3)	1,93 [0,47; 7,90] 0,3605[2]	1,97 [0,46; 8,44] 0,4772[4]	2,1 [-2,4; 6,7] 0,4772[4]
Aromatase inhibitor	149/1169 (12,7)	64/1133 (5,6)	2,26 [1,70; 2,99] <,0001[2]	2,44 [1,80; 3,31] <,0001[3]	7,1 [4,8; 9,4] <,0001[3]
ECOG-PS (Interaction p-value: 0,5029)					
ECOG-PS 0	137/1070 (12,8)	56/1020 (5,5)	2,33 [1,73; 3,14] <,0001[2]	2,53 [1,83; 3,49] <,0001[3]	7,3 [4,9; 9,8] <,0001[3]
ECOG-PS 1	17/213 (8,0)	11/245 (4,5)	1,78 [0,85; 3,71] 0,1255[2]	1,85 [0,84; 4,03] 0,1198[3]	3,5 [-1,0; 8,0] 0,1198[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Alopecia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1687)					
< 65 years	92/918 (10,0)	26/937 (2,8)	3,61 [2,36; 5,53] <,0001[2]	3,90 [2,50; 6,09] <,0001[3]	7,2 [5,0; 9,5] <,0001[3]
≥ 65 years	58/365 (15,9)	8/328 (2,4)	6,52 [3,16; 13,44] <,0001[2]	7,56 [3,55; 16,09] <,0001[3]	13,5 [9,3; 17,6] <,0001[3]
Prior treatment (Interaction p-value: 0,3063)					
Neoadjuvant chemotherapy	52/430 (12,1)	7/415 (1,7)	7,17 [3,29; 15,60] <,0001[2]	8,02 [3,60; 17,87] <,0001[3]	10,4 [7,1; 13,7] <,0001[3]
Adjuvant chemotherapy	90/784 (11,5)	24/769 (3,1)	3,68 [2,37; 5,71] <,0001[2]	4,03 [2,54; 6,39] <,0001[3]	8,4 [5,8; 10,9] <,0001[3]
No chemotherapy	8/69 (11,6)	3/81 (3,7)	3,13 [0,86; 11,34] 0,0823[2]	3,41 [0,87; 13,40] 0,0647[3]	7,9 [-0,7; 16,5] 0,0647[3]
Region (Interaction p-value: 0,2818)					
North America / Europe	109/678 (16,1)	31/650 (4,8)	3,37 [2,30; 4,95] <,0001[2]	3,83 [2,53; 5,79] <,0001[3]	11,3 [8,1; 14,5] <,0001[3]
Asia	14/203 (6,9)	0/201 (0,0)	28,72 [1,72; 478,15] 0,0193[2]	30,84 [1,83; 520,53] 0,0002[3]	6,9 [3,4; 10,4] 0,0002[3]
Other	27/402 (6,7)	3/414 (0,7)	9,27 [2,83; 30,31] 0,0002[2]	9,86 [2,97; 32,78] <,0001[3]	6,0 [3,4; 8,6] <,0001[3]
Primary tumor size (Interaction p-value: 0,1434)					
< 20 mm	36/331 (10,9)	3/335 (0,9)	12,15 [3,78; 39,05] <,0001[2]	13,51 [4,12; 44,31] <,0001[3]	10,0 [6,5; 13,5] <,0001[3]
≥ 20 but < 50 mm	68/646 (10,5)	18/653 (2,8)	3,82 [2,30; 6,35] <,0001[2]	4,15 [2,44; 7,06] <,0001[3]	7,8 [5,1; 10,4] <,0001[3]
≥ 50 mm	43/289 (14,9)	12/265 (4,5)	3,29 [1,77; 6,09] 0,0002[2]	3,69 [1,90; 7,16] <,0001[3]	10,4 [5,5; 15,2] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,0807)					
0-3	47/427 (11,0)	5/418 (1,2)	9,20 [3,70; 22,91] <,0001[2]	10,22 [4,02; 25,96] <,0001[3]	9,8 [6,7; 13,0] <,0001[3]
4-9	63/549 (11,5)	21/542 (3,9)	2,96 [1,83; 4,78] <,0001[2]	3,22 [1,93; 5,35] <,0001[3]	7,6 [4,5; 10,7] <,0001[3]
≥ 10	40/307 (13,0)	8/305 (2,6)	4,97 [2,36; 10,44] <,0001[2]	5,56 [2,56; 12,10] <,0001[3]	10,4 [6,2; 14,6] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,5863)					
IIA	9/113 (8,0)	1/114 (0,9)	9,08 [1,17; 70,50] 0,0349[2]	9,78 [1,22; 78,52] 0,0099[4]	7,1 [1,8; 12,4] 0,0099[4]
IIB	19/151 (12,6)	2/136 (1,5)	8,56 [2,03; 36,06] 0,0034[2]	9,64 [2,20; 42,23] 0,0003[3]	11,1 [5,4; 16,8] 0,0003[3]
IIIA	57/495 (11,5)	18/488 (3,7)	3,12 [1,87; 5,22] <,0001[2]	3,40 [1,97; 5,86] <,0001[3]	7,8 [4,6; 11,1] <,0001[3]
IIIB	6/54 (11,1)	0/45 (0,0)	10,87 [0,63; 187,90] 0,1007[2]	12,20 [0,67; 222,70] 0,0303[4]	11,1 [2,7; 19,5] 0,0303[4]
IIIC	59/468 (12,6)	13/480 (2,7)	4,65 [2,59; 8,37] <,0001[2]	5,18 [2,80; 9,59] <,0001[3]	9,9 [6,6; 13,2] <,0001[3]
Tumor grade (Interaction p-value: 0,6432)					
G1	11/91 (12,1)	4/93 (4,3)	2,81 [0,93; 8,50] 0,0674[2]	3,06 [0,94; 9,99] 0,0536[3]	7,8 [-0,1; 15,7] 0,0536[3]
G2	84/612 (13,7)	17/603 (2,8)	4,87 [2,93; 8,10] <,0001[2]	5,48 [3,21; 9,36] <,0001[3]	10,9 [7,9; 13,9] <,0001[3]
G3	53/527 (10,1)	12/506 (2,4)	4,24 [2,29; 7,84] <,0001[2]	4,60 [2,43; 8,72] <,0001[3]	7,7 [4,8; 10,6] <,0001[3]
GX	1/51 (2,0)	1/59 (1,7)	1,16 [0,07; 18,03] 0,9172[2]	1,16 [0,07; 19,03] 1,0000[4]	0,3 [-4,8; 5,3] 1,0000[4]
Race (Interaction p-value: 0,3910)					
White	128/958 (13,4)	32/944 (3,4)	3,94 [2,70; 5,75] <,0001[2]	4,40 [2,95; 6,55] <,0001[3]	10,0 [7,5; 12,4] <,0001[3]
Asian	17/250 (6,8)	1/242 (0,4)	16,46 [2,21; 122,70] 0,0063[2]	17,58 [2,32; 133,19] 0,0002[3]	6,4 [3,2; 9,6] 0,0002[3]
Other	3/62 (4,8)	0/64 (0,0)	7,22 [0,38; 137,01] 0,1879[2]	7,59 [0,38; 150,00] 0,1162[4]	4,8 [-0,5; 10,2] 0,1162[4]
ECOG-PS (Interaction p-value: 0,4488)					
ECOG-PS 0	127/1070 (11,9)	26/1020 (2,5)	4,66 [3,08; 7,04] <,0001[2]	5,15 [3,35; 7,92] <,0001[3]	9,3 [7,2; 11,5] <,0001[3]
ECOG-PS 1	23/213 (10,8)	8/245 (3,3)	3,31 [1,51; 7,24] 0,0028[2]	3,59 [1,57; 8,20] 0,0014[3]	7,5 [2,8; 12,3] 0,0014[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Anaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7805)					
< 65 years	213/918 (23,2)	32/937 (3,4)	6,79 [4,74; 9,74] <,0001[2]	8,54 [5,82; 12,55] <,0001[3]	19,8 [16,8; 22,8] <,0001[3]
≥ 65 years	116/365 (31,8)	14/328 (4,3)	7,45 [4,36; 12,70] <,0001[2]	10,45 [5,86; 18,64] <,0001[3]	27,5 [22,3; 32,8] <,0001[3]
Prior treatment (Interaction p-value: 0,9879)					
Neoadjuvant chemotherapy	106/430 (24,7)	15/415 (3,6)	6,82 [4,04; 11,51] <,0001[2]	8,72 [4,98; 15,28] <,0001[3]	21,0 [16,6; 25,5] <,0001[3]
Adjuvant chemotherapy	205/784 (26,1)	28/769 (3,6)	7,18 [4,90; 10,52] <,0001[2]	9,37 [6,22; 14,11] <,0001[3]	22,5 [19,2; 25,9] <,0001[3]
No chemotherapy	18/69 (26,1)	3/81 (3,7)	7,04 [2,17; 22,91] 0,0012[2]	9,18 [2,57; 32,75] <,0001[3]	22,4 [11,2; 33,5] <,0001[3]
Region (Interaction p-value: 0,4307)					
North America / Europe	145/678 (21,4)	19/650 (2,9)	7,32 [4,59; 11,66] <,0001[2]	9,03 [5,52; 14,78] <,0001[3]	18,5 [15,1; 21,8] <,0001[3]
Asia	72/203 (35,5)	7/201 (3,5)	10,18 [4,81; 21,58] <,0001[2]	15,23 [6,80; 34,14] <,0001[3]	32,0 [24,9; 39,0] <,0001[3]
Other	112/402 (27,9)	20/414 (4,8)	5,77 [3,66; 9,10] <,0001[2]	7,61 [4,62; 12,54] <,0001[3]	23,0 [18,2; 27,9] <,0001[3]
Primary tumor size (Interaction p-value: 0,5305)					
< 20 mm	78/331 (23,6)	11/335 (3,3)	7,18 [3,89; 13,24] <,0001[2]	9,08 [4,73; 17,44] <,0001[3]	20,3 [15,3; 25,2] <,0001[3]
≥ 20 but < 50 mm	185/646 (28,6)	30/653 (4,6)	6,23 [4,31; 9,03] <,0001[2]	8,33 [5,56; 12,48] <,0001[3]	24,0 [20,2; 27,9] <,0001[3]
≥ 50 mm	59/289 (20,4)	5/265 (1,9)	10,82 [4,41; 26,55] <,0001[2]	13,34 [5,26; 33,81] <,0001[3]	18,5 [13,6; 23,5] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,4475)					
0-3	87/427 (20,4)	12/418 (2,9)	7,10 [3,94; 12,78] <,0001[2]	8,66 [4,65; 16,10] <,0001[3]	17,5 [13,4; 21,6] <,0001[3]
4-9	152/549 (27,7)	25/542 (4,6)	6,00 [4,00; 9,01] <,0001[2]	7,92 [5,09; 12,33] <,0001[3]	23,1 [18,9; 27,2] <,0001[3]
≥ 10	90/307 (29,3)	9/305 (3,0)	9,93 [5,10; 19,35] <,0001[2]	13,64 [6,72; 27,67] <,0001[3]	26,4 [20,9; 31,8] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,2523)					
IIA	20/113 (17,7)	6/114 (5,3)	3,36 [1,40; 8,06] 0,0066[2]	3,87 [1,49; 10,04] 0,0033[3]	12,4 [4,3; 20,6] 0,0033[3]
IIB	40/151 (26,5)	3/136 (2,2)	12,01 [3,80; 37,93] <,0001[2]	15,98 [4,81; 53,04] <,0001[3]	24,3 [16,8; 31,7] <,0001[3]
IIIA	128/495 (25,9)	23/488 (4,7)	5,49 [3,58; 8,40] <,0001[2]	7,05 [4,43; 11,22] <,0001[3]	21,1 [16,9; 25,4] <,0001[3]
IIIB	16/54 (29,6)	0/45 (0,0)	27,60 [1,70; 447,61] 0,0196[2]	39,00 [2,26; 671,56] <,0001[3]	29,6 [17,5; 41,8] <,0001[3]
IIIC	124/468 (26,5)	14/480 (2,9)	9,08 [5,31; 15,55] <,0001[2]	12,00 [6,79; 21,21] <,0001[3]	23,6 [19,3; 27,9] <,0001[3]
Tumor grade (Interaction p-value: 0,4531)					
G1	22/91 (24,2)	1/93 (1,1)	22,48 [3,09; 163,34] 0,0021[2]	29,33 [3,86; 222,94] <,0001[3]	23,1 [14,1; 32,1] <,0001[3]
G2	162/612 (26,5)	20/603 (3,3)	7,98 [5,09; 12,53] <,0001[2]	10,49 [6,49; 16,97] <,0001[3]	23,2 [19,4; 26,9] <,0001[3]
G3	123/527 (23,3)	21/506 (4,2)	5,62 [3,60; 8,79] <,0001[2]	7,03 [4,35; 11,38] <,0001[3]	19,2 [15,2; 23,2] <,0001[3]
GX	21/51 (41,2)	4/59 (6,8)	6,07 [2,23; 16,53] 0,0004[2]	9,63 [3,02; 30,64] <,0001[3]	34,4 [19,4; 49,3] <,0001[3]
Race (Interaction p-value: 0,5404)					
White	224/958 (23,4)	34/944 (3,6)	6,49 [4,58; 9,21] <,0001[2]	8,17 [5,62; 11,87] <,0001[3]	19,8 [16,8; 22,7] <,0001[3]
Asian	83/250 (33,2)	8/242 (3,3)	10,04 [4,97; 20,30] <,0001[2]	14,54 [6,85; 30,85] <,0001[3]	29,9 [23,6; 36,2] <,0001[3]
Other	18/62 (29,0)	3/64 (4,7)	6,19 [1,92; 19,98] 0,0023[2]	8,32 [2,31; 29,99] 0,0002[3]	24,3 [11,9; 36,8] 0,0002[3]
First endocrine therapy (Interaction p-value: 0,2710)					
Tamoxifen	18/114 (15,8)	1/132 (0,8)	20,84 [2,83; 153,70] 0,0029[2]	24,56 [3,22; 187,17] <,0001[3]	15,0 [8,2; 21,9] <,0001[3]
Aromatase inhibitor	311/1169 (26,6)	45/1133 (4,0)	6,70 [4,95; 9,06] <,0001[2]	8,76 [6,33; 12,13] <,0001[3]	22,6 [19,9; 25,4] <,0001[3]
ECOG-PS (Interaction p-value: 0,2908)					
ECOG-PS 0	267/1070 (25,0)	39/1020 (3,8)	6,53 [4,72; 9,03] <,0001[2]	8,36 [5,90; 11,85] <,0001[3]	21,1 [18,3; 24,0] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	62/213 (29,1)	7/245 (2,9)	10,19 [4,77; 21,78] <,0001[2]	13,96 [6,22; 31,31] <,0001[3]	26,3 [19,8; 32,7] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Anxiety from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,3875)					
Neoadjuvant chemotherapy	12/430 (2,8)	15/415 (3,6)	0,77 [0,37; 1,63] 0,4974[2]	0,77 [0,35; 1,66] 0,4961[3]	-0,8 [-3,2; 1,6] 0,4961[3]
Adjuvant chemotherapy	21/784 (2,7)	38/769 (4,9)	0,54 [0,32; 0,92] 0,0219[2]	0,53 [0,31; 0,91] 0,0197[3]	-2,3 [-4,2; -0,4] 0,0197[3]
No chemotherapy	3/69 (4,3)	2/81 (2,5)	1,76 [0,30; 10,24] 0,5287[2]	1,80 [0,29; 11,07] 0,6617[4]	1,9 [-4,0; 7,8] 0,6617[4]
Region (Interaction p-value: 0,8946)					
North America / Europe	26/678 (3,8)	33/650 (5,1)	0,76 [0,46; 1,25] 0,2738[2]	0,75 [0,44; 1,26] 0,2721[3]	-1,2 [-3,5; 1,0] 0,2721[3]
Asia	0/203 (0,0)	5/201 (2,5)	0,09 [0,01; 1,62] 0,1023[2]	0,09 [0,00; 1,60] 0,0297[4]	-2,5 [-4,6; -0,3] 0,0297[4]
Other	10/402 (2,5)	17/414 (4,1)	0,61 [0,28; 1,31] 0,2014[2]	0,60 [0,27; 1,32] 0,1962[3]	-1,6 [-4,1; 0,8] 0,1962[3]
Primary tumor size (Interaction p-value: 0,9615)					
< 20 mm	10/331 (3,0)	16/335 (4,8)	0,63 [0,29; 1,37] 0,2470[2]	0,62 [0,28; 1,39] 0,2423[3]	-1,8 [-4,7; 1,2] 0,2423[3]
≥ 20 but < 50 mm	18/646 (2,8)	26/653 (4,0)	0,70 [0,39; 1,26] 0,2365[2]	0,69 [0,38; 1,27] 0,2338[3]	-1,2 [-3,2; 0,8] 0,2338[3]
≥ 50 mm	8/289 (2,8)	12/265 (4,5)	0,61 [0,25; 1,47] 0,2724[2]	0,60 [0,24; 1,49] 0,2673[3]	-1,8 [-4,9; 1,4] 0,2673[3]
Number of positive lymph nodes (Interaction p-value: 0,1826)					
0-3	16/427 (3,7)	15/418 (3,6)	1,04 [0,52; 2,08] 0,9024[2]	1,05 [0,51; 2,14] 0,9024[3]	0,2 [-2,4; 2,7] 0,9024[3]
4-9	12/549 (2,2)	28/542 (5,2)	0,42 [0,22; 0,82] 0,0113[2]	0,41 [0,21; 0,82] 0,0088[3]	-3,0 [-5,2; -0,8] 0,0088[3]
≥ 10	8/307 (2,6)	12/305 (3,9)	0,66 [0,27; 1,60] 0,3591[2]	0,65 [0,26; 1,62] 0,3553[3]	-1,3 [-4,1; 1,5] 0,3553[3]
Tumor stage (Interaction p-value: 0,5776)					
IIA	4/113 (3,5)	4/114 (3,5)	1,01 [0,26; 3,94] 0,9899[2]	1,01 [0,25; 4,14] 1,0000[4]	0,0 [-4,8; 4,8] 1,0000[4]
IIB	5/151 (3,3)	3/136 (2,2)	1,50 [0,37; 6,16] 0,5730[2]	1,52 [0,36; 6,48] 0,7258[4]	1,1 [-2,7; 4,9] 0,7258[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	12/495 (2,4)	26/488 (5,3)	0,46 [0,23; 0,89] 0,0217[2]	0,44 [0,22; 0,89] 0,0182[3]	-2,9 [-5,3; -0,5] 0,0182[3]
IIIB	1/54 (1,9)	1/45 (2,2)	0,83 [0,05; 12,95] 0,8964[2]	0,83 [0,05; 13,66] 1,0000[4]	-0,4 [-6,0; 5,2] 1,0000[4]
IIIC	14/468 (3,0)	21/480 (4,4)	0,68 [0,35; 1,33] 0,2619[2]	0,67 [0,34; 1,34] 0,2587[3]	-1,4 [-3,8; 1,0] 0,2587[3]
Race (Interaction p-value: 0,4117)					
White	34/958 (3,5)	46/944 (4,9)	0,73 [0,47; 1,12] 0,1523[2]	0,72 [0,46; 1,13] 0,1504[3]	-1,3 [-3,1; 0,5] 0,1504[3]
Asian	1/250 (0,4)	5/242 (2,1)	0,19 [0,02; 1,65] 0,1326[2]	0,19 [0,02; 1,64] 0,1172[4]	-1,7 [-3,6; 0,3] 0,1172[4]
Other	1/62 (1,6)	3/64 (4,7)	0,34 [0,04; 3,22] 0,3497[2]	0,33 [0,03; 3,29] 0,6191[4]	-3,1 [-9,1; 3,0] 0,6191[4]
First endocrine therapy (Interaction p-value: 0,2712)					
Tamoxifen	6/114 (5,3)	6/132 (4,5)	1,16 [0,38; 3,49] 0,7946[2]	1,17 [0,37; 3,72] 0,7944[3]	0,7 [-4,7; 6,1] 0,7944[3]
Aromatase inhibitor	30/1169 (2,6)	49/1133 (4,3)	0,59 [0,38; 0,93] 0,0221[2]	0,58 [0,37; 0,92] 0,0205[3]	-1,8 [-3,3; -0,3] 0,0205[3]
ECOG-PS (Interaction p-value: 0,2279)					
ECOG-PS 0	33/1070 (3,1)	44/1020 (4,3)	0,71 [0,46; 1,11] 0,1378[2]	0,71 [0,45; 1,12] 0,1358[3]	-1,2 [-2,9; 0,4] 0,1358[3]
ECOG-PS 1	3/213 (1,4)	11/245 (4,5)	0,31 [0,09; 1,11] 0,0721[2]	0,30 [0,08; 1,10] 0,0560[3]	-3,1 [-6,1; -0,0] 0,0560[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Arthralgia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8378)					
< 65 years	244/918 (26,6)	358/937 (38,2)	0,70 [0,61; 0,80] <,0001[2]	0,59 [0,48; 0,71] <,0001[3]	-11,6 [-15,9; -7,4] <,0001[3]
≥ 65 years	98/365 (26,8)	130/328 (39,6)	0,68 [0,55; 0,84] 0,0004[2]	0,56 [0,41; 0,77] 0,0003[3]	-12,8 [-19,8; -5,8] 0,0003[3]
Prior treatment (Interaction p-value: 0,6036)					
Neoadjuvant chemotherapy	121/430 (28,1)	158/415 (38,1)	0,74 [0,61; 0,90] 0,0023[2]	0,64 [0,48; 0,85] 0,0021[3]	-9,9 [-16,2; -3,6] 0,0021[3]
Adjuvant chemotherapy	211/784 (26,9)	309/769 (40,2)	0,67 [0,58; 0,77] <,0001[2]	0,55 [0,44; 0,68] <,0001[3]	-13,3 [-17,9; -8,6] <,0001[3]
No chemotherapy	10/69 (14,5)	21/81 (25,9)	0,56 [0,28; 1,10] 0,0942[2]	0,48 [0,21; 1,12] 0,0848[3]	-11,4 [-24,1; 1,2] 0,0848[3]
Region (Interaction p-value: 0,6246)					
North America / Europe	231/678 (34,1)	310/650 (47,7)	0,71 [0,63; 0,82] <,0001[2]	0,57 [0,45; 0,71] <,0001[3]	-13,6 [-18,9; -8,4] <,0001[3]
Asia	38/203 (18,7)	61/201 (30,3)	0,62 [0,43; 0,88] 0,0076[2]	0,53 [0,33; 0,84] 0,0066[3]	-11,6 [-19,9; -3,3] 0,0066[3]
Other	73/402 (18,2)	117/414 (28,3)	0,64 [0,50; 0,83] 0,0008[2]	0,56 [0,40; 0,78] 0,0006[3]	-10,1 [-15,8; -4,4] 0,0006[3]
Primary tumor size (Interaction p-value: 0,9627)					
< 20 mm	91/331 (27,5)	134/335 (40,0)	0,69 [0,55; 0,86] 0,0008[2]	0,57 [0,41; 0,79] 0,0006[3]	-12,5 [-19,6; -5,4] 0,0006[3]
≥ 20 but < 50 mm	161/646 (24,9)	235/653 (36,0)	0,69 [0,59; 0,82] <,0001[2]	0,59 [0,46; 0,75] <,0001[3]	-11,1 [-16,0; -6,1] <,0001[3]
≥ 50 mm	85/289 (29,4)	117/265 (44,2)	0,67 [0,53; 0,83] 0,0004[2]	0,53 [0,37; 0,75] 0,0003[3]	-14,7 [-22,7; -6,8] 0,0003[3]
Number of positive lymph nodes (Interaction p-value: 0,2518)					
0-3	128/427 (30,0)	172/418 (41,1)	0,73 [0,61; 0,88] 0,0008[2]	0,61 [0,46; 0,81] 0,0007[3]	-11,2 [-17,6; -4,8] 0,0007[3]
4-9	150/549 (27,3)	204/542 (37,6)	0,73 [0,61; 0,86] 0,0003[2]	0,62 [0,48; 0,80] 0,0003[3]	-10,3 [-15,8; -4,8] 0,0003[3]
≥ 10	64/307 (20,8)	112/305 (36,7)	0,57 [0,44; 0,74] <,0001[2]	0,45 [0,32; 0,65] <,0001[3]	-15,9 [-22,9; -8,8] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7009)					
IIA	35/113 (31,0)	44/114 (38,6)	0,80 [0,56; 1,15] 0,2305[2]	0,71 [0,41; 1,24] 0,2280[3]	-7,6 [-20,0; 4,7] 0,2280[3]
IIB	42/151 (27,8)	57/136 (41,9)	0,66 [0,48; 0,92] 0,0132[2]	0,53 [0,33; 0,87] 0,0121[3]	-14,1 [-25,0; -3,1] 0,0121[3]
IIIA	137/495 (27,7)	184/488 (37,7)	0,73 [0,61; 0,88] 0,0009[2]	0,63 [0,48; 0,83] 0,0008[3]	-10,0 [-15,9; -4,2] 0,0008[3]
IIIB	15/54 (27,8)	19/45 (42,2)	0,66 [0,38; 1,14] 0,1352[2]	0,53 [0,23; 1,22] 0,1318[3]	-14,4 [-33,2; 4,3] 0,1318[3]
IIIC	112/468 (23,9)	184/480 (38,3)	0,62 [0,51; 0,76] <,0001[2]	0,51 [0,38; 0,67] <,0001[3]	-14,4 [-20,2; -8,6] <,0001[3]
Tumor grade (Interaction p-value: 0,3115)					
G1	27/91 (29,7)	31/93 (33,3)	0,89 [0,58; 1,36] 0,5935[2]	0,84 [0,45; 1,57] 0,5929[3]	-3,7 [-17,1; 9,7] 0,5929[3]
G2	162/612 (26,5)	242/603 (40,1)	0,66 [0,56; 0,78] <,0001[2]	0,54 [0,42; 0,68] <,0001[3]	-13,7 [-18,9; -8,4] <,0001[3]
G3	139/527 (26,4)	201/506 (39,7)	0,66 [0,56; 0,79] <,0001[2]	0,54 [0,42; 0,71] <,0001[3]	-13,3 [-19,0; -7,7] <,0001[3]
GX	13/51 (25,5)	14/59 (23,7)	1,07 [0,56; 2,07] 0,8304[2]	1,10 [0,46; 2,62] 0,8305[3]	1,8 [-14,4; 17,9] 0,8305[3]
Progesterone receptor status (Interaction p-value: 0,5287)					
Negative	42/156 (26,9)	60/169 (35,5)	0,76 [0,55; 1,05] 0,0992[2]	0,67 [0,42; 1,07] 0,0959[3]	-8,6 [-18,6; 1,4] 0,0959[3]
Positive	287/1089 (26,4)	410/1067 (38,4)	0,69 [0,61; 0,78] <,0001[2]	0,57 [0,48; 0,69] <,0001[3]	-12,1 [-16,0; -8,2] <,0001[3]
Unknown	4/10 (40,0)	2/7 (28,6)	1,40 [0,35; 5,65] 0,6366[2]	1,67 [0,21; 13,22] 1,0000[4]	11,4 [-33,8; 56,6] 1,0000[4]
Race (Interaction p-value: 0,8957)					
White	277/958 (28,9)	389/944 (41,2)	0,70 [0,62; 0,80] <,0001[2]	0,58 [0,48; 0,70] <,0001[3]	-12,3 [-16,5; -8,0] <,0001[3]
Asian	46/250 (18,4)	68/242 (28,1)	0,65 [0,47; 0,91] 0,0119[2]	0,58 [0,38; 0,88] 0,0108[3]	-9,7 [-17,1; -2,3] 0,0108[3]
Other	16/62 (25,8)	22/64 (34,4)	0,75 [0,44; 1,29] 0,2990[2]	0,66 [0,31; 1,43] 0,2948[3]	-8,6 [-24,5; 7,4] 0,2948[3]
First endocrine therapy (Interaction p-value: 0,2251)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	21/114 (18,4)	26/132 (19,7)	0,94 [0,56; 1,57] 0,7998[2]	0,92 [0,49; 1,74] 0,7996[3]	-1,3 [-11,1; 8,6] 0,7996[3]
Aromatase inhibitor	321/1169 (27,5)	462/1133 (40,8)	0,67 [0,60; 0,76] <,0001[2]	0,55 [0,46; 0,65] <,0001[3]	-13,3 [-17,2; -9,5] <,0001[3]
ECOG-PS (Interaction p-value: 0,8189)					
ECOG-PS 0	287/1070 (26,8)	399/1020 (39,1)	0,69 [0,61; 0,78] <,0001[2]	0,57 [0,47; 0,69] <,0001[3]	-12,3 [-16,3; -8,3] <,0001[3]
ECOG-PS 1	55/213 (25,8)	89/245 (36,3)	0,71 [0,54; 0,94] 0,0175[2]	0,61 [0,41; 0,91] 0,0157[3]	-10,5 [-18,9; -2,1] 0,0157[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Aspartate aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4422)					
< 65 years	109/918 (11,9)	53/937 (5,7)	2,10 [1,53; 2,88] <,0001[2]	2,25 [1,60; 3,16] <,0001[3]	6,2 [3,7; 8,8] <,0001[3]
≥ 65 years	37/365 (10,1)	12/328 (3,7)	2,77 [1,47; 5,22] 0,0016[2]	2,97 [1,52; 5,80] 0,0009[3]	6,5 [2,8; 10,2] 0,0009[3]
Prior treatment (Interaction p-value: 0,2142)					
Neoadjuvant chemotherapy	59/430 (13,7)	21/415 (5,1)	2,71 [1,68; 4,38] <,0001[2]	2,98 [1,78; 5,01] <,0001[3]	8,7 [4,8; 12,5] <,0001[3]
Adjuvant chemotherapy	78/784 (9,9)	42/769 (5,5)	1,82 [1,27; 2,62] 0,0012[2]	1,91 [1,30; 2,82] 0,0009[3]	4,5 [1,8; 7,1] 0,0009[3]
No chemotherapy	9/69 (13,0)	2/81 (2,5)	5,28 [1,18; 23,63] 0,0294[2]	5,93 [1,23; 28,44] 0,0133[3]	10,6 [1,9; 19,2] 0,0133[3]
Region (Interaction p-value: 0,2779)					
North America / Europe	51/678 (7,5)	21/650 (3,2)	2,33 [1,42; 3,83] 0,0009[2]	2,44 [1,45; 4,10] 0,0006[3]	4,3 [1,9; 6,7] 0,0006[3]
Asia	44/203 (21,7)	14/201 (7,0)	3,11 [1,76; 5,50] <,0001[2]	3,70 [1,95; 6,99] <,0001[3]	14,7 [8,0; 21,4] <,0001[3]
Other	51/402 (12,7)	30/414 (7,2)	1,75 [1,14; 2,69] 0,0106[2]	1,86 [1,16; 2,99] 0,0094[3]	5,4 [1,3; 9,5] 0,0094[3]
Primary tumor size (Interaction p-value: 0,7758)					
< 20 mm	39/331 (11,8)	18/335 (5,4)	2,19 [1,28; 3,75] 0,0042[2]	2,35 [1,32; 4,20] 0,0031[3]	6,4 [2,2; 10,6] 0,0031[3]
≥ 20 but < 50 mm	70/646 (10,8)	34/653 (5,2)	2,08 [1,40; 3,09] 0,0003[2]	2,21 [1,45; 3,38] 0,0002[3]	5,6 [2,7; 8,6] 0,0002[3]
≥ 50 mm	33/289 (11,4)	11/265 (4,2)	2,75 [1,42; 5,33] 0,0027[2]	2,98 [1,47; 6,02] 0,0016[3]	7,3 [2,9; 11,7] 0,0016[3]
Number of positive lymph nodes (Interaction p-value: 0,3742)					
0-3	47/427 (11,0)	18/418 (4,3)	2,56 [1,51; 4,33] 0,0005[2]	2,75 [1,57; 4,82] 0,0003[3]	6,7 [3,2; 10,3] 0,0003[3]
4-9	65/549 (11,8)	26/542 (4,8)	2,47 [1,59; 3,83] <,0001[2]	2,67 [1,66; 4,27] <,0001[3]	7,0 [3,8; 10,3] <,0001[3]
≥ 10	34/307 (11,1)	21/305 (6,9)	1,61 [0,96; 2,71] 0,0734[2]	1,68 [0,95; 2,97] 0,0700[3]	4,2 [-0,3; 8,7] 0,0700[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9862)					
IIA	16/113 (14,2)	8/114 (7,0)	2,02 [0,90; 4,53] 0,0885[2]	2,19 [0,90; 5,33] 0,0802[3]	7,1 [-0,8; 15,1] 0,0802[3]
IIB	11/151 (7,3)	6/136 (4,4)	1,65 [0,63; 4,34] 0,3096[2]	1,70 [0,61; 4,74] 0,3032[3]	2,9 [-2,5; 8,3] 0,3032[3]
IIIA	64/495 (12,9)	28/488 (5,7)	2,25 [1,47; 3,45] 0,0002[2]	2,44 [1,54; 3,88] 0,0001[3]	7,2 [3,6; 10,8] 0,0001[3]
IIIB	7/54 (13,0)	0/45 (0,0)	12,55 [0,74; 213,82] 0,0804[2]	14,37 [0,80; 258,91] 0,0149[4]	13,0 [4,0; 21,9] 0,0149[4]
IIIC	47/468 (10,0)	23/480 (4,8)	2,10 [1,29; 3,39] 0,0026[2]	2,22 [1,32; 3,72] 0,0020[3]	5,3 [1,9; 8,6] 0,0020[3]
Tumor grade (Interaction p-value: 0,3003)					
G1	9/91 (9,9)	1/93 (1,1)	9,20 [1,19; 71,14] 0,0335[2]	10,10 [1,25; 81,42] 0,0091[4]	8,8 [2,3; 15,3] 0,0091[4]
G2	63/612 (10,3)	35/603 (5,8)	1,77 [1,19; 2,64] 0,0047[2]	1,86 [1,21; 2,86] 0,0041[3]	4,5 [1,4; 7,5] 0,0041[3]
G3	63/527 (12,0)	23/506 (4,5)	2,63 [1,66; 4,17] <,0001[2]	2,85 [1,74; 4,67] <,0001[3]	7,4 [4,1; 10,7] <,0001[3]
GX	11/51 (21,6)	5/59 (8,5)	2,55 [0,95; 6,84] 0,0640[2]	2,97 [0,96; 9,23] 0,0521[3]	13,1 [-0,2; 26,4] 0,0521[3]
Progesterone receptor status (Interaction p-value: 0,5847)					
Negative	19/156 (12,2)	11/169 (6,5)	1,87 [0,92; 3,81] 0,0837[2]	1,99 [0,92; 4,33] 0,0777[3]	5,7 [-0,7; 12,0] 0,0777[3]
Positive	126/1089 (11,6)	53/1067 (5,0)	2,33 [1,71; 3,17] <,0001[2]	2,50 [1,79; 3,49] <,0001[3]	6,6 [4,3; 8,9] <,0001[3]
Unknown	1/10 (10,0)	1/7 (14,3)	0,70 [0,05; 9,41] 0,7879[2]	0,67 [0,03; 12,84] 1,0000[4]	-4,3 [-36,2; 27,6] 1,0000[4]
Race (Interaction p-value: 0,5585)					
White	94/958 (9,8)	46/944 (4,9)	2,01 [1,43; 2,83] <,0001[2]	2,12 [1,47; 3,06] <,0001[3]	4,9 [2,6; 7,3] <,0001[3]
Asian	44/250 (17,6)	15/242 (6,2)	2,84 [1,62; 4,96] 0,0003[2]	3,23 [1,75; 5,98] <,0001[3]	11,4 [5,8; 17,0] <,0001[3]
Other	7/62 (11,3)	4/64 (6,3)	1,81 [0,56; 5,87] 0,3251[2]	1,91 [0,53; 6,88] 0,3163[3]	5,0 [-4,8; 14,9] 0,3163[3]
First endocrine therapy (Interaction p-value: 0,9366)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	6/114 (5,3)	3/132 (2,3)	2,32 [0,59; 9,05] 0,2272[2]	2,39 [0,58; 9,78] 0,3097[4]	3,0 [-1,8; 7,8] 0,3097[4]
Aromatase inhibitor	140/1169 (12,0)	62/1133 (5,5)	2,19 [1,64; 2,92] <,0001[2]	2,35 [1,72; 3,21] <,0001[3]	6,5 [4,2; 8,8] <,0001[3]
ECOG-PS (Interaction p-value: 0,5767)					
ECOG-PS 0	125/1070 (11,7)	52/1020 (5,1)	2,29 [1,68; 3,13] <,0001[2]	2,46 [1,76; 3,44] <,0001[3]	6,6 [4,2; 8,9] <,0001[3]
ECOG-PS 1	21/213 (9,9)	13/245 (5,3)	1,86 [0,95; 3,62] 0,0686[2]	1,95 [0,95; 4,00] 0,0638[3]	4,6 [-0,3; 9,4] 0,0638[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Asthenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6560)					
< 65 years	101/918 (11,0)	50/937 (5,3)	2,06 [1,49; 2,86] <,0001[2]	2,19 [1,54; 3,12] <,0001[3]	5,7 [3,2; 8,1] <,0001[3]
≥ 65 years	45/365 (12,3)	17/328 (5,2)	2,38 [1,39; 4,07] 0,0016[2]	2,57 [1,44; 4,59] 0,0010[3]	7,1 [3,0; 11,3] 0,0010[3]
Prior treatment (Interaction p-value: 0,3679)					
Neoadjuvant chemotherapy	54/430 (12,6)	18/415 (4,3)	2,90 [1,73; 4,85] <,0001[2]	3,17 [1,82; 5,50] <,0001[3]	8,2 [4,5; 11,9] <,0001[3]
Adjuvant chemotherapy	85/784 (10,8)	44/769 (5,7)	1,89 [1,34; 2,69] 0,0003[2]	2,00 [1,37; 2,93] 0,0003[3]	5,1 [2,4; 7,8] 0,0003[3]
No chemotherapy	7/69 (10,1)	5/81 (6,2)	1,64 [0,55; 4,95] 0,3768[2]	1,72 [0,52; 5,67] 0,3715[3]	4,0 [-4,9; 12,8] 0,3715[3]
Region (Interaction p-value: 0,6671)					
North America / Europe	81/678 (11,9)	41/650 (6,3)	1,89 [1,32; 2,71] 0,0005[2]	2,02 [1,36; 2,98] 0,0004[3]	5,6 [2,6; 8,7] 0,0004[3]
Asia	3/203 (1,5)	0/201 (0,0)	6,93 [0,36; 133,33] 0,1994[2]	7,03 [0,36; 137,07] 0,2482[4]	1,5 [-0,2; 3,1] 0,2482[4]
Other	62/402 (15,4)	26/414 (6,3)	2,46 [1,59; 3,80] <,0001[2]	2,72 [1,68; 4,40] <,0001[3]	9,1 [4,9; 13,4] <,0001[3]
Primary tumor size (Interaction p-value: 0,4653)					
< 20 mm	38/331 (11,5)	13/335 (3,9)	2,96 [1,61; 5,45] 0,0005[2]	3,21 [1,68; 6,15] 0,0002[3]	7,6 [3,6; 11,6] 0,0002[3]
≥ 20 but < 50 mm	79/646 (12,2)	42/653 (6,4)	1,90 [1,33; 2,72] 0,0004[2]	2,03 [1,37; 3,00] 0,0003[3]	5,8 [2,6; 8,9] 0,0003[3]
≥ 50 mm	26/289 (9,0)	12/265 (4,5)	1,99 [1,02; 3,86] 0,0425[2]	2,08 [1,03; 4,22] 0,0377[3]	4,5 [0,3; 8,6] 0,0377[3]
Number of positive lymph nodes (Interaction p-value: 0,7790)					
0-3	50/427 (11,7)	25/418 (6,0)	1,96 [1,24; 3,10] 0,0043[2]	2,08 [1,26; 3,44] 0,0034[3]	5,7 [1,9; 9,5] 0,0034[3]
4-9	66/549 (12,0)	27/542 (5,0)	2,41 [1,57; 3,72] <,0001[2]	2,61 [1,64; 4,15] <,0001[3]	7,0 [3,8; 10,3] <,0001[3]
≥ 10	30/307 (9,8)	15/305 (4,9)	1,99 [1,09; 3,62] 0,0247[2]	2,09 [1,10; 3,98] 0,0214[3]	4,9 [0,7; 9,0] 0,0214[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8844)					
IIA	13/113 (11,5)	6/114 (5,3)	2,19 [0,86; 5,55] 0,1000[2]	2,34 [0,86; 6,39] 0,0896[3]	6,2 [-0,9; 13,4] 0,0896[3]
IIB	16/151 (10,6)	8/136 (5,9)	1,80 [0,80; 4,08] 0,1577[2]	1,90 [0,78; 4,58] 0,1498[3]	4,7 [-1,6; 11,0] 0,1498[3]
IIIA	64/495 (12,9)	25/488 (5,1)	2,52 [1,62; 3,94] <,0001[2]	2,75 [1,70; 4,45] <,0001[3]	7,8 [4,3; 11,4] <,0001[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	50/468 (10,7)	28/480 (5,8)	1,83 [1,17; 2,86] 0,0077[2]	1,93 [1,19; 3,12] 0,0066[3]	4,9 [1,4; 8,3] 0,0066[3]
Tumor grade (Interaction p-value: 0,7545)					
G1	10/91 (11,0)	7/93 (7,5)	1,46 [0,58; 3,67] 0,4210[2]	1,52 [0,55; 4,17] 0,4175[3]	3,5 [-4,9; 11,8] 0,4175[3]
G2	72/612 (11,8)	30/603 (5,0)	2,36 [1,57; 3,57] <,0001[2]	2,55 [1,64; 3,96] <,0001[3]	6,8 [3,7; 9,9] <,0001[3]
G3	58/527 (11,0)	30/506 (5,9)	1,86 [1,22; 2,84] 0,0042[2]	1,96 [1,24; 3,10] 0,0035[3]	5,1 [1,7; 8,4] 0,0035[3]
GX	5/51 (9,8)	0/59 (0,0)	12,69 [0,72; 224,11] 0,0828[2]	14,08 [0,76; 261,07] 0,0192[4]	9,8 [1,6; 18,0] 0,0192[4]
Race (Interaction p-value: 0,7165)					
White	135/958 (14,1)	60/944 (6,4)	2,22 [1,66; 2,96] <,0001[2]	2,42 [1,76; 3,32] <,0001[3]	7,7 [5,0; 10,4] <,0001[3]
Asian	5/250 (2,0)	0/242 (0,0)	10,65 [0,59; 191,56] 0,1086[2]	10,87 [0,60; 197,57] 0,0614[4]	2,0 [0,3; 3,7] 0,0614[4]
Other	5/62 (8,1)	4/64 (6,3)	1,29 [0,36; 4,58] 0,6935[2]	1,32 [0,34; 5,15] 0,7417[4]	1,8 [-7,2; 10,8] 0,7417[4]
First endocrine therapy (Interaction p-value: 0,8285)					
Tamoxifen	10/114 (8,8)	6/132 (4,5)	1,93 [0,72; 5,15] 0,1888[2]	2,02 [0,71; 5,74] 0,1801[3]	4,2 [-2,1; 10,5] 0,1801[3]
Aromatase inhibitor	136/1169 (11,6)	61/1133 (5,4)	2,16 [1,62; 2,89] <,0001[2]	2,31 [1,69; 3,17] <,0001[3]	6,2 [4,0; 8,5] <,0001[3]
ECOG-PS (Interaction p-value: 0,9292)					
ECOG-PS 0	123/1070 (11,5)	55/1020 (5,4)	2,13 [1,57; 2,90] <,0001[2]	2,28 [1,64; 3,17] <,0001[3]	6,1 [3,7; 8,5] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	23/213 (10,8)	12/245 (4,9)	2,20 [1,12; 4,32] 0,0214[2]	2,35 [1,14; 4,85] 0,0178[3]	5,9 [0,9; 10,9] 0,0178[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Back pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,3744)					
< 65 years	88/918 (9,6)	111/937 (11,8)	0,81 [0,62; 1,05] 0,1167[2]	0,79 [0,59; 1,06] 0,1158[3]	-2,3 [-5,1; 0,6] 0,1158[3]
≥ 65 years	26/365 (7,1)	37/328 (11,3)	0,63 [0,39; 1,02] 0,0599[2]	0,60 [0,36; 1,02] 0,0573[3]	-4,2 [-8,5; 0,2] 0,0573[3]
Prior treatment (Interaction p-value: 0,5424)					
Neoadjuvant chemotherapy	40/430 (9,3)	43/415 (10,4)	0,90 [0,60; 1,35] 0,6052[2]	0,89 [0,56; 1,40] 0,6051[3]	-1,1 [-5,1; 3,0] 0,6051[3]
Adjuvant chemotherapy	71/784 (9,1)	98/769 (12,7)	0,71 [0,53; 0,95] 0,0204[2]	0,68 [0,49; 0,94] 0,0196[3]	-3,7 [-6,8; -0,6] 0,0196[3]
No chemotherapy	3/69 (4,3)	7/81 (8,6)	0,50 [0,14; 1,87] 0,3055[2]	0,48 [0,12; 1,93] 0,3434[4]	-4,3 [-12,1; 3,5] 0,3434[4]
Region (Interaction p-value: 0,5280)					
North America / Europe	82/678 (12,1)	97/650 (14,9)	0,81 [0,62; 1,07] 0,1322[2]	0,78 [0,57; 1,08] 0,1313[3]	-2,8 [-6,5; 0,8] 0,1313[3]
Asia	10/203 (4,9)	19/201 (9,5)	0,52 [0,25; 1,09] 0,0845[2]	0,50 [0,22; 1,10] 0,0780[3]	-4,5 [-9,5; 0,5] 0,0780[3]
Other	22/402 (5,5)	32/414 (7,7)	0,71 [0,42; 1,20] 0,1976[2]	0,69 [0,39; 1,21] 0,1948[3]	-2,3 [-5,7; 1,1] 0,1948[3]
Primary tumor size (Interaction p-value: 0,9178)					
< 20 mm	27/331 (8,2)	35/335 (10,4)	0,78 [0,48; 1,26] 0,3107[2]	0,76 [0,45; 1,29] 0,3090[3]	-2,3 [-6,7; 2,1] 0,3090[3]
≥ 20 but < 50 mm	56/646 (8,7)	78/653 (11,9)	0,73 [0,52; 1,01] 0,0536[2]	0,70 [0,49; 1,00] 0,0523[3]	-3,3 [-6,6; 0,0] 0,0523[3]
≥ 50 mm	31/289 (10,7)	35/265 (13,2)	0,81 [0,52; 1,28] 0,3688[2]	0,79 [0,47; 1,32] 0,3679[3]	-2,5 [-7,9; 2,9] 0,3679[3]
Number of positive lymph nodes (Interaction p-value: 0,0759)					
0-3	52/427 (12,2)	48/418 (11,5)	1,06 [0,73; 1,53] 0,7547[2]	1,07 [0,70; 1,62] 0,7546[3]	0,7 [-3,7; 5,0] 0,7546[3]
4-9	37/549 (6,7)	62/542 (11,4)	0,59 [0,40; 0,87] 0,0078[2]	0,56 [0,37; 0,86] 0,0069[3]	-4,7 [-8,1; -1,3] 0,0069[3]
≥ 10	25/307 (8,1)	38/305 (12,5)	0,65 [0,40; 1,06] 0,0820[2]	0,62 [0,37; 1,06] 0,0790[3]	-4,3 [-9,1; 0,5] 0,0790[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,1132)					
IIA	18/113 (15,9)	9/114 (7,9)	2,02 [0,95; 4,30] 0,0690[2]	2,21 [0,95; 5,16] 0,0615[3]	8,0 [-0,3; 16,4] 0,0615[3]
IIB	16/151 (10,6)	19/136 (14,0)	0,76 [0,41; 1,41] 0,3847[2]	0,73 [0,36; 1,48] 0,3830[3]	-3,4 [-11,0; 4,2] 0,3830[3]
IIIA	39/495 (7,9)	57/488 (11,7)	0,67 [0,46; 0,99] 0,0465[2]	0,65 [0,42; 0,99] 0,0447[3]	-3,8 [-7,5; -0,1] 0,0447[3]
IIIB	4/54 (7,4)	4/45 (8,9)	0,83 [0,22; 3,15] 0,7879[2]	0,82 [0,19; 3,48] 1,0000[4]	-1,5 [-12,3; 9,4] 1,0000[4]
IIIC	37/468 (7,9)	59/480 (12,3)	0,64 [0,44; 0,95] 0,0269[2]	0,61 [0,40; 0,94] 0,0252[3]	-4,4 [-8,2; -0,6] 0,0252[3]
Tumor grade (Interaction p-value: 0,4754)					
G1	5/91 (5,5)	14/93 (15,1)	0,36 [0,14; 0,97] 0,0437[2]	0,33 [0,11; 0,95] 0,0331[3]	-9,6 [-18,2; -0,9] 0,0331[3]
G2	52/612 (8,5)	65/603 (10,8)	0,79 [0,56; 1,12] 0,1788[2]	0,77 [0,52; 1,13] 0,1775[3]	-2,3 [-5,6; 1,0] 0,1775[3]
G3	51/527 (9,7)	62/506 (12,3)	0,79 [0,56; 1,12] 0,1862[2]	0,77 [0,52; 1,14] 0,1849[3]	-2,6 [-6,4; 1,2] 0,1849[3]
GX	6/51 (11,8)	7/59 (11,9)	0,99 [0,36; 2,76] 0,9871[2]	0,99 [0,31; 3,16] 0,9871[3]	-0,1 [-12,2; 12,0] 0,9871[3]
Progesterone receptor status (Interaction p-value: 0,7751)					
Negative	19/156 (12,2)	22/169 (13,0)	0,94 [0,53; 1,66] 0,8202[2]	0,93 [0,48; 1,79] 0,8201[3]	-0,8 [-8,1; 6,4] 0,8201[3]
Positive	92/1089 (8,4)	121/1067 (11,3)	0,74 [0,58; 0,96] 0,0251[2]	0,72 [0,54; 0,96] 0,0244[3]	-2,9 [-5,4; -0,4] 0,0244[3]
Unknown	1/10 (10,0)	1/7 (14,3)	0,70 [0,05; 9,41] 0,7879[2]	0,67 [0,03; 12,84] 1,0000[4]	-4,3 [-36,2; 27,6] 1,0000[4]
Race (Interaction p-value: 0,8277)					
White	94/958 (9,8)	124/944 (13,1)	0,75 [0,58; 0,96] 0,0236[2]	0,72 [0,54; 0,96] 0,0229[3]	-3,3 [-6,2; -0,5] 0,0229[3]
Asian	13/250 (5,2)	18/242 (7,4)	0,70 [0,35; 1,40] 0,3101[2]	0,68 [0,33; 1,43] 0,3071[3]	-2,2 [-6,5; 2,1] 0,3071[3]
Other	6/62 (9,7)	6/64 (9,4)	1,03 [0,35; 3,03] 0,9539[2]	1,04 [0,32; 3,40] 0,9539[3]	0,3 [-10,0; 10,6] 0,9539[3]
First endocrine therapy (Interaction p-value: 0,9621)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	8/114 (7,0)	12/132 (9,1)	0,77 [0,33; 1,82] 0,5547[2]	0,75 [0,30; 1,92] 0,5529[3]	-2,1 [-8,9; 4,7] 0,5529[3]
Aromatase inhibitor	106/1169 (9,1)	136/1133 (12,0)	0,76 [0,59; 0,96] 0,0222[2]	0,73 [0,56; 0,96] 0,0217[3]	-2,9 [-5,4; -0,4] 0,0217[3]
ECOG-PS (Interaction p-value: 0,2712)					
ECOG-PS 0	96/1070 (9,0)	128/1020 (12,5)	0,71 [0,56; 0,92] 0,0086[2]	0,69 [0,52; 0,91] 0,0082[3]	-3,6 [-6,2; -0,9] 0,0082[3]
ECOG-PS 1	18/213 (8,5)	20/245 (8,2)	1,04 [0,56; 1,90] 0,9114[2]	1,04 [0,53; 2,02] 0,9114[3]	0,3 [-4,8; 5,4] 0,9114[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Blood alkaline phosphatase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6780)					
< 65 years	40/918 (4,4)	26/937 (2,8)	1,57 [0,97; 2,55] 0,0684[2]	1,60 [0,97; 2,64] 0,0658[3]	1,6 [-0,1; 3,3] 0,0658[3]
≥ 65 years	19/365 (5,2)	13/328 (4,0)	1,31 [0,66; 2,62] 0,4384[2]	1,33 [0,65; 2,74] 0,4366[3]	1,2 [-1,9; 4,3] 0,4366[3]
Prior treatment (Interaction p-value: 0,8456)					
Neoadjuvant chemotherapy	25/430 (5,8)	16/415 (3,9)	1,51 [0,82; 2,78] 0,1889[2]	1,54 [0,81; 2,93] 0,1853[3]	2,0 [-0,9; 4,8] 0,1853[3]
Adjuvant chemotherapy	30/784 (3,8)	21/769 (2,7)	1,40 [0,81; 2,43] 0,2282[2]	1,42 [0,80; 2,50] 0,2257[3]	1,1 [-0,7; 2,9] 0,2257[3]
No chemotherapy	4/69 (5,8)	2/81 (2,5)	2,35 [0,44; 12,43] 0,3155[2]	2,43 [0,43; 13,69] 0,4143[4]	3,3 [-3,1; 9,8] 0,4143[4]
Region (Interaction p-value: 0,4545)					
North America / Europe	16/678 (2,4)	14/650 (2,2)	1,10 [0,54; 2,23] 0,8007[2]	1,10 [0,53; 2,27] 0,8006[3]	0,2 [-1,4; 1,8] 0,8006[3]
Asia	12/203 (5,9)	5/201 (2,5)	2,38 [0,85; 6,62] 0,0979[2]	2,46 [0,85; 7,12] 0,0866[3]	3,4 [-0,5; 7,3] 0,0866[3]
Other	31/402 (7,7)	20/414 (4,8)	1,60 [0,93; 2,75] 0,0927[2]	1,65 [0,92; 2,94] 0,0892[3]	2,9 [-0,4; 6,2] 0,0892[3]
Primary tumor size (Interaction p-value: 0,4252)					
< 20 mm	10/331 (3,0)	10/335 (3,0)	1,01 [0,43; 2,40] 0,9782[2]	1,01 [0,42; 2,47] 0,9782[3]	0,0 [-2,6; 2,6] 0,9782[3]
≥ 20 but < 50 mm	36/646 (5,6)	19/653 (2,9)	1,92 [1,11; 3,30] 0,0194[2]	1,97 [1,12; 3,47] 0,0172[3]	2,7 [0,5; 4,9] 0,0172[3]
≥ 50 mm	11/289 (3,8)	8/265 (3,0)	1,26 [0,52; 3,09] 0,6119[2]	1,27 [0,50; 3,21] 0,6110[3]	0,8 [-2,2; 3,8] 0,6110[3]
Number of positive lymph nodes (Interaction p-value: 0,5525)					
0-3	20/427 (4,7)	10/418 (2,4)	1,96 [0,93; 4,13] 0,0779[2]	2,00 [0,93; 4,34] 0,0719[3]	2,3 [-0,2; 4,8] 0,0719[3]
4-9	22/549 (4,0)	14/542 (2,6)	1,55 [0,80; 3,00] 0,1918[2]	1,57 [0,80; 3,11] 0,1879[3]	1,4 [-0,7; 3,5] 0,1879[3]
≥ 10	17/307 (5,5)	15/305 (4,9)	1,13 [0,57; 2,21] 0,7309[2]	1,13 [0,56; 2,31] 0,7307[3]	0,6 [-2,9; 4,1] 0,7307[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9768)					
IIA	4/113 (3,5)	3/114 (2,6)	1,35 [0,31; 5,87] 0,6934[2]	1,36 [0,30; 6,21] 0,7216[4]	0,9 [-3,6; 5,4] 0,7216[4]
IIB	9/151 (6,0)	4/136 (2,9)	2,03 [0,64; 6,43] 0,2306[2]	2,09 [0,63; 6,95] 0,2194[3]	3,0 [-1,7; 7,7] 0,2194[3]
IIIA	19/495 (3,8)	13/488 (2,7)	1,44 [0,72; 2,89] 0,3025[2]	1,46 [0,71; 2,99] 0,2995[3]	1,2 [-1,0; 3,4] 0,2995[3]
IIIB	3/54 (5,6)	0/45 (0,0)	5,85 [0,31; 110,43] 0,2383[2]	6,18 [0,31; 122,97] 0,2486[4]	5,6 [-0,6; 11,7] 0,2486[4]
IIIC	24/468 (5,1)	19/480 (4,0)	1,30 [0,72; 2,33] 0,3883[2]	1,31 [0,71; 2,43] 0,3868[3]	1,2 [-1,5; 3,8] 0,3868[3]
Tumor grade (Interaction p-value: 0,2890)					
G1	3/91 (3,3)	5/93 (5,4)	0,61 [0,15; 2,49] 0,4941[2]	0,60 [0,14; 2,59] 0,7206[4]	-2,1 [-8,0; 3,8] 0,7206[4]
G2	20/612 (3,3)	17/603 (2,8)	1,16 [0,61; 2,19] 0,6493[2]	1,16 [0,60; 2,25] 0,6490[3]	0,4 [-1,5; 2,4] 0,6490[3]
G3	29/527 (5,5)	14/506 (2,8)	1,99 [1,06; 3,72] 0,0314[2]	2,05 [1,07; 3,92] 0,0277[3]	2,7 [0,3; 5,2] 0,0277[3]
GX	7/51 (13,7)	3/59 (5,1)	2,70 [0,74; 9,90] 0,1342[2]	2,97 [0,73; 12,15] 0,1829[4]	8,6 [-2,3; 19,6] 0,1829[4]
Progesterone receptor status (Interaction p-value: 0,1109)					
Negative	9/156 (5,8)	6/169 (3,6)	1,63 [0,59; 4,46] 0,3460[2]	1,66 [0,58; 4,79] 0,3408[3]	2,2 [-2,4; 6,8] 0,3408[3]
Positive	50/1089 (4,6)	31/1067 (2,9)	1,58 [1,02; 2,45] 0,0415[2]	1,61 [1,02; 2,54] 0,0396[3]	1,7 [0,1; 3,3] 0,0396[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,6760)					
White	47/958 (4,9)	33/944 (3,5)	1,40 [0,91; 2,17] 0,1276[2]	1,42 [0,90; 2,24] 0,1255[3]	1,4 [-0,4; 3,2] 0,1255[3]
Asian	12/250 (4,8)	5/242 (2,1)	2,32 [0,83; 6,50] 0,1081[2]	2,39 [0,83; 6,89] 0,0969[3]	2,7 [-0,5; 5,9] 0,0969[3]
Other	0/62 (0,0)	1/64 (1,6)	0,34 [0,01; 8,28] 0,5109[2]	0,34 [0,01; 8,47] 1,0000[4]	-1,6 [-4,6; 1,5] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,4349)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	1/114 (0,9)	2/132 (1,5)	0,58 [0,05; 6,30] 0,6536[2]	0,58 [0,05; 6,43] 1,0000[4]	-0,6 [-3,3; 2,1] 1,0000[4]
Aromatase inhibitor	58/1169 (5,0)	37/1133 (3,3)	1,52 [1,01; 2,28] 0,0426[2]	1,55 [1,02; 2,36] 0,0409[3]	1,7 [0,1; 3,3] 0,0409[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Blood creatinine increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6228)					
< 65 years	93/918 (10,1)	10/937 (1,1)	9,49 [4,98; 18,11] <,0001[2]	10,45 [5,41; 20,20] <,0001[3]	9,1 [7,0; 11,1] <,0001[3]
≥ 65 years	57/365 (15,6)	4/328 (1,2)	12,81 [4,70; 34,91] <,0001[2]	14,99 [5,37; 41,81] <,0001[3]	14,4 [10,5; 18,3] <,0001[3]
Prior treatment (Interaction p-value: 0,5189)					
Neoadjuvant chemotherapy	50/430 (11,6)	7/415 (1,7)	6,89 [3,16; 15,03] <,0001[2]	7,67 [3,43; 17,12] <,0001[3]	9,9 [6,7; 13,2] <,0001[3]
Adjuvant chemotherapy	93/784 (11,9)	7/769 (0,9)	13,03 [6,08; 27,91] <,0001[2]	14,65 [6,75; 31,80] <,0001[3]	11,0 [8,6; 13,3] <,0001[3]
No chemotherapy	7/69 (10,1)	0/81 (0,0)	17,57 [1,02; 302,22] 0,0483[2]	19,56 [1,10; 349,01] 0,0037[4]	10,1 [3,0; 17,3] 0,0037[4]
Region (Interaction p-value: 0,2558)					
North America / Europe	81/678 (11,9)	6/650 (0,9)	12,94 [5,69; 29,45] <,0001[2]	14,56 [6,31; 33,62] <,0001[3]	11,0 [8,5; 13,6] <,0001[3]
Asia	27/203 (13,3)	1/201 (0,5)	26,73 [3,67; 194,87] 0,0012[2]	30,68 [4,13; 228,12] <,0001[3]	12,8 [8,0; 17,6] <,0001[3]
Other	42/402 (10,4)	7/414 (1,7)	6,18 [2,81; 13,59] <,0001[2]	6,78 [3,01; 15,29] <,0001[3]	8,8 [5,5; 12,0] <,0001[3]
Primary tumor size (Interaction p-value: 0,5337)					
< 20 mm	37/331 (11,2)	3/335 (0,9)	12,48 [3,89; 40,09] <,0001[2]	13,93 [4,25; 45,64] <,0001[3]	10,3 [6,7; 13,8] <,0001[3]
≥ 20 but < 50 mm	82/646 (12,7)	10/653 (1,5)	8,29 [4,34; 15,84] <,0001[2]	9,35 [4,80; 18,20] <,0001[3]	11,2 [8,4; 13,9] <,0001[3]
≥ 50 mm	27/289 (9,3)	1/265 (0,4)	24,76 [3,39; 180,93] 0,0016[2]	27,21 [3,67; 201,68] <,0001[3]	9,0 [5,5; 12,4] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,7590)					
0-3	49/427 (11,5)	4/418 (1,0)	11,99 [4,37; 32,93] <,0001[2]	13,42 [4,80; 37,53] <,0001[3]	10,5 [7,4; 13,7] <,0001[3]
4-9	60/549 (10,9)	7/542 (1,3)	8,46 [3,90; 18,35] <,0001[2]	9,38 [4,25; 20,71] <,0001[3]	9,6 [6,9; 12,4] <,0001[3]
≥ 10	41/307 (13,4)	3/305 (1,0)	13,58 [4,25; 43,38] <,0001[2]	15,52 [4,75; 50,69] <,0001[3]	12,4 [8,4; 16,3] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,4006)					
IIA	13/113 (11,5)	0/114 (0,0)	27,24 [1,64; 452,75] 0,0212[2]	30,76 [1,81; 524,06] 0,0002[3]	11,5 [5,6; 17,4] 0,0002[3]
IIB	16/151 (10,6)	4/136 (2,9)	3,60 [1,23; 10,51] 0,0190[2]	3,91 [1,27; 12,01] 0,0110[3]	7,7 [2,0; 13,3] 0,0110[3]
IIIA	53/495 (10,7)	6/488 (1,2)	8,71 [3,78; 20,07] <,0001[2]	9,63 [4,10; 22,63] <,0001[3]	9,5 [6,6; 12,4] <,0001[3]
IIIB	4/54 (7,4)	0/45 (0,0)	7,53 [0,42; 136,17] 0,1718[2]	8,11 [0,42; 154,79] 0,1236[4]	7,4 [0,4; 14,4] 0,1236[4]
IIIC	63/468 (13,5)	4/480 (0,8)	16,15 [5,93; 44,02] <,0001[2]	18,51 [6,68; 51,30] <,0001[3]	12,6 [9,4; 15,8] <,0001[3]
Tumor grade (Interaction p-value: 0,9980)					
G1	6/91 (6,6)	0/93 (0,0)	13,28 [0,76; 232,41] 0,0765[2]	14,22 [0,79; 256,15] 0,0134[4]	6,6 [1,5; 11,7] 0,0134[4]
G2	74/612 (12,1)	7/603 (1,2)	10,42 [4,84; 22,43] <,0001[2]	11,71 [5,35; 25,64] <,0001[3]	10,9 [8,2; 13,7] <,0001[3]
G3	60/527 (11,4)	6/506 (1,2)	9,60 [4,19; 22,03] <,0001[2]	10,71 [4,58; 25,02] <,0001[3]	10,2 [7,3; 13,1] <,0001[3]
GX	10/51 (19,6)	1/59 (1,7)	11,57 [1,53; 87,31] 0,0176[2]	14,15 [1,74; 114,85] 0,0018[3]	17,9 [6,5; 29,3] 0,0018[3]
Race (Interaction p-value: 0,5195)					
White	107/958 (11,2)	13/944 (1,4)	8,11 [4,59; 14,32] <,0001[2]	9,00 [5,03; 16,13] <,0001[3]	9,8 [7,7; 11,9] <,0001[3]
Asian	28/250 (11,2)	1/242 (0,4)	27,10 [3,72; 197,65] 0,0011[2]	30,40 [4,10; 225,27] <,0001[3]	10,8 [6,8; 14,8] <,0001[3]
Other	10/62 (16,1)	0/64 (0,0)	21,67 [1,30; 361,97] 0,0323[2]	25,80 [1,48; 450,66] 0,0006[4]	16,1 [7,0; 25,3] 0,0006[4]
ECOG-PS (Interaction p-value: 0,9820)					
ECOG-PS 0	122/1070 (11,4)	11/1020 (1,1)	10,57 [5,74; 19,48] <,0001[2]	11,80 [6,33; 22,02] <,0001[3]	10,3 [8,3; 12,3] <,0001[3]
ECOG-PS 1	28/213 (13,1)	3/245 (1,2)	10,74 [3,31; 34,81] <,0001[2]	12,21 [3,66; 40,78] <,0001[3]	11,9 [7,2; 16,7] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT COVID-19 from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6590)					
< 65 years	26/918 (2,8)	7/937 (0,7)	3,79 [1,65; 8,69] 0,0016[2]	3,87 [1,67; 8,97] 0,0007[3]	2,1 [0,9; 3,3] 0,0007[3]
≥ 65 years	7/365 (1,9)	1/328 (0,3)	6,29 [0,78; 50,86] 0,0846[2]	6,39 [0,78; 52,25] 0,0718[4]	1,6 [0,1; 3,1] 0,0718[4]
Region (Interaction p-value: 0,4042)					
North America / Europe	20/678 (2,9)	6/650 (0,9)	3,20 [1,29; 7,91] 0,0120[2]	3,26 [1,30; 8,18] 0,0077[3]	2,0 [0,6; 3,5] 0,0077[3]
Asia	0/203 (0,0)	0/201 (0,0)	NE	NE	NE
Other	13/402 (3,2)	2/414 (0,5)	6,69 [1,52; 29,48] 0,0119[2]	6,88 [1,54; 30,70] 0,0035[3]	2,8 [0,9; 4,6] 0,0035[3]
Primary tumor size (Interaction p-value: 0,8550)					
< 20 mm	11/331 (3,3)	2/335 (0,6)	5,57 [1,24; 24,92] 0,0248[2]	5,72 [1,26; 26,02] 0,0110[3]	2,7 [0,6; 4,8] 0,0110[3]
≥ 20 but < 50 mm	13/646 (2,0)	4/653 (0,6)	3,29 [1,08; 10,02] 0,0366[2]	3,33 [1,08; 10,27] 0,0264[3]	1,4 [0,2; 2,6] 0,0264[3]
≥ 50 mm	8/289 (2,8)	2/265 (0,8)	3,67 [0,79; 17,12] 0,0982[2]	3,74 [0,79; 17,79] 0,1095[4]	2,0 [-0,1; 4,2] 0,1095[4]
Number of positive lymph nodes (Interaction p-value: 0,5870)					
0-3	8/427 (1,9)	1/418 (0,2)	7,83 [0,98; 62,34] 0,0518[2]	7,96 [0,99; 63,94] 0,0382[4]	1,6 [0,3; 3,0] 0,0382[4]
4-9	18/549 (3,3)	4/542 (0,7)	4,44 [1,51; 13,04] 0,0066[2]	4,56 [1,53; 13,56] 0,0028[3]	2,5 [0,9; 4,2] 0,0028[3]
≥ 10	7/307 (2,3)	3/305 (1,0)	2,32 [0,61; 8,88] 0,2199[2]	2,35 [0,60; 9,17] 0,3397[4]	1,3 [-0,7; 3,3] 0,3397[4]
Tumor stage (Interaction p-value: 0,9999)					
IIA	4/113 (3,5)	0/114 (0,0)	9,08 [0,49; 166,70] 0,1374[2]	9,41 [0,50; 176,86] 0,0598[4]	3,5 [0,1; 6,9] 0,0598[4]
IIB	3/151 (2,0)	0/136 (0,0)	6,31 [0,33; 121,05] 0,2217[2]	6,43 [0,33; 125,70] 0,2494[4]	2,0 [-0,2; 4,2] 0,2494[4]
IIIA	12/495 (2,4)	4/488 (0,8)	2,96 [0,96; 9,11] 0,0588[2]	3,01 [0,96; 9,39] 0,0468[3]	1,6 [0,0; 3,2] 0,0468[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	13/468 (2,8)	4/480 (0,8)	3,33 [1,09; 10,15] 0,0341[2]	3,40 [1,10; 10,50] 0,0241[3]	1,9 [0,2; 3,6] 0,0241[3]
Tumor grade (Interaction p-value: 0,1709)					
G1	2/91 (2,2)	3/93 (3,2)	0,68 [0,12; 3,98] 0,6701[2]	0,67 [0,11; 4,13] 1,0000[4]	-1,0 [-5,7; 3,7] 1,0000[4]
G2	16/612 (2,6)	4/603 (0,7)	3,94 [1,33; 11,72] 0,0136[2]	4,02 [1,34; 12,10] 0,0075[3]	2,0 [0,5; 3,4] 0,0075[3]
G3	14/527 (2,7)	1/506 (0,2)	13,44 [1,77; 101,85] 0,0119[2]	13,78 [1,81; 105,19] 0,0010[3]	2,5 [1,0; 3,9] 0,0010[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,3329)					
Negative	3/156 (1,9)	1/169 (0,6)	3,25 [0,34; 30,92] 0,3051[2]	3,29 [0,34; 32,00] 0,3537[4]	1,3 [-1,1; 3,8] 0,3537[4]
Positive	30/1089 (2,8)	7/1067 (0,7)	4,20 [1,85; 9,52] 0,0006[2]	4,29 [1,88; 9,81] 0,0002[3]	2,1 [1,0; 3,2] 0,0002[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9997)					
White	27/958 (2,8)	8/944 (0,8)	3,33 [1,52; 7,28] 0,0027[2]	3,39 [1,53; 7,51] 0,0014[3]	2,0 [0,8; 3,2] 0,0014[3]
Asian	2/250 (0,8)	0/242 (0,0)	4,84 [0,23; 100,31] 0,3079[2]	4,88 [0,23; 102,16] 0,4991[4]	0,8 [-0,3; 1,9] 0,4991[4]
Other	4/62 (6,5)	0/64 (0,0)	9,29 [0,51; 168,95] 0,1322[2]	9,92 [0,52; 188,28] 0,0557[4]	6,5 [0,3; 12,6] 0,0557[4]
First endocrine therapy (Interaction p-value: 0,9043)					
Tamoxifen	4/114 (3,5)	1/132 (0,8)	4,63 [0,53; 40,85] 0,1675[2]	4,76 [0,52; 43,25] 0,1855[4]	2,8 [-0,9; 6,4] 0,1855[4]
Aromatase inhibitor	29/1169 (2,5)	7/1133 (0,6)	4,02 [1,77; 9,13] 0,0009[2]	4,09 [1,79; 9,38] 0,0003[3]	1,9 [0,9; 2,9] 0,0003[3]
ECOG-PS (Interaction p-value: 0,9713)					
ECOG-PS 0	26/1070 (2,4)	8/1020 (0,8)	3,10 [1,41; 6,81] 0,0049[2]	3,15 [1,42; 6,99] 0,0030[3]	1,6 [0,6; 2,7] 0,0030[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	7/213 (3,3)	0/245 (0,0)	17,24 [0,99; 300,14] 0,0508[2]	17,83 [1,01; 314,11] 0,0045[4]	3,3 [0,9; 5,7] 0,0045[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Cataract from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9722)					
< 65 years	13/918 (1,4)	6/937 (0,6)	2,21 [0,84; 5,79] 0,1063[2]	2,23 [0,84; 5,89] 0,0971[3]	0,8 [-0,1; 1,7] 0,0971[3]
≥ 65 years	12/365 (3,3)	5/328 (1,5)	2,16 [0,77; 6,06] 0,1446[2]	2,20 [0,77; 6,30] 0,1341[3]	1,8 [-0,5; 4,0] 0,1341[3]
Prior treatment (Interaction p-value: 0,3553)					
Neoadjuvant chemotherapy	13/430 (3,0)	3/415 (0,7)	4,18 [1,20; 14,57] 0,0246[2]	4,28 [1,21; 15,14] 0,0142[3]	2,3 [0,5; 4,1] 0,0142[3]
Adjuvant chemotherapy	11/784 (1,4)	8/769 (1,0)	1,35 [0,55; 3,33] 0,5172[2]	1,35 [0,54; 3,38] 0,5156[3]	0,4 [-0,7; 1,5] 0,5156[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,4461)					
North America / Europe	10/678 (1,5)	5/650 (0,8)	1,92 [0,66; 5,58] 0,2323[2]	1,93 [0,66; 5,68] 0,2238[3]	0,7 [-0,4; 1,8] 0,2238[3]
Asia	8/203 (3,9)	5/201 (2,5)	1,58 [0,53; 4,76] 0,4124[2]	1,61 [0,52; 5,00] 0,4079[3]	1,5 [-2,0; 4,9] 0,4079[3]
Other	7/402 (1,7)	1/414 (0,2)	7,21 [0,89; 58,33] 0,0641[2]	7,32 [0,90; 59,76] 0,0357[4]	1,5 [0,1; 2,9] 0,0357[4]
Primary tumor size (Interaction p-value: 0,6176)					
< 20 mm	9/331 (2,7)	4/335 (1,2)	2,28 [0,71; 7,32] 0,1673[2]	2,31 [0,71; 7,59] 0,1549[3]	1,5 [-0,6; 3,6] 0,1549[3]
≥ 20 but < 50 mm	10/646 (1,5)	3/653 (0,5)	3,37 [0,93; 12,19] 0,0640[2]	3,41 [0,93; 12,44] 0,0487[3]	1,1 [0,0; 2,2] 0,0487[3]
≥ 50 mm	6/289 (2,1)	4/265 (1,5)	1,38 [0,39; 4,82] 0,6184[2]	1,38 [0,39; 4,96] 0,7540[4]	0,6 [-1,6; 2,8] 0,7540[4]
Number of positive lymph nodes (Interaction p-value: 0,4346)					
0-3	9/427 (2,1)	3/418 (0,7)	2,94 [0,80; 10,77] 0,1042[2]	2,98 [0,80; 11,08] 0,0877[3]	1,4 [-0,2; 3,0] 0,0877[3]
4-9	8/549 (1,5)	6/542 (1,1)	1,32 [0,46; 3,77] 0,6085[2]	1,32 [0,46; 3,83] 0,6074[3]	0,4 [-1,0; 1,7] 0,6074[3]
≥ 10	8/307 (2,6)	2/305 (0,7)	3,97 [0,85; 18,56] 0,0794[2]	4,05 [0,85; 19,25] 0,1065[4]	2,0 [-0,0; 3,9] 0,1065[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7025)					
IIA	2/113 (1,8)	2/114 (1,8)	1,01 [0,14; 7,04] 0,9929[2]	1,01 [0,14; 7,29] 1,0000[4]	0,0 [-3,4; 3,4] 1,0000[4]
IIB	2/151 (1,3)	0/136 (0,0)	4,51 [0,22; 93,05] 0,3297[2]	4,57 [0,22; 95,94] 0,4996[4]	1,3 [-0,5; 3,1] 0,4996[4]
IIIA	8/495 (1,6)	5/488 (1,0)	1,58 [0,52; 4,79] 0,4211[2]	1,59 [0,52; 4,89] 0,4169[3]	0,6 [-0,8; 2,0] 0,4169[3]
IIIB	0/54 (0,0)	1/45 (2,2)	0,28 [0,01; 6,68] 0,4306[2]	0,27 [0,01; 6,85] 0,4545[4]	-2,2 [-6,5; 2,1] 0,4545[4]
IIIC	13/468 (2,8)	3/480 (0,6)	4,44 [1,27; 15,50] 0,0192[2]	4,54 [1,29; 16,05] 0,0101[3]	2,2 [0,5; 3,8] 0,0101[3]
Tumor grade (Interaction p-value: 0,1052)					
G1	1/91 (1,1)	2/93 (2,2)	0,51 [0,05; 5,54] 0,5808[2]	0,51 [0,05; 5,67] 1,0000[4]	-1,1 [-4,7; 2,6] 1,0000[4]
G2	14/612 (2,3)	3/603 (0,5)	4,60 [1,33; 15,92] 0,0160[2]	4,68 [1,34; 16,38] 0,0079[3]	1,8 [0,5; 3,1] 0,0079[3]
G3	10/527 (1,9)	6/506 (1,2)	1,60 [0,59; 4,37] 0,3591[2]	1,61 [0,58; 4,47] 0,3544[3]	0,7 [-0,8; 2,2] 0,3544[3]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,5949)					
White	17/958 (1,8)	5/944 (0,5)	3,35 [1,24; 9,04] 0,0170[2]	3,39 [1,25; 9,23] 0,0111[3]	1,2 [0,3; 2,2] 0,0111[3]
Asian	8/250 (3,2)	5/242 (2,1)	1,55 [0,51; 4,67] 0,4371[2]	1,57 [0,51; 4,86] 0,4331[3]	1,1 [-1,7; 4,0] 0,4331[3]
Other	0/62 (0,0)	1/64 (1,6)	0,34 [0,01; 8,28] 0,5109[2]	0,34 [0,01; 8,47] 1,0000[4]	-1,6 [-4,6; 1,5] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,0973)					
Tamoxifen	1/114 (0,9)	3/132 (2,3)	0,39 [0,04; 3,66] 0,4068[2]	0,38 [0,04; 3,71] 0,6260[4]	-1,4 [-4,5; 1,7] 0,6260[4]
Aromatase inhibitor	24/1169 (2,1)	8/1133 (0,7)	2,91 [1,31; 6,44] 0,0086[2]	2,95 [1,32; 6,59] 0,0058[3]	1,3 [0,4; 2,3] 0,0058[3]
ECOG-PS (Interaction p-value: 0,5707)					
ECOG-PS 0	21/1070 (2,0)	8/1020 (0,8)	2,50 [1,11; 5,62] 0,0264[2]	2,53 [1,12; 5,74] 0,0213[3]	1,2 [0,2; 2,2] 0,0213[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	4/213 (1,9)	3/245 (1,2)	1,53 [0,35; 6,78] 0,5726[2]	1,54 [0,34; 6,98] 0,7096[4]	0,7 [-1,6; 2,9] 0,7096[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Constipation from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,2479)					
Neoadjuvant chemotherapy	52/430 (12,1)	16/415 (3,9)	3,14 [1,82; 5,40] <,0001[2]	3,43 [1,93; 6,11] <,0001[3]	8,2 [4,6; 11,8] <,0001[3]
Adjuvant chemotherapy	89/784 (11,4)	48/769 (6,2)	1,82 [1,30; 2,55] 0,0005[2]	1,92 [1,33; 2,77] 0,0004[3]	5,1 [2,3; 7,9] 0,0004[3]
No chemotherapy	11/69 (15,9)	6/81 (7,4)	2,15 [0,84; 5,52] 0,1106[2]	2,37 [0,83; 6,79] 0,1003[3]	8,5 [-1,8; 18,9] 0,1003[3]
Region (Interaction p-value: 0,9983)					
North America / Europe	112/678 (16,5)	51/650 (7,8)	2,11 [1,54; 2,88] <,0001[2]	2,32 [1,64; 3,30] <,0001[3]	8,7 [5,2; 12,1] <,0001[3]
Asia	17/203 (8,4)	8/201 (4,0)	2,10 [0,93; 4,76] 0,0745[2]	2,20 [0,93; 5,23] 0,0668[3]	4,4 [-0,3; 9,1] 0,0668[3]
Other	23/402 (5,7)	11/414 (2,7)	2,15 [1,06; 4,36] 0,0330[2]	2,22 [1,07; 4,62] 0,0285[3]	3,1 [0,3; 5,8] 0,0285[3]
Primary tumor size (Interaction p-value: 0,0950)					
< 20 mm	44/331 (13,3)	20/335 (6,0)	2,23 [1,34; 3,69] 0,0019[2]	2,41 [1,39; 4,19] 0,0013[3]	7,3 [2,9; 11,8] 0,0013[3]
≥ 20 but < 50 mm	62/646 (9,6)	38/653 (5,8)	1,65 [1,12; 2,43] 0,0117[2]	1,72 [1,13; 2,61] 0,0106[3]	3,8 [0,9; 6,7] 0,0106[3]
≥ 50 mm	45/289 (15,6)	11/265 (4,2)	3,75 [1,98; 7,10] <,0001[2]	4,26 [2,15; 8,42] <,0001[3]	11,4 [6,6; 16,2] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,1021)					
0-3	57/427 (13,3)	22/418 (5,3)	2,54 [1,58; 4,07] 0,0001[2]	2,77 [1,66; 4,63] <,0001[3]	8,1 [4,2; 12,0] <,0001[3]
4-9	50/549 (9,1)	33/542 (6,1)	1,50 [0,98; 2,28] 0,0622[2]	1,55 [0,98; 2,44] 0,0600[3]	3,0 [-0,1; 6,2] 0,0600[3]
≥ 10	45/307 (14,7)	15/305 (4,9)	2,98 [1,70; 5,23] 0,0001[2]	3,32 [1,81; 6,10] <,0001[3]	9,7 [5,1; 14,4] <,0001[3]
Tumor stage (Interaction p-value: 0,3606)					
IIA	17/113 (15,0)	4/114 (3,5)	4,29 [1,49; 12,35] 0,0070[2]	4,87 [1,58; 14,97] 0,0027[3]	11,5 [4,1; 18,9] 0,0027[3]
IIB	20/151 (13,2)	9/136 (6,6)	2,00 [0,94; 4,24] 0,0705[2]	2,15 [0,95; 4,91] 0,0629[3]	6,6 [-0,2; 13,5] 0,0629[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	47/495 (9,5)	29/488 (5,9)	1,60 [1,02; 2,49] 0,0393[2]	1,66 [1,03; 2,69] 0,0371[3]	3,6 [0,2; 6,9] 0,0371[3]
IIIB	3/54 (5,6)	2/45 (4,4)	1,25 [0,22; 7,16] 0,8021[2]	1,26 [0,20; 7,92] 1,0000[4]	1,1 [-7,5; 9,7] 1,0000[4]
IIIC	65/468 (13,9)	26/480 (5,4)	2,56 [1,66; 3,97] <,0001[2]	2,82 [1,75; 4,53] <,0001[3]	8,5 [4,7; 12,2] <,0001[3]
Tumor grade (Interaction p-value: 0,7654)					
G1	10/91 (11,0)	4/93 (4,3)	2,55 [0,83; 7,85] 0,1016[2]	2,75 [0,83; 9,10] 0,0871[3]	6,7 [-0,9; 14,3] 0,0871[3]
G2	69/612 (11,3)	37/603 (6,1)	1,84 [1,25; 2,70] 0,0019[2]	1,94 [1,28; 2,95] 0,0015[3]	5,1 [2,0; 8,3] 0,0015[3]
G3	68/527 (12,9)	27/506 (5,3)	2,42 [1,57; 3,71] <,0001[2]	2,63 [1,65; 4,18] <,0001[3]	7,6 [4,1; 11,0] <,0001[3]
GX	5/51 (9,8)	2/59 (3,4)	2,89 [0,59; 14,27] 0,1923[2]	3,10 [0,57; 16,71] 0,2463[4]	6,4 [-3,0; 15,8] 0,2463[4]
Race (Interaction p-value: 0,4480)					
White	127/958 (13,3)	56/944 (5,9)	2,23 [1,65; 3,02] <,0001[2]	2,42 [1,75; 3,37] <,0001[3]	7,3 [4,7; 9,9] <,0001[3]
Asian	20/250 (8,0)	8/242 (3,3)	2,42 [1,09; 5,39] 0,0305[2]	2,54 [1,10; 5,89] 0,0246[3]	4,7 [0,6; 8,7] 0,0246[3]
Other	5/62 (8,1)	5/64 (7,8)	1,03 [0,31; 3,39] 0,9583[2]	1,04 [0,28; 3,77] 1,0000[4]	0,3 [-9,2; 9,7] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,3238)					
Tamoxifen	8/114 (7,0)	7/132 (5,3)	1,32 [0,50; 3,54] 0,5764[2]	1,35 [0,47; 3,84] 0,5752[3]	1,7 [-4,3; 7,8] 0,5752[3]
Aromatase inhibitor	144/1169 (12,3)	63/1133 (5,6)	2,22 [1,67; 2,94] <,0001[2]	2,39 [1,75; 3,25] <,0001[3]	6,8 [4,4; 9,1] <,0001[3]
ECOG-PS (Interaction p-value: 0,2201)					
ECOG-PS 0	126/1070 (11,8)	51/1020 (5,0)	2,36 [1,72; 3,22] <,0001[2]	2,54 [1,81; 3,55] <,0001[3]	6,8 [4,4; 9,1] <,0001[3]
ECOG-PS 1	26/213 (12,2)	19/245 (7,8)	1,57 [0,90; 2,76] 0,1139[2]	1,65 [0,89; 3,08] 0,1104[3]	4,5 [-1,1; 10,0] 0,1104[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Cough from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7150)					
< 65 years	132/918 (14,4)	80/937 (8,5)	1,68 [1,30; 2,19] <,0001[2]	1,80 [1,34; 2,41] <,0001[3]	5,8 [3,0; 8,7] <,0001[3]
≥ 65 years	53/365 (14,5)	31/328 (9,5)	1,54 [1,01; 2,33] 0,0437[2]	1,63 [1,02; 2,61] 0,0412[3]	5,1 [0,3; 9,9] 0,0412[3]
Prior treatment (Interaction p-value: 0,2592)					
Neoadjuvant chemotherapy	60/430 (14,0)	29/415 (7,0)	2,00 [1,31; 3,05] 0,0013[2]	2,16 [1,35; 3,44] 0,0010[3]	7,0 [2,9; 11,1] 0,0010[3]
Adjuvant chemotherapy	110/784 (14,0)	75/769 (9,8)	1,44 [1,09; 1,90] 0,0098[2]	1,51 [1,11; 2,06] 0,0093[3]	4,3 [1,1; 7,5] 0,0093[3]
No chemotherapy	15/69 (21,7)	7/81 (8,6)	2,52 [1,09; 5,81] 0,0309[2]	2,94 [1,12; 7,69] 0,0238[3]	13,1 [1,6; 24,6] 0,0238[3]
Region (Interaction p-value: 0,5782)					
North America / Europe	113/678 (16,7)	66/650 (10,2)	1,64 [1,24; 2,18] 0,0006[2]	1,77 [1,28; 2,45] 0,0005[3]	6,5 [2,9; 10,2] 0,0005[3]
Asia	33/203 (16,3)	16/201 (8,0)	2,04 [1,16; 3,59] 0,0131[2]	2,24 [1,19; 4,22] 0,0107[3]	8,3 [2,0; 14,6] 0,0107[3]
Other	39/402 (9,7)	29/414 (7,0)	1,38 [0,87; 2,20] 0,1658[2]	1,43 [0,86; 2,36] 0,1635[3]	2,7 [-1,1; 6,5] 0,1635[3]
Primary tumor size (Interaction p-value: 0,3757)					
< 20 mm	42/331 (12,7)	20/335 (6,0)	2,13 [1,28; 3,54] 0,0038[2]	2,29 [1,31; 3,99] 0,0028[3]	6,7 [2,3; 11,1] 0,0028[3]
≥ 20 but < 50 mm	96/646 (14,9)	57/653 (8,7)	1,70 [1,25; 2,32] 0,0007[2]	1,83 [1,29; 2,58] 0,0006[3]	6,1 [2,6; 9,6] 0,0006[3]
≥ 50 mm	45/289 (15,6)	31/265 (11,7)	1,33 [0,87; 2,04] 0,1883[2]	1,39 [0,85; 2,28] 0,1857[3]	3,9 [-1,8; 9,6] 0,1857[3]
Number of positive lymph nodes (Interaction p-value: 0,8212)					
0-3	63/427 (14,8)	36/418 (8,6)	1,71 [1,16; 2,52] 0,0064[2]	1,84 [1,19; 2,83] 0,0055[3]	6,1 [1,8; 10,4] 0,0055[3]
4-9	70/549 (12,8)	40/542 (7,4)	1,73 [1,19; 2,50] 0,0038[2]	1,83 [1,22; 2,76] 0,0032[3]	5,4 [1,8; 8,9] 0,0032[3]
≥ 10	52/307 (16,9)	35/305 (11,5)	1,48 [0,99; 2,20] 0,0553[2]	1,57 [0,99; 2,50] 0,0530[3]	5,5 [-0,1; 11,0] 0,0530[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,2321)					
IIA	14/113 (12,4)	6/114 (5,3)	2,35 [0,94; 5,91] 0,0683[2]	2,55 [0,94; 6,88] 0,0582[3]	7,1 [-0,2; 14,5] 0,0582[3]
IIB	18/151 (11,9)	16/136 (11,8)	1,01 [0,54; 1,91] 0,9675[2]	1,02 [0,50; 2,08] 0,9675[3]	0,2 [-7,3; 7,6] 0,9675[3]
IIIA	71/495 (14,3)	36/488 (7,4)	1,94 [1,33; 2,85] 0,0006[2]	2,10 [1,38; 3,21] 0,0005[3]	7,0 [3,1; 10,8] 0,0005[3]
IIIB	7/54 (13,0)	1/45 (2,2)	5,83 [0,75; 45,66] 0,0930[2]	6,55 [0,77; 55,43] 0,0682[4]	10,7 [0,8; 20,7] 0,0682[4]
IIIC	73/468 (15,6)	52/480 (10,8)	1,44 [1,03; 2,01] 0,0314[2]	1,52 [1,04; 2,23] 0,0302[3]	4,8 [0,5; 9,1] 0,0302[3]
Tumor grade (Interaction p-value: 0,7189)					
G1	14/91 (15,4)	6/93 (6,5)	2,38 [0,96; 5,93] 0,0617[2]	2,64 [0,97; 7,20] 0,0516[3]	8,9 [-0,0; 17,9] 0,0516[3]
G2	88/612 (14,4)	56/603 (9,3)	1,55 [1,13; 2,12] 0,0066[2]	1,64 [1,15; 2,34] 0,0060[3]	5,1 [1,5; 8,7] 0,0060[3]
G3	76/527 (14,4)	45/506 (8,9)	1,62 [1,15; 2,30] 0,0065[2]	1,73 [1,17; 2,55] 0,0057[3]	5,5 [1,6; 9,4] 0,0057[3]
GX	7/51 (13,7)	3/59 (5,1)	2,70 [0,74; 9,90] 0,1342[2]	2,97 [0,73; 12,15] 0,1829[4]	8,6 [-2,3; 19,6] 0,1829[4]
Race (Interaction p-value: 0,7773)					
White	138/958 (14,4)	86/944 (9,1)	1,58 [1,23; 2,04] 0,0004[2]	1,68 [1,26; 2,23] 0,0003[3]	5,3 [2,4; 8,2] 0,0003[3]
Asian	41/250 (16,4)	21/242 (8,7)	1,89 [1,15; 3,10] 0,0118[2]	2,06 [1,18; 3,61] 0,0099[3]	7,7 [1,9; 13,5] 0,0099[3]
Other	6/62 (9,7)	3/64 (4,7)	2,06 [0,54; 7,89] 0,2894[2]	2,18 [0,52; 9,13] 0,3198[4]	5,0 [-4,0; 14,0] 0,3198[4]
First endocrine therapy (Interaction p-value: 0,6757)					
Tamoxifen	12/114 (10,5)	10/132 (7,6)	1,39 [0,62; 3,10] 0,4209[2]	1,44 [0,60; 3,46] 0,4187[3]	3,0 [-4,3; 10,2] 0,4187[3]
Aromatase inhibitor	173/1169 (14,8)	101/1133 (8,9)	1,66 [1,32; 2,09] <,0001[2]	1,77 [1,37; 2,30] <,0001[3]	5,9 [3,3; 8,5] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Decreased appetite from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1201)					
< 65 years	89/918 (9,7)	29/937 (3,1)	3,13 [2,08; 4,72] <,0001[2]	3,36 [2,19; 5,16] <,0001[3]	6,6 [4,4; 8,8] <,0001[3]
≥ 65 years	74/365 (20,3)	12/328 (3,7)	5,54 [3,07; 10,01] <,0001[2]	6,70 [3,57; 12,58] <,0001[3]	16,6 [12,0; 21,2] <,0001[3]
Prior treatment (Interaction p-value: 0,7552)					
Neoadjuvant chemotherapy	55/430 (12,8)	13/415 (3,1)	4,08 [2,27; 7,36] <,0001[2]	4,54 [2,44; 8,44] <,0001[3]	9,7 [6,1; 13,2] <,0001[3]
Adjuvant chemotherapy	97/784 (12,4)	26/769 (3,4)	3,66 [2,40; 5,58] <,0001[2]	4,03 [2,59; 6,30] <,0001[3]	9,0 [6,4; 11,6] <,0001[3]
No chemotherapy	11/69 (15,9)	2/81 (2,5)	6,46 [1,48; 28,14] 0,0130[2]	7,49 [1,60; 35,09] 0,0035[3]	13,5 [4,2; 22,7] 0,0035[3]
Region (Interaction p-value: 0,5603)					
North America / Europe	91/678 (13,4)	26/650 (4,0)	3,36 [2,20; 5,12] <,0001[2]	3,72 [2,37; 5,84] <,0001[3]	9,4 [6,4; 12,4] <,0001[3]
Asia	21/203 (10,3)	4/201 (2,0)	5,20 [1,82; 14,87] 0,0021[2]	5,68 [1,91; 16,87] 0,0005[3]	8,4 [3,7; 13,0] 0,0005[3]
Other	51/402 (12,7)	11/414 (2,7)	4,77 [2,53; 9,03] <,0001[2]	5,32 [2,73; 10,37] <,0001[3]	10,0 [6,4; 13,6] <,0001[3]
Primary tumor size (Interaction p-value: 0,1662)					
< 20 mm	31/331 (9,4)	13/335 (3,9)	2,41 [1,29; 4,53] 0,0061[2]	2,56 [1,31; 4,98] 0,0044[3]	5,5 [1,7; 9,2] 0,0044[3]
≥ 20 but < 50 mm	84/646 (13,0)	16/653 (2,5)	5,31 [3,14; 8,96] <,0001[2]	5,95 [3,45; 10,28] <,0001[3]	10,6 [7,7; 13,4] <,0001[3]
≥ 50 mm	47/289 (16,3)	12/265 (4,5)	3,59 [1,95; 6,62] <,0001[2]	4,09 [2,12; 7,91] <,0001[3]	11,7 [6,8; 16,7] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,2485)					
0-3	47/427 (11,0)	12/418 (2,9)	3,83 [2,06; 7,12] <,0001[2]	4,18 [2,19; 8,01] <,0001[3]	8,1 [4,8; 11,5] <,0001[3]
4-9	79/549 (14,4)	15/542 (2,8)	5,20 [3,03; 8,91] <,0001[2]	5,91 [3,35; 10,40] <,0001[3]	11,6 [8,4; 14,9] <,0001[3]
≥ 10	37/307 (12,1)	14/305 (4,6)	2,63 [1,45; 4,76] 0,0015[2]	2,85 [1,51; 5,39] 0,0008[3]	7,5 [3,1; 11,8] 0,0008[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor grade (Interaction p-value: 0,7199)					
G1	13/91 (14,3)	2/93 (2,2)	6,64 [1,54; 28,61] 0,0110[2]	7,58 [1,66; 34,64] 0,0026[3]	12,1 [4,4; 19,9] 0,0026[3]
G2	82/612 (13,4)	26/603 (4,3)	3,11 [2,03; 4,76] <,0001[2]	3,43 [2,17; 5,42] <,0001[3]	9,1 [5,9; 12,2] <,0001[3]
G3	56/527 (10,6)	13/506 (2,6)	4,14 [2,29; 7,47] <,0001[2]	4,51 [2,43; 8,35] <,0001[3]	8,1 [5,1; 11,0] <,0001[3]
GX	12/51 (23,5)	0/59 (0,0)	28,85 [1,75; 475,41] 0,0187[2]	37,66 [2,17; 654,41] <,0001[3]	23,5 [11,9; 35,2] <,0001[3]
Race (Interaction p-value: 0,1277)					
White	128/958 (13,4)	30/944 (3,2)	4,20 [2,85; 6,19] <,0001[2]	4,70 [3,12; 7,07] <,0001[3]	10,2 [7,8; 12,6] <,0001[3]
Asian	23/250 (9,2)	5/242 (2,1)	4,45 [1,72; 11,52] 0,0021[2]	4,80 [1,80; 12,85] 0,0006[3]	7,1 [3,1; 11,1] 0,0006[3]
Other	6/62 (9,7)	5/64 (7,8)	1,24 [0,40; 3,85] 0,7115[2]	1,26 [0,37; 4,38] 0,7108[3]	1,9 [-8,0; 11,7] 0,7108[3]
First endocrine therapy (Interaction p-value: 0,7194)					
Tamoxifen	8/114 (7,0)	3/132 (2,3)	3,09 [0,84; 11,36] 0,0899[2]	3,25 [0,84; 12,54] 0,0726[3]	4,7 [-0,6; 10,1] 0,0726[3]
Aromatase inhibitor	155/1169 (13,3)	38/1133 (3,4)	3,95 [2,80; 5,58] <,0001[2]	4,40 [3,06; 6,34] <,0001[3]	9,9 [7,7; 12,1] <,0001[3]
ECOG-PS (Interaction p-value: 0,4689)					
ECOG-PS 0	128/1070 (12,0)	33/1020 (3,2)	3,70 [2,55; 5,37] <,0001[2]	4,06 [2,74; 6,02] <,0001[3]	8,7 [6,5; 11,0] <,0001[3]
ECOG-PS 1	35/213 (16,4)	8/245 (3,3)	5,03 [2,39; 10,61] <,0001[2]	5,83 [2,64; 12,86] <,0001[3]	13,2 [7,7; 18,6] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Deep vein thrombosis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9414)					
Neoadjuvant chemotherapy	8/430 (1,9)	1/415 (0,2)	7,72 [0,97; 61,46] 0,0535[2]	7,85 [0,98; 63,03] 0,0383[4]	1,6 [0,3; 3,0] 0,0383[4]
Adjuvant chemotherapy	10/784 (1,3)	2/769 (0,3)	4,90 [1,08; 22,31] 0,0397[2]	4,95 [1,08; 22,69] 0,0223[3]	1,0 [0,2; 1,9] 0,0223[3]
No chemotherapy	3/69 (4,3)	0/81 (0,0)	8,20 [0,43; 156,04] 0,1615[2]	8,58 [0,44; 169,04] 0,0950[4]	4,3 [-0,5; 9,2] 0,0950[4]
Region (Interaction p-value: 0,9082)					
North America / Europe	15/678 (2,2)	2/650 (0,3)	7,19 [1,65; 31,32] 0,0086[2]	7,33 [1,67; 32,18] 0,0020[3]	1,9 [0,7; 3,1] 0,0020[3]
Asia	0/203 (0,0)	0/201 (0,0)	NE	NE	NE
Other	6/402 (1,5)	1/414 (0,2)	6,18 [0,75; 51,10] 0,0911[2]	6,26 [0,75; 52,21] 0,0655[4]	1,3 [-0,0; 2,5] 0,0655[4]
Primary tumor size (Interaction p-value: 0,9557)					
< 20 mm	4/331 (1,2)	1/335 (0,3)	4,05 [0,45; 36,03] 0,2100[2]	4,09 [0,45; 36,75] 0,2145[4]	0,9 [-0,4; 2,2] 0,2145[4]
≥ 20 but < 50 mm	12/646 (1,9)	2/653 (0,3)	6,07 [1,36; 26,99] 0,0180[2]	6,16 [1,37; 27,64] 0,0068[3]	1,6 [0,4; 2,7] 0,0068[3]
≥ 50 mm	5/289 (1,7)	0/265 (0,0)	10,09 [0,56; 181,60] 0,1170[2]	10,27 [0,56; 186,54] 0,0625[4]	1,7 [0,2; 3,2] 0,0625[4]
Tumor stage (Interaction p-value: 0,9876)					
IIA	2/113 (1,8)	0/114 (0,0)	5,04 [0,24; 103,90] 0,2945[2]	5,13 [0,24; 108,15] 0,2467[4]	1,8 [-0,7; 4,2] 0,2467[4]
IIB	3/151 (2,0)	0/136 (0,0)	6,31 [0,33; 121,05] 0,2217[2]	6,43 [0,33; 125,70] 0,2494[4]	2,0 [-0,2; 4,2] 0,2494[4]
IIIA	9/495 (1,8)	2/488 (0,4)	4,44 [0,96; 20,43] 0,0559[2]	4,50 [0,97; 20,93] 0,0358[3]	1,4 [0,1; 2,7] 0,0358[3]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	7/468 (1,5)	1/480 (0,2)	7,18 [0,89; 58,13] 0,0647[2]	7,27 [0,89; 59,35] 0,0361[4]	1,3 [0,1; 2,5] 0,0361[4]
Tumor grade (Interaction p-value: 0,1851)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	1/91 (1,1)	1/93 (1,1)	1,02 [0,06; 16,09] 0,9877[2]	1,02 [0,06; 16,59] 1,0000[4]	0,0 [-3,0; 3,0] 1,0000[4]
G2	12/612 (2,0)	1/603 (0,2)	11,82 [1,54; 90,65] 0,0175[2]	12,04 [1,56; 92,88] 0,0024[3]	1,8 [0,6; 2,9] 0,0024[3]
G3	8/527 (1,5)	1/506 (0,2)	7,68 [0,96; 61,19] 0,0542[2]	7,78 [0,97; 62,46] 0,0386[4]	1,3 [0,2; 2,4] 0,0386[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9633)					
Negative	3/156 (1,9)	0/169 (0,0)	7,58 [0,39; 145,58] 0,1792[2]	7,73 [0,40; 150,85] 0,1095[4]	1,9 [-0,2; 4,1] 0,1095[4]
Positive	17/1089 (1,6)	3/1067 (0,3)	5,55 [1,63; 18,89] 0,0061[2]	5,62 [1,64; 19,25] 0,0019[3]	1,3 [0,5; 2,1] 0,0019[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,2489)					
White	19/958 (2,0)	1/944 (0,1)	18,72 [2,51; 139,57] 0,0043[2]	19,08 [2,55; 142,82] <,0001[3]	1,9 [1,0; 2,8] <,0001[3]
Asian	1/250 (0,4)	0/242 (0,0)	2,90 [0,12; 70,95] 0,5132[2]	2,92 [0,12; 71,93] 1,0000[4]	0,4 [-0,4; 1,2] 1,0000[4]
Other	1/62 (1,6)	1/64 (1,6)	1,03 [0,07; 16,14] 0,9819[2]	1,03 [0,06; 16,88] 1,0000[4]	0,1 [-4,3; 4,4] 1,0000[4]
ECOG-PS (Interaction p-value: 0,2788)					
ECOG-PS 0	15/1070 (1,4)	1/1020 (0,1)	14,30 [1,89; 108,05] 0,0099[2]	14,49 [1,91; 109,88] 0,0006[3]	1,3 [0,6; 2,0] 0,0006[3]
ECOG-PS 1	6/213 (2,8)	2/245 (0,8)	3,45 [0,70; 16,92] 0,1268[2]	3,52 [0,70; 17,64] 0,1532[4]	2,0 [-0,5; 4,5] 0,1532[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dehydration from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8265)					
Neoadjuvant chemotherapy	11/430 (2,6)	2/415 (0,5)	5,31 [1,18; 23,80] 0,0292[2]	5,42 [1,19; 24,61] 0,0142[3]	2,1 [0,4; 3,7] 0,0142[3]
Adjuvant chemotherapy	12/784 (1,5)	1/769 (0,1)	11,77 [1,53; 90,30] 0,0177[2]	11,94 [1,55; 92,03] 0,0025[3]	1,4 [0,5; 2,3] 0,0025[3]
No chemotherapy	3/69 (4,3)	0/81 (0,0)	8,20 [0,43; 156,04] 0,1615[2]	8,58 [0,44; 169,04] 0,0950[4]	4,3 [-0,5; 9,2] 0,0950[4]
Region (Interaction p-value: 0,9107)					
North America / Europe	19/678 (2,8)	2/650 (0,3)	9,11 [2,13; 38,95] 0,0029[2]	9,34 [2,17; 40,27] 0,0003[3]	2,5 [1,2; 3,8] 0,0003[3]
Asia	2/203 (1,0)	0/201 (0,0)	4,95 [0,24; 102,48] 0,3008[2]	5,00 [0,24; 104,80] 0,4988[4]	1,0 [-0,4; 2,3] 0,4988[4]
Other	5/402 (1,2)	1/414 (0,2)	5,15 [0,60; 43,88] 0,1338[2]	5,20 [0,61; 44,72] 0,1185[4]	1,0 [-0,2; 2,2] 0,1185[4]
Primary tumor size (Interaction p-value: 0,4459)					
< 20 mm	2/331 (0,6)	1/335 (0,3)	2,02 [0,18; 22,22] 0,5640[2]	2,03 [0,18; 22,50] 0,6222[4]	0,3 [-0,7; 1,3] 0,6222[4]
≥ 20 but < 50 mm	15/646 (2,3)	1/653 (0,2)	15,16 [2,01; 114,45] 0,0084[2]	15,50 [2,04; 117,68] 0,0004[3]	2,2 [1,0; 3,4] 0,0004[3]
≥ 50 mm	9/289 (3,1)	1/265 (0,4)	8,25 [1,05; 64,70] 0,0446[2]	8,49 [1,07; 67,44] 0,0215[4]	2,7 [0,6; 4,9] 0,0215[4]
Number of positive lymph nodes (Interaction p-value: 0,8228)					
0-3	9/427 (2,1)	2/418 (0,5)	4,41 [0,96; 20,27] 0,0569[2]	4,48 [0,96; 20,85] 0,0367[3]	1,6 [0,1; 3,1] 0,0367[3]
4-9	7/549 (1,3)	0/542 (0,0)	14,81 [0,85; 258,66] 0,0648[2]	15,00 [0,85; 263,28] 0,0153[4]	1,3 [0,3; 2,2] 0,0153[4]
≥ 10	10/307 (3,3)	1/305 (0,3)	9,93 [1,28; 77,14] 0,0281[2]	10,24 [1,30; 80,46] 0,0064[3]	2,9 [0,8; 5,0] 0,0064[3]
Tumor stage (Interaction p-value: 0,9797)					
IIA	1/113 (0,9)	0/114 (0,0)	3,03 [0,12; 73,51] 0,4963[2]	3,05 [0,12; 75,75] 0,4978[4]	0,9 [-0,8; 2,6] 0,4978[4]
IIB	3/151 (2,0)	1/136 (0,7)	2,70 [0,28; 25,67] 0,3868[2]	2,74 [0,28; 26,62] 0,6244[4]	1,3 [-1,4; 3,9] 0,6244[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	8/495 (1,6)	0/488 (0,0)	16,76 [0,97; 289,58] 0,0525[2]	17,03 [0,98; 295,95] 0,0076[4]	1,6 [0,5; 2,7] 0,0076[4]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	13/468 (2,8)	2/480 (0,4)	6,67 [1,51; 29,38] 0,0122[2]	6,83 [1,53; 30,43] 0,0036[3]	2,4 [0,8; 4,0] 0,0036[3]
Tumor grade (Interaction p-value: 0,8956)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	12/612 (2,0)	1/603 (0,2)	11,82 [1,54; 90,65] 0,0175[2]	12,04 [1,56; 92,88] 0,0024[3]	1,8 [0,6; 2,9] 0,0024[3]
G3	9/527 (1,7)	2/506 (0,4)	4,32 [0,94; 19,90] 0,0604[2]	4,38 [0,94; 20,36] 0,0399[3]	1,3 [0,1; 2,5] 0,0399[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,2718)					
Negative	4/156 (2,6)	1/169 (0,6)	4,33 [0,49; 38,35] 0,1875[2]	4,42 [0,49; 39,99] 0,1985[4]	2,0 [-0,8; 4,7] 0,1985[4]
Positive	22/1089 (2,0)	2/1067 (0,2)	10,78 [2,54; 45,72] 0,0013[2]	10,98 [2,58; 46,81] <,0001[3]	1,8 [1,0; 2,7] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9997)					
White	18/958 (1,9)	3/944 (0,3)	5,91 [1,75; 20,00] 0,0043[2]	6,01 [1,76; 20,46] 0,0011[3]	1,6 [0,6; 2,5] 0,0011[3]
Asian	2/250 (0,8)	0/242 (0,0)	4,84 [0,23; 100,31] 0,3079[2]	4,88 [0,23; 102,16] 0,4991[4]	0,8 [-0,3; 1,9] 0,4991[4]
Other	6/62 (9,7)	0/64 (0,0)	13,41 [0,77; 233,15] 0,0748[2]	14,84 [0,82; 269,32] 0,0125[4]	9,7 [2,3; 17,0] 0,0125[4]
ECOG-PS (Interaction p-value: 0,9744)					
ECOG-PS 0	22/1070 (2,1)	3/1020 (0,3)	6,99 [2,10; 23,28] 0,0015[2]	7,12 [2,12; 23,85] 0,0002[3]	1,8 [0,8; 2,7] 0,0002[3]
ECOG-PS 1	4/213 (1,9)	0/245 (0,0)	10,35 [0,56; 191,06] 0,1163[2]	10,55 [0,56; 197,03] 0,0461[4]	1,9 [0,1; 3,7] 0,0461[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Dermatitis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8656)					
< 65 years	13/918 (1,4)	5/937 (0,5)	2,65 [0,95; 7,41] 0,0626[2]	2,68 [0,95; 7,54] 0,0525[3]	0,9 [-0,0; 1,8] 0,0525[3]
≥ 65 years	5/365 (1,4)	2/328 (0,6)	2,25 [0,44; 11,50] 0,3313[2]	2,26 [0,44; 11,75] 0,4555[4]	0,8 [-0,7; 2,2] 0,4555[4]
Prior treatment (Interaction p-value: 0,8056)					
Neoadjuvant chemotherapy	7/430 (1,6)	2/415 (0,5)	3,38 [0,71; 16,17] 0,1276[2]	3,42 [0,71; 16,55] 0,1780[4]	1,1 [-0,2; 2,5] 0,1780[4]
Adjuvant chemotherapy	10/784 (1,3)	4/769 (0,5)	2,45 [0,77; 7,79] 0,1281[2]	2,47 [0,77; 7,91] 0,1153[3]	0,8 [-0,2; 1,7] 0,1153[3]
No chemotherapy	1/69 (1,4)	1/81 (1,2)	1,17 [0,07; 18,42] 0,9091[2]	1,18 [0,07; 19,17] 1,0000[4]	0,2 [-3,5; 3,9] 1,0000[4]
Region (Interaction p-value: 0,2454)					
North America / Europe	4/678 (0,6)	4/650 (0,6)	0,96 [0,24; 3,82] 0,9523[2]	0,96 [0,24; 3,85] 1,0000[4]	-0,0 [-0,9; 0,8] 1,0000[4]
Asia	9/203 (4,4)	2/201 (1,0)	4,46 [0,97; 20,37] 0,0540[2]	4,62 [0,98; 21,64] 0,0337[3]	3,4 [0,3; 6,6] 0,0337[3]
Other	5/402 (1,2)	1/414 (0,2)	5,15 [0,60; 43,88] 0,1338[2]	5,20 [0,61; 44,72] 0,1185[4]	1,0 [-0,2; 2,2] 0,1185[4]
Primary tumor size (Interaction p-value: 0,3117)					
< 20 mm	3/331 (0,9)	1/335 (0,3)	3,04 [0,32; 29,04] 0,3350[2]	3,05 [0,32; 29,52] 0,3709[4]	0,6 [-0,6; 1,8] 0,3709[4]
≥ 20 but < 50 mm	14/646 (2,2)	4/653 (0,6)	3,54 [1,17; 10,69] 0,0251[2]	3,59 [1,18; 10,98] 0,0165[3]	1,6 [0,3; 2,8] 0,0165[3]
≥ 50 mm	1/289 (0,3)	2/265 (0,8)	0,46 [0,04; 5,03] 0,5233[2]	0,46 [0,04; 5,06] 0,6087[4]	-0,4 [-1,7; 0,8] 0,6087[4]
Number of positive lymph nodes (Interaction p-value: 0,5961)					
0-3	4/427 (0,9)	1/418 (0,2)	3,92 [0,44; 34,89] 0,2213[2]	3,94 [0,44; 35,43] 0,3737[4]	0,7 [-0,3; 1,7] 0,3737[4]
4-9	10/549 (1,8)	3/542 (0,6)	3,29 [0,91; 11,89] 0,0692[2]	3,33 [0,91; 12,18] 0,0536[3]	1,3 [-0,0; 2,5] 0,0536[3]
≥ 10	4/307 (1,3)	3/305 (1,0)	1,32 [0,30; 5,87] 0,7112[2]	1,33 [0,29; 5,99] 1,0000[4]	0,3 [-1,4; 2,0] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9001)					
IIA	1/113 (0,9)	0/114 (0,0)	3,03 [0,12; 73,51] 0,4963[2]	3,05 [0,12; 75,75] 0,4978[4]	0,9 [-0,8; 2,6] 0,4978[4]
IIB	3/151 (2,0)	0/136 (0,0)	6,31 [0,33; 121,05] 0,2217[2]	6,43 [0,33; 125,70] 0,2494[4]	2,0 [-0,2; 4,2] 0,2494[4]
IIIA	7/495 (1,4)	2/488 (0,4)	3,45 [0,72; 16,53] 0,1212[2]	3,49 [0,72; 16,86] 0,1778[4]	1,0 [-0,2; 2,2] 0,1778[4]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	6/468 (1,3)	5/480 (1,0)	1,23 [0,38; 4,01] 0,7302[2]	1,23 [0,37; 4,07] 0,7297[3]	0,2 [-1,1; 1,6] 0,7297[3]
Tumor grade (Interaction p-value: 0,7866)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	10/612 (1,6)	5/603 (0,8)	1,97 [0,68; 5,73] 0,2130[2]	1,99 [0,68; 5,85] 0,2040[3]	0,8 [-0,4; 2,0] 0,2040[3]
G3	6/527 (1,1)	2/506 (0,4)	2,88 [0,58; 14,21] 0,1938[2]	2,90 [0,58; 14,45] 0,2880[4]	0,7 [-0,3; 1,8] 0,2880[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9998)					
Negative	0/156 (0,0)	0/169 (0,0)	NE	NE	NE
Positive	18/1089 (1,7)	7/1067 (0,7)	2,52 [1,06; 6,01] 0,0371[2]	2,55 [1,06; 6,12] 0,0306[3]	1,0 [0,1; 1,9] 0,0306[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,5724)					
White	8/958 (0,8)	5/944 (0,5)	1,58 [0,52; 4,80] 0,4230[2]	1,58 [0,52; 4,85] 0,4189[3]	0,3 [-0,4; 1,0] 0,4189[3]
Asian	9/250 (3,6)	2/242 (0,8)	4,36 [0,95; 19,96] 0,0581[2]	4,48 [0,96; 20,96] 0,0375[3]	2,8 [0,2; 5,3] 0,0375[3]
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
First endocrine therapy (Interaction p-value: 0,1876)					
Tamoxifen	1/114 (0,9)	2/132 (1,5)	0,58 [0,05; 6,30] 0,6536[2]	0,58 [0,05; 6,43] 1,0000[4]	-0,6 [-3,3; 2,1] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aromatase inhibitor	17/1169 (1,5)	5/1133 (0,4)	3,30 [1,22; 8,90] 0,0187[2]	3,33 [1,22; 9,05] 0,0125[3]	1,0 [0,2; 1,8] 0,0125[3]
ECOG-PS (Interaction p-value: 0,2503)					
ECOG-PS 0	15/1070 (1,4)	4/1020 (0,4)	3,57 [1,19; 10,73] 0,0232[2]	3,61 [1,19; 10,92] 0,0151[3]	1,0 [0,2; 1,8] 0,0151[3]
ECOG-PS 1	3/213 (1,4)	3/245 (1,2)	1,15 [0,23; 5,64] 0,8630[2]	1,15 [0,23; 5,77] 1,0000[4]	0,2 [-1,9; 2,3] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Diarrhoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7383)					
Neoadjuvant chemotherapy	352/430 (81,9)	37/415 (8,9)	9,18 [6,73; 12,53] <,0001[2]	46,10 [30,37; 69,98] <,0001[3]	72,9 [68,4; 77,5] <,0001[3]
Adjuvant chemotherapy	651/784 (83,0)	68/769 (8,8)	9,39 [7,47; 11,81] <,0001[2]	50,46 [36,97; 68,87] <,0001[3]	74,2 [70,9; 77,5] <,0001[3]
No chemotherapy	56/69 (81,2)	5/81 (6,2)	13,15 [5,58; 30,97] <,0001[2]	65,48 [22,07; 194,28] <,0001[3]	75,0 [64,4; 85,6] <,0001[3]
Primary tumor size (Interaction p-value: 0,5685)					
< 20 mm	272/331 (82,2)	27/335 (8,1)	10,20 [7,08; 14,69] <,0001[2]	52,59 [32,42; 85,31] <,0001[3]	74,1 [69,1; 79,2] <,0001[3]
≥ 20 but < 50 mm	528/646 (81,7)	53/653 (8,1)	10,07 [7,76; 13,07] <,0001[2]	50,66 [35,89; 71,49] <,0001[3]	73,6 [70,0; 77,3] <,0001[3]
≥ 50 mm	247/289 (85,5)	28/265 (10,6)	8,09 [5,68; 11,52] <,0001[2]	49,78 [29,88; 82,92] <,0001[3]	74,9 [69,4; 80,4] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,8134)					
0-3	346/427 (81,0)	33/418 (7,9)	10,26 [7,37; 14,29] <,0001[2]	49,84 [32,42; 76,61] <,0001[3]	73,1 [68,6; 77,7] <,0001[3]
4-9	462/549 (84,2)	51/542 (9,4)	8,94 [6,87; 11,64] <,0001[2]	51,13 [35,38; 73,89] <,0001[3]	74,7 [70,8; 78,7] <,0001[3]
≥ 10	251/307 (81,8)	26/305 (8,5)	9,59 [6,62; 13,90] <,0001[2]	48,10 [29,31; 78,93] <,0001[3]	73,2 [67,9; 78,6] <,0001[3]
Tumor stage (Interaction p-value: 0,5363)					
IIA	87/113 (77,0)	11/114 (9,6)	7,98 [4,51; 14,12] <,0001[2]	31,33 [14,65; 67,03] <,0001[3]	67,3 [57,9; 76,8] <,0001[3]
IIB	122/151 (80,8)	8/136 (5,9)	13,74 [6,98; 27,02] <,0001[2]	67,31 [29,61; 152,99] <,0001[3]	74,9 [67,5; 82,3] <,0001[3]
IIIA	422/495 (85,3)	39/488 (8,0)	10,67 [7,88; 14,45] <,0001[2]	66,55 [44,13; 100,37] <,0001[3]	77,3 [73,3; 81,2] <,0001[3]
IIIB	41/54 (75,9)	5/45 (11,1)	6,83 [2,95; 15,83] <,0001[2]	25,23 [8,24; 77,30] <,0001[3]	64,8 [50,2; 79,5] <,0001[3]
IIIC	386/468 (82,5)	46/480 (9,6)	8,61 [6,52; 11,36] <,0001[2]	44,41 [30,18; 65,35] <,0001[3]	72,9 [68,6; 77,2] <,0001[3]
Tumor grade (Interaction p-value: 0,4291)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	78/91 (85,7)	8/93 (8,6)	9,96 [5,11; 19,43] <,0001[2]	63,75 [25,08; 162,03] <,0001[3]	77,1 [67,9; 86,3] <,0001[3]
G2	516/612 (84,3)	56/603 (9,3)	9,08 [7,06; 11,68] <,0001[2]	52,50 [36,97; 74,57] <,0001[3]	75,0 [71,3; 78,7] <,0001[3]
G3	422/527 (80,1)	44/506 (8,7)	9,21 [6,92; 12,25] <,0001[2]	42,20 [28,98; 61,46] <,0001[3]	71,4 [67,2; 75,6] <,0001[3]
GX	41/51 (80,4)	1/59 (1,7)	47,43 [6,76; 332,72] 0,0001[2]	237,80 [29,29; 1930,62] <,0001[3]	78,7 [67,3; 90,1] <,0001[3]
Race (Interaction p-value: 0,0559)					
White	791/958 (82,6)	92/944 (9,7)	8,47 [6,96; 10,31] <,0001[2]	43,86 [33,41; 57,59] <,0001[3]	72,8 [69,8; 75,9] <,0001[3]
Asian	204/250 (81,6)	11/242 (4,5)	17,95 [10,05; 32,07] <,0001[2]	93,13 [46,98; 184,61] <,0001[3]	77,1 [71,6; 82,5] <,0001[3]
Other	52/62 (83,9)	6/64 (9,4)	8,95 [4,14; 19,31] <,0001[2]	50,27 [17,09; 147,89] <,0001[3]	74,5 [62,9; 86,1] <,0001[3]
First endocrine therapy (Interaction p-value: 0,4084)					
Tamoxifen	86/114 (75,4)	8/132 (6,1)	12,45 [6,31; 24,56] <,0001[2]	47,61 [20,71; 109,45] <,0001[3]	69,4 [60,5; 78,3] <,0001[3]
Aromatase inhibitor	973/1169 (83,2)	102/1133 (9,0)	9,25 [7,67; 11,15] <,0001[2]	50,18 [38,89; 64,74] <,0001[3]	74,2 [71,5; 76,9] <,0001[3]
ECOG-PS (Interaction p-value: 0,5859)					
ECOG-PS 0	893/1070 (83,5)	92/1020 (9,0)	9,25 [7,60; 11,26] <,0001[2]	50,89 [38,92; 66,54] <,0001[3]	74,4 [71,6; 77,3] <,0001[3]
ECOG-PS 1	166/213 (77,9)	18/245 (7,3)	10,61 [6,76; 16,64] <,0001[2]	44,54 [24,96; 79,47] <,0001[3]	70,6 [64,1; 77,0] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi²-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dizziness from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6982)					
< 65 years	97/918 (10,6)	59/937 (6,3)	1,68 [1,23; 2,29] 0,0011[2]	1,76 [1,25; 2,46] 0,0009[3]	4,3 [1,7; 6,8] 0,0009[3]
≥ 65 years	40/365 (11,0)	24/328 (7,3)	1,50 [0,92; 2,43] 0,1016[2]	1,56 [0,92; 2,65] 0,0983[3]	3,6 [-0,6; 7,9] 0,0983[3]
Prior treatment (Interaction p-value: 0,3818)					
Neoadjuvant chemotherapy	45/430 (10,5)	25/415 (6,0)	1,74 [1,09; 2,78] 0,0213[2]	1,82 [1,10; 3,03] 0,0192[3]	4,4 [0,8; 8,1] 0,0192[3]
Adjuvant chemotherapy	81/784 (10,3)	54/769 (7,0)	1,47 [1,06; 2,05] 0,0217[2]	1,53 [1,06; 2,19] 0,0206[3]	3,3 [0,5; 6,1] 0,0206[3]
No chemotherapy	11/69 (15,9)	4/81 (4,9)	3,23 [1,08; 9,68] 0,0365[2]	3,65 [1,11; 12,05] 0,0252[3]	11,0 [1,2; 20,8] 0,0252[3]
Region (Interaction p-value: 0,6374)					
North America / Europe	82/678 (12,1)	47/650 (7,2)	1,67 [1,19; 2,35] 0,0032[2]	1,77 [1,21; 2,57] 0,0028[3]	4,9 [1,7; 8,0] 0,0028[3]
Asia	23/203 (11,3)	18/201 (9,0)	1,27 [0,70; 2,27] 0,4308[2]	1,30 [0,68; 2,49] 0,4293[3]	2,4 [-3,5; 8,3] 0,4293[3]
Other	32/402 (8,0)	18/414 (4,3)	1,83 [1,04; 3,21] 0,0346[2]	1,90 [1,05; 3,45] 0,0315[3]	3,6 [0,3; 6,9] 0,0315[3]
Primary tumor size (Interaction p-value: 0,3180)					
< 20 mm	27/331 (8,2)	20/335 (6,0)	1,37 [0,78; 2,39] 0,2729[2]	1,40 [0,77; 2,55] 0,2705[3]	2,2 [-1,7; 6,1] 0,2705[3]
≥ 20 but < 50 mm	79/646 (12,2)	41/653 (6,3)	1,95 [1,36; 2,80] 0,0003[2]	2,08 [1,40; 3,08] 0,0002[3]	6,0 [2,8; 9,1] 0,0002[3]
≥ 50 mm	30/289 (10,4)	22/265 (8,3)	1,25 [0,74; 2,11] 0,4035[2]	1,28 [0,72; 2,28] 0,4020[3]	2,1 [-2,8; 6,9] 0,4020[3]
Number of positive lymph nodes (Interaction p-value: 0,6027)					
0-3	45/427 (10,5)	27/418 (6,5)	1,63 [1,03; 2,58] 0,0360[2]	1,71 [1,04; 2,81] 0,0337[3]	4,1 [0,3; 7,8] 0,0337[3]
4-9	60/549 (10,9)	32/542 (5,9)	1,85 [1,23; 2,80] 0,0034[2]	1,96 [1,25; 3,06] 0,0028[3]	5,0 [1,7; 8,3] 0,0028[3]
≥ 10	32/307 (10,4)	24/305 (7,9)	1,32 [0,80; 2,19] 0,2752[2]	1,36 [0,78; 2,37] 0,2731[3]	2,6 [-2,0; 7,1] 0,2731[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7475)					
IIA	10/113 (8,8)	8/114 (7,0)	1,26 [0,52; 3,08] 0,6105[2]	1,29 [0,49; 3,39] 0,6095[3]	1,8 [-5,2; 8,9] 0,6095[3]
IIB	17/151 (11,3)	9/136 (6,6)	1,70 [0,78; 3,69] 0,1785[2]	1,79 [0,77; 4,16] 0,1714[3]	4,6 [-1,9; 11,2] 0,1714[3]
IIIA	56/495 (11,3)	27/488 (5,5)	2,04 [1,31; 3,18] 0,0015[2]	2,18 [1,35; 3,51] 0,0011[3]	5,8 [2,3; 9,2] 0,0011[3]
IIIB	5/54 (9,3)	3/45 (6,7)	1,39 [0,35; 5,50] 0,6397[2]	1,43 [0,32; 6,34] 0,7248[4]	2,6 [-8,0; 13,2] 0,7248[4]
IIIC	49/468 (10,5)	36/480 (7,5)	1,40 [0,93; 2,11] 0,1116[2]	1,44 [0,92; 2,26] 0,1095[3]	3,0 [-0,7; 6,6] 0,1095[3]
Tumor grade (Interaction p-value: 0,9316)					
G1	7/91 (7,7)	6/93 (6,5)	1,19 [0,42; 3,41] 0,7430[2]	1,21 [0,39; 3,74] 0,7426[3]	1,2 [-6,2; 8,7] 0,7426[3]
G2	78/612 (12,7)	45/603 (7,5)	1,71 [1,20; 2,42] 0,0027[2]	1,81 [1,23; 2,66] 0,0023[3]	5,3 [1,9; 8,7] 0,0023[3]
G3	49/527 (9,3)	30/506 (5,9)	1,57 [1,01; 2,43] 0,0439[2]	1,63 [1,01; 2,61] 0,0417[3]	3,4 [0,1; 6,6] 0,0417[3]
GX	3/51 (5,9)	2/59 (3,4)	1,74 [0,30; 9,98] 0,5369[2]	1,78 [0,29; 11,10] 0,6613[4]	2,5 [-5,4; 10,4] 0,6613[4]
Race (Interaction p-value: 0,8703)					
White	100/958 (10,4)	58/944 (6,1)	1,70 [1,25; 2,32] 0,0008[2]	1,78 [1,27; 2,49] 0,0007[3]	4,3 [1,8; 6,8] 0,0007[3]
Asian	27/250 (10,8)	18/242 (7,4)	1,45 [0,82; 2,57] 0,1994[2]	1,51 [0,81; 2,81] 0,1959[3]	3,4 [-1,7; 8,4] 0,1959[3]
Other	9/62 (14,5)	5/64 (7,8)	1,86 [0,66; 5,24] 0,2411[2]	2,00 [0,63; 6,36] 0,2313[3]	6,7 [-4,3; 17,7] 0,2313[3]
First endocrine therapy (Interaction p-value: 0,3393)					
Tamoxifen	13/114 (11,4)	6/132 (4,5)	2,51 [0,99; 6,39] 0,0537[2]	2,70 [0,99; 7,36] 0,0445[3]	6,9 [0,0; 13,7] 0,0445[3]
Aromatase inhibitor	124/1169 (10,6)	77/1133 (6,8)	1,56 [1,19; 2,05] 0,0014[2]	1,63 [1,21; 2,19] 0,0012[3]	3,8 [1,5; 6,1] 0,0012[3]
ECOG-PS (Interaction p-value: 0,8928)					
ECOG-PS 0	109/1070 (10,2)	64/1020 (6,3)	1,62 [1,21; 2,18] 0,0014[2]	1,69 [1,23; 2,34] 0,0012[3]	3,9 [1,6; 6,3] 0,0012[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	28/213 (13,1)	19/245 (7,8)	1,70 [0,98; 2,95] 0,0614[2]	1,80 [0,97; 3,33] 0,0579[3]	5,4 [-0,2; 11,0] 0,0579[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dry eye from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5416)					
< 65 years	31/918 (3,4)	10/937 (1,1)	3,16 [1,56; 6,42] 0,0014[2]	3,24 [1,58; 6,65] 0,0007[3]	2,3 [1,0; 3,7] 0,0007[3]
≥ 65 years	7/365 (1,9)	1/328 (0,3)	6,29 [0,78; 50,86] 0,0846[2]	6,39 [0,78; 52,25] 0,0718[4]	1,6 [0,1; 3,1] 0,0718[4]
Prior treatment (Interaction p-value: 0,9903)					
Neoadjuvant chemotherapy	11/430 (2,6)	3/415 (0,7)	3,54 [0,99; 12,59] 0,0510[2]	3,61 [1,00; 13,02] 0,0367[3]	1,8 [0,1; 3,5] 0,0367[3]
Adjuvant chemotherapy	26/784 (3,3)	8/769 (1,0)	3,19 [1,45; 7,00] 0,0038[2]	3,26 [1,47; 7,25] 0,0022[3]	2,3 [0,8; 3,7] 0,0022[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,6950)					
North America / Europe	26/678 (3,8)	6/650 (0,9)	4,15 [1,72; 10,03] 0,0015[2]	4,28 [1,75; 10,47] 0,0005[3]	2,9 [1,3; 4,5] 0,0005[3]
Asia	6/203 (3,0)	2/201 (1,0)	2,97 [0,61; 14,54] 0,1791[2]	3,03 [0,60; 15,20] 0,2842[4]	2,0 [-0,7; 4,7] 0,2842[4]
Other	6/402 (1,5)	3/414 (0,7)	2,06 [0,52; 8,18] 0,3045[2]	2,08 [0,52; 8,36] 0,3344[4]	0,8 [-0,7; 2,2] 0,3344[4]
Primary tumor size (Interaction p-value: 0,8818)					
< 20 mm	9/331 (2,7)	2/335 (0,6)	4,55 [0,99; 20,92] 0,0513[2]	4,65 [1,00; 21,70] 0,0317[3]	2,1 [0,2; 4,1] 0,0317[3]
≥ 20 but < 50 mm	19/646 (2,9)	6/653 (0,9)	3,20 [1,29; 7,96] 0,0123[2]	3,27 [1,30; 8,24] 0,0080[3]	2,0 [0,5; 3,5] 0,0080[3]
≥ 50 mm	9/289 (3,1)	3/265 (1,1)	2,75 [0,75; 10,05] 0,1259[2]	2,81 [0,75; 10,48] 0,1094[3]	2,0 [-0,4; 4,4] 0,1094[3]
Number of positive lymph nodes (Interaction p-value: 0,5065)					
0-3	18/427 (4,2)	3/418 (0,7)	5,87 [1,74; 19,79] 0,0043[2]	6,09 [1,78; 20,83] 0,0011[3]	3,5 [1,4; 5,6] 0,0011[3]
4-9	12/549 (2,2)	5/542 (0,9)	2,37 [0,84; 6,68] 0,1028[2]	2,40 [0,84; 6,86] 0,0921[3]	1,3 [-0,2; 2,7] 0,0921[3]
≥ 10	8/307 (2,6)	3/305 (1,0)	2,65 [0,71; 9,89] 0,1472[2]	2,69 [0,71; 10,25] 0,1310[3]	1,6 [-0,5; 3,7] 0,1310[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,5145)					
IIA	3/113 (2,7)	0/114 (0,0)	7,06 [0,37; 135,16] 0,1943[2]	7,25 [0,37; 142,05] 0,1217[4]	2,7 [-0,3; 5,6] 0,1217[4]
IIB	5/151 (3,3)	1/136 (0,7)	4,50 [0,53; 38,07] 0,1670[2]	4,62 [0,53; 40,08] 0,2177[4]	2,6 [-0,6; 5,8] 0,2177[4]
IIIA	14/495 (2,8)	3/488 (0,6)	4,60 [1,33; 15,91] 0,0159[2]	4,71 [1,34; 16,48] 0,0078[3]	2,2 [0,6; 3,8] 0,0078[3]
IIIB	1/54 (1,9)	2/45 (4,4)	0,42 [0,04; 4,45] 0,4686[2]	0,41 [0,04; 4,63] 0,5894[4]	-2,6 [-9,6; 4,4] 0,5894[4]
IIIC	15/468 (3,2)	5/480 (1,0)	3,08 [1,13; 8,40] 0,0282[2]	3,15 [1,13; 8,73] 0,0205[3]	2,2 [0,3; 4,0] 0,0205[3]
Tumor grade (Interaction p-value: 0,4793)					
G1	3/91 (3,3)	2/93 (2,2)	1,53 [0,26; 8,96] 0,6354[2]	1,55 [0,25; 9,51] 0,6806[4]	1,1 [-3,6; 5,9] 0,6806[4]
G2	16/612 (2,6)	6/603 (1,0)	2,63 [1,04; 6,67] 0,0421[2]	2,67 [1,04; 6,87] 0,0343[3]	1,6 [0,1; 3,1] 0,0343[3]
G3	17/527 (3,2)	2/506 (0,4)	8,16 [1,90; 35,14] 0,0048[2]	8,40 [1,93; 36,55] 0,0007[3]	2,8 [1,2; 4,4] 0,0007[3]
GX	2/51 (3,9)	1/59 (1,7)	2,31 [0,22; 24,78] 0,4880[2]	2,37 [0,21; 26,90] 0,5957[4]	2,2 [-4,0; 8,5] 0,5957[4]
Progesterone receptor status (Interaction p-value: 0,2708)					
Negative	5/156 (3,2)	2/169 (1,2)	2,71 [0,53; 13,76] 0,2296[2]	2,76 [0,53; 14,46] 0,2669[4]	2,0 [-1,2; 5,2] 0,2669[4]
Positive	32/1089 (2,9)	9/1067 (0,8)	3,48 [1,67; 7,26] 0,0009[2]	3,56 [1,69; 7,49] 0,0004[3]	2,1 [1,0; 3,2] 0,0004[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9645)					
White	28/958 (2,9)	9/944 (1,0)	3,07 [1,45; 6,46] 0,0032[2]	3,13 [1,47; 6,66] 0,0019[3]	2,0 [0,7; 3,2] 0,0019[3]
Asian	8/250 (3,2)	2/242 (0,8)	3,87 [0,83; 18,05] 0,0848[2]	3,97 [0,83; 18,87] 0,1063[4]	2,4 [-0,1; 4,8] 0,1063[4]
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
First endocrine therapy (Interaction p-value: 0,6239)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	4/114 (3,5)	2/132 (1,5)	2,32 [0,43; 12,41] 0,3269[2]	2,36 [0,42; 13,15] 0,4199[4]	2,0 [-2,0; 6,0] 0,4199[4]
Aromatase inhibitor	34/1169 (2,9)	9/1133 (0,8)	3,66 [1,76; 7,60] 0,0005[2]	3,74 [1,79; 7,84] 0,0002[3]	2,1 [1,0; 3,2] 0,0002[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dry mouth from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,3571)					
< 65 years	27/918 (2,9)	8/937 (0,9)	3,44 [1,57; 7,54] 0,0020[2]	3,52 [1,59; 7,79] 0,0010[3]	2,1 [0,8; 3,3] 0,0010[3]
≥ 65 years	18/365 (4,9)	8/328 (2,4)	2,02 [0,89; 4,59] 0,0922[2]	2,07 [0,89; 4,84] 0,0847[3]	2,5 [-0,3; 5,3] 0,0847[3]
Prior treatment (Interaction p-value: 0,7135)					
Neoadjuvant chemotherapy	11/430 (2,6)	6/415 (1,4)	1,77 [0,66; 4,74] 0,2564[2]	1,79 [0,66; 4,88] 0,2496[3]	1,1 [-0,8; 3,0] 0,2496[3]
Adjuvant chemotherapy	30/784 (3,8)	10/769 (1,3)	2,94 [1,45; 5,98] 0,0028[2]	3,02 [1,47; 6,22] 0,0017[3]	2,5 [1,0; 4,1] 0,0017[3]
No chemotherapy	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (Interaction p-value: 0,4059)					
North America / Europe	38/678 (5,6)	12/650 (1,8)	3,04 [1,60; 5,76] 0,0007[2]	3,16 [1,63; 6,10] 0,0003[3]	3,8 [1,7; 5,8] 0,0003[3]
Asia	3/203 (1,5)	3/201 (1,5)	0,99 [0,20; 4,85] 0,9903[2]	0,99 [0,20; 4,96] 1,0000[4]	-0,0 [-2,4; 2,3] 1,0000[4]
Other	4/402 (1,0)	1/414 (0,2)	4,12 [0,46; 36,70] 0,2045[2]	4,15 [0,46; 37,30] 0,2109[4]	0,8 [-0,3; 1,8] 0,2109[4]
Primary tumor size (Interaction p-value: 0,1323)					
< 20 mm	16/331 (4,8)	1/335 (0,3)	16,19 [2,16; 121,41] 0,0067[2]	16,97 [2,24; 128,68] 0,0002[3]	4,5 [2,2; 6,9] 0,0002[3]
≥ 20 but < 50 mm	16/646 (2,5)	9/653 (1,4)	1,80 [0,80; 4,04] 0,1558[2]	1,82 [0,80; 4,14] 0,1496[3]	1,1 [-0,4; 2,6] 0,1496[3]
≥ 50 mm	13/289 (4,5)	6/265 (2,3)	1,99 [0,77; 5,15] 0,1579[2]	2,03 [0,76; 5,43] 0,1489[3]	2,2 [-0,8; 5,2] 0,1489[3]
Number of positive lymph nodes (Interaction p-value: 0,3501)					
0-3	18/427 (4,2)	4/418 (1,0)	4,41 [1,50; 12,91] 0,0069[2]	4,56 [1,53; 13,57] 0,0029[3]	3,3 [1,1; 5,4] 0,0029[3]
4-9	16/549 (2,9)	9/542 (1,7)	1,76 [0,78; 3,94] 0,1724[2]	1,78 [0,78; 4,06] 0,1664[3]	1,3 [-0,5; 3,0] 0,1664[3]
≥ 10	11/307 (3,6)	3/305 (1,0)	3,64 [1,03; 12,93] 0,0455[2]	3,74 [1,03; 13,54] 0,0315[3]	2,6 [0,2; 5,0] 0,0315[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7485)					
IIA	8/113 (7,1)	0/114 (0,0)	17,15 [1,00; 293,63] 0,0499[2]	18,45 [1,05; 323,59] 0,0033[4]	7,1 [2,4; 11,8] 0,0033[4]
IIB	2/151 (1,3)	2/136 (1,5)	0,90 [0,13; 6,31] 0,9161[2]	0,90 [0,12; 6,47] 1,0000[4]	-0,1 [-2,9; 2,6] 1,0000[4]
IIIA	16/495 (3,2)	9/488 (1,8)	1,75 [0,78; 3,93] 0,1730[2]	1,78 [0,78; 4,06] 0,1669[3]	1,4 [-0,6; 3,4] 0,1669[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	17/468 (3,6)	5/480 (1,0)	3,49 [1,30; 9,38] 0,0133[2]	3,58 [1,31; 9,79] 0,0081[3]	2,6 [0,7; 4,5] 0,0081[3]
Tumor grade (Interaction p-value: 0,3477)					
G1	7/91 (7,7)	2/93 (2,2)	3,58 [0,76; 16,76] 0,1058[2]	3,79 [0,77; 18,77] 0,0980[4]	5,5 [-0,7; 11,8] 0,0980[4]
G2	22/612 (3,6)	10/603 (1,7)	2,17 [1,04; 4,54] 0,0402[2]	2,21 [1,04; 4,71] 0,0351[3]	1,9 [0,1; 3,7] 0,0351[3]
G3	16/527 (3,0)	4/506 (0,8)	3,84 [1,29; 11,41] 0,0154[2]	3,93 [1,30; 11,84] 0,0088[3]	2,2 [0,6; 3,9] 0,0088[3]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9617)					
Negative	5/156 (3,2)	0/169 (0,0)	11,91 [0,66; 213,66] 0,0926[2]	12,31 [0,67; 224,42] 0,0246[4]	3,2 [0,4; 6,0] 0,0246[4]
Positive	39/1089 (3,6)	15/1067 (1,4)	2,55 [1,41; 4,59] 0,0019[2]	2,60 [1,43; 4,75] 0,0012[3]	2,2 [0,9; 3,5] 0,0012[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,5650)					
White	38/958 (4,0)	12/944 (1,3)	3,12 [1,64; 5,93] 0,0005[2]	3,21 [1,67; 6,18] 0,0002[3]	2,7 [1,3; 4,1] 0,0002[3]
Asian	4/250 (1,6)	3/242 (1,2)	1,29 [0,29; 5,71] 0,7365[2]	1,30 [0,29; 5,85] 1,0000[4]	0,4 [-1,7; 2,4] 1,0000[4]
Other	2/62 (3,2)	0/64 (0,0)	5,16 [0,25; 105,34] 0,2864[2]	5,33 [0,25; 113,30] 0,2401[4]	3,2 [-1,2; 7,6] 0,2401[4]
First endocrine therapy (Interaction p-value: 0,6272)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	4/114 (3,5)	1/132 (0,8)	4,63 [0,53; 40,85] 0,1675[2]	4,76 [0,52; 43,25] 0,1855[4]	2,8 [-0,9; 6,4] 0,1855[4]
Aromatase inhibitor	41/1169 (3,5)	15/1133 (1,3)	2,65 [1,47; 4,76] 0,0011[2]	2,71 [1,49; 4,92] 0,0007[3]	2,2 [0,9; 3,4] 0,0007[3]
ECOG-PS (Interaction p-value: 0,4836)					
ECOG-PS 0	34/1070 (3,2)	10/1020 (1,0)	3,24 [1,61; 6,53] 0,0010[2]	3,31 [1,63; 6,74] 0,0005[3]	2,2 [1,0; 3,4] 0,0005[3]
ECOG-PS 1	11/213 (5,2)	6/245 (2,4)	2,11 [0,79; 5,61] 0,1347[2]	2,17 [0,79; 5,97] 0,1252[3]	2,7 [-0,8; 6,3] 0,1252[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dry skin from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5096)					
< 65 years	37/918 (4,0)	17/937 (1,8)	2,22 [1,26; 3,92] 0,0058[2]	2,27 [1,27; 4,07] 0,0045[3]	2,2 [0,7; 3,7] 0,0045[3]
≥ 65 years	14/365 (3,8)	8/328 (2,4)	1,57 [0,67; 3,70] 0,2998[2]	1,60 [0,66; 3,85] 0,2951[3]	1,4 [-1,2; 4,0] 0,2951[3]
Prior treatment (Interaction p-value: 0,7986)					
Neoadjuvant chemotherapy	15/430 (3,5)	6/415 (1,4)	2,41 [0,95; 6,16] 0,0654[2]	2,46 [0,95; 6,41] 0,0566[3]	2,0 [-0,0; 4,1] 0,0566[3]
Adjuvant chemotherapy	34/784 (4,3)	17/769 (2,2)	1,96 [1,11; 3,48] 0,0213[2]	2,01 [1,11; 3,62] 0,0187[3]	2,1 [0,4; 3,9] 0,0187[3]
No chemotherapy	2/69 (2,9)	2/81 (2,5)	1,17 [0,17; 8,12] 0,8709[2]	1,18 [0,16; 8,60] 1,0000[4]	0,4 [-4,8; 5,6] 1,0000[4]
Region (Interaction p-value: 0,4602)					
North America / Europe	32/678 (4,7)	15/650 (2,3)	2,05 [1,12; 3,74] 0,0202[2]	2,10 [1,12; 3,91] 0,0174[3]	2,4 [0,4; 4,4] 0,0174[3]
Asia	11/203 (5,4)	8/201 (4,0)	1,36 [0,56; 3,31] 0,4966[2]	1,38 [0,54; 3,51] 0,4947[3]	1,4 [-2,7; 5,6] 0,4947[3]
Other	8/402 (2,0)	2/414 (0,5)	4,12 [0,88; 19,28] 0,0722[2]	4,18 [0,88; 19,82] 0,0604[4]	1,5 [-0,0; 3,0] 0,0604[4]
Primary tumor size (Interaction p-value: 0,4309)					
< 20 mm	12/331 (3,6)	3/335 (0,9)	4,05 [1,15; 14,22] 0,0291[2]	4,16 [1,16; 14,89] 0,0176[3]	2,7 [0,5; 5,0] 0,0176[3]
≥ 20 but < 50 mm	26/646 (4,0)	14/653 (2,1)	1,88 [0,99; 3,56] 0,0540[2]	1,91 [0,99; 3,70] 0,0498[3]	1,9 [0,0; 3,8] 0,0498[3]
≥ 50 mm	13/289 (4,5)	8/265 (3,0)	1,49 [0,63; 3,54] 0,3661[2]	1,51 [0,62; 3,71] 0,3624[3]	1,5 [-1,7; 4,6] 0,3624[3]
Tumor stage (Interaction p-value: 0,1576)					
IIA	3/113 (2,7)	4/114 (3,5)	0,76 [0,17; 3,30] 0,7108[2]	0,75 [0,16; 3,43] 1,0000[4]	-0,9 [-5,3; 3,6] 1,0000[4]
IIB	3/151 (2,0)	5/136 (3,7)	0,54 [0,13; 2,22] 0,3931[2]	0,53 [0,12; 2,27] 0,4833[4]	-1,7 [-5,6; 2,2] 0,4833[4]
IIIA	21/495 (4,2)	6/488 (1,2)	3,45 [1,40; 8,48] 0,0069[2]	3,56 [1,42; 8,90] 0,0039[3]	3,0 [1,0; 5,0] 0,0039[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	3/54 (5,6)	1/45 (2,2)	2,50 [0,27; 23,21] 0,4203[2]	2,59 [0,26; 25,79] 0,6237[4]	3,3 [-4,1; 10,8] 0,6237[4]
IIIC	21/468 (4,5)	9/480 (1,9)	2,39 [1,11; 5,17] 0,0264[2]	2,46 [1,11; 5,43] 0,0216[3]	2,6 [0,4; 4,8] 0,0216[3]
Tumor grade (Interaction p-value: 0,2911)					
G1	4/91 (4,4)	1/93 (1,1)	4,09 [0,47; 35,88] 0,2039[2]	4,23 [0,46; 38,59] 0,2086[4]	3,3 [-1,4; 8,0] 0,2086[4]
G2	26/612 (4,2)	9/603 (1,5)	2,85 [1,35; 6,02] 0,0062[2]	2,93 [1,36; 6,30] 0,0041[3]	2,8 [0,9; 4,6] 0,0041[3]
G3	20/527 (3,8)	12/506 (2,4)	1,60 [0,79; 3,24] 0,1913[2]	1,62 [0,79; 3,36] 0,1868[3]	1,4 [-0,7; 3,5] 0,1868[3]
GX	1/51 (2,0)	3/59 (5,1)	0,39 [0,04; 3,59] 0,4027[2]	0,37 [0,04; 3,71] 0,6221[4]	-3,1 [-9,9; 3,7] 0,6221[4]
Progesterone receptor status (Interaction p-value: 0,1223)					
Negative	13/156 (8,3)	6/169 (3,6)	2,35 [0,91; 6,02] 0,0760[2]	2,47 [0,91; 6,67] 0,0663[3]	4,8 [-0,4; 9,9] 0,0663[3]
Positive	38/1089 (3,5)	19/1067 (1,8)	1,96 [1,14; 3,38] 0,0154[2]	1,99 [1,14; 3,48] 0,0134[3]	1,7 [0,4; 3,1] 0,0134[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,5616)					
White	36/958 (3,8)	14/944 (1,5)	2,53 [1,38; 4,67] 0,0028[2]	2,59 [1,39; 4,84] 0,0019[3]	2,3 [0,8; 3,7] 0,0019[3]
Asian	12/250 (4,8)	8/242 (3,3)	1,45 [0,60; 3,49] 0,4046[2]	1,47 [0,59; 3,67] 0,4014[3]	1,5 [-2,0; 5,0] 0,4014[3]
Other	3/62 (4,8)	2/64 (3,1)	1,55 [0,27; 8,95] 0,6253[2]	1,58 [0,25; 9,77] 0,6774[4]	1,7 [-5,1; 8,5] 0,6774[4]
First endocrine therapy (Interaction p-value: 0,6427)					
Tamoxifen	5/114 (4,4)	2/132 (1,5)	2,89 [0,57; 14,64] 0,1986[2]	2,98 [0,57; 15,67] 0,2546[4]	2,9 [-1,4; 7,2] 0,2546[4]
Aromatase inhibitor	46/1169 (3,9)	23/1133 (2,0)	1,94 [1,18; 3,18] 0,0086[2]	1,98 [1,19; 3,28] 0,0074[3]	1,9 [0,5; 3,3] 0,0074[3]
ECOG-PS (Interaction p-value: 0,3671)					
ECOG-PS 0	42/1070 (3,9)	22/1020 (2,2)	1,82 [1,09; 3,03] 0,0210[2]	1,85 [1,10; 3,13] 0,0190[3]	1,8 [0,3; 3,2] 0,0190[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	9/213 (4,2)	3/245 (1,2)	3,45 [0,95; 12,58] 0,0606[2]	3,56 [0,95; 13,32] 0,0449[3]	3,0 [-0,0; 6,0] 0,0449[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dysgeusia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4205)					
< 65 years	35/918 (3,8)	4/937 (0,4)	8,93 [3,19; 25,03] <,0001[2]	9,25 [3,27; 26,12] <,0001[3]	3,4 [2,1; 4,7] <,0001[3]
≥ 65 years	25/365 (6,8)	1/328 (0,3)	22,47 [3,06; 164,88] 0,0022[2]	24,04 [3,24; 178,47] <,0001[3]	6,5 [3,9; 9,2] <,0001[3]
Prior treatment (Interaction p-value: 0,9678)					
Neoadjuvant chemotherapy	21/430 (4,9)	0/415 (0,0)	41,50 [2,52; 682,93] 0,0091[2]	43,63 [2,63; 722,65] <,0001[3]	4,9 [2,8; 6,9] <,0001[3]
Adjuvant chemotherapy	32/784 (4,1)	5/769 (0,7)	6,28 [2,46; 16,03] 0,0001[2]	6,50 [2,52; 16,78] <,0001[3]	3,4 [1,9; 4,9] <,0001[3]
No chemotherapy	7/69 (10,1)	0/81 (0,0)	17,57 [1,02; 302,22] 0,0483[2]	19,56 [1,10; 349,01] 0,0037[4]	10,1 [3,0; 17,3] 0,0037[4]
Region (Interaction p-value: 0,8841)					
North America / Europe	33/678 (4,9)	3/650 (0,5)	10,55 [3,25; 34,22] <,0001[2]	11,03 [3,37; 36,16] <,0001[3]	4,4 [2,7; 6,1] <,0001[3]
Asia	18/203 (8,9)	1/201 (0,5)	17,82 [2,40; 132,25] 0,0048[2]	19,46 [2,57; 147,22] <,0001[3]	8,4 [4,3; 12,4] <,0001[3]
Other	9/402 (2,2)	1/414 (0,2)	9,27 [1,18; 72,82] 0,0343[2]	9,46 [1,19; 75,00] 0,0102[4]	2,0 [0,5; 3,5] 0,0102[4]
Primary tumor size (Interaction p-value: 0,8644)					
< 20 mm	17/331 (5,1)	1/335 (0,3)	17,21 [2,30; 128,55] 0,0056[2]	18,08 [2,39; 136,68] 0,0001[3]	4,8 [2,4; 7,3] 0,0001[3]
≥ 20 but < 50 mm	28/646 (4,3)	3/653 (0,5)	9,43 [2,88; 30,88] 0,0002[2]	9,82 [2,97; 32,45] <,0001[3]	3,9 [2,2; 5,5] <,0001[3]
≥ 50 mm	15/289 (5,2)	1/265 (0,4)	13,75 [1,83; 103,41] 0,0109[2]	14,45 [1,90; 110,18] 0,0007[3]	4,8 [2,2; 7,5] 0,0007[3]
Number of positive lymph nodes (Interaction p-value: 0,4673)					
0-3	24/427 (5,6)	1/418 (0,2)	23,49 [3,19; 172,88] 0,0019[2]	24,83 [3,34; 184,43] <,0001[3]	5,4 [3,1; 7,6] <,0001[3]
4-9	23/549 (4,2)	4/542 (0,7)	5,68 [1,98; 16,31] 0,0013[2]	5,88 [2,02; 17,12] 0,0002[3]	3,5 [1,6; 5,3] 0,0002[3]
≥ 10	13/307 (4,2)	0/305 (0,0)	26,82 [1,60; 449,24] 0,0222[2]	28,01 [1,66; 473,29] 0,0003[3]	4,2 [2,0; 6,5] 0,0003[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 1,0000)					
IIA	5/113 (4,4)	0/114 (0,0)	11,10 [0,62; 198,36] 0,1019[2]	11,61 [0,63; 212,44] 0,0292[4]	4,4 [0,6; 8,2] 0,0292[4]
IIB	10/151 (6,6)	1/136 (0,7)	9,01 [1,17; 69,44] 0,0349[2]	9,57 [1,21; 75,81] 0,0095[3]	5,9 [1,7; 10,1] 0,0095[3]
IIIA	19/495 (3,8)	2/488 (0,4)	9,37 [2,19; 39,99] 0,0025[2]	9,70 [2,25; 41,87] 0,0002[3]	3,4 [1,6; 5,2] 0,0002[3]
IIIB	6/54 (11,1)	0/45 (0,0)	10,87 [0,63; 187,90] 0,1007[2]	12,20 [0,67; 222,70] 0,0303[4]	11,1 [2,7; 19,5] 0,0303[4]
IIIC	20/468 (4,3)	2/480 (0,4)	10,26 [2,41; 43,64] 0,0016[2]	10,67 [2,48; 45,91] <,0001[3]	3,9 [1,9; 5,8] <,0001[3]
Tumor grade (Interaction p-value: 0,9943)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	27/612 (4,4)	3/603 (0,5)	8,87 [2,70; 29,08] 0,0003[2]	9,23 [2,79; 30,59] <,0001[3]	3,9 [2,2; 5,6] <,0001[3]
G3	24/527 (4,6)	2/506 (0,4)	11,52 [2,74; 48,50] 0,0009[2]	12,02 [2,83; 51,15] <,0001[3]	4,2 [2,3; 6,0] <,0001[3]
GX	7/51 (13,7)	0/59 (0,0)	17,31 [1,01; 295,80] 0,0490[2]	20,06 [1,12; 360,50] 0,0036[4]	13,7 [4,3; 23,2] 0,0036[4]
Progesterone receptor status (Interaction p-value: 0,9978)					
Negative	7/156 (4,5)	0/169 (0,0)	16,24 [0,94; 282,05] 0,0556[2]	17,01 [0,96; 300,29] 0,0055[4]	4,5 [1,2; 7,7] 0,0055[4]
Positive	52/1089 (4,8)	4/1067 (0,4)	12,74 [4,62; 35,09] <,0001[2]	13,33 [4,80; 36,98] <,0001[3]	4,4 [3,1; 5,7] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
Race (Interaction p-value: 0,7622)					
White	32/958 (3,3)	4/944 (0,4)	7,88 [2,80; 22,20] <,0001[2]	8,12 [2,86; 23,05] <,0001[3]	2,9 [1,7; 4,1] <,0001[3]
Asian	19/250 (7,6)	1/242 (0,4)	18,39 [2,48; 136,32] 0,0044[2]	19,82 [2,63; 149,27] <,0001[3]	7,2 [3,8; 10,6] <,0001[3]
Other	7/62 (11,3)	0/64 (0,0)	15,48 [0,90; 265,33] 0,0588[2]	17,43 [0,97; 312,14] 0,0058[4]	11,3 [3,4; 19,2] 0,0058[4]
ECOG-PS (Interaction p-value: 0,9734)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	51/1070 (4,8)	5/1020 (0,5)	9,72 [3,90; 24,26] <,0001[2]	10,16 [4,04; 25,56] <,0001[3]	4,3 [2,9; 5,6] <,0001[3]
ECOG-PS 1	9/213 (4,2)	0/245 (0,0)	21,84 [1,28; 373,05] 0,0332[2]	22,81 [1,32; 394,27] 0,0009[4]	4,2 [1,5; 6,9] 0,0009[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dyspepsia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,1107)					
Neoadjuvant chemotherapy	36/430 (8,4)	5/415 (1,2)	6,95 [2,75; 17,54] <,0001[2]	7,49 [2,91; 19,29] <,0001[3]	7,2 [4,3; 10,0] <,0001[3]
Adjuvant chemotherapy	54/784 (6,9)	23/769 (3,0)	2,30 [1,43; 3,71] 0,0006[2]	2,40 [1,46; 3,95] 0,0004[3]	3,9 [1,8; 6,0] 0,0004[3]
No chemotherapy	6/69 (8,7)	3/81 (3,7)	2,35 [0,61; 9,04] 0,2147[2]	2,48 [0,60; 10,30] 0,3025[4]	5,0 [-2,8; 12,8] 0,3025[4]
Primary tumor size (Interaction p-value: 0,1472)					
< 20 mm	24/331 (7,3)	9/335 (2,7)	2,70 [1,27; 5,72] 0,0096[2]	2,83 [1,30; 6,19] 0,0067[3]	4,6 [1,3; 7,9] 0,0067[3]
≥ 20 but < 50 mm	46/646 (7,1)	9/653 (1,4)	5,17 [2,55; 10,47] <,0001[2]	5,49 [2,66; 11,30] <,0001[3]	5,7 [3,6; 7,9] <,0001[3]
≥ 50 mm	26/289 (9,0)	12/265 (4,5)	1,99 [1,02; 3,86] 0,0425[2]	2,08 [1,03; 4,22] 0,0377[3]	4,5 [0,3; 8,6] 0,0377[3]
Number of positive lymph nodes (Interaction p-value: 0,9577)					
0-3	37/427 (8,7)	11/418 (2,6)	3,29 [1,70; 6,37] 0,0004[2]	3,51 [1,77; 6,98] 0,0002[3]	6,0 [3,0; 9,1] 0,0002[3]
4-9	36/549 (6,6)	12/542 (2,2)	2,96 [1,56; 5,63] 0,0009[2]	3,10 [1,59; 6,02] 0,0005[3]	4,3 [1,9; 6,8] 0,0005[3]
≥ 10	23/307 (7,5)	8/305 (2,6)	2,86 [1,30; 6,29] 0,0091[2]	3,01 [1,32; 6,83] 0,0060[3]	4,9 [1,4; 8,3] 0,0060[3]
Tumor stage (Interaction p-value: 0,8584)					
IIA	11/113 (9,7)	2/114 (1,8)	5,55 [1,26; 24,47] 0,0236[2]	6,04 [1,31; 27,90] 0,0097[3]	8,0 [2,0; 14,0] 0,0097[3]
IIB	13/151 (8,6)	4/136 (2,9)	2,93 [0,98; 8,76] 0,0549[2]	3,11 [0,99; 9,78] 0,0422[3]	5,7 [0,4; 11,0] 0,0422[3]
IIIA	35/495 (7,1)	14/488 (2,9)	2,46 [1,34; 4,52] 0,0036[2]	2,58 [1,37; 4,85] 0,0025[3]	4,2 [1,5; 6,9] 0,0025[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	35/468 (7,5)	10/480 (2,1)	3,59 [1,80; 7,17] 0,0003[2]	3,80 [1,86; 7,76] <,0001[3]	5,4 [2,7; 8,1] <,0001[3]
Tumor grade (Interaction p-value: 0,8732)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G1	5/91 (5,5)	3/93 (3,2)	1,70 [0,42; 6,92] 0,4565[2]	1,74 [0,40; 7,52] 0,4945[4]	2,3 [-3,6; 8,2] 0,4945[4]
G2	47/612 (7,7)	16/603 (2,7)	2,89 [1,66; 5,05] 0,0002[2]	3,05 [1,71; 5,44] <,0001[3]	5,0 [2,6; 7,5] <,0001[3]
G3	41/527 (7,8)	12/506 (2,4)	3,28 [1,74; 6,17] 0,0002[2]	3,47 [1,80; 6,69] <,0001[3]	5,4 [2,8; 8,1] <,0001[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
First endocrine therapy (Interaction p-value: 0,5134)					
Tamoxifen	5/114 (4,4)	3/132 (2,3)	1,93 [0,47; 7,90] 0,3605[2]	1,97 [0,46; 8,44] 0,4772[4]	2,1 [-2,4; 6,7] 0,4772[4]
Aromatase inhibitor	91/1169 (7,8)	28/1133 (2,5)	3,15 [2,08; 4,77] <,0001[2]	3,33 [2,16; 5,13] <,0001[3]	5,3 [3,5; 7,1] <,0001[3]
ECOG-PS (Interaction p-value: 0,2615)					
ECOG-PS 0	80/1070 (7,5)	22/1020 (2,2)	3,47 [2,18; 5,51] <,0001[2]	3,67 [2,27; 5,92] <,0001[3]	5,3 [3,5; 7,1] <,0001[3]
ECOG-PS 1	16/213 (7,5)	9/245 (3,7)	2,04 [0,92; 4,53] 0,0781[2]	2,13 [0,92; 4,92] 0,0713[3]	3,8 [-0,4; 8,1] 0,0713[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Dyspnoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7226)					
< 65 years	62/918 (6,8)	34/937 (3,6)	1,86 [1,24; 2,80] 0,0029[2]	1,92 [1,25; 2,95] 0,0024[3]	3,1 [1,1; 5,1] 0,0024[3]
≥ 65 years	31/365 (8,5)	17/328 (5,2)	1,64 [0,92; 2,90] 0,0908[2]	1,70 [0,92; 3,13] 0,0866[3]	3,3 [-0,4; 7,0] 0,0866[3]
Prior treatment (Interaction p-value: 0,6254)					
Neoadjuvant chemotherapy	29/430 (6,7)	12/415 (2,9)	2,33 [1,21; 4,51] 0,0118[2]	2,43 [1,22; 4,83] 0,0092[3]	3,9 [1,0; 6,7] 0,0092[3]
Adjuvant chemotherapy	57/784 (7,3)	33/769 (4,3)	1,69 [1,12; 2,57] 0,0132[2]	1,75 [1,13; 2,72] 0,0120[3]	3,0 [0,7; 5,3] 0,0120[3]
No chemotherapy	7/69 (10,1)	6/81 (7,4)	1,37 [0,48; 3,88] 0,5542[2]	1,41 [0,45; 4,42] 0,5526[3]	2,7 [-6,4; 11,9] 0,5526[3]
Region (Interaction p-value: 0,0884)					
North America / Europe	79/678 (11,7)	37/650 (5,7)	2,05 [1,41; 2,98] 0,0002[2]	2,19 [1,46; 3,28] 0,0001[3]	6,0 [3,0; 9,0] 0,0001[3]
Asia	4/203 (2,0)	1/201 (0,5)	3,96 [0,45; 35,13] 0,2165[2]	4,02 [0,45; 36,28] 0,3719[4]	1,5 [-0,7; 3,6] 0,3719[4]
Other	10/402 (2,5)	13/414 (3,1)	0,79 [0,35; 1,79] 0,5743[2]	0,79 [0,34; 1,82] 0,5734[3]	-0,7 [-2,9; 1,6] 0,5734[3]
Primary tumor size (Interaction p-value: 0,2347)					
< 20 mm	23/331 (6,9)	19/335 (5,7)	1,23 [0,68; 2,21] 0,4987[2]	1,24 [0,66; 2,33] 0,4979[3]	1,3 [-2,4; 5,0] 0,4979[3]
≥ 20 but < 50 mm	47/646 (7,3)	25/653 (3,8)	1,90 [1,18; 3,05] 0,0078[2]	1,97 [1,20; 3,24] 0,0066[3]	3,4 [1,0; 5,9] 0,0066[3]
≥ 50 mm	22/289 (7,6)	7/265 (2,6)	2,88 [1,25; 6,64] 0,0129[2]	3,04 [1,28; 7,23] 0,0087[3]	5,0 [1,4; 8,6] 0,0087[3]
Number of positive lymph nodes (Interaction p-value: 0,5236)					
0-3	32/427 (7,5)	14/418 (3,3)	2,24 [1,21; 4,13] 0,0101[2]	2,34 [1,23; 4,45] 0,0079[3]	4,1 [1,1; 7,2] 0,0079[3]
4-9	36/549 (6,6)	19/542 (3,5)	1,87 [1,09; 3,22] 0,0238[2]	1,93 [1,09; 3,41] 0,0212[3]	3,1 [0,5; 5,6] 0,0212[3]
≥ 10	25/307 (8,1)	18/305 (5,9)	1,38 [0,77; 2,48] 0,2805[2]	1,41 [0,75; 2,65] 0,2780[3]	2,2 [-1,8; 6,3] 0,2780[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7923)					
IIA	7/113 (6,2)	2/114 (1,8)	3,53 [0,75; 16,63] 0,1106[2]	3,70 [0,75; 18,20] 0,1016[4]	4,4 [-0,6; 9,5] 0,1016[4]
IIB	9/151 (6,0)	4/136 (2,9)	2,03 [0,64; 6,43] 0,2306[2]	2,09 [0,63; 6,95] 0,2194[3]	3,0 [-1,7; 7,7] 0,2194[3]
IIIA	34/495 (6,9)	16/488 (3,3)	2,09 [1,17; 3,75] 0,0126[2]	2,18 [1,18; 4,00] 0,0104[3]	3,6 [0,9; 6,3] 0,0104[3]
IIIB	3/54 (5,6)	2/45 (4,4)	1,25 [0,22; 7,16] 0,8021[2]	1,26 [0,20; 7,92] 1,0000[4]	1,1 [-7,5; 9,7] 1,0000[4]
IIIC	40/468 (8,5)	27/480 (5,6)	1,52 [0,95; 2,43] 0,0819[2]	1,57 [0,95; 2,60] 0,0792[3]	2,9 [-0,3; 6,2] 0,0792[3]
Tumor grade (Interaction p-value: 0,5210)					
G1	6/91 (6,6)	1/93 (1,1)	6,13 [0,75; 49,93] 0,0901[2]	6,49 [0,77; 55,06] 0,0630[4]	5,5 [0,0; 11,0] 0,0630[4]
G2	47/612 (7,7)	23/603 (3,8)	2,01 [1,24; 3,27] 0,0048[2]	2,10 [1,26; 3,50] 0,0038[3]	3,9 [1,3; 6,5] 0,0038[3]
G3	35/527 (6,6)	23/506 (4,5)	1,46 [0,88; 2,44] 0,1464[2]	1,49 [0,87; 2,57] 0,1435[3]	2,1 [-0,7; 4,9] 0,1435[3]
GX	5/51 (9,8)	4/59 (6,8)	1,45 [0,41; 5,10] 0,5662[2]	1,49 [0,38; 5,89] 0,7306[4]	3,0 [-7,4; 13,4] 0,7306[4]
Race (Interaction p-value: 0,2524)					
White	78/958 (8,1)	43/944 (4,6)	1,79 [1,25; 2,57] 0,0016[2]	1,86 [1,27; 2,73] 0,0014[3]	3,6 [1,4; 5,8] 0,0014[3]
Asian	6/250 (2,4)	1/242 (0,4)	5,81 [0,70; 47,89] 0,1022[2]	5,93 [0,71; 49,59] 0,1227[4]	2,0 [-0,1; 4,0] 0,1227[4]
Other	5/62 (8,1)	6/64 (9,4)	0,86 [0,28; 2,67] 0,7947[2]	0,85 [0,24; 2,94] 0,7945[3]	-1,3 [-11,2; 8,5] 0,7945[3]
First endocrine therapy (Interaction p-value: 0,5208)					
Tamoxifen	4/114 (3,5)	4/132 (3,0)	1,16 [0,30; 4,53] 0,8330[2]	1,16 [0,28; 4,76] 1,0000[4]	0,5 [-4,0; 4,9] 1,0000[4]
Aromatase inhibitor	89/1169 (7,6)	47/1133 (4,1)	1,84 [1,30; 2,59] 0,0005[2]	1,90 [1,32; 2,74] 0,0004[3]	3,5 [1,6; 5,4] 0,0004[3]
ECOG-PS (Interaction p-value: 0,6578)					
ECOG-PS 0	72/1070 (6,7)	36/1020 (3,5)	1,91 [1,29; 2,82] 0,0012[2]	1,97 [1,31; 2,97] 0,0010[3]	3,2 [1,3; 5,1] 0,0010[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	21/213 (9,9)	15/245 (6,1)	1,61 [0,85; 3,04] 0,1424[2]	1,68 [0,84; 3,34] 0,1383[3]	3,7 [-1,3; 8,7] 0,1383[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Epistaxis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9889)					
Neoadjuvant chemotherapy	8/430 (1,9)	1/415 (0,2)	7,72 [0,97; 61,46] 0,0535[2]	7,85 [0,98; 63,03] 0,0383[4]	1,6 [0,3; 3,0] 0,0383[4]
Adjuvant chemotherapy	13/784 (1,7)	2/769 (0,3)	6,38 [1,44; 28,16] 0,0145[2]	6,47 [1,45; 28,75] 0,0049[3]	1,4 [0,4; 2,4] 0,0049[3]
No chemotherapy	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (Interaction p-value: 0,3978)					
North America / Europe	18/678 (2,7)	2/650 (0,3)	8,63 [2,01; 37,04] 0,0037[2]	8,84 [2,04; 38,24] 0,0004[3]	2,3 [1,1; 3,6] 0,0004[3]
Asia	1/203 (0,5)	1/201 (0,5)	0,99 [0,06; 15,72] 0,9944[2]	0,99 [0,06; 15,94] 1,0000[4]	-0,0 [-1,4; 1,4] 1,0000[4]
Other	4/402 (1,0)	0/414 (0,0)	9,27 [0,50; 171,59] 0,1348[2]	9,36 [0,50; 174,44] 0,0585[4]	1,0 [0,0; 2,0] 0,0585[4]
Primary tumor size (Interaction p-value: 0,9937)					
< 20 mm	5/331 (1,5)	0/335 (0,0)	11,13 [0,62; 200,53] 0,1023[2]	11,30 [0,62; 205,23] 0,0299[4]	1,5 [0,2; 2,8] 0,0299[4]
≥ 20 but < 50 mm	11/646 (1,7)	2/653 (0,3)	5,56 [1,24; 24,98] 0,0253[2]	5,64 [1,24; 25,54] 0,0115[3]	1,4 [0,3; 2,5] 0,0115[3]
≥ 50 mm	7/289 (2,4)	1/265 (0,4)	6,42 [0,79; 51,82] 0,0810[2]	6,55 [0,80; 53,62] 0,0704[4]	2,0 [0,1; 4,0] 0,0704[4]
Number of positive lymph nodes (Interaction p-value: 0,6671)					
0-3	12/427 (2,8)	1/418 (0,2)	11,75 [1,53; 89,94] 0,0177[2]	12,06 [1,56; 93,15] 0,0024[3]	2,6 [0,9; 4,2] 0,0024[3]
4-9	8/549 (1,5)	1/542 (0,2)	7,90 [0,99; 62,93] 0,0510[2]	8,00 [1,00; 64,18] 0,0383[4]	1,3 [0,2; 2,3] 0,0383[4]
≥ 10	3/307 (1,0)	1/305 (0,3)	2,98 [0,31; 28,49] 0,3431[2]	3,00 [0,31; 29,00] 0,6238[4]	0,6 [-0,6; 1,9] 0,6238[4]
Tumor grade (Interaction p-value: 0,6201)					
G1	0/91 (0,0)	1/93 (1,1)	0,34 [0,01; 8,25] 0,5078[2]	0,34 [0,01; 8,38] 1,0000[4]	-1,1 [-3,2; 1,0] 1,0000[4]
G2	12/612 (2,0)	1/603 (0,2)	11,82 [1,54; 90,65] 0,0175[2]	12,04 [1,56; 92,88] 0,0024[3]	1,8 [0,6; 2,9] 0,0024[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G3	10/527 (1,9)	0/506 (0,0)	20,16 [1,18; 343,21] 0,0378[2]	20,55 [1,20; 351,68] 0,0019[4]	1,9 [0,7; 3,1] 0,0019[4]
GX	1/51 (2,0)	1/59 (1,7)	1,16 [0,07; 18,03] 0,9172[2]	1,16 [0,07; 19,03] 1,0000[4]	0,3 [-4,8; 5,3] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,2732)					
Negative	4/156 (2,6)	1/169 (0,6)	4,33 [0,49; 38,35] 0,1875[2]	4,42 [0,49; 39,99] 0,1985[4]	2,0 [-0,8; 4,7] 0,1985[4]
Positive	18/1089 (1,7)	2/1067 (0,2)	8,82 [2,05; 37,91] 0,0034[2]	8,95 [2,07; 38,67] 0,0004[3]	1,5 [0,7; 2,3] 0,0004[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,3165)					
White	22/958 (2,3)	2/944 (0,2)	10,84 [2,56; 45,97] 0,0012[2]	11,07 [2,60; 47,21] <,0001[3]	2,1 [1,1; 3,1] <,0001[3]
Asian	1/250 (0,4)	1/242 (0,4)	0,97 [0,06; 15,39] 0,9816[2]	0,97 [0,06; 15,56] 1,0000[4]	-0,0 [-1,1; 1,1] 1,0000[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9729)					
ECOG-PS 0	17/1070 (1,6)	3/1020 (0,3)	5,40 [1,59; 18,38] 0,0069[2]	5,47 [1,60; 18,73] 0,0024[3]	1,3 [0,5; 2,1] 0,0024[3]
ECOG-PS 1	6/213 (2,8)	0/245 (0,0)	14,94 [0,85; 263,72] 0,0648[2]	15,38 [0,86; 274,65] 0,0097[4]	2,8 [0,6; 5,0] 0,0097[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Fatigue from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5699)					
< 65 years	266/918 (29,0)	108/937 (11,5)	2,51 [2,05; 3,08] <,0001[2]	3,13 [2,45; 4,01] <,0001[3]	17,4 [13,9; 21,0] <,0001[3]
≥ 65 years	128/365 (35,1)	41/328 (12,5)	2,81 [2,04; 3,86] <,0001[2]	3,78 [2,56; 5,59] <,0001[3]	22,6 [16,5; 28,6] <,0001[3]
Prior treatment (Interaction p-value: 0,3293)					
Neoadjuvant chemotherapy	121/430 (28,1)	51/415 (12,3)	2,29 [1,70; 3,09] <,0001[2]	2,79 [1,95; 4,01] <,0001[3]	15,9 [10,6; 21,1] <,0001[3]
Adjuvant chemotherapy	248/784 (31,6)	91/769 (11,8)	2,67 [2,15; 3,33] <,0001[2]	3,45 [2,64; 4,50] <,0001[3]	19,8 [15,8; 23,8] <,0001[3]
No chemotherapy	25/69 (36,2)	7/81 (8,6)	4,19 [1,93; 9,09] 0,0003[2]	6,01 [2,40; 15,03] <,0001[3]	27,6 [14,7; 40,5] <,0001[3]
Region (Interaction p-value: 0,1480)					
North America / Europe	283/678 (41,7)	117/650 (18,0)	2,32 [1,92; 2,79] <,0001[2]	3,26 [2,54; 4,20] <,0001[3]	23,7 [19,0; 28,5] <,0001[3]
Asia	36/203 (17,7)	10/201 (5,0)	3,56 [1,82; 6,99] 0,0002[2]	4,12 [1,98; 8,55] <,0001[3]	12,8 [6,7; 18,8] <,0001[3]
Other	75/402 (18,7)	22/414 (5,3)	3,51 [2,23; 5,53] <,0001[2]	4,09 [2,49; 6,72] <,0001[3]	13,3 [9,0; 17,7] <,0001[3]
Primary tumor size (Interaction p-value: 0,5116)					
< 20 mm	99/331 (29,9)	45/335 (13,4)	2,23 [1,62; 3,06] <,0001[2]	2,75 [1,86; 4,07] <,0001[3]	16,5 [10,3; 22,6] <,0001[3]
≥ 20 but < 50 mm	189/646 (29,3)	70/653 (10,7)	2,73 [2,12; 3,51] <,0001[2]	3,44 [2,55; 4,65] <,0001[3]	18,5 [14,3; 22,8] <,0001[3]
≥ 50 mm	106/289 (36,7)	34/265 (12,8)	2,86 [2,02; 4,05] <,0001[2]	3,94 [2,55; 6,06] <,0001[3]	23,8 [17,0; 30,7] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9661)					
0-3	124/427 (29,0)	48/418 (11,5)	2,53 [1,86; 3,43] <,0001[2]	3,15 [2,19; 4,55] <,0001[3]	17,6 [12,3; 22,8] <,0001[3]
4-9	165/549 (30,1)	61/542 (11,3)	2,67 [2,04; 3,49] <,0001[2]	3,39 [2,45; 4,68] <,0001[3]	18,8 [14,1; 23,5] <,0001[3]
≥ 10	105/307 (34,2)	40/305 (13,1)	2,61 [1,88; 3,62] <,0001[2]	3,44 [2,29; 5,18] <,0001[3]	21,1 [14,6; 27,6] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,1648)					
IIA	31/113 (27,4)	15/114 (13,2)	2,08 [1,19; 3,65] 0,0100[2]	2,50 [1,26; 4,94] 0,0075[3]	14,3 [4,0; 24,6] 0,0075[3]
IIB	42/151 (27,8)	13/136 (9,6)	2,91 [1,63; 5,18] 0,0003[2]	3,65 [1,86; 7,15] <,0001[3]	18,3 [9,6; 26,9] <,0001[3]
IIIA	151/495 (30,5)	49/488 (10,0)	3,04 [2,26; 4,09] <,0001[2]	3,93 [2,77; 5,59] <,0001[3]	20,5 [15,6; 25,3] <,0001[3]
IIIB	12/54 (22,2)	9/45 (20,0)	1,11 [0,52; 2,40] 0,7881[2]	1,14 [0,43; 3,02] 0,7877[3]	2,2 [-13,9; 18,3] 0,7877[3]
IIIC	158/468 (33,8)	63/480 (13,1)	2,57 [1,98; 3,35] <,0001[2]	3,37 [2,43; 4,68] <,0001[3]	20,6 [15,4; 25,9] <,0001[3]
Tumor grade (Interaction p-value: 0,9718)					
G1	27/91 (29,7)	10/93 (10,8)	2,76 [1,42; 5,37] 0,0028[2]	3,50 [1,58; 7,76] 0,0014[3]	18,9 [7,6; 30,2] 0,0014[3]
G2	193/612 (31,5)	76/603 (12,6)	2,50 [1,97; 3,18] <,0001[2]	3,19 [2,38; 4,29] <,0001[3]	18,9 [14,4; 23,5] <,0001[3]
G3	161/527 (30,6)	57/506 (11,3)	2,71 [2,06; 3,58] <,0001[2]	3,47 [2,49; 4,83] <,0001[3]	19,3 [14,5; 24,1] <,0001[3]
GX	12/51 (23,5)	5/59 (8,5)	2,78 [1,05; 7,35] 0,0398[2]	3,32 [1,08; 10,20] 0,0294[3]	15,1 [1,4; 28,7] 0,0294[3]
Progesterone receptor status (Interaction p-value: 0,6413)					
Negative	54/156 (34,6)	26/169 (15,4)	2,25 [1,49; 3,40] 0,0001[2]	2,91 [1,71; 4,96] <,0001[3]	19,2 [10,0; 28,5] <,0001[3]
Positive	321/1089 (29,5)	114/1067 (10,7)	2,76 [2,27; 3,36] <,0001[2]	3,49 [2,77; 4,41] <,0001[3]	18,8 [15,5; 22,1] <,0001[3]
Unknown	6/10 (60,0)	2/7 (28,6)	2,10 [0,59; 7,52] 0,2544[2]	3,75 [0,47; 29,75] 0,3348[4]	31,4 [-13,8; 76,6] 0,3348[4]
Race (Interaction p-value: 0,3825)					
White	330/958 (34,4)	127/944 (13,5)	2,56 [2,13; 3,08] <,0001[2]	3,38 [2,69; 4,25] <,0001[3]	21,0 [17,3; 24,7] <,0001[3]
Asian	43/250 (17,2)	10/242 (4,1)	4,16 [2,14; 8,09] <,0001[2]	4,82 [2,36; 9,83] <,0001[3]	13,1 [7,8; 18,4] <,0001[3]
Other	17/62 (27,4)	7/64 (10,9)	2,51 [1,12; 5,62] 0,0258[2]	3,08 [1,17; 8,06] 0,0185[3]	16,5 [3,0; 30,0] 0,0185[3]
First endocrine therapy (Interaction p-value: 0,2998)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	34/114 (29,8)	11/132 (8,3)	3,58 [1,90; 6,73] <,0001[2]	4,68 [2,24; 9,76] <,0001[3]	21,5 [11,9; 31,1] <,0001[3]
Aromatase inhibitor	360/1169 (30,8)	138/1133 (12,2)	2,53 [2,12; 3,02] <,0001[2]	3,21 [2,58; 3,99] <,0001[3]	18,6 [15,4; 21,9] <,0001[3]
ECOG-PS (Interaction p-value: 0,1324)					
ECOG-PS 0	316/1070 (29,5)	123/1020 (12,1)	2,45 [2,03; 2,96] <,0001[2]	3,06 [2,43; 3,85] <,0001[3]	17,5 [14,1; 20,9] <,0001[3]
ECOG-PS 1	78/213 (36,6)	26/245 (10,6)	3,45 [2,30; 5,17] <,0001[2]	4,87 [2,97; 7,97] <,0001[3]	26,0 [18,5; 33,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Flatulence from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1023)					
< 65 years	32/918 (3,5)	4/937 (0,4)	8,17 [2,90; 23,00] <,0001[2]	8,42 [2,97; 23,92] <,0001[3]	3,1 [1,8; 4,3] <,0001[3]
≥ 65 years	10/365 (2,7)	4/328 (1,2)	2,25 [0,71; 7,09] 0,1677[2]	2,28 [0,71; 7,35] 0,1555[3]	1,5 [-0,5; 3,6] 0,1555[3]
Prior treatment (Interaction p-value: 0,7405)					
Neoadjuvant chemotherapy	16/430 (3,7)	2/415 (0,5)	7,72 [1,79; 33,37] 0,0062[2]	7,98 [1,82; 34,93] 0,0011[3]	3,2 [1,3; 5,1] 0,0011[3]
Adjuvant chemotherapy	24/784 (3,1)	6/769 (0,8)	3,92 [1,61; 9,55] 0,0026[2]	4,02 [1,63; 9,88] 0,0011[3]	2,3 [0,9; 3,6] 0,0011[3]
No chemotherapy	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (Interaction p-value: 0,9925)					
North America / Europe	37/678 (5,5)	6/650 (0,9)	5,91 [2,51; 13,91] <,0001[2]	6,20 [2,60; 14,78] <,0001[3]	4,5 [2,7; 6,4] <,0001[3]
Asia	0/203 (0,0)	1/201 (0,5)	0,33 [0,01; 8,05] 0,4965[2]	0,33 [0,01; 8,11] 0,4975[4]	-0,5 [-1,5; 0,5] 0,4975[4]
Other	5/402 (1,2)	1/414 (0,2)	5,15 [0,60; 43,88] 0,1338[2]	5,20 [0,61; 44,72] 0,1185[4]	1,0 [-0,2; 2,2] 0,1185[4]
Primary tumor size (Interaction p-value: 0,7549)					
< 20 mm	9/331 (2,7)	1/335 (0,3)	9,11 [1,16; 71,50] 0,0356[2]	9,34 [1,18; 74,10] 0,0108[4]	2,4 [0,6; 4,3] 0,0108[4]
≥ 20 but < 50 mm	20/646 (3,1)	5/653 (0,8)	4,04 [1,53; 10,71] 0,0049[2]	4,14 [1,54; 11,10] 0,0022[3]	2,3 [0,8; 3,8] 0,0022[3]
≥ 50 mm	13/289 (4,5)	2/265 (0,8)	5,96 [1,36; 26,17] 0,0180[2]	6,19 [1,38; 27,71] 0,0067[3]	3,7 [1,1; 6,4] 0,0067[3]
Number of positive lymph nodes (Interaction p-value: 0,1580)					
0-3	19/427 (4,4)	1/418 (0,2)	18,60 [2,50; 138,31] 0,0043[2]	19,42 [2,59; 145,73] <,0001[3]	4,2 [2,2; 6,2] <,0001[3]
4-9	15/549 (2,7)	3/542 (0,6)	4,94 [1,44; 16,95] 0,0112[2]	5,05 [1,45; 17,53] 0,0047[3]	2,2 [0,7; 3,7] 0,0047[3]
≥ 10	8/307 (2,6)	4/305 (1,3)	1,99 [0,60; 6,53] 0,2580[2]	2,01 [0,60; 6,76] 0,2482[3]	1,3 [-0,9; 3,5] 0,2482[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,5290)					
IIA	3/113 (2,7)	0/114 (0,0)	7,06 [0,37; 135,16] 0,1943[2]	7,25 [0,37; 142,05] 0,1217[4]	2,7 [-0,3; 5,6] 0,1217[4]
IIB	7/151 (4,6)	1/136 (0,7)	6,30 [0,79; 50,59] 0,0831[2]	6,56 [0,80; 54,04] 0,0695[4]	3,9 [0,3; 7,5] 0,0695[4]
IIIA	20/495 (4,0)	2/488 (0,4)	9,86 [2,32; 41,95] 0,0020[2]	10,23 [2,38; 44,01] 0,0001[3]	3,6 [1,8; 5,5] 0,0001[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	10/468 (2,1)	5/480 (1,0)	2,05 [0,71; 5,96] 0,1865[2]	2,07 [0,70; 6,12] 0,1767[3]	1,1 [-0,5; 2,7] 0,1767[3]
Tumor grade (Interaction p-value: 0,6636)					
G1	1/91 (1,1)	0/93 (0,0)	3,07 [0,13; 74,28] 0,4910[2]	3,10 [0,12; 77,08] 0,4946[4]	1,1 [-1,0; 3,2] 0,4946[4]
G2	27/612 (4,4)	3/603 (0,5)	8,87 [2,70; 29,08] 0,0003[2]	9,23 [2,79; 30,59] <,0001[3]	3,9 [2,2; 5,6] <,0001[3]
G3	13/527 (2,5)	4/506 (0,8)	3,12 [1,02; 9,51] 0,0453[2]	3,17 [1,03; 9,80] 0,0343[3]	1,7 [0,1; 3,2] 0,0343[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,9644)					
Negative	2/156 (1,3)	0/169 (0,0)	5,41 [0,26; 111,90] 0,2744[2]	5,49 [0,26; 115,15] 0,2296[4]	1,3 [-0,5; 3,0] 0,2296[4]
Positive	40/1089 (3,7)	8/1067 (0,7)	4,90 [2,30; 10,42] <,0001[2]	5,05 [2,35; 10,84] <,0001[3]	2,9 [1,7; 4,2] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9996)					
White	41/958 (4,3)	6/944 (0,6)	6,73 [2,87; 15,79] <,0001[2]	6,99 [2,95; 16,54] <,0001[3]	3,6 [2,3; 5,0] <,0001[3]
Asian	0/250 (0,0)	1/242 (0,4)	0,32 [0,01; 7,88] 0,4879[2]	0,32 [0,01; 7,93] 0,4919[4]	-0,4 [-1,2; 0,4] 0,4919[4]
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
First endocrine therapy (Interaction p-value: 0,9142)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	4/114 (3,5)	1/132 (0,8)	4,63 [0,53; 40,85] 0,1675[2]	4,76 [0,52; 43,25] 0,1855[4]	2,8 [-0,9; 6,4] 0,1855[4]
Aromatase inhibitor	38/1169 (3,3)	7/1133 (0,6)	5,26 [2,36; 11,73] <,0001[2]	5,40 [2,40; 12,15] <,0001[3]	2,6 [1,5; 3,7] <,0001[3]
ECOG-PS (Interaction p-value: 0,3879)					
ECOG-PS 0	32/1070 (3,0)	7/1020 (0,7)	4,36 [1,93; 9,83] 0,0004[2]	4,46 [1,96; 10,15] <,0001[3]	2,3 [1,2; 3,4] <,0001[3]
ECOG-PS 1	10/213 (4,7)	1/245 (0,4)	11,50 [1,48; 89,12] 0,0194[2]	12,02 [1,53; 94,69] 0,0028[3]	4,3 [1,3; 7,2] 0,0028[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Gamma-glutamyltransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9341)					
< 65 years	30/918 (3,3)	12/937 (1,3)	2,55 [1,31; 4,95] 0,0056[2]	2,60 [1,32; 5,12] 0,0040[3]	2,0 [0,6; 3,3] 0,0040[3]
≥ 65 years	12/365 (3,3)	4/328 (1,2)	2,70 [0,88; 8,28] 0,0831[2]	2,75 [0,88; 8,62] 0,0703[3]	2,1 [-0,1; 4,2] 0,0703[3]
Prior treatment (Interaction p-value: 0,7491)					
Neoadjuvant chemotherapy	13/430 (3,0)	4/415 (1,0)	3,14 [1,03; 9,54] 0,0440[2]	3,20 [1,04; 9,91] 0,0330[3]	2,1 [0,2; 3,9] 0,0330[3]
Adjuvant chemotherapy	25/784 (3,2)	11/769 (1,4)	2,23 [1,10; 4,50] 0,0252[2]	2,27 [1,11; 4,65] 0,0213[3]	1,8 [0,3; 3,2] 0,0213[3]
No chemotherapy	4/69 (5,8)	1/81 (1,2)	4,70 [0,54; 41,03] 0,1620[2]	4,92 [0,54; 45,13] 0,1807[4]	4,6 [-1,5; 10,6] 0,1807[4]
Region (Interaction p-value: 0,6060)					
North America / Europe	16/678 (2,4)	8/650 (1,2)	1,92 [0,83; 4,45] 0,1296[2]	1,94 [0,82; 4,56] 0,1226[3]	1,1 [-0,3; 2,6] 0,1226[3]
Asia	8/203 (3,9)	3/201 (1,5)	2,64 [0,71; 9,81] 0,1471[2]	2,71 [0,71; 10,36] 0,1306[3]	2,4 [-0,7; 5,6] 0,1306[3]
Other	18/402 (4,5)	5/414 (1,2)	3,71 [1,39; 9,89] 0,0089[2]	3,83 [1,41; 10,43] 0,0048[3]	3,3 [1,0; 5,5] 0,0048[3]
Primary tumor size (Interaction p-value: 0,9625)					
< 20 mm	7/331 (2,1)	3/335 (0,9)	2,36 [0,62; 9,05] 0,2101[2]	2,39 [0,61; 9,33] 0,2206[4]	1,2 [-0,6; 3,1] 0,2206[4]
≥ 20 but < 50 mm	26/646 (4,0)	10/653 (1,5)	2,63 [1,28; 5,41] 0,0086[2]	2,70 [1,29; 5,64] 0,0062[3]	2,5 [0,7; 4,3] 0,0062[3]
≥ 50 mm	7/289 (2,4)	3/265 (1,1)	2,14 [0,56; 8,19] 0,2667[2]	2,17 [0,55; 8,47] 0,3440[4]	1,3 [-0,9; 3,5] 0,3440[4]
Number of positive lymph nodes (Interaction p-value: 0,7644)					
0-3	12/427 (2,8)	4/418 (1,0)	2,94 [0,95; 9,03] 0,0602[2]	2,99 [0,96; 9,36] 0,0481[3]	1,9 [0,0; 3,7] 0,0481[3]
4-9	16/549 (2,9)	5/542 (0,9)	3,16 [1,17; 8,56] 0,0238[2]	3,22 [1,17; 8,86] 0,0167[3]	2,0 [0,4; 3,6] 0,0167[3]
≥ 10	14/307 (4,6)	7/305 (2,3)	1,99 [0,81; 4,85] 0,1320[2]	2,03 [0,81; 5,11] 0,1238[3]	2,3 [-0,6; 5,1] 0,1238[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7794)					
IIA	3/113 (2,7)	1/114 (0,9)	3,03 [0,32; 28,66] 0,3343[2]	3,08 [0,32; 30,08] 0,3695[4]	1,8 [-1,6; 5,2] 0,3695[4]
IIB	4/151 (2,6)	3/136 (2,2)	1,20 [0,27; 5,27] 0,8083[2]	1,21 [0,27; 5,49] 1,0000[4]	0,4 [-3,1; 4,0] 1,0000[4]
IIIA	13/495 (2,6)	3/488 (0,6)	4,27 [1,23; 14,90] 0,0227[2]	4,36 [1,23; 15,40] 0,0127[3]	2,0 [0,4; 3,6] 0,0127[3]
IIIB	3/54 (5,6)	0/45 (0,0)	5,85 [0,31; 110,43] 0,2383[2]	6,18 [0,31; 122,97] 0,2486[4]	5,6 [-0,6; 11,7] 0,2486[4]
IIIC	19/468 (4,1)	9/480 (1,9)	2,17 [0,99; 4,74] 0,0531[2]	2,21 [0,99; 4,95] 0,0470[3]	2,2 [0,0; 4,3] 0,0470[3]
Tumor grade (Interaction p-value: 0,7561)					
G1	3/91 (3,3)	0/93 (0,0)	7,15 [0,37; 136,54] 0,1910[2]	7,40 [0,38; 145,22] 0,1189[4]	3,3 [-0,4; 7,0] 0,1189[4]
G2	19/612 (3,1)	7/603 (1,2)	2,67 [1,13; 6,32] 0,0248[2]	2,73 [1,14; 6,54] 0,0192[3]	1,9 [0,3; 3,6] 0,0192[3]
G3	16/527 (3,0)	9/506 (1,8)	1,71 [0,76; 3,83] 0,1943[2]	1,73 [0,76; 3,95] 0,1886[3]	1,3 [-0,6; 3,1] 0,1886[3]
GX	4/51 (7,8)	0/59 (0,0)	10,38 [0,57; 188,36] 0,1135[2]	11,27 [0,59; 214,65] 0,0433[4]	7,8 [0,5; 15,2] 0,0433[4]
Progesterone receptor status (Interaction p-value: 0,9971)					
Negative	6/156 (3,8)	0/169 (0,0)	14,08 [0,80; 247,83] 0,0708[2]	14,64 [0,82; 262,08] 0,0116[4]	3,8 [0,8; 6,9] 0,0116[4]
Positive	35/1089 (3,2)	16/1067 (1,5)	2,14 [1,19; 3,85] 0,0107[2]	2,18 [1,20; 3,97] 0,0088[3]	1,7 [0,4; 3,0] 0,0088[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
Race (Interaction p-value: 0,9865)					
White	31/958 (3,2)	12/944 (1,3)	2,55 [1,32; 4,93] 0,0055[2]	2,60 [1,33; 5,09] 0,0040[3]	2,0 [0,6; 3,3] 0,0040[3]
Asian	8/250 (3,2)	3/242 (1,2)	2,58 [0,69; 9,62] 0,1576[2]	2,63 [0,69; 10,05] 0,1415[3]	2,0 [-0,6; 4,5] 0,1415[3]
Other	3/62 (4,8)	1/64 (1,6)	3,10 [0,33; 28,97] 0,3218[2]	3,20 [0,32; 31,66] 0,3610[4]	3,3 [-2,9; 9,4] 0,3610[4]
ECOG-PS (Interaction p-value: 0,8163)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	34/1070 (3,2)	12/1020 (1,2)	2,70 [1,41; 5,19] 0,0028[2]	2,76 [1,42; 5,35] 0,0018[3]	2,0 [0,8; 3,2] 0,0018[3]
ECOG-PS 1	8/213 (3,8)	4/245 (1,6)	2,30 [0,70; 7,53] 0,1686[2]	2,35 [0,70; 7,92] 0,1559[3]	2,1 [-0,9; 5,1] 0,1559[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Tabl: Subgroups - adverse events according PT Gastrointestinal pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,9699)					
Negative	3/156 (1,9)	0/169 (0,0)	7,58 [0,39; 145,58] 0,1792[2]	7,73 [0,40; 150,85] 0,1095[4]	1,9 [-0,2; 4,1] 0,1095[4]
Positive	13/1089 (1,2)	0/1067 (0,0)	26,46 [1,57; 444,46] 0,0229[2]	26,77 [1,59; 450,96] 0,0003[3]	1,2 [0,5; 1,8] 0,0003[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 1,0000)					
White	16/958 (1,7)	0/944 (0,0)	32,52 [1,95; 541,24] 0,0152[2]	33,07 [1,98; 552,01] <,0001[3]	1,7 [0,9; 2,5] <,0001[3]
Asian	0/250 (0,0)	0/242 (0,0)	NE	NE	NE
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gbac1_bp_aesocpt_sub.sas
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Table: Subgroups - adverse events according PT Gastrooesophageal reflux disease from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,3983)					
< 65 years	28/918 (3,1)	14/937 (1,5)	2,04 [1,08; 3,85] 0,0276[2]	2,07 [1,08; 3,97] 0,0243[3]	1,6 [0,2; 2,9] 0,0243[3]
≥ 65 years	13/365 (3,6)	9/328 (2,7)	1,30 [0,56; 3,00] 0,5412[2]	1,31 [0,55; 3,10] 0,5398[3]	0,8 [-1,8; 3,4] 0,5398[3]
Prior treatment (Interaction p-value: 0,3354)					
Neoadjuvant chemotherapy	15/430 (3,5)	12/415 (2,9)	1,21 [0,57; 2,55] 0,6225[2]	1,21 [0,56; 2,63] 0,6219[3]	0,6 [-1,8; 3,0] 0,6219[3]
Adjuvant chemotherapy	24/784 (3,1)	9/769 (1,2)	2,62 [1,22; 5,59] 0,0131[2]	2,67 [1,23; 5,77] 0,0098[3]	1,9 [0,5; 3,3] 0,0098[3]
No chemotherapy	2/69 (2,9)	2/81 (2,5)	1,17 [0,17; 8,12] 0,8709[2]	1,18 [0,16; 8,60] 1,0000[4]	0,4 [-4,8; 5,6] 1,0000[4]
Region (Interaction p-value: 0,1226)					
North America / Europe	31/678 (4,6)	12/650 (1,8)	2,48 [1,28; 4,78] 0,0069[2]	2,55 [1,30; 5,00] 0,0050[3]	2,7 [0,8; 4,6] 0,0050[3]
Asia	5/203 (2,5)	3/201 (1,5)	1,65 [0,40; 6,81] 0,4887[2]	1,67 [0,39; 7,07] 0,7238[4]	1,0 [-1,7; 3,7] 0,7238[4]
Other	5/402 (1,2)	8/414 (1,9)	0,64 [0,21; 1,95] 0,4361[2]	0,64 [0,21; 1,97] 0,4322[3]	-0,7 [-2,4; 1,0] 0,4322[3]
Primary tumor size (Interaction p-value: 0,3282)					
< 20 mm	12/331 (3,6)	8/335 (2,4)	1,52 [0,63; 3,67] 0,3533[2]	1,54 [0,62; 3,81] 0,3496[3]	1,2 [-1,4; 3,8] 0,3496[3]
≥ 20 but < 50 mm	16/646 (2,5)	12/653 (1,8)	1,35 [0,64; 2,83] 0,4296[2]	1,36 [0,64; 2,89] 0,4277[3]	0,6 [-0,9; 2,2] 0,4277[3]
≥ 50 mm	13/289 (4,5)	3/265 (1,1)	3,97 [1,14; 13,79] 0,0298[2]	4,11 [1,16; 14,60] 0,0181[3]	3,4 [0,7; 6,1] 0,0181[3]
Number of positive lymph nodes (Interaction p-value: 0,1006)					
0-3	13/427 (3,0)	4/418 (1,0)	3,18 [1,05; 9,68] 0,0415[2]	3,25 [1,05; 10,05] 0,0307[3]	2,1 [0,2; 4,0] 0,0307[3]
4-9	19/549 (3,5)	8/542 (1,5)	2,34 [1,04; 5,31] 0,0410[2]	2,39 [1,04; 5,51] 0,0349[3]	2,0 [0,1; 3,8] 0,0349[3]
≥ 10	9/307 (2,9)	11/305 (3,6)	0,81 [0,34; 1,93] 0,6393[2]	0,81 [0,33; 1,98] 0,6387[3]	-0,7 [-3,5; 2,1] 0,6387[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,4008)					
IIA	3/113 (2,7)	0/114 (0,0)	7,06 [0,37; 135,16] 0,1943[2]	7,25 [0,37; 142,05] 0,1217[4]	2,7 [-0,3; 5,6] 0,1217[4]
IIB	4/151 (2,6)	3/136 (2,2)	1,20 [0,27; 5,27] 0,8083[2]	1,21 [0,27; 5,49] 1,0000[4]	0,4 [-3,1; 4,0] 1,0000[4]
IIIA	18/495 (3,6)	5/488 (1,0)	3,55 [1,33; 9,48] 0,0115[2]	3,65 [1,34; 9,90] 0,0068[3]	2,6 [0,7; 4,5] 0,0068[3]
IIIB	2/54 (3,7)	2/45 (4,4)	0,83 [0,12; 5,68] 0,8523[2]	0,83 [0,11; 6,12] 1,0000[4]	-0,7 [-8,6; 7,1] 1,0000[4]
IIIC	14/468 (3,0)	13/480 (2,7)	1,10 [0,52; 2,32] 0,7934[2]	1,11 [0,52; 2,38] 0,7933[3]	0,3 [-1,8; 2,4] 0,7933[3]
Tumor grade (Interaction p-value: 0,6776)					
G1	2/91 (2,2)	3/93 (3,2)	0,68 [0,12; 3,98] 0,6701[2]	0,67 [0,11; 4,13] 1,0000[4]	-1,0 [-5,7; 3,7] 1,0000[4]
G2	25/612 (4,1)	12/603 (2,0)	2,05 [1,04; 4,05] 0,0379[2]	2,10 [1,04; 4,21] 0,0336[3]	2,1 [0,2; 4,0] 0,0336[3]
G3	12/527 (2,3)	6/506 (1,2)	1,92 [0,73; 5,08] 0,1884[2]	1,94 [0,72; 5,21] 0,1803[3]	1,1 [-0,5; 2,7] 0,1803[3]
GX	2/51 (3,9)	2/59 (3,4)	1,16 [0,17; 7,92] 0,8820[2]	1,16 [0,16; 8,57] 1,0000[4]	0,5 [-6,5; 7,6] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,9086)					
Negative	4/156 (2,6)	4/169 (2,4)	1,08 [0,28; 4,26] 0,9087[2]	1,09 [0,27; 4,42] 1,0000[4]	0,2 [-3,2; 3,6] 1,0000[4]
Positive	35/1089 (3,2)	19/1067 (1,8)	1,80 [1,04; 3,13] 0,0361[2]	1,83 [1,04; 3,22] 0,0332[3]	1,4 [0,1; 2,7] 0,0332[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8672)					
White	30/958 (3,1)	19/944 (2,0)	1,56 [0,88; 2,74] 0,1269[2]	1,57 [0,88; 2,82] 0,1236[3]	1,1 [-0,3; 2,5] 0,1236[3]
Asian	7/250 (2,8)	3/242 (1,2)	2,26 [0,59; 8,63] 0,2337[2]	2,29 [0,59; 8,98] 0,3394[4]	1,6 [-0,9; 4,0] 0,3394[4]
Other	2/62 (3,2)	1/64 (1,6)	2,06 [0,19; 22,19] 0,5497[2]	2,10 [0,19; 23,77] 0,6160[4]	1,7 [-3,7; 7,0] 0,6160[4]
First endocrine therapy (Interaction p-value: 0,8107)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	2/114 (1,8)	1/132 (0,8)	2,32 [0,21; 25,21] 0,4906[2]	2,34 [0,21; 26,14] 0,5979[4]	1,0 [-1,8; 3,8] 0,5979[4]
Aromatase inhibitor	39/1169 (3,3)	22/1133 (1,9)	1,72 [1,03; 2,88] 0,0399[2]	1,74 [1,03; 2,96] 0,0373[3]	1,4 [0,1; 2,7] 0,0373[3]
ECOG-PS (Interaction p-value: 0,4624)					
ECOG-PS 0	36/1070 (3,4)	18/1020 (1,8)	1,91 [1,09; 3,34] 0,0237[2]	1,94 [1,09; 3,44] 0,0212[3]	1,6 [0,3; 2,9] 0,0212[3]
ECOG-PS 1	5/213 (2,3)	5/245 (2,0)	1,15 [0,34; 3,92] 0,8229[2]	1,15 [0,33; 4,04] 1,0000[4]	0,3 [-2,4; 3,0] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Haemorrhoids from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5596)					
< 65 years	19/918 (2,1)	9/937 (1,0)	2,15 [0,98; 4,74] 0,0562[2]	2,18 [0,98; 4,84] 0,0501[3]	1,1 [-0,0; 2,2] 0,0501[3]
≥ 65 years	8/365 (2,2)	5/328 (1,5)	1,44 [0,48; 4,35] 0,5204[2]	1,45 [0,47; 4,47] 0,5179[3]	0,7 [-1,3; 2,7] 0,5179[3]
Prior treatment (Interaction p-value: 0,9169)					
Neoadjuvant chemotherapy	8/430 (1,9)	3/415 (0,7)	2,57 [0,69; 9,63] 0,1604[2]	2,60 [0,69; 9,88] 0,1447[3]	1,1 [-0,4; 2,7] 0,1447[3]
Adjuvant chemotherapy	19/784 (2,4)	10/769 (1,3)	1,86 [0,87; 3,98] 0,1080[2]	1,89 [0,87; 4,08] 0,1021[3]	1,1 [-0,2; 2,5] 0,1021[3]
No chemotherapy	0/69 (0,0)	1/81 (1,2)	0,39 [0,02; 9,43] 0,5628[2]	0,39 [0,02; 9,63] 1,0000[4]	-1,2 [-3,6; 1,2] 1,0000[4]
Region (Interaction p-value: 0,7326)					
North America / Europe	19/678 (2,8)	10/650 (1,5)	1,82 [0,85; 3,89] 0,1211[2]	1,85 [0,85; 4,00] 0,1152[3]	1,3 [-0,3; 2,8] 0,1152[3]
Asia	4/203 (2,0)	1/201 (0,5)	3,96 [0,45; 35,13] 0,2165[2]	4,02 [0,45; 36,28] 0,3719[4]	1,5 [-0,7; 3,6] 0,3719[4]
Other	4/402 (1,0)	3/414 (0,7)	1,37 [0,31; 6,10] 0,6767[2]	1,38 [0,31; 6,19] 0,7217[4]	0,3 [-1,0; 1,5] 0,7217[4]
Primary tumor size (Interaction p-value: 0,5100)					
< 20 mm	8/331 (2,4)	2/335 (0,6)	4,05 [0,87; 18,92] 0,0755[2]	4,12 [0,87; 19,57] 0,0621[4]	1,8 [-0,0; 3,7] 0,0621[4]
≥ 20 but < 50 mm	13/646 (2,0)	9/653 (1,4)	1,46 [0,63; 3,39] 0,3788[2]	1,47 [0,62; 3,46] 0,3758[3]	0,6 [-0,8; 2,0] 0,3758[3]
≥ 50 mm	5/289 (1,7)	3/265 (1,1)	1,53 [0,37; 6,33] 0,5587[2]	1,54 [0,36; 6,50] 0,7267[4]	0,6 [-1,4; 2,6] 0,7267[4]
Number of positive lymph nodes (Interaction p-value: 0,5855)					
0-3	9/427 (2,1)	4/418 (1,0)	2,20 [0,68; 7,10] 0,1859[2]	2,23 [0,68; 7,29] 0,1742[3]	1,2 [-0,5; 2,8] 0,1742[3]
4-9	14/549 (2,6)	6/542 (1,1)	2,30 [0,89; 5,95] 0,0848[2]	2,34 [0,89; 6,13] 0,0756[3]	1,4 [-0,1; 3,0] 0,0756[3]
≥ 10	4/307 (1,3)	4/305 (1,3)	0,99 [0,25; 3,94] 0,9926[2]	0,99 [0,25; 4,01] 1,0000[4]	-0,0 [-1,8; 1,8] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8784)					
IIA	4/113 (3,5)	1/114 (0,9)	4,04 [0,46; 35,55] 0,2089[2]	4,15 [0,46; 37,69] 0,2125[4]	2,7 [-1,2; 6,5] 0,2125[4]
IIB	2/151 (1,3)	1/136 (0,7)	1,80 [0,17; 19,64] 0,6293[2]	1,81 [0,16; 20,21] 1,0000[4]	0,6 [-1,7; 2,9] 1,0000[4]
IIIA	13/495 (2,6)	6/488 (1,2)	2,14 [0,82; 5,57] 0,1210[2]	2,17 [0,82; 5,75] 0,1118[3]	1,4 [-0,3; 3,1] 0,1118[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	7/468 (1,5)	6/480 (1,3)	1,20 [0,41; 3,53] 0,7453[2]	1,20 [0,40; 3,60] 0,7450[3]	0,2 [-1,2; 1,7] 0,7450[3]
Tumor grade (Interaction p-value: 0,6993)					
G1	0/91 (0,0)	2/93 (2,2)	0,20 [0,01; 4,20] 0,3032[2]	0,20 [0,01; 4,22] 0,4973[4]	-2,2 [-5,1; 0,8] 0,4973[4]
G2	14/612 (2,3)	9/603 (1,5)	1,53 [0,67; 3,51] 0,3132[2]	1,55 [0,66; 3,60] 0,3093[3]	0,8 [-0,7; 2,3] 0,3093[3]
G3	12/527 (2,3)	3/506 (0,6)	3,84 [1,09; 13,53] 0,0362[2]	3,91 [1,10; 13,93] 0,0237[3]	1,7 [0,2; 3,1] 0,0237[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,2672)					
Negative	5/156 (3,2)	2/169 (1,2)	2,71 [0,53; 13,76] 0,2296[2]	2,76 [0,53; 14,46] 0,2669[4]	2,0 [-1,2; 5,2] 0,2669[4]
Positive	21/1089 (1,9)	12/1067 (1,1)	1,71 [0,85; 3,47] 0,1334[2]	1,73 [0,85; 3,53] 0,1286[3]	0,8 [-0,2; 1,8] 0,1286[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8087)					
White	22/958 (2,3)	12/944 (1,3)	1,81 [0,90; 3,63] 0,0966[2]	1,83 [0,90; 3,71] 0,0916[3]	1,0 [-0,2; 2,2] 0,0916[3]
Asian	4/250 (1,6)	1/242 (0,4)	3,87 [0,44; 34,40] 0,2244[2]	3,92 [0,43; 35,31] 0,3728[4]	1,2 [-0,6; 2,9] 0,3728[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,2066)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	23/1070 (2,1)	9/1020 (0,9)	2,44 [1,13; 5,24] 0,0227[2]	2,47 [1,14; 5,36] 0,0184[3]	1,3 [0,2; 2,3] 0,0184[3]
ECOG-PS 1	4/213 (1,9)	5/245 (2,0)	0,92 [0,25; 3,38] 0,9003[2]	0,92 [0,24; 3,47] 1,0000[4]	-0,2 [-2,7; 2,4] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Headache from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,2661)					
< 65 years	179/918 (19,5)	115/937 (12,3)	1,59 [1,28; 1,97] <,0001[2]	1,73 [1,34; 2,23] <,0001[3]	7,2 [3,9; 10,5] <,0001[3]
≥ 65 years	43/365 (11,8)	32/328 (9,8)	1,21 [0,78; 1,86] 0,3929[2]	1,24 [0,76; 2,00] 0,3917[3]	2,0 [-2,6; 6,6] 0,3917[3]
Prior treatment (Interaction p-value: 0,9698)					
Neoadjuvant chemotherapy	76/430 (17,7)	48/415 (11,6)	1,53 [1,09; 2,14] 0,0132[2]	1,64 [1,11; 2,42] 0,0121[3]	6,1 [1,4; 10,8] 0,0121[3]
Adjuvant chemotherapy	134/784 (17,1)	90/769 (11,7)	1,46 [1,14; 1,87] 0,0028[2]	1,56 [1,17; 2,07] 0,0025[3]	5,4 [1,9; 8,9] 0,0025[3]
No chemotherapy	12/69 (17,4)	9/81 (11,1)	1,57 [0,70; 3,49] 0,2738[2]	1,68 [0,66; 4,28] 0,2692[3]	6,3 [-5,0; 17,5] 0,2692[3]
Region (Interaction p-value: 0,6320)					
North America / Europe	136/678 (20,1)	94/650 (14,5)	1,39 [1,09; 1,76] 0,0075[2]	1,48 [1,11; 1,98] 0,0070[3]	5,6 [1,5; 9,6] 0,0070[3]
Asia	30/203 (14,8)	20/201 (10,0)	1,49 [0,87; 2,53] 0,1444[2]	1,57 [0,86; 2,87] 0,1406[3]	4,8 [-1,6; 11,2] 0,1406[3]
Other	56/402 (13,9)	33/414 (8,0)	1,75 [1,16; 2,63] 0,0073[2]	1,87 [1,19; 2,94] 0,0063[3]	6,0 [1,7; 10,2] 0,0063[3]
Primary tumor size (Interaction p-value: 0,5729)					
< 20 mm	50/331 (15,1)	38/335 (11,3)	1,33 [0,90; 1,97] 0,1537[2]	1,39 [0,88; 2,19] 0,1517[3]	3,8 [-1,4; 8,9] 0,1517[3]
≥ 20 but < 50 mm	117/646 (18,1)	73/653 (11,2)	1,62 [1,24; 2,13] 0,0005[2]	1,76 [1,28; 2,41] 0,0004[3]	6,9 [3,1; 10,8] 0,0004[3]
≥ 50 mm	51/289 (17,6)	36/265 (13,6)	1,30 [0,88; 1,92] 0,1917[2]	1,36 [0,86; 2,17] 0,1893[3]	4,1 [-2,0; 10,1] 0,1893[3]
Number of positive lymph nodes (Interaction p-value: 0,8346)					
0-3	87/427 (20,4)	56/418 (13,4)	1,52 [1,12; 2,07] 0,0075[2]	1,65 [1,15; 2,39] 0,0068[3]	7,0 [2,0; 12,0] 0,0068[3]
4-9	86/549 (15,7)	61/542 (11,3)	1,39 [1,03; 1,89] 0,0341[2]	1,46 [1,03; 2,08] 0,0329[3]	4,4 [0,4; 8,5] 0,0329[3]
≥ 10	49/307 (16,0)	30/305 (9,8)	1,62 [1,06; 2,48] 0,0259[2]	1,74 [1,07; 2,83] 0,0239[3]	6,1 [0,8; 11,4] 0,0239[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9185)					
IIA	21/113 (18,6)	14/114 (12,3)	1,51 [0,81; 2,82] 0,1933[2]	1,63 [0,78; 3,39] 0,1885[3]	6,3 [-3,1; 15,7] 0,1885[3]
IIB	32/151 (21,2)	22/136 (16,2)	1,31 [0,80; 2,14] 0,2809[2]	1,39 [0,76; 2,54] 0,2777[3]	5,0 [-4,0; 14,0] 0,2777[3]
IIIA	85/495 (17,2)	51/488 (10,5)	1,64 [1,19; 2,27] 0,0027[2]	1,78 [1,22; 2,58] 0,0023[3]	6,7 [2,4; 11,0] 0,0023[3]
IIIB	7/54 (13,0)	5/45 (11,1)	1,17 [0,40; 3,43] 0,7791[2]	1,19 [0,35; 4,05] 0,7786[3]	1,9 [-11,0; 14,7] 0,7786[3]
IIIC	75/468 (16,0)	55/480 (11,5)	1,40 [1,01; 1,93] 0,0423[2]	1,47 [1,01; 2,14] 0,0410[3]	4,6 [0,2; 8,9] 0,0410[3]
Tumor grade (Interaction p-value: 0,2567)					
G1	13/91 (14,3)	5/93 (5,4)	2,66 [0,99; 7,15] 0,0530[2]	2,93 [1,00; 8,60] 0,0420[3]	8,9 [0,4; 17,4] 0,0420[3]
G2	115/612 (18,8)	83/603 (13,8)	1,37 [1,05; 1,77] 0,0185[2]	1,45 [1,07; 1,97] 0,0177[3]	5,0 [0,9; 9,2] 0,0177[3]
G3	84/527 (15,9)	56/506 (11,1)	1,44 [1,05; 1,97] 0,0234[2]	1,52 [1,06; 2,19] 0,0222[3]	4,9 [0,7; 9,0] 0,0222[3]
GX	10/51 (19,6)	3/59 (5,1)	3,86 [1,12; 13,25] 0,0321[2]	4,55 [1,18; 17,59] 0,0186[3]	14,5 [2,3; 26,8] 0,0186[3]
Race (Interaction p-value: 0,9915)					
White	174/958 (18,2)	115/944 (12,2)	1,49 [1,20; 1,85] 0,0003[2]	1,60 [1,24; 2,06] 0,0003[3]	6,0 [2,8; 9,2] 0,0003[3]
Asian	32/250 (12,8)	20/242 (8,3)	1,55 [0,91; 2,63] 0,1057[2]	1,63 [0,90; 2,94] 0,1019[3]	4,5 [-0,9; 9,9] 0,1019[3]
Other	13/62 (21,0)	9/64 (14,1)	1,49 [0,69; 3,24] 0,3123[2]	1,62 [0,64; 4,12] 0,3074[3]	6,9 [-6,3; 20,1] 0,3074[3]
First endocrine therapy (Interaction p-value: 0,9465)					
Tamoxifen	21/114 (18,4)	16/132 (12,1)	1,52 [0,83; 2,77] 0,1717[2]	1,64 [0,81; 3,31] 0,1681[3]	6,3 [-2,7; 15,3] 0,1681[3]
Aromatase inhibitor	201/1169 (17,2)	131/1133 (11,6)	1,49 [1,21; 1,82] 0,0001[2]	1,59 [1,25; 2,01] 0,0001[3]	5,6 [2,8; 8,5] 0,0001[3]
ECOG-PS (Interaction p-value: 0,6451)					
ECOG-PS 0	189/1070 (17,7)	124/1020 (12,2)	1,45 [1,18; 1,79] 0,0005[2]	1,55 [1,21; 1,98] 0,0004[3]	5,5 [2,5; 8,5] 0,0004[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	33/213 (15,5)	23/245 (9,4)	1,65 [1,00; 2,72] 0,0494[2]	1,77 [1,00; 3,12] 0,0467[3]	6,1 [0,0; 12,2] 0,0467[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Hot flush from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,3646)					
< 65 years	116/918 (12,6)	170/937 (18,1)	0,70 [0,56; 0,87] 0,0011[2]	0,65 [0,51; 0,84] 0,0010[3]	-5,5 [-8,8; -2,2] 0,0010[3]
≥ 65 years	27/365 (7,4)	44/328 (13,4)	0,55 [0,35; 0,87] 0,0104[2]	0,52 [0,31; 0,85] 0,0091[3]	-6,0 [-10,6; -1,5] 0,0091[3]
Prior treatment (Interaction p-value: 0,2670)					
Neoadjuvant chemotherapy	52/430 (12,1)	66/415 (15,9)	0,76 [0,54; 1,07] 0,1116[2]	0,73 [0,49; 1,08] 0,1101[3]	-3,8 [-8,5; 0,9] 0,1101[3]
Adjuvant chemotherapy	87/784 (11,1)	133/769 (17,3)	0,64 [0,50; 0,82] 0,0005[2]	0,60 [0,45; 0,80] 0,0005[3]	-6,2 [-9,7; -2,7] 0,0005[3]
No chemotherapy	4/69 (5,8)	15/81 (18,5)	0,31 [0,11; 0,90] 0,0310[2]	0,27 [0,09; 0,86] 0,0196[3]	-12,7 [-22,8; -2,6] 0,0196[3]
Region (Interaction p-value: 0,2477)					
North America / Europe	114/678 (16,8)	154/650 (23,7)	0,71 [0,57; 0,88] 0,0019[2]	0,65 [0,50; 0,85] 0,0018[3]	-6,9 [-11,2; -2,6] 0,0018[3]
Asia	9/203 (4,4)	23/201 (11,4)	0,39 [0,18; 0,82] 0,0127[2]	0,36 [0,16; 0,80] 0,0091[3]	-7,0 [-12,2; -1,8] 0,0091[3]
Other	20/402 (5,0)	37/414 (8,9)	0,56 [0,33; 0,94] 0,0292[2]	0,53 [0,30; 0,94] 0,0264[3]	-4,0 [-7,4; -0,5] 0,0264[3]
Primary tumor size (Interaction p-value: 0,8597)					
< 20 mm	39/331 (11,8)	55/335 (16,4)	0,72 [0,49; 1,05] 0,0880[2]	0,68 [0,44; 1,06] 0,0858[3]	-4,6 [-9,9; 0,6] 0,0858[3]
≥ 20 but < 50 mm	67/646 (10,4)	102/653 (15,6)	0,66 [0,50; 0,89] 0,0054[2]	0,63 [0,45; 0,87] 0,0049[3]	-5,2 [-8,9; -1,6] 0,0049[3]
≥ 50 mm	37/289 (12,8)	55/265 (20,8)	0,62 [0,42; 0,90] 0,0132[2]	0,56 [0,36; 0,88] 0,0120[3]	-8,0 [-14,2; -1,7] 0,0120[3]
Number of positive lymph nodes (Interaction p-value: 0,7879)					
0-3	56/427 (13,1)	90/418 (21,5)	0,61 [0,45; 0,83] 0,0014[2]	0,55 [0,38; 0,79] 0,0012[3]	-8,4 [-13,5; -3,3] 0,0012[3]
4-9	59/549 (10,7)	82/542 (15,1)	0,71 [0,52; 0,97] 0,0321[2]	0,68 [0,47; 0,97] 0,0310[3]	-4,4 [-8,4; -0,4] 0,0310[3]
≥ 10	28/307 (9,1)	42/305 (13,8)	0,66 [0,42; 1,04] 0,0735[2]	0,63 [0,38; 1,04] 0,0707[3]	-4,6 [-9,7; 0,4] 0,0707[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,6090)					
IIA	13/113 (11,5)	23/114 (20,2)	0,57 [0,30; 1,07] 0,0797[2]	0,51 [0,25; 1,07] 0,0738[3]	-8,7 [-18,1; 0,8] 0,0738[3]
IIB	21/151 (13,9)	26/136 (19,1)	0,73 [0,43; 1,23] 0,2360[2]	0,68 [0,36; 1,28] 0,2337[3]	-5,2 [-13,8; 3,4] 0,2337[3]
IIIA	51/495 (10,3)	80/488 (16,4)	0,63 [0,45; 0,87] 0,0055[2]	0,59 [0,40; 0,85] 0,0050[3]	-6,1 [-10,3; -1,9] 0,0050[3]
IIIB	2/54 (3,7)	7/45 (15,6)	0,24 [0,05; 1,09] 0,0644[2]	0,21 [0,04; 1,06] 0,0749[4]	-11,9 [-23,6; -0,1] 0,0749[4]
IIIC	56/468 (12,0)	77/480 (16,0)	0,75 [0,54; 1,03] 0,0724[2]	0,71 [0,49; 1,03] 0,0708[3]	-4,1 [-8,5; 0,3] 0,0708[3]
Tumor grade (Interaction p-value: 0,7045)					
G1	5/91 (5,5)	12/93 (12,9)	0,43 [0,16; 1,16] 0,0951[2]	0,39 [0,13; 1,16] 0,0827[3]	-7,4 [-15,7; 0,9] 0,0827[3]
G2	70/612 (11,4)	98/603 (16,3)	0,70 [0,53; 0,94] 0,0158[2]	0,67 [0,48; 0,93] 0,0151[3]	-4,8 [-8,7; -0,9] 0,0151[3]
G3	66/527 (12,5)	98/506 (19,4)	0,65 [0,49; 0,86] 0,0029[2]	0,60 [0,42; 0,84] 0,0026[3]	-6,8 [-11,3; -2,4] 0,0026[3]
GX	2/51 (3,9)	6/59 (10,2)	0,39 [0,08; 1,83] 0,2300[2]	0,36 [0,07; 1,87] 0,2815[4]	-6,2 [-15,6; 3,1] 0,2815[4]
Race (Interaction p-value: 0,6711)					
White	117/958 (12,2)	172/944 (18,2)	0,67 [0,54; 0,83] 0,0003[2]	0,62 [0,48; 0,81] 0,0003[3]	-6,0 [-9,2; -2,8] 0,0003[3]
Asian	14/250 (5,6)	27/242 (11,2)	0,50 [0,27; 0,93] 0,0295[2]	0,47 [0,24; 0,92] 0,0258[3]	-5,6 [-10,4; -0,7] 0,0258[3]
Other	9/62 (14,5)	13/64 (20,3)	0,71 [0,33; 1,55] 0,3954[2]	0,67 [0,26; 1,69] 0,3915[3]	-5,8 [-19,0; 7,4] 0,3915[3]
First endocrine therapy (Interaction p-value: 0,2847)					
Tamoxifen	12/114 (10,5)	29/132 (22,0)	0,48 [0,26; 0,89] 0,0209[2]	0,42 [0,20; 0,86] 0,0163[3]	-11,4 [-20,5; -2,4] 0,0163[3]
Aromatase inhibitor	131/1169 (11,2)	185/1133 (16,3)	0,69 [0,56; 0,85] 0,0004[2]	0,65 [0,51; 0,82] 0,0004[3]	-5,1 [-7,9; -2,3] 0,0004[3]
ECOG-PS (Interaction p-value: 0,9781)					
ECOG-PS 0	117/1070 (10,9)	169/1020 (16,6)	0,66 [0,53; 0,82] 0,0002[2]	0,62 [0,48; 0,80] 0,0002[3]	-5,6 [-8,6; -2,7] 0,0002[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	26/213 (12,2)	45/245 (18,4)	0,66 [0,43; 1,04] 0,0729[2]	0,62 [0,37; 1,04] 0,0692[3]	-6,2 [-12,7; 0,4] 0,0692[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Hypokalaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8384)					
< 65 years	36/918 (3,9)	11/937 (1,2)	3,34 [1,71; 6,52] 0,0004[2]	3,44 [1,74; 6,79] 0,0002[3]	2,7 [1,3; 4,2] 0,0002[3]
≥ 65 years	21/365 (5,8)	5/328 (1,5)	3,77 [1,44; 9,90] 0,0069[2]	3,94 [1,47; 10,58] 0,0034[3]	4,2 [1,5; 7,0] 0,0034[3]
Prior treatment (Interaction p-value: 0,6420)					
Neoadjuvant chemotherapy	17/430 (4,0)	7/415 (1,7)	2,34 [0,98; 5,59] 0,0549[2]	2,40 [0,98; 5,85] 0,0474[3]	2,3 [0,0; 4,5] 0,0474[3]
Adjuvant chemotherapy	37/784 (4,7)	9/769 (1,2)	4,03 [1,96; 8,30] 0,0002[2]	4,18 [2,00; 8,73] <,0001[3]	3,5 [1,9; 5,2] <,0001[3]
No chemotherapy	3/69 (4,3)	0/81 (0,0)	8,20 [0,43; 156,04] 0,1615[2]	8,58 [0,44; 169,04] 0,0950[4]	4,3 [-0,5; 9,2] 0,0950[4]
Region (Interaction p-value: 0,9637)					
North America / Europe	36/678 (5,3)	10/650 (1,5)	3,45 [1,73; 6,90] 0,0005[2]	3,59 [1,77; 7,29] 0,0002[3]	3,8 [1,8; 5,7] 0,0002[3]
Asia	12/203 (5,9)	3/201 (1,5)	3,96 [1,13; 13,82] 0,0309[2]	4,15 [1,15; 14,92] 0,0188[3]	4,4 [0,8; 8,1] 0,0188[3]
Other	9/402 (2,2)	3/414 (0,7)	3,09 [0,84; 11,33] 0,0889[2]	3,14 [0,84; 11,67] 0,0724[3]	1,5 [-0,1; 3,2] 0,0724[3]
Primary tumor size (Interaction p-value: 0,8428)					
< 20 mm	20/331 (6,0)	7/335 (2,1)	2,89 [1,24; 6,75] 0,0140[2]	3,01 [1,26; 7,23] 0,0097[3]	4,0 [1,0; 6,9] 0,0097[3]
≥ 20 but < 50 mm	21/646 (3,3)	5/653 (0,8)	4,25 [1,61; 11,19] 0,0035[2]	4,35 [1,63; 11,62] 0,0014[3]	2,5 [1,0; 4,0] 0,0014[3]
≥ 50 mm	15/289 (5,2)	4/265 (1,5)	3,44 [1,16; 10,23] 0,0264[2]	3,57 [1,17; 10,90] 0,0174[3]	3,7 [0,7; 6,6] 0,0174[3]
Number of positive lymph nodes (Interaction p-value: 0,9112)					
0-3	19/427 (4,4)	6/418 (1,4)	3,10 [1,25; 7,68] 0,0146[2]	3,20 [1,26; 8,09] 0,0097[3]	3,0 [0,8; 5,3] 0,0097[3]
4-9	21/549 (3,8)	6/542 (1,1)	3,46 [1,41; 8,49] 0,0069[2]	3,55 [1,42; 8,87] 0,0039[3]	2,7 [0,9; 4,5] 0,0039[3]
≥ 10	17/307 (5,5)	4/305 (1,3)	4,22 [1,44; 12,40] 0,0088[2]	4,41 [1,47; 13,27] 0,0041[3]	4,2 [1,4; 7,1] 0,0041[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,2335)					
IIA	10/113 (8,8)	2/114 (1,8)	5,04 [1,13; 22,51] 0,0340[2]	5,44 [1,16; 25,40] 0,0169[3]	7,1 [1,3; 12,9] 0,0169[3]
IIB	2/151 (1,3)	0/136 (0,0)	4,51 [0,22; 93,05] 0,3297[2]	4,57 [0,22; 95,94] 0,4996[4]	1,3 [-0,5; 3,1] 0,4996[4]
IIIA	20/495 (4,0)	6/488 (1,2)	3,29 [1,33; 8,11] 0,0099[2]	3,38 [1,35; 8,50] 0,0060[3]	2,8 [0,8; 4,8] 0,0060[3]
IIIB	1/54 (1,9)	3/45 (6,7)	0,28 [0,03; 2,58] 0,2599[2]	0,26 [0,03; 2,63] 0,3271[4]	-4,8 [-12,9; 3,3] 0,3271[4]
IIIC	23/468 (4,9)	5/480 (1,0)	4,72 [1,81; 12,31] 0,0015[2]	4,91 [1,85; 13,03] 0,0004[3]	3,9 [1,7; 6,0] 0,0004[3]
Tumor grade (Interaction p-value: 0,8408)					
G1	6/91 (6,6)	1/93 (1,1)	6,13 [0,75; 49,93] 0,0901[2]	6,49 [0,77; 55,06] 0,0630[4]	5,5 [0,0; 11,0] 0,0630[4]
G2	23/612 (3,8)	9/603 (1,5)	2,52 [1,17; 5,40] 0,0176[2]	2,58 [1,18; 5,62] 0,0137[3]	2,3 [0,5; 4,1] 0,0137[3]
G3	23/527 (4,4)	6/506 (1,2)	3,68 [1,51; 8,96] 0,0041[2]	3,80 [1,54; 9,42] 0,0020[3]	3,2 [1,2; 5,2] 0,0020[3]
GX	5/51 (9,8)	0/59 (0,0)	12,69 [0,72; 224,11] 0,0828[2]	14,08 [0,76; 261,07] 0,0192[4]	9,8 [1,6; 18,0] 0,0192[4]
Progesterone receptor status (Interaction p-value: 0,1698)					
Negative	6/156 (3,8)	2/169 (1,2)	3,25 [0,67; 15,86] 0,1451[2]	3,34 [0,66; 16,80] 0,1598[4]	2,7 [-0,8; 6,1] 0,1598[4]
Positive	50/1089 (4,6)	14/1067 (1,3)	3,50 [1,95; 6,29] <,0001[2]	3,62 [1,99; 6,59] <,0001[3]	3,3 [1,9; 4,7] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8956)					
White	39/958 (4,1)	11/944 (1,2)	3,49 [1,80; 6,78] 0,0002[2]	3,60 [1,83; 7,07] <,0001[3]	2,9 [1,5; 4,3] <,0001[3]
Asian	13/250 (5,2)	3/242 (1,2)	4,19 [1,21; 14,54] 0,0238[2]	4,37 [1,23; 15,53] 0,0133[3]	4,0 [0,9; 7,0] 0,0133[3]
Other	5/62 (8,1)	2/64 (3,1)	2,58 [0,52; 12,81] 0,2462[2]	2,72 [0,51; 14,57] 0,2693[4]	4,9 [-3,1; 12,9] 0,2693[4]
First endocrine therapy (Interaction p-value: 0,7323)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	2/114 (1,8)	1/132 (0,8)	2,32 [0,21; 25,21] 0,4906[2]	2,34 [0,21; 26,14] 0,5979[4]	1,0 [-1,8; 3,8] 0,5979[4]
Aromatase inhibitor	55/1169 (4,7)	15/1133 (1,3)	3,55 [2,02; 6,25] <,0001[2]	3,68 [2,07; 6,55] <,0001[3]	3,4 [2,0; 4,8] <,0001[3]
ECOG-PS (Interaction p-value: 0,9570)					
ECOG-PS 0	45/1070 (4,2)	12/1020 (1,2)	3,57 [1,90; 6,72] <,0001[2]	3,69 [1,94; 7,01] <,0001[3]	3,0 [1,7; 4,4] <,0001[3]
ECOG-PS 1	12/213 (5,6)	4/245 (1,6)	3,45 [1,13; 10,54] 0,0297[2]	3,60 [1,14; 11,33] 0,0200[3]	4,0 [0,5; 7,5] 0,0200[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Tabl: Subgroups - adverse events according PT Hyponatraemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,3720)					
Neoadjuvant chemotherapy	4/430 (0,9)	4/415 (1,0)	0,97 [0,24; 3,83] 0,9598[2]	0,96 [0,24; 3,88] 1,0000[4]	-0,0 [-1,3; 1,3] 1,0000[4]
Adjuvant chemotherapy	14/784 (1,8)	4/769 (0,5)	3,43 [1,14; 10,38] 0,0289[2]	3,48 [1,14; 10,61] 0,0198[3]	1,3 [0,2; 2,3] 0,0198[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,9048)					
North America / Europe	11/678 (1,6)	4/650 (0,6)	2,64 [0,84; 8,24] 0,0954[2]	2,66 [0,84; 8,41] 0,0826[3]	1,0 [-0,1; 2,1] 0,0826[3]
Asia	1/203 (0,5)	0/201 (0,0)	2,97 [0,12; 72,49] 0,5042[2]	2,99 [0,12; 73,71] 1,0000[4]	0,5 [-0,5; 1,5] 1,0000[4]
Other	7/402 (1,7)	4/414 (1,0)	1,80 [0,53; 6,11] 0,3443[2]	1,82 [0,53; 6,25] 0,3371[3]	0,8 [-0,8; 2,4] 0,3371[3]
Primary tumor size (Interaction p-value: 0,6007)					
< 20 mm	4/331 (1,2)	1/335 (0,3)	4,05 [0,45; 36,03] 0,2100[2]	4,09 [0,45; 36,75] 0,2145[4]	0,9 [-0,4; 2,2] 0,2145[4]
≥ 20 but < 50 mm	10/646 (1,5)	6/653 (0,9)	1,68 [0,62; 4,61] 0,3096[2]	1,70 [0,61; 4,69] 0,3040[3]	0,6 [-0,6; 1,8] 0,3040[3]
≥ 50 mm	5/289 (1,7)	1/265 (0,4)	4,58 [0,54; 38,99] 0,1632[2]	4,65 [0,54; 40,04] 0,2189[4]	1,4 [-0,3; 3,0] 0,2189[4]
Number of positive lymph nodes (Interaction p-value: 0,3719)					
0-3	6/427 (1,4)	4/418 (1,0)	1,47 [0,42; 5,17] 0,5495[2]	1,48 [0,41; 5,27] 0,7526[4]	0,4 [-1,0; 1,9] 0,7526[4]
4-9	8/549 (1,5)	1/542 (0,2)	7,90 [0,99; 62,93] 0,0510[2]	8,00 [1,00; 64,18] 0,0383[4]	1,3 [0,2; 2,3] 0,0383[4]
≥ 10	5/307 (1,6)	3/305 (1,0)	1,66 [0,40; 6,87] 0,4872[2]	1,67 [0,39; 7,04] 0,7248[4]	0,6 [-1,2; 2,4] 0,7248[4]
Tumor stage (Interaction p-value: 0,4081)					
IIA	0/113 (0,0)	0/114 (0,0)	NE	NE	NE
IIB	3/151 (2,0)	3/136 (2,2)	0,90 [0,18; 4,39] 0,8970[2]	0,90 [0,18; 4,53] 1,0000[4]	-0,2 [-3,5; 3,1] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	7/495 (1,4)	2/488 (0,4)	3,45 [0,72; 16,53] 0,1212[2]	3,49 [0,72; 16,86] 0,1778[4]	1,0 [-0,2; 2,2] 0,1778[4]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	9/468 (1,9)	3/480 (0,6)	3,08 [0,84; 11,29] 0,0903[2]	3,12 [0,84; 11,59] 0,0739[3]	1,3 [-0,1; 2,7] 0,0739[3]
Tumor grade (Interaction p-value: 0,4813)					
G1	1/91 (1,1)	0/93 (0,0)	3,07 [0,13; 74,28] 0,4910[2]	3,10 [0,12; 77,08] 0,4946[4]	1,1 [-1,0; 3,2] 0,4946[4]
G2	12/612 (2,0)	3/603 (0,5)	3,94 [1,12; 13,90] 0,0329[2]	4,00 [1,12; 14,25] 0,0209[3]	1,5 [0,2; 2,7] 0,0209[3]
G3	5/527 (0,9)	5/506 (1,0)	0,96 [0,28; 3,30] 0,9485[2]	0,96 [0,28; 3,34] 1,0000[4]	-0,0 [-1,2; 1,2] 1,0000[4]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,9644)					
Negative	2/156 (1,3)	0/169 (0,0)	5,41 [0,26; 111,90] 0,2744[2]	5,49 [0,26; 115,15] 0,2296[4]	1,3 [-0,5; 3,0] 0,2296[4]
Positive	17/1089 (1,6)	8/1067 (0,7)	2,08 [0,90; 4,80] 0,0856[2]	2,10 [0,90; 4,89] 0,0785[3]	0,8 [-0,1; 1,7] 0,0785[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,6303)					
White	17/958 (1,8)	6/944 (0,6)	2,79 [1,11; 7,05] 0,0298[2]	2,82 [1,11; 7,19] 0,0231[3]	1,1 [0,2; 2,1] 0,0231[3]
Asian	2/250 (0,8)	2/242 (0,8)	0,97 [0,14; 6,82] 0,9739[2]	0,97 [0,14; 6,93] 1,0000[4]	-0,0 [-1,6; 1,6] 1,0000[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,2067)					
ECOG-PS 0	15/1070 (1,4)	4/1020 (0,4)	3,57 [1,19; 10,73] 0,0232[2]	3,61 [1,19; 10,92] 0,0151[3]	1,0 [0,2; 1,8] 0,0151[3]
ECOG-PS 1	4/213 (1,9)	4/245 (1,6)	1,15 [0,29; 4,54] 0,8417[2]	1,15 [0,28; 4,67] 1,0000[4]	0,2 [-2,2; 2,7] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Hypotension from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9063)					
< 65 years	13/918 (1,4)	4/937 (0,4)	3,32 [1,09; 10,14] 0,0354[2]	3,35 [1,09; 10,31] 0,0254[3]	1,0 [0,1; 1,9] 0,0254[3]
≥ 65 years	10/365 (2,7)	3/328 (0,9)	3,00 [0,83; 10,79] 0,0934[2]	3,05 [0,83; 11,19] 0,0770[3]	1,8 [-0,1; 3,8] 0,0770[3]
Prior treatment (Interaction p-value: 0,9365)					
Neoadjuvant chemotherapy	8/430 (1,9)	2/415 (0,5)	3,86 [0,82; 18,07] 0,0863[2]	3,91 [0,83; 18,54] 0,1078[4]	1,4 [-0,1; 2,8] 0,1078[4]
Adjuvant chemotherapy	14/784 (1,8)	5/769 (0,7)	2,75 [0,99; 7,59] 0,0514[2]	2,78 [1,00; 7,75] 0,0418[3]	1,1 [0,0; 2,2] 0,0418[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,2009)					
North America / Europe	19/678 (2,8)	4/650 (0,6)	4,55 [1,56; 13,31] 0,0056[2]	4,66 [1,58; 13,76] 0,0023[3]	2,2 [0,8; 3,6] 0,0023[3]
Asia	0/203 (0,0)	0/201 (0,0)	NE	NE	NE
Other	4/402 (1,0)	3/414 (0,7)	1,37 [0,31; 6,10] 0,6767[2]	1,38 [0,31; 6,19] 0,7217[4]	0,3 [-1,0; 1,5] 0,7217[4]
Primary tumor size (Interaction p-value: 0,5031)					
< 20 mm	8/331 (2,4)	1/335 (0,3)	8,10 [1,02; 64,38] 0,0480[2]	8,27 [1,03; 66,51] 0,0200[4]	2,1 [0,4; 3,9] 0,0200[4]
≥ 20 but < 50 mm	8/646 (1,2)	3/653 (0,5)	2,70 [0,72; 10,12] 0,1417[2]	2,72 [0,72; 10,29] 0,1255[3]	0,8 [-0,2; 1,8] 0,1255[3]
≥ 50 mm	6/289 (2,1)	3/265 (1,1)	1,83 [0,46; 7,26] 0,3876[2]	1,85 [0,46; 7,48] 0,5080[4]	0,9 [-1,1; 3,0] 0,5080[4]
Number of positive lymph nodes (Interaction p-value: 0,9576)					
0-3	8/427 (1,9)	2/418 (0,5)	3,92 [0,84; 18,33] 0,0831[2]	3,97 [0,84; 18,81] 0,1075[4]	1,4 [-0,1; 2,8] 0,1075[4]
4-9	9/549 (1,6)	3/542 (0,6)	2,96 [0,81; 10,88] 0,1020[2]	2,99 [0,81; 11,12] 0,0856[3]	1,1 [-0,1; 2,3] 0,0856[3]
≥ 10	6/307 (2,0)	2/305 (0,7)	2,98 [0,61; 14,65] 0,1789[2]	3,02 [0,60; 15,08] 0,2858[4]	1,3 [-0,5; 3,1] 0,2858[4]
Tumor stage (Interaction p-value: 0,8994)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIA	2/113 (1,8)	0/114 (0,0)	5,04 [0,24; 103,90] 0,2945[2]	5,13 [0,24; 108,15] 0,2467[4]	1,8 [-0,7; 4,2] 0,2467[4]
IIB	2/151 (1,3)	0/136 (0,0)	4,51 [0,22; 93,05] 0,3297[2]	4,57 [0,22; 95,94] 0,4996[4]	1,3 [-0,5; 3,1] 0,4996[4]
IIIA	9/495 (1,8)	2/488 (0,4)	4,44 [0,96; 20,43] 0,0559[2]	4,50 [0,97; 20,93] 0,0358[3]	1,4 [0,1; 2,7] 0,0358[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	8/468 (1,7)	5/480 (1,0)	1,64 [0,54; 4,98] 0,3818[2]	1,65 [0,54; 5,09] 0,3768[3]	0,7 [-0,8; 2,2] 0,3768[3]
Tumor grade (Interaction p-value: 0,3621)					
G1	3/91 (3,3)	0/93 (0,0)	7,15 [0,37; 136,54] 0,1910[2]	7,40 [0,38; 145,22] 0,1189[4]	3,3 [-0,4; 7,0] 0,1189[4]
G2	5/612 (0,8)	5/603 (0,8)	0,99 [0,29; 3,39] 0,9812[2]	0,99 [0,28; 3,42] 1,0000[4]	-0,0 [-1,0; 1,0] 1,0000[4]
G3	12/527 (2,3)	2/506 (0,4)	5,76 [1,30; 25,61] 0,0214[2]	5,87 [1,31; 26,37] 0,0089[3]	1,9 [0,5; 3,3] 0,0089[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,2224)					
Negative	4/156 (2,6)	1/169 (0,6)	4,33 [0,49; 38,35] 0,1875[2]	4,42 [0,49; 39,99] 0,1985[4]	2,0 [-0,8; 4,7] 0,1985[4]
Positive	19/1089 (1,7)	6/1067 (0,6)	3,10 [1,24; 7,74] 0,0152[2]	3,14 [1,25; 7,89] 0,0103[3]	1,2 [0,3; 2,1] 0,0103[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9909)					
White	22/958 (2,3)	7/944 (0,7)	3,10 [1,33; 7,22] 0,0088[2]	3,15 [1,34; 7,40] 0,0057[3]	1,6 [0,5; 2,7] 0,0057[3]
Asian	0/250 (0,0)	0/242 (0,0)	NE	NE	NE
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
First endocrine therapy (Interaction p-value: 0,7695)					
Tamoxifen	2/114 (1,8)	1/132 (0,8)	2,32 [0,21; 25,21] 0,4906[2]	2,34 [0,21; 26,14] 0,5979[4]	1,0 [-1,8; 3,8] 0,5979[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aromatase inhibitor	21/1169 (1,8)	6/1133 (0,5)	3,39 [1,37; 8,37] 0,0081[2]	3,44 [1,38; 8,54] 0,0048[3]	1,3 [0,4; 2,1] 0,0048[3]
ECOG-PS (Interaction p-value: 0,4539)					
ECOG-PS 0	22/1070 (2,1)	6/1020 (0,6)	3,50 [1,42; 8,59] 0,0063[2]	3,55 [1,43; 8,79] 0,0035[3]	1,5 [0,5; 2,4] 0,0035[3]
ECOG-PS 1	1/213 (0,5)	1/245 (0,4)	1,15 [0,07; 18,28] 0,9210[2]	1,15 [0,07; 18,51] 1,0000[4]	0,1 [-1,2; 1,3] 1,0000[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Joint stiffness from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6952)					
< 65 years	10/918 (1,1)	24/937 (2,6)	0,43 [0,20; 0,88] 0,0221[2]	0,42 [0,20; 0,88] 0,0181[3]	-1,5 [-2,7; -0,3] 0,0181[3]
≥ 65 years	2/365 (0,5)	6/328 (1,8)	0,30 [0,06; 1,47] 0,1381[2]	0,30 [0,06; 1,48] 0,1585[4]	-1,3 [-2,9; 0,4] 0,1585[4]
Prior treatment (Interaction p-value: 0,9989)					
Neoadjuvant chemotherapy	3/430 (0,7)	7/415 (1,7)	0,41 [0,11; 1,59] 0,1985[2]	0,41 [0,11; 1,59] 0,2164[4]	-1,0 [-2,5; 0,5] 0,2164[4]
Adjuvant chemotherapy	9/784 (1,1)	22/769 (2,9)	0,40 [0,19; 0,87] 0,0200[2]	0,39 [0,18; 0,86] 0,0158[3]	-1,7 [-3,1; -0,3] 0,0158[3]
No chemotherapy	0/69 (0,0)	1/81 (1,2)	0,39 [0,02; 9,43] 0,5628[2]	0,39 [0,02; 9,63] 1,0000[4]	-1,2 [-3,6; 1,2] 1,0000[4]
Region (Interaction p-value: 0,2017)					
North America / Europe	9/678 (1,3)	22/650 (3,4)	0,39 [0,18; 0,85] 0,0169[2]	0,38 [0,18; 0,84] 0,0131[3]	-2,1 [-3,7; -0,4] 0,0131[3]
Asia	3/203 (1,5)	8/201 (4,0)	0,37 [0,10; 1,38] 0,1390[2]	0,36 [0,09; 1,38] 0,1223[3]	-2,5 [-5,7; 0,7] 0,1223[3]
Other	0/402 (0,0)	0/414 (0,0)	NE	NE	NE
Primary tumor size (Interaction p-value: 0,3220)					
< 20 mm	5/331 (1,5)	6/335 (1,8)	0,84 [0,26; 2,74] 0,7767[2]	0,84 [0,25; 2,78] 0,7764[3]	-0,3 [-2,2; 1,7] 0,7764[3]
≥ 20 but < 50 mm	4/646 (0,6)	16/653 (2,5)	0,25 [0,08; 0,75] 0,0134[2]	0,25 [0,08; 0,75] 0,0074[3]	-1,8 [-3,2; -0,5] 0,0074[3]
≥ 50 mm	3/289 (1,0)	8/265 (3,0)	0,34 [0,09; 1,28] 0,1120[2]	0,34 [0,09; 1,28] 0,0950[3]	-2,0 [-4,3; 0,4] 0,0950[3]
Number of positive lymph nodes (Interaction p-value: 0,1750)					
0-3	3/427 (0,7)	8/418 (1,9)	0,37 [0,10; 1,37] 0,1368[2]	0,36 [0,10; 1,38] 0,1204[3]	-1,2 [-2,7; 0,3] 0,1204[3]
4-9	8/549 (1,5)	11/542 (2,0)	0,72 [0,29; 1,77] 0,4721[2]	0,71 [0,28; 1,79] 0,4700[3]	-0,6 [-2,1; 1,0] 0,4700[3]
≥ 10	1/307 (0,3)	11/305 (3,6)	0,09 [0,01; 0,70] 0,0209[2]	0,09 [0,01; 0,68] 0,0034[3]	-3,3 [-5,5; -1,1] 0,0034[3]
Tumor stage (Interaction p-value: 0,8119)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIA	2/113 (1,8)	2/114 (1,8)	1,01 [0,14; 7,04] 0,9929[2]	1,01 [0,14; 7,29] 1,0000[4]	0,0 [-3,4; 3,4] 1,0000[4]
IIB	0/151 (0,0)	2/136 (1,5)	0,18 [0,01; 3,72] 0,2674[2]	0,18 [0,01; 3,73] 0,2237[4]	-1,5 [-3,5; 0,6] 0,2237[4]
IIIA	6/495 (1,2)	11/488 (2,3)	0,54 [0,20; 1,44] 0,2179[2]	0,53 [0,20; 1,45] 0,2102[3]	-1,0 [-2,7; 0,6] 0,2102[3]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	4/468 (0,9)	15/480 (3,1)	0,27 [0,09; 0,82] 0,0204[2]	0,27 [0,09; 0,81] 0,0126[3]	-2,3 [-4,0; -0,5] 0,0126[3]
Tumor grade (Interaction p-value: 0,6173)					
G1	0/91 (0,0)	2/93 (2,2)	0,20 [0,01; 4,20] 0,3032[2]	0,20 [0,01; 4,22] 0,4973[4]	-2,2 [-5,1; 0,8] 0,4973[4]
G2	8/612 (1,3)	16/603 (2,7)	0,49 [0,21; 1,14] 0,0990[2]	0,49 [0,21; 1,14] 0,0918[3]	-1,3 [-2,9; 0,2] 0,0918[3]
G3	4/527 (0,8)	12/506 (2,4)	0,32 [0,10; 0,99] 0,0472[2]	0,31 [0,10; 0,98] 0,0359[3]	-1,6 [-3,1; -0,1] 0,0359[3]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,6179)					
Negative	3/156 (1,9)	2/169 (1,2)	1,63 [0,28; 9,60] 0,5921[2]	1,64 [0,27; 9,93] 0,6739[4]	0,7 [-2,0; 3,4] 0,6739[4]
Positive	9/1089 (0,8)	28/1067 (2,6)	0,31 [0,15; 0,66] 0,0024[2]	0,31 [0,15; 0,66] 0,0013[3]	-1,8 [-2,9; -0,7] 0,0013[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,7789)					
White	8/958 (0,8)	21/944 (2,2)	0,38 [0,17; 0,84] 0,0177[2]	0,37 [0,16; 0,84] 0,0134[3]	-1,4 [-2,5; -0,3] 0,0134[3]
Asian	3/250 (1,2)	8/242 (3,3)	0,36 [0,10; 1,35] 0,1310[2]	0,36 [0,09; 1,36] 0,1142[3]	-2,1 [-4,7; 0,5] 0,1142[3]
Other	1/62 (1,6)	1/64 (1,6)	1,03 [0,07; 16,14] 0,9819[2]	1,03 [0,06; 16,88] 1,0000[4]	0,1 [-4,3; 4,4] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,1280)					
Tamoxifen	2/114 (1,8)	1/132 (0,8)	2,32 [0,21; 25,21] 0,4906[2]	2,34 [0,21; 26,14] 0,5979[4]	1,0 [-1,8; 3,8] 0,5979[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aromatase inhibitor	10/1169 (0,9)	29/1133 (2,6)	0,33 [0,16; 0,68] 0,0026[2]	0,33 [0,16; 0,68] 0,0015[3]	-1,7 [-2,8; -0,6] 0,0015[3]
ECOG-PS (Interaction p-value: 0,9915)					
ECOG-PS 0	11/1070 (1,0)	27/1020 (2,6)	0,39 [0,19; 0,78] 0,0077[2]	0,38 [0,19; 0,77] 0,0056[3]	-1,6 [-2,8; -0,5] 0,0056[3]
ECOG-PS 1	1/213 (0,5)	3/245 (1,2)	0,38 [0,04; 3,66] 0,4049[2]	0,38 [0,04; 3,69] 0,6270[4]	-0,8 [-2,4; 0,9] 0,6270[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Lacrimation increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1329)					
< 65 years	51/918 (5,6)	2/937 (0,2)	26,03 [6,36; 106,60] <,0001[2]	27,50 [6,67; 113,30] <,0001[3]	5,3 [3,8; 6,9] <,0001[3]
≥ 65 years	21/365 (5,8)	3/328 (0,9)	6,29 [1,89; 20,90] 0,0027[2]	6,61 [1,95; 22,38] 0,0005[3]	4,8 [2,2; 7,4] 0,0005[3]
Prior treatment (Interaction p-value: 0,6993)					
Neoadjuvant chemotherapy	28/430 (6,5)	1/415 (0,2)	27,02 [3,69; 197,71] 0,0012[2]	28,84 [3,90; 212,94] <,0001[3]	6,3 [3,9; 8,6] <,0001[3]
Adjuvant chemotherapy	42/784 (5,4)	4/769 (0,5)	10,30 [3,71; 28,58] <,0001[2]	10,83 [3,86; 30,34] <,0001[3]	4,8 [3,2; 6,5] <,0001[3]
No chemotherapy	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (Interaction p-value: 0,9706)					
North America / Europe	52/678 (7,7)	4/650 (0,6)	12,46 [4,53; 34,26] <,0001[2]	13,42 [4,82; 37,31] <,0001[3]	7,1 [5,0; 9,1] <,0001[3]
Asia	4/203 (2,0)	0/201 (0,0)	8,91 [0,48; 164,45] 0,1414[2]	9,09 [0,49; 169,95] 0,1232[4]	2,0 [0,1; 3,9] 0,1232[4]
Other	16/402 (4,0)	1/414 (0,2)	16,48 [2,20; 123,67] 0,0064[2]	17,12 [2,26; 129,70] 0,0002[3]	3,7 [1,8; 5,7] 0,0002[3]
Primary tumor size (Interaction p-value: 0,7061)					
< 20 mm	16/331 (4,8)	2/335 (0,6)	8,10 [1,88; 34,94] 0,0051[2]	8,46 [1,93; 37,08] 0,0007[3]	4,2 [1,8; 6,7] 0,0007[3]
≥ 20 but < 50 mm	35/646 (5,4)	2/653 (0,3)	17,69 [4,27; 73,24] <,0001[2]	18,65 [4,47; 77,85] <,0001[3]	5,1 [3,3; 6,9] <,0001[3]
≥ 50 mm	20/289 (6,9)	1/265 (0,4)	18,34 [2,48; 135,70] 0,0044[2]	19,63 [2,62; 147,30] <,0001[3]	6,5 [3,5; 9,6] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9973)					
0-3	19/427 (4,4)	2/418 (0,5)	9,30 [2,18; 39,68] 0,0026[2]	9,69 [2,24; 41,85] 0,0002[3]	4,0 [1,9; 6,0] 0,0002[3]
4-9	30/549 (5,5)	3/542 (0,6)	9,87 [3,03; 32,16] 0,0001[2]	10,39 [3,15; 34,24] <,0001[3]	4,9 [2,9; 6,9] <,0001[3]
≥ 10	23/307 (7,5)	0/305 (0,0)	46,69 [2,85; 765,33] 0,0071[2]	50,47 [3,05; 834,77] <,0001[3]	7,5 [4,5; 10,4] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7214)					
IIA	6/113 (5,3)	1/114 (0,9)	6,05 [0,74; 49,48] 0,0930[2]	6,34 [0,75; 53,50] 0,0655[4]	4,4 [-0,0; 8,9] 0,0655[4]
IIB	5/151 (3,3)	1/136 (0,7)	4,50 [0,53; 38,07] 0,1670[2]	4,62 [0,53; 40,08] 0,2177[4]	2,6 [-0,6; 5,8] 0,2177[4]
IIIA	27/495 (5,5)	2/488 (0,4)	13,31 [3,18; 55,66] 0,0004[2]	14,02 [3,32; 59,28] <,0001[3]	5,0 [3,0; 7,1] <,0001[3]
IIIB	4/54 (7,4)	0/45 (0,0)	7,53 [0,42; 136,17] 0,1718[2]	8,11 [0,42; 154,79] 0,1236[4]	7,4 [0,4; 14,4] 0,1236[4]
IIIC	30/468 (6,4)	1/480 (0,2)	30,77 [4,21; 224,71] 0,0007[2]	32,81 [4,46; 241,59] <,0001[3]	6,2 [3,9; 8,5] <,0001[3]
Tumor grade (Interaction p-value: 0,3816)					
G1	3/91 (3,3)	1/93 (1,1)	3,07 [0,32; 28,93] 0,3279[2]	3,14 [0,32; 30,72] 0,3655[4]	2,2 [-2,0; 6,4] 0,3655[4]
G2	41/612 (6,7)	1/603 (0,2)	40,40 [5,57; 292,74] 0,0003[2]	43,23 [5,93; 315,28] <,0001[3]	6,5 [4,5; 8,5] <,0001[3]
G3	26/527 (4,9)	3/506 (0,6)	8,32 [2,53; 27,32] 0,0005[2]	8,70 [2,62; 28,93] <,0001[3]	4,3 [2,4; 6,3] <,0001[3]
GX	2/51 (3,9)	0/59 (0,0)	5,77 [0,28; 117,46] 0,2544[2]	6,01 [0,28; 128,14] 0,2127[4]	3,9 [-1,4; 9,2] 0,2127[4]
Progesterone receptor status (Interaction p-value: 0,9587)					
Negative	13/156 (8,3)	0/169 (0,0)	29,24 [1,75; 487,71] 0,0187[2]	31,89 [1,88; 541,19] 0,0001[3]	8,3 [4,0; 12,7] 0,0001[3]
Positive	58/1089 (5,3)	5/1067 (0,5)	11,37 [4,58; 28,23] <,0001[2]	11,95 [4,77; 29,91] <,0001[3]	4,9 [3,5; 6,3] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9997)					
White	64/958 (6,7)	5/944 (0,5)	12,61 [5,10; 31,20] <,0001[2]	13,44 [5,39; 33,56] <,0001[3]	6,2 [4,5; 7,8] <,0001[3]
Asian	5/250 (2,0)	0/242 (0,0)	10,65 [0,59; 191,56] 0,1086[2]	10,87 [0,60; 197,57] 0,0614[4]	2,0 [0,3; 3,7] 0,0614[4]
Other	3/62 (4,8)	0/64 (0,0)	7,22 [0,38; 137,01] 0,1879[2]	7,59 [0,38; 150,00] 0,1162[4]	4,8 [-0,5; 10,2] 0,1162[4]
First endocrine therapy (Interaction p-value: 0,6601)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	8/114 (7,0)	1/132 (0,8)	9,26 [1,18; 72,95] 0,0345[2]	9,89 [1,22; 80,30] 0,0133[4]	6,3 [1,3; 11,2] 0,0133[4]
Aromatase inhibitor	64/1169 (5,5)	4/1133 (0,4)	15,51 [5,67; 42,44] <,0001[2]	16,35 [5,93; 45,04] <,0001[3]	5,1 [3,8; 6,5] <,0001[3]
ECOG-PS (Interaction p-value: 0,9048)					
ECOG-PS 0	61/1070 (5,7)	4/1020 (0,4)	14,54 [5,31; 39,83] <,0001[2]	15,36 [5,56; 42,39] <,0001[3]	5,3 [3,9; 6,8] <,0001[3]
ECOG-PS 1	11/213 (5,2)	1/245 (0,4)	12,65 [1,65; 97,20] 0,0147[2]	13,29 [1,70; 103,79] 0,0015[3]	4,8 [1,7; 7,8] 0,0015[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Leukopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6569)					
< 65 years	137/918 (14,9)	20/937 (2,1)	6,99 [4,41; 11,08] <,0001[2]	8,04 [4,98; 12,98] <,0001[3]	12,8 [10,3; 15,3] <,0001[3]
≥ 65 years	49/365 (13,4)	5/328 (1,5)	8,81 [3,55; 21,83] <,0001[2]	10,02 [3,94; 25,47] <,0001[3]	11,9 [8,2; 15,6] <,0001[3]
Prior treatment (Interaction p-value: 0,9362)					
Neoadjuvant chemotherapy	59/430 (13,7)	8/415 (1,9)	7,12 [3,44; 14,71] <,0001[2]	8,09 [3,82; 17,16] <,0001[3]	11,8 [8,3; 15,3] <,0001[3]
Adjuvant chemotherapy	118/784 (15,1)	16/769 (2,1)	7,23 [4,33; 12,08] <,0001[2]	8,34 [4,90; 14,20] <,0001[3]	13,0 [10,3; 15,7] <,0001[3]
No chemotherapy	9/69 (13,0)	1/81 (1,2)	10,57 [1,37; 81,32] 0,0236[2]	12,00 [1,48; 97,30] 0,0058[4]	11,8 [3,5; 20,1] 0,0058[4]
Region (Interaction p-value: 0,2306)					
North America / Europe	66/678 (9,7)	5/650 (0,8)	12,65 [5,13; 31,21] <,0001[2]	13,91 [5,57; 34,76] <,0001[3]	9,0 [6,6; 11,3] <,0001[3]
Asia	15/203 (7,4)	1/201 (0,5)	14,85 [1,98; 111,38] 0,0087[2]	15,96 [2,09; 121,99] 0,0004[3]	6,9 [3,2; 10,6] 0,0004[3]
Other	105/402 (26,1)	19/414 (4,6)	5,69 [3,56; 9,10] <,0001[2]	7,35 [4,41; 12,26] <,0001[3]	21,5 [16,8; 26,3] <,0001[3]
Primary tumor size (Interaction p-value: 0,5714)					
< 20 mm	48/331 (14,5)	6/335 (1,8)	8,10 [3,51; 18,66] <,0001[2]	9,30 [3,92; 22,05] <,0001[3]	12,7 [8,7; 16,8] <,0001[3]
≥ 20 but < 50 mm	95/646 (14,7)	15/653 (2,3)	6,40 [3,75; 10,92] <,0001[2]	7,33 [4,20; 12,79] <,0001[3]	12,4 [9,4; 15,4] <,0001[3]
≥ 50 mm	41/289 (14,2)	3/265 (1,1)	12,53 [3,93; 39,99] <,0001[2]	14,44 [4,41; 47,22] <,0001[3]	13,1 [8,8; 17,3] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,8811)					
0-3	53/427 (12,4)	6/418 (1,4)	8,65 [3,76; 19,90] <,0001[2]	9,73 [4,14; 22,90] <,0001[3]	11,0 [7,6; 14,3] <,0001[3]
4-9	88/549 (16,0)	13/542 (2,4)	6,68 [3,78; 11,82] <,0001[2]	7,77 [4,28; 14,09] <,0001[3]	13,6 [10,3; 17,0] <,0001[3]
≥ 10	45/307 (14,7)	6/305 (2,0)	7,45 [3,23; 17,21] <,0001[2]	8,56 [3,59; 20,39] <,0001[3]	12,7 [8,4; 16,9] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9605)					
IIA	14/113 (12,4)	1/114 (0,9)	14,12 [1,89; 105,62] 0,0099[2]	15,98 [2,06; 123,71] 0,0005[3]	11,5 [5,2; 17,8] 0,0005[3]
IIB	19/151 (12,6)	3/136 (2,2)	5,70 [1,73; 18,85] 0,0043[2]	6,38 [1,84; 22,08] 0,0010[3]	10,4 [4,5; 16,2] 0,0010[3]
IIIA	74/495 (14,9)	10/488 (2,0)	7,30 [3,81; 13,95] <,0001[2]	8,40 [4,29; 16,47] <,0001[3]	12,9 [9,5; 16,3] <,0001[3]
IIIB	7/54 (13,0)	1/45 (2,2)	5,83 [0,75; 45,66] 0,0930[2]	6,55 [0,77; 55,43] 0,0682[4]	10,7 [0,8; 20,7] 0,0682[4]
IIIC	72/468 (15,4)	10/480 (2,1)	7,38 [3,86; 14,13] <,0001[2]	8,55 [4,35; 16,78] <,0001[3]	13,3 [9,8; 16,8] <,0001[3]
Tumor grade (Interaction p-value: 0,6185)					
G1	11/91 (12,1)	0/93 (0,0)	23,50 [1,41; 392,99] 0,0280[2]	26,71 [1,55; 460,48] 0,0005[3]	12,1 [5,4; 18,8] 0,0005[3]
G2	85/612 (13,9)	15/603 (2,5)	5,58 [3,26; 9,55] <,0001[2]	6,32 [3,61; 11,08] <,0001[3]	11,4 [8,4; 14,4] <,0001[3]
G3	82/527 (15,6)	8/506 (1,6)	9,84 [4,81; 20,13] <,0001[2]	11,47 [5,49; 23,97] <,0001[3]	14,0 [10,7; 17,3] <,0001[3]
GX	8/51 (15,7)	2/59 (3,4)	4,63 [1,03; 20,81] 0,0458[2]	5,30 [1,07; 26,24] 0,0423[4]	12,3 [1,3; 23,3] 0,0423[4]
Progesterone receptor status (Interaction p-value: 0,3113)					
Negative	25/156 (16,0)	5/169 (3,0)	5,42 [2,13; 13,80] 0,0004[2]	6,26 [2,33; 16,80] <,0001[3]	13,1 [6,8; 19,4] <,0001[3]
Positive	160/1089 (14,7)	20/1067 (1,9)	7,84 [4,96; 12,38] <,0001[2]	9,02 [5,62; 14,47] <,0001[3]	12,8 [10,6; 15,1] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8110)					
White	159/958 (16,6)	21/944 (2,2)	7,46 [4,78; 11,66] <,0001[2]	8,75 [5,49; 13,92] <,0001[3]	14,4 [11,8; 16,9] <,0001[3]
Asian	18/250 (7,2)	2/242 (0,8)	8,71 [2,04; 37,15] 0,0034[2]	9,31 [2,14; 40,57] 0,0003[3]	6,4 [3,0; 9,8] 0,0003[3]
Other	9/62 (14,5)	2/64 (3,1)	4,65 [1,04; 20,65] 0,0436[2]	5,26 [1,09; 25,44] 0,0235[3]	11,4 [1,6; 21,1] 0,0235[3]
ECOG-PS (Interaction p-value: 0,1962)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	153/1070 (14,3)	17/1020 (1,7)	8,58 [5,24; 14,06] <,0001[2]	9,84 [5,92; 16,38] <,0001[3]	12,6 [10,4; 14,9] <,0001[3]
ECOG-PS 1	33/213 (15,5)	8/245 (3,3)	4,74 [2,24; 10,05] <,0001[2]	5,43 [2,45; 12,04] <,0001[3]	12,2 [6,9; 17,6] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Lymphocyte count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7497)					
< 65 years	74/918 (8,1)	21/937 (2,2)	3,60 [2,23; 5,79] <,0001[2]	3,82 [2,33; 6,26] <,0001[3]	5,8 [3,8; 7,8] <,0001[3]
≥ 65 years	37/365 (10,1)	8/328 (2,4)	4,16 [1,96; 8,79] 0,0002[2]	4,51 [2,07; 9,84] <,0001[3]	7,7 [4,2; 11,2] <,0001[3]
Prior treatment (Interaction p-value: 0,9516)					
Neoadjuvant chemotherapy	40/430 (9,3)	10/415 (2,4)	3,86 [1,96; 7,62] <,0001[2]	4,15 [2,05; 8,42] <,0001[3]	6,9 [3,8; 10,0] <,0001[3]
Adjuvant chemotherapy	66/784 (8,4)	17/769 (2,2)	3,81 [2,26; 6,43] <,0001[2]	4,07 [2,36; 7,00] <,0001[3]	6,2 [4,0; 8,4] <,0001[3]
No chemotherapy	5/69 (7,2)	2/81 (2,5)	2,93 [0,59; 14,65] 0,1894[2]	3,09 [0,58; 16,44] 0,2485[4]	4,8 [-2,2; 11,8] 0,2485[4]
Region (Interaction p-value: 0,6806)					
North America / Europe	49/678 (7,2)	11/650 (1,7)	4,27 [2,24; 8,14] <,0001[2]	4,53 [2,33; 8,78] <,0001[3]	5,5 [3,3; 7,7] <,0001[3]
Asia	27/203 (13,3)	6/201 (3,0)	4,46 [1,88; 10,56] 0,0007[2]	4,99 [2,01; 12,36] 0,0002[3]	10,3 [5,1; 15,5] 0,0002[3]
Other	35/402 (8,7)	12/414 (2,9)	3,00 [1,58; 5,70] 0,0008[2]	3,19 [1,63; 6,25] 0,0004[3]	5,8 [2,6; 9,0] 0,0004[3]
Primary tumor size (Interaction p-value: 0,8490)					
< 20 mm	28/331 (8,5)	6/335 (1,8)	4,72 [1,98; 11,26] 0,0005[2]	5,07 [2,07; 12,41] <,0001[3]	6,7 [3,4; 10,0] <,0001[3]
≥ 20 but < 50 mm	49/646 (7,6)	14/653 (2,1)	3,54 [1,97; 6,34] <,0001[2]	3,75 [2,05; 6,86] <,0001[3]	5,4 [3,1; 7,8] <,0001[3]
≥ 50 mm	31/289 (10,7)	8/265 (3,0)	3,55 [1,66; 7,59] 0,0011[2]	3,86 [1,74; 8,56] 0,0004[3]	7,7 [3,6; 11,8] 0,0004[3]
Number of positive lymph nodes (Interaction p-value: 0,9597)					
0-3	36/427 (8,4)	10/418 (2,4)	3,52 [1,77; 7,01] 0,0003[2]	3,76 [1,84; 7,67] 0,0001[3]	6,0 [3,0; 9,1] 0,0001[3]
4-9	46/549 (8,4)	12/542 (2,2)	3,78 [2,03; 7,06] <,0001[2]	4,04 [2,12; 7,71] <,0001[3]	6,2 [3,5; 8,8] <,0001[3]
≥ 10	29/307 (9,4)	7/305 (2,3)	4,12 [1,83; 9,25] 0,0006[2]	4,44 [1,91; 10,30] 0,0002[3]	7,2 [3,5; 10,8] 0,0002[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8842)					
IIA	11/113 (9,7)	3/114 (2,6)	3,70 [1,06; 12,91] 0,0402[2]	3,99 [1,08; 14,71] 0,0261[3]	7,1 [0,9; 13,3] 0,0261[3]
IIB	13/151 (8,6)	2/136 (1,5)	5,85 [1,35; 25,48] 0,0185[2]	6,31 [1,40; 28,50] 0,0067[3]	7,1 [2,2; 12,0] 0,0067[3]
IIIA	44/495 (8,9)	15/488 (3,1)	2,89 [1,63; 5,13] 0,0003[2]	3,08 [1,69; 5,61] 0,0001[3]	5,8 [2,9; 8,8] 0,0001[3]
IIIB	5/54 (9,3)	0/45 (0,0)	9,20 [0,52; 162,01] 0,1294[2]	10,11 [0,54; 188,02] 0,0613[4]	9,3 [1,5; 17,0] 0,0613[4]
IIIC	37/468 (7,9)	9/480 (1,9)	4,22 [2,06; 8,64] <,0001[2]	4,49 [2,14; 9,42] <,0001[3]	6,0 [3,3; 8,8] <,0001[3]
Tumor grade (Interaction p-value: 0,4692)					
G1	10/91 (11,0)	0/93 (0,0)	21,46 [1,28; 360,85] 0,0332[2]	24,09 [1,39; 417,56] 0,0007[4]	11,0 [4,6; 17,4] 0,0007[4]
G2	48/612 (7,8)	18/603 (3,0)	2,63 [1,55; 4,46] 0,0004[2]	2,77 [1,59; 4,81] 0,0002[3]	4,9 [2,3; 7,4] 0,0002[3]
G3	47/527 (8,9)	9/506 (1,8)	5,01 [2,48; 10,12] <,0001[2]	5,41 [2,62; 11,15] <,0001[3]	7,1 [4,4; 9,8] <,0001[3]
GX	6/51 (11,8)	1/59 (1,7)	6,94 [0,86; 55,76] 0,0684[2]	7,73 [0,90; 66,56] 0,0477[4]	10,1 [0,6; 19,5] 0,0477[4]
Race (Interaction p-value: 0,9068)					
White	79/958 (8,2)	22/944 (2,3)	3,54 [2,23; 5,63] <,0001[2]	3,77 [2,33; 6,10] <,0001[3]	5,9 [3,9; 7,9] <,0001[3]
Asian	27/250 (10,8)	6/242 (2,5)	4,36 [1,83; 10,36] 0,0009[2]	4,76 [1,93; 11,75] 0,0002[3]	8,3 [4,0; 12,6] 0,0002[3]
Other	3/62 (4,8)	1/64 (1,6)	3,10 [0,33; 28,97] 0,3218[2]	3,20 [0,32; 31,66] 0,3610[4]	3,3 [-2,9; 9,4] 0,3610[4]
First endocrine therapy (Interaction p-value: 0,1327)					
Tamoxifen	5/114 (4,4)	4/132 (3,0)	1,45 [0,40; 5,26] 0,5745[2]	1,47 [0,38; 5,60] 0,7368[4]	1,4 [-3,4; 6,1] 0,7368[4]
Aromatase inhibitor	106/1169 (9,1)	25/1133 (2,2)	4,11 [2,68; 6,30] <,0001[2]	4,42 [2,84; 6,89] <,0001[3]	6,9 [5,0; 8,7] <,0001[3]
ECOG-PS (Interaction p-value: 0,0962)					
ECOG-PS 0	91/1070 (8,5)	27/1020 (2,6)	3,21 [2,11; 4,89] <,0001[2]	3,42 [2,20; 5,30] <,0001[3]	5,9 [3,9; 7,8] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	20/213 (9,4)	2/245 (0,8)	11,50 [2,72; 48,64] 0,0009[2]	12,59 [2,91; 54,53] <,0001[3]	8,6 [4,5; 12,6] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Lymphoedema from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1911)					
< 65 years	116/918 (12,6)	72/937 (7,7)	1,64 [1,24; 2,17] 0,0005[2]	1,74 [1,28; 2,37] 0,0004[3]	5,0 [2,2; 7,7] 0,0004[3]
≥ 65 years	37/365 (10,1)	29/328 (8,8)	1,15 [0,72; 1,82] 0,5624[2]	1,16 [0,70; 1,94] 0,5619[3]	1,3 [-3,1; 5,7] 0,5619[3]
Prior treatment (Interaction p-value: 0,4143)					
Neoadjuvant chemotherapy	60/430 (14,0)	41/415 (9,9)	1,41 [0,97; 2,05] 0,0700[2]	1,48 [0,97; 2,26] 0,0680[3]	4,1 [-0,3; 8,4] 0,0680[3]
Adjuvant chemotherapy	86/784 (11,0)	58/769 (7,5)	1,45 [1,06; 2,00] 0,0209[2]	1,51 [1,07; 2,14] 0,0199[3]	3,4 [0,6; 6,3] 0,0199[3]
No chemotherapy	7/69 (10,1)	2/81 (2,5)	4,11 [0,88; 19,13] 0,0718[2]	4,46 [0,89; 22,23] 0,0809[4]	7,7 [-0,2; 15,6] 0,0809[4]
Region (Interaction p-value: 0,1143)					
North America / Europe	89/678 (13,1)	70/650 (10,8)	1,22 [0,91; 1,64] 0,1870[2]	1,25 [0,90; 1,75] 0,1859[3]	2,4 [-1,1; 5,8] 0,1859[3]
Asia	30/203 (14,8)	14/201 (7,0)	2,12 [1,16; 3,88] 0,0146[2]	2,32 [1,19; 4,51] 0,0117[3]	7,8 [1,8; 13,8] 0,0117[3]
Other	34/402 (8,5)	17/414 (4,1)	2,06 [1,17; 3,63] 0,0123[2]	2,16 [1,19; 3,93] 0,0102[3]	4,4 [1,0; 7,7] 0,0102[3]
Primary tumor size (Interaction p-value: 0,4732)					
< 20 mm	39/331 (11,8)	31/335 (9,3)	1,27 [0,81; 1,99] 0,2889[2]	1,31 [0,80; 2,16] 0,2874[3]	2,5 [-2,1; 7,2] 0,2874[3]
≥ 20 but < 50 mm	65/646 (10,1)	47/653 (7,2)	1,40 [0,98; 2,00] 0,0675[2]	1,44 [0,97; 2,14] 0,0659[3]	2,9 [-0,2; 5,9] 0,0659[3]
≥ 50 mm	47/289 (16,3)	23/265 (8,7)	1,87 [1,17; 3,00] 0,0088[2]	2,04 [1,20; 3,47] 0,0073[3]	7,6 [2,1; 13,0] 0,0073[3]
Number of positive lymph nodes (Interaction p-value: 0,2562)					
0-3	47/427 (11,0)	25/418 (6,0)	1,84 [1,15; 2,93] 0,0103[2]	1,94 [1,17; 3,22] 0,0089[3]	5,0 [1,3; 8,8] 0,0089[3]
4-9	64/549 (11,7)	39/542 (7,2)	1,62 [1,11; 2,37] 0,0128[2]	1,70 [1,12; 2,58] 0,0117[3]	4,5 [1,0; 7,9] 0,0117[3]
≥ 10	42/307 (13,7)	37/305 (12,1)	1,13 [0,75; 1,70] 0,5679[2]	1,15 [0,72; 1,84] 0,5675[3]	1,5 [-3,8; 6,9] 0,5675[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,5239)					
IIA	13/113 (11,5)	11/114 (9,6)	1,19 [0,56; 2,55] 0,6500[2]	1,22 [0,52; 2,84] 0,6494[3]	1,9 [-6,1; 9,9] 0,6494[3]
IIB	15/151 (9,9)	6/136 (4,4)	2,25 [0,90; 5,64] 0,0831[2]	2,39 [0,90; 6,35] 0,0729[3]	5,5 [-0,4; 11,4] 0,0729[3]
IIIA	57/495 (11,5)	33/488 (6,8)	1,70 [1,13; 2,57] 0,0110[2]	1,79 [1,15; 2,81] 0,0098[3]	4,8 [1,2; 8,3] 0,0098[3]
IIIB	5/54 (9,3)	1/45 (2,2)	4,17 [0,51; 34,38] 0,1850[2]	4,49 [0,50; 39,93] 0,2162[4]	7,0 [-1,8; 15,9] 0,2162[4]
IIIC	62/468 (13,2)	50/480 (10,4)	1,27 [0,90; 1,80] 0,1783[2]	1,31 [0,88; 1,95] 0,1769[3]	2,8 [-1,3; 6,9] 0,1769[3]
Tumor grade (Interaction p-value: 0,3179)					
G1	14/91 (15,4)	8/93 (8,6)	1,79 [0,79; 4,06] 0,1642[2]	1,93 [0,77; 4,86] 0,1563[3]	6,8 [-2,6; 16,1] 0,1563[3]
G2	83/612 (13,6)	49/603 (8,1)	1,67 [1,19; 2,33] 0,0027[2]	1,77 [1,22; 2,58] 0,0023[3]	5,4 [2,0; 8,9] 0,0023[3]
G3	50/527 (9,5)	42/506 (8,3)	1,14 [0,77; 1,69] 0,5035[2]	1,16 [0,75; 1,78] 0,5030[3]	1,2 [-2,3; 4,7] 0,5030[3]
GX	6/51 (11,8)	2/59 (3,4)	3,47 [0,73; 16,45] 0,1170[2]	3,80 [0,73; 19,73] 0,1413[4]	8,4 [-1,6; 18,4] 0,1413[4]
Race (Interaction p-value: 0,2852)					
White	109/958 (11,4)	79/944 (8,4)	1,36 [1,03; 1,79] 0,0287[2]	1,41 [1,04; 1,91] 0,0279[3]	3,0 [0,3; 5,7] 0,0279[3]
Asian	34/250 (13,6)	15/242 (6,2)	2,19 [1,23; 3,92] 0,0081[2]	2,38 [1,26; 4,50] 0,0061[3]	7,4 [2,2; 12,6] 0,0061[3]
Other	10/62 (16,1)	5/64 (7,8)	2,06 [0,75; 5,70] 0,1616[2]	2,27 [0,73; 7,07] 0,1495[3]	8,3 [-3,0; 19,6] 0,1495[3]
ECOG-PS (Interaction p-value: 0,8379)					
ECOG-PS 0	131/1070 (12,2)	83/1020 (8,1)	1,50 [1,16; 1,95] 0,0022[2]	1,57 [1,18; 2,10] 0,0020[3]	4,1 [1,5; 6,7] 0,0020[3]
ECOG-PS 1	22/213 (10,3)	18/245 (7,3)	1,41 [0,78; 2,55] 0,2620[2]	1,45 [0,76; 2,79] 0,2596[3]	3,0 [-2,3; 8,2] 0,2596[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Lymphopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4393)					
< 65 years	42/918 (4,6)	7/937 (0,7)	6,12 [2,77; 13,56] <,0001[2]	6,37 [2,85; 14,25] <,0001[3]	3,8 [2,4; 5,3] <,0001[3]
≥ 65 years	26/365 (7,1)	2/328 (0,6)	11,68 [2,79; 48,84] 0,0008[2]	12,50 [2,94; 53,09] <,0001[3]	6,5 [3,7; 9,3] <,0001[3]
Prior treatment (Interaction p-value: 0,0877)					
Neoadjuvant chemotherapy	23/430 (5,3)	3/415 (0,7)	7,40 [2,24; 24,46] 0,0010[2]	7,76 [2,31; 26,05] <,0001[3]	4,6 [2,3; 6,9] <,0001[3]
Adjuvant chemotherapy	44/784 (5,6)	4/769 (0,5)	10,79 [3,90; 29,88] <,0001[2]	11,37 [4,07; 31,81] <,0001[3]	5,1 [3,4; 6,8] <,0001[3]
No chemotherapy	1/69 (1,4)	2/81 (2,5)	0,59 [0,05; 6,33] 0,6607[2]	0,58 [0,05; 6,55] 1,0000[4]	-1,0 [-5,4; 3,4] 1,0000[4]
Region (Interaction p-value: 0,9887)					
North America / Europe	24/678 (3,5)	3/650 (0,5)	7,67 [2,32; 25,35] 0,0008[2]	7,91 [2,37; 26,41] <,0001[3]	3,1 [1,6; 4,6] <,0001[3]
Asia	4/203 (2,0)	0/201 (0,0)	8,91 [0,48; 164,45] 0,1414[2]	9,09 [0,49; 169,95] 0,1232[4]	2,0 [0,1; 3,9] 0,1232[4]
Other	40/402 (10,0)	6/414 (1,4)	6,87 [2,94; 16,02] <,0001[2]	7,51 [3,15; 17,93] <,0001[3]	8,5 [5,4; 11,6] <,0001[3]
Primary tumor size (Interaction p-value: 0,8140)					
< 20 mm	17/331 (5,1)	2/335 (0,6)	8,60 [2,00; 36,94] 0,0038[2]	9,01 [2,07; 39,33] 0,0004[3]	4,5 [2,0; 7,1] 0,0004[3]
≥ 20 but < 50 mm	33/646 (5,1)	4/653 (0,6)	8,34 [2,97; 23,41] <,0001[2]	8,73 [3,08; 24,80] <,0001[3]	4,5 [2,7; 6,3] <,0001[3]
≥ 50 mm	17/289 (5,9)	3/265 (1,1)	5,20 [1,54; 17,53] 0,0079[2]	5,46 [1,58; 18,84] 0,0028[3]	4,8 [1,8; 7,7] 0,0028[3]
Number of positive lymph nodes (Interaction p-value: 0,6951)					
0-3	12/427 (2,8)	2/418 (0,5)	5,87 [1,32; 26,08] 0,0199[2]	6,01 [1,34; 27,04] 0,0079[3]	2,3 [0,6; 4,0] 0,0079[3]
4-9	33/549 (6,0)	3/542 (0,6)	10,86 [3,35; 35,20] <,0001[2]	11,49 [3,50; 37,70] <,0001[3]	5,5 [3,4; 7,5] <,0001[3]
≥ 10	23/307 (7,5)	4/305 (1,3)	5,71 [2,00; 16,32] 0,0011[2]	6,09 [2,08; 17,84] 0,0002[3]	6,2 [3,0; 9,4] 0,0002[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7160)					
IIA	3/113 (2,7)	1/114 (0,9)	3,03 [0,32; 28,66] 0,3343[2]	3,08 [0,32; 30,08] 0,3695[4]	1,8 [-1,6; 5,2] 0,3695[4]
IIB	3/151 (2,0)	1/136 (0,7)	2,70 [0,28; 25,67] 0,3868[2]	2,74 [0,28; 26,62] 0,6244[4]	1,3 [-1,4; 3,9] 0,6244[4]
IIIA	28/495 (5,7)	2/488 (0,4)	13,80 [3,31; 57,62] 0,0003[2]	14,57 [3,45; 61,50] <,0001[3]	5,2 [3,1; 7,4] <,0001[3]
IIIB	4/54 (7,4)	0/45 (0,0)	7,53 [0,42; 136,17] 0,1718[2]	8,11 [0,42; 154,79] 0,1236[4]	7,4 [0,4; 14,4] 0,1236[4]
IIIC	30/468 (6,4)	5/480 (1,0)	6,15 [2,41; 15,72] 0,0001[2]	6,51 [2,50; 16,92] <,0001[3]	5,4 [3,0; 7,8] <,0001[3]
Tumor grade (Interaction p-value: 0,9978)					
G1	5/91 (5,5)	0/93 (0,0)	11,24 [0,63; 200,37] 0,0997[2]	11,89 [0,65; 218,22] 0,0280[4]	5,5 [0,8; 10,2] 0,0280[4]
G2	37/612 (6,0)	6/603 (1,0)	6,08 [2,58; 14,29] <,0001[2]	6,40 [2,68; 15,28] <,0001[3]	5,1 [3,0; 7,1] <,0001[3]
G3	22/527 (4,2)	3/506 (0,6)	7,04 [2,12; 23,38] 0,0014[2]	7,30 [2,17; 24,56] 0,0002[3]	3,6 [1,7; 5,4] 0,0002[3]
GX	4/51 (7,8)	0/59 (0,0)	10,38 [0,57; 188,36] 0,1135[2]	11,27 [0,59; 214,65] 0,0433[4]	7,8 [0,5; 15,2] 0,0433[4]
Race (Interaction p-value: 0,9599)					
White	58/958 (6,1)	8/944 (0,8)	7,14 [3,43; 14,88] <,0001[2]	7,54 [3,58; 15,88] <,0001[3]	5,2 [3,6; 6,8] <,0001[3]
Asian	4/250 (1,6)	0/242 (0,0)	8,71 [0,47; 160,97] 0,1457[2]	8,85 [0,47; 165,34] 0,1237[4]	1,6 [0,0; 3,2] 0,1237[4]
Other	5/62 (8,1)	1/64 (1,6)	5,16 [0,62; 42,93] 0,1289[2]	5,53 [0,63; 48,73] 0,1118[4]	6,5 [-0,9; 13,9] 0,1118[4]
ECOG-PS (Interaction p-value: 0,3230)					
ECOG-PS 0	57/1070 (5,3)	6/1020 (0,6)	9,06 [3,92; 20,91] <,0001[2]	9,51 [4,08; 22,15] <,0001[3]	4,7 [3,3; 6,2] <,0001[3]
ECOG-PS 1	11/213 (5,2)	3/245 (1,2)	4,22 [1,19; 14,92] 0,0256[2]	4,39 [1,21; 15,96] 0,0146[3]	3,9 [0,7; 7,2] 0,0146[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Malaise from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5649)					
< 65 years	24/918 (2,6)	8/937 (0,9)	3,06 [1,38; 6,78] 0,0058[2]	3,12 [1,39; 6,98] 0,0036[3]	1,8 [0,6; 2,9] 0,0036[3]
≥ 65 years	9/365 (2,5)	4/328 (1,2)	2,02 [0,63; 6,50] 0,2376[2]	2,05 [0,62; 6,71] 0,2273[3]	1,2 [-0,7; 3,2] 0,2273[3]
Prior treatment (Interaction p-value: 0,8834)					
Neoadjuvant chemotherapy	13/430 (3,0)	4/415 (1,0)	3,14 [1,03; 9,54] 0,0440[2]	3,20 [1,04; 9,91] 0,0330[3]	2,1 [0,2; 3,9] 0,0330[3]
Adjuvant chemotherapy	18/784 (2,3)	8/769 (1,0)	2,21 [0,97; 5,05] 0,0606[2]	2,24 [0,97; 5,17] 0,0538[3]	1,3 [-0,0; 2,5] 0,0538[3]
No chemotherapy	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (Interaction p-value: 0,6898)					
North America / Europe	10/678 (1,5)	4/650 (0,6)	2,40 [0,76; 7,60] 0,1378[2]	2,42 [0,75; 7,75] 0,1252[3]	0,9 [-0,2; 1,9] 0,1252[3]
Asia	18/203 (8,9)	5/201 (2,5)	3,56 [1,35; 9,42] 0,0103[2]	3,81 [1,39; 10,48] 0,0057[3]	6,4 [1,9; 10,8] 0,0057[3]
Other	5/402 (1,2)	3/414 (0,7)	1,72 [0,41; 7,13] 0,4574[2]	1,73 [0,41; 7,27] 0,4998[4]	0,5 [-0,8; 1,9] 0,4998[4]
Primary tumor size (Interaction p-value: 0,4421)					
< 20 mm	5/331 (1,5)	2/335 (0,6)	2,53 [0,49; 12,95] 0,2651[2]	2,55 [0,49; 13,26] 0,2839[4]	0,9 [-0,6; 2,5] 0,2839[4]
≥ 20 but < 50 mm	19/646 (2,9)	5/653 (0,8)	3,84 [1,44; 10,23] 0,0071[2]	3,93 [1,46; 10,58] 0,0036[3]	2,2 [0,7; 3,6] 0,0036[3]
≥ 50 mm	8/289 (2,8)	5/265 (1,9)	1,47 [0,49; 4,43] 0,4965[2]	1,48 [0,48; 4,58] 0,4936[3]	0,9 [-1,6; 3,4] 0,4936[3]
Number of positive lymph nodes (Interaction p-value: 0,7563)					
0-3	5/427 (1,2)	1/418 (0,2)	4,89 [0,57; 41,72] 0,1463[2]	4,94 [0,57; 42,47] 0,2172[4]	0,9 [-0,2; 2,1] 0,2172[4]
4-9	13/549 (2,4)	6/542 (1,1)	2,14 [0,82; 5,59] 0,1206[2]	2,17 [0,82; 5,74] 0,1114[3]	1,3 [-0,3; 2,8] 0,1114[3]
≥ 10	15/307 (4,9)	5/305 (1,6)	2,98 [1,10; 8,10] 0,0323[2]	3,08 [1,11; 8,59] 0,0239[3]	3,2 [0,4; 6,0] 0,0239[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9387)					
IIA	0/113 (0,0)	0/114 (0,0)	NE	NE	NE
IIB	3/151 (2,0)	0/136 (0,0)	6,31 [0,33; 121,05] 0,2217[2]	6,43 [0,33; 125,70] 0,2494[4]	2,0 [-0,2; 4,2] 0,2494[4]
IIIA	9/495 (1,8)	5/488 (1,0)	1,77 [0,60; 5,26] 0,3006[2]	1,79 [0,60; 5,38] 0,2938[3]	0,8 [-0,7; 2,3] 0,2938[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	19/468 (4,1)	7/480 (1,5)	2,78 [1,18; 6,56] 0,0192[2]	2,86 [1,19; 6,87] 0,0142[3]	2,6 [0,5; 4,7] 0,0142[3]
Tumor grade (Interaction p-value: 0,6842)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	15/612 (2,5)	9/603 (1,5)	1,64 [0,72; 3,72] 0,2351[2]	1,66 [0,72; 3,82] 0,2300[3]	1,0 [-0,6; 2,5] 0,2300[3]
G3	13/527 (2,5)	3/506 (0,6)	4,16 [1,19; 14,51] 0,0253[2]	4,24 [1,20; 14,97] 0,0148[3]	1,9 [0,4; 3,4] 0,0148[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,9617)					
Negative	5/156 (3,2)	0/169 (0,0)	11,91 [0,66; 213,66] 0,0926[2]	12,31 [0,67; 224,42] 0,0246[4]	3,2 [0,4; 6,0] 0,0246[4]
Positive	27/1089 (2,5)	12/1067 (1,1)	2,20 [1,12; 4,33] 0,0217[2]	2,24 [1,13; 4,44] 0,0183[3]	1,4 [0,2; 2,5] 0,0183[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,7589)					
White	15/958 (1,6)	7/944 (0,7)	2,11 [0,86; 5,16] 0,1008[2]	2,13 [0,86; 5,25] 0,0928[3]	0,8 [-0,1; 1,8] 0,0928[3]
Asian	18/250 (7,2)	5/242 (2,1)	3,48 [1,31; 9,24] 0,0121[2]	3,68 [1,34; 10,07] 0,0070[3]	5,1 [1,5; 8,8] 0,0070[3]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: 0,3664)					
Tamoxifen	2/114 (1,8)	2/132 (1,5)	1,16 [0,17; 8,09] 0,8825[2]	1,16 [0,16; 8,37] 1,0000[4]	0,2 [-2,9; 3,4] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aromatase inhibitor	31/1169 (2,7)	10/1133 (0,9)	3,00 [1,48; 6,10] 0,0023[2]	3,06 [1,49; 6,27] 0,0013[3]	1,8 [0,7; 2,8] 0,0013[3]
ECOG-PS (Interaction p-value: 0,8139)					
ECOG-PS 0	30/1070 (2,8)	11/1020 (1,1)	2,60 [1,31; 5,16] 0,0063[2]	2,65 [1,32; 5,31] 0,0045[3]	1,7 [0,6; 2,9] 0,0045[3]
ECOG-PS 1	3/213 (1,4)	1/245 (0,4)	3,45 [0,36; 32,93] 0,2818[2]	3,49 [0,36; 33,76] 0,3420[4]	1,0 [-0,8; 2,8] 0,3420[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Tabl: Subgroups - adverse events according PT Mucosal inflammation from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6623)					
< 65 years	30/918 (3,3)	8/937 (0,9)	3,83 [1,76; 8,30] 0,0007[2]	3,92 [1,79; 8,60] 0,0002[3]	2,4 [1,1; 3,7] 0,0002[3]
≥ 65 years	7/365 (1,9)	1/328 (0,3)	6,29 [0,78; 50,86] 0,0846[2]	6,39 [0,78; 52,25] 0,0718[4]	1,6 [0,1; 3,1] 0,0718[4]
Prior treatment (Interaction p-value: 0,2715)					
Neoadjuvant chemotherapy	8/430 (1,9)	4/415 (1,0)	1,93 [0,59; 6,36] 0,2798[2]	1,95 [0,58; 6,52] 0,2708[3]	0,9 [-0,7; 2,5] 0,2708[3]
Adjuvant chemotherapy	29/784 (3,7)	4/769 (0,5)	7,11 [2,51; 20,13] 0,0002[2]	7,35 [2,57; 21,00] <,0001[3]	3,2 [1,8; 4,6] <,0001[3]
No chemotherapy	0/69 (0,0)	1/81 (1,2)	0,39 [0,02; 9,43] 0,5628[2]	0,39 [0,02; 9,63] 1,0000[4]	-1,2 [-3,6; 1,2] 1,0000[4]
Region (Interaction p-value: 0,9722)					
North America / Europe	25/678 (3,7)	8/650 (1,2)	3,00 [1,36; 6,59] 0,0064[2]	3,07 [1,38; 6,86] 0,0040[3]	2,5 [0,8; 4,1] 0,0040[3]
Asia	4/203 (2,0)	1/201 (0,5)	3,96 [0,45; 35,13] 0,2165[2]	4,02 [0,45; 36,28] 0,3719[4]	1,5 [-0,7; 3,6] 0,3719[4]
Other	8/402 (2,0)	0/414 (0,0)	17,51 [1,01; 302,30] 0,0489[2]	17,86 [1,03; 310,49] 0,0033[4]	2,0 [0,6; 3,4] 0,0033[4]
Primary tumor size (Interaction p-value: 0,3821)					
< 20 mm	9/331 (2,7)	1/335 (0,3)	9,11 [1,16; 71,50] 0,0356[2]	9,34 [1,18; 74,10] 0,0108[4]	2,4 [0,6; 4,3] 0,0108[4]
≥ 20 but < 50 mm	19/646 (2,9)	4/653 (0,6)	4,80 [1,64; 14,04] 0,0041[2]	4,92 [1,66; 14,53] 0,0015[3]	2,3 [0,9; 3,8] 0,0015[3]
≥ 50 mm	9/289 (3,1)	4/265 (1,5)	2,06 [0,64; 6,62] 0,2234[2]	2,10 [0,64; 6,89] 0,2126[3]	1,6 [-0,9; 4,1] 0,2126[3]
Number of positive lymph nodes (Interaction p-value: 0,8516)					
0-3	15/427 (3,5)	3/418 (0,7)	4,89 [1,43; 16,78] 0,0115[2]	5,04 [1,45; 17,53] 0,0049[3]	2,8 [0,9; 4,7] 0,0049[3]
4-9	9/549 (1,6)	3/542 (0,6)	2,96 [0,81; 10,88] 0,1020[2]	2,99 [0,81; 11,12] 0,0856[3]	1,1 [-0,1; 2,3] 0,0856[3]
≥ 10	13/307 (4,2)	3/305 (1,0)	4,31 [1,24; 14,96] 0,0216[2]	4,45 [1,26; 15,78] 0,0117[3]	3,3 [0,7; 5,8] 0,0117[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9885)					
IIA	4/113 (3,5)	1/114 (0,9)	4,04 [0,46; 35,55] 0,2089[2]	4,15 [0,46; 37,69] 0,2125[4]	2,7 [-1,2; 6,5] 0,2125[4]
IIB	3/151 (2,0)	0/136 (0,0)	6,31 [0,33; 121,05] 0,2217[2]	6,43 [0,33; 125,70] 0,2494[4]	2,0 [-0,2; 4,2] 0,2494[4]
IIIA	12/495 (2,4)	4/488 (0,8)	2,96 [0,96; 9,11] 0,0588[2]	3,01 [0,96; 9,39] 0,0468[3]	1,6 [0,0; 3,2] 0,0468[3]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	18/468 (3,8)	4/480 (0,8)	4,62 [1,57; 13,54] 0,0053[2]	4,76 [1,60; 14,17] 0,0021[3]	3,0 [1,1; 4,9] 0,0021[3]
Tumor grade (Interaction p-value: 0,8846)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	20/612 (3,3)	4/603 (0,7)	4,93 [1,69; 14,33] 0,0034[2]	5,06 [1,72; 14,89] 0,0011[3]	2,6 [1,1; 4,2] 0,0011[3]
G3	14/527 (2,7)	5/506 (1,0)	2,69 [0,98; 7,41] 0,0559[2]	2,73 [0,98; 7,65] 0,0460[3]	1,7 [0,0; 3,3] 0,0460[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,1007)					
Negative	6/156 (3,8)	1/169 (0,6)	6,50 [0,79; 53,39] 0,0815[2]	6,72 [0,80; 56,46] 0,0582[4]	3,3 [0,0; 6,5] 0,0582[4]
Positive	31/1089 (2,8)	8/1067 (0,7)	3,80 [1,75; 8,22] 0,0007[2]	3,88 [1,77; 8,48] 0,0003[3]	2,1 [1,0; 3,2] 0,0003[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9883)					
White	33/958 (3,4)	7/944 (0,7)	4,65 [2,07; 10,45] 0,0002[2]	4,78 [2,10; 10,85] <,0001[3]	2,7 [1,4; 4,0] <,0001[3]
Asian	4/250 (1,6)	1/242 (0,4)	3,87 [0,44; 34,40] 0,2244[2]	3,92 [0,43; 35,31] 0,3728[4]	1,2 [-0,6; 2,9] 0,3728[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,8942)					
ECOG-PS 0	33/1070 (3,1)	8/1020 (0,8)	3,93 [1,83; 8,47] 0,0005[2]	4,03 [1,85; 8,76] 0,0002[3]	2,3 [1,1; 3,5] 0,0002[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	4/213 (1,9)	1/245 (0,4)	4,60 [0,52; 40,85] 0,1707[2]	4,67 [0,52; 42,11] 0,1885[4]	1,5 [-0,5; 3,5] 0,1885[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Muscle spasms from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1602)					
< 65 years	53/918 (5,8)	31/937 (3,3)	1,75 [1,13; 2,69] 0,0119[2]	1,79 [1,14; 2,82] 0,0107[3]	2,5 [0,6; 4,4] 0,0107[3]
≥ 65 years	19/365 (5,2)	17/328 (5,2)	1,00 [0,53; 1,90] 0,9893[2]	1,00 [0,51; 1,97] 0,9893[3]	0,0 [-3,3; 3,3] 0,9893[3]
Prior treatment (Interaction p-value: 0,9956)					
Neoadjuvant chemotherapy	22/430 (5,1)	15/415 (3,6)	1,42 [0,74; 2,69] 0,2890[2]	1,44 [0,74; 2,81] 0,2862[3]	1,5 [-1,2; 4,3] 0,2862[3]
Adjuvant chemotherapy	46/784 (5,9)	33/769 (4,3)	1,37 [0,88; 2,11] 0,1596[2]	1,39 [0,88; 2,20] 0,1576[3]	1,6 [-0,6; 3,8] 0,1576[3]
No chemotherapy	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (Interaction p-value: 0,8144)					
North America / Europe	52/678 (7,7)	36/650 (5,5)	1,38 [0,92; 2,09] 0,1206[2]	1,42 [0,91; 2,20] 0,1186[3]	2,1 [-0,5; 4,8] 0,1186[3]
Asia	7/203 (3,4)	5/201 (2,5)	1,39 [0,45; 4,30] 0,5714[2]	1,40 [0,44; 4,49] 0,5695[3]	1,0 [-2,3; 4,3] 0,5695[3]
Other	13/402 (3,2)	7/414 (1,7)	1,91 [0,77; 4,74] 0,1618[2]	1,94 [0,77; 4,92] 0,1541[3]	1,5 [-0,6; 3,7] 0,1541[3]
Primary tumor size (Interaction p-value: 0,1377)					
< 20 mm	17/331 (5,1)	13/335 (3,9)	1,32 [0,65; 2,68] 0,4365[2]	1,34 [0,64; 2,81] 0,4348[3]	1,3 [-1,9; 4,4] 0,4348[3]
≥ 20 but < 50 mm	33/646 (5,1)	29/653 (4,4)	1,15 [0,71; 1,87] 0,5731[2]	1,16 [0,69; 1,93] 0,5727[3]	0,7 [-1,7; 3,0] 0,5727[3]
≥ 50 mm	21/289 (7,3)	6/265 (2,3)	3,21 [1,32; 7,83] 0,0104[2]	3,38 [1,34; 8,51] 0,0063[3]	5,0 [1,5; 8,5] 0,0063[3]
Number of positive lymph nodes (Interaction p-value: 0,8654)					
0-3	29/427 (6,8)	17/418 (4,1)	1,67 [0,93; 2,99] 0,0849[2]	1,72 [0,93; 3,18] 0,0809[3]	2,7 [-0,3; 5,8] 0,0809[3]
4-9	30/549 (5,5)	22/542 (4,1)	1,35 [0,79; 2,30] 0,2780[2]	1,37 [0,78; 2,40] 0,2760[3]	1,4 [-1,1; 3,9] 0,2760[3]
≥ 10	13/307 (4,2)	9/305 (3,0)	1,44 [0,62; 3,31] 0,3965[2]	1,45 [0,61; 3,45] 0,3937[3]	1,3 [-1,7; 4,2] 0,3937[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,1162)					
IIA	6/113 (5,3)	10/114 (8,8)	0,61 [0,23; 1,61] 0,3144[2]	0,58 [0,20; 1,66] 0,3082[3]	-3,5 [-10,1; 3,2] 0,3082[3]
IIB	13/151 (8,6)	4/136 (2,9)	2,93 [0,98; 8,76] 0,0549[2]	3,11 [0,99; 9,78] 0,0422[3]	5,7 [0,4; 11,0] 0,0422[3]
IIIA	28/495 (5,7)	17/488 (3,5)	1,62 [0,90; 2,93] 0,1070[2]	1,66 [0,90; 3,08] 0,1031[3]	2,2 [-0,4; 4,8] 0,1031[3]
IIIB	2/54 (3,7)	4/45 (8,9)	0,42 [0,08; 2,17] 0,2986[2]	0,39 [0,07; 2,26] 0,4065[4]	-5,2 [-14,9; 4,5] 0,4065[4]
IIIC	23/468 (4,9)	13/480 (2,7)	1,81 [0,93; 3,54] 0,0804[2]	1,86 [0,93; 3,71] 0,0756[3]	2,2 [-0,2; 4,6] 0,0756[3]
Tumor grade (Interaction p-value: 0,7573)					
G1	8/91 (8,8)	4/93 (4,3)	2,04 [0,64; 6,55] 0,2291[2]	2,14 [0,62; 7,39] 0,2175[3]	4,5 [-2,6; 11,6] 0,2175[3]
G2	31/612 (5,1)	24/603 (4,0)	1,27 [0,76; 2,14] 0,3643[2]	1,29 [0,75; 2,22] 0,3629[3]	1,1 [-1,2; 3,4] 0,3629[3]
G3	30/527 (5,7)	19/506 (3,8)	1,52 [0,86; 2,66] 0,1464[2]	1,55 [0,86; 2,79] 0,1430[3]	1,9 [-0,6; 4,5] 0,1430[3]
GX	3/51 (5,9)	1/59 (1,7)	3,47 [0,37; 32,34] 0,2745[2]	3,63 [0,37; 35,99] 0,3349[4]	4,2 [-3,1; 11,4] 0,3349[4]
Race (Interaction p-value: 0,5606)					
White	62/958 (6,5)	39/944 (4,1)	1,57 [1,06; 2,31] 0,0242[2]	1,61 [1,06; 2,42] 0,0229[3]	2,3 [0,3; 4,4] 0,0229[3]
Asian	8/250 (3,2)	7/242 (2,9)	1,11 [0,41; 3,00] 0,8429[2]	1,11 [0,40; 3,11] 0,8428[3]	0,3 [-2,7; 3,3] 0,8428[3]
Other	1/62 (1,6)	2/64 (3,1)	0,52 [0,05; 5,55] 0,5852[2]	0,51 [0,04; 5,75] 1,0000[4]	-1,5 [-6,8; 3,8] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,2670)					
Tamoxifen	7/114 (6,1)	9/132 (6,8)	0,90 [0,35; 2,34] 0,8299[2]	0,89 [0,32; 2,48] 0,8298[3]	-0,7 [-6,8; 5,5] 0,8298[3]
Aromatase inhibitor	65/1169 (5,6)	39/1133 (3,4)	1,62 [1,10; 2,38] 0,0155[2]	1,65 [1,10; 2,48] 0,0144[3]	2,1 [0,4; 3,8] 0,0144[3]
ECOG-PS (Interaction p-value: 0,1489)					
ECOG-PS 0	56/1070 (5,2)	41/1020 (4,0)	1,30 [0,88; 1,93] 0,1888[2]	1,32 [0,87; 1,99] 0,1873[3]	1,2 [-0,6; 3,0] 0,1873[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	16/213 (7,5)	7/245 (2,9)	2,63 [1,10; 6,27] 0,0292[2]	2,76 [1,11; 6,85] 0,0229[3]	4,7 [0,5; 8,8] 0,0229[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Nail disorder from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9813)					
Neoadjuvant chemotherapy	4/430 (0,9)	0/415 (0,0)	8,69 [0,47; 160,84] 0,1466[2]	8,77 [0,47; 163,36] 0,1243[4]	0,9 [0,0; 1,8] 0,1243[4]
Adjuvant chemotherapy	19/784 (2,4)	2/769 (0,3)	9,32 [2,18; 39,87] 0,0026[2]	9,52 [2,21; 41,03] 0,0002[3]	2,2 [1,0; 3,3] 0,0002[3]
No chemotherapy	0/69 (0,0)	0/81 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,4542)					
North America / Europe	16/678 (2,4)	1/650 (0,2)	15,34 [2,04; 115,33] 0,0080[2]	15,69 [2,07; 118,62] 0,0004[3]	2,2 [1,0; 3,4] 0,0004[3]
Asia	5/203 (2,5)	0/201 (0,0)	10,89 [0,61; 195,70] 0,1052[2]	11,17 [0,61; 203,28] 0,0610[4]	2,5 [0,3; 4,6] 0,0610[4]
Other	2/402 (0,5)	1/414 (0,2)	2,06 [0,19; 22,63] 0,5546[2]	2,07 [0,19; 22,86] 0,6191[4]	0,3 [-0,6; 1,1] 0,6191[4]
Primary tumor size (Interaction p-value: 0,9210)					
< 20 mm	6/331 (1,8)	0/335 (0,0)	13,16 [0,74; 232,61] 0,0787[2]	13,40 [0,75; 238,81] 0,0147[4]	1,8 [0,4; 3,2] 0,0147[4]
≥ 20 but < 50 mm	10/646 (1,5)	1/653 (0,2)	10,11 [1,30; 78,74] 0,0272[2]	10,25 [1,31; 80,32] 0,0061[3]	1,4 [0,4; 2,4] 0,0061[3]
≥ 50 mm	6/289 (2,1)	1/265 (0,4)	5,50 [0,67; 45,40] 0,1133[2]	5,60 [0,67; 46,80] 0,1251[4]	1,7 [-0,1; 3,5] 0,1251[4]
Number of positive lymph nodes (Interaction p-value: 0,9643)					
0-3	3/427 (0,7)	2/418 (0,5)	1,47 [0,25; 8,74] 0,6730[2]	1,47 [0,24; 8,85] 1,0000[4]	0,2 [-0,8; 1,3] 1,0000[4]
4-9	12/549 (2,2)	0/542 (0,0)	24,68 [1,46; 415,83] 0,0261[2]	25,23 [1,49; 427,24] 0,0005[3]	2,2 [1,0; 3,4] 0,0005[3]
≥ 10	8/307 (2,6)	0/305 (0,0)	16,89 [0,98; 291,34] 0,0517[2]	17,34 [1,00; 301,77] 0,0075[4]	2,6 [0,8; 4,4] 0,0075[4]
Tumor stage (Interaction p-value: 0,5712)					
IIA	0/113 (0,0)	0/114 (0,0)	NE	NE	NE
IIB	2/151 (1,3)	1/136 (0,7)	1,80 [0,17; 19,64] 0,6293[2]	1,81 [0,16; 20,21] 1,0000[4]	0,6 [-1,7; 2,9] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	10/495 (2,0)	1/488 (0,2)	9,86 [1,27; 76,72] 0,0288[2]	10,04 [1,28; 78,74] 0,0068[3]	1,8 [0,5; 3,1] 0,0068[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	10/468 (2,1)	0/480 (0,0)	21,54 [1,27; 366,49] 0,0338[2]	22,01 [1,29; 376,65] 0,0008[4]	2,1 [0,8; 3,4] 0,0008[4]
Tumor grade (Interaction p-value: 0,9999)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	18/612 (2,9)	0/603 (0,0)	36,46 [2,20; 603,59] 0,0120[2]	37,56 [2,26; 624,68] <,0001[3]	2,9 [1,6; 4,3] <,0001[3]
G3	2/527 (0,4)	2/506 (0,4)	0,96 [0,14; 6,79] 0,9675[2]	0,96 [0,13; 6,84] 1,0000[4]	-0,0 [-0,8; 0,7] 1,0000[4]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,9634)					
Negative	2/156 (1,3)	0/169 (0,0)	5,41 [0,26; 111,90] 0,2744[2]	5,49 [0,26; 115,15] 0,2296[4]	1,3 [-0,5; 3,0] 0,2296[4]
Positive	19/1089 (1,7)	2/1067 (0,2)	9,31 [2,17; 39,86] 0,0026[2]	9,46 [2,20; 40,69] 0,0002[3]	1,6 [0,7; 2,4] 0,0002[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9993)					
White	17/958 (1,8)	1/944 (0,1)	16,75 [2,23; 125,62] 0,0061[2]	17,04 [2,26; 128,27] 0,0002[3]	1,7 [0,8; 2,5] 0,0002[3]
Asian	6/250 (2,4)	0/242 (0,0)	12,59 [0,71; 222,20] 0,0838[2]	12,89 [0,72; 230,13] 0,0304[4]	2,4 [0,5; 4,3] 0,0304[4]
Other	0/62 (0,0)	1/64 (1,6)	0,34 [0,01; 8,28] 0,5109[2]	0,34 [0,01; 8,47] 1,0000[4]	-1,6 [-4,6; 1,5] 1,0000[4]
ECOG-PS (Interaction p-value: 0,0957)					
ECOG-PS 0	22/1070 (2,1)	1/1020 (0,1)	20,97 [2,83; 155,30] 0,0029[2]	21,39 [2,88; 158,99] <,0001[3]	2,0 [1,1; 2,8] <,0001[3]
ECOG-PS 1	1/213 (0,5)	1/245 (0,4)	1,15 [0,07; 18,28] 0,9210[2]	1,15 [0,07; 18,51] 1,0000[4]	0,1 [-1,2; 1,3] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Nausea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8363)					
< 65 years	262/918 (28,5)	68/937 (7,3)	3,93 [3,06; 5,05] <,0001[2]	5,10 [3,84; 6,79] <,0001[3]	21,3 [17,9; 24,6] <,0001[3]
≥ 65 years	121/365 (33,2)	29/328 (8,8)	3,75 [2,57; 5,47] <,0001[2]	5,11 [3,30; 7,93] <,0001[3]	24,3 [18,6; 30,0] <,0001[3]
Prior treatment (Interaction p-value: 0,4923)					
Neoadjuvant chemotherapy	125/430 (29,1)	32/415 (7,7)	3,77 [2,62; 5,43] <,0001[2]	4,91 [3,23; 7,44] <,0001[3]	21,4 [16,4; 26,4] <,0001[3]
Adjuvant chemotherapy	234/784 (29,8)	61/769 (7,9)	3,76 [2,89; 4,90] <,0001[2]	4,94 [3,65; 6,69] <,0001[3]	21,9 [18,2; 25,6] <,0001[3]
No chemotherapy	24/69 (34,8)	4/81 (4,9)	7,04 [2,57; 19,31] 0,0001[2]	10,27 [3,35; 31,48] <,0001[3]	29,8 [17,7; 42,0] <,0001[3]
Region (Interaction p-value: 0,2860)					
North America / Europe	268/678 (39,5)	74/650 (11,4)	3,47 [2,75; 4,39] <,0001[2]	5,09 [3,82; 6,78] <,0001[3]	28,1 [23,7; 32,6] <,0001[3]
Asia	37/203 (18,2)	6/201 (3,0)	6,11 [2,64; 14,15] <,0001[2]	7,24 [2,98; 17,59] <,0001[3]	15,2 [9,4; 21,1] <,0001[3]
Other	78/402 (19,4)	17/414 (4,1)	4,73 [2,85; 7,84] <,0001[2]	5,62 [3,26; 9,69] <,0001[3]	15,3 [11,0; 19,6] <,0001[3]
Primary tumor size (Interaction p-value: 0,9731)					
< 20 mm	99/331 (29,9)	25/335 (7,5)	4,01 [2,66; 6,05] <,0001[2]	5,29 [3,31; 8,47] <,0001[3]	22,4 [16,8; 28,1] <,0001[3]
≥ 20 but < 50 mm	191/646 (29,6)	51/653 (7,8)	3,79 [2,84; 5,05] <,0001[2]	4,96 [3,56; 6,91] <,0001[3]	21,8 [17,7; 25,8] <,0001[3]
≥ 50 mm	90/289 (31,1)	21/265 (7,9)	3,93 [2,52; 6,13] <,0001[2]	5,25 [3,15; 8,76] <,0001[3]	23,2 [17,0; 29,5] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,0789)					
0-3	147/427 (34,4)	29/418 (6,9)	4,96 [3,41; 7,22] <,0001[2]	7,04 [4,60; 10,79] <,0001[3]	27,5 [22,4; 32,6] <,0001[3]
4-9	148/549 (27,0)	49/542 (9,0)	2,98 [2,21; 4,03] <,0001[2]	3,71 [2,62; 5,26] <,0001[3]	17,9 [13,5; 22,3] <,0001[3]
≥ 10	88/307 (28,7)	19/305 (6,2)	4,60 [2,88; 7,36] <,0001[2]	6,05 [3,57; 10,24] <,0001[3]	22,4 [16,7; 28,2] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,2689)					
IIA	39/113 (34,5)	8/114 (7,0)	4,92 [2,41; 10,05] <,0001[2]	6,98 [3,09; 15,80] <,0001[3]	27,5 [17,6; 37,4] <,0001[3]
IIB	50/151 (33,1)	6/136 (4,4)	7,51 [3,32; 16,95] <,0001[2]	10,73 [4,42; 26,01] <,0001[3]	28,7 [20,4; 37,0] <,0001[3]
IIIA	146/495 (29,5)	43/488 (8,8)	3,35 [2,44; 4,59] <,0001[2]	4,33 [3,00; 6,25] <,0001[3]	20,7 [15,9; 25,4] <,0001[3]
IIIB	13/54 (24,1)	5/45 (11,1)	2,17 [0,84; 5,62] 0,1116[2]	2,54 [0,83; 7,77] 0,0959[3]	13,0 [-1,7; 27,6] 0,0959[3]
IIIC	135/468 (28,8)	35/480 (7,3)	3,96 [2,79; 5,61] <,0001[2]	5,15 [3,46; 7,67] <,0001[3]	21,6 [16,8; 26,3] <,0001[3]
Tumor grade (Interaction p-value: 0,1426)					
G1	26/91 (28,6)	5/93 (5,4)	5,31 [2,13; 13,23] 0,0003[2]	7,04 [2,57; 19,32] <,0001[3]	23,2 [12,8; 33,5] <,0001[3]
G2	180/612 (29,4)	60/603 (10,0)	2,96 [2,26; 3,87] <,0001[2]	3,77 [2,74; 5,18] <,0001[3]	19,5 [15,1; 23,8] <,0001[3]
G3	162/527 (30,7)	32/506 (6,3)	4,86 [3,39; 6,96] <,0001[2]	6,57 [4,39; 9,84] <,0001[3]	24,4 [19,9; 28,9] <,0001[3]
GX	15/51 (29,4)	0/59 (0,0)	35,77 [2,19; 583,27] 0,0120[2]	50,53 [2,93; 870,27] <,0001[3]	29,4 [16,9; 41,9] <,0001[3]
Progesterone receptor status (Interaction p-value: 0,9310)					
Negative	53/156 (34,0)	14/169 (8,3)	4,10 [2,37; 7,09] <,0001[2]	5,70 [3,01; 10,80] <,0001[3]	25,7 [17,2; 34,2] <,0001[3]
Positive	313/1089 (28,7)	79/1067 (7,4)	3,88 [3,08; 4,90] <,0001[2]	5,04 [3,87; 6,57] <,0001[3]	21,3 [18,2; 24,5] <,0001[3]
Unknown	4/10 (40,0)	1/7 (14,3)	2,80 [0,39; 20,02] 0,3049[2]	4,00 [0,34; 47,11] 0,3382[4]	25,7 [-14,2; 65,6] 0,3382[4]
Race (Interaction p-value: 0,4204)					
White	315/958 (32,9)	83/944 (8,8)	3,74 [2,99; 4,68] <,0001[2]	5,08 [3,91; 6,61] <,0001[3]	24,1 [20,6; 27,6] <,0001[3]
Asian	41/250 (16,4)	6/242 (2,5)	6,61 [2,86; 15,30] <,0001[2]	7,72 [3,21; 18,54] <,0001[3]	13,9 [8,9; 18,9] <,0001[3]
Other	20/62 (32,3)	6/64 (9,4)	3,44 [1,48; 7,99] 0,0041[2]	4,60 [1,70; 12,45] 0,0015[3]	22,9 [9,2; 36,5] 0,0015[3]
First endocrine therapy (Interaction p-value: 0,5206)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	30/114 (26,3)	7/132 (5,3)	4,96 [2,27; 10,86] <,0001[2]	6,38 [2,68; 15,19] <,0001[3]	21,0 [12,1; 30,0] <,0001[3]
Aromatase inhibitor	353/1169 (30,2)	90/1133 (7,9)	3,80 [3,06; 4,72] <,0001[2]	5,01 [3,91; 6,43] <,0001[3]	22,3 [19,2; 25,3] <,0001[3]
ECOG-PS (Interaction p-value: 0,2930)					
ECOG-PS 0	320/1070 (29,9)	74/1020 (7,3)	4,12 [3,25; 5,23] <,0001[2]	5,45 [4,16; 7,15] <,0001[3]	22,7 [19,5; 25,8] <,0001[3]
ECOG-PS 1	63/213 (29,6)	23/245 (9,4)	3,15 [2,03; 4,90] <,0001[2]	4,05 [2,41; 6,82] <,0001[3]	20,2 [13,1; 27,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Neutropenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4891)					
< 65 years	221/918 (24,1)	24/937 (2,6)	9,40 [6,23; 14,18] <,0001[2]	12,06 [7,83; 18,59] <,0001[3]	21,5 [18,6; 24,5] <,0001[3]
≥ 65 years	74/365 (20,3)	5/328 (1,5)	13,30 [5,44; 32,49] <,0001[2]	16,43 [6,55; 41,20] <,0001[3]	18,7 [14,4; 23,1] <,0001[3]
Prior treatment (Interaction p-value: 0,9880)					
Neoadjuvant chemotherapy	115/430 (26,7)	12/415 (2,9)	9,25 [5,18; 16,50] <,0001[2]	12,26 [6,64; 22,62] <,0001[3]	23,9 [19,4; 28,3] <,0001[3]
Adjuvant chemotherapy	170/784 (21,7)	17/769 (2,2)	9,81 [6,02; 15,99] <,0001[2]	12,25 [7,36; 20,39] <,0001[3]	19,5 [16,4; 22,5] <,0001[3]
No chemotherapy	10/69 (14,5)	0/81 (0,0)	24,60 [1,47; 412,32] 0,0260[2]	28,76 [1,65; 500,60] 0,0003[4]	14,5 [6,2; 22,8] 0,0003[4]
Primary tumor size (Interaction p-value: 0,9199)					
< 20 mm	80/331 (24,2)	8/335 (2,4)	10,12 [4,97; 20,60] <,0001[2]	13,03 [6,18; 27,45] <,0001[3]	21,8 [16,9; 26,7] <,0001[3]
≥ 20 but < 50 mm	133/646 (20,6)	14/653 (2,1)	9,60 [5,60; 16,48] <,0001[2]	11,83 [6,74; 20,77] <,0001[3]	18,4 [15,1; 21,8] <,0001[3]
≥ 50 mm	77/289 (26,6)	6/265 (2,3)	11,77 [5,21; 26,55] <,0001[2]	15,68 [6,70; 36,69] <,0001[3]	24,4 [19,0; 29,8] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,7528)					
0-3	97/427 (22,7)	8/418 (1,9)	11,87 [5,85; 24,10] <,0001[2]	15,06 [7,22; 31,43] <,0001[3]	20,8 [16,6; 25,0] <,0001[3]
4-9	133/549 (24,2)	13/542 (2,4)	10,10 [5,79; 17,63] <,0001[2]	13,01 [7,26; 23,33] <,0001[3]	21,8 [18,0; 25,6] <,0001[3]
≥ 10	65/307 (21,2)	8/305 (2,6)	8,07 [3,94; 16,53] <,0001[2]	9,97 [4,69; 21,19] <,0001[3]	18,5 [13,6; 23,5] <,0001[3]
Tumor stage (Interaction p-value: 0,6048)					
IIA	21/113 (18,6)	3/114 (2,6)	7,06 [2,17; 23,01] 0,0012[2]	8,45 [2,44; 29,21] <,0001[3]	16,0 [8,2; 23,7] <,0001[3]
IIB	38/151 (25,2)	1/136 (0,7)	34,23 [4,76; 245,91] 0,0004[2]	45,40 [6,14; 335,87] <,0001[3]	24,4 [17,4; 31,5] <,0001[3]
IIIA	114/495 (23,0)	10/488 (2,0)	11,24 [5,96; 21,19] <,0001[2]	14,30 [7,39; 27,68] <,0001[3]	21,0 [17,1; 24,9] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	14/54 (25,9)	2/45 (4,4)	5,83 [1,40; 24,32] 0,0155[2]	7,53 [1,61; 35,20] 0,0038[3]	21,5 [8,3; 34,6] 0,0038[3]
IIIC	108/468 (23,1)	13/480 (2,7)	8,52 [4,86; 14,93] <,0001[2]	10,78 [5,96; 19,47] <,0001[3]	20,4 [16,3; 24,5] <,0001[3]
Tumor grade (Interaction p-value: 0,1753)					
G1	18/91 (19,8)	1/93 (1,1)	18,40 [2,51; 134,95] 0,0042[2]	22,68 [2,96; 173,93] <,0001[3]	18,7 [10,3; 27,2] <,0001[3]
G2	139/612 (22,7)	20/603 (3,3)	6,85 [4,34; 10,79] <,0001[2]	8,57 [5,28; 13,90] <,0001[3]	19,4 [15,8; 23,0] <,0001[3]
G3	127/527 (24,1)	7/506 (1,4)	17,42 [8,22; 36,92] <,0001[2]	22,63 [10,46; 48,99] <,0001[3]	22,7 [18,9; 26,5] <,0001[3]
GX	11/51 (21,6)	1/59 (1,7)	12,73 [1,70; 95,21] 0,0132[2]	15,95 [1,98; 128,49] 0,0009[3]	19,9 [8,1; 31,6] 0,0009[3]
Race (Interaction p-value: 0,3960)					
White	243/958 (25,4)	27/944 (2,9)	8,87 [6,02; 13,06] <,0001[2]	11,54 [7,66; 17,38] <,0001[3]	22,5 [19,6; 25,5] <,0001[3]
Asian	32/250 (12,8)	1/242 (0,4)	30,98 [4,27; 224,91] 0,0007[2]	35,38 [4,79; 261,07] <,0001[3]	12,4 [8,2; 16,6] <,0001[3]
Other	17/62 (27,4)	1/64 (1,6)	17,55 [2,41; 127,90] 0,0047[2]	23,80 [3,06; 185,38] <,0001[3]	25,9 [14,3; 37,4] <,0001[3]
First endocrine therapy (Interaction p-value: 0,4820)					
Tamoxifen	28/114 (24,6)	2/132 (1,5)	16,21 [3,95; 66,56] 0,0001[2]	21,16 [4,91; 91,14] <,0001[3]	23,0 [14,9; 31,2] <,0001[3]
Aromatase inhibitor	267/1169 (22,8)	27/1133 (2,4)	9,58 [6,51; 14,12] <,0001[2]	12,13 [8,08; 18,19] <,0001[3]	20,5 [17,9; 23,0] <,0001[3]
ECOG-PS (Interaction p-value: 0,2859)					
ECOG-PS 0	238/1070 (22,2)	20/1020 (2,0)	11,34 [7,25; 17,76] <,0001[2]	14,30 [8,98; 22,78] <,0001[3]	20,3 [17,6; 22,9] <,0001[3]
ECOG-PS 1	57/213 (26,8)	9/245 (3,7)	7,28 [3,70; 14,36] <,0001[2]	9,58 [4,61; 19,91] <,0001[3]	23,1 [16,7; 29,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Neutrophil count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1769)					
< 65 years	198/918 (21,6)	19/937 (2,0)	10,64 [6,70; 16,88] <,0001[2]	13,29 [8,22; 21,49] <,0001[3]	19,5 [16,7; 22,4] <,0001[3]
≥ 65 years	83/365 (22,7)	3/328 (0,9)	24,86 [7,93; 77,91] <,0001[2]	31,89 [9,97; 102,00] <,0001[3]	21,8 [17,4; 26,2] <,0001[3]
Prior treatment (Interaction p-value: 0,3434)					
Neoadjuvant chemotherapy	95/430 (22,1)	11/415 (2,7)	8,34 [4,53; 15,33] <,0001[2]	10,42 [5,49; 19,77] <,0001[3]	19,4 [15,2; 23,7] <,0001[3]
Adjuvant chemotherapy	177/784 (22,6)	11/769 (1,4)	15,78 [8,65; 28,78] <,0001[2]	20,09 [10,83; 37,29] <,0001[3]	21,1 [18,1; 24,2] <,0001[3]
No chemotherapy	9/69 (13,0)	0/81 (0,0)	22,26 [1,32; 375,60] 0,0314[2]	25,60 [1,46; 448,36] 0,0007[4]	13,0 [5,1; 21,0] 0,0007[4]
Region (Interaction p-value: 0,5243)					
North America / Europe	105/678 (15,5)	6/650 (0,9)	16,78 [7,42; 37,93] <,0001[2]	19,67 [8,57; 45,12] <,0001[3]	14,6 [11,7; 17,4] <,0001[3]
Asia	119/203 (58,6)	12/201 (6,0)	9,82 [5,60; 17,20] <,0001[2]	22,31 [11,68; 42,61] <,0001[3]	52,7 [45,1; 60,2] <,0001[3]
Other	57/402 (14,2)	4/414 (1,0)	14,68 [5,37; 40,07] <,0001[2]	16,93 [6,08; 47,14] <,0001[3]	13,2 [9,7; 16,8] <,0001[3]
Primary tumor size (Interaction p-value: 0,1695)					
< 20 mm	65/331 (19,6)	9/335 (2,7)	7,31 [3,70; 14,43] <,0001[2]	8,85 [4,33; 18,11] <,0001[3]	17,0 [12,3; 21,6] <,0001[3]
≥ 20 but < 50 mm	156/646 (24,1)	9/653 (1,4)	17,52 [9,03; 34,00] <,0001[2]	22,78 [11,52; 45,06] <,0001[3]	22,8 [19,4; 26,2] <,0001[3]
≥ 50 mm	53/289 (18,3)	3/265 (1,1)	16,20 [5,12; 51,22] <,0001[2]	19,61 [6,05; 63,60] <,0001[3]	17,2 [12,6; 21,8] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,5321)					
0-3	85/427 (19,9)	6/418 (1,4)	13,87 [6,13; 31,39] <,0001[2]	17,07 [7,37; 39,54] <,0001[3]	18,5 [14,5; 22,4] <,0001[3]
4-9	121/549 (22,0)	12/542 (2,2)	9,95 [5,57; 17,80] <,0001[2]	12,49 [6,81; 22,90] <,0001[3]	19,8 [16,1; 23,5] <,0001[3]
≥ 10	75/307 (24,4)	4/305 (1,3)	18,63 [6,90; 50,29] <,0001[2]	24,33 [8,77; 67,48] <,0001[3]	23,1 [18,1; 28,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8583)					
IIA	25/113 (22,1)	1/114 (0,9)	25,22 [3,48; 183,00] 0,0014[2]	32,10 [4,27; 241,54] <,0001[3]	21,2 [13,4; 29,1] <,0001[3]
IIB	35/151 (23,2)	4/136 (2,9)	7,88 [2,88; 21,60] <,0001[2]	9,96 [3,44; 28,86] <,0001[3]	20,2 [12,9; 27,5] <,0001[3]
IIIA	104/495 (21,0)	8/488 (1,6)	12,82 [6,31; 26,02] <,0001[2]	15,96 [7,68; 33,16] <,0001[3]	19,4 [15,6; 23,1] <,0001[3]
IIIB	13/54 (24,1)	1/45 (2,2)	10,83 [1,47; 79,66] 0,0192[2]	13,95 [1,75; 111,45] 0,0019[3]	21,9 [9,7; 34,0] 0,0019[3]
IIIC	103/468 (22,0)	8/480 (1,7)	13,21 [6,51; 26,81] <,0001[2]	16,65 [8,01; 34,63] <,0001[3]	20,3 [16,4; 24,3] <,0001[3]
Tumor grade (Interaction p-value: 0,2095)					
G1	16/91 (17,6)	1/93 (1,1)	16,35 [2,21; 120,76] 0,0062[2]	19,63 [2,54; 151,42] 0,0001[3]	16,5 [8,4; 24,6] 0,0001[3]
G2	121/612 (19,8)	6/603 (1,0)	19,87 [8,82; 44,76] <,0001[2]	24,52 [10,71; 56,14] <,0001[3]	18,8 [15,5; 22,0] <,0001[3]
G3	126/527 (23,9)	11/506 (2,2)	11,00 [6,01; 20,12] <,0001[2]	14,14 [7,53; 26,55] <,0001[3]	21,7 [17,9; 25,6] <,0001[3]
GX	17/51 (33,3)	4/59 (6,8)	4,92 [1,77; 13,67] 0,0023[2]	6,88 [2,13; 22,15] 0,0004[3]	26,6 [12,1; 41,0] 0,0004[3]
Race (Interaction p-value: 0,7209)					
White	143/958 (14,9)	10/944 (1,1)	14,09 [7,47; 26,58] <,0001[2]	16,39 [8,57; 31,33] <,0001[3]	13,9 [11,5; 16,2] <,0001[3]
Asian	123/250 (49,2)	12/242 (5,0)	9,92 [5,63; 17,47] <,0001[2]	18,56 [9,88; 34,89] <,0001[3]	44,2 [37,5; 51,0] <,0001[3]
Other	13/62 (21,0)	0/64 (0,0)	27,86 [1,69; 458,71] 0,0199[2]	35,18 [2,04; 606,31] 0,0001[3]	21,0 [10,8; 31,1] 0,0001[3]
First endocrine therapy (Interaction p-value: 0,1084)					
Tamoxifen	19/114 (16,7)	4/132 (3,0)	5,50 [1,93; 15,70] 0,0014[2]	6,40 [2,11; 19,43] 0,0002[3]	13,6 [6,2; 21,1] 0,0002[3]
Aromatase inhibitor	262/1169 (22,4)	18/1133 (1,6)	14,11 [8,81; 22,58] <,0001[2]	17,89 [11,01; 29,08] <,0001[3]	20,8 [18,3; 23,3] <,0001[3]
ECOG-PS (Interaction p-value: 0,8172)					
ECOG-PS 0	244/1070 (22,8)	19/1020 (1,9)	12,24 [7,74; 19,37] <,0001[2]	15,56 [9,67; 25,05] <,0001[3]	20,9 [18,3; 23,6] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	37/213 (17,4)	3/245 (1,2)	14,19 [4,44; 45,35] <,0001[2]	16,96 [5,15; 55,88] <,0001[3]	16,1 [10,9; 21,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Oedema peripheral from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6710)					
< 65 years	58/918 (6,3)	33/937 (3,5)	1,79 [1,18; 2,72] 0,0061[2]	1,85 [1,19; 2,86] 0,0053[3]	2,8 [0,8; 4,8] 0,0053[3]
≥ 65 years	35/365 (9,6)	15/328 (4,6)	2,10 [1,17; 3,77] 0,0133[2]	2,21 [1,19; 4,13] 0,0108[3]	5,0 [1,2; 8,8] 0,0108[3]
Prior treatment (Interaction p-value: 0,5552)					
Neoadjuvant chemotherapy	30/430 (7,0)	11/415 (2,7)	2,63 [1,34; 5,18] 0,0051[2]	2,75 [1,36; 5,57] 0,0034[3]	4,3 [1,5; 7,2] 0,0034[3]
Adjuvant chemotherapy	56/784 (7,1)	32/769 (4,2)	1,72 [1,12; 2,62] 0,0123[2]	1,77 [1,13; 2,77] 0,0111[3]	3,0 [0,7; 5,3] 0,0111[3]
No chemotherapy	7/69 (10,1)	5/81 (6,2)	1,64 [0,55; 4,95] 0,3768[2]	1,72 [0,52; 5,67] 0,3715[3]	4,0 [-4,9; 12,8] 0,3715[3]
Region (Interaction p-value: 0,7172)					
North America / Europe	51/678 (7,5)	28/650 (4,3)	1,75 [1,12; 2,73] 0,0148[2]	1,81 [1,12; 2,90] 0,0133[3]	3,2 [0,7; 5,7] 0,0133[3]
Asia	16/203 (7,9)	9/201 (4,5)	1,76 [0,80; 3,89] 0,1622[2]	1,83 [0,79; 4,23] 0,1556[3]	3,4 [-1,3; 8,1] 0,1556[3]
Other	26/402 (6,5)	11/414 (2,7)	2,43 [1,22; 4,86] 0,0117[2]	2,53 [1,23; 5,20] 0,0089[3]	3,8 [1,0; 6,7] 0,0089[3]
Primary tumor size (Interaction p-value: 0,5834)					
< 20 mm	30/331 (9,1)	12/335 (3,6)	2,53 [1,32; 4,86] 0,0053[2]	2,68 [1,35; 5,34] 0,0036[3]	5,5 [1,8; 9,2] 0,0036[3]
≥ 20 but < 50 mm	46/646 (7,1)	28/653 (4,3)	1,66 [1,05; 2,62] 0,0296[2]	1,71 [1,06; 2,77] 0,0276[3]	2,8 [0,3; 5,4] 0,0276[3]
≥ 50 mm	15/289 (5,2)	7/265 (2,6)	1,96 [0,81; 4,74] 0,1332[2]	2,02 [0,81; 5,03] 0,1249[3]	2,5 [-0,7; 5,8] 0,1249[3]
Number of positive lymph nodes (Interaction p-value: 0,9450)					
0-3	27/427 (6,3)	15/418 (3,6)	1,76 [0,95; 3,26] 0,0718[2]	1,81 [0,95; 3,46] 0,0674[3]	2,7 [-0,2; 5,7] 0,0674[3]
4-9	41/549 (7,5)	20/542 (3,7)	2,02 [1,20; 3,41] 0,0080[2]	2,11 [1,22; 3,65] 0,0066[3]	3,8 [1,1; 6,5] 0,0066[3]
≥ 10	25/307 (8,1)	13/305 (4,3)	1,91 [1,00; 3,66] 0,0514[2]	1,99 [1,00; 3,97] 0,0467[3]	3,9 [0,1; 7,7] 0,0467[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7053)					
IIA	9/113 (8,0)	4/114 (3,5)	2,27 [0,72; 7,16] 0,1619[2]	2,38 [0,71; 7,96] 0,1486[3]	4,5 [-1,6; 10,5] 0,1486[3]
IIB	8/151 (5,3)	6/136 (4,4)	1,20 [0,43; 3,37] 0,7283[2]	1,21 [0,41; 3,59] 0,7278[3]	0,9 [-4,1; 5,9] 0,7278[3]
IIIA	36/495 (7,3)	18/488 (3,7)	1,97 [1,14; 3,42] 0,0159[2]	2,05 [1,15; 3,66] 0,0137[3]	3,6 [0,8; 6,4] 0,0137[3]
IIIB	3/54 (5,6)	3/45 (6,7)	0,83 [0,18; 3,93] 0,8177[2]	0,82 [0,16; 4,29] 1,0000[4]	-1,1 [-10,6; 8,4] 1,0000[4]
IIIC	36/468 (7,7)	17/480 (3,5)	2,17 [1,24; 3,81] 0,0069[2]	2,27 [1,26; 4,10] 0,0054[3]	4,2 [1,2; 7,1] 0,0054[3]
Tumor grade (Interaction p-value: 0,5440)					
G1	7/91 (7,7)	5/93 (5,4)	1,43 [0,47; 4,34] 0,5273[2]	1,47 [0,45; 4,80] 0,5247[3]	2,3 [-4,8; 9,5] 0,5247[3]
G2	41/612 (6,7)	18/603 (3,0)	2,24 [1,30; 3,86] 0,0035[2]	2,33 [1,32; 4,11] 0,0026[3]	3,7 [1,3; 6,1] 0,0026[3]
G3	40/527 (7,6)	24/506 (4,7)	1,60 [0,98; 2,62] 0,0606[2]	1,65 [0,98; 2,78] 0,0578[3]	2,8 [-0,1; 5,8] 0,0578[3]
GX	5/51 (9,8)	1/59 (1,7)	5,78 [0,70; 47,91] 0,1037[2]	6,30 [0,71; 55,86] 0,0942[4]	8,1 [-0,7; 16,9] 0,0942[4]
Race (Interaction p-value: 0,8260)					
White	67/958 (7,0)	35/944 (3,7)	1,89 [1,27; 2,81] 0,0018[2]	1,95 [1,28; 2,97] 0,0015[3]	3,3 [1,3; 5,3] 0,0015[3]
Asian	16/250 (6,4)	9/242 (3,7)	1,72 [0,78; 3,82] 0,1821[2]	1,77 [0,77; 4,09] 0,1758[3]	2,7 [-1,2; 6,5] 0,1758[3]
Other	8/62 (12,9)	3/64 (4,7)	2,75 [0,77; 9,90] 0,1211[2]	3,01 [0,76; 11,93] 0,1024[3]	8,2 [-1,6; 18,0] 0,1024[3]
First endocrine therapy (Interaction p-value: 0,7681)					
Tamoxifen	6/114 (5,3)	3/132 (2,3)	2,32 [0,59; 9,05] 0,2272[2]	2,39 [0,58; 9,78] 0,3097[4]	3,0 [-1,8; 7,8] 0,3097[4]
Aromatase inhibitor	87/1169 (7,4)	45/1133 (4,0)	1,87 [1,32; 2,66] 0,0004[2]	1,94 [1,34; 2,81] 0,0003[3]	3,5 [1,6; 5,4] 0,0003[3]
ECOG-PS (Interaction p-value: 0,6512)					
ECOG-PS 0	74/1070 (6,9)	35/1020 (3,4)	2,02 [1,36; 2,99] 0,0005[2]	2,09 [1,39; 3,16] 0,0003[3]	3,5 [1,6; 5,4] 0,0003[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	19/213 (8,9)	13/245 (5,3)	1,68 [0,85; 3,32] 0,1350[2]	1,75 [0,84; 3,63] 0,1302[3]	3,6 [-1,1; 8,4] 0,1302[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Onychoclasis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6190)					
< 65 years	17/918 (1,9)	2/937 (0,2)	8,68 [2,01; 37,45] 0,0038[2]	8,82 [2,03; 38,29] 0,0005[3]	1,6 [0,7; 2,6] 0,0005[3]
≥ 65 years	5/365 (1,4)	1/328 (0,3)	4,49 [0,53; 38,26] 0,1691[2]	4,54 [0,53; 39,08] 0,2207[4]	1,1 [-0,3; 2,4] 0,2207[4]
Prior treatment (Interaction p-value: 0,9941)					
Neoadjuvant chemotherapy	7/430 (1,6)	1/415 (0,2)	6,76 [0,83; 54,67] 0,0733[2]	6,85 [0,84; 55,93] 0,0694[4]	1,4 [0,1; 2,7] 0,0694[4]
Adjuvant chemotherapy	12/784 (1,5)	2/769 (0,3)	5,89 [1,32; 26,21] 0,0200[2]	5,96 [1,33; 26,72] 0,0081[3]	1,3 [0,3; 2,2] 0,0081[3]
No chemotherapy	3/69 (4,3)	0/81 (0,0)	8,20 [0,43; 156,04] 0,1615[2]	8,58 [0,44; 169,04] 0,0950[4]	4,3 [-0,5; 9,2] 0,0950[4]
Region (Interaction p-value: 0,9780)					
North America / Europe	20/678 (2,9)	3/650 (0,5)	6,39 [1,91; 21,41] 0,0026[2]	6,56 [1,94; 22,17] 0,0005[3]	2,5 [1,1; 3,9] 0,0005[3]
Asia	0/203 (0,0)	0/201 (0,0)	NE	NE	NE
Other	2/402 (0,5)	0/414 (0,0)	5,15 [0,25; 106,92] 0,2896[2]	5,17 [0,25; 108,12] 0,2424[4]	0,5 [-0,2; 1,2] 0,2424[4]
Primary tumor size (Interaction p-value: 0,8909)					
< 20 mm	8/331 (2,4)	1/335 (0,3)	8,10 [1,02; 64,38] 0,0480[2]	8,27 [1,03; 66,51] 0,0200[4]	2,1 [0,4; 3,9] 0,0200[4]
≥ 20 but < 50 mm	9/646 (1,4)	1/653 (0,2)	9,10 [1,16; 71,60] 0,0359[2]	9,21 [1,16; 72,92] 0,0110[4]	1,2 [0,3; 2,2] 0,0110[4]
≥ 50 mm	5/289 (1,7)	1/265 (0,4)	4,58 [0,54; 38,99] 0,1632[2]	4,65 [0,54; 40,04] 0,2189[4]	1,4 [-0,3; 3,0] 0,2189[4]
Number of positive lymph nodes (Interaction p-value: 0,8058)					
0-3	11/427 (2,6)	1/418 (0,2)	10,77 [1,40; 83,03] 0,0226[2]	11,03 [1,42; 85,79] 0,0041[3]	2,3 [0,8; 3,9] 0,0041[3]
4-9	4/549 (0,7)	1/542 (0,2)	3,95 [0,44; 35,22] 0,2186[2]	3,97 [0,44; 35,64] 0,3739[4]	0,5 [-0,3; 1,3] 0,3739[4]
≥ 10	7/307 (2,3)	1/305 (0,3)	6,95 [0,86; 56,19] 0,0689[2]	7,09 [0,87; 58,00] 0,0685[4]	2,0 [0,2; 3,7] 0,0685[4]
Tumor stage (Interaction p-value: 0,9556)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIA	3/113 (2,7)	0/114 (0,0)	7,06 [0,37; 135,16] 0,1943[2]	7,25 [0,37; 142,05] 0,1217[4]	2,7 [-0,3; 5,6] 0,1217[4]
IIB	3/151 (2,0)	1/136 (0,7)	2,70 [0,28; 25,67] 0,3868[2]	2,74 [0,28; 26,62] 0,6244[4]	1,3 [-1,4; 3,9] 0,6244[4]
IIIA	7/495 (1,4)	1/488 (0,2)	6,90 [0,85; 55,88] 0,0703[2]	6,99 [0,86; 56,99] 0,0693[4]	1,2 [0,1; 2,3] 0,0693[4]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	9/468 (1,9)	1/480 (0,2)	9,23 [1,17; 72,57] 0,0346[2]	9,39 [1,19; 74,43] 0,0104[4]	1,7 [0,4; 3,0] 0,0104[4]
Tumor grade (Interaction p-value: 0,9991)					
G1	0/91 (0,0)	1/93 (1,1)	0,34 [0,01; 8,25] 0,5078[2]	0,34 [0,01; 8,38] 1,0000[4]	-1,1 [-3,2; 1,0] 1,0000[4]
G2	15/612 (2,5)	0/603 (0,0)	30,54 [1,83; 509,34] 0,0172[2]	31,31 [1,87; 524,48] 0,0001[3]	2,5 [1,2; 3,7] 0,0001[3]
G3	7/527 (1,3)	2/506 (0,4)	3,36 [0,70; 16,10] 0,1294[2]	3,39 [0,70; 16,41] 0,1786[4]	0,9 [-0,2; 2,1] 0,1786[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9644)					
Negative	2/156 (1,3)	0/169 (0,0)	5,41 [0,26; 111,90] 0,2744[2]	5,49 [0,26; 115,15] 0,2296[4]	1,3 [-0,5; 3,0] 0,2296[4]
Positive	18/1089 (1,7)	3/1067 (0,3)	5,88 [1,74; 19,90] 0,0044[2]	5,96 [1,75; 20,30] 0,0012[3]	1,4 [0,6; 2,2] 0,0012[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9853)					
White	21/958 (2,2)	3/944 (0,3)	6,90 [2,06; 23,05] 0,0017[2]	7,03 [2,09; 23,65] 0,0003[3]	1,9 [0,9; 2,9] 0,0003[3]
Asian	1/250 (0,4)	0/242 (0,0)	2,90 [0,12; 70,95] 0,5132[2]	2,92 [0,12; 71,93] 1,0000[4]	0,4 [-0,4; 1,2] 1,0000[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: 0,3153)					
Tamoxifen	2/114 (1,8)	1/132 (0,8)	2,32 [0,21; 25,21] 0,4906[2]	2,34 [0,21; 26,14] 0,5979[4]	1,0 [-1,8; 3,8] 0,5979[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aromatase inhibitor	20/1169 (1,7)	2/1133 (0,2)	9,69 [2,27; 41,37] 0,0022[2]	9,84 [2,30; 42,21] 0,0002[3]	1,5 [0,8; 2,3] 0,0002[3]
ECOG-PS (Interaction p-value: 0,3196)					
ECOG-PS 0	20/1070 (1,9)	2/1020 (0,2)	9,53 [2,23; 40,68] 0,0023[2]	9,70 [2,26; 41,58] 0,0002[3]	1,7 [0,8; 2,5] 0,0002[3]
ECOG-PS 1	2/213 (0,9)	1/245 (0,4)	2,30 [0,21; 25,19] 0,4951[2]	2,31 [0,21; 25,69] 0,5998[4]	0,5 [-1,0; 2,1] 0,5998[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Oral herpes from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6291)					
< 65 years	11/918 (1,2)	3/937 (0,3)	3,74 [1,05; 13,37] 0,0422[2]	3,78 [1,05; 13,58] 0,0289[3]	0,9 [0,1; 1,7] 0,0289[3]
≥ 65 years	5/365 (1,4)	2/328 (0,6)	2,25 [0,44; 11,50] 0,3313[2]	2,26 [0,44; 11,75] 0,4555[4]	0,8 [-0,7; 2,2] 0,4555[4]
Prior treatment (Interaction p-value: 0,9995)					
Neoadjuvant chemotherapy	6/430 (1,4)	2/415 (0,5)	2,90 [0,59; 14,26] 0,1913[2]	2,92 [0,59; 14,56] 0,2873[4]	0,9 [-0,4; 2,2] 0,2873[4]
Adjuvant chemotherapy	9/784 (1,1)	3/769 (0,4)	2,94 [0,80; 10,83] 0,1044[2]	2,97 [0,80; 10,99] 0,0881[3]	0,8 [-0,1; 1,6] 0,0881[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Primary tumor size (Interaction p-value: 0,7506)					
< 20 mm	4/331 (1,2)	0/335 (0,0)	9,11 [0,49; 168,51] 0,1378[2]	9,22 [0,49; 171,93] 0,0605[4]	1,2 [0,0; 2,4] 0,0605[4]
≥ 20 but < 50 mm	7/646 (1,1)	4/653 (0,6)	1,77 [0,52; 6,01] 0,3609[2]	1,78 [0,52; 6,10] 0,3543[3]	0,5 [-0,5; 1,5] 0,3543[3]
≥ 50 mm	5/289 (1,7)	1/265 (0,4)	4,58 [0,54; 38,99] 0,1632[2]	4,65 [0,54; 40,04] 0,2189[4]	1,4 [-0,3; 3,0] 0,2189[4]
Number of positive lymph nodes (Interaction p-value: 0,6521)					
0-3	9/427 (2,1)	2/418 (0,5)	4,41 [0,96; 20,27] 0,0569[2]	4,48 [0,96; 20,85] 0,0367[3]	1,6 [0,1; 3,1] 0,0367[3]
4-9	6/549 (1,1)	2/542 (0,4)	2,96 [0,60; 14,61] 0,1824[2]	2,98 [0,60; 14,85] 0,2873[4]	0,7 [-0,3; 1,7] 0,2873[4]
≥ 10	1/307 (0,3)	1/305 (0,3)	0,99 [0,06; 15,81] 0,9963[2]	0,99 [0,06; 15,96] 1,0000[4]	-0,0 [-0,9; 0,9] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,9624)					
Negative	4/156 (2,6)	0/169 (0,0)	9,75 [0,53; 179,55] 0,1256[2]	10,00 [0,53; 187,32] 0,0520[4]	2,6 [0,1; 5,0] 0,0520[4]
Positive	12/1089 (1,1)	5/1067 (0,5)	2,35 [0,83; 6,65] 0,1070[2]	2,37 [0,83; 6,74] 0,0964[3]	0,6 [-0,1; 1,4] 0,0964[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9576)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
White	13/958 (1,4)	3/944 (0,3)	4,27 [1,22; 14,94] 0,0231[2]	4,31 [1,23; 15,19] 0,0131[3]	1,0 [0,2; 1,9] 0,0131[3]
Asian	3/250 (1,2)	1/242 (0,4)	2,90 [0,30; 27,73] 0,3544[2]	2,93 [0,30; 28,34] 0,6237[4]	0,8 [-0,8; 2,4] 0,6237[4]
Other	0/62 (0,0)	1/64 (1,6)	0,34 [0,01; 8,28] 0,5109[2]	0,34 [0,01; 8,47] 1,0000[4]	-1,6 [-4,6; 1,5] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,5297)					
Tamoxifen	5/114 (4,4)	1/132 (0,8)	5,79 [0,69; 48,83] 0,1065[2]	6,01 [0,69; 52,21] 0,0988[4]	3,6 [-0,4; 7,7] 0,0988[4]
Aromatase inhibitor	11/1169 (0,9)	4/1133 (0,4)	2,67 [0,85; 8,35] 0,0923[2]	2,68 [0,85; 8,44] 0,0796[3]	0,6 [-0,1; 1,2] 0,0796[3]
ECOG-PS (Interaction p-value: 0,9331)					
ECOG-PS 0	13/1070 (1,2)	4/1020 (0,4)	3,10 [1,01; 9,47] 0,0473[2]	3,12 [1,02; 9,61] 0,0363[3]	0,8 [0,1; 1,6] 0,0363[3]
ECOG-PS 1	3/213 (1,4)	1/245 (0,4)	3,45 [0,36; 32,93] 0,2818[2]	3,49 [0,36; 33,76] 0,3420[4]	1,0 [-0,8; 2,8] 0,3420[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Oropharyngeal pain from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1609)					
< 65 years	33/918 (3,6)	26/937 (2,8)	1,30 [0,78; 2,15] 0,3158[2]	1,31 [0,78; 2,20] 0,3143[3]	0,8 [-0,8; 2,4] 0,3143[3]
≥ 65 years	16/365 (4,4)	5/328 (1,5)	2,88 [1,07; 7,76] 0,0371[2]	2,96 [1,07; 8,18] 0,0284[3]	2,9 [0,4; 5,3] 0,0284[3]
Prior treatment (Interaction p-value: 0,6185)					
Neoadjuvant chemotherapy	22/430 (5,1)	12/415 (2,9)	1,77 [0,89; 3,53] 0,1052[2]	1,81 [0,88; 3,71] 0,0999[3]	2,2 [-0,4; 4,9] 0,0999[3]
Adjuvant chemotherapy	24/784 (3,1)	18/769 (2,3)	1,31 [0,72; 2,39] 0,3830[2]	1,32 [0,71; 2,45] 0,3815[3]	0,7 [-0,9; 2,3] 0,3815[3]
No chemotherapy	3/69 (4,3)	1/81 (1,2)	3,52 [0,37; 33,09] 0,2707[2]	3,64 [0,37; 35,78] 0,3343[4]	3,1 [-2,3; 8,5] 0,3343[4]
Region (Interaction p-value: 0,2567)					
North America / Europe	35/678 (5,2)	20/650 (3,1)	1,68 [0,98; 2,88] 0,0598[2]	1,71 [0,98; 3,00] 0,0566[3]	2,1 [-0,0; 4,2] 0,0566[3]
Asia	6/203 (3,0)	8/201 (4,0)	0,74 [0,26; 2,10] 0,5751[2]	0,73 [0,25; 2,16] 0,5735[3]	-1,0 [-4,6; 2,5] 0,5735[3]
Other	8/402 (2,0)	3/414 (0,7)	2,75 [0,73; 10,28] 0,1335[2]	2,78 [0,73; 10,56] 0,1171[3]	1,3 [-0,3; 2,9] 0,1171[3]
Primary tumor size (Interaction p-value: 0,8828)					
< 20 mm	13/331 (3,9)	7/335 (2,1)	1,88 [0,76; 4,65] 0,1723[2]	1,92 [0,75; 4,86] 0,1647[3]	1,8 [-0,8; 4,4] 0,1647[3]
≥ 20 but < 50 mm	24/646 (3,7)	16/653 (2,5)	1,52 [0,81; 2,83] 0,1905[2]	1,54 [0,81; 2,92] 0,1870[3]	1,3 [-0,6; 3,1] 0,1870[3]
≥ 50 mm	12/289 (4,2)	8/265 (3,0)	1,38 [0,57; 3,31] 0,4772[2]	1,39 [0,56; 3,46] 0,4750[3]	1,1 [-2,0; 4,2] 0,4750[3]
Number of positive lymph nodes (Interaction p-value: 0,5920)					
0-3	21/427 (4,9)	12/418 (2,9)	1,71 [0,85; 3,44] 0,1297[2]	1,75 [0,85; 3,60] 0,1246[3]	2,0 [-0,6; 4,6] 0,1246[3]
4-9	20/549 (3,6)	11/542 (2,0)	1,79 [0,87; 3,71] 0,1143[2]	1,83 [0,87; 3,85] 0,1088[3]	1,6 [-0,4; 3,6] 0,1088[3]
≥ 10	8/307 (2,6)	8/305 (2,6)	0,99 [0,38; 2,61] 0,9894[2]	0,99 [0,37; 2,68] 0,9894[3]	-0,0 [-2,5; 2,5] 0,9894[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9953)					
IIA	7/113 (6,2)	4/114 (3,5)	1,77 [0,53; 5,87] 0,3534[2]	1,82 [0,52; 6,38] 0,3461[3]	2,7 [-2,9; 8,3] 0,3461[3]
IIB	6/151 (4,0)	4/136 (2,9)	1,35 [0,39; 4,69] 0,6354[2]	1,37 [0,38; 4,95] 0,7530[4]	1,0 [-3,2; 5,2] 0,7530[4]
IIIA	17/495 (3,4)	10/488 (2,0)	1,68 [0,78; 3,62] 0,1893[2]	1,70 [0,77; 3,75] 0,1840[3]	1,4 [-0,7; 3,4] 0,1840[3]
IIIB	3/54 (5,6)	2/45 (4,4)	1,25 [0,22; 7,16] 0,8021[2]	1,26 [0,20; 7,92] 1,0000[4]	1,1 [-7,5; 9,7] 1,0000[4]
IIIC	16/468 (3,4)	11/480 (2,3)	1,49 [0,70; 3,18] 0,3004[2]	1,51 [0,69; 3,29] 0,2969[3]	1,1 [-1,0; 3,2] 0,2969[3]
Tumor grade (Interaction p-value: 0,9304)					
G1	1/91 (1,1)	0/93 (0,0)	3,07 [0,13; 74,28] 0,4910[2]	3,10 [0,12; 77,08] 0,4946[4]	1,1 [-1,0; 3,2] 0,4946[4]
G2	26/612 (4,2)	15/603 (2,5)	1,71 [0,91; 3,19] 0,0935[2]	1,74 [0,91; 3,32] 0,0892[3]	1,8 [-0,3; 3,8] 0,0892[3]
G3	21/527 (4,0)	16/506 (3,2)	1,26 [0,67; 2,39] 0,4780[2]	1,27 [0,66; 2,46] 0,4769[3]	0,8 [-1,4; 3,1] 0,4769[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,1352)					
Negative	11/156 (7,1)	5/169 (3,0)	2,38 [0,85; 6,71] 0,0999[2]	2,49 [0,84; 7,33] 0,0884[3]	4,1 [-0,7; 8,9] 0,0884[3]
Positive	38/1089 (3,5)	26/1067 (2,4)	1,43 [0,88; 2,34] 0,1523[2]	1,45 [0,87; 2,40] 0,1499[3]	1,1 [-0,4; 2,5] 0,1499[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,5494)					
White	37/958 (3,9)	23/944 (2,4)	1,59 [0,95; 2,65] 0,0782[2]	1,61 [0,95; 2,73] 0,0753[3]	1,4 [-0,1; 3,0] 0,0753[3]
Asian	7/250 (2,8)	8/242 (3,3)	0,85 [0,31; 2,30] 0,7446[2]	0,84 [0,30; 2,36] 0,7443[3]	-0,5 [-3,5; 2,5] 0,7443[3]
Other	3/62 (4,8)	0/64 (0,0)	7,22 [0,38; 137,01] 0,1879[2]	7,59 [0,38; 150,00] 0,1162[4]	4,8 [-0,5; 10,2] 0,1162[4]
ECOG-PS (Interaction p-value: 0,2456)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	39/1070 (3,6)	27/1020 (2,6)	1,38 [0,85; 2,23] 0,1944[2]	1,39 [0,85; 2,29] 0,1923[3]	1,0 [-0,5; 2,5] 0,1923[3]
ECOG-PS 1	10/213 (4,7)	4/245 (1,6)	2,88 [0,92; 9,04] 0,0706[2]	2,97 [0,92; 9,61] 0,0576[3]	3,1 [-0,2; 6,3] 0,0576[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Osteoporosis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5273)					
< 65 years	21/918 (2,3)	31/937 (3,3)	0,69 [0,40; 1,19] 0,1857[2]	0,68 [0,39; 1,20] 0,1829[3]	-1,0 [-2,5; 0,5] 0,1829[3]
≥ 65 years	9/365 (2,5)	16/328 (4,9)	0,51 [0,23; 1,13] 0,0958[2]	0,49 [0,21; 1,13] 0,0891[3]	-2,4 [-5,2; 0,4] 0,0891[3]
Prior treatment (Interaction p-value: 0,8709)					
Neoadjuvant chemotherapy	9/430 (2,1)	15/415 (3,6)	0,58 [0,26; 1,31] 0,1891[2]	0,57 [0,25; 1,32] 0,1832[3]	-1,5 [-3,8; 0,7] 0,1832[3]
Adjuvant chemotherapy	20/784 (2,6)	29/769 (3,8)	0,68 [0,39; 1,19] 0,1720[2]	0,67 [0,37; 1,19] 0,1691[3]	-1,2 [-3,0; 0,5] 0,1691[3]
No chemotherapy	1/69 (1,4)	3/81 (3,7)	0,39 [0,04; 3,68] 0,4117[2]	0,38 [0,04; 3,76] 0,6248[4]	-2,3 [-7,2; 2,7] 0,6248[4]
Region (Interaction p-value: 0,6236)					
North America / Europe	14/678 (2,1)	17/650 (2,6)	0,79 [0,39; 1,59] 0,5076[2]	0,79 [0,38; 1,61] 0,5066[3]	-0,6 [-2,2; 1,1] 0,5066[3]
Asia	10/203 (4,9)	16/201 (8,0)	0,62 [0,29; 1,33] 0,2193[2]	0,60 [0,27; 1,35] 0,2140[3]	-3,0 [-7,8; 1,7] 0,2140[3]
Other	6/402 (1,5)	14/414 (3,4)	0,44 [0,17; 1,14] 0,0903[2]	0,43 [0,16; 1,14] 0,0810[3]	-1,9 [-4,0; 0,2] 0,0810[3]
Primary tumor size (Interaction p-value: 0,6596)					
< 20 mm	10/331 (3,0)	17/335 (5,1)	0,60 [0,28; 1,28] 0,1846[2]	0,58 [0,26; 1,29] 0,1791[3]	-2,1 [-5,0; 0,9] 0,1791[3]
≥ 20 but < 50 mm	14/646 (2,2)	18/653 (2,8)	0,79 [0,39; 1,57] 0,4944[2]	0,78 [0,39; 1,58] 0,4933[3]	-0,6 [-2,3; 1,1] 0,4933[3]
≥ 50 mm	6/289 (2,1)	12/265 (4,5)	0,46 [0,17; 1,20] 0,1135[2]	0,45 [0,17; 1,21] 0,1039[3]	-2,5 [-5,4; 0,5] 0,1039[3]
Number of positive lymph nodes (Interaction p-value: 0,4533)					
0-3	13/427 (3,0)	14/418 (3,3)	0,91 [0,43; 1,91] 0,8012[2]	0,91 [0,42; 1,95] 0,8011[3]	-0,3 [-2,7; 2,1] 0,8011[3]
4-9	11/549 (2,0)	23/542 (4,2)	0,47 [0,23; 0,96] 0,0379[2]	0,46 [0,22; 0,96] 0,0333[3]	-2,2 [-4,3; -0,2] 0,0333[3]
≥ 10	6/307 (2,0)	10/305 (3,3)	0,60 [0,22; 1,62] 0,3104[2]	0,59 [0,21; 1,64] 0,3046[3]	-1,3 [-3,9; 1,2] 0,3046[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,2917)					
IIA	2/113 (1,8)	6/114 (5,3)	0,34 [0,07; 1,63] 0,1761[2]	0,32 [0,06; 1,64] 0,2803[4]	-3,5 [-8,3; 1,3] 0,2803[4]
IIB	6/151 (4,0)	1/136 (0,7)	5,40 [0,66; 44,32] 0,1161[2]	5,59 [0,66; 47,00] 0,1240[4]	3,2 [-0,2; 6,7] 0,1240[4]
IIIA	11/495 (2,2)	19/488 (3,9)	0,57 [0,27; 1,19] 0,1332[2]	0,56 [0,26; 1,19] 0,1277[3]	-1,7 [-3,8; 0,5] 0,1277[3]
IIIB	2/54 (3,7)	4/45 (8,9)	0,42 [0,08; 2,17] 0,2986[2]	0,39 [0,07; 2,26] 0,4065[4]	-5,2 [-14,9; 4,5] 0,4065[4]
IIIC	9/468 (1,9)	17/480 (3,5)	0,54 [0,24; 1,21] 0,1336[2]	0,53 [0,24; 1,21] 0,1271[3]	-1,6 [-3,7; 0,5] 0,1271[3]
Tumor grade (Interaction p-value: 0,5696)					
G1	2/91 (2,2)	2/93 (2,2)	1,02 [0,15; 7,10] 0,9825[2]	1,02 [0,14; 7,42] 1,0000[4]	0,0 [-4,2; 4,3] 1,0000[4]
G2	13/612 (2,1)	26/603 (4,3)	0,49 [0,26; 0,95] 0,0345[2]	0,48 [0,25; 0,95] 0,0305[3]	-2,2 [-4,2; -0,2] 0,0305[3]
G3	15/527 (2,8)	15/506 (3,0)	0,96 [0,47; 1,94] 0,9100[2]	0,96 [0,46; 1,98] 0,9100[3]	-0,1 [-2,2; 1,9] 0,9100[3]
GX	0/51 (0,0)	4/59 (6,8)	0,13 [0,01; 2,33] 0,1648[2]	0,12 [0,01; 2,28] 0,1221[4]	-6,8 [-13,2; -0,4] 0,1221[4]
Progesterone receptor status (Interaction p-value: 0,2959)					
Negative	2/156 (1,3)	10/169 (5,9)	0,22 [0,05; 0,97] 0,0460[2]	0,21 [0,04; 0,96] 0,0268[3]	-4,6 [-8,6; -0,7] 0,0268[3]
Positive	28/1089 (2,6)	36/1067 (3,4)	0,76 [0,47; 1,24] 0,2737[2]	0,76 [0,46; 1,25] 0,2722[3]	-0,8 [-2,2; 0,6] 0,2722[3]
Unknown	0/10 (0,0)	1/7 (14,3)	0,24 [0,01; 5,21] 0,3654[2]	0,21 [0,01; 5,86] 0,4118[4]	-14,3 [-40,2; 11,6] 0,4118[4]
Race (Interaction p-value: 0,9976)					
White	19/958 (2,0)	29/944 (3,1)	0,65 [0,36; 1,14] 0,1334[2]	0,64 [0,36; 1,15] 0,1301[3]	-1,1 [-2,5; 0,3] 0,1301[3]
Asian	11/250 (4,4)	17/242 (7,0)	0,63 [0,30; 1,31] 0,2138[2]	0,61 [0,28; 1,33] 0,2090[3]	-2,6 [-6,7; 1,5] 0,2090[3]
Other	0/62 (0,0)	1/64 (1,6)	0,34 [0,01; 8,28] 0,5109[2]	0,34 [0,01; 8,47] 1,0000[4]	-1,6 [-4,6; 1,5] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,9512)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	1/114 (0,9)	2/132 (1,5)	0,58 [0,05; 6,30] 0,6536[2]	0,58 [0,05; 6,43] 1,0000[4]	-0,6 [-3,3; 2,1] 1,0000[4]
Aromatase inhibitor	29/1169 (2,5)	45/1133 (4,0)	0,62 [0,39; 0,99] 0,0447[2]	0,62 [0,38; 0,99] 0,0426[3]	-1,5 [-2,9; -0,0] 0,0426[3]
ECOG-PS (Interaction p-value: 0,3258)					
ECOG-PS 0	26/1070 (2,4)	35/1020 (3,4)	0,71 [0,43; 1,17] 0,1762[2]	0,70 [0,42; 1,17] 0,1740[3]	-1,0 [-2,5; 0,4] 0,1740[3]
ECOG-PS 1	4/213 (1,9)	12/245 (4,9)	0,38 [0,13; 1,17] 0,0924[2]	0,37 [0,12; 1,17] 0,0791[3]	-3,0 [-6,3; 0,2] 0,0791[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Palpitations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,3716)					
< 65 years	21/918 (2,3)	11/937 (1,2)	1,95 [0,94; 4,02] 0,0708[2]	1,97 [0,94; 4,11] 0,0655[3]	1,1 [-0,1; 2,3] 0,0655[3]
≥ 65 years	6/365 (1,6)	1/328 (0,3)	5,39 [0,65; 44,55] 0,1179[2]	5,47 [0,65; 45,64] 0,1269[4]	1,3 [-0,1; 2,8] 0,1269[4]
Prior treatment (Interaction p-value: 0,7696)					
Neoadjuvant chemotherapy	12/430 (2,8)	4/415 (1,0)	2,90 [0,94; 8,91] 0,0637[2]	2,95 [0,94; 9,22] 0,0514[3]	1,8 [0,0; 3,6] 0,0514[3]
Adjuvant chemotherapy	14/784 (1,8)	8/769 (1,0)	1,72 [0,72; 4,07] 0,2198[2]	1,73 [0,72; 4,15] 0,2139[3]	0,7 [-0,4; 1,9] 0,2139[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,5773)					
North America / Europe	18/678 (2,7)	9/650 (1,4)	1,92 [0,87; 4,24] 0,1076[2]	1,94 [0,87; 4,36] 0,1011[3]	1,3 [-0,2; 2,8] 0,1011[3]
Asia	6/203 (3,0)	1/201 (0,5)	5,94 [0,72; 48,90] 0,0976[2]	6,09 [0,73; 51,06] 0,1218[4]	2,5 [-0,1; 5,0] 0,1218[4]
Other	3/402 (0,7)	2/414 (0,5)	1,54 [0,26; 9,20] 0,6328[2]	1,55 [0,26; 9,32] 0,6822[4]	0,3 [-0,8; 1,3] 0,6822[4]
Primary tumor size (Interaction p-value: 0,6042)					
< 20 mm	7/331 (2,1)	2/335 (0,6)	3,54 [0,74; 16,93] 0,1130[2]	3,60 [0,74; 17,45] 0,1052[4]	1,5 [-0,2; 3,3] 0,1052[4]
≥ 20 but < 50 mm	13/646 (2,0)	8/653 (1,2)	1,64 [0,69; 3,94] 0,2657[2]	1,66 [0,68; 4,02] 0,2606[3]	0,8 [-0,6; 2,2] 0,2606[3]
≥ 50 mm	7/289 (2,4)	2/265 (0,8)	3,21 [0,67; 15,31] 0,1436[2]	3,26 [0,67; 15,85] 0,1798[4]	1,7 [-0,4; 3,7] 0,1798[4]
Number of positive lymph nodes (Interaction p-value: 0,9506)					
0-3	10/427 (2,3)	4/418 (1,0)	2,45 [0,77; 7,74] 0,1277[2]	2,48 [0,77; 7,98] 0,1148[3]	1,4 [-0,3; 3,1] 0,1148[3]
4-9	12/549 (2,2)	6/542 (1,1)	1,97 [0,75; 5,22] 0,1705[2]	2,00 [0,74; 5,36] 0,1619[3]	1,1 [-0,4; 2,6] 0,1619[3]
≥ 10	5/307 (1,6)	2/305 (0,7)	2,48 [0,49; 12,70] 0,2746[2]	2,51 [0,48; 13,03] 0,4504[4]	1,0 [-0,7; 2,7] 0,4504[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9421)					
IIA	2/113 (1,8)	2/114 (1,8)	1,01 [0,14; 7,04] 0,9929[2]	1,01 [0,14; 7,29] 1,0000[4]	0,0 [-3,4; 3,4] 1,0000[4]
IIB	2/151 (1,3)	1/136 (0,7)	1,80 [0,17; 19,64] 0,6293[2]	1,81 [0,16; 20,21] 1,0000[4]	0,6 [-1,7; 2,9] 1,0000[4]
IIIA	11/495 (2,2)	4/488 (0,8)	2,71 [0,87; 8,46] 0,0857[2]	2,75 [0,87; 8,70] 0,0729[3]	1,4 [-0,1; 2,9] 0,0729[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	11/468 (2,4)	5/480 (1,0)	2,26 [0,79; 6,44] 0,1286[2]	2,29 [0,79; 6,63] 0,1178[3]	1,3 [-0,3; 3,0] 0,1178[3]
Tumor grade (Interaction p-value: 0,9992)					
G1	2/91 (2,2)	1/93 (1,1)	2,04 [0,19; 22,15] 0,5565[2]	2,07 [0,18; 23,21] 0,6189[4]	1,1 [-2,5; 4,8] 0,6189[4]
G2	13/612 (2,1)	6/603 (1,0)	2,13 [0,82; 5,58] 0,1218[2]	2,16 [0,82; 5,72] 0,1127[3]	1,1 [-0,3; 2,5] 0,1127[3]
G3	10/527 (1,9)	5/506 (1,0)	1,92 [0,66; 5,58] 0,2305[2]	1,94 [0,66; 5,71] 0,2219[3]	0,9 [-0,5; 2,4] 0,2219[3]
GX	2/51 (3,9)	0/59 (0,0)	5,77 [0,28; 117,46] 0,2544[2]	6,01 [0,28; 128,14] 0,2127[4]	3,9 [-1,4; 9,2] 0,2127[4]
Progesterone receptor status (Interaction p-value: 0,6594)					
Negative	4/156 (2,6)	3/169 (1,8)	1,44 [0,33; 6,35] 0,6265[2]	1,46 [0,32; 6,61] 0,7142[4]	0,8 [-2,4; 4,0] 0,7142[4]
Positive	23/1089 (2,1)	9/1067 (0,8)	2,50 [1,16; 5,39] 0,0188[2]	2,54 [1,17; 5,51] 0,0149[3]	1,3 [0,3; 2,3] 0,0149[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,4467)					
White	18/958 (1,9)	11/944 (1,2)	1,61 [0,77; 3,40] 0,2086[2]	1,62 [0,76; 3,46] 0,2041[3]	0,7 [-0,4; 1,8] 0,2041[3]
Asian	7/250 (2,8)	1/242 (0,4)	6,78 [0,84; 54,66] 0,0725[2]	6,94 [0,85; 56,85] 0,0684[4]	2,4 [0,2; 4,6] 0,0684[4]
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
ECOG-PS (Interaction p-value: 0,9592)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	23/1070 (2,1)	10/1020 (1,0)	2,19 [1,05; 4,58] 0,0369[2]	2,22 [1,05; 4,68] 0,0321[3]	1,2 [0,1; 2,2] 0,0321[3]
ECOG-PS 1	4/213 (1,9)	2/245 (0,8)	2,30 [0,43; 12,44] 0,3332[2]	2,33 [0,42; 12,82] 0,4235[4]	1,1 [-1,1; 3,2] 0,4235[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Paronychia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8273)					
< 65 years	10/918 (1,1)	3/937 (0,3)	3,40 [0,94; 12,32] 0,0622[2]	3,43 [0,94; 12,50] 0,0471[3]	0,8 [0,0; 1,5] 0,0471[3]
≥ 65 years	5/365 (1,4)	1/328 (0,3)	4,49 [0,53; 38,26] 0,1691[2]	4,54 [0,53; 39,08] 0,2207[4]	1,1 [-0,3; 2,4] 0,2207[4]
Prior treatment (Interaction p-value: 0,9667)					
Neoadjuvant chemotherapy	1/430 (0,2)	0/415 (0,0)	2,90 [0,12; 70,88] 0,5146[2]	2,90 [0,12; 71,44] 1,0000[4]	0,2 [-0,2; 0,7] 1,0000[4]
Adjuvant chemotherapy	13/784 (1,7)	4/769 (0,5)	3,19 [1,04; 9,73] 0,0418[2]	3,22 [1,05; 9,93] 0,0312[3]	1,1 [0,1; 2,2] 0,0312[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,9933)					
North America / Europe	8/678 (1,2)	3/650 (0,5)	2,56 [0,68; 9,59] 0,1642[2]	2,58 [0,68; 9,75] 0,1488[3]	0,7 [-0,2; 1,7] 0,1488[3]
Asia	3/203 (1,5)	1/201 (0,5)	2,97 [0,31; 28,32] 0,3440[2]	3,00 [0,31; 29,09] 0,6232[4]	1,0 [-0,9; 2,9] 0,6232[4]
Other	4/402 (1,0)	0/414 (0,0)	9,27 [0,50; 171,59] 0,1348[2]	9,36 [0,50; 174,44] 0,0585[4]	1,0 [0,0; 2,0] 0,0585[4]
Progesterone receptor status (Interaction p-value: 0,5742)					
Negative	2/156 (1,3)	1/169 (0,6)	2,17 [0,20; 23,66] 0,5261[2]	2,18 [0,20; 24,30] 0,6093[4]	0,7 [-1,4; 2,8] 0,6093[4]
Positive	13/1089 (1,2)	3/1067 (0,3)	4,25 [1,21; 14,86] 0,0237[2]	4,29 [1,22; 15,08] 0,0136[3]	0,9 [0,2; 1,6] 0,0136[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9735)					
White	12/958 (1,3)	3/944 (0,3)	3,94 [1,12; 13,92] 0,0332[2]	3,98 [1,12; 14,14] 0,0212[3]	0,9 [0,1; 1,7] 0,0212[3]
Asian	3/250 (1,2)	1/242 (0,4)	2,90 [0,30; 27,73] 0,3544[2]	2,93 [0,30; 28,34] 0,6237[4]	0,8 [-0,8; 2,4] 0,6237[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9731)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	12/1070 (1,1)	4/1020 (0,4)	2,86 [0,93; 8,84] 0,0680[2]	2,88 [0,93; 8,96] 0,0559[3]	0,7 [-0,0; 1,5] 0,0559[3]
ECOG-PS 1	3/213 (1,4)	0/245 (0,0)	8,05 [0,42; 154,90] 0,1670[2]	8,16 [0,42; 158,96] 0,0998[4]	1,4 [-0,2; 3,0] 0,0998[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Platelet count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8800)					
< 65 years	71/918 (7,7)	6/937 (0,6)	12,08 [5,28; 27,65] <,0001[2]	13,01 [5,62; 30,08] <,0001[3]	7,1 [5,3; 8,9] <,0001[3]
≥ 65 years	45/365 (12,3)	3/328 (0,9)	13,48 [4,23; 42,96] <,0001[2]	15,23 [4,69; 49,52] <,0001[3]	11,4 [7,9; 14,9] <,0001[3]
Prior treatment (Interaction p-value: 0,9964)					
Neoadjuvant chemotherapy	35/430 (8,1)	3/415 (0,7)	11,26 [3,49; 36,33] <,0001[2]	12,17 [3,71; 39,89] <,0001[3]	7,4 [4,7; 10,1] <,0001[3]
Adjuvant chemotherapy	73/784 (9,3)	6/769 (0,8)	11,93 [5,22; 27,27] <,0001[2]	13,06 [5,64; 30,20] <,0001[3]	8,5 [6,4; 10,7] <,0001[3]
No chemotherapy	8/69 (11,6)	0/81 (0,0)	19,91 [1,17; 338,90] 0,0386[2]	22,53 [1,28; 397,86] 0,0016[4]	11,6 [4,0; 19,1] 0,0016[4]
Region (Interaction p-value: 0,1250)					
North America / Europe	34/678 (5,0)	2/650 (0,3)	16,30 [3,93; 67,56] 0,0001[2]	17,11 [4,09; 71,50] <,0001[3]	4,7 [3,0; 6,4] <,0001[3]
Asia	56/203 (27,6)	2/201 (1,0)	27,72 [6,86; 112,08] <,0001[2]	37,90 [9,10; 157,83] <,0001[3]	26,6 [20,3; 32,9] <,0001[3]
Other	26/402 (6,5)	5/414 (1,2)	5,36 [2,08; 13,81] 0,0005[2]	5,66 [2,15; 14,88] <,0001[3]	5,3 [2,6; 7,9] <,0001[3]
Primary tumor size (Interaction p-value: 0,1521)					
< 20 mm	25/331 (7,6)	1/335 (0,3)	25,30 [3,45; 185,65] 0,0015[2]	27,29 [3,68; 202,60] <,0001[3]	7,3 [4,3; 10,2] <,0001[3]
≥ 20 but < 50 mm	68/646 (10,5)	4/653 (0,6)	17,18 [6,31; 46,83] <,0001[2]	19,09 [6,92; 52,65] <,0001[3]	9,9 [7,5; 12,4] <,0001[3]
≥ 50 mm	21/289 (7,3)	4/265 (1,5)	4,81 [1,67; 13,84] 0,0035[2]	5,11 [1,73; 15,10] 0,0011[3]	5,8 [2,4; 9,1] 0,0011[3]
Number of positive lymph nodes (Interaction p-value: 0,4736)					
0-3	29/427 (6,8)	1/418 (0,2)	28,39 [3,88; 207,45] 0,0010[2]	30,38 [4,12; 224,11] <,0001[3]	6,6 [4,1; 9,0] <,0001[3]
4-9	53/549 (9,7)	6/542 (1,1)	8,72 [3,78; 20,12] <,0001[2]	9,55 [4,07; 22,40] <,0001[3]	8,5 [5,9; 11,2] <,0001[3]
≥ 10	34/307 (11,1)	2/305 (0,7)	16,89 [4,09; 69,68] <,0001[2]	18,87 [4,49; 79,27] <,0001[3]	10,4 [6,8; 14,0] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,4729)					
IIA	9/113 (8,0)	0/114 (0,0)	19,17 [1,13; 325,44] 0,0410[2]	20,82 [1,20; 362,12] 0,0016[4]	8,0 [3,0; 13,0] 0,0016[4]
IIB	15/151 (9,9)	0/136 (0,0)	27,94 [1,69; 462,56] 0,0200[2]	31,00 [1,84; 523,28] 0,0002[3]	9,9 [5,2; 14,7] 0,0002[3]
IIIA	37/495 (7,5)	7/488 (1,4)	5,21 [2,35; 11,58] <,0001[2]	5,55 [2,45; 12,58] <,0001[3]	6,0 [3,5; 8,6] <,0001[3]
IIIB	7/54 (13,0)	0/45 (0,0)	12,55 [0,74; 213,82] 0,0804[2]	14,37 [0,80; 258,91] 0,0149[4]	13,0 [4,0; 21,9] 0,0149[4]
IIIC	48/468 (10,3)	2/480 (0,4)	24,62 [6,02; 100,70] <,0001[2]	27,31 [6,60; 113,06] <,0001[3]	9,8 [7,0; 12,6] <,0001[3]
Tumor grade (Interaction p-value: 0,5950)					
G1	6/91 (6,6)	0/93 (0,0)	13,28 [0,76; 232,41] 0,0765[2]	14,22 [0,79; 256,15] 0,0134[4]	6,6 [1,5; 11,7] 0,0134[4]
G2	54/612 (8,8)	7/603 (1,2)	7,60 [3,49; 16,57] <,0001[2]	8,24 [3,72; 18,26] <,0001[3]	7,7 [5,3; 10,1] <,0001[3]
G3	49/527 (9,3)	2/506 (0,4)	23,52 [5,75; 96,22] <,0001[2]	25,83 [6,25; 106,81] <,0001[3]	8,9 [6,4; 11,4] <,0001[3]
GX	6/51 (11,8)	0/59 (0,0)	15,00 [0,87; 259,93] 0,0628[2]	17,00 [0,93; 309,65] 0,0084[4]	11,8 [2,9; 20,6] 0,0084[4]
Race (Interaction p-value: 0,2783)					
White	56/958 (5,8)	6/944 (0,6)	9,20 [3,98; 21,24] <,0001[2]	9,71 [4,16; 22,64] <,0001[3]	5,2 [3,6; 6,8] <,0001[3]
Asian	56/250 (22,4)	2/242 (0,8)	27,10 [6,69; 109,84] <,0001[2]	34,64 [8,35; 143,75] <,0001[3]	21,6 [16,3; 26,9] <,0001[3]
Other	4/62 (6,5)	1/64 (1,6)	4,13 [0,47; 35,92] 0,1989[2]	4,34 [0,47; 40,01] 0,2039[4]	4,9 [-1,9; 11,7] 0,2039[4]
First endocrine therapy (Interaction p-value: 0,4626)					
Tamoxifen	5/114 (4,4)	1/132 (0,8)	5,79 [0,69; 48,83] 0,1065[2]	6,01 [0,69; 52,21] 0,0988[4]	3,6 [-0,4; 7,7] 0,0988[4]
Aromatase inhibitor	111/1169 (9,5)	8/1133 (0,7)	13,45 [6,59; 27,43] <,0001[2]	14,75 [7,16; 30,38] <,0001[3]	8,8 [7,0; 10,5] <,0001[3]
ECOG-PS (Interaction p-value: 0,6406)					
ECOG-PS 0	100/1070 (9,3)	7/1020 (0,7)	13,62 [6,36; 29,16] <,0001[2]	14,92 [6,90; 32,26] <,0001[3]	8,7 [6,8; 10,5] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	16/213 (7,5)	2/245 (0,8)	9,20 [2,14; 39,56] 0,0029[2]	9,87 [2,24; 43,43] 0,0002[3]	6,7 [3,0; 10,4] 0,0002[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Tabl: Subgroups - adverse events according PT Pneumonitis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,7206)					
Neoadjuvant chemotherapy	7/430 (1,6)	2/415 (0,5)	3,38 [0,71; 16,17] 0,1276[2]	3,42 [0,71; 16,55] 0,1780[4]	1,1 [-0,2; 2,5] 0,1780[4]
Adjuvant chemotherapy	10/784 (1,3)	1/769 (0,1)	9,81 [1,26; 76,44] 0,0293[2]	9,92 [1,27; 77,70] 0,0071[3]	1,1 [0,3; 2,0] 0,0071[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,7872)					
North America / Europe	9/678 (1,3)	1/650 (0,2)	8,63 [1,10; 67,91] 0,0406[2]	8,73 [1,10; 69,11] 0,0213[4]	1,2 [0,3; 2,1] 0,0213[4]
Asia	7/203 (3,4)	2/201 (1,0)	3,47 [0,73; 16,48] 0,1182[2]	3,55 [0,73; 17,32] 0,1748[4]	2,5 [-0,4; 5,3] 0,1748[4]
Other	2/402 (0,5)	0/414 (0,0)	5,15 [0,25; 106,92] 0,2896[2]	5,17 [0,25; 108,12] 0,2424[4]	0,5 [-0,2; 1,2] 0,2424[4]
Primary tumor size (Interaction p-value: 0,5329)					
< 20 mm	4/331 (1,2)	0/335 (0,0)	9,11 [0,49; 168,51] 0,1378[2]	9,22 [0,49; 171,93] 0,0605[4]	1,2 [0,0; 2,4] 0,0605[4]
≥ 20 but < 50 mm	11/646 (1,7)	1/653 (0,2)	11,12 [1,44; 85,88] 0,0209[2]	11,29 [1,45; 87,74] 0,0035[3]	1,5 [0,5; 2,6] 0,0035[3]
≥ 50 mm	2/289 (0,7)	1/265 (0,4)	1,83 [0,17; 20,11] 0,6196[2]	1,84 [0,17; 20,41] 1,0000[4]	0,3 [-0,9; 1,5] 1,0000[4]
Tumor grade (Interaction p-value: 0,9956)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	6/612 (1,0)	1/603 (0,2)	5,91 [0,71; 48,96] 0,0995[2]	5,96 [0,72; 49,66] 0,1240[4]	0,8 [-0,0; 1,7] 0,1240[4]
G3	9/527 (1,7)	1/506 (0,2)	8,64 [1,10; 67,96] 0,0404[2]	8,77 [1,11; 69,51] 0,0211[4]	1,5 [0,3; 2,7] 0,0211[4]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,3906)					
Negative	3/156 (1,9)	1/169 (0,6)	3,25 [0,34; 30,92] 0,3051[2]	3,29 [0,34; 32,00] 0,3537[4]	1,3 [-1,1; 3,8] 0,3537[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Positive	15/1089 (1,4)	2/1067 (0,2)	7,35 [1,68; 32,06] 0,0080[2]	7,44 [1,70; 32,60] 0,0018[3]	1,2 [0,5; 1,9] 0,0018[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,7754)					
White	10/958 (1,0)	1/944 (0,1)	9,85 [1,26; 76,82] 0,0290[2]	9,95 [1,27; 77,86] 0,0070[3]	0,9 [0,3; 1,6] 0,0070[3]
Asian	8/250 (3,2)	2/242 (0,8)	3,87 [0,83; 18,05] 0,0848[2]	3,97 [0,83; 18,87] 0,1063[4]	2,4 [-0,1; 4,8] 0,1063[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Pruritus from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6434)					
< 65 years	67/918 (7,3)	40/937 (4,3)	1,71 [1,17; 2,50] 0,0058[2]	1,77 [1,18; 2,64] 0,0051[3]	3,0 [0,9; 5,2] 0,0051[3]
≥ 65 years	40/365 (11,0)	18/328 (5,5)	2,00 [1,17; 3,41] 0,0114[2]	2,12 [1,19; 3,78] 0,0094[3]	5,5 [1,4; 9,5] 0,0094[3]
Prior treatment (Interaction p-value: 0,1008)					
Neoadjuvant chemotherapy	35/430 (8,1)	14/415 (3,4)	2,41 [1,32; 4,42] 0,0043[2]	2,54 [1,34; 4,79] 0,0030[3]	4,8 [1,7; 7,9] 0,0030[3]
Adjuvant chemotherapy	62/784 (7,9)	42/769 (5,5)	1,45 [0,99; 2,11] 0,0555[2]	1,49 [0,99; 2,23] 0,0538[3]	2,4 [-0,0; 4,9] 0,0538[3]
No chemotherapy	10/69 (14,5)	2/81 (2,5)	5,87 [1,33; 25,88] 0,0194[2]	6,69 [1,41; 31,71] 0,0068[3]	12,0 [3,1; 21,0] 0,0068[3]
Region (Interaction p-value: 0,2287)					
North America / Europe	43/678 (6,3)	28/650 (4,3)	1,47 [0,93; 2,34] 0,1020[2]	1,50 [0,92; 2,45] 0,0995[3]	2,0 [-0,4; 4,4] 0,0995[3]
Asia	22/203 (10,8)	14/201 (7,0)	1,56 [0,82; 2,95] 0,1765[2]	1,62 [0,81; 3,27] 0,1720[3]	3,9 [-1,7; 9,4] 0,1720[3]
Other	42/402 (10,4)	16/414 (3,9)	2,70 [1,55; 4,73] 0,0005[2]	2,90 [1,60; 5,25] 0,0003[3]	6,6 [3,1; 10,1] 0,0003[3]
Primary tumor size (Interaction p-value: 0,1486)					
< 20 mm	17/331 (5,1)	16/335 (4,8)	1,08 [0,55; 2,09] 0,8306[2]	1,08 [0,54; 2,17] 0,8306[3]	0,4 [-2,9; 3,7] 0,8306[3]
≥ 20 but < 50 mm	55/646 (8,5)	30/653 (4,6)	1,85 [1,20; 2,85] 0,0051[2]	1,93 [1,22; 3,06] 0,0043[3]	3,9 [1,2; 6,6] 0,0043[3]
≥ 50 mm	35/289 (12,1)	12/265 (4,5)	2,67 [1,42; 5,04] 0,0024[2]	2,91 [1,47; 5,73] 0,0014[3]	7,6 [3,1; 12,1] 0,0014[3]
Number of positive lymph nodes (Interaction p-value: 0,4927)					
0-3	32/427 (7,5)	22/418 (5,3)	1,42 [0,84; 2,41] 0,1877[2]	1,46 [0,83; 2,55] 0,1849[3]	2,2 [-1,1; 5,5] 0,1849[3]
4-9	47/549 (8,6)	21/542 (3,9)	2,21 [1,34; 3,65] 0,0019[2]	2,32 [1,37; 3,94] 0,0014[3]	4,7 [1,8; 7,5] 0,0014[3]
≥ 10	28/307 (9,1)	15/305 (4,9)	1,85 [1,01; 3,40] 0,0460[2]	1,94 [1,01; 3,71] 0,0420[3]	4,2 [0,2; 8,2] 0,0420[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,2233)					
IIA	7/113 (6,2)	6/114 (5,3)	1,18 [0,41; 3,39] 0,7629[2]	1,19 [0,39; 3,65] 0,7626[3]	0,9 [-5,1; 7,0] 0,7626[3]
IIB	10/151 (6,6)	11/136 (8,1)	0,82 [0,36; 1,87] 0,6346[2]	0,81 [0,33; 1,96] 0,6340[3]	-1,5 [-7,5; 4,6] 0,6340[3]
IIIA	46/495 (9,3)	19/488 (3,9)	2,39 [1,42; 4,01] 0,0010[2]	2,53 [1,46; 4,38] 0,0007[3]	5,4 [2,3; 8,5] 0,0007[3]
IIIB	7/54 (13,0)	4/45 (8,9)	1,46 [0,46; 4,67] 0,5249[2]	1,53 [0,42; 5,59] 0,5207[3]	4,1 [-8,1; 16,3] 0,5207[3]
IIIC	37/468 (7,9)	18/480 (3,8)	2,11 [1,22; 3,65] 0,0077[2]	2,20 [1,24; 3,93] 0,0062[3]	4,2 [1,2; 7,1] 0,0062[3]
Tumor grade (Interaction p-value: 0,2640)					
G1	6/91 (6,6)	4/93 (4,3)	1,53 [0,45; 5,25] 0,4966[2]	1,57 [0,43; 5,76] 0,5339[4]	2,3 [-4,3; 8,8] 0,5339[4]
G2	63/612 (10,3)	25/603 (4,1)	2,48 [1,58; 3,89] <,0001[2]	2,65 [1,65; 4,28] <,0001[3]	6,1 [3,3; 9,0] <,0001[3]
G3	36/527 (6,8)	27/506 (5,3)	1,28 [0,79; 2,08] 0,3170[2]	1,30 [0,78; 2,18] 0,3155[3]	1,5 [-1,4; 4,4] 0,3155[3]
GX	2/51 (3,9)	1/59 (1,7)	2,31 [0,22; 24,78] 0,4880[2]	2,37 [0,21; 26,90] 0,5957[4]	2,2 [-4,0; 8,5] 0,5957[4]
Race (Interaction p-value: 0,0513)					
White	76/958 (7,9)	33/944 (3,5)	2,27 [1,52; 3,38] <,0001[2]	2,38 [1,56; 3,62] <,0001[3]	4,4 [2,4; 6,5] <,0001[3]
Asian	25/250 (10,0)	15/242 (6,2)	1,61 [0,87; 2,98] 0,1276[2]	1,68 [0,86; 3,27] 0,1229[3]	3,8 [-1,0; 8,6] 0,1229[3]
Other	4/62 (6,5)	8/64 (12,5)	0,52 [0,16; 1,63] 0,2589[2]	0,48 [0,14; 1,69] 0,2476[3]	-6,0 [-16,2; 4,1] 0,2476[3]
First endocrine therapy (Interaction p-value: 0,5912)					
Tamoxifen	10/114 (8,8)	8/132 (6,1)	1,45 [0,59; 3,54] 0,4183[2]	1,49 [0,57; 3,91] 0,4155[3]	2,7 [-3,9; 9,3] 0,4155[3]
Aromatase inhibitor	97/1169 (8,3)	50/1133 (4,4)	1,88 [1,35; 2,62] 0,0002[2]	1,96 [1,38; 2,79] 0,0001[3]	3,9 [1,9; 5,9] 0,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events according PT Pyrexia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9528)					
< 65 years	82/918 (8,9)	36/937 (3,8)	2,32 [1,59; 3,40] <,0001[2]	2,45 [1,64; 3,67] <,0001[3]	5,1 [2,9; 7,3] <,0001[3]
≥ 65 years	16/365 (4,4)	6/328 (1,8)	2,40 [0,95; 6,05] 0,0644[2]	2,46 [0,95; 6,36] 0,0555[3]	2,6 [0,0; 5,1] 0,0555[3]
Prior treatment (Interaction p-value: 0,6865)					
Neoadjuvant chemotherapy	31/430 (7,2)	13/415 (3,1)	2,30 [1,22; 4,34] 0,0099[2]	2,40 [1,24; 4,66] 0,0077[3]	4,1 [1,1; 7,0] 0,0077[3]
Adjuvant chemotherapy	64/784 (8,2)	26/769 (3,4)	2,41 [1,55; 3,77] 0,0001[2]	2,54 [1,59; 4,05] <,0001[3]	4,8 [2,5; 7,1] <,0001[3]
No chemotherapy	3/69 (4,3)	3/81 (3,7)	1,17 [0,24; 5,63] 0,8411[2]	1,18 [0,23; 6,05] 1,0000[4]	0,6 [-5,7; 7,0] 1,0000[4]
Region (Interaction p-value: 0,7952)					
North America / Europe	49/678 (7,2)	23/650 (3,5)	2,04 [1,26; 3,31] 0,0038[2]	2,12 [1,28; 3,53] 0,0030[3]	3,7 [1,3; 6,1] 0,0030[3]
Asia	24/203 (11,8)	9/201 (4,5)	2,64 [1,26; 5,54] 0,0102[2]	2,86 [1,29; 6,32] 0,0070[3]	7,3 [2,1; 12,6] 0,0070[3]
Other	25/402 (6,2)	10/414 (2,4)	2,57 [1,25; 5,29] 0,0101[2]	2,68 [1,27; 5,65] 0,0073[3]	3,8 [1,0; 6,6] 0,0073[3]
Primary tumor size (Interaction p-value: 0,3841)					
< 20 mm	16/331 (4,8)	10/335 (3,0)	1,62 [0,75; 3,52] 0,2230[2]	1,65 [0,74; 3,69] 0,2181[3]	1,8 [-1,1; 4,8] 0,2181[3]
≥ 20 but < 50 mm	53/646 (8,2)	25/653 (3,8)	2,14 [1,35; 3,40] 0,0013[2]	2,25 [1,38; 3,66] 0,0009[3]	4,4 [1,8; 7,0] 0,0009[3]
≥ 50 mm	27/289 (9,3)	7/265 (2,6)	3,54 [1,57; 7,99] 0,0024[2]	3,80 [1,63; 8,88] 0,0010[3]	6,7 [2,8; 10,6] 0,0010[3]
Number of positive lymph nodes (Interaction p-value: 0,0873)					
0-3	35/427 (8,2)	13/418 (3,1)	2,64 [1,41; 4,91] 0,0023[2]	2,78 [1,45; 5,34] 0,0014[3]	5,1 [2,0; 8,2] 0,0014[3]
4-9	31/549 (5,6)	21/542 (3,9)	1,46 [0,85; 2,50] 0,1725[2]	1,48 [0,84; 2,62] 0,1696[3]	1,8 [-0,8; 4,3] 0,1696[3]
≥ 10	32/307 (10,4)	8/305 (2,6)	3,97 [1,86; 8,48] 0,0004[2]	4,32 [1,96; 9,54] <,0001[3]	7,8 [3,9; 11,7] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,0737)					
IIA	6/113 (5,3)	4/114 (3,5)	1,51 [0,44; 5,22] 0,5119[2]	1,54 [0,42; 5,62] 0,5386[4]	1,8 [-3,5; 7,1] 0,5386[4]
IIB	17/151 (11,3)	6/136 (4,4)	2,55 [1,04; 6,29] 0,0417[2]	2,75 [1,05; 7,19] 0,0329[3]	6,8 [0,7; 13,0] 0,0329[3]
IIIA	30/495 (6,1)	20/488 (4,1)	1,48 [0,85; 2,57] 0,1647[2]	1,51 [0,85; 2,70] 0,1615[3]	2,0 [-0,8; 4,7] 0,1615[3]
IIIB	3/54 (5,6)	3/45 (6,7)	0,83 [0,18; 3,93] 0,8177[2]	0,82 [0,16; 4,29] 1,0000[4]	-1,1 [-10,6; 8,4] 1,0000[4]
IIIC	42/468 (9,0)	9/480 (1,9)	4,79 [2,36; 9,72] <,0001[2]	5,16 [2,48; 10,73] <,0001[3]	7,1 [4,2; 10,0] <,0001[3]
Tumor grade (Interaction p-value: 0,3366)					
G1	4/91 (4,4)	5/93 (5,4)	0,82 [0,23; 2,95] 0,7583[2]	0,81 [0,21; 3,11] 1,0000[4]	-1,0 [-7,2; 5,2] 1,0000[4]
G2	49/612 (8,0)	17/603 (2,8)	2,84 [1,65; 4,87] 0,0002[2]	3,00 [1,71; 5,27] <,0001[3]	5,2 [2,7; 7,7] <,0001[3]
G3	40/527 (7,6)	20/506 (4,0)	1,92 [1,14; 3,24] 0,0144[2]	2,00 [1,15; 3,46] 0,0125[3]	3,6 [0,8; 6,5] 0,0125[3]
GX	5/51 (9,8)	0/59 (0,0)	12,69 [0,72; 224,11] 0,0828[2]	14,08 [0,76; 261,07] 0,0192[4]	9,8 [1,6; 18,0] 0,0192[4]
Race (Interaction p-value: 0,8847)					
White	65/958 (6,8)	27/944 (2,9)	2,37 [1,53; 3,68] 0,0001[2]	2,47 [1,56; 3,91] <,0001[3]	3,9 [2,0; 5,8] <,0001[3]
Asian	29/250 (11,6)	13/242 (5,4)	2,16 [1,15; 4,05] 0,0166[2]	2,31 [1,17; 4,56] 0,0134[3]	6,2 [1,3; 11,1] 0,0134[3]
Other	3/62 (4,8)	2/64 (3,1)	1,55 [0,27; 8,95] 0,6253[2]	1,58 [0,25; 9,77] 0,6774[4]	1,7 [-5,1; 8,5] 0,6774[4]
First endocrine therapy (Interaction p-value: 0,5072)					
Tamoxifen	9/114 (7,9)	3/132 (2,3)	3,47 [0,96; 12,52] 0,0570[2]	3,69 [0,97; 13,96] 0,0412[3]	5,6 [0,1; 11,2] 0,0412[3]
Aromatase inhibitor	89/1169 (7,6)	39/1133 (3,4)	2,21 [1,53; 3,19] <,0001[2]	2,31 [1,57; 3,40] <,0001[3]	4,2 [2,3; 6,0] <,0001[3]
ECOG-PS (Interaction p-value: 0,1677)					
ECOG-PS 0	82/1070 (7,7)	38/1020 (3,7)	2,06 [1,41; 2,99] 0,0002[2]	2,14 [1,45; 3,18] 0,0001[3]	3,9 [2,0; 5,9] 0,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	16/213 (7,5)	4/245 (1,6)	4,60 [1,56; 13,55] 0,0056[2]	4,89 [1,61; 14,87] 0,0021[3]	5,9 [2,0; 9,8] 0,0021[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Rash from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5596)					
< 65 years	77/918 (8,4)	28/937 (3,0)	2,81 [1,84; 4,28] <,0001[2]	2,97 [1,91; 4,63] <,0001[3]	5,4 [3,3; 7,5] <,0001[3]
≥ 65 years	36/365 (9,9)	9/328 (2,7)	3,59 [1,76; 7,35] 0,0005[2]	3,88 [1,84; 8,18] 0,0001[3]	7,1 [3,6; 10,7] 0,0001[3]
Prior treatment (Interaction p-value: 0,1762)					
Neoadjuvant chemotherapy	28/430 (6,5)	14/415 (3,4)	1,93 [1,03; 3,61] 0,0399[2]	2,00 [1,03; 3,85] 0,0359[3]	3,1 [0,2; 6,0] 0,0359[3]
Adjuvant chemotherapy	73/784 (9,3)	21/769 (2,7)	3,41 [2,12; 5,48] <,0001[2]	3,66 [2,23; 6,01] <,0001[3]	6,6 [4,2; 8,9] <,0001[3]
No chemotherapy	12/69 (17,4)	2/81 (2,5)	7,04 [1,63; 30,39] 0,0089[2]	8,32 [1,79; 38,60] 0,0017[3]	14,9 [5,4; 24,5] 0,0017[3]
Region (Interaction p-value: 0,8358)					
North America / Europe	71/678 (10,5)	24/650 (3,7)	2,84 [1,81; 4,45] <,0001[2]	3,05 [1,90; 4,91] <,0001[3]	6,8 [4,1; 9,5] <,0001[3]
Asia	23/203 (11,3)	8/201 (4,0)	2,85 [1,30; 6,21] 0,0086[2]	3,08 [1,34; 7,07] 0,0055[3]	7,3 [2,2; 12,5] 0,0055[3]
Other	19/402 (4,7)	5/414 (1,2)	3,91 [1,48; 10,38] 0,0061[2]	4,06 [1,50; 10,97] 0,0029[3]	3,5 [1,2; 5,8] 0,0029[3]
Primary tumor size (Interaction p-value: 0,3994)					
< 20 mm	22/331 (6,6)	8/335 (2,4)	2,78 [1,26; 6,16] 0,0116[2]	2,91 [1,28; 6,63] 0,0081[3]	4,3 [1,1; 7,4] 0,0081[3]
≥ 20 but < 50 mm	62/646 (9,6)	17/653 (2,6)	3,69 [2,18; 6,23] <,0001[2]	3,97 [2,30; 6,87] <,0001[3]	7,0 [4,4; 9,6] <,0001[3]
≥ 50 mm	27/289 (9,3)	12/265 (4,5)	2,06 [1,07; 3,99] 0,0313[2]	2,17 [1,08; 4,38] 0,0269[3]	4,8 [0,6; 9,0] 0,0269[3]
Number of positive lymph nodes (Interaction p-value: 0,5879)					
0-3	37/427 (8,7)	11/418 (2,6)	3,29 [1,70; 6,37] 0,0004[2]	3,51 [1,77; 6,98] 0,0002[3]	6,0 [3,0; 9,1] 0,0002[3]
4-9	49/549 (8,9)	14/542 (2,6)	3,46 [1,93; 6,18] <,0001[2]	3,70 [2,02; 6,78] <,0001[3]	6,3 [3,6; 9,1] <,0001[3]
≥ 10	27/307 (8,8)	12/305 (3,9)	2,24 [1,15; 4,33] 0,0171[2]	2,35 [1,17; 4,74] 0,0138[3]	4,9 [1,0; 8,7] 0,0138[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8983)					
IIA	8/113 (7,1)	4/114 (3,5)	2,02 [0,63; 6,51] 0,2403[2]	2,10 [0,61; 7,17] 0,2293[3]	3,6 [-2,2; 9,4] 0,2293[3]
IIB	17/151 (11,3)	4/136 (2,9)	3,83 [1,32; 11,10] 0,0134[2]	4,19 [1,37; 12,77] 0,0069[3]	8,3 [2,5; 14,1] 0,0069[3]
IIIA	41/495 (8,3)	12/488 (2,5)	3,37 [1,79; 6,33] 0,0002[2]	3,58 [1,86; 6,90] <,0001[3]	5,8 [3,0; 8,6] <,0001[3]
IIIB	4/54 (7,4)	0/45 (0,0)	7,53 [0,42; 136,17] 0,1718[2]	8,11 [0,42; 154,79] 0,1236[4]	7,4 [0,4; 14,4] 0,1236[4]
IIIC	42/468 (9,0)	17/480 (3,5)	2,53 [1,46; 4,39] 0,0009[2]	2,69 [1,51; 4,79] 0,0005[3]	5,4 [2,4; 8,5] 0,0005[3]
Tumor grade (Interaction p-value: 0,7125)					
G1	9/91 (9,9)	4/93 (4,3)	2,30 [0,73; 7,20] 0,1529[2]	2,44 [0,72; 8,23] 0,1391[3]	5,6 [-1,8; 13,0] 0,1391[3]
G2	58/612 (9,5)	15/603 (2,5)	3,81 [2,18; 6,65] <,0001[2]	4,10 [2,30; 7,33] <,0001[3]	7,0 [4,4; 9,6] <,0001[3]
G3	43/527 (8,2)	15/506 (3,0)	2,75 [1,55; 4,89] 0,0006[2]	2,91 [1,59; 5,30] 0,0003[3]	5,2 [2,4; 8,0] 0,0003[3]
GX	3/51 (5,9)	2/59 (3,4)	1,74 [0,30; 9,98] 0,5369[2]	1,78 [0,29; 11,10] 0,6613[4]	2,5 [-5,4; 10,4] 0,6613[4]
Progesterone receptor status (Interaction p-value: 0,2676)					
Negative	12/156 (7,7)	5/169 (3,0)	2,60 [0,94; 7,21] 0,0664[2]	2,73 [0,94; 7,94] 0,0555[3]	4,7 [-0,2; 9,6] 0,0555[3]
Positive	100/1089 (9,2)	31/1067 (2,9)	3,16 [2,13; 4,69] <,0001[2]	3,38 [2,24; 5,10] <,0001[3]	6,3 [4,3; 8,3] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,6837)					
White	84/958 (8,8)	25/944 (2,6)	3,31 [2,14; 5,13] <,0001[2]	3,53 [2,24; 5,57] <,0001[3]	6,1 [4,1; 8,2] <,0001[3]
Asian	26/250 (10,4)	9/242 (3,7)	2,80 [1,34; 5,84] 0,0063[2]	3,00 [1,38; 6,55] 0,0040[3]	6,7 [2,2; 11,2] 0,0040[3]
Other	3/62 (4,8)	2/64 (3,1)	1,55 [0,27; 8,95] 0,6253[2]	1,58 [0,25; 9,77] 0,6774[4]	1,7 [-5,1; 8,5] 0,6774[4]
First endocrine therapy (Interaction p-value: 0,9424)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	10/114 (8,8)	4/132 (3,0)	2,89 [0,93; 8,98] 0,0658[2]	3,08 [0,94; 10,09] 0,0526[3]	5,7 [-0,2; 11,7] 0,0526[3]
Aromatase inhibitor	103/1169 (8,8)	33/1133 (2,9)	3,03 [2,06; 4,44] <,0001[2]	3,22 [2,16; 4,81] <,0001[3]	5,9 [4,0; 7,8] <,0001[3]
ECOG-PS (Interaction p-value: 0,5844)					
ECOG-PS 0	96/1070 (9,0)	29/1020 (2,8)	3,16 [2,10; 4,74] <,0001[2]	3,37 [2,20; 5,15] <,0001[3]	6,1 [4,1; 8,1] <,0001[3]
ECOG-PS 1	17/213 (8,0)	8/245 (3,3)	2,44 [1,08; 5,55] 0,0327[2]	2,57 [1,09; 6,08] 0,0267[3]	4,7 [0,5; 9,0] 0,0267[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Rash maculo-papular from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8911)					
Neoadjuvant chemotherapy	4/430 (0,9)	1/415 (0,2)	3,86 [0,43; 34,40] 0,2261[2]	3,89 [0,43; 34,92] 0,3739[4]	0,7 [-0,3; 1,7] 0,3739[4]
Adjuvant chemotherapy	15/784 (1,9)	2/769 (0,3)	7,36 [1,69; 32,06] 0,0079[2]	7,48 [1,70; 32,82] 0,0017[3]	1,7 [0,6; 2,7] 0,0017[3]
No chemotherapy	3/69 (4,3)	0/81 (0,0)	8,20 [0,43; 156,04] 0,1615[2]	8,58 [0,44; 169,04] 0,0950[4]	4,3 [-0,5; 9,2] 0,0950[4]
Region (Interaction p-value: 0,9994)					
North America / Europe	12/678 (1,8)	3/650 (0,5)	3,83 [1,09; 13,53] 0,0366[2]	3,89 [1,09; 13,83] 0,0241[3]	1,3 [0,2; 2,4] 0,0241[3]
Asia	4/203 (2,0)	0/201 (0,0)	8,91 [0,48; 164,45] 0,1414[2]	9,09 [0,49; 169,95] 0,1232[4]	2,0 [0,1; 3,9] 0,1232[4]
Other	6/402 (1,5)	0/414 (0,0)	13,39 [0,76; 236,86] 0,0768[2]	13,59 [0,76; 242,03] 0,0140[4]	1,5 [0,3; 2,7] 0,0140[4]
Primary tumor size (Interaction p-value: 0,8964)					
< 20 mm	4/331 (1,2)	1/335 (0,3)	4,05 [0,45; 36,03] 0,2100[2]	4,09 [0,45; 36,75] 0,2145[4]	0,9 [-0,4; 2,2] 0,2145[4]
≥ 20 but < 50 mm	15/646 (2,3)	2/653 (0,3)	7,58 [1,74; 33,02] 0,0070[2]	7,74 [1,76; 33,97] 0,0014[3]	2,0 [0,8; 3,3] 0,0014[3]
≥ 50 mm	2/289 (0,7)	0/265 (0,0)	4,59 [0,22; 95,09] 0,3248[2]	4,62 [0,22; 96,62] 0,5000[4]	0,7 [-0,3; 1,6] 0,5000[4]
Number of positive lymph nodes (Interaction p-value: 0,9624)					
0-3	6/427 (1,4)	1/418 (0,2)	5,87 [0,71; 48,58] 0,1005[2]	5,94 [0,71; 49,58] 0,1236[4]	1,2 [-0,0; 2,4] 0,1236[4]
4-9	9/549 (1,6)	1/542 (0,2)	8,89 [1,13; 69,89] 0,0379[2]	9,02 [1,14; 71,41] 0,0209[4]	1,5 [0,3; 2,6] 0,0209[4]
≥ 10	7/307 (2,3)	1/305 (0,3)	6,95 [0,86; 56,19] 0,0689[2]	7,09 [0,87; 58,00] 0,0685[4]	2,0 [0,2; 3,7] 0,0685[4]
Tumor stage (Interaction p-value: 0,8611)					
IIA	2/113 (1,8)	0/114 (0,0)	5,04 [0,24; 103,90] 0,2945[2]	5,13 [0,24; 108,15] 0,2467[4]	1,8 [-0,7; 4,2] 0,2467[4]
IIB	2/151 (1,3)	1/136 (0,7)	1,80 [0,17; 19,64] 0,6293[2]	1,81 [0,16; 20,21] 1,0000[4]	0,6 [-1,7; 2,9] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	8/495 (1,6)	1/488 (0,2)	7,89 [0,99; 62,82] 0,0511[2]	8,00 [1,00; 64,21] 0,0382[4]	1,4 [0,2; 2,6] 0,0382[4]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	10/468 (2,1)	1/480 (0,2)	10,26 [1,32; 79,80] 0,0262[2]	10,46 [1,33; 82,03] 0,0056[3]	1,9 [0,6; 3,3] 0,0056[3]
Tumor grade (Interaction p-value: 0,9858)					
G1	3/91 (3,3)	0/93 (0,0)	7,15 [0,37; 136,54] 0,1910[2]	7,40 [0,38; 145,22] 0,1189[4]	3,3 [-0,4; 7,0] 0,1189[4]
G2	8/612 (1,3)	1/603 (0,2)	7,88 [0,99; 62,83] 0,0512[2]	7,97 [0,99; 63,95] 0,0384[4]	1,1 [0,2; 2,1] 0,0384[4]
G3	10/527 (1,9)	2/506 (0,4)	4,80 [1,06; 21,80] 0,0422[2]	4,87 [1,06; 22,36] 0,0243[3]	1,5 [0,2; 2,8] 0,0243[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,9645)					
Negative	2/156 (1,3)	0/169 (0,0)	5,41 [0,26; 111,90] 0,2744[2]	5,49 [0,26; 115,15] 0,2296[4]	1,3 [-0,5; 3,0] 0,2296[4]
Positive	20/1089 (1,8)	3/1067 (0,3)	6,53 [1,95; 21,92] 0,0024[2]	6,64 [1,97; 22,40] 0,0004[3]	1,6 [0,7; 2,4] 0,0004[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9997)					
White	15/958 (1,6)	3/944 (0,3)	4,93 [1,43; 16,96] 0,0115[2]	4,99 [1,44; 17,29] 0,0049[3]	1,2 [0,4; 2,1] 0,0049[3]
Asian	4/250 (1,6)	0/242 (0,0)	8,71 [0,47; 160,97] 0,1457[2]	8,85 [0,47; 165,34] 0,1237[4]	1,6 [0,0; 3,2] 0,1237[4]
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
ECOG-PS (Interaction p-value: 0,9393)					
ECOG-PS 0	16/1070 (1,5)	2/1020 (0,2)	7,63 [1,76; 33,08] 0,0067[2]	7,73 [1,77; 33,69] 0,0013[3]	1,3 [0,5; 2,1] 0,0013[3]
ECOG-PS 1	6/213 (2,8)	1/245 (0,4)	6,90 [0,84; 56,87] 0,0726[2]	7,07 [0,84; 59,22] 0,0535[4]	2,4 [0,0; 4,8] 0,0535[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk					

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Tabl: Subgroups - adverse events according PT Seroma from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6291)					
< 65 years	11/918 (1,2)	3/937 (0,3)	3,74 [1,05; 13,37] 0,0422[2]	3,78 [1,05; 13,58] 0,0289[3]	0,9 [0,1; 1,7] 0,0289[3]
≥ 65 years	5/365 (1,4)	2/328 (0,6)	2,25 [0,44; 11,50] 0,3313[2]	2,26 [0,44; 11,75] 0,4555[4]	0,8 [-0,7; 2,2] 0,4555[4]
Prior treatment (Interaction p-value: 0,3491)					
Neoadjuvant chemotherapy	1/430 (0,2)	2/415 (0,5)	0,48 [0,04; 5,30] 0,5513[2]	0,48 [0,04; 5,33] 0,6180[4]	-0,2 [-1,1; 0,6] 0,6180[4]
Adjuvant chemotherapy	11/784 (1,4)	3/769 (0,4)	3,60 [1,01; 12,84] 0,0487[2]	3,63 [1,01; 13,07] 0,0347[3]	1,0 [0,1; 1,9] 0,0347[3]
No chemotherapy	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (Interaction p-value: 0,7171)					
North America / Europe	14/678 (2,1)	4/650 (0,6)	3,36 [1,11; 10,14] 0,0319[2]	3,41 [1,11; 10,40] 0,0224[3]	1,4 [0,2; 2,7] 0,0224[3]
Asia	0/203 (0,0)	0/201 (0,0)	NE	NE	NE
Other	2/402 (0,5)	1/414 (0,2)	2,06 [0,19; 22,63] 0,5546[2]	2,07 [0,19; 22,86] 0,6191[4]	0,3 [-0,6; 1,1] 0,6191[4]
Tumor stage (Interaction p-value: 0,7481)					
IIA	0/113 (0,0)	1/114 (0,9)	0,34 [0,01; 8,17] 0,5031[2]	0,33 [0,01; 8,27] 1,0000[4]	-0,9 [-2,6; 0,8] 1,0000[4]
IIB	1/151 (0,7)	0/136 (0,0)	2,70 [0,11; 65,82] 0,5414[2]	2,72 [0,11; 67,35] 1,0000[4]	0,7 [-0,6; 2,0] 1,0000[4]
IIIA	9/495 (1,8)	1/488 (0,2)	8,87 [1,13; 69,77] 0,0380[2]	9,02 [1,14; 71,46] 0,0209[4]	1,6 [0,4; 2,9] 0,0209[4]
IIIB	1/54 (1,9)	1/45 (2,2)	0,83 [0,05; 12,95] 0,8964[2]	0,83 [0,05; 13,66] 1,0000[4]	-0,4 [-6,0; 5,2] 1,0000[4]
IIIC	5/468 (1,1)	2/480 (0,4)	2,56 [0,50; 13,15] 0,2590[2]	2,58 [0,50; 13,37] 0,2815[4]	0,7 [-0,4; 1,7] 0,2815[4]
Race (Interaction p-value: 0,9909)					
White	15/958 (1,6)	5/944 (0,5)	2,96 [1,08; 8,10] 0,0351[2]	2,99 [1,08; 8,25] 0,0268[3]	1,0 [0,1; 1,9] 0,0268[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Asian	0/250 (0,0)	0/242 (0,0)	NE	NE	NE
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
ECOG-PS (Interaction p-value: 0,7046)					
ECOG-PS 0	12/1070 (1,1)	4/1020 (0,4)	2,86 [0,93; 8,84] 0,0680[2]	2,88 [0,93; 8,96] 0,0559[3]	0,7 [-0,0; 1,5] 0,0559[3]
ECOG-PS 1	4/213 (1,9)	1/245 (0,4)	4,60 [0,52; 40,85] 0,1707[2]	4,67 [0,52; 42,11] 0,1885[4]	1,5 [-0,5; 3,5] 0,1885[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Stomatitis from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6398)					
< 65 years	48/918 (5,2)	8/937 (0,9)	6,12 [2,91; 12,87] <,0001[2]	6,41 [3,01; 13,62] <,0001[3]	4,4 [2,8; 5,9] <,0001[3]
≥ 65 years	20/365 (5,5)	4/328 (1,2)	4,49 [1,55; 13,01] 0,0056[2]	4,70 [1,59; 13,88] 0,0022[3]	4,3 [1,6; 6,9] 0,0022[3]
Prior treatment (Interaction p-value: 0,7122)					
Neoadjuvant chemotherapy	16/430 (3,7)	4/415 (1,0)	3,86 [1,30; 11,45] 0,0149[2]	3,97 [1,32; 11,98] 0,0084[3]	2,8 [0,7; 4,8] 0,0084[3]
Adjuvant chemotherapy	48/784 (6,1)	7/769 (0,9)	6,73 [3,06; 14,77] <,0001[2]	7,10 [3,19; 15,79] <,0001[3]	5,2 [3,4; 7,0] <,0001[3]
No chemotherapy	4/69 (5,8)	1/81 (1,2)	4,70 [0,54; 41,03] 0,1620[2]	4,92 [0,54; 45,13] 0,1807[4]	4,6 [-1,5; 10,6] 0,1807[4]
Region (Interaction p-value: 0,9298)					
North America / Europe	31/678 (4,6)	6/650 (0,9)	4,95 [2,08; 11,79] 0,0003[2]	5,14 [2,13; 12,41] <,0001[3]	3,6 [1,9; 5,4] <,0001[3]
Asia	26/203 (12,8)	4/201 (2,0)	6,44 [2,29; 18,11] 0,0004[2]	7,23 [2,48; 21,13] <,0001[3]	10,8 [5,8; 15,8] <,0001[3]
Other	11/402 (2,7)	2/414 (0,5)	5,66 [1,26; 25,39] 0,0235[2]	5,80 [1,28; 26,31] 0,0102[3]	2,3 [0,5; 4,0] 0,0102[3]
Primary tumor size (Interaction p-value: 0,3252)					
< 20 mm	16/331 (4,8)	1/335 (0,3)	16,19 [2,16; 121,41] 0,0067[2]	16,97 [2,24; 128,68] 0,0002[3]	4,5 [2,2; 6,9] 0,0002[3]
≥ 20 but < 50 mm	33/646 (5,1)	6/653 (0,9)	5,56 [2,35; 13,18] <,0001[2]	5,81 [2,42; 13,95] <,0001[3]	4,2 [2,3; 6,0] <,0001[3]
≥ 50 mm	17/289 (5,9)	5/265 (1,9)	3,12 [1,17; 8,33] 0,0234[2]	3,25 [1,18; 8,94] 0,0161[3]	4,0 [0,8; 7,2] 0,0161[3]
Number of positive lymph nodes (Interaction p-value: 0,2777)					
0-3	23/427 (5,4)	1/418 (0,2)	22,52 [3,05; 165,96] 0,0022[2]	23,74 [3,19; 176,61] <,0001[3]	5,1 [3,0; 7,3] <,0001[3]
4-9	29/549 (5,3)	7/542 (1,3)	4,09 [1,81; 9,26] 0,0007[2]	4,26 [1,85; 9,82] 0,0002[3]	4,0 [1,9; 6,1] 0,0002[3]
≥ 10	16/307 (5,2)	4/305 (1,3)	3,97 [1,34; 11,75] 0,0126[2]	4,14 [1,37; 12,52] 0,0067[3]	3,9 [1,1; 6,7] 0,0067[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9979)					
IIA	6/113 (5,3)	1/114 (0,9)	6,05 [0,74; 49,48] 0,0930[2]	6,34 [0,75; 53,50] 0,0655[4]	4,4 [-0,0; 8,9] 0,0655[4]
IIB	7/151 (4,6)	0/136 (0,0)	13,52 [0,78; 234,52] 0,0737[2]	14,17 [0,80; 250,47] 0,0154[4]	4,6 [1,3; 8,0] 0,0154[4]
IIIA	26/495 (5,3)	5/488 (1,0)	5,13 [1,98; 13,24] 0,0007[2]	5,36 [2,04; 14,06] 0,0001[3]	4,2 [2,1; 6,4] 0,0001[3]
IIIB	3/54 (5,6)	0/45 (0,0)	5,85 [0,31; 110,43] 0,2383[2]	6,18 [0,31; 122,97] 0,2486[4]	5,6 [-0,6; 11,7] 0,2486[4]
IIIC	25/468 (5,3)	6/480 (1,3)	4,27 [1,77; 10,32] 0,0012[2]	4,46 [1,81; 10,97] 0,0004[3]	4,1 [1,8; 6,4] 0,0004[3]
Tumor grade (Interaction p-value: 0,5414)					
G1	4/91 (4,4)	0/93 (0,0)	9,20 [0,50; 168,39] 0,1348[2]	9,62 [0,51; 181,24] 0,0578[4]	4,4 [0,2; 8,6] 0,0578[4]
G2	31/612 (5,1)	9/603 (1,5)	3,39 [1,63; 7,07] 0,0011[2]	3,52 [1,66; 7,46] 0,0005[3]	3,6 [1,6; 5,6] 0,0005[3]
G3	30/527 (5,7)	3/506 (0,6)	9,60 [2,95; 31,26] 0,0002[2]	10,12 [3,07; 33,38] <,0001[3]	5,1 [3,0; 7,2] <,0001[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,9385)					
Negative	17/156 (10,9)	0/169 (0,0)	37,90 [2,30; 624,93] 0,0110[2]	42,53 [2,53; 713,50] <,0001[3]	10,9 [6,0; 15,8] <,0001[3]
Positive	51/1089 (4,7)	12/1067 (1,1)	4,16 [2,23; 7,77] <,0001[2]	4,32 [2,29; 8,15] <,0001[3]	3,6 [2,2; 5,0] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,8247)					
White	38/958 (4,0)	8/944 (0,8)	4,68 [2,20; 9,98] <,0001[2]	4,83 [2,24; 10,41] <,0001[3]	3,1 [1,8; 4,5] <,0001[3]
Asian	29/250 (11,6)	4/242 (1,7)	7,02 [2,50; 19,66] 0,0002[2]	7,81 [2,70; 22,57] <,0001[3]	9,9 [5,7; 14,2] <,0001[3]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: 0,3273)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	8/114 (7,0)	3/132 (2,3)	3,09 [0,84; 11,36] 0,0899[2]	3,25 [0,84; 12,54] 0,0726[3]	4,7 [-0,6; 10,1] 0,0726[3]
Aromatase inhibitor	60/1169 (5,1)	9/1133 (0,8)	6,46 [3,22; 12,96] <,0001[2]	6,76 [3,34; 13,68] <,0001[3]	4,3 [3,0; 5,7] <,0001[3]
ECOG-PS (Interaction p-value: 0,4494)					
ECOG-PS 0	58/1070 (5,4)	11/1020 (1,1)	5,03 [2,65; 9,52] <,0001[2]	5,26 [2,74; 10,07] <,0001[3]	4,3 [2,8; 5,8] <,0001[3]
ECOG-PS 1	10/213 (4,7)	1/245 (0,4)	11,50 [1,48; 89,12] 0,0194[2]	12,02 [1,53; 94,69] 0,0028[3]	4,3 [1,3; 7,2] 0,0028[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Taste disorder from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7790)					
< 65 years	12/918 (1,3)	1/937 (0,1)	12,25 [1,60; 94,01] 0,0160[2]	12,40 [1,61; 95,54] 0,0019[3]	1,2 [0,4; 2,0] 0,0019[3]
≥ 65 years	9/365 (2,5)	1/328 (0,3)	8,09 [1,03; 63,49] 0,0468[2]	8,27 [1,04; 65,61] 0,0223[4]	2,2 [0,5; 3,9] 0,0223[4]
Prior treatment (Interaction p-value: 0,9719)					
Neoadjuvant chemotherapy	3/430 (0,7)	0/415 (0,0)	6,76 [0,35; 130,40] 0,2059[2]	6,80 [0,35; 132,12] 0,2493[4]	0,7 [-0,1; 1,5] 0,2493[4]
Adjuvant chemotherapy	17/784 (2,2)	2/769 (0,3)	8,34 [1,93; 35,96] 0,0045[2]	8,50 [1,96; 36,92] 0,0006[3]	1,9 [0,8; 3,0] 0,0006[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,9756)					
North America / Europe	14/678 (2,1)	2/650 (0,3)	6,71 [1,53; 29,41] 0,0116[2]	6,83 [1,55; 30,18] 0,0033[3]	1,8 [0,6; 2,9] 0,0033[3]
Asia	0/203 (0,0)	0/201 (0,0)	NE	NE	NE
Other	7/402 (1,7)	0/414 (0,0)	15,45 [0,89; 269,57] 0,0606[2]	15,72 [0,89; 276,16] 0,0069[4]	1,7 [0,5; 3,0] 0,0069[4]
Primary tumor size (Interaction p-value: 0,9210)					
< 20 mm	5/331 (1,5)	0/335 (0,0)	11,13 [0,62; 200,53] 0,1023[2]	11,30 [0,62; 205,23] 0,0299[4]	1,5 [0,2; 2,8] 0,0299[4]
≥ 20 but < 50 mm	10/646 (1,5)	1/653 (0,2)	10,11 [1,30; 78,74] 0,0272[2]	10,25 [1,31; 80,32] 0,0061[3]	1,4 [0,4; 2,4] 0,0061[3]
≥ 50 mm	6/289 (2,1)	1/265 (0,4)	5,50 [0,67; 45,40] 0,1133[2]	5,60 [0,67; 46,80] 0,1251[4]	1,7 [-0,1; 3,5] 0,1251[4]
Number of positive lymph nodes (Interaction p-value: 0,8195)					
0-3	3/427 (0,7)	0/418 (0,0)	6,85 [0,36; 132,26] 0,2025[2]	6,90 [0,36; 134,01] 0,2492[4]	0,7 [-0,1; 1,5] 0,2492[4]
4-9	13/549 (2,4)	1/542 (0,2)	12,83 [1,68; 97,77] 0,0138[2]	13,12 [1,71; 100,65] 0,0014[3]	2,2 [0,9; 3,5] 0,0014[3]
≥ 10	5/307 (1,6)	1/305 (0,3)	4,97 [0,58; 42,27] 0,1423[2]	5,03 [0,58; 43,34] 0,2165[4]	1,3 [-0,3; 2,9] 0,2165[4]
Tumor stage (Interaction p-value: 1,0000)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIA	1/113 (0,9)	0/114 (0,0)	3,03 [0,12; 73,51] 0,4963[2]	3,05 [0,12; 75,75] 0,4978[4]	0,9 [-0,8; 2,6] 0,4978[4]
IIB	0/151 (0,0)	0/136 (0,0)	NE	NE	NE
IIIA	10/495 (2,0)	0/488 (0,0)	20,70 [1,22; 352,34] 0,0361[2]	21,13 [1,23; 361,59] 0,0019[4]	2,0 [0,8; 3,3] 0,0019[4]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	8/468 (1,7)	2/480 (0,4)	4,10 [0,88; 19,22] 0,0732[2]	4,16 [0,88; 19,68] 0,0610[4]	1,3 [-0,0; 2,6] 0,0610[4]
Tumor grade (Interaction p-value: 0,5164)					
G1	2/91 (2,2)	1/93 (1,1)	2,04 [0,19; 22,15] 0,5565[2]	2,07 [0,18; 23,21] 0,6189[4]	1,1 [-2,5; 4,8] 0,6189[4]
G2	13/612 (2,1)	1/603 (0,2)	12,81 [1,68; 97,61] 0,0138[2]	13,07 [1,70; 100,19] 0,0014[3]	2,0 [0,8; 3,1] 0,0014[3]
G3	6/527 (1,1)	0/506 (0,0)	12,48 [0,71; 221,01] 0,0851[2]	12,63 [0,71; 224,71] 0,0310[4]	1,1 [0,2; 2,0] 0,0310[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,2089)					
Negative	6/156 (3,8)	1/169 (0,6)	6,50 [0,79; 53,39] 0,0815[2]	6,72 [0,80; 56,46] 0,0582[4]	3,3 [0,0; 6,5] 0,0582[4]
Positive	15/1089 (1,4)	1/1067 (0,1)	14,70 [1,94; 111,07] 0,0092[2]	14,89 [1,96; 112,91] 0,0005[3]	1,3 [0,6; 2,0] 0,0005[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9867)					
White	20/958 (2,1)	1/944 (0,1)	19,71 [2,65; 146,55] 0,0036[2]	20,11 [2,69; 150,12] <,0001[3]	2,0 [1,1; 2,9] <,0001[3]
Asian	1/250 (0,4)	0/242 (0,0)	2,90 [0,12; 70,95] 0,5132[2]	2,92 [0,12; 71,93] 1,0000[4]	0,4 [-0,4; 1,2] 1,0000[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: 0,2947)					
Tamoxifen	3/114 (2,6)	1/132 (0,8)	3,47 [0,37; 32,93] 0,2779[2]	3,54 [0,36; 34,52] 0,3391[4]	1,9 [-1,4; 5,2] 0,3391[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aromatase inhibitor	18/1169 (1,5)	1/1133 (0,1)	17,45 [2,33; 130,47] 0,0054[2]	17,70 [2,36; 132,83] 0,0001[3]	1,5 [0,7; 2,2] 0,0001[3]
ECOG-PS (Interaction p-value: 0,5158)					
ECOG-PS 0	16/1070 (1,5)	1/1020 (0,1)	15,25 [2,03; 114,80] 0,0082[2]	15,47 [2,05; 116,86] 0,0004[3]	1,4 [0,6; 2,1] 0,0004[3]
ECOG-PS 1	5/213 (2,3)	1/245 (0,4)	5,75 [0,68; 48,84] 0,1090[2]	5,87 [0,68; 50,61] 0,1013[4]	1,9 [-0,2; 4,1] 0,1013[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Thrombocytopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1114)					
< 65 years	48/918 (5,2)	8/937 (0,9)	6,12 [2,91; 12,87] <,0001[2]	6,41 [3,01; 13,62] <,0001[3]	4,4 [2,8; 5,9] <,0001[3]
≥ 65 years	38/365 (10,4)	1/328 (0,3)	34,15 [4,71; 247,32] 0,0005[2]	38,00 [5,19; 278,41] <,0001[3]	10,1 [6,9; 13,3] <,0001[3]
Prior treatment (Interaction p-value: 0,9420)					
Neoadjuvant chemotherapy	24/430 (5,6)	3/415 (0,7)	7,72 [2,34; 25,45] 0,0008[2]	8,12 [2,43; 27,17] <,0001[3]	4,9 [2,5; 7,2] <,0001[3]
Adjuvant chemotherapy	61/784 (7,8)	6/769 (0,8)	9,97 [4,34; 22,93] <,0001[2]	10,73 [4,61; 24,97] <,0001[3]	7,0 [5,0; 9,0] <,0001[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,5748)					
North America / Europe	42/678 (6,2)	3/650 (0,5)	13,42 [4,18; 43,09] <,0001[2]	14,24 [4,39; 46,18] <,0001[3]	5,7 [3,8; 7,6] <,0001[3]
Asia	8/203 (3,9)	0/201 (0,0)	16,83 [0,98; 289,71] 0,0518[2]	17,52 [1,00; 305,63] 0,0073[4]	3,9 [1,3; 6,6] 0,0073[4]
Other	36/402 (9,0)	6/414 (1,4)	6,18 [2,63; 14,50] <,0001[2]	6,69 [2,79; 16,06] <,0001[3]	7,5 [4,5; 10,5] <,0001[3]
Primary tumor size (Interaction p-value: 0,6587)					
< 20 mm	19/331 (5,7)	2/335 (0,6)	9,61 [2,26; 40,95] 0,0022[2]	10,14 [2,34; 43,89] 0,0001[3]	5,1 [2,5; 7,8] 0,0001[3]
≥ 20 but < 50 mm	44/646 (6,8)	6/653 (0,9)	7,41 [3,18; 17,27] <,0001[2]	7,88 [3,33; 18,63] <,0001[3]	5,9 [3,8; 8,0] <,0001[3]
≥ 50 mm	22/289 (7,6)	1/265 (0,4)	20,17 [2,74; 148,62] 0,0032[2]	21,75 [2,91; 162,55] <,0001[3]	7,2 [4,1; 10,4] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,3433)					
0-3	25/427 (5,9)	4/418 (1,0)	6,12 [2,15; 17,43] 0,0007[2]	6,44 [2,22; 18,66] <,0001[3]	4,9 [2,5; 7,3] <,0001[3]
4-9	42/549 (7,7)	2/542 (0,4)	20,73 [5,04; 85,22] <,0001[2]	22,37 [5,39; 92,88] <,0001[3]	7,3 [5,0; 9,6] <,0001[3]
≥ 10	19/307 (6,2)	3/305 (1,0)	6,29 [1,88; 21,04] 0,0028[2]	6,64 [1,94; 22,68] 0,0005[3]	5,2 [2,3; 8,1] 0,0005[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9665)					
IIA	5/113 (4,4)	1/114 (0,9)	5,04 [0,60; 42,50] 0,1367[2]	5,23 [0,60; 45,51] 0,1192[4]	3,5 [-0,6; 7,7] 0,1192[4]
IIB	10/151 (6,6)	1/136 (0,7)	9,01 [1,17; 69,44] 0,0349[2]	9,57 [1,21; 75,81] 0,0095[3]	5,9 [1,7; 10,1] 0,0095[3]
IIIA	37/495 (7,5)	3/488 (0,6)	12,16 [3,77; 39,17] <,0001[2]	13,06 [4,00; 42,65] <,0001[3]	6,9 [4,4; 9,3] <,0001[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	32/468 (6,8)	4/480 (0,8)	8,21 [2,92; 23,02] <,0001[2]	8,73 [3,06; 24,90] <,0001[3]	6,0 [3,6; 8,4] <,0001[3]
Tumor grade (Interaction p-value: 0,9985)					
G1	4/91 (4,4)	0/93 (0,0)	9,20 [0,50; 168,39] 0,1348[2]	9,62 [0,51; 181,24] 0,0578[4]	4,4 [0,2; 8,6] 0,0578[4]
G2	37/612 (6,0)	4/603 (0,7)	9,11 [3,27; 25,41] <,0001[2]	9,64 [3,41; 27,21] <,0001[3]	5,4 [3,4; 7,4] <,0001[3]
G3	42/527 (8,0)	5/506 (1,0)	8,07 [3,22; 20,22] <,0001[2]	8,68 [3,40; 22,12] <,0001[3]	7,0 [4,5; 9,4] <,0001[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,5670)					
Negative	13/156 (8,3)	2/169 (1,2)	7,04 [1,61; 30,71] 0,0094[2]	7,59 [1,68; 34,20] 0,0021[3]	7,1 [2,5; 11,8] 0,0021[3]
Positive	73/1089 (6,7)	7/1067 (0,7)	10,22 [4,73; 22,09] <,0001[2]	10,88 [4,99; 23,74] <,0001[3]	6,0 [4,5; 7,6] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,1625)					
White	71/958 (7,4)	7/944 (0,7)	9,99 [4,62; 21,61] <,0001[2]	10,71 [4,90; 23,42] <,0001[3]	6,7 [4,9; 8,4] <,0001[3]
Asian	12/250 (4,8)	0/242 (0,0)	24,20 [1,44; 406,54] 0,0268[2]	25,42 [1,50; 431,75] 0,0006[3]	4,8 [2,2; 7,4] 0,0006[3]
Other	3/62 (4,8)	2/64 (3,1)	1,55 [0,27; 8,95] 0,6253[2]	1,58 [0,25; 9,77] 0,6774[4]	1,7 [-5,1; 8,5] 0,6774[4]
ECOG-PS (Interaction p-value: 0,4661)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	60/1070 (5,6)	7/1020 (0,7)	8,17 [3,75; 17,79] <,0001[2]	8,60 [3,91; 18,90] <,0001[3]	4,9 [3,5; 6,4] <,0001[3]
ECOG-PS 1	26/213 (12,2)	2/245 (0,8)	14,95 [3,59; 62,26] 0,0002[2]	16,89 [3,96; 72,07] <,0001[3]	11,4 [6,9; 15,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Urinary tract infection from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8305)					
< 65 years	80/918 (8,7)	50/937 (5,3)	1,63 [1,16; 2,30] 0,0049[2]	1,69 [1,17; 2,44] 0,0044[3]	3,4 [1,1; 5,7] 0,0044[3]
≥ 65 years	37/365 (10,1)	19/328 (5,8)	1,75 [1,03; 2,98] 0,0395[2]	1,83 [1,03; 3,26] 0,0362[3]	4,3 [0,3; 8,3] 0,0362[3]
Prior treatment (Interaction p-value: 0,1169)					
Neoadjuvant chemotherapy	35/430 (8,1)	11/415 (2,7)	3,07 [1,58; 5,96] 0,0009[2]	3,25 [1,63; 6,50] 0,0004[3]	5,5 [2,5; 8,5] 0,0004[3]
Adjuvant chemotherapy	76/784 (9,7)	53/769 (6,9)	1,41 [1,00; 1,97] 0,0468[2]	1,45 [1,01; 2,09] 0,0455[3]	2,8 [0,1; 5,5] 0,0455[3]
No chemotherapy	6/69 (8,7)	5/81 (6,2)	1,41 [0,45; 4,42] 0,5567[2]	1,45 [0,42; 4,97] 0,5547[3]	2,5 [-5,9; 11,0] 0,5547[3]
Region (Interaction p-value: 0,6684)					
North America / Europe	83/678 (12,2)	52/650 (8,0)	1,53 [1,10; 2,13] 0,0114[2]	1,60 [1,11; 2,31] 0,0106[3]	4,2 [1,0; 7,5] 0,0106[3]
Asia	5/203 (2,5)	2/201 (1,0)	2,48 [0,49; 12,61] 0,2752[2]	2,51 [0,48; 13,10] 0,4491[4]	1,5 [-1,1; 4,0] 0,4491[4]
Other	29/402 (7,2)	15/414 (3,6)	1,99 [1,08; 3,66] 0,0264[2]	2,07 [1,09; 3,92] 0,0232[3]	3,6 [0,5; 6,7] 0,0232[3]
Primary tumor size (Interaction p-value: 0,9052)					
< 20 mm	24/331 (7,3)	13/335 (3,9)	1,87 [0,97; 3,61] 0,0625[2]	1,94 [0,97; 3,87] 0,0576[3]	3,4 [-0,1; 6,8] 0,0576[3]
≥ 20 but < 50 mm	53/646 (8,2)	33/653 (5,1)	1,62 [1,07; 2,47] 0,0240[2]	1,68 [1,07; 2,63] 0,0224[3]	3,2 [0,4; 5,9] 0,0224[3]
≥ 50 mm	39/289 (13,5)	23/265 (8,7)	1,55 [0,95; 2,53] 0,0760[2]	1,64 [0,95; 2,83] 0,0725[3]	4,8 [-0,4; 10,0] 0,0725[3]
Number of positive lymph nodes (Interaction p-value: 0,8497)					
0-3	36/427 (8,4)	20/418 (4,8)	1,76 [1,04; 2,99] 0,0361[2]	1,83 [1,04; 3,22] 0,0331[3]	3,6 [0,3; 7,0] 0,0331[3]
4-9	50/549 (9,1)	28/542 (5,2)	1,76 [1,13; 2,76] 0,0129[2]	1,84 [1,14; 2,97] 0,0115[3]	3,9 [0,9; 7,0] 0,0115[3]
≥ 10	31/307 (10,1)	21/305 (6,9)	1,47 [0,86; 2,49] 0,1574[2]	1,52 [0,85; 2,71] 0,1541[3]	3,2 [-1,2; 7,6] 0,1541[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,6657)					
IIA	13/113 (11,5)	6/114 (5,3)	2,19 [0,86; 5,55] 0,1000[2]	2,34 [0,86; 6,39] 0,0896[3]	6,2 [-0,9; 13,4] 0,0896[3]
IIB	9/151 (6,0)	9/136 (6,6)	0,90 [0,37; 2,20] 0,8187[2]	0,89 [0,34; 2,32] 0,8186[3]	-0,7 [-6,3; 5,0] 0,8186[3]
IIIA	48/495 (9,7)	28/488 (5,7)	1,69 [1,08; 2,65] 0,0220[2]	1,76 [1,09; 2,86] 0,0201[3]	4,0 [0,6; 7,3] 0,0201[3]
IIIB	3/54 (5,6)	1/45 (2,2)	2,50 [0,27; 23,21] 0,4203[2]	2,59 [0,26; 25,79] 0,6237[4]	3,3 [-4,1; 10,8] 0,6237[4]
IIIC	44/468 (9,4)	25/480 (5,2)	1,81 [1,12; 2,90] 0,0146[2]	1,89 [1,14; 3,14] 0,0130[3]	4,2 [0,9; 7,5] 0,0130[3]
Tumor grade (Interaction p-value: 0,7026)					
G1	7/91 (7,7)	4/93 (4,3)	1,79 [0,54; 5,90] 0,3399[2]	1,85 [0,52; 6,56] 0,3320[3]	3,4 [-3,5; 10,2] 0,3320[3]
G2	62/612 (10,1)	38/603 (6,3)	1,61 [1,09; 2,37] 0,0164[2]	1,68 [1,10; 2,55] 0,0152[3]	3,8 [0,8; 6,9] 0,0152[3]
G3	43/527 (8,2)	26/506 (5,1)	1,59 [0,99; 2,54] 0,0545[2]	1,64 [0,99; 2,71] 0,0519[3]	3,0 [-0,0; 6,0] 0,0519[3]
GX	5/51 (9,8)	1/59 (1,7)	5,78 [0,70; 47,91] 0,1037[2]	6,30 [0,71; 55,86] 0,0942[4]	8,1 [-0,7; 16,9] 0,0942[4]
Race (Interaction p-value: 0,7814)					
White	104/958 (10,9)	58/944 (6,1)	1,77 [1,30; 2,41] 0,0003[2]	1,86 [1,33; 2,60] 0,0002[3]	4,7 [2,2; 7,2] 0,0002[3]
Asian	5/250 (2,0)	4/242 (1,7)	1,21 [0,33; 4,45] 0,7743[2]	1,21 [0,32; 4,58] 1,0000[4]	0,3 [-2,0; 2,7] 1,0000[4]
Other	8/62 (12,9)	6/64 (9,4)	1,38 [0,51; 3,74] 0,5309[2]	1,43 [0,47; 4,40] 0,5287[3]	3,5 [-7,5; 14,5] 0,5287[3]
First endocrine therapy (Interaction p-value: 0,1254)					
Tamoxifen	9/114 (7,9)	2/132 (1,5)	5,21 [1,15; 23,62] 0,0323[2]	5,57 [1,18; 26,34] 0,0158[3]	6,4 [1,0; 11,8] 0,0158[3]
Aromatase inhibitor	108/1169 (9,2)	67/1133 (5,9)	1,56 [1,16; 2,10] 0,0029[2]	1,62 [1,18; 2,22] 0,0026[3]	3,3 [1,2; 5,5] 0,0026[3]
ECOG-PS (Interaction p-value: 0,5396)					
ECOG-PS 0	91/1070 (8,5)	54/1020 (5,3)	1,61 [1,16; 2,22] 0,0043[2]	1,66 [1,17; 2,36] 0,0039[3]	3,2 [1,0; 5,4] 0,0039[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	26/213 (12,2)	15/245 (6,1)	1,99 [1,09; 3,66] 0,0262[2]	2,13 [1,10; 4,14] 0,0229[3]	6,1 [0,8; 11,4] 0,0229[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Viral infection from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,2124)					
< 65 years	13/918 (1,4)	1/937 (0,1)	13,27 [1,74; 101,23] 0,0126[2]	13,45 [1,76; 102,99] 0,0011[3]	1,3 [0,5; 2,1] 0,0011[3]
≥ 65 years	2/365 (0,5)	1/328 (0,3)	1,80 [0,16; 19,73] 0,6315[2]	1,80 [0,16; 19,96] 1,0000[4]	0,2 [-0,7; 1,2] 1,0000[4]
Prior treatment (Interaction p-value: 0,9831)					
Neoadjuvant chemotherapy	6/430 (1,4)	0/415 (0,0)	12,55 [0,71; 222,03] 0,0844[2]	12,72 [0,71; 226,59] 0,0308[4]	1,4 [0,3; 2,5] 0,0308[4]
Adjuvant chemotherapy	9/784 (1,1)	2/769 (0,3)	4,41 [0,96; 20,36] 0,0570[2]	4,45 [0,96; 20,68] 0,0370[3]	0,9 [0,1; 1,7] 0,0370[3]
No chemotherapy	0/69 (0,0)	0/81 (0,0)	NE	NE	NE
Region (Interaction p-value: 0,9779)					
North America / Europe	13/678 (1,9)	2/650 (0,3)	6,23 [1,41; 27,51] 0,0157[2]	6,33 [1,42; 28,18] 0,0055[3]	1,6 [0,5; 2,7] 0,0055[3]
Asia	0/203 (0,0)	0/201 (0,0)	NE	NE	NE
Other	2/402 (0,5)	0/414 (0,0)	5,15 [0,25; 106,92] 0,2896[2]	5,17 [0,25; 108,12] 0,2424[4]	0,5 [-0,2; 1,2] 0,2424[4]
Tumor grade (Interaction p-value: 0,5758)					
G1	1/91 (1,1)	0/93 (0,0)	3,07 [0,13; 74,28] 0,4910[2]	3,10 [0,12; 77,08] 0,4946[4]	1,1 [-1,0; 3,2] 0,4946[4]
G2	5/612 (0,8)	1/603 (0,2)	4,93 [0,58; 42,04] 0,1449[2]	4,96 [0,58; 42,57] 0,2177[4]	0,7 [-0,1; 1,4] 0,2177[4]
G3	9/527 (1,7)	1/506 (0,2)	8,64 [1,10; 67,96] 0,0404[2]	8,77 [1,11; 69,51] 0,0211[4]	1,5 [0,3; 2,7] 0,0211[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,9634)					
Negative	2/156 (1,3)	0/169 (0,0)	5,41 [0,26; 111,90] 0,2744[2]	5,49 [0,26; 115,15] 0,2296[4]	1,3 [-0,5; 3,0] 0,2296[4]
Positive	13/1089 (1,2)	2/1067 (0,2)	6,37 [1,44; 28,15] 0,0146[2]	6,43 [1,45; 28,58] 0,0049[3]	1,0 [0,3; 1,7] 0,0049[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Race (Interaction p-value: 0,9853)					
White	14/958 (1,5)	2/944 (0,2)	6,90 [1,57; 30,27] 0,0105[2]	6,99 [1,58; 30,82] 0,0029[3]	1,2 [0,4; 2,1] 0,0029[3]
Asian	1/250 (0,4)	0/242 (0,0)	2,90 [0,12; 70,95] 0,5132[2]	2,92 [0,12; 71,93] 1,0000[4]	0,4 [-0,4; 1,2] 1,0000[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9757)					
ECOG-PS 0	13/1070 (1,2)	2/1020 (0,2)	6,20 [1,40; 27,39] 0,0162[2]	6,26 [1,41; 27,81] 0,0058[3]	1,0 [0,3; 1,7] 0,0058[3]
ECOG-PS 1	2/213 (0,9)	0/245 (0,0)	5,75 [0,28; 119,06] 0,2581[2]	5,80 [0,28; 121,56] 0,2157[4]	0,9 [-0,4; 2,2] 0,2157[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Vision blurred from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1757)					
< 65 years	23/918 (2,5)	6/937 (0,6)	3,91 [1,60; 9,56] 0,0028[2]	3,99 [1,62; 9,84] 0,0012[3]	1,9 [0,7; 3,0] 0,0012[3]
≥ 65 years	6/365 (1,6)	4/328 (1,2)	1,35 [0,38; 4,73] 0,6414[2]	1,35 [0,38; 4,84] 0,7557[4]	0,4 [-1,3; 2,2] 0,7557[4]
Prior treatment (Interaction p-value: 0,7750)					
Neoadjuvant chemotherapy	11/430 (2,6)	4/415 (1,0)	2,65 [0,85; 8,27] 0,0923[2]	2,70 [0,85; 8,54] 0,0793[3]	1,6 [-0,2; 3,4] 0,0793[3]
Adjuvant chemotherapy	17/784 (2,2)	5/769 (0,7)	3,33 [1,24; 8,99] 0,0173[2]	3,39 [1,24; 9,23] 0,0114[3]	1,5 [0,4; 2,7] 0,0114[3]
No chemotherapy	1/69 (1,4)	1/81 (1,2)	1,17 [0,07; 18,42] 0,9091[2]	1,18 [0,07; 19,17] 1,0000[4]	0,2 [-3,5; 3,9] 1,0000[4]
Region (Interaction p-value: 0,5694)					
North America / Europe	22/678 (3,2)	6/650 (0,9)	3,52 [1,43; 8,61] 0,0060[2]	3,60 [1,45; 8,94] 0,0032[3]	2,3 [0,8; 3,8] 0,0032[3]
Asia	3/203 (1,5)	1/201 (0,5)	2,97 [0,31; 28,32] 0,3440[2]	3,00 [0,31; 29,09] 0,6232[4]	1,0 [-0,9; 2,9] 0,6232[4]
Other	4/402 (1,0)	3/414 (0,7)	1,37 [0,31; 6,10] 0,6767[2]	1,38 [0,31; 6,19] 0,7217[4]	0,3 [-1,0; 1,5] 0,7217[4]
Primary tumor size (Interaction p-value: 0,2515)					
< 20 mm	11/331 (3,3)	2/335 (0,6)	5,57 [1,24; 24,92] 0,0248[2]	5,72 [1,26; 26,02] 0,0110[3]	2,7 [0,6; 4,8] 0,0110[3]
≥ 20 but < 50 mm	11/646 (1,7)	7/653 (1,1)	1,59 [0,62; 4,07] 0,3353[2]	1,60 [0,62; 4,15] 0,3308[3]	0,6 [-0,6; 1,9] 0,3308[3]
≥ 50 mm	7/289 (2,4)	1/265 (0,4)	6,42 [0,79; 51,82] 0,0810[2]	6,55 [0,80; 53,62] 0,0704[4]	2,0 [0,1; 4,0] 0,0704[4]
Number of positive lymph nodes (Interaction p-value: 0,9363)					
0-3	12/427 (2,8)	4/418 (1,0)	2,94 [0,95; 9,03] 0,0602[2]	2,99 [0,96; 9,36] 0,0481[3]	1,9 [0,0; 3,7] 0,0481[3]
4-9	13/549 (2,4)	5/542 (0,9)	2,57 [0,92; 7,15] 0,0713[2]	2,60 [0,92; 7,36] 0,0609[3]	1,4 [-0,1; 3,0] 0,0609[3]
≥ 10	4/307 (1,3)	1/305 (0,3)	3,97 [0,45; 35,35] 0,2160[2]	4,01 [0,45; 36,11] 0,3730[4]	1,0 [-0,4; 2,4] 0,3730[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,5698)					
IIA	3/113 (2,7)	0/114 (0,0)	7,06 [0,37; 135,16] 0,1943[2]	7,25 [0,37; 142,05] 0,1217[4]	2,7 [-0,3; 5,6] 0,1217[4]
IIB	3/151 (2,0)	1/136 (0,7)	2,70 [0,28; 25,67] 0,3868[2]	2,74 [0,28; 26,62] 0,6244[4]	1,3 [-1,4; 3,9] 0,6244[4]
IIIA	13/495 (2,6)	3/488 (0,6)	4,27 [1,23; 14,90] 0,0227[2]	4,36 [1,23; 15,40] 0,0127[3]	2,0 [0,4; 3,6] 0,0127[3]
IIIB	1/54 (1,9)	2/45 (4,4)	0,42 [0,04; 4,45] 0,4686[2]	0,41 [0,04; 4,63] 0,5894[4]	-2,6 [-9,6; 4,4] 0,5894[4]
IIIC	9/468 (1,9)	4/480 (0,8)	2,31 [0,72; 7,44] 0,1616[2]	2,33 [0,71; 7,63] 0,1492[3]	1,1 [-0,4; 2,6] 0,1492[3]
Tumor grade (Interaction p-value: 0,7477)					
G1	0/91 (0,0)	0/93 (0,0)	NE	NE	NE
G2	15/612 (2,5)	7/603 (1,2)	2,11 [0,87; 5,14] 0,0998[2]	2,14 [0,87; 5,28] 0,0917[3]	1,3 [-0,2; 2,8] 0,0917[3]
G3	12/527 (2,3)	3/506 (0,6)	3,84 [1,09; 13,53] 0,0362[2]	3,91 [1,10; 13,93] 0,0237[3]	1,7 [0,2; 3,1] 0,0237[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,2114)					
Negative	4/156 (2,6)	1/169 (0,6)	4,33 [0,49; 38,35] 0,1875[2]	4,42 [0,49; 39,99] 0,1985[4]	2,0 [-0,8; 4,7] 0,1985[4]
Positive	24/1089 (2,2)	9/1067 (0,8)	2,61 [1,22; 5,59] 0,0134[2]	2,65 [1,23; 5,73] 0,0101[3]	1,4 [0,3; 2,4] 0,0101[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9531)					
White	22/958 (2,3)	8/944 (0,8)	2,71 [1,21; 6,06] 0,0151[2]	2,75 [1,22; 6,21] 0,0112[3]	1,4 [0,3; 2,6] 0,0112[3]
Asian	4/250 (1,6)	1/242 (0,4)	3,87 [0,44; 34,40] 0,2244[2]	3,92 [0,43; 35,31] 0,3728[4]	1,2 [-0,6; 2,9] 0,3728[4]
Other	3/62 (4,8)	1/64 (1,6)	3,10 [0,33; 28,97] 0,3218[2]	3,20 [0,32; 31,66] 0,3610[4]	3,3 [-2,9; 9,4] 0,3610[4]
First endocrine therapy (Interaction p-value: 0,9962)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	5/114 (4,4)	2/132 (1,5)	2,89 [0,57; 14,64] 0,1986[2]	2,98 [0,57; 15,67] 0,2546[4]	2,9 [-1,4; 7,2] 0,2546[4]
Aromatase inhibitor	24/1169 (2,1)	8/1133 (0,7)	2,91 [1,31; 6,44] 0,0086[2]	2,95 [1,32; 6,59] 0,0058[3]	1,3 [0,4; 2,3] 0,0058[3]
ECOG-PS (Interaction p-value: 0,7858)					
ECOG-PS 0	25/1070 (2,3)	8/1020 (0,8)	2,98 [1,35; 6,57] 0,0069[2]	3,03 [1,36; 6,74] 0,0044[3]	1,6 [0,5; 2,6] 0,0044[3]
ECOG-PS 1	4/213 (1,9)	2/245 (0,8)	2,30 [0,43; 12,44] 0,3332[2]	2,33 [0,42; 12,82] 0,4235[4]	1,1 [-1,1; 3,2] 0,4235[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Vitamin B12 deficiency from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0712)					
< 65 years	12/918 (1,3)	1/937 (0,1)	12,25 [1,60; 94,01] 0,0160[2]	12,40 [1,61; 95,54] 0,0019[3]	1,2 [0,4; 2,0] 0,0019[3]
≥ 65 years	4/365 (1,1)	3/328 (0,9)	1,20 [0,27; 5,31] 0,8120[2]	1,20 [0,27; 5,40] 1,0000[4]	0,2 [-1,3; 1,7] 1,0000[4]
Region (Interaction p-value: 0,5269)					
North America / Europe	11/678 (1,6)	2/650 (0,3)	5,27 [1,17; 23,70] 0,0301[2]	5,34 [1,18; 24,20] 0,0150[3]	1,3 [0,3; 2,4] 0,0150[3]
Asia	0/203 (0,0)	0/201 (0,0)	NE	NE	NE
Other	5/402 (1,2)	2/414 (0,5)	2,57 [0,50; 13,19] 0,2567[2]	2,59 [0,50; 13,45] 0,2803[4]	0,8 [-0,5; 2,0] 0,2803[4]
Primary tumor size (Interaction p-value: 0,8845)					
< 20 mm	3/331 (0,9)	0/335 (0,0)	7,08 [0,37; 136,62] 0,1947[2]	7,15 [0,37; 138,95] 0,1222[4]	0,9 [-0,1; 1,9] 0,1222[4]
≥ 20 but < 50 mm	8/646 (1,2)	2/653 (0,3)	4,04 [0,86; 18,97] 0,0765[2]	4,08 [0,86; 19,29] 0,0631[4]	0,9 [-0,0; 1,9] 0,0631[4]
≥ 50 mm	5/289 (1,7)	2/265 (0,8)	2,29 [0,45; 11,72] 0,3189[2]	2,32 [0,45; 12,04] 0,4533[4]	1,0 [-0,9; 2,8] 0,4533[4]
Tumor stage (Interaction p-value: 1,0000)					
IIA	1/113 (0,9)	0/114 (0,0)	3,03 [0,12; 73,51] 0,4963[2]	3,05 [0,12; 75,75] 0,4978[4]	0,9 [-0,8; 2,6] 0,4978[4]
IIB	2/151 (1,3)	0/136 (0,0)	4,51 [0,22; 93,05] 0,3297[2]	4,57 [0,22; 95,94] 0,4996[4]	1,3 [-0,5; 3,1] 0,4996[4]
IIIA	6/495 (1,2)	0/488 (0,0)	12,82 [0,72; 226,89] 0,0819[2]	12,97 [0,73; 230,92] 0,0308[4]	1,2 [0,2; 2,2] 0,0308[4]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	7/468 (1,5)	4/480 (0,8)	1,79 [0,53; 6,09] 0,3481[2]	1,81 [0,53; 6,21] 0,3410[3]	0,7 [-0,7; 2,0] 0,3410[3]
Tumor grade (Interaction p-value: 0,8821)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G2	10/612 (1,6)	2/603 (0,3)	4,93 [1,08; 22,39] 0,0390[2]	4,99 [1,09; 22,88] 0,0217[3]	1,3 [0,2; 2,4] 0,0217[3]
G3	4/527 (0,8)	2/506 (0,4)	1,92 [0,35; 10,44] 0,4500[2]	1,93 [0,35; 10,57] 0,6870[4]	0,4 [-0,6; 1,3] 0,6870[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,5736)					
Negative	2/156 (1,3)	1/169 (0,6)	2,17 [0,20; 23,66] 0,5261[2]	2,18 [0,20; 24,30] 0,6093[4]	0,7 [-1,4; 2,8] 0,6093[4]
Positive	14/1089 (1,3)	3/1067 (0,3)	4,57 [1,32; 15,87] 0,0166[2]	4,62 [1,32; 16,12] 0,0084[3]	1,0 [0,3; 1,7] 0,0084[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9844)					
White	14/958 (1,5)	4/944 (0,4)	3,45 [1,14; 10,44] 0,0285[2]	3,49 [1,14; 10,63] 0,0194[3]	1,0 [0,2; 1,9] 0,0194[3]
Asian	1/250 (0,4)	0/242 (0,0)	2,90 [0,12; 70,95] 0,5132[2]	2,92 [0,12; 71,93] 1,0000[4]	0,4 [-0,4; 1,2] 1,0000[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,8913)					
ECOG-PS 0	13/1070 (1,2)	3/1020 (0,3)	4,13 [1,18; 14,45] 0,0264[2]	4,17 [1,18; 14,67] 0,0158[3]	0,9 [0,2; 1,7] 0,0158[3]
ECOG-PS 1	3/213 (1,4)	1/245 (0,4)	3,45 [0,36; 32,93] 0,2818[2]	3,49 [0,36; 33,76] 0,3420[4]	1,0 [-0,8; 2,8] 0,3420[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Vomiting from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5712)					
< 65 years	158/918 (17,2)	41/937 (4,4)	3,93 [2,82; 5,48] <,0001[2]	4,54 [3,18; 6,49] <,0001[3]	12,8 [10,1; 15,6] <,0001[3]
≥ 65 years	64/365 (17,5)	12/328 (3,7)	4,79 [2,63; 8,72] <,0001[2]	5,60 [2,96; 10,58] <,0001[3]	13,9 [9,5; 18,3] <,0001[3]
Prior treatment (Interaction p-value: 0,9722)					
Neoadjuvant chemotherapy	78/430 (18,1)	18/415 (4,3)	4,18 [2,55; 6,86] <,0001[2]	4,89 [2,87; 8,32] <,0001[3]	13,8 [9,7; 17,9] <,0001[3]
Adjuvant chemotherapy	132/784 (16,8)	32/769 (4,2)	4,05 [2,79; 5,88] <,0001[2]	4,66 [3,12; 6,96] <,0001[3]	12,7 [9,7; 15,7] <,0001[3]
No chemotherapy	12/69 (17,4)	3/81 (3,7)	4,70 [1,38; 15,96] 0,0132[2]	5,47 [1,48; 20,30] 0,0054[3]	13,7 [3,8; 23,5] 0,0054[3]
Region (Interaction p-value: 0,0774)					
North America / Europe	140/678 (20,6)	41/650 (6,3)	3,27 [2,35; 4,56] <,0001[2]	3,87 [2,68; 5,58] <,0001[3]	14,3 [10,8; 17,9] <,0001[3]
Asia	26/203 (12,8)	2/201 (1,0)	12,87 [3,10; 53,52] 0,0004[2]	14,62 [3,42; 62,46] <,0001[3]	11,8 [7,0; 16,6] <,0001[3]
Other	56/402 (13,9)	10/414 (2,4)	5,77 [2,98; 11,14] <,0001[2]	6,54 [3,29; 13,01] <,0001[3]	11,5 [7,8; 15,2] <,0001[3]
Primary tumor size (Interaction p-value: 0,7189)					
< 20 mm	53/331 (16,0)	11/335 (3,3)	4,88 [2,59; 9,17] <,0001[2]	5,62 [2,88; 10,96] <,0001[3]	12,7 [8,3; 17,1] <,0001[3]
≥ 20 but < 50 mm	109/646 (16,9)	30/653 (4,6)	3,67 [2,49; 5,42] <,0001[2]	4,22 [2,77; 6,42] <,0001[3]	12,3 [9,0; 15,6] <,0001[3]
≥ 50 mm	58/289 (20,1)	12/265 (4,5)	4,43 [2,44; 8,07] <,0001[2]	5,29 [2,77; 10,11] <,0001[3]	15,5 [10,3; 20,8] <,0001[3]
Tumor stage (Interaction p-value: 0,0560)					
IIA	17/113 (15,0)	4/114 (3,5)	4,29 [1,49; 12,35] 0,0070[2]	4,87 [1,58; 14,97] 0,0027[3]	11,5 [4,1; 18,9] 0,0027[3]
IIB	24/151 (15,9)	10/136 (7,4)	2,16 [1,07; 4,35] 0,0310[2]	2,38 [1,09; 5,18] 0,0254[3]	8,5 [1,2; 15,8] 0,0254[3]
IIIA	87/495 (17,6)	25/488 (5,1)	3,43 [2,24; 5,26] <,0001[2]	3,95 [2,48; 6,28] <,0001[3]	12,5 [8,6; 16,3] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	4/54 (7,4)	2/45 (4,4)	1,67 [0,32; 8,68] 0,5441[2]	1,72 [0,30; 9,85] 0,6859[4]	3,0 [-6,3; 12,2] 0,6859[4]
IIIC	90/468 (19,2)	12/480 (2,5)	7,69 [4,27; 13,86] <,0001[2]	9,29 [5,01; 17,22] <,0001[3]	16,7 [12,9; 20,6] <,0001[3]
Tumor grade (Interaction p-value: 0,7829)					
G1	13/91 (14,3)	3/93 (3,2)	4,43 [1,31; 15,03] 0,0170[2]	5,00 [1,37; 18,19] 0,0078[3]	11,1 [3,0; 19,1] 0,0078[3]
G2	106/612 (17,3)	28/603 (4,6)	3,73 [2,50; 5,57] <,0001[2]	4,30 [2,79; 6,63] <,0001[3]	12,7 [9,2; 16,1] <,0001[3]
G3	94/527 (17,8)	21/506 (4,2)	4,30 [2,72; 6,79] <,0001[2]	5,01 [3,07; 8,19] <,0001[3]	13,7 [10,0; 17,4] <,0001[3]
GX	9/51 (17,6)	1/59 (1,7)	10,41 [1,37; 79,41] 0,0238[2]	12,43 [1,52; 101,88] 0,0054[4]	16,0 [5,0; 26,9] 0,0054[4]
Race (Interaction p-value: 0,3578)					
White	180/958 (18,8)	46/944 (4,9)	3,86 [2,83; 5,26] <,0001[2]	4,52 [3,22; 6,33] <,0001[3]	13,9 [11,1; 16,7] <,0001[3]
Asian	29/250 (11,6)	3/242 (1,2)	9,36 [2,89; 30,31] 0,0002[2]	10,45 [3,14; 34,80] <,0001[3]	10,4 [6,2; 14,6] <,0001[3]
Other	11/62 (17,7)	3/64 (4,7)	3,78 [1,11; 12,92] 0,0336[2]	4,39 [1,16; 16,58] 0,0197[3]	13,1 [2,2; 23,9] 0,0197[3]
First endocrine therapy (Interaction p-value: 0,3704)					
Tamoxifen	18/114 (15,8)	3/132 (2,3)	6,95 [2,10; 22,98] 0,0015[2]	8,06 [2,31; 28,15] 0,0002[3]	13,5 [6,4; 20,7] 0,0002[3]
Aromatase inhibitor	204/1169 (17,5)	50/1133 (4,4)	3,95 [2,93; 5,33] <,0001[2]	4,58 [3,32; 6,31] <,0001[3]	13,0 [10,6; 15,5] <,0001[3]
ECOG-PS (Interaction p-value: 0,0929)					
ECOG-PS 0	181/1070 (16,9)	36/1020 (3,5)	4,79 [3,39; 6,78] <,0001[2]	5,57 [3,85; 8,05] <,0001[3]	13,4 [10,9; 15,9] <,0001[3]
ECOG-PS 1	41/213 (19,2)	17/245 (6,9)	2,77 [1,63; 4,74] 0,0002[2]	3,20 [1,76; 5,82] <,0001[3]	12,3 [6,1; 18,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT Weight decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9699)					
< 65 years	31/918 (3,4)	9/937 (1,0)	3,52 [1,68; 7,34] 0,0008[2]	3,60 [1,71; 7,61] 0,0003[3]	2,4 [1,1; 3,7] 0,0003[3]
≥ 65 years	24/365 (6,6)	6/328 (1,8)	3,59 [1,49; 8,68] 0,0045[2]	3,78 [1,52; 9,36] 0,0022[3]	4,7 [1,8; 7,7] 0,0022[3]
Prior treatment (Interaction p-value: 0,6748)					
Neoadjuvant chemotherapy	22/430 (5,1)	5/415 (1,2)	4,25 [1,62; 11,11] 0,0032[2]	4,42 [1,66; 11,79] 0,0012[3]	3,9 [1,6; 6,2] 0,0012[3]
Adjuvant chemotherapy	27/784 (3,4)	9/769 (1,2)	2,94 [1,39; 6,22] 0,0047[2]	3,01 [1,41; 6,45] 0,0029[3]	2,3 [0,8; 3,8] 0,0029[3]
No chemotherapy	6/69 (8,7)	1/81 (1,2)	7,04 [0,87; 57,09] 0,0675[2]	7,62 [0,89; 64,93] 0,0485[4]	7,5 [0,4; 14,5] 0,0485[4]
Region (Interaction p-value: 0,8340)					
North America / Europe	31/678 (4,6)	9/650 (1,4)	3,30 [1,58; 6,88] 0,0014[2]	3,41 [1,61; 7,23] 0,0007[3]	3,2 [1,4; 5,0] 0,0007[3]
Asia	11/203 (5,4)	2/201 (1,0)	5,45 [1,22; 24,26] 0,0262[2]	5,70 [1,25; 26,05] 0,0118[3]	4,4 [1,0; 7,8] 0,0118[3]
Other	13/402 (3,2)	4/414 (1,0)	3,35 [1,10; 10,18] 0,0333[2]	3,43 [1,11; 10,60] 0,0234[3]	2,3 [0,3; 4,2] 0,0234[3]
Primary tumor size (Interaction p-value: 0,2082)					
< 20 mm	8/331 (2,4)	5/335 (1,5)	1,62 [0,54; 4,90] 0,3934[2]	1,63 [0,53; 5,05] 0,3886[3]	0,9 [-1,2; 3,0] 0,3886[3]
≥ 20 but < 50 mm	34/646 (5,3)	6/653 (0,9)	5,73 [2,42; 13,55] <,0001[2]	5,99 [2,50; 14,37] <,0001[3]	4,3 [2,5; 6,2] <,0001[3]
≥ 50 mm	13/289 (4,5)	3/265 (1,1)	3,97 [1,14; 13,79] 0,0298[2]	4,11 [1,16; 14,60] 0,0181[3]	3,4 [0,7; 6,1] 0,0181[3]
Number of positive lymph nodes (Interaction p-value: 0,9276)					
0-3	12/427 (2,8)	3/418 (0,7)	3,92 [1,11; 13,78] 0,0334[2]	4,00 [1,12; 14,28] 0,0213[3]	2,1 [0,3; 3,9] 0,0213[3]
4-9	31/549 (5,6)	8/542 (1,5)	3,83 [1,77; 8,25] 0,0006[2]	3,99 [1,82; 8,77] 0,0002[3]	4,2 [2,0; 6,4] 0,0002[3]
≥ 10	12/307 (3,9)	4/305 (1,3)	2,98 [0,97; 9,14] 0,0561[2]	3,06 [0,98; 9,60] 0,0441[3]	2,6 [0,1; 5,1] 0,0441[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8894)					
IIA	1/113 (0,9)	1/114 (0,9)	1,01 [0,06; 15,93] 0,9950[2]	1,01 [0,06; 16,33] 1,0000[4]	0,0 [-2,4; 2,4] 1,0000[4]
IIB	8/151 (5,3)	2/136 (1,5)	3,60 [0,78; 16,67] 0,1011[2]	3,75 [0,78; 17,97] 0,1080[4]	3,8 [-0,3; 7,9] 0,1080[4]
IIIA	30/495 (6,1)	7/488 (1,4)	4,23 [1,87; 9,53] 0,0005[2]	4,43 [1,93; 10,19] 0,0001[3]	4,6 [2,3; 7,0] 0,0001[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	14/468 (3,0)	5/480 (1,0)	2,87 [1,04; 7,91] 0,0413[2]	2,93 [1,05; 8,20] 0,0322[3]	1,9 [0,2; 3,7] 0,0322[3]
Tumor grade (Interaction p-value: 0,3963)					
G1	4/91 (4,4)	3/93 (3,2)	1,36 [0,31; 5,92] 0,6797[2]	1,38 [0,30; 6,34] 0,7190[4]	1,2 [-4,4; 6,7] 0,7190[4]
G2	34/612 (5,6)	6/603 (1,0)	5,58 [2,36; 13,20] <,0001[2]	5,85 [2,44; 14,05] <,0001[3]	4,6 [2,6; 6,5] <,0001[3]
G3	14/527 (2,7)	5/506 (1,0)	2,69 [0,98; 7,41] 0,0559[2]	2,73 [0,98; 7,65] 0,0460[3]	1,7 [0,0; 3,3] 0,0460[3]
GX	3/51 (5,9)	1/59 (1,7)	3,47 [0,37; 32,34] 0,2745[2]	3,63 [0,37; 35,99] 0,3349[4]	4,2 [-3,1; 11,4] 0,3349[4]
Progesterone receptor status (Interaction p-value: 0,8297)					
Negative	6/156 (3,8)	1/169 (0,6)	6,50 [0,79; 53,39] 0,0815[2]	6,72 [0,80; 56,46] 0,0582[4]	3,3 [0,0; 6,5] 0,0582[4]
Positive	47/1089 (4,3)	14/1067 (1,3)	3,29 [1,82; 5,94] <,0001[2]	3,39 [1,86; 6,20] <,0001[3]	3,0 [1,6; 4,4] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
Race (Interaction p-value: 0,6838)					
White	37/958 (3,9)	11/944 (1,2)	3,31 [1,70; 6,46] 0,0004[2]	3,41 [1,73; 6,72] 0,0002[3]	2,7 [1,3; 4,1] 0,0002[3]
Asian	14/250 (5,6)	2/242 (0,8)	6,78 [1,56; 29,50] 0,0108[2]	7,12 [1,60; 31,66] 0,0028[3]	4,8 [1,7; 7,8] 0,0028[3]
Other	4/62 (6,5)	1/64 (1,6)	4,13 [0,47; 35,92] 0,1989[2]	4,34 [0,47; 40,01] 0,2039[4]	4,9 [-1,9; 11,7] 0,2039[4]
First endocrine therapy (Interaction p-value: 0,7136)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	2/114 (1,8)	1/132 (0,8)	2,32 [0,21; 25,21] 0,4906[2]	2,34 [0,21; 26,14] 0,5979[4]	1,0 [-1,8; 3,8] 0,5979[4]
Aromatase inhibitor	53/1169 (4,5)	14/1133 (1,2)	3,67 [2,05; 6,57] <,0001[2]	3,80 [2,09; 6,88] <,0001[3]	3,3 [1,9; 4,7] <,0001[3]
ECOG-PS (Interaction p-value: 0,5729)					
ECOG-PS 0	42/1070 (3,9)	12/1020 (1,2)	3,34 [1,77; 6,30] 0,0002[2]	3,43 [1,80; 6,56] <,0001[3]	2,7 [1,4; 4,1] <,0001[3]
ECOG-PS 1	13/213 (6,1)	3/245 (1,2)	4,98 [1,44; 17,26] 0,0112[2]	5,24 [1,47; 18,66] 0,0046[3]	4,9 [1,4; 8,4] 0,0046[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according PT White blood cell count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,2645)					
< 65 years	199/918 (21,7)	40/937 (4,3)	5,08 [3,66; 7,04] <,0001[2]	6,21 [4,36; 8,84] <,0001[3]	17,4 [14,4; 20,4] <,0001[3]
≥ 65 years	85/365 (23,3)	10/328 (3,0)	7,64 [4,04; 14,46] <,0001[2]	9,65 [4,92; 18,95] <,0001[3]	20,2 [15,5; 25,0] <,0001[3]
Prior treatment (Interaction p-value: 0,6387)					
Neoadjuvant chemotherapy	99/430 (23,0)	16/415 (3,9)	5,97 [3,58; 9,95] <,0001[2]	7,46 [4,31; 12,90] <,0001[3]	19,2 [14,8; 23,6] <,0001[3]
Adjuvant chemotherapy	174/784 (22,2)	33/769 (4,3)	5,17 [3,61; 7,40] <,0001[2]	6,36 [4,32; 9,37] <,0001[3]	17,9 [14,7; 21,1] <,0001[3]
No chemotherapy	11/69 (15,9)	1/81 (1,2)	12,91 [1,71; 97,52] 0,0131[2]	15,17 [1,91; 120,82] 0,0009[3]	14,7 [5,7; 23,7] 0,0009[3]
Region (Interaction p-value: 0,7683)					
North America / Europe	102/678 (15,0)	15/650 (2,3)	6,52 [3,83; 11,09] <,0001[2]	7,50 [4,31; 13,04] <,0001[3]	12,7 [9,8; 15,7] <,0001[3]
Asia	113/203 (55,7)	22/201 (10,9)	5,09 [3,37; 7,69] <,0001[2]	10,22 [6,06; 17,22] <,0001[3]	44,7 [36,6; 52,8] <,0001[3]
Other	69/402 (17,2)	13/414 (3,1)	5,47 [3,07; 9,73] <,0001[2]	6,39 [3,47; 11,76] <,0001[3]	14,0 [10,0; 18,1] <,0001[3]
Primary tumor size (Interaction p-value: 0,6750)					
< 20 mm	73/331 (22,1)	11/335 (3,3)	6,72 [3,63; 12,43] <,0001[2]	8,33 [4,33; 16,04] <,0001[3]	18,8 [13,9; 23,6] <,0001[3]
≥ 20 but < 50 mm	142/646 (22,0)	29/653 (4,4)	4,95 [3,37; 7,27] <,0001[2]	6,06 [4,00; 9,19] <,0001[3]	17,5 [14,0; 21,1] <,0001[3]
≥ 50 mm	60/289 (20,8)	9/265 (3,4)	6,11 [3,10; 12,07] <,0001[2]	7,45 [3,62; 15,36] <,0001[3]	17,4 [12,2; 22,5] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9900)					
0-3	88/427 (20,6)	15/418 (3,6)	5,74 [3,38; 9,76] <,0001[2]	6,97 [3,96; 12,29] <,0001[3]	17,0 [12,8; 21,3] <,0001[3]
4-9	122/549 (22,2)	22/542 (4,1)	5,47 [3,53; 8,49] <,0001[2]	6,75 [4,21; 10,82] <,0001[3]	18,2 [14,3; 22,0] <,0001[3]
≥ 10	74/307 (24,1)	13/305 (4,3)	5,66 [3,21; 9,98] <,0001[2]	7,13 [3,86; 13,18] <,0001[3]	19,8 [14,5; 25,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,6965)					
IIA	26/113 (23,0)	2/114 (1,8)	13,12 [3,19; 53,96] 0,0004[2]	16,74 [3,87; 72,44] <,0001[3]	21,3 [13,1; 29,4] <,0001[3]
IIB	35/151 (23,2)	6/136 (4,4)	5,25 [2,28; 12,10] <,0001[2]	6,54 [2,65; 16,10] <,0001[3]	18,8 [11,2; 26,3] <,0001[3]
IIIA	108/495 (21,8)	21/488 (4,3)	5,07 [3,23; 7,95] <,0001[2]	6,21 [3,82; 10,09] <,0001[3]	17,5 [13,5; 21,6] <,0001[3]
IIIB	14/54 (25,9)	1/45 (2,2)	11,67 [1,60; 85,33] 0,0155[2]	15,40 [1,94; 122,46] 0,0011[3]	23,7 [11,2; 36,2] 0,0011[3]
IIIC	100/468 (21,4)	20/480 (4,2)	5,13 [3,23; 8,15] <,0001[2]	6,25 [3,79; 10,30] <,0001[3]	17,2 [13,1; 21,3] <,0001[3]
Tumor grade (Interaction p-value: 0,7645)					
G1	17/91 (18,7)	2/93 (2,2)	8,69 [2,07; 36,53] 0,0032[2]	10,45 [2,34; 46,70] 0,0002[3]	16,5 [8,0; 25,1] 0,0002[3]
G2	127/612 (20,8)	26/603 (4,3)	4,81 [3,20; 7,23] <,0001[2]	5,81 [3,75; 9,01] <,0001[3]	16,4 [12,8; 20,0] <,0001[3]
G3	119/527 (22,6)	18/506 (3,6)	6,35 [3,93; 10,26] <,0001[2]	7,91 [4,73; 13,21] <,0001[3]	19,0 [15,1; 22,9] <,0001[3]
GX	20/51 (39,2)	4/59 (6,8)	5,78 [2,12; 15,82] 0,0006[2]	8,87 [2,78; 28,31] <,0001[3]	32,4 [17,6; 47,3] <,0001[3]
Race (Interaction p-value: 0,7497)					
White	158/958 (16,5)	27/944 (2,9)	5,77 [3,87; 8,59] <,0001[2]	6,71 [4,41; 10,20] <,0001[3]	13,6 [11,1; 16,2] <,0001[3]
Asian	115/250 (46,0)	22/242 (9,1)	5,06 [3,32; 7,70] <,0001[2]	8,52 [5,15; 14,10] <,0001[3]	36,9 [29,7; 44,1] <,0001[3]
Other	10/62 (16,1)	1/64 (1,6)	10,32 [1,36; 78,26] 0,0239[2]	12,12 [1,50; 97,77] 0,0038[3]	14,6 [4,9; 24,2] 0,0038[3]
First endocrine therapy (Interaction p-value: 0,3940)					
Tamoxifen	16/114 (14,0)	5/132 (3,8)	3,71 [1,40; 9,80] 0,0083[2]	4,15 [1,47; 11,71] 0,0041[3]	10,2 [3,1; 17,4] 0,0041[3]
Aromatase inhibitor	268/1169 (22,9)	45/1133 (4,0)	5,77 [4,25; 7,83] <,0001[2]	7,19 [5,18; 9,98] <,0001[3]	19,0 [16,3; 21,6] <,0001[3]
ECOG-PS (Interaction p-value: 0,3787)					
ECOG-PS 0	243/1070 (22,7)	44/1020 (4,3)	5,26 [3,86; 7,17] <,0001[2]	6,52 [4,67; 9,10] <,0001[3]	18,4 [15,6; 21,2] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	41/213 (19,2)	6/245 (2,4)	7,86 [3,40; 18,15] <,0001[2]	9,50 [3,94; 22,87] <,0001[3]	16,8 [11,2; 22,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events according SOC Blood and lymphatic system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1441)					
< 65 years	405/918 (44,1)	88/937 (9,4)	4,70 [3,80; 5,81] <,0001[2]	7,62 [5,90; 9,83] <,0001[3]	34,7 [31,0; 38,4] <,0001[3]
≥ 65 years	182/365 (49,9)	25/328 (7,6)	6,54 [4,43; 9,67] <,0001[2]	12,05 [7,64; 19,03] <,0001[3]	42,2 [36,4; 48,1] <,0001[3]
Prior treatment (Interaction p-value: 0,9719)					
Neoadjuvant chemotherapy	202/430 (47,0)	37/415 (8,9)	5,27 [3,81; 7,28] <,0001[2]	9,05 [6,15; 13,33] <,0001[3]	38,1 [32,6; 43,5] <,0001[3]
Adjuvant chemotherapy	356/784 (45,4)	69/769 (9,0)	5,06 [3,99; 6,42] <,0001[2]	8,44 [6,35; 11,22] <,0001[3]	36,4 [32,4; 40,5] <,0001[3]
No chemotherapy	29/69 (42,0)	7/81 (8,6)	4,86 [2,27; 10,40] <,0001[2]	7,66 [3,08; 19,05] <,0001[3]	33,4 [20,2; 46,5] <,0001[3]
Primary tumor size (Interaction p-value: 0,6928)					
< 20 mm	148/331 (44,7)	29/335 (8,7)	5,17 [3,58; 7,46] <,0001[2]	8,53 [5,51; 13,23] <,0001[3]	36,1 [29,9; 42,2] <,0001[3]
≥ 20 but < 50 mm	303/646 (46,9)	64/653 (9,8)	4,79 [3,74; 6,12] <,0001[2]	8,13 [6,02; 10,98] <,0001[3]	37,1 [32,6; 41,6] <,0001[3]
≥ 50 mm	124/289 (42,9)	19/265 (7,2)	5,98 [3,80; 9,42] <,0001[2]	9,73 [5,78; 16,39] <,0001[3]	35,7 [29,2; 42,2] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,6660)					
0-3	170/427 (39,8)	30/418 (7,2)	5,55 [3,85; 7,98] <,0001[2]	8,56 [5,63; 13,01] <,0001[3]	32,6 [27,4; 37,9] <,0001[3]
4-9	268/549 (48,8)	50/542 (9,2)	5,29 [4,01; 6,98] <,0001[2]	9,38 [6,71; 13,13] <,0001[3]	39,6 [34,8; 44,4] <,0001[3]
≥ 10	149/307 (48,5)	33/305 (10,8)	4,49 [3,19; 6,32] <,0001[2]	7,77 [5,08; 11,89] <,0001[3]	37,7 [31,1; 44,3] <,0001[3]
Tumor stage (Interaction p-value: 0,4628)					
IIA	42/113 (37,2)	11/114 (9,6)	3,85 [2,09; 7,09] <,0001[2]	5,54 [2,67; 11,49] <,0001[3]	27,5 [17,1; 37,9] <,0001[3]
IIB	70/151 (46,4)	7/136 (5,1)	9,01 [4,29; 18,91] <,0001[2]	15,93 [6,98; 36,35] <,0001[3]	41,2 [32,4; 50,0] <,0001[3]
IIIA	228/495 (46,1)	45/488 (9,2)	5,00 [3,72; 6,70] <,0001[2]	8,41 [5,90; 11,98] <,0001[3]	36,8 [31,8; 41,9] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	26/54 (48,1)	3/45 (6,7)	7,22 [2,34; 22,31] 0,0006[2]	13,00 [3,59; 47,09] <,0001[3]	41,5 [26,3; 56,7] <,0001[3]
IIIC	220/468 (47,0)	47/480 (9,8)	4,80 [3,60; 6,40] <,0001[2]	8,17 [5,75; 11,61] <,0001[3]	37,2 [32,0; 42,5] <,0001[3]
Tumor grade (Interaction p-value: 0,5781)					
G1	36/91 (39,6)	4/93 (4,3)	9,20 [3,41; 24,80] <,0001[2]	14,56 [4,91; 43,16] <,0001[3]	35,3 [24,4; 46,1] <,0001[3]
G2	290/612 (47,4)	61/603 (10,1)	4,68 [3,64; 6,03] <,0001[2]	8,00 [5,88; 10,90] <,0001[3]	37,3 [32,6; 41,9] <,0001[3]
G3	229/527 (43,5)	42/506 (8,3)	5,24 [3,86; 7,11] <,0001[2]	8,49 [5,92; 12,17] <,0001[3]	35,2 [30,3; 40,0] <,0001[3]
GX	31/51 (60,8)	6/59 (10,2)	5,98 [2,71; 13,17] <,0001[2]	13,69 [4,97; 37,75] <,0001[3]	50,6 [35,2; 66,1] <,0001[3]
ECOG-PS (Interaction p-value: 0,2584)					
ECOG-PS 0	484/1070 (45,2)	85/1020 (8,3)	5,43 [4,38; 6,72] <,0001[2]	9,09 [7,06; 11,70] <,0001[3]	36,9 [33,5; 40,3] <,0001[3]
ECOG-PS 1	103/213 (48,4)	28/245 (11,4)	4,23 [2,91; 6,16] <,0001[2]	7,26 [4,51; 11,69] <,0001[3]	36,9 [29,1; 44,7] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Cardiac disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6036)					
< 65 years	60/918 (6,5)	38/937 (4,1)	1,61 [1,08; 2,39] 0,0182[2]	1,65 [1,09; 2,51] 0,0170[3]	2,5 [0,4; 4,5] 0,0170[3]
≥ 65 years	30/365 (8,2)	20/328 (6,1)	1,35 [0,78; 2,33] 0,2836[2]	1,38 [0,77; 2,48] 0,2811[3]	2,1 [-1,7; 5,9] 0,2811[3]
Prior treatment (Interaction p-value: 0,9337)					
Neoadjuvant chemotherapy	35/430 (8,1)	22/415 (5,3)	1,54 [0,92; 2,57] 0,1033[2]	1,58 [0,91; 2,75] 0,1001[3]	2,8 [-0,5; 6,2] 0,1001[3]
Adjuvant chemotherapy	50/784 (6,4)	33/769 (4,3)	1,49 [0,97; 2,28] 0,0697[2]	1,52 [0,97; 2,39] 0,0676[3]	2,1 [-0,1; 4,3] 0,0676[3]
No chemotherapy	5/69 (7,2)	3/81 (3,7)	1,96 [0,48; 7,89] 0,3456[2]	2,03 [0,47; 8,83] 0,4711[4]	3,5 [-3,8; 10,9] 0,4711[4]
Region (Interaction p-value: 0,6679)					
North America / Europe	64/678 (9,4)	43/650 (6,6)	1,43 [0,98; 2,07] 0,0605[2]	1,47 [0,98; 2,20] 0,0587[3]	2,8 [-0,1; 5,7] 0,0587[3]
Asia	10/203 (4,9)	4/201 (2,0)	2,48 [0,79; 7,76] 0,1201[2]	2,55 [0,79; 8,27] 0,1067[3]	2,9 [-0,6; 6,5] 0,1067[3]
Other	16/402 (4,0)	11/414 (2,7)	1,50 [0,70; 3,19] 0,2943[2]	1,52 [0,70; 3,31] 0,2908[3]	1,3 [-1,1; 3,8] 0,2908[3]
Primary tumor size (Interaction p-value: 0,0856)					
< 20 mm	23/331 (6,9)	12/335 (3,6)	1,94 [0,98; 3,83] 0,0566[2]	2,01 [0,98; 4,11] 0,0516[3]	3,4 [-0,0; 6,8] 0,0516[3]
≥ 20 but < 50 mm	44/646 (6,8)	39/653 (6,0)	1,14 [0,75; 1,73] 0,5369[2]	1,15 [0,74; 1,80] 0,5366[3]	0,8 [-1,8; 3,5] 0,5366[3]
≥ 50 mm	23/289 (8,0)	7/265 (2,6)	3,01 [1,31; 6,91] 0,0092[2]	3,19 [1,34; 7,56] 0,0057[3]	5,3 [1,6; 9,0] 0,0057[3]
Tumor stage (Interaction p-value: 0,7704)					
IIA	10/113 (8,8)	5/114 (4,4)	2,02 [0,71; 5,72] 0,1865[2]	2,12 [0,70; 6,40] 0,1759[3]	4,5 [-2,0; 10,9] 0,1759[3]
IIB	9/151 (6,0)	4/136 (2,9)	2,03 [0,64; 6,43] 0,2306[2]	2,09 [0,63; 6,95] 0,2194[3]	3,0 [-1,7; 7,7] 0,2194[3]
IIIA	36/495 (7,3)	24/488 (4,9)	1,48 [0,90; 2,44] 0,1260[2]	1,52 [0,89; 2,58] 0,1231[3]	2,4 [-0,6; 5,3] 0,1231[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	2/54 (3,7)	3/45 (6,7)	0,56 [0,10; 3,18] 0,5091[2]	0,54 [0,09; 3,37] 0,6567[4]	-3,0 [-11,8; 5,9] 0,6567[4]
IIIC	33/468 (7,1)	22/480 (4,6)	1,54 [0,91; 2,60] 0,1073[2]	1,58 [0,91; 2,75] 0,1041[3]	2,5 [-0,5; 5,4] 0,1041[3]
Tumor grade (Interaction p-value: 0,8844)					
G1	6/91 (6,6)	4/93 (4,3)	1,53 [0,45; 5,25] 0,4966[2]	1,57 [0,43; 5,76] 0,5339[4]	2,3 [-4,3; 8,8] 0,5339[4]
G2	46/612 (7,5)	28/603 (4,6)	1,62 [1,03; 2,55] 0,0385[2]	1,67 [1,03; 2,71] 0,0363[3]	2,9 [0,2; 5,6] 0,0363[3]
G3	36/527 (6,8)	23/506 (4,5)	1,50 [0,90; 2,50] 0,1166[2]	1,54 [0,90; 2,64] 0,1135[3]	2,3 [-0,5; 5,1] 0,1135[3]
GX	2/51 (3,9)	3/59 (5,1)	0,77 [0,13; 4,44] 0,7711[2]	0,76 [0,12; 4,75] 1,0000[4]	-1,2 [-8,9; 6,6] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,0548)					
Negative	7/156 (4,5)	7/169 (4,1)	1,08 [0,39; 3,02] 0,8783[2]	1,09 [0,37; 3,17] 0,8783[3]	0,3 [-4,1; 4,8] 0,8783[3]
Positive	83/1089 (7,6)	51/1067 (4,8)	1,59 [1,14; 2,24] 0,0069[2]	1,64 [1,15; 2,35] 0,0063[3]	2,8 [0,8; 4,9] 0,0063[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,3400)					
White	71/958 (7,4)	50/944 (5,3)	1,40 [0,99; 1,99] 0,0603[2]	1,43 [0,99; 2,08] 0,0589[3]	2,1 [-0,1; 4,3] 0,0589[3]
Asian	13/250 (5,2)	4/242 (1,7)	3,15 [1,04; 9,51] 0,0424[2]	3,26 [1,05; 10,15] 0,0313[3]	3,5 [0,4; 6,7] 0,0313[3]
Other	4/62 (6,5)	4/64 (6,3)	1,03 [0,27; 3,95] 0,9630[2]	1,03 [0,25; 4,33] 1,0000[4]	0,2 [-8,3; 8,7] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,2000)					
Tamoxifen	7/114 (6,1)	2/132 (1,5)	4,05 [0,86; 19,12] 0,0771[2]	4,25 [0,87; 20,90] 0,0855[4]	4,6 [-0,2; 9,5] 0,0855[4]
Aromatase inhibitor	83/1169 (7,1)	56/1133 (4,9)	1,44 [1,03; 2,00] 0,0309[2]	1,47 [1,04; 2,08] 0,0298[3]	2,2 [0,2; 4,1] 0,0298[3]
ECOG-PS (Interaction p-value: 0,6612)					
ECOG-PS 0	71/1070 (6,6)	42/1020 (4,1)	1,61 [1,11; 2,34] 0,0119[2]	1,65 [1,12; 2,45] 0,0110[3]	2,5 [0,6; 4,4] 0,0110[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	19/213 (8,9)	16/245 (6,5)	1,37 [0,72; 2,59] 0,3390[2]	1,40 [0,70; 2,80] 0,3370[3]	2,4 [-2,5; 7,3] 0,3370[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Eye disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8501)					
< 65 years	136/918 (14,8)	47/937 (5,0)	2,95 [2,15; 4,06] <,0001[2]	3,29 [2,33; 4,65] <,0001[3]	9,8 [7,1; 12,5] <,0001[3]
≥ 65 years	59/365 (16,2)	19/328 (5,8)	2,79 [1,70; 4,58] <,0001[2]	3,14 [1,83; 5,38] <,0001[3]	10,4 [5,8; 14,9] <,0001[3]
Prior treatment (Interaction p-value: 0,6986)					
Neoadjuvant chemotherapy	69/430 (16,0)	21/415 (5,1)	3,17 [1,98; 5,07] <,0001[2]	3,59 [2,16; 5,97] <,0001[3]	11,0 [6,9; 15,0] <,0001[3]
Adjuvant chemotherapy	118/784 (15,1)	43/769 (5,6)	2,69 [1,93; 3,76] <,0001[2]	2,99 [2,08; 4,31] <,0001[3]	9,5 [6,5; 12,4] <,0001[3]
No chemotherapy	8/69 (11,6)	2/81 (2,5)	4,70 [1,03; 21,38] 0,0455[2]	5,18 [1,06; 25,28] 0,0444[4]	9,1 [0,8; 17,4] 0,0444[4]
Region (Interaction p-value: 0,2854)					
North America / Europe	123/678 (18,1)	38/650 (5,8)	3,10 [2,19; 4,39] <,0001[2]	3,57 [2,44; 5,23] <,0001[3]	12,3 [8,9; 15,7] <,0001[3]
Asia	31/203 (15,3)	16/201 (8,0)	1,92 [1,08; 3,40] 0,0253[2]	2,08 [1,10; 3,94] 0,0219[3]	7,3 [1,1; 13,5] 0,0219[3]
Other	41/402 (10,2)	12/414 (2,9)	3,52 [1,88; 6,60] <,0001[2]	3,80 [1,97; 7,35] <,0001[3]	7,3 [3,9; 10,7] <,0001[3]
Primary tumor size (Interaction p-value: 0,6996)					
< 20 mm	48/331 (14,5)	14/335 (4,2)	3,47 [1,95; 6,17] <,0001[2]	3,89 [2,10; 7,20] <,0001[3]	10,3 [6,0; 14,7] <,0001[3]
≥ 20 but < 50 mm	94/646 (14,6)	34/653 (5,2)	2,79 [1,92; 4,07] <,0001[2]	3,10 [2,06; 4,67] <,0001[3]	9,3 [6,1; 12,6] <,0001[3]
≥ 50 mm	49/289 (17,0)	18/265 (6,8)	2,50 [1,49; 4,17] 0,0005[2]	2,80 [1,59; 4,95] 0,0002[3]	10,2 [4,9; 15,4] 0,0002[3]
Number of positive lymph nodes (Interaction p-value: 0,7961)					
0-3	66/427 (15,5)	20/418 (4,8)	3,23 [2,00; 5,23] <,0001[2]	3,64 [2,16; 6,12] <,0001[3]	10,7 [6,7; 14,7] <,0001[3]
4-9	77/549 (14,0)	29/542 (5,4)	2,62 [1,74; 3,95] <,0001[2]	2,89 [1,85; 4,50] <,0001[3]	8,7 [5,2; 12,1] <,0001[3]
≥ 10	52/307 (16,9)	17/305 (5,6)	3,04 [1,80; 5,13] <,0001[2]	3,45 [1,95; 6,13] <,0001[3]	11,4 [6,4; 16,3] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,4508)					
IIA	16/113 (14,2)	5/114 (4,4)	3,23 [1,22; 8,52] 0,0179[2]	3,60 [1,27; 10,18] 0,0111[3]	9,8 [2,3; 17,2] 0,0111[3]
IIB	21/151 (13,9)	7/136 (5,1)	2,70 [1,19; 6,16] 0,0180[2]	2,98 [1,22; 7,24] 0,0125[3]	8,8 [2,1; 15,4] 0,0125[3]
IIIA	74/495 (14,9)	20/488 (4,1)	3,65 [2,26; 5,88] <,0001[2]	4,11 [2,47; 6,86] <,0001[3]	10,9 [7,3; 14,5] <,0001[3]
IIIB	5/54 (9,3)	4/45 (8,9)	1,04 [0,30; 3,65] 0,9491[2]	1,05 [0,26; 4,15] 1,0000[4]	0,4 [-11,0; 11,7] 1,0000[4]
IIIC	78/468 (16,7)	30/480 (6,3)	2,67 [1,79; 3,98] <,0001[2]	3,00 [1,93; 4,67] <,0001[3]	10,4 [6,4; 14,4] <,0001[3]
Tumor grade (Interaction p-value: 0,3885)					
G1	9/91 (9,9)	6/93 (6,5)	1,53 [0,57; 4,13] 0,3985[2]	1,59 [0,54; 4,67] 0,3941[3]	3,4 [-4,5; 11,3] 0,3941[3]
G2	98/612 (16,0)	31/603 (5,1)	3,11 [2,11; 4,59] <,0001[2]	3,52 [2,31; 5,36] <,0001[3]	10,9 [7,5; 14,3] <,0001[3]
G3	82/527 (15,6)	25/506 (4,9)	3,15 [2,05; 4,85] <,0001[2]	3,55 [2,22; 5,65] <,0001[3]	10,6 [7,0; 14,2] <,0001[3]
GX	5/51 (9,8)	4/59 (6,8)	1,45 [0,41; 5,10] 0,5662[2]	1,49 [0,38; 5,89] 0,7306[4]	3,0 [-7,4; 13,4] 0,7306[4]
Race (Interaction p-value: 0,2669)					
White	148/958 (15,4)	43/944 (4,6)	3,39 [2,44; 4,71] <,0001[2]	3,83 [2,69; 5,45] <,0001[3]	10,9 [8,2; 13,5] <,0001[3]
Asian	35/250 (14,0)	17/242 (7,0)	1,99 [1,15; 3,46] 0,0143[2]	2,15 [1,17; 3,96] 0,0119[3]	7,0 [1,6; 12,3] 0,0119[3]
Other	9/62 (14,5)	3/64 (4,7)	3,10 [0,88; 10,91] 0,0785[2]	3,45 [0,89; 13,42] 0,0602[3]	9,8 [-0,4; 20,0] 0,0602[3]
First endocrine therapy (Interaction p-value: 0,3008)					
Tamoxifen	22/114 (19,3)	12/132 (9,1)	2,12 [1,10; 4,10] 0,0248[2]	2,39 [1,13; 5,08] 0,0207[3]	10,2 [1,5; 19,0] 0,0207[3]
Aromatase inhibitor	173/1169 (14,8)	54/1133 (4,8)	3,11 [2,31; 4,17] <,0001[2]	3,47 [2,53; 4,77] <,0001[3]	10,0 [7,6; 12,4] <,0001[3]
ECOG-PS (Interaction p-value: 0,3495)					
ECOG-PS 0	168/1070 (15,7)	52/1020 (5,1)	3,08 [2,28; 4,15] <,0001[2]	3,47 [2,51; 4,79] <,0001[3]	10,6 [8,0; 13,2] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	27/213 (12,7)	14/245 (5,7)	2,22 [1,19; 4,12] 0,0116[2]	2,40 [1,22; 4,70] 0,0092[3]	7,0 [1,6; 12,3] 0,0092[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Gastrointestinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0813)					
< 65 years	822/918 (89,5)	291/937 (31,1)	2,88 [2,61; 3,18] <,0001[2]	19,01 [14,76; 24,47] <,0001[3]	58,5 [54,9; 62,0] <,0001[3]
≥ 65 years	320/365 (87,7)	117/328 (35,7)	2,46 [2,11; 2,86] <,0001[2]	12,82 [8,72; 18,85] <,0001[3]	52,0 [45,8; 58,2] <,0001[3]
Prior treatment (Interaction p-value: 0,6865)					
Neoadjuvant chemotherapy	377/430 (87,7)	126/415 (30,4)	2,89 [2,49; 3,35] <,0001[2]	16,32 [11,43; 23,28] <,0001[3]	57,3 [51,9; 62,7] <,0001[3]
Adjuvant chemotherapy	705/784 (89,9)	254/769 (33,0)	2,72 [2,46; 3,02] <,0001[2]	18,09 [13,72; 23,87] <,0001[3]	56,9 [53,0; 60,8] <,0001[3]
No chemotherapy	60/69 (87,0)	28/81 (34,6)	2,52 [1,84; 3,44] <,0001[2]	12,62 [5,46; 29,14] <,0001[3]	52,4 [39,3; 65,4] <,0001[3]
Primary tumor size (Interaction p-value: 0,0667)					
< 20 mm	294/331 (88,8)	105/335 (31,3)	2,83 [2,41; 3,34] <,0001[2]	17,41 [11,52; 26,29] <,0001[3]	57,5 [51,5; 63,5] <,0001[3]
≥ 20 but < 50 mm	570/646 (88,2)	195/653 (29,9)	2,95 [2,62; 3,33] <,0001[2]	17,62 [13,15; 23,59] <,0001[3]	58,4 [54,1; 62,7] <,0001[3]
≥ 50 mm	264/289 (91,3)	103/265 (38,9)	2,35 [2,01; 2,74] <,0001[2]	16,61 [10,29; 26,81] <,0001[3]	52,5 [45,8; 59,2] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,3183)					
0-3	377/427 (88,3)	129/418 (30,9)	2,86 [2,47; 3,32] <,0001[2]	16,89 [11,78; 24,23] <,0001[3]	57,4 [52,1; 62,8] <,0001[3]
4-9	487/549 (88,7)	168/542 (31,0)	2,86 [2,52; 3,26] <,0001[2]	17,49 [12,69; 24,10] <,0001[3]	57,7 [53,0; 62,4] <,0001[3]
≥ 10	278/307 (90,6)	111/305 (36,4)	2,49 [2,14; 2,90] <,0001[2]	16,75 [10,70; 26,22] <,0001[3]	54,2 [47,8; 60,5] <,0001[3]
Tumor stage (Interaction p-value: 0,1063)					
IIA	99/113 (87,6)	32/114 (28,1)	3,12 [2,31; 4,22] <,0001[2]	18,12 [9,06; 36,23] <,0001[3]	59,5 [49,3; 69,8] <,0001[3]
IIB	131/151 (86,8)	37/136 (27,2)	3,19 [2,41; 4,23] <,0001[2]	17,53 [9,59; 32,04] <,0001[3]	59,5 [50,3; 68,8] <,0001[3]
IIIA	445/495 (89,9)	145/488 (29,7)	3,03 [2,63; 3,48] <,0001[2]	21,05 [14,82; 29,90] <,0001[3]	60,2 [55,3; 65,0] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	45/54 (83,3)	16/45 (35,6)	2,34 [1,55; 3,54] <,0001[2]	9,06 [3,54; 23,21] <,0001[3]	47,8 [30,6; 64,9] <,0001[3]
IIIC	420/468 (89,7)	176/480 (36,7)	2,45 [2,17; 2,76] <,0001[2]	15,11 [10,63; 21,48] <,0001[3]	53,1 [48,0; 58,2] <,0001[3]
Tumor grade (Interaction p-value: 0,0652)					
G1	83/91 (91,2)	32/93 (34,4)	2,65 [1,99; 3,53] <,0001[2]	19,78 [8,52; 45,92] <,0001[3]	56,8 [45,5; 68,1] <,0001[3]
G2	550/612 (89,9)	214/603 (35,5)	2,53 [2,27; 2,83] <,0001[2]	16,13 [11,81; 22,01] <,0001[3]	54,4 [49,9; 58,9] <,0001[3]
G3	463/527 (87,9)	148/506 (29,2)	3,00 [2,61; 3,45] <,0001[2]	17,50 [12,66; 24,20] <,0001[3]	58,6 [53,8; 63,5] <,0001[3]
GX	44/51 (86,3)	11/59 (18,6)	4,63 [2,69; 7,97] <,0001[2]	27,43 [9,77; 76,99] <,0001[3]	67,6 [53,9; 81,3] <,0001[3]
Progesterone receptor status (Interaction p-value: 0,5174)					
Negative	140/156 (89,7)	59/169 (34,9)	2,57 [2,08; 3,18] <,0001[2]	16,31 [8,90; 29,91] <,0001[3]	54,8 [46,2; 63,5] <,0001[3]
Positive	967/1089 (88,8)	338/1067 (31,7)	2,80 [2,56; 3,07] <,0001[2]	17,10 [13,61; 21,48] <,0001[3]	57,1 [53,8; 60,5] <,0001[3]
Unknown	9/10 (90,0)	1/7 (14,3)	6,30 [1,01; 39,13] 0,0482[2]	54,00 [2,80; 1040,05] 0,0037[4]	75,7 [43,8; 100,0] 0,0037[4]
Race (Interaction p-value: 0,1825)					
White	851/958 (88,8)	313/944 (33,2)	2,68 [2,44; 2,94] <,0001[2]	16,03 [12,58; 20,43] <,0001[3]	55,7 [52,1; 59,3] <,0001[3]
Asian	222/250 (88,8)	66/242 (27,3)	3,26 [2,64; 4,02] <,0001[2]	21,14 [13,03; 34,32] <,0001[3]	61,5 [54,7; 68,4] <,0001[3]
Other	56/62 (90,3)	24/64 (37,5)	2,41 [1,74; 3,34] <,0001[2]	15,56 [5,82; 41,54] <,0001[3]	52,8 [38,9; 66,8] <,0001[3]
First endocrine therapy (Interaction p-value: 0,8958)					
Tamoxifen	96/114 (84,2)	41/132 (31,1)	2,71 [2,08; 3,54] <,0001[2]	11,84 [6,34; 22,09] <,0001[3]	53,1 [42,8; 63,5] <,0001[3]
Aromatase inhibitor	1046/1169 (89,5)	367/1133 (32,4)	2,76 [2,53; 3,01] <,0001[2]	17,75 [14,18; 22,22] <,0001[3]	57,1 [53,8; 60,3] <,0001[3]
ECOG-PS (Interaction p-value: 0,1328)					
ECOG-PS 0	955/1070 (89,3)	320/1020 (31,4)	2,84 [2,59; 3,12] <,0001[2]	18,17 [14,37; 22,96] <,0001[3]	57,9 [54,5; 61,3] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	187/213 (87,8)	88/245 (35,9)	2,44 [2,05; 2,91] <,0001[2]	12,83 [7,89; 20,87] <,0001[3]	51,9 [44,4; 59,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC General disorders and administration site conditions from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8971)					
< 65 years	496/918 (54,0)	292/937 (31,2)	1,73 [1,55; 1,94] <,0001[2]	2,60 [2,15; 3,14] <,0001[3]	22,9 [18,5; 27,2] <,0001[3]
≥ 65 years	217/365 (59,5)	114/328 (34,8)	1,71 [1,44; 2,03] <,0001[2]	2,75 [2,02; 3,75] <,0001[3]	24,7 [17,5; 31,9] <,0001[3]
Prior treatment (Interaction p-value: 0,6830)					
Neoadjuvant chemotherapy	241/430 (56,0)	132/415 (31,8)	1,76 [1,50; 2,08] <,0001[2]	2,73 [2,06; 3,62] <,0001[3]	24,2 [17,8; 30,7] <,0001[3]
Adjuvant chemotherapy	434/784 (55,4)	252/769 (32,8)	1,69 [1,50; 1,90] <,0001[2]	2,54 [2,07; 3,13] <,0001[3]	22,6 [17,8; 27,4] <,0001[3]
No chemotherapy	38/69 (55,1)	22/81 (27,2)	2,03 [1,34; 3,07] 0,0009[2]	3,29 [1,66; 6,50] 0,0005[3]	27,9 [12,7; 43,1] 0,0005[3]
Primary tumor size (Interaction p-value: 0,8944)					
< 20 mm	179/331 (54,1)	101/335 (30,1)	1,79 [1,48; 2,17] <,0001[2]	2,73 [1,98; 3,75] <,0001[3]	23,9 [16,7; 31,2] <,0001[3]
≥ 20 but < 50 mm	356/646 (55,1)	212/653 (32,5)	1,70 [1,49; 1,93] <,0001[2]	2,55 [2,04; 3,20] <,0001[3]	22,6 [17,4; 27,9] <,0001[3]
≥ 50 mm	172/289 (59,5)	92/265 (34,7)	1,71 [1,42; 2,07] <,0001[2]	2,76 [1,96; 3,90] <,0001[3]	24,8 [16,7; 32,9] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,6074)					
0-3	232/427 (54,3)	140/418 (33,5)	1,62 [1,38; 1,90] <,0001[2]	2,36 [1,79; 3,12] <,0001[3]	20,8 [14,3; 27,4] <,0001[3]
4-9	290/549 (52,8)	158/542 (29,2)	1,81 [1,55; 2,11] <,0001[2]	2,72 [2,12; 3,49] <,0001[3]	23,7 [18,0; 29,3] <,0001[3]
≥ 10	191/307 (62,2)	108/305 (35,4)	1,76 [1,48; 2,09] <,0001[2]	3,00 [2,16; 4,17] <,0001[3]	26,8 [19,2; 34,4] <,0001[3]
Tumor stage (Interaction p-value: 0,4042)					
IIA	55/113 (48,7)	38/114 (33,3)	1,46 [1,06; 2,01] 0,0209[2]	1,90 [1,11; 3,24] 0,0188[3]	15,3 [2,7; 28,0] 0,0188[3]
IIB	82/151 (54,3)	45/136 (33,1)	1,64 [1,24; 2,17] 0,0005[2]	2,40 [1,49; 3,88] 0,0003[3]	21,2 [10,0; 32,4] 0,0003[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	268/495 (54,1)	140/488 (28,7)	1,89 [1,61; 2,22] <,0001[2]	2,93 [2,25; 3,82] <,0001[3]	25,5 [19,5; 31,4] <,0001[3]
IIIB	22/54 (40,7)	15/45 (33,3)	1,22 [0,72; 2,06] 0,4526[2]	1,38 [0,60; 3,13] 0,4481[3]	7,4 [-11,6; 26,4] 0,4481[3]
IIIC	285/468 (60,9)	168/480 (35,0)	1,74 [1,51; 2,01] <,0001[2]	2,89 [2,22; 3,77] <,0001[3]	25,9 [19,8; 32,0] <,0001[3]
Tumor grade (Interaction p-value: 0,0849)					
G1	51/91 (56,0)	27/93 (29,0)	1,93 [1,34; 2,78] 0,0004[2]	3,12 [1,69; 5,73] 0,0002[3]	27,0 [13,3; 40,8] 0,0002[3]
G2	339/612 (55,4)	207/603 (34,3)	1,61 [1,42; 1,84] <,0001[2]	2,38 [1,88; 2,99] <,0001[3]	21,1 [15,6; 26,5] <,0001[3]
G3	294/527 (55,8)	163/506 (32,2)	1,73 [1,49; 2,01] <,0001[2]	2,66 [2,06; 3,42] <,0001[3]	23,6 [17,7; 29,5] <,0001[3]
GX	27/51 (52,9)	8/59 (13,6)	3,90 [1,95; 7,82] 0,0001[2]	7,17 [2,84; 18,11] <,0001[3]	39,4 [23,1; 55,6] <,0001[3]
Progesterone receptor status (Interaction p-value: 0,6939)					
Negative	95/156 (60,9)	63/169 (37,3)	1,63 [1,29; 2,06] <,0001[2]	2,62 [1,67; 4,10] <,0001[3]	23,6 [13,0; 34,2] <,0001[3]
Positive	592/1089 (54,4)	328/1067 (30,7)	1,77 [1,59; 1,96] <,0001[2]	2,68 [2,25; 3,20] <,0001[3]	23,6 [19,6; 27,7] <,0001[3]
Unknown	8/10 (80,0)	4/7 (57,1)	1,40 [0,69; 2,85] 0,3546[2]	3,00 [0,35; 25,87] 0,5928[4]	22,9 [-21,4; 67,1] 0,5928[4]
Race (Interaction p-value: 0,6870)					
White	567/958 (59,2)	326/944 (34,5)	1,71 [1,55; 1,90] <,0001[2]	2,75 [2,28; 3,31] <,0001[3]	24,7 [20,3; 29,0] <,0001[3]
Asian	107/250 (42,8)	56/242 (23,1)	1,85 [1,41; 2,42] <,0001[2]	2,49 [1,68; 3,67] <,0001[3]	19,7 [11,5; 27,8] <,0001[3]
Other	32/62 (51,6)	16/64 (25,0)	2,06 [1,27; 3,36] 0,0036[2]	3,20 [1,51; 6,80] 0,0021[3]	26,6 [10,3; 43,0] 0,0021[3]
First endocrine therapy (Interaction p-value: 0,3668)					
Tamoxifen	62/114 (54,4)	36/132 (27,3)	1,99 [1,44; 2,76] <,0001[2]	3,18 [1,87; 5,41] <,0001[3]	27,1 [15,2; 39,0] <,0001[3]
Aromatase inhibitor	651/1169 (55,7)	370/1133 (32,7)	1,71 [1,55; 1,88] <,0001[2]	2,59 [2,19; 3,07] <,0001[3]	23,0 [19,1; 27,0] <,0001[3]
ECOG-PS (Interaction p-value: 0,8743)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	589/1070 (55,0)	325/1020 (31,9)	1,73 [1,56; 1,92] <,0001[2]	2,62 [2,19; 3,13] <,0001[3]	23,2 [19,1; 27,3] <,0001[3]
ECOG-PS 1	124/213 (58,2)	81/245 (33,1)	1,76 [1,43; 2,18] <,0001[2]	2,82 [1,93; 4,13] <,0001[3]	25,2 [16,3; 34,0] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Infections and infestations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,3729)					
< 65 years	442/918 (48,1)	343/937 (36,6)	1,32 [1,18; 1,46] <,0001[2]	1,61 [1,34; 1,94] <,0001[3]	11,5 [7,1; 16,0] <,0001[3]
≥ 65 years	158/365 (43,3)	119/328 (36,3)	1,19 [0,99; 1,44] 0,0619[2]	1,34 [0,99; 1,82] 0,0601[3]	7,0 [-0,3; 14,3] 0,0601[3]
Prior treatment (Interaction p-value: 0,4327)					
Neoadjuvant chemotherapy	202/430 (47,0)	141/415 (34,0)	1,38 [1,17; 1,63] 0,0002[2]	1,72 [1,30; 2,27] 0,0001[3]	13,0 [6,4; 19,6] 0,0001[3]
Adjuvant chemotherapy	368/784 (46,9)	296/769 (38,5)	1,22 [1,09; 1,37] 0,0008[2]	1,41 [1,16; 1,73] 0,0008[3]	8,4 [3,5; 13,3] 0,0008[3]
No chemotherapy	30/69 (43,5)	25/81 (30,9)	1,41 [0,92; 2,15] 0,1120[2]	1,72 [0,88; 3,37] 0,1101[3]	12,6 [-2,8; 28,0] 0,1101[3]
Region (Interaction p-value: 0,0832)					
North America / Europe	347/678 (51,2)	268/650 (41,2)	1,24 [1,10; 1,40] 0,0003[2]	1,49 [1,20; 1,86] 0,0003[3]	9,9 [4,6; 15,3] 0,0003[3]
Asia	102/203 (50,2)	92/201 (45,8)	1,10 [0,90; 1,35] 0,3688[2]	1,20 [0,81; 1,77] 0,3680[3]	4,5 [-5,3; 14,2] 0,3680[3]
Other	151/402 (37,6)	102/414 (24,6)	1,52 [1,24; 1,88] <,0001[2]	1,84 [1,36; 2,49] <,0001[3]	12,9 [6,6; 19,2] <,0001[3]
Primary tumor size (Interaction p-value: 0,2290)					
< 20 mm	154/331 (46,5)	107/335 (31,9)	1,46 [1,20; 1,77] 0,0001[2]	1,85 [1,35; 2,54] 0,0001[3]	14,6 [7,3; 21,9] 0,0001[3]
≥ 20 but < 50 mm	280/646 (43,3)	238/653 (36,4)	1,19 [1,04; 1,36] 0,0114[2]	1,33 [1,07; 1,67] 0,0111[3]	6,9 [1,6; 12,2] 0,0111[3]
≥ 50 mm	158/289 (54,7)	110/265 (41,5)	1,32 [1,10; 1,57] 0,0023[2]	1,70 [1,21; 2,38] 0,0020[3]	13,2 [4,9; 21,4] 0,0020[3]
Number of positive lymph nodes (Interaction p-value: 0,9843)					
0-3	201/427 (47,1)	152/418 (36,4)	1,29 [1,10; 1,52] 0,0018[2]	1,56 [1,18; 2,05] 0,0016[3]	10,7 [4,1; 17,3] 0,0016[3]
4-9	252/549 (45,9)	196/542 (36,2)	1,27 [1,10; 1,47] 0,0012[2]	1,50 [1,18; 1,91] 0,0011[3]	9,7 [3,9; 15,5] 0,0011[3]
≥ 10	147/307 (47,9)	114/305 (37,4)	1,28 [1,06; 1,54] 0,0092[2]	1,54 [1,12; 2,12] 0,0086[3]	10,5 [2,7; 18,3] 0,0086[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8578)					
IIA	58/113 (51,3)	44/114 (38,6)	1,33 [0,99; 1,78] 0,0565[2]	1,68 [0,99; 2,84] 0,0539[3]	12,7 [-0,1; 25,6] 0,0539[3]
IIB	68/151 (45,0)	49/136 (36,0)	1,25 [0,94; 1,66] 0,1250[2]	1,45 [0,90; 2,34] 0,1212[3]	9,0 [-2,3; 20,3] 0,1212[3]
IIIA	235/495 (47,5)	171/488 (35,0)	1,35 [1,16; 1,58] <,0001[2]	1,68 [1,30; 2,17] <,0001[3]	12,4 [6,3; 18,5] <,0001[3]
IIIB	21/54 (38,9)	16/45 (35,6)	1,09 [0,65; 1,83] 0,7337[2]	1,15 [0,51; 2,62] 0,7328[3]	3,3 [-15,8; 22,4] 0,7328[3]
IIIC	216/468 (46,2)	181/480 (37,7)	1,22 [1,05; 1,42] 0,0087[2]	1,42 [1,09; 1,83] 0,0084[3]	8,4 [2,2; 14,7] 0,0084[3]
Tumor grade (Interaction p-value: 0,7092)					
G1	41/91 (45,1)	27/93 (29,0)	1,55 [1,05; 2,29] 0,0274[2]	2,00 [1,09; 3,69] 0,0244[3]	16,0 [2,3; 29,8] 0,0244[3]
G2	288/612 (47,1)	223/603 (37,0)	1,27 [1,11; 1,45] 0,0004[2]	1,51 [1,20; 1,90] 0,0004[3]	10,1 [4,6; 15,6] 0,0004[3]
G3	244/527 (46,3)	189/506 (37,4)	1,24 [1,07; 1,43] 0,0038[2]	1,45 [1,13; 1,85] 0,0036[3]	8,9 [3,0; 14,9] 0,0036[3]
GX	26/51 (51,0)	21/59 (35,6)	1,43 [0,93; 2,22] 0,1064[2]	1,88 [0,88; 4,04] 0,1038[3]	15,4 [-3,0; 33,8] 0,1038[3]
Progesterone receptor status (Interaction p-value: 0,6511)					
Negative	78/156 (50,0)	71/169 (42,0)	1,19 [0,94; 1,51] 0,1494[2]	1,38 [0,89; 2,14] 0,1488[3]	8,0 [-2,8; 18,8] 0,1488[3]
Positive	506/1089 (46,5)	376/1067 (35,2)	1,32 [1,19; 1,46] <,0001[2]	1,60 [1,34; 1,90] <,0001[3]	11,2 [7,1; 15,3] <,0001[3]
Unknown	6/10 (60,0)	4/7 (57,1)	1,05 [0,46; 2,38] 0,9068[2]	1,13 [0,16; 7,99] 1,0000[4]	2,9 [-44,7; 50,5] 1,0000[4]
Race (Interaction p-value: 0,0990)					
White	446/958 (46,6)	343/944 (36,3)	1,28 [1,15; 1,43] <,0001[2]	1,53 [1,27; 1,83] <,0001[3]	10,2 [5,8; 14,6] <,0001[3]
Asian	116/250 (46,4)	96/242 (39,7)	1,17 [0,95; 1,44] 0,1334[2]	1,32 [0,92; 1,88] 0,1318[3]	6,7 [-2,0; 15,5] 0,1318[3]
Other	31/62 (50,0)	15/64 (23,4)	2,13 [1,28; 3,55] 0,0035[2]	3,27 [1,52; 7,01] 0,0020[3]	26,6 [10,4; 42,8] 0,0020[3]
First endocrine therapy (Interaction p-value: 0,9764)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	63/114 (55,3)	57/132 (43,2)	1,28 [0,99; 1,65] 0,0590[2]	1,63 [0,98; 2,69] 0,0587[3]	12,1 [-0,4; 24,5] 0,0587[3]
Aromatase inhibitor	537/1169 (45,9)	405/1133 (35,7)	1,29 [1,16; 1,42] <,0001[2]	1,53 [1,29; 1,81] <,0001[3]	10,2 [6,2; 14,2] <,0001[3]
ECOG-PS (Interaction p-value: 0,6788)					
ECOG-PS 0	499/1070 (46,6)	375/1020 (36,8)	1,27 [1,14; 1,41] <,0001[2]	1,50 [1,26; 1,79] <,0001[3]	9,9 [5,7; 14,1] <,0001[3]
ECOG-PS 1	101/213 (47,4)	87/245 (35,5)	1,34 [1,07; 1,66] 0,0100[2]	1,64 [1,13; 2,38] 0,0098[3]	11,9 [2,9; 20,9] 0,0098[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Investigations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,2239)					
< 65 years	440/918 (47,9)	193/937 (20,6)	2,33 [2,02; 2,68] <,0001[2]	3,55 [2,89; 4,35] <,0001[3]	27,3 [23,2; 31,5] <,0001[3]
≥ 65 years	181/365 (49,6)	82/328 (25,0)	1,98 [1,60; 2,46] <,0001[2]	2,95 [2,14; 4,08] <,0001[3]	24,6 [17,6; 31,5] <,0001[3]
Prior treatment (Interaction p-value: 0,8181)					
Neoadjuvant chemotherapy	217/430 (50,5)	97/415 (23,4)	2,16 [1,77; 2,63] <,0001[2]	3,34 [2,49; 4,49] <,0001[3]	27,1 [20,9; 33,3] <,0001[3]
Adjuvant chemotherapy	375/784 (47,8)	165/769 (21,5)	2,23 [1,91; 2,60] <,0001[2]	3,36 [2,69; 4,19] <,0001[3]	26,4 [21,8; 30,9] <,0001[3]
No chemotherapy	29/69 (42,0)	13/81 (16,0)	2,62 [1,48; 4,63] 0,0009[2]	3,79 [1,77; 8,12] 0,0004[3]	26,0 [11,9; 40,1] 0,0004[3]
Primary tumor size (Interaction p-value: 0,4580)					
< 20 mm	160/331 (48,3)	64/335 (19,1)	2,53 [1,98; 3,24] <,0001[2]	3,96 [2,80; 5,61] <,0001[3]	29,2 [22,4; 36,1] <,0001[3]
≥ 20 but < 50 mm	316/646 (48,9)	145/653 (22,2)	2,20 [1,87; 2,59] <,0001[2]	3,35 [2,64; 4,27] <,0001[3]	26,7 [21,7; 31,7] <,0001[3]
≥ 50 mm	135/289 (46,7)	61/265 (23,0)	2,03 [1,58; 2,61] <,0001[2]	2,93 [2,03; 4,23] <,0001[3]	23,7 [16,0; 31,4] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,2999)					
0-3	205/427 (48,0)	78/418 (18,7)	2,57 [2,06; 3,22] <,0001[2]	4,03 [2,95; 5,49] <,0001[3]	29,3 [23,3; 35,4] <,0001[3]
4-9	256/549 (46,6)	122/542 (22,5)	2,07 [1,73; 2,48] <,0001[2]	3,01 [2,31; 3,91] <,0001[3]	24,1 [18,7; 29,6] <,0001[3]
≥ 10	160/307 (52,1)	75/305 (24,6)	2,12 [1,69; 2,65] <,0001[2]	3,34 [2,37; 4,71] <,0001[3]	27,5 [20,1; 34,9] <,0001[3]
Tumor stage (Interaction p-value: 0,4600)					
IIA	59/113 (52,2)	19/114 (16,7)	3,13 [2,00; 4,90] <,0001[2]	5,46 [2,95; 10,11] <,0001[3]	35,5 [24,1; 47,0] <,0001[3]
IIB	69/151 (45,7)	29/136 (21,3)	2,14 [1,49; 3,09] <,0001[2]	3,10 [1,84; 5,22] <,0001[3]	24,4 [13,9; 34,9] <,0001[3]
IIIA	235/495 (47,5)	113/488 (23,2)	2,05 [1,70; 2,47] <,0001[2]	3,00 [2,28; 3,95] <,0001[3]	24,3 [18,5; 30,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	25/54 (46,3)	7/45 (15,6)	2,98 [1,42; 6,23] 0,0038[2]	4,68 [1,78; 12,31] 0,0011[3]	30,7 [13,7; 47,7] 0,0011[3]
IIIC	232/468 (49,6)	107/480 (22,3)	2,22 [1,84; 2,69] <,0001[2]	3,43 [2,59; 4,54] <,0001[3]	27,3 [21,4; 33,1] <,0001[3]
Tumor grade (Interaction p-value: 0,9526)					
G1	34/91 (37,4)	17/93 (18,3)	2,04 [1,23; 3,39] 0,0056[2]	2,67 [1,36; 5,24] 0,0038[3]	19,1 [6,4; 31,8] 0,0038[3]
G2	300/612 (49,0)	135/603 (22,4)	2,19 [1,85; 2,59] <,0001[2]	3,33 [2,60; 4,27] <,0001[3]	26,6 [21,5; 31,8] <,0001[3]
G3	256/527 (48,6)	106/506 (20,9)	2,32 [1,92; 2,81] <,0001[2]	3,56 [2,71; 4,69] <,0001[3]	27,6 [22,1; 33,2] <,0001[3]
GX	30/51 (58,8)	15/59 (25,4)	2,31 [1,41; 3,79] 0,0009[2]	4,19 [1,87; 9,41] 0,0004[3]	33,4 [15,9; 50,9] 0,0004[3]
Progesterone receptor status (Interaction p-value: 0,8237)					
Negative	79/156 (50,6)	36/169 (21,3)	2,38 [1,71; 3,30] <,0001[2]	3,79 [2,34; 6,15] <,0001[3]	29,3 [19,4; 39,3] <,0001[3]
Positive	522/1089 (47,9)	232/1067 (21,7)	2,20 [1,94; 2,51] <,0001[2]	3,31 [2,75; 4,00] <,0001[3]	26,2 [22,3; 30,1] <,0001[3]
Unknown	5/10 (50,0)	1/7 (14,3)	3,50 [0,51; 23,81] 0,2004[2]	6,00 [0,52; 69,75] 0,3043[4]	35,7 [-4,7; 76,1] 0,3043[4]
Race (Interaction p-value: 0,1113)					
White	418/958 (43,6)	200/944 (21,2)	2,06 [1,79; 2,37] <,0001[2]	2,88 [2,35; 3,52] <,0001[3]	22,4 [18,4; 26,5] <,0001[3]
Asian	163/250 (65,2)	63/242 (26,0)	2,50 [1,99; 3,15] <,0001[2]	5,32 [3,61; 7,84] <,0001[3]	39,2 [31,1; 47,3] <,0001[3]
Other	32/62 (51,6)	9/64 (14,1)	3,67 [1,91; 7,04] <,0001[2]	6,52 [2,75; 15,45] <,0001[3]	37,6 [22,5; 52,6] <,0001[3]
First endocrine therapy (Interaction p-value: 0,3096)					
Tamoxifen	46/114 (40,4)	19/132 (14,4)	2,80 [1,75; 4,49] <,0001[2]	4,02 [2,18; 7,43] <,0001[3]	26,0 [15,1; 36,8] <,0001[3]
Aromatase inhibitor	575/1169 (49,2)	256/1133 (22,6)	2,18 [1,93; 2,46] <,0001[2]	3,32 [2,77; 3,97] <,0001[3]	26,6 [22,8; 30,4] <,0001[3]
ECOG-PS (Interaction p-value: 0,4161)					
ECOG-PS 0	531/1070 (49,6)	223/1020 (21,9)	2,27 [1,99; 2,59] <,0001[2]	3,52 [2,91; 4,26] <,0001[3]	27,8 [23,8; 31,7] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	90/213 (42,3)	52/245 (21,2)	1,99 [1,49; 2,65] <,0001[2]	2,72 [1,80; 4,09] <,0001[3]	21,0 [12,6; 29,4] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Metabolism and nutrition disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4166)					
< 65 years	231/918 (25,2)	142/937 (15,2)	1,66 [1,38; 2,00] <,0001[2]	1,88 [1,49; 2,38] <,0001[3]	10,0 [6,4; 13,6] <,0001[3]
≥ 65 years	127/365 (34,8)	60/328 (18,3)	1,90 [1,45; 2,49] <,0001[2]	2,38 [1,67; 3,39] <,0001[3]	16,5 [10,1; 22,9] <,0001[3]
Prior treatment (Interaction p-value: 0,4378)					
Neoadjuvant chemotherapy	115/430 (26,7)	73/415 (17,6)	1,52 [1,17; 1,97] 0,0016[2]	1,71 [1,23; 2,38] 0,0014[3]	9,2 [3,6; 14,7] 0,0014[3]
Adjuvant chemotherapy	223/784 (28,4)	117/769 (15,2)	1,87 [1,53; 2,28] <,0001[2]	2,22 [1,72; 2,85] <,0001[3]	13,2 [9,2; 17,3] <,0001[3]
No chemotherapy	20/69 (29,0)	12/81 (14,8)	1,96 [1,03; 3,71] 0,0397[2]	2,35 [1,05; 5,24] 0,0347[3]	14,2 [1,0; 27,4] 0,0347[3]
Number of positive lymph nodes (Interaction p-value: 0,2235)					
0-3	114/427 (26,7)	63/418 (15,1)	1,77 [1,34; 2,34] <,0001[2]	2,05 [1,46; 2,89] <,0001[3]	11,6 [6,2; 17,0] <,0001[3]
4-9	160/549 (29,1)	80/542 (14,8)	1,97 [1,55; 2,51] <,0001[2]	2,38 [1,76; 3,21] <,0001[3]	14,4 [9,5; 19,2] <,0001[3]
≥ 10	84/307 (27,4)	59/305 (19,3)	1,41 [1,06; 1,90] 0,0203[2]	1,57 [1,08; 2,29] 0,0191[3]	8,0 [1,3; 14,7] 0,0191[3]
Tumor stage (Interaction p-value: 0,1890)					
IIA	29/113 (25,7)	21/114 (18,4)	1,39 [0,85; 2,29] 0,1916[2]	1,53 [0,81; 2,88] 0,1880[3]	7,2 [-3,5; 18,0] 0,1880[3]
IIB	32/151 (21,2)	16/136 (11,8)	1,80 [1,04; 3,13] 0,0372[2]	2,02 [1,05; 3,87] 0,0326[3]	9,4 [1,0; 17,9] 0,0326[3]
IIIA	147/495 (29,7)	68/488 (13,9)	2,13 [1,65; 2,76] <,0001[2]	2,61 [1,89; 3,60] <,0001[3]	15,8 [10,7; 20,8] <,0001[3]
IIIB	11/54 (20,4)	10/45 (22,2)	0,92 [0,43; 1,96] 0,8223[2]	0,90 [0,34; 2,35] 0,8224[3]	-1,9 [-18,1; 14,4] 0,8224[3]
IIIC	137/468 (29,3)	86/480 (17,9)	1,63 [1,29; 2,07] <,0001[2]	1,90 [1,40; 2,58] <,0001[3]	11,4 [6,0; 16,7] <,0001[3]
Tumor grade (Interaction p-value: 0,2085)					
G1	28/91 (30,8)	13/93 (14,0)	2,20 [1,22; 3,97] 0,0089[2]	2,74 [1,31; 5,71] 0,0062[3]	16,8 [5,0; 28,6] 0,0062[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G2	185/612 (30,2)	100/603 (16,6)	1,82 [1,47; 2,26] <,0001[2]	2,18 [1,65; 2,87] <,0001[3]	13,6 [8,9; 18,3] <,0001[3]
G3	125/527 (23,7)	81/506 (16,0)	1,48 [1,15; 1,91] 0,0022[2]	1,63 [1,20; 2,23] 0,0019[3]	7,7 [2,9; 12,5] 0,0019[3]
GX	19/51 (37,3)	7/59 (11,9)	3,14 [1,44; 6,86] 0,0041[2]	4,41 [1,67; 11,66] 0,0018[3]	25,4 [9,8; 41,0] 0,0018[3]
Progesterone receptor status (Interaction p-value: 0,8137)					
Negative	48/156 (30,8)	26/169 (15,4)	2,00 [1,31; 3,06] 0,0014[2]	2,44 [1,43; 4,19] 0,0010[3]	15,4 [6,3; 24,4] 0,0010[3]
Positive	303/1089 (27,8)	171/1067 (16,0)	1,74 [1,47; 2,05] <,0001[2]	2,02 [1,64; 2,49] <,0001[3]	11,8 [8,3; 15,3] <,0001[3]
Unknown	2/10 (20,0)	1/7 (14,3)	1,40 [0,16; 12,60] 0,7641[2]	1,50 [0,11; 20,68] 1,0000[4]	5,7 [-30,2; 41,6] 1,0000[4]
Race (Interaction p-value: 0,2756)					
White	264/958 (27,6)	157/944 (16,6)	1,66 [1,39; 1,98] <,0001[2]	1,91 [1,53; 2,38] <,0001[3]	10,9 [7,2; 14,6] <,0001[3]
Asian	58/250 (23,2)	23/242 (9,5)	2,44 [1,56; 3,83] <,0001[2]	2,88 [1,71; 4,84] <,0001[3]	13,7 [7,3; 20,1] <,0001[3]
Other	28/62 (45,2)	18/64 (28,1)	1,61 [1,00; 2,59] 0,0522[2]	2,10 [1,00; 4,41] 0,0471[3]	17,0 [0,5; 33,6] 0,0471[3]
First endocrine therapy (Interaction p-value: 0,3232)					
Tamoxifen	28/114 (24,6)	14/132 (10,6)	2,32 [1,28; 4,18] 0,0053[2]	2,74 [1,36; 5,52] 0,0037[3]	14,0 [4,5; 23,4] 0,0037[3]
Aromatase inhibitor	330/1169 (28,2)	188/1133 (16,6)	1,70 [1,45; 2,00] <,0001[2]	1,98 [1,62; 2,42] <,0001[3]	11,6 [8,3; 15,0] <,0001[3]
ECOG-PS (Interaction p-value: 0,9135)					
ECOG-PS 0	292/1070 (27,3)	158/1020 (15,5)	1,76 [1,48; 2,10] <,0001[2]	2,05 [1,65; 2,54] <,0001[3]	11,8 [8,3; 15,3] <,0001[3]
ECOG-PS 1	66/213 (31,0)	44/245 (18,0)	1,73 [1,24; 2,41] 0,0014[2]	2,05 [1,33; 3,17] 0,0011[3]	13,0 [5,2; 20,9] 0,0011[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Musculoskeletal and connective tissue disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0795)					
< 65 years	457/918 (49,8)	542/937 (57,8)	0,86 [0,79; 0,94] 0,0005[2]	0,72 [0,60; 0,87] 0,0005[3]	-8,1 [-12,6; -3,5] 0,0005[3]
≥ 65 years	167/365 (45,8)	202/328 (61,6)	0,74 [0,65; 0,86] <,0001[2]	0,53 [0,39; 0,71] <,0001[3]	-15,8 [-23,2; -8,5] <,0001[3]
Prior treatment (Interaction p-value: 0,9046)					
Neoadjuvant chemotherapy	216/430 (50,2)	247/415 (59,5)	0,84 [0,75; 0,95] 0,0069[2]	0,69 [0,52; 0,90] 0,0067[3]	-9,3 [-16,0; -2,6] 0,0067[3]
Adjuvant chemotherapy	382/784 (48,7)	459/769 (59,7)	0,82 [0,74; 0,90] <,0001[2]	0,64 [0,52; 0,78] <,0001[3]	-11,0 [-15,9; -6,0] <,0001[3]
No chemotherapy	26/69 (37,7)	38/81 (46,9)	0,80 [0,55; 1,18] 0,2605[2]	0,68 [0,36; 1,32] 0,2545[3]	-9,2 [-25,0; 6,5] 0,2545[3]
Region (Interaction p-value: 0,9094)					
North America / Europe	395/678 (58,3)	455/650 (70,0)	0,83 [0,77; 0,90] <,0001[2]	0,60 [0,48; 0,75] <,0001[3]	-11,7 [-16,9; -6,6] <,0001[3]
Asia	86/203 (42,4)	106/201 (52,7)	0,80 [0,65; 0,99] 0,0382[2]	0,66 [0,44; 0,98] 0,0369[3]	-10,4 [-20,1; -0,7] 0,0369[3]
Other	143/402 (35,6)	183/414 (44,2)	0,80 [0,68; 0,95] 0,0124[2]	0,70 [0,53; 0,92] 0,0119[3]	-8,6 [-15,3; -1,9] 0,0119[3]
Primary tumor size (Interaction p-value: 0,8529)					
< 20 mm	168/331 (50,8)	199/335 (59,4)	0,85 [0,74; 0,98] 0,0257[2]	0,70 [0,52; 0,96] 0,0249[3]	-8,6 [-16,2; -1,1] 0,0249[3]
≥ 20 but < 50 mm	295/646 (45,7)	367/653 (56,2)	0,81 [0,73; 0,91] 0,0002[2]	0,65 [0,53; 0,82] 0,0001[3]	-10,5 [-15,9; -5,1] 0,0001[3]
≥ 50 mm	156/289 (54,0)	172/265 (64,9)	0,83 [0,72; 0,96] 0,0091[2]	0,63 [0,45; 0,89] 0,0089[3]	-10,9 [-19,1; -2,8] 0,0089[3]
Number of positive lymph nodes (Interaction p-value: 0,1501)					
0-3	220/427 (51,5)	243/418 (58,1)	0,89 [0,78; 1,00] 0,0540[2]	0,77 [0,58; 1,00] 0,0535[3]	-6,6 [-13,3; 0,1] 0,0535[3]
4-9	269/549 (49,0)	317/542 (58,5)	0,84 [0,75; 0,94] 0,0018[2]	0,68 [0,54; 0,87] 0,0017[3]	-9,5 [-15,4; -3,6] 0,0017[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	135/307 (44,0)	184/305 (60,3)	0,73 [0,62; 0,85] <,0001[2]	0,52 [0,37; 0,71] <,0001[3]	-16,4 [-24,2; -8,5] <,0001[3]
Tumor stage (Interaction p-value: 0,2938)					
IIA	61/113 (54,0)	65/114 (57,0)	0,95 [0,75; 1,20] 0,6457[2]	0,88 [0,52; 1,49] 0,6454[3]	-3,0 [-16,0; 9,9] 0,6454[3]
IIB	77/151 (51,0)	78/136 (57,4)	0,89 [0,72; 1,10] 0,2799[2]	0,77 [0,49; 1,23] 0,2804[3]	-6,4 [-17,9; 5,2] 0,2804[3]
IIIA	247/495 (49,9)	282/488 (57,8)	0,86 [0,77; 0,97] 0,0134[2]	0,73 [0,57; 0,94] 0,0131[3]	-7,9 [-14,1; -1,7] 0,0131[3]
IIIB	21/54 (38,9)	26/45 (57,8)	0,67 [0,44; 1,02] 0,0630[2]	0,47 [0,21; 1,04] 0,0609[3]	-18,9 [-38,3; 0,5] 0,0609[3]
IIIC	217/468 (46,4)	292/480 (60,8)	0,76 [0,68; 0,86] <,0001[2]	0,56 [0,43; 0,72] <,0001[3]	-14,5 [-20,7; -8,2] <,0001[3]
Tumor grade (Interaction p-value: 0,4852)					
G1	50/91 (54,9)	51/93 (54,8)	1,00 [0,77; 1,30] 0,9884[2]	1,00 [0,56; 1,80] 0,9884[3]	0,1 [-14,3; 14,5] 0,9884[3]
G2	311/612 (50,8)	380/603 (63,0)	0,81 [0,73; 0,89] <,0001[2]	0,61 [0,48; 0,76] <,0001[3]	-12,2 [-17,7; -6,7] <,0001[3]
G3	243/527 (46,1)	287/506 (56,7)	0,81 [0,72; 0,92] 0,0007[2]	0,65 [0,51; 0,83] 0,0006[3]	-10,6 [-16,7; -4,5] 0,0006[3]
GX	19/51 (37,3)	25/59 (42,4)	0,88 [0,55; 1,40] 0,5867[2]	0,81 [0,37; 1,74] 0,5848[3]	-5,1 [-23,4; 13,2] 0,5848[3]
Progesterone receptor status (Interaction p-value: 0,5538)					
Negative	78/156 (50,0)	99/169 (58,6)	0,85 [0,70; 1,04] 0,1239[2]	0,71 [0,46; 1,10] 0,1207[3]	-8,6 [-19,4; 2,2] 0,1207[3]
Positive	524/1089 (48,1)	624/1067 (58,5)	0,82 [0,76; 0,89] <,0001[2]	0,66 [0,56; 0,78] <,0001[3]	-10,4 [-14,6; -6,2] <,0001[3]
Unknown	6/10 (60,0)	3/7 (42,9)	1,40 [0,52; 3,78] 0,5070[2]	2,00 [0,28; 14,20] 0,6372[4]	17,1 [-30,5; 64,7] 0,6372[4]
Race (Interaction p-value: 0,8598)					
White	493/958 (51,5)	582/944 (61,7)	0,83 [0,77; 0,90] <,0001[2]	0,66 [0,55; 0,79] <,0001[3]	-10,2 [-14,6; -5,8] <,0001[3]
Asian	95/250 (38,0)	115/242 (47,5)	0,80 [0,65; 0,98] 0,0337[2]	0,68 [0,47; 0,97] 0,0328[3]	-9,5 [-18,2; -0,8] 0,0328[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Other	31/62 (50,0)	36/64 (56,3)	0,89 [0,64; 1,24] 0,4837[2]	0,78 [0,39; 1,57] 0,4821[3]	-6,3 [-23,6; 11,1] 0,4821[3]
First endocrine therapy (Interaction p-value: 0,2030)					
Tamoxifen	50/114 (43,9)	59/132 (44,7)	0,98 [0,74; 1,30] 0,8952[2]	0,97 [0,58; 1,60] 0,8951[3]	-0,8 [-13,3; 11,6] 0,8951[3]
Aromatase inhibitor	574/1169 (49,1)	685/1133 (60,5)	0,81 [0,75; 0,88] <,0001[2]	0,63 [0,53; 0,74] <,0001[3]	-11,4 [-15,4; -7,3] <,0001[3]
ECOG-PS (Interaction p-value: 0,8779)					
ECOG-PS 0	524/1070 (49,0)	603/1020 (59,1)	0,83 [0,76; 0,90] <,0001[2]	0,66 [0,56; 0,79] <,0001[3]	-10,1 [-14,4; -5,9] <,0001[3]
ECOG-PS 1	100/213 (46,9)	141/245 (57,6)	0,82 [0,68; 0,98] 0,0256[2]	0,65 [0,45; 0,94] 0,0234[3]	-10,6 [-19,7; -1,5] 0,0234[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Nervous system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4778)					
< 65 years	357/918 (38,9)	251/937 (26,8)	1,45 [1,27; 1,66] <,0001[2]	1,74 [1,43; 2,12] <,0001[3]	12,1 [7,9; 16,3] <,0001[3]
≥ 65 years	137/365 (37,5)	93/328 (28,4)	1,32 [1,07; 1,64] 0,0113[2]	1,52 [1,10; 2,09] 0,0104[3]	9,2 [2,2; 16,1] 0,0104[3]
Prior treatment (Interaction p-value: 0,3863)					
Neoadjuvant chemotherapy	164/430 (38,1)	111/415 (26,7)	1,43 [1,17; 1,74] 0,0005[2]	1,69 [1,26; 2,26] 0,0004[3]	11,4 [5,1; 17,7] 0,0004[3]
Adjuvant chemotherapy	300/784 (38,3)	215/769 (28,0)	1,37 [1,18; 1,58] <,0001[2]	1,60 [1,29; 1,98] <,0001[3]	10,3 [5,7; 15,0] <,0001[3]
No chemotherapy	30/69 (43,5)	18/81 (22,2)	1,96 [1,20; 3,19] 0,0071[2]	2,69 [1,33; 5,46] 0,0054[3]	21,3 [6,5; 36,0] 0,0054[3]
Region (Interaction p-value: 0,3340)					
North America / Europe	314/678 (46,3)	225/650 (34,6)	1,34 [1,17; 1,53] <,0001[2]	1,63 [1,31; 2,03] <,0001[3]	11,7 [6,5; 16,9] <,0001[3]
Asia	68/203 (33,5)	50/201 (24,9)	1,35 [0,99; 1,83] 0,0588[2]	1,52 [0,99; 2,34] 0,0567[3]	8,6 [-0,2; 17,4] 0,0567[3]
Other	112/402 (27,9)	69/414 (16,7)	1,67 [1,28; 2,18] 0,0002[2]	1,93 [1,38; 2,71] 0,0001[3]	11,2 [5,5; 16,9] 0,0001[3]
Primary tumor size (Interaction p-value: 0,7760)					
< 20 mm	117/331 (35,3)	84/335 (25,1)	1,41 [1,11; 1,78] 0,0043[2]	1,63 [1,17; 2,28] 0,0039[3]	10,3 [3,3; 17,2] 0,0039[3]
≥ 20 but < 50 mm	253/646 (39,2)	176/653 (27,0)	1,45 [1,24; 1,70] <,0001[2]	1,74 [1,38; 2,21] <,0001[3]	12,2 [7,1; 17,3] <,0001[3]
≥ 50 mm	119/289 (41,2)	83/265 (31,3)	1,31 [1,05; 1,65] 0,0173[2]	1,53 [1,08; 2,18] 0,0161[3]	9,9 [1,9; 17,8] 0,0161[3]
Number of positive lymph nodes (Interaction p-value: 0,9121)					
0-3	178/427 (41,7)	120/418 (28,7)	1,45 [1,20; 1,75] 0,0001[2]	1,78 [1,33; 2,36] <,0001[3]	13,0 [6,6; 19,4] <,0001[3]
4-9	201/549 (36,6)	140/542 (25,8)	1,42 [1,18; 1,70] 0,0001[2]	1,66 [1,28; 2,15] 0,0001[3]	10,8 [5,3; 16,2] 0,0001[3]
≥ 10	115/307 (37,5)	84/305 (27,5)	1,36 [1,08; 1,72] 0,0095[2]	1,58 [1,12; 2,22] 0,0088[3]	9,9 [2,5; 17,3] 0,0088[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8015)					
IIA	40/113 (35,4)	32/114 (28,1)	1,26 [0,86; 1,85] 0,2379[2]	1,40 [0,80; 2,46] 0,2355[3]	7,3 [-4,7; 19,4] 0,2355[3]
IIB	69/151 (45,7)	45/136 (33,1)	1,38 [1,03; 1,86] 0,0323[2]	1,70 [1,05; 2,75] 0,0293[3]	12,6 [1,4; 23,8] 0,0293[3]
IIIA	193/495 (39,0)	126/488 (25,8)	1,51 [1,25; 1,82] <,0001[2]	1,84 [1,40; 2,41] <,0001[3]	13,2 [7,4; 19,0] <,0001[3]
IIIB	19/54 (35,2)	9/45 (20,0)	1,76 [0,88; 3,50] 0,1072[2]	2,17 [0,87; 5,45] 0,0948[3]	15,2 [-2,1; 32,5] 0,0948[3]
IIIC	171/468 (36,5)	132/480 (27,5)	1,33 [1,10; 1,60] 0,0031[2]	1,52 [1,15; 2,00] 0,0028[3]	9,0 [3,1; 15,0] 0,0028[3]
Tumor grade (Interaction p-value: 0,1438)					
G1	34/91 (37,4)	19/93 (20,4)	1,83 [1,13; 2,96] 0,0140[2]	2,32 [1,20; 4,49] 0,0112[3]	16,9 [4,1; 29,8] 0,0112[3]
G2	253/612 (41,3)	181/603 (30,0)	1,38 [1,18; 1,61] <,0001[2]	1,64 [1,30; 2,08] <,0001[3]	11,3 [6,0; 16,7] <,0001[3]
G3	187/527 (35,5)	136/506 (26,9)	1,32 [1,10; 1,59] 0,0031[2]	1,50 [1,15; 1,95] 0,0029[3]	8,6 [3,0; 14,2] 0,0029[3]
GX	20/51 (39,2)	8/59 (13,6)	2,89 [1,39; 6,00] 0,0043[2]	4,11 [1,62; 10,46] 0,0021[3]	25,7 [9,7; 41,7] 0,0021[3]
Progesterone receptor status (Interaction p-value: 0,2257)					
Negative	55/156 (35,3)	53/169 (31,4)	1,12 [0,83; 1,53] 0,4565[2]	1,19 [0,75; 1,89] 0,4564[3]	3,9 [-6,4; 14,1] 0,4564[3]
Positive	425/1089 (39,0)	283/1067 (26,5)	1,47 [1,30; 1,67] <,0001[2]	1,77 [1,48; 2,13] <,0001[3]	12,5 [8,6; 16,4] <,0001[3]
Unknown	4/10 (40,0)	1/7 (14,3)	2,80 [0,39; 20,02] 0,3049[2]	4,00 [0,34; 47,11] 0,3382[4]	25,7 [-14,2; 65,6] 0,3382[4]
Race (Interaction p-value: 0,9466)					
White	384/958 (40,1)	261/944 (27,6)	1,45 [1,27; 1,65] <,0001[2]	1,75 [1,44; 2,12] <,0001[3]	12,4 [8,2; 16,7] <,0001[3]
Asian	79/250 (31,6)	54/242 (22,3)	1,42 [1,05; 1,91] 0,0219[2]	1,61 [1,07; 2,41] 0,0204[3]	9,3 [1,5; 17,1] 0,0204[3]
Other	26/62 (41,9)	20/64 (31,3)	1,34 [0,84; 2,14] 0,2168[2]	1,59 [0,77; 3,30] 0,2130[3]	10,7 [-6,0; 27,4] 0,2130[3]
First endocrine therapy (Interaction p-value: 0,3437)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	38/114 (33,3)	37/132 (28,0)	1,19 [0,82; 1,73] 0,3677[2]	1,28 [0,75; 2,21] 0,3676[3]	5,3 [-6,3; 16,9] 0,3676[3]
Aromatase inhibitor	456/1169 (39,0)	307/1133 (27,1)	1,44 [1,28; 1,62] <,0001[2]	1,72 [1,44; 2,05] <,0001[3]	11,9 [8,1; 15,7] <,0001[3]
ECOG-PS (Interaction p-value: 0,3231)					
ECOG-PS 0	409/1070 (38,2)	283/1020 (27,7)	1,38 [1,22; 1,56] <,0001[2]	1,61 [1,34; 1,94] <,0001[3]	10,5 [6,5; 14,5] <,0001[3]
ECOG-PS 1	85/213 (39,9)	61/245 (24,9)	1,60 [1,22; 2,11] 0,0007[2]	2,00 [1,34; 2,98] 0,0006[3]	15,0 [6,5; 23,5] 0,0006[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Renal and urinary disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8217)					
< 65 years	63/918 (6,9)	47/937 (5,0)	1,37 [0,95; 1,97] 0,0938[2]	1,40 [0,95; 2,06] 0,0922[3]	1,8 [-0,3; 4,0] 0,0922[3]
≥ 65 years	36/365 (9,9)	22/328 (6,7)	1,47 [0,88; 2,45] 0,1376[2]	1,52 [0,88; 2,65] 0,1342[3]	3,2 [-0,9; 7,2] 0,1342[3]
Prior treatment (Interaction p-value: 0,3188)					
Neoadjuvant chemotherapy	29/430 (6,7)	16/415 (3,9)	1,75 [0,96; 3,17] 0,0656[2]	1,80 [0,96; 3,37] 0,0615[3]	2,9 [-0,1; 5,9] 0,0615[3]
Adjuvant chemotherapy	61/784 (7,8)	49/769 (6,4)	1,22 [0,85; 1,75] 0,2803[2]	1,24 [0,84; 1,83] 0,2793[3]	1,4 [-1,1; 4,0] 0,2793[3]
No chemotherapy	9/69 (13,0)	4/81 (4,9)	2,64 [0,85; 8,20] 0,0930[2]	2,89 [0,85; 9,83] 0,0787[3]	8,1 [-1,1; 17,3] 0,0787[3]
Region (Interaction p-value: 0,7167)					
North America / Europe	63/678 (9,3)	43/650 (6,6)	1,40 [0,97; 2,04] 0,0738[2]	1,45 [0,97; 2,17] 0,0720[3]	2,7 [-0,2; 5,6] 0,0720[3]
Asia	12/203 (5,9)	11/201 (5,5)	1,08 [0,49; 2,39] 0,8491[2]	1,09 [0,47; 2,52] 0,8491[3]	0,4 [-4,1; 5,0] 0,8491[3]
Other	24/402 (6,0)	15/414 (3,6)	1,65 [0,88; 3,09] 0,1205[2]	1,69 [0,87; 3,27] 0,1161[3]	2,3 [-0,6; 5,3] 0,1161[3]
Primary tumor size (Interaction p-value: 0,1325)					
< 20 mm	29/331 (8,8)	15/335 (4,5)	1,96 [1,07; 3,58] 0,0295[2]	2,05 [1,08; 3,90] 0,0261[3]	4,3 [0,5; 8,0] 0,0261[3]
≥ 20 but < 50 mm	46/646 (7,1)	44/653 (6,7)	1,06 [0,71; 1,57] 0,7860[2]	1,06 [0,69; 1,63] 0,7860[3]	0,4 [-2,4; 3,1] 0,7860[3]
≥ 50 mm	22/289 (7,6)	10/265 (3,8)	2,02 [0,97; 4,18] 0,0591[2]	2,10 [0,98; 4,52] 0,0530[3]	3,8 [0,0; 7,7] 0,0530[3]
Number of positive lymph nodes (Interaction p-value: 0,7713)					
0-3	31/427 (7,3)	25/418 (6,0)	1,21 [0,73; 2,02] 0,4558[2]	1,23 [0,71; 2,12] 0,4549[3]	1,3 [-2,1; 4,6] 0,4549[3]
4-9	45/549 (8,2)	29/542 (5,4)	1,53 [0,98; 2,41] 0,0640[2]	1,58 [0,97; 2,56] 0,0616[3]	2,8 [-0,1; 5,8] 0,0616[3]
≥ 10	23/307 (7,5)	15/305 (4,9)	1,52 [0,81; 2,86] 0,1910[2]	1,57 [0,80; 3,06] 0,1871[3]	2,6 [-1,2; 6,4] 0,1871[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,3374)					
IIA	11/113 (9,7)	5/114 (4,4)	2,22 [0,80; 6,18] 0,1272[2]	2,35 [0,79; 7,00] 0,1155[3]	5,3 [-1,3; 12,0] 0,1155[3]
IIB	10/151 (6,6)	9/136 (6,6)	1,00 [0,42; 2,39] 0,9987[2]	1,00 [0,39; 2,54] 0,9987[3]	0,0 [-5,8; 5,8] 0,9987[3]
IIIA	38/495 (7,7)	25/488 (5,1)	1,50 [0,92; 2,44] 0,1050[2]	1,54 [0,91; 2,59] 0,1021[3]	2,6 [-0,5; 5,6] 0,1021[3]
IIIB	1/54 (1,9)	4/45 (8,9)	0,21 [0,02; 1,80] 0,1537[2]	0,19 [0,02; 1,80] 0,1738[4]	-7,0 [-16,1; 2,0] 0,1738[4]
IIIC	39/468 (8,3)	26/480 (5,4)	1,54 [0,95; 2,49] 0,0783[2]	1,59 [0,95; 2,65] 0,0756[3]	2,9 [-0,3; 6,1] 0,0756[3]
Tumor grade (Interaction p-value: 0,9962)					
G1	6/91 (6,6)	4/93 (4,3)	1,53 [0,45; 5,25] 0,4966[2]	1,57 [0,43; 5,76] 0,5339[4]	2,3 [-4,3; 8,8] 0,5339[4]
G2	44/612 (7,2)	31/603 (5,1)	1,40 [0,90; 2,18] 0,1402[2]	1,43 [0,89; 2,30] 0,1379[3]	2,0 [-0,7; 4,7] 0,1379[3]
G3	47/527 (8,9)	32/506 (6,3)	1,41 [0,92; 2,17] 0,1191[2]	1,45 [0,91; 2,31] 0,1168[3]	2,6 [-0,6; 5,8] 0,1168[3]
GX	2/51 (3,9)	2/59 (3,4)	1,16 [0,17; 7,92] 0,8820[2]	1,16 [0,16; 8,57] 1,0000[4]	0,5 [-6,5; 7,6] 1,0000[4]
First endocrine therapy (Interaction p-value: 0,7175)					
Tamoxifen	6/114 (5,3)	6/132 (4,5)	1,16 [0,38; 3,49] 0,7946[2]	1,17 [0,37; 3,72] 0,7944[3]	0,7 [-4,7; 6,1] 0,7944[3]
Aromatase inhibitor	93/1169 (8,0)	63/1133 (5,6)	1,43 [1,05; 1,95] 0,0232[2]	1,47 [1,05; 2,04] 0,0223[3]	2,4 [0,3; 4,4] 0,0223[3]
ECOG-PS (Interaction p-value: 0,4340)					
ECOG-PS 0	80/1070 (7,5)	57/1020 (5,6)	1,34 [0,96; 1,86] 0,0826[2]	1,37 [0,96; 1,94] 0,0812[3]	1,9 [-0,2; 4,0] 0,0812[3]
ECOG-PS 1	19/213 (8,9)	12/245 (4,9)	1,82 [0,91; 3,66] 0,0928[2]	1,90 [0,90; 4,02] 0,0874[3]	4,0 [-0,7; 8,7] 0,0874[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Reproductive system and breast disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,2682)					
< 65 years	97/918 (10,6)	128/937 (13,7)	0,77 [0,60; 0,99] 0,0421[2]	0,75 [0,56; 0,99] 0,0413[3]	-3,1 [-6,1; -0,1] 0,0413[3]
≥ 65 years	24/365 (6,6)	38/328 (11,6)	0,57 [0,35; 0,93] 0,0231[2]	0,54 [0,31; 0,92] 0,0210[3]	-5,0 [-9,3; -0,7] 0,0210[3]
Prior treatment (Interaction p-value: 0,9435)					
Neoadjuvant chemotherapy	33/430 (7,7)	47/415 (11,3)	0,68 [0,44; 1,04] 0,0722[2]	0,65 [0,41; 1,04] 0,0700[3]	-3,7 [-7,6; 0,3] 0,0700[3]
Adjuvant chemotherapy	84/784 (10,7)	112/769 (14,6)	0,74 [0,56; 0,96] 0,0231[2]	0,70 [0,52; 0,95] 0,0224[3]	-3,9 [-7,2; -0,5] 0,0224[3]
No chemotherapy	4/69 (5,8)	7/81 (8,6)	0,67 [0,20; 2,20] 0,5093[2]	0,65 [0,18; 2,32] 0,5053[3]	-2,8 [-11,1; 5,4] 0,5053[3]
Region (Interaction p-value: 0,8749)					
North America / Europe	79/678 (11,7)	106/650 (16,3)	0,71 [0,55; 0,94] 0,0149[2]	0,68 [0,49; 0,93] 0,0143[3]	-4,7 [-8,4; -0,9] 0,0143[3]
Asia	9/203 (4,4)	15/201 (7,5)	0,59 [0,27; 1,33] 0,2038[2]	0,58 [0,25; 1,35] 0,1978[3]	-3,0 [-7,6; 1,6] 0,1978[3]
Other	33/402 (8,2)	45/414 (10,9)	0,76 [0,49; 1,16] 0,1983[2]	0,73 [0,46; 1,18] 0,1963[3]	-2,7 [-6,7; 1,4] 0,1963[3]
Primary tumor size (Interaction p-value: 0,9378)					
< 20 mm	29/331 (8,8)	39/335 (11,6)	0,75 [0,48; 1,19] 0,2217[2]	0,73 [0,44; 1,21] 0,2196[3]	-2,9 [-7,5; 1,7] 0,2196[3]
≥ 20 but < 50 mm	61/646 (9,4)	86/653 (13,2)	0,72 [0,53; 0,98] 0,0352[2]	0,69 [0,49; 0,97] 0,0340[3]	-3,7 [-7,2; -0,3] 0,0340[3]
≥ 50 mm	30/289 (10,4)	41/265 (15,5)	0,67 [0,43; 1,04] 0,0757[2]	0,63 [0,38; 1,05] 0,0733[3]	-5,1 [-10,7; 0,5] 0,0733[3]
Number of positive lymph nodes (Interaction p-value: 0,8417)					
0-3	44/427 (10,3)	55/418 (13,2)	0,78 [0,54; 1,14] 0,1987[2]	0,76 [0,50; 1,16] 0,1972[3]	-2,9 [-7,2; 1,5] 0,1972[3]
4-9	47/549 (8,6)	69/542 (12,7)	0,67 [0,47; 0,96] 0,0268[2]	0,64 [0,43; 0,95] 0,0255[3]	-4,2 [-7,8; -0,5] 0,0255[3]
≥ 10	30/307 (9,8)	42/305 (13,8)	0,71 [0,46; 1,10] 0,1273[2]	0,68 [0,41; 1,12] 0,1248[3]	-4,0 [-9,1; 1,1] 0,1248[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,6333)					
IIA	13/113 (11,5)	11/114 (9,6)	1,19 [0,56; 2,55] 0,6500[2]	1,22 [0,52; 2,84] 0,6494[3]	1,9 [-6,1; 9,9] 0,6494[3]
IIB	16/151 (10,6)	24/136 (17,6)	0,60 [0,33; 1,08] 0,0894[2]	0,55 [0,28; 1,09] 0,0850[3]	-7,1 [-15,1; 1,0] 0,0850[3]
IIIA	43/495 (8,7)	66/488 (13,5)	0,64 [0,45; 0,92] 0,0169[2]	0,61 [0,41; 0,91] 0,0157[3]	-4,8 [-8,8; -0,9] 0,0157[3]
IIIB	3/54 (5,6)	3/45 (6,7)	0,83 [0,18; 3,93] 0,8177[2]	0,82 [0,16; 4,29] 1,0000[4]	-1,1 [-10,6; 8,4] 1,0000[4]
IIIC	46/468 (9,8)	62/480 (12,9)	0,76 [0,53; 1,09] 0,1364[2]	0,73 [0,49; 1,10] 0,1347[3]	-3,1 [-7,1; 0,9] 0,1347[3]
Tumor grade (Interaction p-value: 0,2693)					
G1	3/91 (3,3)	12/93 (12,9)	0,26 [0,07; 0,88] 0,0299[2]	0,23 [0,06; 0,84] 0,0173[3]	-9,6 [-17,3; -1,9] 0,0173[3]
G2	70/612 (11,4)	86/603 (14,3)	0,80 [0,60; 1,08] 0,1423[2]	0,78 [0,55; 1,09] 0,1412[3]	-2,8 [-6,6; 0,9] 0,1412[3]
G3	44/527 (8,3)	64/506 (12,6)	0,66 [0,46; 0,95] 0,0253[2]	0,63 [0,42; 0,94] 0,0240[3]	-4,3 [-8,0; -0,6] 0,0240[3]
GX	4/51 (7,8)	4/59 (6,8)	1,16 [0,30; 4,39] 0,8305[2]	1,17 [0,28; 4,94] 1,0000[4]	1,1 [-8,7; 10,8] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,3366)					
Negative	13/156 (8,3)	12/169 (7,1)	1,17 [0,55; 2,49] 0,6772[2]	1,19 [0,53; 2,69] 0,6769[3]	1,2 [-4,6; 7,0] 0,6769[3]
Positive	103/1089 (9,5)	147/1067 (13,8)	0,69 [0,54; 0,87] 0,0019[2]	0,65 [0,50; 0,85] 0,0017[3]	-4,3 [-7,0; -1,6] 0,0017[3]
Unknown	1/10 (10,0)	2/7 (28,6)	0,35 [0,04; 3,15] 0,3491[2]	0,28 [0,02; 3,88] 0,5368[4]	-18,6 [-56,9; 19,7] 0,5368[4]
Race (Interaction p-value: 0,6838)					
White	103/958 (10,8)	133/944 (14,1)	0,76 [0,60; 0,97] 0,0279[2]	0,73 [0,56; 0,97] 0,0273[3]	-3,3 [-6,3; -0,4] 0,0273[3]
Asian	11/250 (4,4)	19/242 (7,9)	0,56 [0,27; 1,15] 0,1156[2]	0,54 [0,25; 1,16] 0,1097[3]	-3,5 [-7,7; 0,8] 0,1097[3]
Other	6/62 (9,7)	10/64 (15,6)	0,62 [0,24; 1,60] 0,3229[2]	0,58 [0,20; 1,70] 0,3161[3]	-5,9 [-17,5; 5,6] 0,3161[3]
First endocrine therapy (Interaction p-value: 0,8616)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tamoxifen	13/114 (11,4)	22/132 (16,7)	0,68 [0,36; 1,30] 0,2438[2]	0,64 [0,31; 1,34] 0,2387[3]	-5,3 [-13,9; 3,4] 0,2387[3]
Aromatase inhibitor	108/1169 (9,2)	144/1133 (12,7)	0,73 [0,57; 0,92] 0,0080[2]	0,70 [0,54; 0,91] 0,0077[3]	-3,5 [-6,0; -0,9] 0,0077[3]
ECOG-PS (Interaction p-value: 0,2184)					
ECOG-PS 0	104/1070 (9,7)	129/1020 (12,6)	0,77 [0,60; 0,98] 0,0342[2]	0,74 [0,57; 0,98] 0,0335[3]	-2,9 [-5,6; -0,2] 0,0335[3]
ECOG-PS 1	17/213 (8,0)	37/245 (15,1)	0,53 [0,31; 0,91] 0,0216[2]	0,49 [0,27; 0,89] 0,0184[3]	-7,1 [-12,9; -1,3] 0,0184[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Respiratory, thoracic and mediastinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,3445)					
< 65 years	256/918 (27,9)	185/937 (19,7)	1,41 [1,20; 1,67] <,0001[2]	1,57 [1,27; 1,95] <,0001[3]	8,1 [4,3; 12,0] <,0001[3]
≥ 65 years	117/365 (32,1)	64/328 (19,5)	1,64 [1,26; 2,14] 0,0003[2]	1,95 [1,37; 2,76] 0,0002[3]	12,5 [6,1; 19,0] 0,0002[3]
Prior treatment (Interaction p-value: 0,6611)					
Neoadjuvant chemotherapy	124/430 (28,8)	80/415 (19,3)	1,50 [1,17; 1,91] 0,0014[2]	1,70 [1,23; 2,34] 0,0012[3]	9,6 [3,8; 15,3] 0,0012[3]
Adjuvant chemotherapy	225/784 (28,7)	154/769 (20,0)	1,43 [1,20; 1,71] <,0001[2]	1,61 [1,27; 2,03] <,0001[3]	8,7 [4,4; 12,9] <,0001[3]
No chemotherapy	24/69 (34,8)	15/81 (18,5)	1,88 [1,07; 3,29] 0,0272[2]	2,35 [1,11; 4,96] 0,0236[3]	16,3 [2,2; 30,3] 0,0236[3]
Region (Interaction p-value: 0,7407)					
North America / Europe	245/678 (36,1)	154/650 (23,7)	1,53 [1,29; 1,81] <,0001[2]	1,82 [1,43; 2,31] <,0001[3]	12,4 [7,6; 17,3] <,0001[3]
Asia	57/203 (28,1)	40/201 (19,9)	1,41 [0,99; 2,01] 0,0567[2]	1,57 [0,99; 2,49] 0,0543[3]	8,2 [-0,1; 16,5] 0,0543[3]
Other	71/402 (17,7)	55/414 (13,3)	1,33 [0,96; 1,84] 0,0852[2]	1,40 [0,96; 2,05] 0,0837[3]	4,4 [-0,6; 9,3] 0,0837[3]
Primary tumor size (Interaction p-value: 0,9353)					
< 20 mm	85/331 (25,7)	61/335 (18,2)	1,41 [1,05; 1,89] 0,0209[2]	1,55 [1,07; 2,25] 0,0198[3]	7,5 [1,2; 13,7] 0,0198[3]
≥ 20 but < 50 mm	189/646 (29,3)	128/653 (19,6)	1,49 [1,23; 1,82] <,0001[2]	1,70 [1,31; 2,19] <,0001[3]	9,7 [5,0; 14,3] <,0001[3]
≥ 50 mm	94/289 (32,5)	57/265 (21,5)	1,51 [1,14; 2,01] 0,0043[2]	1,76 [1,20; 2,58] 0,0036[3]	11,0 [3,7; 18,3] 0,0036[3]
Number of positive lymph nodes (Interaction p-value: 0,6749)					
0-3	137/427 (32,1)	86/418 (20,6)	1,56 [1,23; 1,97] 0,0002[2]	1,82 [1,33; 2,49] 0,0001[3]	11,5 [5,6; 17,4] 0,0001[3]
4-9	139/549 (25,3)	91/542 (16,8)	1,51 [1,19; 1,91] 0,0007[2]	1,68 [1,25; 2,26] 0,0006[3]	8,5 [3,7; 13,3] 0,0006[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	97/307 (31,6)	72/305 (23,6)	1,34 [1,03; 1,74] 0,0283[2]	1,49 [1,05; 2,14] 0,0271[3]	8,0 [0,9; 15,0] 0,0271[3]
Tumor stage (Interaction p-value: 0,7141)					
IIA	30/113 (26,5)	21/114 (18,4)	1,44 [0,88; 2,36] 0,1464[2]	1,60 [0,85; 3,01] 0,1424[3]	8,1 [-2,7; 18,9] 0,1424[3]
IIB	49/151 (32,5)	30/136 (22,1)	1,47 [1,00; 2,17] 0,0529[2]	1,70 [1,00; 2,88] 0,0491[3]	10,4 [0,2; 20,6] 0,0491[3]
IIIA	135/495 (27,3)	80/488 (16,4)	1,66 [1,30; 2,13] <,0001[2]	1,91 [1,40; 2,61] <,0001[3]	10,9 [5,8; 16,0] <,0001[3]
IIIB	16/54 (29,6)	8/45 (17,8)	1,67 [0,79; 3,53] 0,1824[2]	1,95 [0,74; 5,10] 0,1706[3]	11,9 [-4,7; 28,4] 0,1706[3]
IIIC	141/468 (30,1)	110/480 (22,9)	1,31 [1,06; 1,63] 0,0124[2]	1,45 [1,08; 1,94] 0,0119[3]	7,2 [1,6; 12,8] 0,0119[3]
Tumor grade (Interaction p-value: 0,4042)					
G1	24/91 (26,4)	12/93 (12,9)	2,04 [1,09; 3,84] 0,0261[2]	2,42 [1,13; 5,20] 0,0213[3]	13,5 [2,1; 24,8] 0,0213[3]
G2	175/612 (28,6)	126/603 (20,9)	1,37 [1,12; 1,67] 0,0021[2]	1,52 [1,17; 1,97] 0,0019[3]	7,7 [2,9; 12,5] 0,0019[3]
G3	158/527 (30,0)	102/506 (20,2)	1,49 [1,20; 1,85] 0,0003[2]	1,70 [1,27; 2,26] 0,0003[3]	9,8 [4,6; 15,1] 0,0003[3]
GX	16/51 (31,4)	8/59 (13,6)	2,31 [1,08; 4,95] 0,0308[2]	2,91 [1,13; 7,55] 0,0241[3]	17,8 [2,4; 33,3] 0,0241[3]
Race (Interaction p-value: 0,8144)					
White	284/958 (29,6)	187/944 (19,8)	1,50 [1,27; 1,76] <,0001[2]	1,71 [1,38; 2,11] <,0001[3]	9,8 [6,0; 13,7] <,0001[3]
Asian	69/250 (27,6)	48/242 (19,8)	1,39 [1,01; 1,92] 0,0451[2]	1,54 [1,01; 2,35] 0,0431[3]	7,8 [0,3; 15,2] 0,0431[3]
Other	13/62 (21,0)	11/64 (17,2)	1,22 [0,59; 2,51] 0,5899[2]	1,28 [0,52; 3,12] 0,5890[3]	3,8 [-9,9; 17,5] 0,5890[3]
First endocrine therapy (Interaction p-value: 0,5055)					
Tamoxifen	30/114 (26,3)	20/132 (15,2)	1,74 [1,05; 2,88] 0,0329[2]	2,00 [1,06; 3,76] 0,0300[3]	11,2 [1,0; 21,3] 0,0300[3]
Aromatase inhibitor	343/1169 (29,3)	229/1133 (20,2)	1,45 [1,25; 1,68] <,0001[2]	1,64 [1,35; 1,99] <,0001[3]	9,1 [5,6; 12,6] <,0001[3]
ECOG-PS (Interaction p-value: 0,0500)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	293/1070 (27,4)	202/1020 (19,8)	1,38 [1,18; 1,62] <,0001[2]	1,53 [1,24; 1,87] <,0001[3]	7,6 [4,0; 11,2] <,0001[3]
ECOG-PS 1	80/213 (37,6)	47/245 (19,2)	1,96 [1,44; 2,67] <,0001[2]	2,53 [1,66; 3,86] <,0001[3]	18,4 [10,2; 26,5] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events according SOC Skin and subcutaneous tissue disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,0788)					
< 65 years	342/918 (37,3)	210/937 (22,4)	1,66 [1,44; 1,92] <,0001[2]	2,06 [1,68; 2,52] <,0001[3]	14,8 [10,7; 19,0] <,0001[3]
≥ 65 years	164/365 (44,9)	69/328 (21,0)	2,14 [1,68; 2,71] <,0001[2]	3,06 [2,19; 4,29] <,0001[3]	23,9 [17,1; 30,6] <,0001[3]
Prior treatment (Interaction p-value: 0,1090)					
Neoadjuvant chemotherapy	165/430 (38,4)	87/415 (21,0)	1,83 [1,47; 2,29] <,0001[2]	2,35 [1,73; 3,19] <,0001[3]	17,4 [11,4; 23,4] <,0001[3]
Adjuvant chemotherapy	305/784 (38,9)	178/769 (23,1)	1,68 [1,44; 1,96] <,0001[2]	2,11 [1,70; 2,64] <,0001[3]	15,8 [11,2; 20,3] <,0001[3]
No chemotherapy	36/69 (52,2)	14/81 (17,3)	3,02 [1,78; 5,11] <,0001[2]	5,22 [2,48; 11,00] <,0001[3]	34,9 [20,5; 49,3] <,0001[3]
Primary tumor size (Interaction p-value: 0,7933)					
< 20 mm	113/331 (34,1)	62/335 (18,5)	1,84 [1,41; 2,42] <,0001[2]	2,28 [1,60; 3,26] <,0001[3]	15,6 [9,0; 22,2] <,0001[3]
≥ 20 but < 50 mm	256/646 (39,6)	143/653 (21,9)	1,81 [1,52; 2,15] <,0001[2]	2,34 [1,84; 2,99] <,0001[3]	17,7 [12,8; 22,7] <,0001[3]
≥ 50 mm	130/289 (45,0)	72/265 (27,2)	1,66 [1,31; 2,09] <,0001[2]	2,19 [1,53; 3,13] <,0001[3]	17,8 [10,0; 25,7] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,7840)					
0-3	170/427 (39,8)	91/418 (21,8)	1,83 [1,47; 2,27] <,0001[2]	2,38 [1,76; 3,22] <,0001[3]	18,0 [11,9; 24,1] <,0001[3]
4-9	207/549 (37,7)	111/542 (20,5)	1,84 [1,51; 2,24] <,0001[2]	2,35 [1,79; 3,08] <,0001[3]	17,2 [11,9; 22,5] <,0001[3]
≥ 10	129/307 (42,0)	77/305 (25,2)	1,66 [1,32; 2,10] <,0001[2]	2,15 [1,52; 3,03] <,0001[3]	16,8 [9,4; 24,1] <,0001[3]
Tumor stage (Interaction p-value: 0,9836)					
IIA	41/113 (36,3)	24/114 (21,1)	1,72 [1,12; 2,65] 0,0134[2]	2,14 [1,18; 3,86] 0,0111[3]	15,2 [3,6; 26,8] 0,0111[3]
IIB	61/151 (40,4)	31/136 (22,8)	1,77 [1,23; 2,55] 0,0021[2]	2,30 [1,37; 3,85] 0,0014[3]	17,6 [7,1; 28,1] 0,0014[3]
IIIA	196/495 (39,6)	105/488 (21,5)	1,84 [1,50; 2,25] <,0001[2]	2,39 [1,81; 3,17] <,0001[3]	18,1 [12,4; 23,7] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	20/54 (37,0)	11/45 (24,4)	1,52 [0,81; 2,82] 0,1892[2]	1,82 [0,76; 4,37] 0,1785[3]	12,6 [-5,4; 30,6] 0,1785[3]
IIIC	187/468 (40,0)	108/480 (22,5)	1,78 [1,45; 2,17] <,0001[2]	2,29 [1,73; 3,04] <,0001[3]	17,5 [11,7; 23,3] <,0001[3]
Tumor grade (Interaction p-value: 0,2329)					
G1	37/91 (40,7)	19/93 (20,4)	1,99 [1,24; 3,19] 0,0042[2]	2,67 [1,39; 5,14] 0,0029[3]	20,2 [7,2; 33,2] 0,0029[3]
G2	260/612 (42,5)	130/603 (21,6)	1,97 [1,65; 2,35] <,0001[2]	2,69 [2,09; 3,46] <,0001[3]	20,9 [15,8; 26,0] <,0001[3]
G3	196/527 (37,2)	115/506 (22,7)	1,64 [1,35; 1,99] <,0001[2]	2,01 [1,53; 2,64] <,0001[3]	14,5 [9,0; 20,0] <,0001[3]
GX	12/51 (23,5)	13/59 (22,0)	1,07 [0,54; 2,13] 0,8519[2]	1,09 [0,45; 2,66] 0,8519[3]	1,5 [-14,2; 17,2] 0,8519[3]
Progesterone receptor status (Interaction p-value: 0,4762)					
Negative	62/156 (39,7)	45/169 (26,6)	1,49 [1,09; 2,05] 0,0130[2]	1,82 [1,14; 2,90] 0,0119[3]	13,1 [2,9; 23,3] 0,0119[3]
Positive	429/1089 (39,4)	231/1067 (21,6)	1,82 [1,59; 2,08] <,0001[2]	2,35 [1,95; 2,84] <,0001[3]	17,7 [13,9; 21,6] <,0001[3]
Unknown	4/10 (40,0)	1/7 (14,3)	2,80 [0,39; 20,02] 0,3049[2]	4,00 [0,34; 47,11] 0,3382[4]	25,7 [-14,2; 65,6] 0,3382[4]
Race (Interaction p-value: 0,1023)					
White	378/958 (39,5)	193/944 (20,4)	1,93 [1,66; 2,24] <,0001[2]	2,54 [2,07; 3,11] <,0001[3]	19,0 [15,0; 23,0] <,0001[3]
Asian	101/250 (40,4)	63/242 (26,0)	1,55 [1,20; 2,01] 0,0009[2]	1,93 [1,31; 2,82] 0,0007[3]	14,4 [6,1; 22,6] 0,0007[3]
Other	19/62 (30,6)	17/64 (26,6)	1,15 [0,66; 2,01] 0,6125[2]	1,22 [0,56; 2,65] 0,6120[3]	4,1 [-11,7; 19,9] 0,6120[3]
First endocrine therapy (Interaction p-value: 0,5269)					
Tamoxifen	44/114 (38,6)	32/132 (24,2)	1,59 [1,09; 2,33] 0,0165[2]	1,96 [1,14; 3,40] 0,0151[3]	14,4 [2,8; 25,9] 0,0151[3]
Aromatase inhibitor	462/1169 (39,5)	247/1133 (21,8)	1,81 [1,59; 2,07] <,0001[2]	2,34 [1,95; 2,82] <,0001[3]	17,7 [14,0; 21,4] <,0001[3]
ECOG-PS (Interaction p-value: 0,4863)					
ECOG-PS 0	422/1070 (39,4)	220/1020 (21,6)	1,83 [1,59; 2,10] <,0001[2]	2,37 [1,95; 2,87] <,0001[3]	17,9 [14,0; 21,7] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	84/213 (39,4)	59/245 (24,1)	1,64 [1,24; 2,16] 0,0005[2]	2,05 [1,37; 3,07] 0,0004[3]	15,4 [6,9; 23,8] 0,0004[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - serious adverse events according SOC Gastrointestinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9576)					
Neoadjuvant chemotherapy	8/430 (1,9)	3/415 (0,7)	2,57 [0,69; 9,63] 0,1604[2]	2,60 [0,69; 9,88] 0,1447[3]	1,1 [-0,4; 2,7] 0,1447[3]
Adjuvant chemotherapy	21/784 (2,7)	10/769 (1,3)	2,06 [0,98; 4,35] 0,0578[2]	2,09 [0,98; 4,47] 0,0522[3]	1,4 [-0,0; 2,8] 0,0522[3]
No chemotherapy	2/69 (2,9)	1/81 (1,2)	2,35 [0,22; 25,34] 0,4819[2]	2,39 [0,21; 26,92] 0,5945[4]	1,7 [-3,0; 6,3] 0,5945[4]
Region (Interaction p-value: 0,5645)					
North America / Europe	21/678 (3,1)	11/650 (1,7)	1,83 [0,89; 3,77] 0,1006[2]	1,86 [0,89; 3,88] 0,0951[3]	1,4 [-0,2; 3,0] 0,0951[3]
Asia	4/203 (2,0)	2/201 (1,0)	1,98 [0,37; 10,69] 0,4271[2]	2,00 [0,36; 11,04] 0,6852[4]	1,0 [-1,4; 3,3] 0,6852[4]
Other	6/402 (1,5)	1/414 (0,2)	6,18 [0,75; 51,10] 0,0911[2]	6,26 [0,75; 52,21] 0,0655[4]	1,3 [-0,0; 2,5] 0,0655[4]
Primary tumor size (Interaction p-value: 0,9402)					
< 20 mm	5/331 (1,5)	2/335 (0,6)	2,53 [0,49; 12,95] 0,2651[2]	2,55 [0,49; 13,26] 0,2839[4]	0,9 [-0,6; 2,5] 0,2839[4]
≥ 20 but < 50 mm	18/646 (2,8)	8/653 (1,2)	2,27 [1,00; 5,19] 0,0511[2]	2,31 [1,00; 5,35] 0,0446[3]	1,6 [0,0; 3,1] 0,0446[3]
≥ 50 mm	8/289 (2,8)	4/265 (1,5)	1,83 [0,56; 6,02] 0,3173[2]	1,86 [0,55; 6,24] 0,3093[3]	1,3 [-1,1; 3,7] 0,3093[3]
Number of positive lymph nodes (Interaction p-value: 0,2714)					
0-3	12/427 (2,8)	3/418 (0,7)	3,92 [1,11; 13,78] 0,0334[2]	4,00 [1,12; 14,28] 0,0213[3]	2,1 [0,3; 3,9] 0,0213[3]
4-9	8/549 (1,5)	7/542 (1,3)	1,13 [0,41; 3,09] 0,8143[2]	1,13 [0,41; 3,14] 0,8142[3]	0,2 [-1,2; 1,5] 0,8142[3]
≥ 10	11/307 (3,6)	4/305 (1,3)	2,73 [0,88; 8,49] 0,0822[2]	2,80 [0,88; 8,88] 0,0692[3]	2,3 [-0,2; 4,7] 0,0692[3]
Tumor stage (Interaction p-value: 0,9730)					
IIA	2/113 (1,8)	0/114 (0,0)	5,04 [0,24; 103,90] 0,2945[2]	5,13 [0,24; 108,15] 0,2467[4]	1,8 [-0,7; 4,2] 0,2467[4]
IIB	5/151 (3,3)	0/136 (0,0)	9,91 [0,55; 177,65] 0,1192[2]	10,25 [0,56; 187,10] 0,0620[4]	3,3 [0,5; 6,2] 0,0620[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	9/495 (1,8)	7/488 (1,4)	1,27 [0,48; 3,38] 0,6353[2]	1,27 [0,47; 3,44] 0,6345[3]	0,4 [-1,2; 2,0] 0,6345[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	14/468 (3,0)	7/480 (1,5)	2,05 [0,84; 5,04] 0,1170[2]	2,08 [0,83; 5,21] 0,1088[3]	1,5 [-0,3; 3,4] 0,1088[3]
Tumor grade (Interaction p-value: 0,2748)					
G1	1/91 (1,1)	3/93 (3,2)	0,34 [0,04; 3,21] 0,3471[2]	0,33 [0,03; 3,27] 0,6210[4]	-2,1 [-6,3; 2,1] 0,6210[4]
G2	13/612 (2,1)	6/603 (1,0)	2,13 [0,82; 5,58] 0,1218[2]	2,16 [0,82; 5,72] 0,1127[3]	1,1 [-0,3; 2,5] 0,1127[3]
G3	17/527 (3,2)	4/506 (0,8)	4,08 [1,38; 12,04] 0,0109[2]	4,18 [1,40; 12,52] 0,0056[3]	2,4 [0,7; 4,1] 0,0056[3]
GX	0/51 (0,0)	1/59 (1,7)	0,38 [0,02; 9,24] 0,5558[2]	0,38 [0,02; 9,50] 1,0000[4]	-1,7 [-5,0; 1,6] 1,0000[4]
Race (Interaction p-value: 0,8628)					
White	22/958 (2,3)	11/944 (1,2)	1,97 [0,96; 4,04] 0,0641[2]	1,99 [0,96; 4,13] 0,0589[3]	1,1 [-0,0; 2,3] 0,0589[3]
Asian	6/250 (2,4)	2/242 (0,8)	2,90 [0,59; 14,25] 0,1889[2]	2,95 [0,59; 14,77] 0,2856[4]	1,6 [-0,6; 3,8] 0,2856[4]
Other	3/62 (4,8)	1/64 (1,6)	3,10 [0,33; 28,97] 0,3218[2]	3,20 [0,32; 31,66] 0,3610[4]	3,3 [-2,9; 9,4] 0,3610[4]
ECOG-PS (Interaction p-value: 0,1449)					
ECOG-PS 0	21/1070 (2,0)	12/1020 (1,2)	1,67 [0,83; 3,37] 0,1543[2]	1,68 [0,82; 3,44] 0,1496[3]	0,8 [-0,3; 1,8] 0,1496[3]
ECOG-PS 1	10/213 (4,7)	2/245 (0,8)	5,75 [1,27; 25,96] 0,0229[2]	5,99 [1,30; 27,63] 0,0095[3]	3,9 [0,8; 6,9] 0,0095[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - serious adverse events according SOC Infections and infestations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,4685)					
< 65 years	44/918 (4,8)	25/937 (2,7)	1,80 [1,11; 2,91] 0,0173[2]	1,84 [1,11; 3,03] 0,0156[3]	2,1 [0,4; 3,8] 0,0156[3]
≥ 65 years	25/365 (6,8)	9/328 (2,7)	2,50 [1,18; 5,27] 0,0164[2]	2,61 [1,20; 5,67] 0,0125[3]	4,1 [1,0; 7,2] 0,0125[3]
Prior treatment (Interaction p-value: 0,1971)					
Neoadjuvant chemotherapy	26/430 (6,0)	12/415 (2,9)	2,09 [1,07; 4,09] 0,0311[2]	2,16 [1,08; 4,34] 0,0269[3]	3,2 [0,4; 5,9] 0,0269[3]
Adjuvant chemotherapy	42/784 (5,4)	18/769 (2,3)	2,29 [1,33; 3,94] 0,0028[2]	2,36 [1,35; 4,14] 0,0020[3]	3,0 [1,1; 4,9] 0,0020[3]
No chemotherapy	1/69 (1,4)	4/81 (4,9)	0,29 [0,03; 2,56] 0,2677[2]	0,28 [0,03; 2,59] 0,3747[4]	-3,5 [-9,0; 2,0] 0,3747[4]
Region (Interaction p-value: 0,1281)					
North America / Europe	42/678 (6,2)	25/650 (3,8)	1,61 [0,99; 2,61] 0,0532[2]	1,65 [0,99; 2,74] 0,0506[3]	2,3 [0,0; 4,7] 0,0506[3]
Asia	7/203 (3,4)	5/201 (2,5)	1,39 [0,45; 4,30] 0,5714[2]	1,40 [0,44; 4,49] 0,5695[3]	1,0 [-2,3; 4,3] 0,5695[3]
Other	20/402 (5,0)	4/414 (1,0)	5,15 [1,78; 14,93] 0,0026[2]	5,37 [1,82; 15,84] 0,0007[3]	4,0 [1,7; 6,3] 0,0007[3]
Number of positive lymph nodes (Interaction p-value: 0,8691)					
0-3	25/427 (5,9)	14/418 (3,3)	1,75 [0,92; 3,32] 0,0873[2]	1,79 [0,92; 3,50] 0,0826[3]	2,5 [-0,3; 5,3] 0,0826[3]
4-9	27/549 (4,9)	12/542 (2,2)	2,22 [1,14; 4,34] 0,0195[2]	2,28 [1,15; 4,56] 0,0162[3]	2,7 [0,5; 4,9] 0,0162[3]
≥ 10	17/307 (5,5)	8/305 (2,6)	2,11 [0,92; 4,82] 0,0760[2]	2,18 [0,92; 5,12] 0,0686[3]	2,9 [-0,2; 6,0] 0,0686[3]
Tumor stage (Interaction p-value: 0,1905)					
IIA	5/113 (4,4)	2/114 (1,8)	2,52 [0,50; 12,73] 0,2628[2]	2,59 [0,49; 13,65] 0,2803[4]	2,7 [-1,8; 7,2] 0,2803[4]
IIB	8/151 (5,3)	9/136 (6,6)	0,80 [0,32; 2,02] 0,6370[2]	0,79 [0,30; 2,11] 0,6363[3]	-1,3 [-6,8; 4,2] 0,6363[3]
IIIA	31/495 (6,3)	9/488 (1,8)	3,40 [1,63; 7,06] 0,0011[2]	3,56 [1,67; 7,55] 0,0005[3]	4,4 [2,0; 6,9] 0,0005[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	3/54 (5,6)	2/45 (4,4)	1,25 [0,22; 7,16] 0,8021[2]	1,26 [0,20; 7,92] 1,0000[4]	1,1 [-7,5; 9,7] 1,0000[4]
IIIC	22/468 (4,7)	12/480 (2,5)	1,88 [0,94; 3,76] 0,0736[2]	1,92 [0,94; 3,93] 0,0685[3]	2,2 [-0,2; 4,6] 0,0685[3]
Race (Interaction p-value: 0,7666)					
White	56/958 (5,8)	27/944 (2,9)	2,04 [1,30; 3,21] 0,0019[2]	2,11 [1,32; 3,37] 0,0014[3]	3,0 [1,2; 4,8] 0,0014[3]
Asian	10/250 (4,0)	7/242 (2,9)	1,38 [0,54; 3,57] 0,5035[2]	1,40 [0,52; 3,74] 0,5013[3]	1,1 [-2,1; 4,3] 0,5013[3]
Other	3/62 (4,8)	0/64 (0,0)	7,22 [0,38; 137,01] 0,1879[2]	7,59 [0,38; 150,00] 0,1162[4]	4,8 [-0,5; 10,2] 0,1162[4]
ECOG-PS (Interaction p-value: 0,6051)					
ECOG-PS 0	52/1070 (4,9)	26/1020 (2,5)	1,91 [1,20; 3,03] 0,0063[2]	1,95 [1,21; 3,15] 0,0053[3]	2,3 [0,7; 3,9] 0,0053[3]
ECOG-PS 1	17/213 (8,0)	8/245 (3,3)	2,44 [1,08; 5,55] 0,0327[2]	2,57 [1,09; 6,08] 0,0267[3]	4,7 [0,5; 9,0] 0,0267[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - serious adverse events according SOC Vascular disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7527)					
< 65 years	9/918 (1,0)	4/937 (0,4)	2,30 [0,71; 7,43] 0,1652[2]	2,31 [0,71; 7,53] 0,1531[3]	0,6 [-0,2; 1,3] 0,1531[3]
≥ 65 years	7/365 (1,9)	2/328 (0,6)	3,15 [0,66; 15,03] 0,1511[2]	3,19 [0,66; 15,45] 0,1825[4]	1,3 [-0,3; 2,9] 0,1825[4]
Prior treatment (Interaction p-value: 0,7223)					
Neoadjuvant chemotherapy	8/430 (1,9)	2/415 (0,5)	3,86 [0,82; 18,07] 0,0863[2]	3,91 [0,83; 18,54] 0,1078[4]	1,4 [-0,1; 2,8] 0,1078[4]
Adjuvant chemotherapy	7/784 (0,9)	4/769 (0,5)	1,72 [0,50; 5,84] 0,3871[2]	1,72 [0,50; 5,91] 0,3812[3]	0,4 [-0,5; 1,2] 0,3812[3]
No chemotherapy	1/69 (1,4)	0/81 (0,0)	3,51 [0,15; 84,90] 0,4392[2]	3,57 [0,14; 89,04] 0,4600[4]	1,4 [-1,4; 4,3] 0,4600[4]
Region (Interaction p-value: 0,9319)					
North America / Europe	10/678 (1,5)	5/650 (0,8)	1,92 [0,66; 5,58] 0,2323[2]	1,93 [0,66; 5,68] 0,2238[3]	0,7 [-0,4; 1,8] 0,2238[3]
Asia	3/203 (1,5)	0/201 (0,0)	6,93 [0,36; 133,33] 0,1994[2]	7,03 [0,36; 137,07] 0,2482[4]	1,5 [-0,2; 3,1] 0,2482[4]
Other	3/402 (0,7)	1/414 (0,2)	3,09 [0,32; 29,58] 0,3277[2]	3,11 [0,32; 29,98] 0,3669[4]	0,5 [-0,5; 1,5] 0,3669[4]
Primary tumor size (Interaction p-value: 0,3049)					
< 20 mm	3/331 (0,9)	3/335 (0,9)	1,01 [0,21; 4,98] 0,9882[2]	1,01 [0,20; 5,05] 1,0000[4]	0,0 [-1,4; 1,4] 1,0000[4]
≥ 20 but < 50 mm	11/646 (1,7)	2/653 (0,3)	5,56 [1,24; 24,98] 0,0253[2]	5,64 [1,24; 25,54] 0,0115[3]	1,4 [0,3; 2,5] 0,0115[3]
≥ 50 mm	2/289 (0,7)	1/265 (0,4)	1,83 [0,17; 20,11] 0,6196[2]	1,84 [0,17; 20,41] 1,0000[4]	0,3 [-0,9; 1,5] 1,0000[4]
Tumor stage (Interaction p-value: 0,7369)					
IIA	0/113 (0,0)	0/114 (0,0)	NE	NE	NE
IIB	2/151 (1,3)	0/136 (0,0)	4,51 [0,22; 93,05] 0,3297[2]	4,57 [0,22; 95,94] 0,4996[4]	1,3 [-0,5; 3,1] 0,4996[4]
IIIA	5/495 (1,0)	3/488 (0,6)	1,64 [0,39; 6,84] 0,4949[2]	1,65 [0,39; 6,94] 0,7255[4]	0,4 [-0,7; 1,5] 0,7255[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIB	1/54 (1,9)	1/45 (2,2)	0,83 [0,05; 12,95] 0,8964[2]	0,83 [0,05; 13,66] 1,0000[4]	-0,4 [-6,0; 5,2] 1,0000[4]
IIIC	8/468 (1,7)	2/480 (0,4)	4,10 [0,88; 19,22] 0,0732[2]	4,16 [0,88; 19,68] 0,0610[4]	1,3 [-0,0; 2,6] 0,0610[4]
Tumor grade (Interaction p-value: 0,8553)					
G1	1/91 (1,1)	1/93 (1,1)	1,02 [0,06; 16,09] 0,9877[2]	1,02 [0,06; 16,59] 1,0000[4]	0,0 [-3,0; 3,0] 1,0000[4]
G2	12/612 (2,0)	5/603 (0,8)	2,36 [0,84; 6,67] 0,1039[2]	2,39 [0,84; 6,83] 0,0931[3]	1,1 [-0,2; 2,4] 0,0931[3]
G3	3/527 (0,6)	0/506 (0,0)	6,72 [0,35; 129,80] 0,2072[2]	6,76 [0,35; 131,20] 0,2496[4]	0,6 [-0,1; 1,2] 0,2496[4]
GX	0/51 (0,0)	0/59 (0,0)	NE	NE	NE
Progesterone receptor status (Interaction p-value: 0,5572)					
Negative	2/156 (1,3)	1/169 (0,6)	2,17 [0,20; 23,66] 0,5261[2]	2,18 [0,20; 24,30] 0,6093[4]	0,7 [-1,4; 2,8] 0,6093[4]
Positive	14/1089 (1,3)	5/1067 (0,5)	2,74 [0,99; 7,59] 0,0519[2]	2,77 [0,99; 7,71] 0,0424[3]	0,8 [0,0; 1,6] 0,0424[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9997)					
White	11/958 (1,1)	5/944 (0,5)	2,17 [0,76; 6,22] 0,1499[2]	2,18 [0,76; 6,30] 0,1397[3]	0,6 [-0,2; 1,4] 0,1397[3]
Asian	4/250 (1,6)	0/242 (0,0)	8,71 [0,47; 160,97] 0,1457[2]	8,85 [0,47; 165,34] 0,1237[4]	1,6 [0,0; 3,2] 0,1237[4]
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
First endocrine therapy (Interaction p-value: 0,5759)					
Tamoxifen	4/114 (3,5)	1/132 (0,8)	4,63 [0,53; 40,85] 0,1675[2]	4,76 [0,52; 43,25] 0,1855[4]	2,8 [-0,9; 6,4] 0,1855[4]
Aromatase inhibitor	12/1169 (1,0)	5/1133 (0,4)	2,33 [0,82; 6,58] 0,1116[2]	2,34 [0,82; 6,66] 0,1011[3]	0,6 [-0,1; 1,3] 0,1011[3]
ECOG-PS (Interaction p-value: 0,4071)					
ECOG-PS 0	11/1070 (1,0)	5/1020 (0,5)	2,10 [0,73; 6,01] 0,1683[2]	2,11 [0,73; 6,09] 0,1585[3]	0,5 [-0,2; 1,3] 0,1585[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	5/213 (2,3)	1/245 (0,4)	5,75 [0,68; 48,84] 0,1090[2]	5,87 [0,68; 50,61] 0,1013[4]	1,9 [-0,2; 4,1] 0,1013[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Alanine aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5420)					
< 65 years	24/918 (2,6)	5/937 (0,5)	4,90 [1,88; 12,79] 0,0012[2]	5,00 [1,90; 13,17] 0,0003[3]	2,1 [0,9; 3,2] 0,0003[3]
≥ 65 years	11/365 (3,0)	1/328 (0,3)	9,88 [1,28; 76,15] 0,0279[2]	10,16 [1,30; 79,14] 0,0063[3]	2,7 [0,9; 4,6] 0,0063[3]
Prior treatment (Interaction p-value: 0,2629)					
Neoadjuvant chemotherapy	17/430 (4,0)	1/415 (0,2)	16,41 [2,19; 122,73] 0,0064[2]	17,04 [2,26; 128,64] 0,0002[3]	3,7 [1,8; 5,6] 0,0002[3]
Adjuvant chemotherapy	11/784 (1,4)	4/769 (0,5)	2,70 [0,86; 8,43] 0,0880[2]	2,72 [0,86; 8,58] 0,0753[3]	0,9 [-0,1; 1,9] 0,0753[3]
No chemotherapy	7/69 (10,1)	1/81 (1,2)	8,22 [1,04; 65,16] 0,0462[2]	9,03 [1,08; 75,35] 0,0243[4]	8,9 [1,4; 16,4] 0,0243[4]
Region (Interaction p-value: 0,7023)					
North America / Europe	12/678 (1,8)	1/650 (0,2)	11,50 [1,50; 88,22] 0,0188[2]	11,69 [1,52; 90,19] 0,0028[3]	1,6 [0,6; 2,7] 0,0028[3]
Asia	11/203 (5,4)	2/201 (1,0)	5,45 [1,22; 24,26] 0,0262[2]	5,70 [1,25; 26,05] 0,0118[3]	4,4 [1,0; 7,8] 0,0118[3]
Other	12/402 (3,0)	3/414 (0,7)	4,12 [1,17; 14,49] 0,0274[2]	4,22 [1,18; 15,05] 0,0163[3]	2,3 [0,4; 4,1] 0,0163[3]
Primary tumor size (Interaction p-value: 0,9677)					
< 20 mm	8/331 (2,4)	1/335 (0,3)	8,10 [1,02; 64,38] 0,0480[2]	8,27 [1,03; 66,51] 0,0200[4]	2,1 [0,4; 3,9] 0,0200[4]
≥ 20 but < 50 mm	20/646 (3,1)	3/653 (0,5)	6,74 [2,01; 22,57] 0,0020[2]	6,92 [2,05; 23,41] 0,0003[3]	2,6 [1,2; 4,1] 0,0003[3]
≥ 50 mm	6/289 (2,1)	1/265 (0,4)	5,50 [0,67; 45,40] 0,1133[2]	5,60 [0,67; 46,80] 0,1251[4]	1,7 [-0,1; 3,5] 0,1251[4]
Number of positive lymph nodes (Interaction p-value: 0,6165)					
0-3	13/427 (3,0)	2/418 (0,5)	6,36 [1,44; 28,02] 0,0144[2]	6,53 [1,46; 29,12] 0,0047[3]	2,6 [0,8; 4,3] 0,0047[3]
4-9	12/549 (2,2)	0/542 (0,0)	24,68 [1,46; 415,83] 0,0261[2]	25,23 [1,49; 427,24] 0,0005[3]	2,2 [1,0; 3,4] 0,0005[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	10/307 (3,3)	4/305 (1,3)	2,48 [0,79; 7,83] 0,1206[2]	2,53 [0,79; 8,17] 0,1074[3]	1,9 [-0,4; 4,3] 0,1074[3]
Tumor stage (Interaction p-value: 0,9397)					
IIA	1/113 (0,9)	1/114 (0,9)	1,01 [0,06; 15,93] 0,9950[2]	1,01 [0,06; 16,33] 1,0000[4]	0,0 [-2,4; 2,4] 1,0000[4]
IIB	4/151 (2,6)	1/136 (0,7)	3,60 [0,41; 31,84] 0,2490[2]	3,67 [0,41; 33,28] 0,3741[4]	1,9 [-1,0; 4,9] 0,3741[4]
IIIA	12/495 (2,4)	0/488 (0,0)	24,65 [1,46; 415,13] 0,0261[2]	25,26 [1,49; 427,80] 0,0005[3]	2,4 [1,1; 3,8] 0,0005[3]
IIIB	3/54 (5,6)	0/45 (0,0)	5,85 [0,31; 110,43] 0,2383[2]	6,18 [0,31; 122,97] 0,2486[4]	5,6 [-0,6; 11,7] 0,2486[4]
IIIC	15/468 (3,2)	4/480 (0,8)	3,85 [1,29; 11,50] 0,0160[2]	3,94 [1,30; 11,96] 0,0092[3]	2,4 [0,6; 4,2] 0,0092[3]
Tumor grade (Interaction p-value: 0,9346)					
G1	1/91 (1,1)	0/93 (0,0)	3,07 [0,13; 74,28] 0,4910[2]	3,10 [0,12; 77,08] 0,4946[4]	1,1 [-1,0; 3,2] 0,4946[4]
G2	17/612 (2,8)	4/603 (0,7)	4,19 [1,42; 12,37] 0,0096[2]	4,28 [1,43; 12,79] 0,0047[3]	2,1 [0,7; 3,6] 0,0047[3]
G3	16/527 (3,0)	2/506 (0,4)	7,68 [1,78; 33,24] 0,0064[2]	7,89 [1,80; 34,49] 0,0012[3]	2,6 [1,1; 4,2] 0,0012[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,4403)					
Negative	4/156 (2,6)	2/169 (1,2)	2,17 [0,40; 11,66] 0,3680[2]	2,20 [0,40; 12,17] 0,4323[4]	1,4 [-1,6; 4,3] 0,4323[4]
Positive	31/1089 (2,8)	4/1067 (0,4)	7,59 [2,69; 21,44] 0,0001[2]	7,79 [2,74; 22,14] <,0001[3]	2,5 [1,4; 3,5] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,6527)					
White	22/958 (2,3)	3/944 (0,3)	7,23 [2,17; 24,06] 0,0013[2]	7,37 [2,20; 24,72] 0,0002[3]	2,0 [1,0; 3,0] 0,0002[3]
Asian	11/250 (4,4)	2/242 (0,8)	5,32 [1,19; 23,77] 0,0285[2]	5,52 [1,21; 25,18] 0,0135[3]	3,6 [0,8; 6,4] 0,0135[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Other	2/62 (3,2)	1/64 (1,6)	2,06 [0,19; 22,19] 0,5497[2]	2,10 [0,19; 23,77] 0,6160[4]	1,7 [-3,7; 7,0] 0,6160[4]
ECOG-PS (Interaction p-value: 0,9736)					
ECOG-PS 0	31/1070 (2,9)	6/1020 (0,6)	4,93 [2,06; 11,76] 0,0003[2]	5,04 [2,09; 12,14] <,0001[3]	2,3 [1,2; 3,4] <,0001[3]
ECOG-PS 1	4/213 (1,9)	0/245 (0,0)	10,35 [0,56; 191,06] 0,1163[2]	10,55 [0,56; 197,03] 0,0461[4]	1,9 [0,1; 3,7] 0,0461[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Anaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7391)					
< 65 years	17/918 (1,9)	2/937 (0,2)	8,68 [2,01; 37,45] 0,0038[2]	8,82 [2,03; 38,29] 0,0005[3]	1,6 [0,7; 2,6] 0,0005[3]
≥ 65 years	21/365 (5,8)	3/328 (0,9)	6,29 [1,89; 20,90] 0,0027[2]	6,61 [1,95; 22,38] 0,0005[3]	4,8 [2,2; 7,4] 0,0005[3]
Prior treatment (Interaction p-value: 0,8958)					
Neoadjuvant chemotherapy	11/430 (2,6)	1/415 (0,2)	10,62 [1,38; 81,86] 0,0234[2]	10,87 [1,40; 84,56] 0,0044[3]	2,3 [0,8; 3,9] 0,0044[3]
Adjuvant chemotherapy	25/784 (3,2)	4/769 (0,5)	6,13 [2,14; 17,53] 0,0007[2]	6,30 [2,18; 18,19] 0,0001[3]	2,7 [1,3; 4,0] 0,0001[3]
No chemotherapy	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (Interaction p-value: 0,6800)					
North America / Europe	20/678 (2,9)	4/650 (0,6)	4,79 [1,65; 13,95] 0,0040[2]	4,91 [1,67; 14,44] 0,0014[3]	2,3 [0,9; 3,7] 0,0014[3]
Asia	5/203 (2,5)	0/201 (0,0)	10,89 [0,61; 195,70] 0,1052[2]	11,17 [0,61; 203,28] 0,0610[4]	2,5 [0,3; 4,6] 0,0610[4]
Other	13/402 (3,2)	1/414 (0,2)	13,39 [1,76; 101,87] 0,0122[2]	13,80 [1,80; 106,00] 0,0010[3]	3,0 [1,2; 4,8] 0,0010[3]
Primary tumor size (Interaction p-value: 0,9159)					
< 20 mm	9/331 (2,7)	1/335 (0,3)	9,11 [1,16; 71,50] 0,0356[2]	9,34 [1,18; 74,10] 0,0108[4]	2,4 [0,6; 4,3] 0,0108[4]
≥ 20 but < 50 mm	22/646 (3,4)	4/653 (0,6)	5,56 [1,93; 16,04] 0,0015[2]	5,72 [1,96; 16,69] 0,0003[3]	2,8 [1,3; 4,3] 0,0003[3]
≥ 50 mm	7/289 (2,4)	0/265 (0,0)	13,76 [0,79; 239,74] 0,0722[2]	14,10 [0,80; 248,04] 0,0156[4]	2,4 [0,6; 4,2] 0,0156[4]
Number of positive lymph nodes (Interaction p-value: 0,6517)					
0-3	8/427 (1,9)	1/418 (0,2)	7,83 [0,98; 62,34] 0,0518[2]	7,96 [0,99; 63,94] 0,0382[4]	1,6 [0,3; 3,0] 0,0382[4]
4-9	15/549 (2,7)	3/542 (0,6)	4,94 [1,44; 16,95] 0,0112[2]	5,05 [1,45; 17,53] 0,0047[3]	2,2 [0,7; 3,7] 0,0047[3]
≥ 10	15/307 (4,9)	1/305 (0,3)	14,90 [1,98; 112,12] 0,0087[2]	15,62 [2,05; 118,98] 0,0004[3]	4,6 [2,1; 7,1] 0,0004[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9915)					
IIA	1/113 (0,9)	0/114 (0,0)	3,03 [0,12; 73,51] 0,4963[2]	3,05 [0,12; 75,75] 0,4978[4]	0,9 [-0,8; 2,6] 0,4978[4]
IIB	5/151 (3,3)	0/136 (0,0)	9,91 [0,55; 177,65] 0,1192[2]	10,25 [0,56; 187,10] 0,0620[4]	3,3 [0,5; 6,2] 0,0620[4]
IIIA	15/495 (3,0)	3/488 (0,6)	4,93 [1,44; 16,92] 0,0112[2]	5,05 [1,45; 17,56] 0,0047[3]	2,4 [0,8; 4,1] 0,0047[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	16/468 (3,4)	2/480 (0,4)	8,21 [1,90; 35,49] 0,0048[2]	8,46 [1,93; 37,00] 0,0007[3]	3,0 [1,3; 4,7] 0,0007[3]
Tumor grade (Interaction p-value: 0,9559)					
G1	3/91 (3,3)	0/93 (0,0)	7,15 [0,37; 136,54] 0,1910[2]	7,40 [0,38; 145,22] 0,1189[4]	3,3 [-0,4; 7,0] 0,1189[4]
G2	23/612 (3,8)	3/603 (0,5)	7,55 [2,28; 25,03] 0,0009[2]	7,81 [2,33; 26,15] <,0001[3]	3,3 [1,7; 4,9] <,0001[3]
G3	9/527 (1,7)	2/506 (0,4)	4,32 [0,94; 19,90] 0,0604[2]	4,38 [0,94; 20,36] 0,0399[3]	1,3 [0,1; 2,5] 0,0399[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,6514)					
Negative	3/156 (1,9)	2/169 (1,2)	1,63 [0,28; 9,60] 0,5921[2]	1,64 [0,27; 9,93] 0,6739[4]	0,7 [-2,0; 3,4] 0,6739[4]
Positive	35/1089 (3,2)	3/1067 (0,3)	11,43 [3,53; 37,05] <,0001[2]	11,78 [3,61; 38,41] <,0001[3]	2,9 [1,8; 4,0] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9997)					
White	25/958 (2,6)	5/944 (0,5)	4,93 [1,89; 12,82] 0,0011[2]	5,03 [1,92; 13,20] 0,0003[3]	2,1 [1,0; 3,2] 0,0003[3]
Asian	9/250 (3,6)	0/242 (0,0)	18,39 [1,08; 314,31] 0,0443[2]	19,08 [1,10; 329,63] 0,0037[4]	3,6 [1,3; 5,9] 0,0037[4]
Other	4/62 (6,5)	0/64 (0,0)	9,29 [0,51; 168,95] 0,1322[2]	9,92 [0,52; 188,28] 0,0557[4]	6,5 [0,3; 12,6] 0,0557[4]
ECOG-PS (Interaction p-value: 0,9709)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	25/1070 (2,3)	5/1020 (0,5)	4,77 [1,83; 12,40] 0,0014[2]	4,86 [1,85; 12,74] 0,0004[3]	1,8 [0,8; 2,8] 0,0004[3]
ECOG-PS 1	13/213 (6,1)	0/245 (0,0)	31,04 [1,86; 519,00] 0,0168[2]	33,06 [1,95; 559,56] <,0001[3]	6,1 [2,9; 9,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Aspartate aminotransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8660)					
< 65 years	15/918 (1,6)	3/937 (0,3)	5,10 [1,48; 17,57] 0,0098[2]	5,17 [1,49; 17,92] 0,0039[3]	1,3 [0,4; 2,2] 0,0039[3]
≥ 65 years	7/365 (1,9)	1/328 (0,3)	6,29 [0,78; 50,86] 0,0846[2]	6,39 [0,78; 52,25] 0,0718[4]	1,6 [0,1; 3,1] 0,0718[4]
Prior treatment (Interaction p-value: 0,2497)					
Neoadjuvant chemotherapy	15/430 (3,5)	1/415 (0,2)	14,48 [1,92; 109,10] 0,0095[2]	14,96 [1,97; 113,80] 0,0005[3]	3,2 [1,5; 5,0] 0,0005[3]
Adjuvant chemotherapy	3/784 (0,4)	2/769 (0,3)	1,47 [0,25; 8,78] 0,6718[2]	1,47 [0,25; 8,84] 1,0000[4]	0,1 [-0,4; 0,7] 1,0000[4]
No chemotherapy	4/69 (5,8)	1/81 (1,2)	4,70 [0,54; 41,03] 0,1620[2]	4,92 [0,54; 45,13] 0,1807[4]	4,6 [-1,5; 10,6] 0,1807[4]
Region (Interaction p-value: 0,8121)					
North America / Europe	6/678 (0,9)	0/650 (0,0)	12,46 [0,70; 220,80] 0,0854[2]	12,57 [0,71; 223,66] 0,0311[4]	0,9 [0,2; 1,6] 0,0311[4]
Asia	7/203 (3,4)	1/201 (0,5)	6,93 [0,86; 55,82] 0,0689[2]	7,14 [0,87; 58,59] 0,0676[4]	3,0 [0,3; 5,6] 0,0676[4]
Other	9/402 (2,2)	3/414 (0,7)	3,09 [0,84; 11,33] 0,0889[2]	3,14 [0,84; 11,67] 0,0724[3]	1,5 [-0,1; 3,2] 0,0724[3]
Primary tumor size (Interaction p-value: 0,9031)					
< 20 mm	7/331 (2,1)	1/335 (0,3)	7,08 [0,88; 57,27] 0,0663[2]	7,22 [0,88; 58,98] 0,0370[4]	1,8 [0,2; 3,5] 0,0370[4]
≥ 20 but < 50 mm	12/646 (1,9)	3/653 (0,5)	4,04 [1,15; 14,26] 0,0298[2]	4,10 [1,15; 14,60] 0,0184[3]	1,4 [0,2; 2,6] 0,0184[3]
≥ 50 mm	3/289 (1,0)	0/265 (0,0)	6,42 [0,33; 123,72] 0,2180[2]	6,49 [0,33; 126,18] 0,2501[4]	1,0 [-0,1; 2,2] 0,2501[4]
Number of positive lymph nodes (Interaction p-value: 0,7711)					
0-3	9/427 (2,1)	1/418 (0,2)	8,81 [1,12; 69,23] 0,0386[2]	8,98 [1,13; 71,18] 0,0208[4]	1,9 [0,4; 3,3] 0,0208[4]
4-9	6/549 (1,1)	1/542 (0,2)	5,92 [0,72; 49,04] 0,0990[2]	5,98 [0,72; 49,82] 0,1238[4]	0,9 [-0,0; 1,9] 0,1238[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	7/307 (2,3)	2/305 (0,7)	3,48 [0,73; 16,60] 0,1182[2]	3,54 [0,73; 17,15] 0,1765[4]	1,6 [-0,3; 3,5] 0,1765[4]
Tumor stage (Interaction p-value: 0,9710)					
IIA	2/113 (1,8)	1/114 (0,9)	2,02 [0,19; 21,94] 0,5642[2]	2,04 [0,18; 22,78] 0,6217[4]	0,9 [-2,1; 3,9] 0,6217[4]
IIB	3/151 (2,0)	0/136 (0,0)	6,31 [0,33; 121,05] 0,2217[2]	6,43 [0,33; 125,70] 0,2494[4]	2,0 [-0,2; 4,2] 0,2494[4]
IIIA	6/495 (1,2)	1/488 (0,2)	5,92 [0,71; 48,95] 0,0992[2]	5,98 [0,72; 49,82] 0,1237[4]	1,0 [-0,0; 2,1] 0,1237[4]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	10/468 (2,1)	2/480 (0,4)	5,13 [1,13; 23,28] 0,0342[2]	5,22 [1,14; 23,95] 0,0179[3]	1,7 [0,3; 3,2] 0,0179[3]
Tumor grade (Interaction p-value: 0,7857)					
G1	1/91 (1,1)	0/93 (0,0)	3,07 [0,13; 74,28] 0,4910[2]	3,10 [0,12; 77,08] 0,4946[4]	1,1 [-1,0; 3,2] 0,4946[4]
G2	9/612 (1,5)	3/603 (0,5)	2,96 [0,80; 10,87] 0,1027[2]	2,99 [0,80; 11,08] 0,0864[3]	1,0 [-0,1; 2,1] 0,0864[3]
G3	11/527 (2,1)	1/506 (0,2)	10,56 [1,37; 81,51] 0,0238[2]	10,77 [1,38; 83,69] 0,0046[3]	1,9 [0,6; 3,2] 0,0046[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,3666)					
Negative	3/156 (1,9)	1/169 (0,6)	3,25 [0,34; 30,92] 0,3051[2]	3,29 [0,34; 32,00] 0,3537[4]	1,3 [-1,1; 3,8] 0,3537[4]
Positive	19/1089 (1,7)	3/1067 (0,3)	6,21 [1,84; 20,91] 0,0032[2]	6,30 [1,86; 21,34] 0,0007[3]	1,5 [0,6; 2,3] 0,0007[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,1049)					
White	14/958 (1,5)	1/944 (0,1)	13,80 [1,82; 104,70] 0,0112[2]	13,99 [1,84; 106,57] 0,0008[3]	1,4 [0,6; 2,1] 0,0008[3]
Asian	7/250 (2,8)	1/242 (0,4)	6,78 [0,84; 54,66] 0,0725[2]	6,94 [0,85; 56,85] 0,0684[4]	2,4 [0,2; 4,6] 0,0684[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Other	1/62 (1,6)	2/64 (3,1)	0,52 [0,05; 5,55] 0,5852[2]	0,51 [0,04; 5,75] 1,0000[4]	-1,5 [-6,8; 3,8] 1,0000[4]
ECOG-PS (Interaction p-value: 0,6687)					
ECOG-PS 0	19/1070 (1,8)	3/1020 (0,3)	6,04 [1,79; 20,34] 0,0037[2]	6,13 [1,81; 20,77] 0,0009[3]	1,5 [0,6; 2,3] 0,0009[3]
ECOG-PS 1	3/213 (1,4)	1/245 (0,4)	3,45 [0,36; 32,93] 0,2818[2]	3,49 [0,36; 33,76] 0,3420[4]	1,0 [-0,8; 2,8] 0,3420[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Diarrhoea from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,6734)					
< 65 years	77/918 (8,4)	1/937 (0,1)	78,59 [10,95; 563,88] <,0001[2]	85,70 [11,89; 617,50] <,0001[3]	8,3 [6,5; 10,1] <,0001[3]
≥ 65 years	48/365 (13,2)	1/328 (0,3)	43,13 [5,99; 310,74] 0,0002[2]	49,51 [6,79; 360,88] <,0001[3]	12,8 [9,3; 16,4] <,0001[3]
Prior treatment (Interaction p-value: 0,9540)					
Neoadjuvant chemotherapy	48/430 (11,2)	1/415 (0,2)	46,33 [6,42; 334,08] 0,0001[2]	52,02 [7,15; 378,72] <,0001[3]	10,9 [7,9; 13,9] <,0001[3]
Adjuvant chemotherapy	73/784 (9,3)	1/769 (0,1)	71,60 [9,98; 513,87] <,0001[2]	78,85 [10,93; 568,81] <,0001[3]	9,2 [7,1; 11,2] <,0001[3]
No chemotherapy	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (Interaction p-value: 0,9994)					
North America / Europe	67/678 (9,9)	2/650 (0,3)	32,12 [7,90; 130,54] <,0001[2]	35,53 [8,67; 145,64] <,0001[3]	9,6 [7,3; 11,9] <,0001[3]
Asia	13/203 (6,4)	0/201 (0,0)	26,74 [1,60; 446,72] 0,0222[2]	28,56 [1,69; 483,76] 0,0003[3]	6,4 [3,0; 9,8] 0,0003[3]
Other	45/402 (11,2)	0/414 (0,0)	93,71 [5,79; 1515,99] 0,0014[2]	105,51 [6,48; 1718,80] <,0001[3]	11,2 [8,1; 14,3] <,0001[3]
Primary tumor size (Interaction p-value: 0,7882)					
< 20 mm	27/331 (8,2)	0/335 (0,0)	55,66 [3,41; 908,76] 0,0048[2]	60,60 [3,68; 997,72] <,0001[3]	8,2 [5,2; 11,1] <,0001[3]
≥ 20 but < 50 mm	68/646 (10,5)	1/653 (0,2)	68,74 [9,57; 493,54] <,0001[2]	76,71 [10,62; 554,17] <,0001[3]	10,4 [8,0; 12,8] <,0001[3]
≥ 50 mm	28/289 (9,7)	1/265 (0,4)	25,67 [3,52; 187,39] 0,0014[2]	28,32 [3,83; 209,69] <,0001[3]	9,3 [5,8; 12,8] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9946)					
0-3	51/427 (11,9)	1/418 (0,2)	49,93 [6,93; 359,61] 0,0001[2]	56,56 [7,78; 411,30] <,0001[3]	11,7 [8,6; 14,8] <,0001[3]
4-9	44/549 (8,0)	1/542 (0,2)	43,44 [6,01; 314,16] 0,0002[2]	47,14 [6,47; 343,39] <,0001[3]	7,8 [5,5; 10,1] <,0001[3]
≥ 10	30/307 (9,8)	0/305 (0,0)	60,60 [3,72; 986,65] 0,0039[2]	67,15 [4,09; 1103,41] <,0001[3]	9,8 [6,5; 13,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9968)					
IIA	11/113 (9,7)	0/114 (0,0)	23,20 [1,38; 389,08] 0,0288[2]	25,69 [1,50; 441,49] 0,0006[3]	9,7 [4,3; 15,2] 0,0006[3]
IIB	16/151 (10,6)	0/136 (0,0)	29,74 [1,80; 491,08] 0,0177[2]	33,24 [1,97; 559,68] <,0001[3]	10,6 [5,7; 15,5] <,0001[3]
IIIA	35/495 (7,1)	1/488 (0,2)	34,51 [4,75; 250,87] 0,0005[2]	37,05 [5,06; 271,57] <,0001[3]	6,9 [4,6; 9,2] <,0001[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	60/468 (12,8)	1/480 (0,2)	61,54 [8,56; 442,21] <,0001[2]	70,44 [9,72; 510,51] <,0001[3]	12,6 [9,6; 15,7] <,0001[3]
Race (Interaction p-value: 0,9998)					
White	103/958 (10,8)	2/944 (0,2)	50,75 [12,56; 205,05] <,0001[2]	56,74 [13,96; 230,64] <,0001[3]	10,5 [8,6; 12,5] <,0001[3]
Asian	14/250 (5,6)	0/242 (0,0)	28,08 [1,68; 468,05] 0,0202[2]	29,74 [1,76; 501,31] 0,0002[3]	5,6 [2,7; 8,5] 0,0002[3]
Other	6/62 (9,7)	0/64 (0,0)	13,41 [0,77; 233,15] 0,0748[2]	14,84 [0,82; 269,32] 0,0125[4]	9,7 [2,3; 17,0] 0,0125[4]
ECOG-PS (Interaction p-value: 0,9752)					
ECOG-PS 0	105/1070 (9,8)	2/1020 (0,2)	50,05 [12,39; 202,22] <,0001[2]	55,38 [13,63; 225,00] <,0001[3]	9,6 [7,8; 11,4] <,0001[3]
ECOG-PS 1	20/213 (9,4)	0/245 (0,0)	47,13 [2,87; 774,60] 0,0070[2]	52,02 [3,13; 865,51] <,0001[3]	9,4 [5,5; 13,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Tabl: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Fatigue from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9301)					
< 65 years	17/918 (1,9)	1/937 (0,1)	17,35 [2,31; 130,12] 0,0055[2]	17,66 [2,35; 132,98] 0,0001[3]	1,7 [0,8; 2,6] 0,0001[3]
≥ 65 years	17/365 (4,7)	1/328 (0,3)	15,28 [2,04; 114,16] 0,0079[2]	15,97 [2,11; 120,71] 0,0003[3]	4,4 [2,1; 6,6] 0,0003[3]
Prior treatment (Interaction p-value: 0,8086)					
Neoadjuvant chemotherapy	9/430 (2,1)	1/415 (0,2)	8,69 [1,11; 68,26] 0,0399[2]	8,85 [1,12; 70,17] 0,0210[4]	1,9 [0,4; 3,3] 0,0210[4]
Adjuvant chemotherapy	23/784 (2,9)	1/769 (0,1)	22,56 [3,05; 166,64] 0,0023[2]	23,21 [3,13; 172,31] <,0001[3]	2,8 [1,6; 4,0] <,0001[3]
No chemotherapy	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (Interaction p-value: 0,9995)					
North America / Europe	23/678 (3,4)	2/650 (0,3)	11,03 [2,61; 46,58] 0,0011[2]	11,38 [2,67; 48,45] <,0001[3]	3,1 [1,7; 4,5] <,0001[3]
Asia	1/203 (0,5)	0/201 (0,0)	2,97 [0,12; 72,49] 0,5042[2]	2,99 [0,12; 73,71] 1,0000[4]	0,5 [-0,5; 1,5] 1,0000[4]
Other	10/402 (2,5)	0/414 (0,0)	21,63 [1,27; 367,82] 0,0335[2]	22,18 [1,30; 379,73] 0,0008[4]	2,5 [1,0; 4,0] 0,0008[4]
Primary tumor size (Interaction p-value: 0,9993)					
< 20 mm	8/331 (2,4)	0/335 (0,0)	17,20 [1,00; 296,88] 0,0502[2]	17,63 [1,01; 306,71] 0,0036[4]	2,4 [0,8; 4,1] 0,0036[4]
≥ 20 but < 50 mm	15/646 (2,3)	2/653 (0,3)	7,58 [1,74; 33,02] 0,0070[2]	7,74 [1,76; 33,97] 0,0014[3]	2,0 [0,8; 3,3] 0,0014[3]
≥ 50 mm	11/289 (3,8)	0/265 (0,0)	21,10 [1,25; 356,25] 0,0345[2]	21,93 [1,29; 373,94] 0,0013[3]	3,8 [1,6; 6,0] 0,0013[3]
Number of positive lymph nodes (Interaction p-value: 0,9979)					
0-3	12/427 (2,8)	1/418 (0,2)	11,75 [1,53; 89,94] 0,0177[2]	12,06 [1,56; 93,15] 0,0024[3]	2,6 [0,9; 4,2] 0,0024[3]
4-9	11/549 (2,0)	1/542 (0,2)	10,86 [1,41; 83,83] 0,0222[2]	11,06 [1,42; 85,97] 0,0040[3]	1,8 [0,6; 3,0] 0,0040[3]
≥ 10	11/307 (3,6)	0/305 (0,0)	22,85 [1,35; 386,06] 0,0301[2]	23,70 [1,39; 403,96] 0,0009[3]	3,6 [1,5; 5,7] 0,0009[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9981)					
IIA	4/113 (3,5)	0/114 (0,0)	9,08 [0,49; 166,70] 0,1374[2]	9,41 [0,50; 176,86] 0,0598[4]	3,5 [0,1; 6,9] 0,0598[4]
IIB	5/151 (3,3)	0/136 (0,0)	9,91 [0,55; 177,65] 0,1192[2]	10,25 [0,56; 187,10] 0,0620[4]	3,3 [0,5; 6,2] 0,0620[4]
IIIA	11/495 (2,2)	1/488 (0,2)	10,84 [1,41; 83,68] 0,0222[2]	11,07 [1,42; 86,06] 0,0040[3]	2,0 [0,7; 3,4] 0,0040[3]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	14/468 (3,0)	1/480 (0,2)	14,36 [1,90; 108,76] 0,0099[2]	14,77 [1,93; 112,78] 0,0006[3]	2,8 [1,2; 4,4] 0,0006[3]
Tumor grade (Interaction p-value: 1,0000)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	14/612 (2,3)	0/603 (0,0)	28,57 [1,71; 477,93] 0,0197[2]	29,24 [1,74; 491,31] 0,0002[3]	2,3 [1,1; 3,5] 0,0002[3]
G3	17/527 (3,2)	2/506 (0,4)	8,16 [1,90; 35,14] 0,0048[2]	8,40 [1,93; 36,55] 0,0007[3]	2,8 [1,2; 4,4] 0,0007[3]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,9606)					
Negative	5/156 (3,2)	0/169 (0,0)	11,91 [0,66; 213,66] 0,0926[2]	12,31 [0,67; 224,42] 0,0246[4]	3,2 [0,4; 6,0] 0,0246[4]
Positive	29/1089 (2,7)	2/1067 (0,2)	14,21 [3,40; 59,39] 0,0003[2]	14,57 [3,47; 61,21] <,0001[3]	2,5 [1,5; 3,5] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9864)					
White	32/958 (3,3)	2/944 (0,2)	15,77 [3,79; 65,60] 0,0001[2]	16,28 [3,89; 68,11] <,0001[3]	3,1 [2,0; 4,3] <,0001[3]
Asian	1/250 (0,4)	0/242 (0,0)	2,90 [0,12; 70,95] 0,5132[2]	2,92 [0,12; 71,93] 1,0000[4]	0,4 [-0,4; 1,2] 1,0000[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
ECOG-PS (Interaction p-value: 0,9742)					
ECOG-PS 0	26/1070 (2,4)	2/1020 (0,2)	12,39 [2,95; 52,08] 0,0006[2]	12,68 [3,00; 53,55] <,0001[3]	2,2 [1,3; 3,2] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	8/213 (3,8)	0/245 (0,0)	19,54 [1,13; 336,58] 0,0407[2]	20,31 [1,17; 353,98] 0,0020[4]	3,8 [1,2; 6,3] 0,0020[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Gamma-glutamyltransferase increased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,8567)					
Neoadjuvant chemotherapy	6/430 (1,4)	1/415 (0,2)	5,79 [0,70; 47,89] 0,1033[2]	5,86 [0,70; 48,87] 0,1239[4]	1,2 [-0,1; 2,4] 0,1239[4]
Adjuvant chemotherapy	12/784 (1,5)	3/769 (0,4)	3,92 [1,11; 13,85] 0,0336[2]	3,97 [1,12; 14,12] 0,0216[3]	1,1 [0,2; 2,1] 0,0216[3]
No chemotherapy	2/69 (2,9)	1/81 (1,2)	2,35 [0,22; 25,34] 0,4819[2]	2,39 [0,21; 26,92] 0,5945[4]	1,7 [-3,0; 6,3] 0,5945[4]
Region (Interaction p-value: 0,9490)					
North America / Europe	8/678 (1,2)	2/650 (0,3)	3,83 [0,82; 17,99] 0,0883[2]	3,87 [0,82; 18,29] 0,1088[4]	0,9 [-0,0; 1,8] 0,1088[4]
Asia	4/203 (2,0)	0/201 (0,0)	8,91 [0,48; 164,45] 0,1414[2]	9,09 [0,49; 169,95] 0,1232[4]	2,0 [0,1; 3,9] 0,1232[4]
Other	8/402 (2,0)	3/414 (0,7)	2,75 [0,73; 10,28] 0,1335[2]	2,78 [0,73; 10,56] 0,1171[3]	1,3 [-0,3; 2,9] 0,1171[3]
Primary tumor size (Interaction p-value: 0,0941)					
< 20 mm	2/331 (0,6)	3/335 (0,9)	0,67 [0,11; 4,01] 0,6653[2]	0,67 [0,11; 4,05] 1,0000[4]	-0,3 [-1,6; 1,0] 1,0000[4]
≥ 20 but < 50 mm	13/646 (2,0)	1/653 (0,2)	13,14 [1,72; 100,16] 0,0129[2]	13,39 [1,75; 102,66] 0,0012[3]	1,9 [0,7; 3,0] 0,0012[3]
≥ 50 mm	4/289 (1,4)	1/265 (0,4)	3,67 [0,41; 32,61] 0,2437[2]	3,71 [0,41; 33,36] 0,3751[4]	1,0 [-0,5; 2,5] 0,3751[4]
Number of positive lymph nodes (Interaction p-value: 0,2469)					
0-3	7/427 (1,6)	1/418 (0,2)	6,85 [0,85; 55,45] 0,0712[2]	6,95 [0,85; 56,74] 0,0691[4]	1,4 [0,1; 2,7] 0,0691[4]
4-9	9/549 (1,6)	1/542 (0,2)	8,89 [1,13; 69,89] 0,0379[2]	9,02 [1,14; 71,41] 0,0209[4]	1,5 [0,3; 2,6] 0,0209[4]
≥ 10	4/307 (1,3)	3/305 (1,0)	1,32 [0,30; 5,87] 0,7112[2]	1,33 [0,29; 5,99] 1,0000[4]	0,3 [-1,4; 2,0] 1,0000[4]
Tumor grade (Interaction p-value: 0,8954)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
G2	9/612 (1,5)	4/603 (0,7)	2,22 [0,69; 7,16] 0,1832[2]	2,24 [0,68; 7,30] 0,1715[3]	0,8 [-0,3; 2,0] 0,1715[3]
G3	6/527 (1,1)	1/506 (0,2)	5,76 [0,70; 47,68] 0,1044[2]	5,82 [0,70; 48,48] 0,1243[4]	0,9 [-0,0; 1,9] 0,1243[4]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,9644)					
Negative	2/156 (1,3)	0/169 (0,0)	5,41 [0,26; 111,90] 0,2744[2]	5,49 [0,26; 115,15] 0,2296[4]	1,3 [-0,5; 3,0] 0,2296[4]
Positive	18/1089 (1,7)	5/1067 (0,5)	3,53 [1,31; 9,47] 0,0123[2]	3,57 [1,32; 9,65] 0,0074[3]	1,2 [0,3; 2,0] 0,0074[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9285)					
White	14/958 (1,5)	4/944 (0,4)	3,45 [1,14; 10,44] 0,0285[2]	3,49 [1,14; 10,63] 0,0194[3]	1,0 [0,2; 1,9] 0,0194[3]
Asian	4/250 (1,6)	0/242 (0,0)	8,71 [0,47; 160,97] 0,1457[2]	8,85 [0,47; 165,34] 0,1237[4]	1,6 [0,0; 3,2] 0,1237[4]
Other	2/62 (3,2)	1/64 (1,6)	2,06 [0,19; 22,19] 0,5497[2]	2,10 [0,19; 23,77] 0,6160[4]	1,7 [-3,7; 7,0] 0,6160[4]
ECOG-PS (Interaction p-value: 0,8802)					
ECOG-PS 0	16/1070 (1,5)	4/1020 (0,4)	3,81 [1,28; 11,37] 0,0163[2]	3,86 [1,28; 11,57] 0,0096[3]	1,1 [0,3; 1,9] 0,0096[3]
ECOG-PS 1	4/213 (1,9)	1/245 (0,4)	4,60 [0,52; 40,85] 0,1707[2]	4,67 [0,52; 42,11] 0,1885[4]	1,5 [-0,5; 3,5] 0,1885[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Hypokalaemia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9572)					
< 65 years	10/918 (1,1)	3/937 (0,3)	3,40 [0,94; 12,32] 0,0622[2]	3,43 [0,94; 12,50] 0,0471[3]	0,8 [0,0; 1,5] 0,0471[3]
≥ 65 years	8/365 (2,2)	2/328 (0,6)	3,59 [0,77; 16,81] 0,1040[2]	3,65 [0,77; 17,33] 0,1119[4]	1,6 [-0,1; 3,3] 0,1119[4]
Prior treatment (Interaction p-value: 0,6716)					
Neoadjuvant chemotherapy	6/430 (1,4)	3/415 (0,7)	1,93 [0,49; 7,67] 0,3501[2]	1,94 [0,48; 7,82] 0,5061[4]	0,7 [-0,7; 2,0] 0,5061[4]
Adjuvant chemotherapy	10/784 (1,3)	2/769 (0,3)	4,90 [1,08; 22,31] 0,0397[2]	4,95 [1,08; 22,69] 0,0223[3]	1,0 [0,2; 1,9] 0,0223[3]
No chemotherapy	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (Interaction p-value: 0,5783)					
North America / Europe	11/678 (1,6)	2/650 (0,3)	5,27 [1,17; 23,70] 0,0301[2]	5,34 [1,18; 24,20] 0,0150[3]	1,3 [0,3; 2,4] 0,0150[3]
Asia	4/203 (2,0)	1/201 (0,5)	3,96 [0,45; 35,13] 0,2165[2]	4,02 [0,45; 36,28] 0,3719[4]	1,5 [-0,7; 3,6] 0,3719[4]
Other	3/402 (0,7)	2/414 (0,5)	1,54 [0,26; 9,20] 0,6328[2]	1,55 [0,26; 9,32] 0,6822[4]	0,3 [-0,8; 1,3] 0,6822[4]
Primary tumor size (Interaction p-value: 0,9874)					
< 20 mm	5/331 (1,5)	2/335 (0,6)	2,53 [0,49; 12,95] 0,2651[2]	2,55 [0,49; 13,26] 0,2839[4]	0,9 [-0,6; 2,5] 0,2839[4]
≥ 20 but < 50 mm	6/646 (0,9)	0/653 (0,0)	13,14 [0,74; 232,78] 0,0790[2]	13,26 [0,75; 235,93] 0,0150[4]	0,9 [0,2; 1,7] 0,0150[4]
≥ 50 mm	7/289 (2,4)	3/265 (1,1)	2,14 [0,56; 8,19] 0,2667[2]	2,17 [0,55; 8,47] 0,3440[4]	1,3 [-0,9; 3,5] 0,3440[4]
Number of positive lymph nodes (Interaction p-value: 0,3597)					
0-3	2/427 (0,5)	2/418 (0,5)	0,98 [0,14; 6,92] 0,9830[2]	0,98 [0,14; 6,98] 1,0000[4]	-0,0 [-0,9; 0,9] 1,0000[4]
4-9	11/549 (2,0)	2/542 (0,4)	5,43 [1,21; 24,38] 0,0273[2]	5,52 [1,22; 25,02] 0,0128[3]	1,6 [0,4; 2,9] 0,0128[3]
≥ 10	5/307 (1,6)	1/305 (0,3)	4,97 [0,58; 42,27] 0,1423[2]	5,03 [0,58; 43,34] 0,2165[4]	1,3 [-0,3; 2,9] 0,2165[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,8990)					
IIA	1/113 (0,9)	0/114 (0,0)	3,03 [0,12; 73,51] 0,4963[2]	3,05 [0,12; 75,75] 0,4978[4]	0,9 [-0,8; 2,6] 0,4978[4]
IIB	0/151 (0,0)	0/136 (0,0)	NE	NE	NE
IIIA	10/495 (2,0)	1/488 (0,2)	9,86 [1,27; 76,72] 0,0288[2]	10,04 [1,28; 78,74] 0,0068[3]	1,8 [0,5; 3,1] 0,0068[3]
IIIB	0/54 (0,0)	2/45 (4,4)	0,17 [0,01; 3,40] 0,2444[2]	0,16 [0,01; 3,41] 0,2041[4]	-4,4 [-10,5; 1,6] 0,2041[4]
IIIC	7/468 (1,5)	2/480 (0,4)	3,59 [0,75; 17,19] 0,1098[2]	3,63 [0,75; 17,56] 0,1037[4]	1,1 [-0,2; 2,3] 0,1037[4]
Tumor grade (Interaction p-value: 0,9069)					
G1	5/91 (5,5)	0/93 (0,0)	11,24 [0,63; 200,37] 0,0997[2]	11,89 [0,65; 218,22] 0,0280[4]	5,5 [0,8; 10,2] 0,0280[4]
G2	6/612 (1,0)	4/603 (0,7)	1,48 [0,42; 5,21] 0,5435[2]	1,48 [0,42; 5,28] 0,7530[4]	0,3 [-0,7; 1,3] 0,7530[4]
G3	4/527 (0,8)	1/506 (0,2)	3,84 [0,43; 34,24] 0,2280[2]	3,86 [0,43; 34,67] 0,3743[4]	0,6 [-0,3; 1,4] 0,3743[4]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,9576)					
Negative	1/156 (0,6)	1/169 (0,6)	1,08 [0,07; 17,17] 0,9547[2]	1,08 [0,07; 17,48] 1,0000[4]	0,0 [-1,7; 1,8] 1,0000[4]
Positive	17/1089 (1,6)	4/1067 (0,4)	4,16 [1,41; 12,33] 0,0100[2]	4,21 [1,41; 12,57] 0,0050[3]	1,2 [0,4; 2,0] 0,0050[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9882)					
White	13/958 (1,4)	4/944 (0,4)	3,20 [1,05; 9,79] 0,0411[2]	3,23 [1,05; 9,95] 0,0306[3]	0,9 [0,1; 1,8] 0,0306[3]
Asian	4/250 (1,6)	1/242 (0,4)	3,87 [0,44; 34,40] 0,2244[2]	3,92 [0,43; 35,31] 0,3728[4]	1,2 [-0,6; 2,9] 0,3728[4]
Other	1/62 (1,6)	0/64 (0,0)	3,10 [0,13; 74,56] 0,4864[2]	3,15 [0,13; 78,72] 0,4921[4]	1,6 [-1,5; 4,7] 0,4921[4]
ECOG-PS (Interaction p-value: 0,9780)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	15/1070 (1,4)	4/1020 (0,4)	3,57 [1,19; 10,73] 0,0232[2]	3,61 [1,19; 10,92] 0,0151[3]	1,0 [0,2; 1,8] 0,0151[3]
ECOG-PS 1	3/213 (1,4)	1/245 (0,4)	3,45 [0,36; 32,93] 0,2818[2]	3,49 [0,36; 33,76] 0,3420[4]	1,0 [-0,8; 2,8] 0,3420[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Leukopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5851)					
< 65 years	31/918 (3,4)	1/937 (0,1)	31,64 [4,33; 231,30] 0,0007[2]	32,71 [4,46; 240,13] <,0001[3]	3,3 [2,1; 4,5] <,0001[3]
≥ 65 years	16/365 (4,4)	1/328 (0,3)	14,38 [1,92; 107,82] 0,0095[2]	14,99 [1,98; 113,68] 0,0005[3]	4,1 [1,9; 6,3] 0,0005[3]
Prior treatment (Interaction p-value: 0,9717)					
Neoadjuvant chemotherapy	14/430 (3,3)	0/415 (0,0)	27,99 [1,68; 467,71] 0,0204[2]	28,93 [1,72; 486,56] 0,0002[3]	3,3 [1,6; 4,9] 0,0002[3]
Adjuvant chemotherapy	31/784 (4,0)	2/769 (0,3)	15,20 [3,65; 63,31] 0,0002[2]	15,79 [3,77; 66,20] <,0001[3]	3,7 [2,3; 5,1] <,0001[3]
No chemotherapy	2/69 (2,9)	0/81 (0,0)	5,86 [0,29; 119,97] 0,2512[2]	6,04 [0,28; 127,91] 0,2099[4]	2,9 [-1,1; 6,9] 0,2099[4]
Region (Interaction p-value: 0,9992)					
North America / Europe	20/678 (2,9)	0/650 (0,0)	39,31 [2,38; 648,59] 0,0103[2]	40,50 [2,44; 671,05] <,0001[3]	2,9 [1,7; 4,2] <,0001[3]
Asia	5/203 (2,5)	0/201 (0,0)	10,89 [0,61; 195,70] 0,1052[2]	11,17 [0,61; 203,28] 0,0610[4]	2,5 [0,3; 4,6] 0,0610[4]
Other	22/402 (5,5)	2/414 (0,5)	11,33 [2,68; 47,86] 0,0010[2]	11,93 [2,79; 51,06] <,0001[3]	5,0 [2,7; 7,3] <,0001[3]
Primary tumor size (Interaction p-value: 0,9996)					
< 20 mm	10/331 (3,0)	0/335 (0,0)	21,25 [1,25; 361,22] 0,0345[2]	21,91 [1,28; 375,52] 0,0009[4]	3,0 [1,2; 4,9] 0,0009[4]
≥ 20 but < 50 mm	25/646 (3,9)	2/653 (0,3)	12,64 [3,01; 53,13] 0,0005[2]	13,10 [3,09; 55,55] <,0001[3]	3,6 [2,0; 5,1] <,0001[3]
≥ 50 mm	11/289 (3,8)	0/265 (0,0)	21,10 [1,25; 356,25] 0,0345[2]	21,93 [1,29; 373,94] 0,0013[3]	3,8 [1,6; 6,0] 0,0013[3]
Number of positive lymph nodes (Interaction p-value: 0,9830)					
0-3	10/427 (2,3)	0/418 (0,0)	20,56 [1,21; 349,71] 0,0365[2]	21,05 [1,23; 360,39] 0,0019[4]	2,3 [0,9; 3,8] 0,0019[4]
4-9	21/549 (3,8)	1/542 (0,2)	20,73 [2,80; 153,59] 0,0030[2]	21,52 [2,88; 160,54] <,0001[3]	3,6 [2,0; 5,3] <,0001[3]
≥ 10	16/307 (5,2)	1/305 (0,3)	15,90 [2,12; 119,12] 0,0071[2]	16,71 [2,20; 126,84] 0,0002[3]	4,9 [2,3; 7,5] 0,0002[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,9999)					
IIA	3/113 (2,7)	0/114 (0,0)	7,06 [0,37; 135,16] 0,1943[2]	7,25 [0,37; 142,05] 0,1217[4]	2,7 [-0,3; 5,6] 0,1217[4]
IIB	5/151 (3,3)	0/136 (0,0)	9,91 [0,55; 177,65] 0,1192[2]	10,25 [0,56; 187,10] 0,0620[4]	3,3 [0,5; 6,2] 0,0620[4]
IIIA	19/495 (3,8)	1/488 (0,2)	18,73 [2,52; 139,38] 0,0042[2]	19,44 [2,59; 145,78] <,0001[3]	3,6 [1,9; 5,4] <,0001[3]
IIIB	0/54 (0,0)	0/45 (0,0)	NE	NE	NE
IIIC	20/468 (4,3)	1/480 (0,2)	20,51 [2,76; 152,23] 0,0031[2]	21,38 [2,86; 159,99] <,0001[3]	4,1 [2,2; 5,9] <,0001[3]
Tumor grade (Interaction p-value: 0,9991)					
G1	4/91 (4,4)	0/93 (0,0)	9,20 [0,50; 168,39] 0,1348[2]	9,62 [0,51; 181,24] 0,0578[4]	4,4 [0,2; 8,6] 0,0578[4]
G2	20/612 (3,3)	2/603 (0,3)	9,85 [2,31; 41,97] 0,0020[2]	10,15 [2,36; 43,63] 0,0001[3]	2,9 [1,5; 4,4] 0,0001[3]
G3	20/527 (3,8)	0/506 (0,0)	39,37 [2,39; 649,20] 0,0102[2]	40,92 [2,47; 678,38] <,0001[3]	3,8 [2,2; 5,4] <,0001[3]
GX	3/51 (5,9)	0/59 (0,0)	8,08 [0,43; 152,76] 0,1637[2]	8,59 [0,43; 170,32] 0,0965[4]	5,9 [-0,6; 12,3] 0,0965[4]
Progesterone receptor status (Interaction p-value: 0,9595)					
Negative	7/156 (4,5)	0/169 (0,0)	16,24 [0,94; 282,05] 0,0556[2]	17,01 [0,96; 300,29] 0,0055[4]	4,5 [1,2; 7,7] 0,0055[4]
Positive	40/1089 (3,7)	2/1067 (0,2)	19,60 [4,75; 80,88] <,0001[2]	20,31 [4,89; 84,23] <,0001[3]	3,5 [2,3; 4,6] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9997)					
White	37/958 (3,9)	2/944 (0,2)	18,23 [4,41; 75,42] <,0001[2]	18,92 [4,55; 78,73] <,0001[3]	3,7 [2,4; 4,9] <,0001[3]
Asian	6/250 (2,4)	0/242 (0,0)	12,59 [0,71; 222,20] 0,0838[2]	12,89 [0,72; 230,13] 0,0304[4]	2,4 [0,5; 4,3] 0,0304[4]
Other	4/62 (6,5)	0/64 (0,0)	9,29 [0,51; 168,95] 0,1322[2]	9,92 [0,52; 188,28] 0,0557[4]	6,5 [0,3; 12,6] 0,0557[4]
ECOG-PS (Interaction p-value: 0,5427)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	35/1070 (3,3)	1/1020 (0,1)	33,36 [4,58; 243,08] 0,0005[2]	34,46 [4,71; 252,00] <,0001[3]	3,2 [2,1; 4,3] <,0001[3]
ECOG-PS 1	12/213 (5,6)	1/245 (0,4)	13,80 [1,81; 105,28] 0,0113[2]	14,57 [1,88; 112,99] 0,0008[3]	5,2 [2,0; 8,4] 0,0008[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Lymphocyte count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,9109)					
< 65 years	25/918 (2,7)	3/937 (0,3)	8,51 [2,58; 28,07] 0,0004[2]	8,72 [2,62; 28,97] <,0001[3]	2,4 [1,3; 3,5] <,0001[3]
≥ 65 years	17/365 (4,7)	2/328 (0,6)	7,64 [1,78; 32,81] 0,0063[2]	7,96 [1,83; 34,73] 0,0011[3]	4,0 [1,7; 6,4] 0,0011[3]
Prior treatment (Interaction p-value: 0,8981)					
Neoadjuvant chemotherapy	18/430 (4,2)	4/415 (1,0)	4,34 [1,48; 12,72] 0,0074[2]	4,49 [1,51; 13,38] 0,0033[3]	3,2 [1,1; 5,3] 0,0033[3]
Adjuvant chemotherapy	22/784 (2,8)	0/769 (0,0)	44,14 [2,68; 726,36] 0,0080[2]	45,41 [2,75; 749,96] <,0001[3]	2,8 [1,7; 4,0] <,0001[3]
No chemotherapy	2/69 (2,9)	1/81 (1,2)	2,35 [0,22; 25,34] 0,4819[2]	2,39 [0,21; 26,92] 0,5945[4]	1,7 [-3,0; 6,3] 0,5945[4]
Region (Interaction p-value: 0,5944)					
North America / Europe	27/678 (4,0)	2/650 (0,3)	12,94 [3,09; 54,21] 0,0005[2]	13,44 [3,18; 56,74] <,0001[3]	3,7 [2,1; 5,2] <,0001[3]
Asia	9/203 (4,4)	2/201 (1,0)	4,46 [0,97; 20,37] 0,0540[2]	4,62 [0,98; 21,64] 0,0337[3]	3,4 [0,3; 6,6] 0,0337[3]
Other	6/402 (1,5)	1/414 (0,2)	6,18 [0,75; 51,10] 0,0911[2]	6,26 [0,75; 52,21] 0,0655[4]	1,3 [-0,0; 2,5] 0,0655[4]
Primary tumor size (Interaction p-value: 0,9875)					
< 20 mm	12/331 (3,6)	0/335 (0,0)	25,30 [1,50; 425,59] 0,0249[2]	26,25 [1,55; 445,23] 0,0004[3]	3,6 [1,6; 5,6] 0,0004[3]
≥ 20 but < 50 mm	15/646 (2,3)	2/653 (0,3)	7,58 [1,74; 33,02] 0,0070[2]	7,74 [1,76; 33,97] 0,0014[3]	2,0 [0,8; 3,3] 0,0014[3]
≥ 50 mm	14/289 (4,8)	2/265 (0,8)	6,42 [1,47; 27,98] 0,0133[2]	6,69 [1,51; 29,74] 0,0041[3]	4,1 [1,4; 6,8] 0,0041[3]
Number of positive lymph nodes (Interaction p-value: 0,8190)					
0-3	13/427 (3,0)	0/418 (0,0)	26,43 [1,58; 443,21] 0,0228[2]	27,26 [1,62; 460,07] 0,0003[3]	3,0 [1,4; 4,7] 0,0003[3]
4-9	13/549 (2,4)	3/542 (0,6)	4,28 [1,23; 14,93] 0,0226[2]	4,36 [1,23; 15,38] 0,0127[3]	1,8 [0,4; 3,2] 0,0127[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	16/307 (5,2)	2/305 (0,7)	7,95 [1,84; 34,27] 0,0054[2]	8,33 [1,90; 36,55] 0,0009[3]	4,6 [1,9; 7,2] 0,0009[3]
Tumor stage (Interaction p-value: 0,9166)					
IIA	4/113 (3,5)	0/114 (0,0)	9,08 [0,49; 166,70] 0,1374[2]	9,41 [0,50; 176,86] 0,0598[4]	3,5 [0,1; 6,9] 0,0598[4]
IIB	5/151 (3,3)	0/136 (0,0)	9,91 [0,55; 177,65] 0,1192[2]	10,25 [0,56; 187,10] 0,0620[4]	3,3 [0,5; 6,2] 0,0620[4]
IIIA	12/495 (2,4)	3/488 (0,6)	3,94 [1,12; 13,89] 0,0327[2]	4,02 [1,13; 14,32] 0,0207[3]	1,8 [0,3; 3,3] 0,0207[3]
IIIB	1/54 (1,9)	0/45 (0,0)	2,51 [0,10; 60,13] 0,5703[2]	2,55 [0,10; 64,17] 1,0000[4]	1,9 [-1,7; 5,4] 1,0000[4]
IIIC	20/468 (4,3)	2/480 (0,4)	10,26 [2,41; 43,64] 0,0016[2]	10,67 [2,48; 45,91] <,0001[3]	3,9 [1,9; 5,8] <,0001[3]
Tumor grade (Interaction p-value: 0,9020)					
G1	5/91 (5,5)	0/93 (0,0)	11,24 [0,63; 200,37] 0,0997[2]	11,89 [0,65; 218,22] 0,0280[4]	5,5 [0,8; 10,2] 0,0280[4]
G2	19/612 (3,1)	3/603 (0,5)	6,24 [1,86; 20,98] 0,0031[2]	6,41 [1,89; 21,77] 0,0007[3]	2,6 [1,1; 4,1] 0,0007[3]
G3	14/527 (2,7)	1/506 (0,2)	13,44 [1,77; 101,85] 0,0119[2]	13,78 [1,81; 105,19] 0,0010[3]	2,5 [1,0; 3,9] 0,0010[3]
GX	4/51 (7,8)	1/59 (1,7)	4,63 [0,53; 40,09] 0,1643[2]	4,94 [0,53; 45,67] 0,1806[4]	6,1 [-1,9; 14,2] 0,1806[4]
Race (Interaction p-value: 0,6885)					
White	31/958 (3,2)	3/944 (0,3)	10,18 [3,12; 33,19] 0,0001[2]	10,49 [3,20; 34,43] <,0001[3]	2,9 [1,7; 4,1] <,0001[3]
Asian	9/250 (3,6)	2/242 (0,8)	4,36 [0,95; 19,96] 0,0581[2]	4,48 [0,96; 20,96] 0,0375[3]	2,8 [0,2; 5,3] 0,0375[3]
Other	2/62 (3,2)	0/64 (0,0)	5,16 [0,25; 105,34] 0,2864[2]	5,33 [0,25; 113,30] 0,2401[4]	3,2 [-1,2; 7,6] 0,2401[4]
ECOG-PS (Interaction p-value: 0,9727)					
ECOG-PS 0	34/1070 (3,2)	5/1020 (0,5)	6,48 [2,55; 16,51] <,0001[2]	6,66 [2,60; 17,10] <,0001[3]	2,7 [1,6; 3,8] <,0001[3]
ECOG-PS 1	8/213 (3,8)	0/245 (0,0)	19,54 [1,13; 336,58] 0,0407[2]	20,31 [1,17; 353,98] 0,0020[4]	3,8 [1,2; 6,3] 0,0020[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk					

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Lymphopenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Prior treatment (Interaction p-value: 0,9355)					
Neoadjuvant chemotherapy	9/430 (2,1)	0/415 (0,0)	18,34 [1,07; 314,08] 0,0447[2]	18,73 [1,09; 322,84] 0,0038[4]	2,1 [0,7; 3,4] 0,0038[4]
Adjuvant chemotherapy	13/784 (1,7)	0/769 (0,0)	26,48 [1,58; 444,73] 0,0228[2]	26,93 [1,60; 453,81] 0,0003[3]	1,7 [0,8; 2,6] 0,0003[3]
No chemotherapy	0/69 (0,0)	1/81 (1,2)	0,39 [0,02; 9,43] 0,5628[2]	0,39 [0,02; 9,63] 1,0000[4]	-1,2 [-3,6; 1,2] 1,0000[4]
Region (Interaction p-value: 0,9994)					
North America / Europe	6/678 (0,9)	1/650 (0,2)	5,75 [0,69; 47,65] 0,1048[2]	5,79 [0,70; 48,26] 0,1246[4]	0,7 [-0,0; 1,5] 0,1246[4]
Asia	2/203 (1,0)	0/201 (0,0)	4,95 [0,24; 102,48] 0,3008[2]	5,00 [0,24; 104,80] 0,4988[4]	1,0 [-0,4; 2,3] 0,4988[4]
Other	14/402 (3,5)	0/414 (0,0)	29,86 [1,79; 498,95] 0,0181[2]	30,94 [1,84; 520,43] 0,0001[3]	3,5 [1,7; 5,3] 0,0001[3]
Primary tumor size (Interaction p-value: 0,9990)					
< 20 mm	3/331 (0,9)	0/335 (0,0)	7,08 [0,37; 136,62] 0,1947[2]	7,15 [0,37; 138,95] 0,1222[4]	0,9 [-0,1; 1,9] 0,1222[4]
≥ 20 but < 50 mm	14/646 (2,2)	0/653 (0,0)	29,31 [1,75; 490,37] 0,0188[2]	29,96 [1,78; 503,34] 0,0002[3]	2,2 [1,0; 3,3] 0,0002[3]
≥ 50 mm	4/289 (1,4)	1/265 (0,4)	3,67 [0,41; 32,61] 0,2437[2]	3,71 [0,41; 33,36] 0,3751[4]	1,0 [-0,5; 2,5] 0,3751[4]
Number of positive lymph nodes (Interaction p-value: 0,9992)					
0-3	2/427 (0,5)	0/418 (0,0)	4,89 [0,24; 101,65] 0,3048[2]	4,92 [0,24; 102,74] 0,4995[4]	0,5 [-0,2; 1,1] 0,4995[4]
4-9	13/549 (2,4)	0/542 (0,0)	26,66 [1,59; 447,29] 0,0225[2]	27,30 [1,62; 460,43] 0,0003[3]	2,4 [1,1; 3,6] 0,0003[3]
≥ 10	7/307 (2,3)	1/305 (0,3)	6,95 [0,86; 56,19] 0,0689[2]	7,09 [0,87; 58,00] 0,0685[4]	2,0 [0,2; 3,7] 0,0685[4]
Tumor stage (Interaction p-value: 1,0000)					
IIA	0/113 (0,0)	0/114 (0,0)	NE	NE	NE
IIB	1/151 (0,7)	0/136 (0,0)	2,70 [0,11; 65,82] 0,5414[2]	2,72 [0,11; 67,35] 1,0000[4]	0,7 [-0,6; 2,0] 1,0000[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
IIIA	9/495 (1,8)	0/488 (0,0)	18,73 [1,09; 320,95] 0,0432[2]	19,08 [1,11; 328,69] 0,0038[4]	1,8 [0,6; 3,0] 0,0038[4]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	10/468 (2,1)	1/480 (0,2)	10,26 [1,32; 79,80] 0,0262[2]	10,46 [1,33; 82,03] 0,0056[3]	1,9 [0,6; 3,3] 0,0056[3]
Tumor grade (Interaction p-value: 0,9999)					
G1	2/91 (2,2)	0/93 (0,0)	5,11 [0,25; 104,97] 0,2903[2]	5,22 [0,25; 110,31] 0,2432[4]	2,2 [-0,8; 5,2] 0,2432[4]
G2	13/612 (2,1)	1/603 (0,2)	12,81 [1,68; 97,61] 0,0138[2]	13,07 [1,70; 100,19] 0,0014[3]	2,0 [0,8; 3,1] 0,0014[3]
G3	6/527 (1,1)	0/506 (0,0)	12,48 [0,71; 221,01] 0,0851[2]	12,63 [0,71; 224,71] 0,0310[4]	1,1 [0,2; 2,0] 0,0310[4]
GX	1/51 (2,0)	0/59 (0,0)	3,46 [0,14; 83,15] 0,4439[2]	3,53 [0,14; 88,69] 0,4636[4]	2,0 [-1,8; 5,8] 0,4636[4]
Progesterone receptor status (Interaction p-value: 0,9994)					
Negative	1/156 (0,6)	1/169 (0,6)	1,08 [0,07; 17,17] 0,9547[2]	1,08 [0,07; 17,48] 1,0000[4]	0,0 [-1,7; 1,8] 1,0000[4]
Positive	21/1089 (1,9)	0/1067 (0,0)	42,13 [2,56; 694,64] 0,0089[2]	42,96 [2,60; 710,10] <,0001[3]	1,9 [1,1; 2,7] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9998)					
White	17/958 (1,8)	1/944 (0,1)	16,75 [2,23; 125,62] 0,0061[2]	17,04 [2,26; 128,27] 0,0002[3]	1,7 [0,8; 2,5] 0,0002[3]
Asian	2/250 (0,8)	0/242 (0,0)	4,84 [0,23; 100,31] 0,3079[2]	4,88 [0,23; 102,16] 0,4991[4]	0,8 [-0,3; 1,9] 0,4991[4]
Other	3/62 (4,8)	0/64 (0,0)	7,22 [0,38; 137,01] 0,1879[2]	7,59 [0,38; 150,00] 0,1162[4]	4,8 [-0,5; 10,2] 0,1162[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Neutropenia from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,8935)					
< 65 years	105/918 (11,4)	3/937 (0,3)	35,72 [11,38; 112,15] <,0001[2]	40,21 [12,71; 127,18] <,0001[3]	11,1 [9,0; 13,2] <,0001[3]
≥ 65 years	34/365 (9,3)	1/328 (0,3)	30,55 [4,21; 221,95] 0,0007[2]	33,59 [4,57; 246,82] <,0001[3]	9,0 [6,0; 12,1] <,0001[3]
Prior treatment (Interaction p-value: 0,8443)					
Neoadjuvant chemotherapy	54/430 (12,6)	1/415 (0,2)	52,12 [7,24; 374,99] <,0001[2]	59,46 [8,19; 431,91] <,0001[3]	12,3 [9,1; 15,5] <,0001[3]
Adjuvant chemotherapy	81/784 (10,3)	3/769 (0,4)	26,48 [8,40; 83,48] <,0001[2]	29,42 [9,25; 93,56] <,0001[3]	9,9 [7,8; 12,1] <,0001[3]
No chemotherapy	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (Interaction p-value: 0,9781)					
North America / Europe	69/678 (10,2)	2/650 (0,3)	33,08 [8,14; 134,36] <,0001[2]	36,71 [8,96; 150,39] <,0001[3]	9,9 [7,6; 12,2] <,0001[3]
Asia	18/203 (8,9)	0/201 (0,0)	36,64 [2,22; 603,86] 0,0118[2]	40,19 [2,41; 671,65] <,0001[3]	8,9 [5,0; 12,8] <,0001[3]
Other	52/402 (12,9)	2/414 (0,5)	26,78 [6,57; 109,19] <,0001[2]	30,61 [7,40; 126,55] <,0001[3]	12,5 [9,1; 15,8] <,0001[3]
Primary tumor size (Interaction p-value: 0,9260)					
< 20 mm	40/331 (12,1)	0/335 (0,0)	81,98 [5,06; 1327,65] 0,0019[2]	93,23 [5,71; 1522,80] <,0001[3]	12,1 [8,6; 15,6] <,0001[3]
≥ 20 but < 50 mm	62/646 (9,6)	3/653 (0,5)	20,89 [6,59; 66,21] <,0001[2]	23,00 [7,18; 73,67] <,0001[3]	9,1 [6,8; 11,5] <,0001[3]
≥ 50 mm	36/289 (12,5)	1/265 (0,4)	33,01 [4,56; 239,08] 0,0005[2]	37,57 [5,11; 276,04] <,0001[3]	12,1 [8,2; 16,0] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9079)					
0-3	50/427 (11,7)	1/418 (0,2)	48,95 [6,79; 352,69] 0,0001[2]	55,31 [7,60; 402,31] <,0001[3]	11,5 [8,4; 14,6] <,0001[3]
4-9	60/549 (10,9)	2/542 (0,4)	29,62 [7,28; 120,56] <,0001[2]	33,13 [8,05; 136,25] <,0001[3]	10,6 [7,9; 13,2] <,0001[3]
≥ 10	29/307 (9,4)	1/305 (0,3)	28,81 [3,95; 210,17] 0,0009[2]	31,71 [4,29; 234,35] <,0001[3]	9,1 [5,8; 12,5] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,5961)					
IIA	10/113 (8,8)	0/114 (0,0)	21,18 [1,26; 357,25] 0,0342[2]	23,23 [1,34; 401,41] 0,0008[4]	8,8 [3,6; 14,1] 0,0008[4]
IIB	21/151 (13,9)	0/136 (0,0)	38,76 [2,37; 633,73] 0,0103[2]	44,98 [2,70; 750,14] <,0001[3]	13,9 [8,4; 19,4] <,0001[3]
IIIA	56/495 (11,3)	1/488 (0,2)	55,21 [7,67; 397,24] <,0001[2]	62,12 [8,56; 450,66] <,0001[3]	11,1 [8,3; 13,9] <,0001[3]
IIIB	6/54 (11,1)	1/45 (2,2)	5,00 [0,62; 40,01] 0,1293[2]	5,50 [0,64; 47,51] 0,1226[4]	8,9 [-0,5; 18,3] 0,1226[4]
IIIC	46/468 (9,8)	2/480 (0,4)	23,59 [5,76; 96,62] <,0001[2]	26,05 [6,29; 107,97] <,0001[3]	9,4 [6,7; 12,2] <,0001[3]
Progesterone receptor status (Interaction p-value: 0,9274)					
Negative	21/156 (13,5)	0/169 (0,0)	46,56 [2,84; 762,19] 0,0071[2]	53,79 [3,23; 896,07] <,0001[3]	13,5 [8,1; 18,8] <,0001[3]
Positive	118/1089 (10,8)	4/1067 (0,4)	28,90 [10,71; 78,01] <,0001[2]	32,30 [11,88; 87,81] <,0001[3]	10,5 [8,6; 12,3] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9997)					
White	104/958 (10,9)	4/944 (0,4)	25,62 [9,48; 69,27] <,0001[2]	28,62 [10,50; 78,02] <,0001[3]	10,4 [8,4; 12,4] <,0001[3]
Asian	24/250 (9,6)	0/242 (0,0)	47,44 [2,90; 775,74] 0,0068[2]	52,46 [3,17; 867,73] <,0001[3]	9,6 [5,9; 13,3] <,0001[3]
Other	11/62 (17,7)	0/64 (0,0)	23,73 [1,43; 394,21] 0,0272[2]	28,81 [1,66; 500,49] 0,0004[3]	17,7 [8,2; 27,3] 0,0004[3]
ECOG-PS (Interaction p-value: 0,9073)					
ECOG-PS 0	112/1070 (10,5)	3/1020 (0,3)	35,59 [11,34; 111,66] <,0001[2]	39,63 [12,55; 125,17] <,0001[3]	10,2 [8,3; 12,0] <,0001[3]
ECOG-PS 1	27/213 (12,7)	1/245 (0,4)	31,06 [4,26; 226,62] 0,0007[2]	35,42 [4,77; 263,03] <,0001[3]	12,3 [7,7; 16,8] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Neutrophil count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1737)					
< 65 years	90/918 (9,8)	1/937 (0,1)	91,86 [12,83; 657,88] <,0001[2]	101,74 [14,15; 731,76] <,0001[3]	9,7 [7,8; 11,6] <,0001[3]
≥ 65 years	38/365 (10,4)	2/328 (0,6)	17,07 [4,15; 70,22] <,0001[2]	18,94 [4,53; 79,16] <,0001[3]	9,8 [6,6; 13,0] <,0001[3]
Prior treatment (Interaction p-value: 0,9600)					
Neoadjuvant chemotherapy	52/430 (12,1)	1/415 (0,2)	50,19 [6,97; 361,35] 0,0001[2]	56,95 [7,83; 413,99] <,0001[3]	11,9 [8,7; 15,0] <,0001[3]
Adjuvant chemotherapy	72/784 (9,2)	2/769 (0,3)	35,31 [8,69; 143,41] <,0001[2]	38,78 [9,48; 158,64] <,0001[3]	8,9 [6,9; 11,0] <,0001[3]
No chemotherapy	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (Interaction p-value: 0,9563)					
North America / Europe	47/678 (6,9)	1/650 (0,2)	45,06 [6,24; 325,63] 0,0002[2]	48,34 [6,65; 351,43] <,0001[3]	6,8 [4,8; 8,7] <,0001[3]
Asia	63/203 (31,0)	2/201 (1,0)	31,19 [7,74; 125,74] <,0001[2]	44,78 [10,78; 186,03] <,0001[3]	30,0 [23,5; 36,5] <,0001[3]
Other	18/402 (4,5)	0/414 (0,0)	38,10 [2,30; 630,13] 0,0110[2]	39,89 [2,40; 664,14] <,0001[3]	4,5 [2,5; 6,5] <,0001[3]
Primary tumor size (Interaction p-value: 0,4542)					
< 20 mm	29/331 (8,8)	2/335 (0,6)	14,68 [3,53; 61,01] 0,0002[2]	15,99 [3,78; 67,57] <,0001[3]	8,2 [5,0; 11,3] <,0001[3]
≥ 20 but < 50 mm	69/646 (10,7)	1/653 (0,2)	69,75 [9,72; 500,70] <,0001[2]	77,97 [10,79; 563,18] <,0001[3]	10,5 [8,1; 12,9] <,0001[3]
≥ 50 mm	29/289 (10,0)	0/265 (0,0)	54,12 [3,32; 881,30] 0,0051[2]	60,13 [3,66; 989,27] <,0001[3]	10,0 [6,6; 13,5] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,9644)					
0-3	44/427 (10,3)	1/418 (0,2)	43,07 [5,96; 311,19] 0,0002[2]	47,91 [6,57; 349,39] <,0001[3]	10,1 [7,1; 13,0] <,0001[3]
4-9	50/549 (9,1)	1/542 (0,2)	49,36 [6,84; 356,06] 0,0001[2]	54,21 [7,46; 393,88] <,0001[3]	8,9 [6,5; 11,4] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	34/307 (11,1)	1/305 (0,3)	33,78 [4,65; 245,20] 0,0005[2]	37,86 [5,15; 278,44] <,0001[3]	10,7 [7,2; 14,3] <,0001[3]
Tumor stage (Interaction p-value: 0,9974)					
IIA	12/113 (10,6)	0/114 (0,0)	25,22 [1,51; 420,91] 0,0246[2]	28,20 [1,65; 482,36] 0,0003[3]	10,6 [4,9; 16,3] 0,0003[3]
IIB	18/151 (11,9)	1/136 (0,7)	16,21 [2,19; 119,83] 0,0063[2]	18,27 [2,40; 138,82] 0,0001[3]	11,2 [5,8; 16,5] 0,0001[3]
IIIA	43/495 (8,7)	0/488 (0,0)	85,77 [5,30; 1389,34] 0,0017[2]	93,92 [5,77; 1530,09] <,0001[3]	8,7 [6,2; 11,2] <,0001[3]
IIIB	3/54 (5,6)	0/45 (0,0)	5,85 [0,31; 110,43] 0,2383[2]	6,18 [0,31; 122,97] 0,2486[4]	5,6 [-0,6; 11,7] 0,2486[4]
IIIC	51/468 (10,9)	2/480 (0,4)	26,15 [6,40; 106,81] <,0001[2]	29,23 [7,07; 120,80] <,0001[3]	10,5 [7,6; 13,4] <,0001[3]
Tumor grade (Interaction p-value: 0,8649)					
G1	6/91 (6,6)	0/93 (0,0)	13,28 [0,76; 232,41] 0,0765[2]	14,22 [0,79; 256,15] 0,0134[4]	6,6 [1,5; 11,7] 0,0134[4]
G2	57/612 (9,3)	0/603 (0,0)	113,31 [7,02; 1829,33] 0,0009[2]	124,94 [7,70; 2026,42] <,0001[3]	9,3 [7,0; 11,6] <,0001[3]
G3	57/527 (10,8)	2/506 (0,4)	27,36 [6,72; 111,49] <,0001[2]	30,56 [7,42; 125,88] <,0001[3]	10,4 [7,7; 13,1] <,0001[3]
GX	8/51 (15,7)	1/59 (1,7)	9,25 [1,20; 71,52] 0,0329[2]	10,79 [1,30; 89,53] 0,0115[4]	14,0 [3,5; 24,5] 0,0115[4]
Progesterone receptor status (Interaction p-value: 0,9965)					
Negative	20/156 (12,8)	0/169 (0,0)	44,39 [2,71; 727,88] 0,0079[2]	50,91 [3,05; 849,41] <,0001[3]	12,8 [7,6; 18,1] <,0001[3]
Positive	106/1089 (9,7)	2/1067 (0,2)	51,93 [12,85; 209,82] <,0001[2]	57,42 [14,14; 233,23] <,0001[3]	9,5 [7,8; 11,3] <,0001[3]
Unknown	2/10 (20,0)	0/7 (0,0)	3,64 [0,20; 65,86] 0,3824[2]	4,41 [0,18; 107,28] 0,4853[4]	20,0 [-4,8; 44,8] 0,4853[4]
Race (Interaction p-value: 0,8953)					
White	57/958 (5,9)	1/944 (0,1)	56,17 [7,79; 404,79] <,0001[2]	59,66 [8,24; 431,73] <,0001[3]	5,8 [4,3; 7,4] <,0001[3]
Asian	65/250 (26,0)	2/242 (0,8)	31,46 [7,79; 127,06] <,0001[2]	42,16 [10,19; 174,44] <,0001[3]	25,2 [19,6; 30,7] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Other	5/62 (8,1)	0/64 (0,0)	11,35 [0,64; 201,02] 0,0976[2]	12,34 [0,67; 228,05] 0,0265[4]	8,1 [1,3; 14,8] 0,0265[4]
ECOG-PS (Interaction p-value: 0,9753)					
ECOG-PS 0	114/1070 (10,7)	3/1020 (0,3)	36,22 [11,55; 113,62] <,0001[2]	40,42 [12,80; 127,64] <,0001[3]	10,4 [8,5; 12,2] <,0001[3]
ECOG-PS 1	14/213 (6,6)	0/245 (0,0)	33,34 [2,00; 555,51] 0,0146[2]	35,69 [2,12; 601,94] <,0001[3]	6,6 [3,2; 9,9] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT Platelet count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Progesterone receptor status (Interaction p-value: 0,9724)					
Negative	1/156 (0,6)	0/169 (0,0)	3,25 [0,13; 79,16] 0,4696[2]	3,27 [0,13; 80,87] 0,4800[4]	0,6 [-0,6; 1,9] 0,4800[4]
Positive	12/1089 (1,1)	0/1067 (0,0)	24,50 [1,45; 413,20] 0,0265[2]	24,77 [1,46; 418,85] 0,0006[3]	1,1 [0,5; 1,7] 0,0006[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according PT White blood cell count decreased from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1282)					
< 65 years	73/918 (8,0)	1/937 (0,1)	74,51 [10,38; 534,96] <,0001[2]	80,86 [11,21; 583,05] <,0001[3]	7,8 [6,1; 9,6] <,0001[3]
≥ 65 years	25/365 (6,8)	2/328 (0,6)	11,23 [2,68; 47,06] 0,0009[2]	11,99 [2,82; 51,01] <,0001[3]	6,2 [3,5; 9,0] <,0001[3]
Prior treatment (Interaction p-value: 0,9438)					
Neoadjuvant chemotherapy	41/430 (9,5)	1/415 (0,2)	39,57 [5,47; 286,34] 0,0003[2]	43,63 [5,97; 318,75] <,0001[3]	9,3 [6,5; 12,1] <,0001[3]
Adjuvant chemotherapy	53/784 (6,8)	2/769 (0,3)	25,99 [6,36; 106,29] <,0001[2]	27,81 [6,75; 114,51] <,0001[3]	6,5 [4,7; 8,3] <,0001[3]
No chemotherapy	4/69 (5,8)	0/81 (0,0)	10,54 [0,58; 192,43] 0,1119[2]	11,20 [0,59; 211,78] 0,0427[4]	5,8 [0,3; 11,3] 0,0427[4]
Region (Interaction p-value: 0,9734)					
North America / Europe	33/678 (4,9)	1/650 (0,2)	31,64 [4,34; 230,64] 0,0007[2]	33,20 [4,53; 243,50] <,0001[3]	4,7 [3,1; 6,4] <,0001[3]
Asia	48/203 (23,6)	2/201 (1,0)	23,76 [5,85; 96,46] <,0001[2]	30,81 [7,37; 128,76] <,0001[3]	22,7 [16,6; 28,7] <,0001[3]
Other	17/402 (4,2)	0/414 (0,0)	36,04 [2,17; 597,33] 0,0123[2]	37,63 [2,26; 627,93] <,0001[3]	4,2 [2,3; 6,2] <,0001[3]
Primary tumor size (Interaction p-value: 0,9636)					
< 20 mm	23/331 (6,9)	3/335 (0,9)	7,76 [2,35; 25,59] 0,0008[2]	8,26 [2,46; 27,80] <,0001[3]	6,1 [3,1; 9,0] <,0001[3]
≥ 20 but < 50 mm	47/646 (7,3)	0/653 (0,0)	96,03 [5,93; 1554,45] 0,0013[2]	103,56 [6,37; 1683,59] <,0001[3]	7,3 [5,3; 9,3] <,0001[3]
≥ 50 mm	27/289 (9,3)	0/265 (0,0)	50,45 [3,09; 822,94] 0,0059[2]	55,63 [3,38; 916,71] <,0001[3]	9,3 [6,0; 12,7] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,5108)					
0-3	29/427 (6,8)	0/418 (0,0)	57,76 [3,54; 942,22] 0,0044[2]	61,96 [3,77; 1017,47] <,0001[3]	6,8 [4,4; 9,2] <,0001[3]
4-9	47/549 (8,6)	1/542 (0,2)	46,40 [6,42; 335,11] 0,0001[2]	50,65 [6,96; 368,48] <,0001[3]	8,4 [6,0; 10,7] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	22/307 (7,2)	2/305 (0,7)	10,93 [2,59; 46,07] 0,0011[2]	11,69 [2,73; 50,18] <,0001[3]	6,5 [3,5; 9,5] <,0001[3]
Tumor stage (Interaction p-value: 1,0000)					
IIA	7/113 (6,2)	0/114 (0,0)	15,13 [0,87; 261,84] 0,0618[2]	16,13 [0,91; 285,81] 0,0069[4]	6,2 [1,8; 10,6] 0,0069[4]
IIB	12/151 (7,9)	0/136 (0,0)	22,53 [1,35; 376,99] 0,0302[2]	24,46 [1,43; 417,24] 0,0008[3]	7,9 [3,6; 12,3] 0,0008[3]
IIIA	42/495 (8,5)	0/488 (0,0)	83,80 [5,17; 1357,91] 0,0018[2]	91,56 [5,62; 1492,17] <,0001[3]	8,5 [6,0; 10,9] <,0001[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	34/468 (7,3)	3/480 (0,6)	11,62 [3,59; 37,59] <,0001[2]	12,46 [3,80; 40,85] <,0001[3]	6,6 [4,2; 9,1] <,0001[3]
Tumor grade (Interaction p-value: 0,6983)					
G1	8/91 (8,8)	1/93 (1,1)	8,18 [1,04; 64,06] 0,0455[2]	8,87 [1,09; 72,41] 0,0177[4]	7,7 [1,5; 13,9] 0,0177[4]
G2	45/612 (7,4)	0/603 (0,0)	89,66 [5,54; 1452,15] 0,0016[2]	96,77 [5,95; 1574,54] <,0001[3]	7,4 [5,3; 9,4] <,0001[3]
G3	38/527 (7,2)	1/506 (0,2)	36,49 [5,03; 264,74] 0,0004[2]	39,24 [5,37; 286,94] <,0001[3]	7,0 [4,8; 9,3] <,0001[3]
GX	7/51 (13,7)	1/59 (1,7)	8,10 [1,03; 63,63] 0,0467[2]	9,23 [1,09; 77,77] 0,0236[4]	12,0 [2,0; 22,0] 0,0236[4]
Progesterone receptor status (Interaction p-value: 0,9999)					
Negative	15/156 (9,6)	0/169 (0,0)	33,57 [2,03; 556,31] 0,0142[2]	37,13 [2,20; 626,11] <,0001[3]	9,6 [5,0; 14,2] <,0001[3]
Positive	82/1089 (7,5)	3/1067 (0,3)	26,78 [8,49; 84,50] <,0001[2]	28,88 [9,10; 91,70] <,0001[3]	7,2 [5,6; 8,8] <,0001[3]
Unknown	1/10 (10,0)	0/7 (0,0)	2,18 [0,10; 46,92] 0,6182[2]	2,37 [0,08; 66,88] 1,0000[4]	10,0 [-8,6; 28,6] 1,0000[4]
Race (Interaction p-value: 0,8718)					
White	46/958 (4,8)	1/944 (0,1)	45,33 [6,26; 328,01] 0,0002[2]	47,56 [6,55; 345,61] <,0001[3]	4,7 [3,3; 6,1] <,0001[3]
Asian	49/250 (19,6)	2/242 (0,8)	23,72 [5,83; 96,44] <,0001[2]	29,25 [7,03; 121,79] <,0001[3]	18,8 [13,7; 23,8] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Other	2/62 (3,2)	0/64 (0,0)	5,16 [0,25; 105,34] 0,2864[2]	5,33 [0,25; 113,30] 0,2401[4]	3,2 [-1,2; 7,6] 0,2401[4]
ECOG-PS (Interaction p-value: 0,9748)					
ECOG-PS 0	85/1070 (7,9)	3/1020 (0,3)	27,01 [8,57; 85,15] <,0001[2]	29,25 [9,22; 92,83] <,0001[3]	7,6 [6,0; 9,3] <,0001[3]
ECOG-PS 1	13/213 (6,1)	0/245 (0,0)	31,04 [1,86; 519,00] 0,0168[2]	33,06 [1,95; 559,56] <,0001[3]	6,1 [2,9; 9,3] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Blood and lymphatic system disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5066)					
< 65 years	141/918 (15,4)	8/937 (0,9)	17,99 [8,88; 36,46] <,0001[2]	21,07 [10,27; 43,24] <,0001[3]	14,5 [12,1; 16,9] <,0001[3]
≥ 65 years	68/365 (18,6)	5/328 (1,5)	12,22 [4,99; 29,94] <,0001[2]	14,79 [5,88; 37,18] <,0001[3]	17,1 [12,9; 21,3] <,0001[3]
Prior treatment (Interaction p-value: 0,8030)					
Neoadjuvant chemotherapy	74/430 (17,2)	4/415 (1,0)	17,85 [6,59; 48,39] <,0001[2]	21,36 [7,73; 59,00] <,0001[3]	16,2 [12,6; 19,9] <,0001[3]
Adjuvant chemotherapy	128/784 (16,3)	8/769 (1,0)	15,69 [7,74; 31,84] <,0001[2]	18,56 [9,02; 38,20] <,0001[3]	15,3 [12,6; 18,0] <,0001[3]
No chemotherapy	7/69 (10,1)	1/81 (1,2)	8,22 [1,04; 65,16] 0,0462[2]	9,03 [1,08; 75,35] 0,0243[4]	8,9 [1,4; 16,4] 0,0243[4]
Region (Interaction p-value: 0,9090)					
North America / Europe	104/678 (15,3)	8/650 (1,2)	12,46 [6,12; 25,38] <,0001[2]	14,54 [7,02; 30,11] <,0001[3]	14,1 [11,3; 17,0] <,0001[3]
Asia	27/203 (13,3)	0/201 (0,0)	54,46 [3,34; 886,78] 0,0050[2]	62,79 [3,80; 1036,89] <,0001[3]	13,3 [8,6; 18,0] <,0001[3]
Other	78/402 (19,4)	5/414 (1,2)	16,07 [6,57; 39,27] <,0001[2]	19,69 [7,88; 49,21] <,0001[3]	18,2 [14,2; 22,2] <,0001[3]
Primary tumor size (Interaction p-value: 0,2477)					
< 20 mm	55/331 (16,6)	1/335 (0,3)	55,66 [7,75; 399,90] <,0001[2]	66,56 [9,15; 484,05] <,0001[3]	16,3 [12,3; 20,4] <,0001[3]
≥ 20 but < 50 mm	107/646 (16,6)	10/653 (1,5)	10,82 [5,71; 20,49] <,0001[2]	12,76 [6,61; 24,65] <,0001[3]	15,0 [12,0; 18,0] <,0001[3]
≥ 50 mm	45/289 (15,6)	2/265 (0,8)	20,63 [5,05; 84,21] <,0001[2]	24,25 [5,82; 101,04] <,0001[3]	14,8 [10,5; 19,1] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,4720)					
0-3	62/427 (14,5)	2/418 (0,5)	30,35 [7,47; 123,26] <,0001[2]	35,33 [8,58; 145,45] <,0001[3]	14,0 [10,6; 17,4] <,0001[3]
4-9	93/549 (16,9)	6/542 (1,1)	15,30 [6,76; 34,64] <,0001[2]	18,22 [7,91; 41,99] <,0001[3]	15,8 [12,6; 19,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	54/307 (17,6)	5/305 (1,6)	10,73 [4,35; 26,45] <,0001[2]	12,81 [5,05; 32,50] <,0001[3]	16,0 [11,5; 20,4] <,0001[3]
Tumor stage (Interaction p-value: 0,9467)					
IIA	13/113 (11,5)	0/114 (0,0)	27,24 [1,64; 452,75] 0,0212[2]	30,76 [1,81; 524,06] 0,0002[3]	11,5 [5,6; 17,4] 0,0002[3]
IIB	28/151 (18,5)	0/136 (0,0)	51,38 [3,17; 833,49] 0,0056[2]	63,00 [3,81; 1042,86] <,0001[3]	18,5 [12,3; 24,7] <,0001[3]
IIIA	82/495 (16,6)	5/488 (1,0)	16,17 [6,61; 39,54] <,0001[2]	19,18 [7,70; 47,76] <,0001[3]	15,5 [12,1; 18,9] <,0001[3]
IIIB	8/54 (14,8)	1/45 (2,2)	6,67 [0,87; 51,32] 0,0685[2]	7,65 [0,92; 63,72] 0,0374[4]	12,6 [2,2; 23,0] 0,0374[4]
IIIC	78/468 (16,7)	7/480 (1,5)	11,43 [5,33; 24,51] <,0001[2]	13,51 [6,17; 29,62] <,0001[3]	15,2 [11,7; 18,8] <,0001[3]
Progesterone receptor status (Interaction p-value: 0,7451)					
Negative	27/156 (17,3)	3/169 (1,8)	9,75 [3,02; 31,50] 0,0001[2]	11,58 [3,44; 39,02] <,0001[3]	15,5 [9,3; 21,8] <,0001[3]
Positive	182/1089 (16,7)	10/1067 (0,9)	17,83 [9,49; 33,51] <,0001[2]	21,21 [11,15; 40,33] <,0001[3]	15,8 [13,5; 18,1] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,9505)					
White	153/958 (16,0)	12/944 (1,3)	12,56 [7,03; 22,45] <,0001[2]	14,76 [8,14; 26,77] <,0001[3]	14,7 [12,3; 17,1] <,0001[3]
Asian	39/250 (15,6)	0/242 (0,0)	76,48 [4,73; 1237,40] 0,0023[2]	90,58 [5,53; 1482,68] <,0001[3]	15,6 [11,1; 20,1] <,0001[3]
Other	17/62 (27,4)	1/64 (1,6)	17,55 [2,41; 127,90] 0,0047[2]	23,80 [3,06; 185,38] <,0001[3]	25,9 [14,3; 37,4] <,0001[3]
ECOG-PS (Interaction p-value: 0,8503)					
ECOG-PS 0	163/1070 (15,2)	10/1020 (1,0)	15,54 [8,25; 29,25] <,0001[2]	18,15 [9,53; 34,59] <,0001[3]	14,3 [12,0; 16,5] <,0001[3]
ECOG-PS 1	46/213 (21,6)	3/245 (1,2)	17,64 [5,57; 55,89] <,0001[2]	22,22 [6,80; 72,63] <,0001[3]	20,4 [14,7; 26,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Gastrointestinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,2058)					
< 65 years	92/918 (10,0)	9/937 (1,0)	10,43 [5,29; 20,56] <,0001[2]	11,48 [5,76; 22,92] <,0001[3]	9,1 [7,0; 11,1] <,0001[3]
≥ 65 years	56/365 (15,3)	9/328 (2,7)	5,59 [2,81; 11,12] <,0001[2]	6,42 [3,12; 13,21] <,0001[3]	12,6 [8,5; 16,7] <,0001[3]
Prior treatment (Interaction p-value: 0,7029)					
Neoadjuvant chemotherapy	57/430 (13,3)	5/415 (1,2)	11,00 [4,45; 27,17] <,0001[2]	12,53 [4,97; 31,60] <,0001[3]	12,1 [8,7; 15,4] <,0001[3]
Adjuvant chemotherapy	85/784 (10,8)	12/769 (1,6)	6,95 [3,83; 12,61] <,0001[2]	7,67 [4,16; 14,16] <,0001[3]	9,3 [6,9; 11,6] <,0001[3]
No chemotherapy	6/69 (8,7)	1/81 (1,2)	7,04 [0,87; 57,09] 0,0675[2]	7,62 [0,89; 64,93] 0,0485[4]	7,5 [0,4; 14,5] 0,0485[4]
Region (Interaction p-value: 0,3038)					
North America / Europe	85/678 (12,5)	13/650 (2,0)	6,27 [3,53; 11,13] <,0001[2]	7,02 [3,88; 12,73] <,0001[3]	10,5 [7,8; 13,3] <,0001[3]
Asia	13/203 (6,4)	2/201 (1,0)	6,44 [1,47; 28,16] 0,0134[2]	6,81 [1,52; 30,57] 0,0040[3]	5,4 [1,8; 9,0] 0,0040[3]
Other	50/402 (12,4)	3/414 (0,7)	17,16 [5,40; 54,58] <,0001[2]	19,46 [6,02; 62,93] <,0001[3]	11,7 [8,4; 15,0] <,0001[3]
Primary tumor size (Interaction p-value: 0,8657)					
< 20 mm	30/331 (9,1)	4/335 (1,2)	7,59 [2,70; 21,31] 0,0001[2]	8,25 [2,87; 23,68] <,0001[3]	7,9 [4,6; 11,2] <,0001[3]
≥ 20 but < 50 mm	80/646 (12,4)	9/653 (1,4)	8,99 [4,55; 17,74] <,0001[2]	10,11 [5,03; 20,33] <,0001[3]	11,0 [8,3; 13,7] <,0001[3]
≥ 50 mm	36/289 (12,5)	5/265 (1,9)	6,60 [2,63; 16,57] <,0001[2]	7,40 [2,86; 19,16] <,0001[3]	10,6 [6,4; 14,7] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,4932)					
0-3	63/427 (14,8)	5/418 (1,2)	12,33 [5,01; 30,36] <,0001[2]	14,30 [5,69; 35,93] <,0001[3]	13,6 [10,0; 17,1] <,0001[3]
4-9	51/549 (9,3)	8/542 (1,5)	6,29 [3,02; 13,14] <,0001[2]	6,84 [3,21; 14,55] <,0001[3]	7,8 [5,2; 10,4] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	34/307 (11,1)	5/305 (1,6)	6,76 [2,68; 17,04] <,0001[2]	7,47 [2,88; 19,38] <,0001[3]	9,4 [5,6; 13,2] <,0001[3]
Tumor stage (Interaction p-value: 0,8896)					
IIA	14/113 (12,4)	1/114 (0,9)	14,12 [1,89; 105,62] 0,0099[2]	15,98 [2,06; 123,71] 0,0005[3]	11,5 [5,2; 17,8] 0,0005[3]
IIB	22/151 (14,6)	0/136 (0,0)	40,56 [2,48; 662,27] 0,0094[2]	47,43 [2,85; 790,00] <,0001[3]	14,6 [8,9; 20,2] <,0001[3]
IIIA	42/495 (8,5)	8/488 (1,6)	5,18 [2,46; 10,91] <,0001[2]	5,56 [2,58; 11,98] <,0001[3]	6,8 [4,1; 9,5] <,0001[3]
IIIB	2/54 (3,7)	0/45 (0,0)	4,18 [0,21; 84,92] 0,3517[2]	4,33 [0,20; 92,62] 0,4991[4]	3,7 [-1,3; 8,7] 0,4991[4]
IIIC	67/468 (14,3)	9/480 (1,9)	7,64 [3,85; 15,13] <,0001[2]	8,74 [4,31; 17,76] <,0001[3]	12,4 [9,0; 15,8] <,0001[3]
Tumor grade (Interaction p-value: 0,2055)					
G1	10/91 (11,0)	3/93 (3,2)	3,41 [0,97; 11,98] 0,0561[2]	3,70 [0,98; 13,93] 0,0399[3]	7,8 [0,4; 15,1] 0,0399[3]
G2	61/612 (10,0)	9/603 (1,5)	6,68 [3,35; 13,32] <,0001[2]	7,31 [3,59; 14,85] <,0001[3]	8,5 [5,9; 11,0] <,0001[3]
G3	75/527 (14,2)	5/506 (1,0)	14,40 [5,87; 35,32] <,0001[2]	16,63 [6,66; 41,48] <,0001[3]	13,2 [10,1; 16,3] <,0001[3]
GX	2/51 (3,9)	1/59 (1,7)	2,31 [0,22; 24,78] 0,4880[2]	2,37 [0,21; 26,90] 0,5957[4]	2,2 [-4,0; 8,5] 0,5957[4]
Race (Interaction p-value: 0,9913)					
White	122/958 (12,7)	14/944 (1,5)	8,59 [4,98; 14,82] <,0001[2]	9,69 [5,53; 16,99] <,0001[3]	11,3 [9,0; 13,5] <,0001[3]
Asian	16/250 (6,4)	2/242 (0,8)	7,74 [1,80; 33,32] 0,0060[2]	8,21 [1,87; 36,08] 0,0010[3]	5,6 [2,3; 8,8] 0,0010[3]
Other	8/62 (12,9)	1/64 (1,6)	8,26 [1,06; 64,10] 0,0435[2]	9,33 [1,13; 77,01] 0,0160[4]	11,3 [2,5; 20,2] 0,0160[4]
ECOG-PS (Interaction p-value: 0,7578)					
ECOG-PS 0	123/1070 (11,5)	15/1020 (1,5)	7,82 [4,61; 13,27] <,0001[2]	8,70 [5,05; 14,98] <,0001[3]	10,0 [8,0; 12,1] <,0001[3]
ECOG-PS 1	25/213 (11,7)	3/245 (1,2)	9,59 [2,94; 31,30] 0,0002[2]	10,73 [3,19; 36,07] <,0001[3]	10,5 [6,0; 15,0] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC General disorders and administration site conditions from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7471)					
< 65 years	32/918 (3,5)	4/937 (0,4)	8,17 [2,90; 23,00] <,0001[2]	8,42 [2,97; 23,92] <,0001[3]	3,1 [1,8; 4,3] <,0001[3]
≥ 65 years	21/365 (5,8)	3/328 (0,9)	6,29 [1,89; 20,90] 0,0027[2]	6,61 [1,95; 22,38] 0,0005[3]	4,8 [2,2; 7,4] 0,0005[3]
Prior treatment (Interaction p-value: 0,4961)					
Neoadjuvant chemotherapy	16/430 (3,7)	1/415 (0,2)	15,44 [2,06; 115,92] 0,0078[2]	16,00 [2,11; 121,20] 0,0003[3]	3,5 [1,6; 5,3] 0,0003[3]
Adjuvant chemotherapy	35/784 (4,5)	5/769 (0,7)	6,87 [2,70; 17,43] <,0001[2]	7,14 [2,78; 18,32] <,0001[3]	3,8 [2,3; 5,4] <,0001[3]
No chemotherapy	2/69 (2,9)	1/81 (1,2)	2,35 [0,22; 25,34] 0,4819[2]	2,39 [0,21; 26,92] 0,5945[4]	1,7 [-3,0; 6,3] 0,5945[4]
Region (Interaction p-value: 0,4844)					
North America / Europe	32/678 (4,7)	6/650 (0,9)	5,11 [2,15; 12,15] 0,0002[2]	5,32 [2,21; 12,80] <,0001[3]	3,8 [2,0; 5,6] <,0001[3]
Asia	2/203 (1,0)	0/201 (0,0)	4,95 [0,24; 102,48] 0,3008[2]	5,00 [0,24; 104,80] 0,4988[4]	1,0 [-0,4; 2,3] 0,4988[4]
Other	19/402 (4,7)	1/414 (0,2)	19,57 [2,63; 145,48] 0,0037[2]	20,49 [2,73; 153,78] <,0001[3]	4,5 [2,4; 6,6] <,0001[3]
Primary tumor size (Interaction p-value: 0,6858)					
< 20 mm	13/331 (3,9)	1/335 (0,3)	13,16 [1,73; 100,01] 0,0128[2]	13,65 [1,78; 104,98] 0,0011[3]	3,6 [1,5; 5,8] 0,0011[3]
≥ 20 but < 50 mm	28/646 (4,3)	5/653 (0,8)	5,66 [2,20; 14,57] 0,0003[2]	5,87 [2,25; 15,30] <,0001[3]	3,6 [1,9; 5,3] <,0001[3]
≥ 50 mm	12/289 (4,2)	1/265 (0,4)	11,00 [1,44; 84,05] 0,0208[2]	11,44 [1,48; 88,57] 0,0034[3]	3,8 [1,4; 6,2] 0,0034[3]
Number of positive lymph nodes (Interaction p-value: 0,6983)					
0-3	15/427 (3,5)	1/418 (0,2)	14,68 [1,95; 110,66] 0,0091[2]	15,18 [2,00; 115,46] 0,0005[3]	3,3 [1,5; 5,1] 0,0005[3]
4-9	22/549 (4,0)	3/542 (0,6)	7,24 [2,18; 24,05] 0,0012[2]	7,50 [2,23; 25,21] 0,0001[3]	3,5 [1,7; 5,2] 0,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	16/307 (5,2)	3/305 (1,0)	5,30 [1,56; 18,00] 0,0075[2]	5,53 [1,60; 19,20] 0,0026[3]	4,2 [1,5; 6,9] 0,0026[3]
Tumor stage (Interaction p-value: 0,4385)					
IIA	6/113 (5,3)	0/114 (0,0)	13,11 [0,75; 230,08] 0,0783[2]	13,85 [0,77; 248,76] 0,0142[4]	5,3 [1,2; 9,4] 0,0142[4]
IIB	6/151 (4,0)	0/136 (0,0)	11,72 [0,67; 206,07] 0,0925[2]	12,20 [0,68; 218,55] 0,0309[4]	4,0 [0,9; 7,1] 0,0309[4]
IIIA	21/495 (4,2)	1/488 (0,2)	20,70 [2,80; 153,31] 0,0030[2]	21,58 [2,89; 161,04] <,0001[3]	4,0 [2,2; 5,9] <,0001[3]
IIIB	1/54 (1,9)	1/45 (2,2)	0,83 [0,05; 12,95] 0,8964[2]	0,83 [0,05; 13,66] 1,0000[4]	-0,4 [-6,0; 5,2] 1,0000[4]
IIIC	19/468 (4,1)	5/480 (1,0)	3,90 [1,47; 10,35] 0,0063[2]	4,02 [1,49; 10,86] 0,0031[3]	3,0 [1,0; 5,0] 0,0031[3]
Tumor grade (Interaction p-value: 0,9168)					
G1	3/91 (3,3)	0/93 (0,0)	7,15 [0,37; 136,54] 0,1910[2]	7,40 [0,38; 145,22] 0,1189[4]	3,3 [-0,4; 7,0] 0,1189[4]
G2	20/612 (3,3)	3/603 (0,5)	6,57 [1,96; 21,99] 0,0023[2]	6,76 [2,00; 22,86] 0,0004[3]	2,8 [1,3; 4,3] 0,0004[3]
G3	27/527 (5,1)	3/506 (0,6)	8,64 [2,64; 28,31] 0,0004[2]	9,05 [2,73; 30,04] <,0001[3]	4,5 [2,5; 6,5] <,0001[3]
GX	3/51 (5,9)	1/59 (1,7)	3,47 [0,37; 32,34] 0,2745[2]	3,63 [0,37; 35,99] 0,3349[4]	4,2 [-3,1; 11,4] 0,3349[4]
Race (Interaction p-value: 0,9844)					
White	50/958 (5,2)	7/944 (0,7)	7,04 [3,21; 15,44] <,0001[2]	7,37 [3,32; 16,34] <,0001[3]	4,5 [3,0; 6,0] <,0001[3]
Asian	2/250 (0,8)	0/242 (0,0)	4,84 [0,23; 100,31] 0,3079[2]	4,88 [0,23; 102,16] 0,4991[4]	0,8 [-0,3; 1,9] 0,4991[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE
First endocrine therapy (Interaction p-value: 0,4912)					
Tamoxifen	3/114 (2,6)	1/132 (0,8)	3,47 [0,37; 32,93] 0,2779[2]	3,54 [0,36; 34,52] 0,3391[4]	1,9 [-1,4; 5,2] 0,3391[4]
Aromatase inhibitor	50/1169 (4,3)	6/1133 (0,5)	8,08 [3,48; 18,76] <,0001[2]	8,39 [3,58; 19,65] <,0001[3]	3,7 [2,5; 5,0] <,0001[3]
ECOG-PS (Interaction p-value: 0,2387)					

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 0	43/1070 (4,0)	4/1020 (0,4)	10,25 [3,69; 28,45] <,0001[2]	10,63 [3,80; 29,74] <,0001[3]	3,6 [2,4; 4,9] <,0001[3]
ECOG-PS 1	10/213 (4,7)	3/245 (1,2)	3,83 [1,07; 13,75] 0,0392[2]	3,97 [1,08; 14,63] 0,0257[3]	3,5 [0,3; 6,6] 0,0257[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Infections and infestations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,5500)					
< 65 years	44/918 (4,8)	26/937 (2,8)	1,73 [1,07; 2,78] 0,0245[2]	1,76 [1,08; 2,89] 0,0226[3]	2,0 [0,3; 3,8] 0,0226[3]
≥ 65 years	25/365 (6,8)	10/328 (3,0)	2,25 [1,10; 4,61] 0,0271[2]	2,34 [1,11; 4,95] 0,0225[3]	3,8 [0,6; 7,0] 0,0225[3]
Prior treatment (Interaction p-value: 0,2967)					
Neoadjuvant chemotherapy	24/430 (5,6)	13/415 (3,1)	1,78 [0,92; 3,45] 0,0869[2]	1,83 [0,92; 3,64] 0,0820[3]	2,4 [-0,3; 5,2] 0,0820[3]
Adjuvant chemotherapy	42/784 (5,4)	18/769 (2,3)	2,29 [1,33; 3,94] 0,0028[2]	2,36 [1,35; 4,14] 0,0020[3]	3,0 [1,1; 4,9] 0,0020[3]
No chemotherapy	3/69 (4,3)	5/81 (6,2)	0,70 [0,17; 2,84] 0,6224[2]	0,69 [0,16; 3,00] 0,7264[4]	-1,8 [-8,9; 5,3] 0,7264[4]
Region (Interaction p-value: 0,1715)					
North America / Europe	46/678 (6,8)	25/650 (3,8)	1,76 [1,10; 2,84] 0,0192[2]	1,82 [1,10; 3,00] 0,0173[3]	2,9 [0,5; 5,3] 0,0173[3]
Asia	7/203 (3,4)	7/201 (3,5)	0,99 [0,35; 2,77] 0,9850[2]	0,99 [0,34; 2,87] 0,9850[3]	-0,0 [-3,6; 3,5] 0,9850[3]
Other	16/402 (4,0)	4/414 (1,0)	4,12 [1,39; 12,22] 0,0107[2]	4,25 [1,41; 12,82] 0,0054[3]	3,0 [0,9; 5,1] 0,0054[3]
Primary tumor size (Interaction p-value: 0,0751)					
< 20 mm	17/331 (5,1)	5/335 (1,5)	3,44 [1,28; 9,22] 0,0140[2]	3,57 [1,30; 9,80] 0,0085[3]	3,6 [0,9; 6,4] 0,0085[3]
≥ 20 but < 50 mm	33/646 (5,1)	26/653 (4,0)	1,28 [0,78; 2,12] 0,3309[2]	1,30 [0,77; 2,20] 0,3295[3]	1,1 [-1,1; 3,4] 0,3295[3]
≥ 50 mm	19/289 (6,6)	5/265 (1,9)	3,48 [1,32; 9,20] 0,0117[2]	3,66 [1,35; 9,94] 0,0068[3]	4,7 [1,4; 8,0] 0,0068[3]
Number of positive lymph nodes (Interaction p-value: 0,8242)					
0-3	27/427 (6,3)	15/418 (3,6)	1,76 [0,95; 3,26] 0,0718[2]	1,81 [0,95; 3,46] 0,0674[3]	2,7 [-0,2; 5,7] 0,0674[3]
4-9	21/549 (3,8)	12/542 (2,2)	1,73 [0,86; 3,48] 0,1254[2]	1,76 [0,86; 3,61] 0,1203[3]	1,6 [-0,4; 3,6] 0,1203[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	21/307 (6,8)	9/305 (3,0)	2,32 [1,08; 4,98] 0,0312[2]	2,41 [1,09; 5,36] 0,0259[3]	3,9 [0,5; 7,3] 0,0259[3]
Tumor stage (Interaction p-value: 0,6341)					
IIA	6/113 (5,3)	3/114 (2,6)	2,02 [0,52; 7,87] 0,3122[2]	2,07 [0,51; 8,51] 0,3327[4]	2,7 [-2,4; 7,8] 0,3327[4]
IIB	10/151 (6,6)	9/136 (6,6)	1,00 [0,42; 2,39] 0,9987[2]	1,00 [0,39; 2,54] 0,9987[3]	0,0 [-5,8; 5,8] 0,9987[3]
IIIA	24/495 (4,8)	10/488 (2,0)	2,37 [1,14; 4,90] 0,0202[2]	2,44 [1,15; 5,15] 0,0163[3]	2,8 [0,5; 5,1] 0,0163[3]
IIIB	2/54 (3,7)	1/45 (2,2)	1,67 [0,16; 17,79] 0,6724[2]	1,69 [0,15; 19,30] 1,0000[4]	1,5 [-5,1; 8,1] 1,0000[4]
IIIC	27/468 (5,8)	13/480 (2,7)	2,13 [1,11; 4,08] 0,0224[2]	2,20 [1,12; 4,32] 0,0191[3]	3,1 [0,5; 5,6] 0,0191[3]
Tumor grade (Interaction p-value: 0,1246)					
G1	5/91 (5,5)	4/93 (4,3)	1,28 [0,35; 4,61] 0,7083[2]	1,29 [0,34; 4,98] 0,7457[4]	1,2 [-5,0; 7,4] 0,7457[4]
G2	34/612 (5,6)	10/603 (1,7)	3,35 [1,67; 6,72] 0,0007[2]	3,49 [1,71; 7,13] 0,0003[3]	3,9 [1,8; 6,0] 0,0003[3]
G3	26/527 (4,9)	21/506 (4,2)	1,19 [0,68; 2,09] 0,5465[2]	1,20 [0,67; 2,16] 0,5459[3]	0,8 [-1,8; 3,3] 0,5459[3]
GX	3/51 (5,9)	1/59 (1,7)	3,47 [0,37; 32,34] 0,2745[2]	3,63 [0,37; 35,99] 0,3349[4]	4,2 [-3,1; 11,4] 0,3349[4]
Race (Interaction p-value: 0,6629)					
White	55/958 (5,7)	28/944 (3,0)	1,94 [1,24; 3,02] 0,0037[2]	1,99 [1,25; 3,17] 0,0031[3]	2,8 [0,9; 4,6] 0,0031[3]
Asian	10/250 (4,0)	8/242 (3,3)	1,21 [0,49; 3,01] 0,6823[2]	1,22 [0,47; 3,14] 0,6818[3]	0,7 [-2,6; 4,0] 0,6818[3]
Other	4/62 (6,5)	0/64 (0,0)	9,29 [0,51; 168,95] 0,1322[2]	9,92 [0,52; 188,28] 0,0557[4]	6,5 [0,3; 12,6] 0,0557[4]
ECOG-PS (Interaction p-value: 0,7656)					
ECOG-PS 0	54/1070 (5,0)	26/1020 (2,5)	1,98 [1,25; 3,14] 0,0036[2]	2,03 [1,26; 3,27] 0,0029[3]	2,5 [0,9; 4,1] 0,0029[3]
ECOG-PS 1	15/213 (7,0)	10/245 (4,1)	1,73 [0,79; 3,76] 0,1699[2]	1,78 [0,78; 4,05] 0,1642[3]	3,0 [-1,3; 7,2] 0,1642[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class					

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Investigations from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,1773)					
< 65 years	175/918 (19,1)	18/937 (1,9)	9,92 [6,16; 15,98] <,0001[2]	12,03 [7,33; 19,72] <,0001[3]	17,1 [14,5; 19,8] <,0001[3]
≥ 65 years	71/365 (19,5)	11/328 (3,4)	5,80 [3,13; 10,75] <,0001[2]	6,96 [3,62; 13,39] <,0001[3]	16,1 [11,6; 20,6] <,0001[3]
Prior treatment (Interaction p-value: 0,3053)					
Neoadjuvant chemotherapy	102/430 (23,7)	12/415 (2,9)	8,20 [4,58; 14,69] <,0001[2]	10,44 [5,64; 19,33] <,0001[3]	20,8 [16,5; 25,2] <,0001[3]
Adjuvant chemotherapy	131/784 (16,7)	13/769 (1,7)	9,88 [5,64; 17,32] <,0001[2]	11,67 [6,54; 20,83] <,0001[3]	15,0 [12,3; 17,8] <,0001[3]
No chemotherapy	13/69 (18,8)	4/81 (4,9)	3,82 [1,30; 11,16] 0,0145[2]	4,47 [1,38; 14,43] 0,0074[3]	13,9 [3,5; 24,3] 0,0074[3]
Region (Interaction p-value: 0,3436)					
North America / Europe	110/678 (16,2)	12/650 (1,8)	8,79 [4,89; 15,79] <,0001[2]	10,30 [5,61; 18,88] <,0001[3]	14,4 [11,4; 17,3] <,0001[3]
Asia	89/203 (43,8)	8/201 (4,0)	11,02 [5,49; 22,11] <,0001[2]	18,83 [8,81; 40,26] <,0001[3]	39,9 [32,5; 47,2] <,0001[3]
Other	47/402 (11,7)	9/414 (2,2)	5,38 [2,67; 10,83] <,0001[2]	5,96 [2,88; 12,33] <,0001[3]	9,5 [6,1; 13,0] <,0001[3]
Primary tumor size (Interaction p-value: 0,8394)					
< 20 mm	51/331 (15,4)	7/335 (2,1)	7,37 [3,40; 16,01] <,0001[2]	8,53 [3,81; 19,11] <,0001[3]	13,3 [9,1; 17,5] <,0001[3]
≥ 20 but < 50 mm	134/646 (20,7)	15/653 (2,3)	9,03 [5,36; 15,23] <,0001[2]	11,13 [6,45; 19,22] <,0001[3]	18,4 [15,1; 21,8] <,0001[3]
≥ 50 mm	57/289 (19,7)	5/265 (1,9)	10,45 [4,25; 25,68] <,0001[2]	12,78 [5,04; 32,42] <,0001[3]	17,8 [13,0; 22,7] <,0001[3]
Number of positive lymph nodes (Interaction p-value: 0,0897)					
0-3	80/427 (18,7)	4/418 (1,0)	19,58 [7,24; 52,96] <,0001[2]	23,86 [8,65; 65,79] <,0001[3]	17,8 [14,0; 21,6] <,0001[3]
4-9	95/549 (17,3)	12/542 (2,2)	7,82 [4,34; 14,08] <,0001[2]	9,24 [5,00; 17,07] <,0001[3]	15,1 [11,7; 18,5] <,0001[3]
≥ 10	71/307 (23,1)	13/305 (4,3)	5,43 [3,07; 9,59] <,0001[2]	6,76 [3,65; 12,51] <,0001[3]	18,9 [13,6; 24,1] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tumor stage (Interaction p-value: 0,7337)					
IIA	18/113 (15,9)	1/114 (0,9)	18,16 [2,47; 133,75] 0,0044[2]	21,41 [2,81; 163,36] <,0001[3]	15,1 [8,1; 22,0] <,0001[3]
IIB	28/151 (18,5)	3/136 (2,2)	8,41 [2,61; 27,03] 0,0004[2]	10,09 [2,99; 34,04] <,0001[3]	16,3 [9,7; 23,0] <,0001[3]
IIIA	88/495 (17,8)	8/488 (1,6)	10,84 [5,32; 22,12] <,0001[2]	12,97 [6,22; 27,07] <,0001[3]	16,1 [12,6; 19,7] <,0001[3]
IIIB	10/54 (18,5)	1/45 (2,2)	8,33 [1,11; 62,64] 0,0394[2]	10,00 [1,23; 81,47] 0,0102[3]	16,3 [5,1; 27,5] 0,0102[3]
IIIC	101/468 (21,6)	16/480 (3,3)	6,47 [3,88; 10,80] <,0001[2]	7,98 [4,63; 13,76] <,0001[3]	18,2 [14,2; 22,3] <,0001[3]
Tumor grade (Interaction p-value: 0,6727)					
G1	16/91 (17,6)	1/93 (1,1)	16,35 [2,21; 120,76] 0,0062[2]	19,63 [2,54; 151,42] 0,0001[3]	16,5 [8,4; 24,6] 0,0001[3]
G2	117/612 (19,1)	16/603 (2,7)	7,20 [4,33; 12,00] <,0001[2]	8,67 [5,07; 14,82] <,0001[3]	16,5 [13,1; 19,8] <,0001[3]
G3	98/527 (18,6)	9/506 (1,8)	10,45 [5,34; 20,47] <,0001[2]	12,61 [6,30; 25,27] <,0001[3]	16,8 [13,3; 20,3] <,0001[3]
GX	15/51 (29,4)	3/59 (5,1)	5,78 [1,77; 18,85] 0,0036[2]	7,78 [2,10; 28,78] 0,0006[3]	24,3 [10,6; 38,0] 0,0006[3]
Race (Interaction p-value: 0,5921)					
White	139/958 (14,5)	19/944 (2,0)	7,21 [4,50; 11,54] <,0001[2]	8,26 [5,07; 13,47] <,0001[3]	12,5 [10,1; 14,9] <,0001[3]
Asian	92/250 (36,8)	8/242 (3,3)	11,13 [5,53; 22,43] <,0001[2]	17,03 [8,04; 36,06] <,0001[3]	33,5 [27,1; 39,9] <,0001[3]
Other	14/62 (22,6)	2/64 (3,1)	7,23 [1,71; 30,49] 0,0071[2]	9,04 [1,96; 41,70] 0,0010[3]	19,5 [8,2; 30,7] 0,0010[3]
First endocrine therapy (Interaction p-value: 0,8074)					
Tamoxifen	12/114 (10,5)	2/132 (1,5)	6,95 [1,59; 30,39] 0,0100[2]	7,65 [1,67; 34,94] 0,0023[3]	9,0 [3,0; 15,0] 0,0023[3]
Aromatase inhibitor	234/1169 (20,0)	27/1133 (2,4)	8,40 [5,69; 12,40] <,0001[2]	10,25 [6,82; 15,41] <,0001[3]	17,6 [15,2; 20,1] <,0001[3]
ECOG-PS (Interaction p-value: 0,9379)					
ECOG-PS 0	211/1070 (19,7)	24/1020 (2,4)	8,38 [5,54; 12,67] <,0001[2]	10,19 [6,62; 15,70] <,0001[3]	17,4 [14,8; 19,9] <,0001[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS 1	35/213 (16,4)	5/245 (2,0)	8,05 [3,21; 20,18] <,0001[2]	9,44 [3,63; 24,57] <,0001[3]	14,4 [9,1; 19,7] <,0001[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Metabolism and nutrition disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,7852)					
< 65 years	35/918 (3,8)	12/937 (1,3)	2,98 [1,56; 5,70] 0,0010[2]	3,06 [1,58; 5,92] 0,0005[3]	2,5 [1,1; 4,0] 0,0005[3]
≥ 65 years	29/365 (7,9)	10/328 (3,0)	2,61 [1,29; 5,26] 0,0076[2]	2,74 [1,32; 5,72] 0,0052[3]	4,9 [1,6; 8,2] 0,0052[3]
Prior treatment (Interaction p-value: 0,2503)					
Neoadjuvant chemotherapy	18/430 (4,2)	10/415 (2,4)	1,74 [0,81; 3,72] 0,1550[2]	1,77 [0,81; 3,88] 0,1492[3]	1,8 [-0,6; 4,2] 0,1492[3]
Adjuvant chemotherapy	40/784 (5,1)	11/769 (1,4)	3,57 [1,84; 6,90] 0,0002[2]	3,70 [1,89; 7,28] <,0001[3]	3,7 [1,9; 5,4] <,0001[3]
No chemotherapy	6/69 (8,7)	1/81 (1,2)	7,04 [0,87; 57,09] 0,0675[2]	7,62 [0,89; 64,93] 0,0485[4]	7,5 [0,4; 14,5] 0,0485[4]
Region (Interaction p-value: 0,3325)					
North America / Europe	33/678 (4,9)	13/650 (2,0)	2,43 [1,29; 4,58] 0,0059[2]	2,51 [1,31; 4,81] 0,0043[3]	2,9 [0,9; 4,8] 0,0043[3]
Asia	12/203 (5,9)	1/201 (0,5)	11,88 [1,56; 90,53] 0,0169[2]	12,57 [1,62; 97,57] 0,0020[3]	5,4 [2,0; 8,8] 0,0020[3]
Other	19/402 (4,7)	8/414 (1,9)	2,45 [1,08; 5,52] 0,0314[2]	2,52 [1,09; 5,82] 0,0257[3]	2,8 [0,3; 5,3] 0,0257[3]
Primary tumor size (Interaction p-value: 0,3553)					
< 20 mm	17/331 (5,1)	9/335 (2,7)	1,91 [0,86; 4,23] 0,1095[2]	1,96 [0,86; 4,46] 0,1027[3]	2,4 [-0,5; 5,4] 0,1027[3]
≥ 20 but < 50 mm	28/646 (4,3)	10/653 (1,5)	2,83 [1,39; 5,78] 0,0043[2]	2,91 [1,40; 6,05] 0,0027[3]	2,8 [1,0; 4,6] 0,0027[3]
≥ 50 mm	18/289 (6,2)	3/265 (1,1)	5,50 [1,64; 18,47] 0,0058[2]	5,80 [1,69; 19,93] 0,0017[3]	5,1 [2,0; 8,2] 0,0017[3]
Number of positive lymph nodes (Interaction p-value: 0,6392)					
0-3	17/427 (4,0)	8/418 (1,9)	2,08 [0,91; 4,77] 0,0835[2]	2,13 [0,91; 4,98] 0,0762[3]	2,1 [-0,2; 4,3] 0,0762[3]
4-9	29/549 (5,3)	8/542 (1,5)	3,58 [1,65; 7,76] 0,0012[2]	3,72 [1,69; 8,22] 0,0005[3]	3,8 [1,7; 5,9] 0,0005[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	18/307 (5,9)	6/305 (2,0)	2,98 [1,20; 7,41] 0,0187[2]	3,10 [1,21; 7,93] 0,0130[3]	3,9 [0,8; 7,0] 0,0130[3]
Tumor stage (Interaction p-value: 0,3366)					
IIA	4/113 (3,5)	1/114 (0,9)	4,04 [0,46; 35,55] 0,2089[2]	4,15 [0,46; 37,69] 0,2125[4]	2,7 [-1,2; 6,5] 0,2125[4]
IIB	4/151 (2,6)	3/136 (2,2)	1,20 [0,27; 5,27] 0,8083[2]	1,21 [0,27; 5,49] 1,0000[4]	0,4 [-3,1; 4,0] 1,0000[4]
IIIA	24/495 (4,8)	6/488 (1,2)	3,94 [1,63; 9,56] 0,0024[2]	4,09 [1,66; 10,10] 0,0010[3]	3,6 [1,5; 5,7] 0,0010[3]
IIIB	1/54 (1,9)	2/45 (4,4)	0,42 [0,04; 4,45] 0,4686[2]	0,41 [0,04; 4,63] 0,5894[4]	-2,6 [-9,6; 4,4] 0,5894[4]
IIIC	31/468 (6,6)	10/480 (2,1)	3,18 [1,58; 6,41] 0,0012[2]	3,33 [1,62; 6,88] 0,0006[3]	4,5 [2,0; 7,1] 0,0006[3]
Tumor grade (Interaction p-value: 0,6269)					
G1	7/91 (7,7)	0/93 (0,0)	15,33 [0,89; 264,49] 0,0603[2]	16,60 [0,93; 295,02] 0,0064[4]	7,7 [2,2; 13,2] 0,0064[4]
G2	29/612 (4,7)	16/603 (2,7)	1,79 [0,98; 3,25] 0,0582[2]	1,82 [0,98; 3,40] 0,0543[3]	2,1 [-0,0; 4,2] 0,0543[3]
G3	23/527 (4,4)	6/506 (1,2)	3,68 [1,51; 8,96] 0,0041[2]	3,80 [1,54; 9,42] 0,0020[3]	3,2 [1,2; 5,2] 0,0020[3]
GX	5/51 (9,8)	0/59 (0,0)	12,69 [0,72; 224,11] 0,0828[2]	14,08 [0,76; 261,07] 0,0192[4]	9,8 [1,6; 18,0] 0,0192[4]
Progesterone receptor status (Interaction p-value: 0,0916)					
Negative	4/156 (2,6)	4/169 (2,4)	1,08 [0,28; 4,26] 0,9087[2]	1,09 [0,27; 4,42] 1,0000[4]	0,2 [-3,2; 3,6] 1,0000[4]
Positive	60/1089 (5,5)	18/1067 (1,7)	3,27 [1,94; 5,49] <,0001[2]	3,40 [1,99; 5,79] <,0001[3]	3,8 [2,3; 5,4] <,0001[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,2878)					
White	44/958 (4,6)	19/944 (2,0)	2,28 [1,34; 3,88] 0,0023[2]	2,34 [1,36; 4,04] 0,0017[3]	2,6 [1,0; 4,2] 0,0017[3]
Asian	12/250 (4,8)	1/242 (0,4)	11,62 [1,52; 88,65] 0,0180[2]	12,15 [1,57; 94,19] 0,0024[3]	4,4 [1,6; 7,2] 0,0024[3]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Other	7/62 (11,3)	2/64 (3,1)	3,61 [0,78; 16,72] 0,1003[2]	3,95 [0,79; 19,79] 0,0929[4]	8,2 [-0,8; 17,1] 0,0929[4]
First endocrine therapy (Interaction p-value: 0,8024)					
Tamoxifen	6/114 (5,3)	2/132 (1,5)	3,47 [0,72; 16,87] 0,1226[2]	3,61 [0,71; 18,26] 0,1495[4]	3,7 [-0,9; 8,3] 0,1495[4]
Aromatase inhibitor	58/1169 (5,0)	20/1133 (1,8)	2,81 [1,70; 4,64] <,0001[2]	2,91 [1,74; 4,86] <,0001[3]	3,2 [1,7; 4,7] <,0001[3]
ECOG-PS (Interaction p-value: 0,2656)					
ECOG-PS 0	50/1070 (4,7)	19/1020 (1,9)	2,51 [1,49; 4,22] 0,0005[2]	2,58 [1,51; 4,41] 0,0003[3]	2,8 [1,3; 4,3] 0,0003[3]
ECOG-PS 1	14/213 (6,6)	3/245 (1,2)	5,37 [1,56; 18,43] 0,0076[2]	5,68 [1,61; 20,03] 0,0025[3]	5,3 [1,7; 8,9] 0,0025[3]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Subgroups - adverse events with CTCAE Grade ≥ 3 according SOC Respiratory, thoracic and mediastinal disorders from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Age (Interaction p-value: 0,2635)					
< 65 years	13/918 (1,4)	8/937 (0,9)	1,66 [0,69; 3,98] 0,2576[2]	1,67 [0,69; 4,04] 0,2524[3]	0,6 [-0,4; 1,5] 0,2524[3]
≥ 65 years	10/365 (2,7)	2/328 (0,6)	4,49 [0,99; 20,36] 0,0513[2]	4,59 [1,00; 21,11] 0,0319[3]	2,1 [0,3; 4,0] 0,0319[3]
Prior treatment (Interaction p-value: 0,8206)					
Neoadjuvant chemotherapy	4/430 (0,9)	3/415 (0,7)	1,29 [0,29; 5,71] 0,7402[2]	1,29 [0,29; 5,80] 1,0000[4]	0,2 [-1,0; 1,4] 1,0000[4]
Adjuvant chemotherapy	16/784 (2,0)	7/769 (0,9)	2,24 [0,93; 5,42] 0,0730[2]	2,27 [0,93; 5,54] 0,0652[3]	1,1 [-0,1; 2,3] 0,0652[3]
No chemotherapy	3/69 (4,3)	0/81 (0,0)	8,20 [0,43; 156,04] 0,1615[2]	8,58 [0,44; 169,04] 0,0950[4]	4,3 [-0,5; 9,2] 0,0950[4]
Region (Interaction p-value: 0,7592)					
North America / Europe	16/678 (2,4)	6/650 (0,9)	2,56 [1,01; 6,49] 0,0484[2]	2,59 [1,01; 6,67] 0,0403[3]	1,4 [0,1; 2,8] 0,0403[3]
Asia	3/203 (1,5)	1/201 (0,5)	2,97 [0,31; 28,32] 0,3440[2]	3,00 [0,31; 29,09] 0,6232[4]	1,0 [-0,9; 2,9] 0,6232[4]
Other	4/402 (1,0)	3/414 (0,7)	1,37 [0,31; 6,10] 0,6767[2]	1,38 [0,31; 6,19] 0,7217[4]	0,3 [-1,0; 1,5] 0,7217[4]
Primary tumor size (Interaction p-value: 0,4954)					
< 20 mm	3/331 (0,9)	2/335 (0,6)	1,52 [0,26; 9,03] 0,6462[2]	1,52 [0,25; 9,17] 0,6847[4]	0,3 [-1,0; 1,6] 0,6847[4]
≥ 20 but < 50 mm	18/646 (2,8)	6/653 (0,9)	3,03 [1,21; 7,59] 0,0178[2]	3,09 [1,22; 7,84] 0,0125[3]	1,9 [0,4; 3,3] 0,0125[3]
≥ 50 mm	2/289 (0,7)	2/265 (0,8)	0,92 [0,13; 6,46] 0,9307[2]	0,92 [0,13; 6,55] 1,0000[4]	-0,1 [-1,5; 1,4] 1,0000[4]
Number of positive lymph nodes (Interaction p-value: 0,8880)					
0-3	9/427 (2,1)	3/418 (0,7)	2,94 [0,80; 10,77] 0,1042[2]	2,98 [0,80; 11,08] 0,0877[3]	1,4 [-0,2; 3,0] 0,0877[3]
4-9	6/549 (1,1)	3/542 (0,6)	1,97 [0,50; 7,85] 0,3342[2]	1,99 [0,49; 7,98] 0,5061[4]	0,5 [-0,5; 1,6] 0,5061[4]

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
≥ 10	8/307 (2,6)	4/305 (1,3)	1,99 [0,60; 6,53] 0,2580[2]	2,01 [0,60; 6,76] 0,2482[3]	1,3 [-0,9; 3,5] 0,2482[3]
Tumor stage (Interaction p-value: 0,9138)					
IIA	2/113 (1,8)	0/114 (0,0)	5,04 [0,24; 103,90] 0,2945[2]	5,13 [0,24; 108,15] 0,2467[4]	1,8 [-0,7; 4,2] 0,2467[4]
IIB	6/151 (4,0)	1/136 (0,7)	5,40 [0,66; 44,32] 0,1161[2]	5,59 [0,66; 47,00] 0,1240[4]	3,2 [-0,2; 6,7] 0,1240[4]
IIIA	7/495 (1,4)	3/488 (0,6)	2,30 [0,60; 8,84] 0,2254[2]	2,32 [0,60; 9,02] 0,3414[4]	0,8 [-0,5; 2,0] 0,3414[4]
IIIB	0/54 (0,0)	1/45 (2,2)	0,28 [0,01; 6,68] 0,4306[2]	0,27 [0,01; 6,85] 0,4545[4]	-2,2 [-6,5; 2,1] 0,4545[4]
IIIC	8/468 (1,7)	5/480 (1,0)	1,64 [0,54; 4,98] 0,3818[2]	1,65 [0,54; 5,09] 0,3768[3]	0,7 [-0,8; 2,2] 0,3768[3]
Tumor grade (Interaction p-value: 0,8373)					
G1	2/91 (2,2)	1/93 (1,1)	2,04 [0,19; 22,15] 0,5565[2]	2,07 [0,18; 23,21] 0,6189[4]	1,1 [-2,5; 4,8] 0,6189[4]
G2	9/612 (1,5)	5/603 (0,8)	1,77 [0,60; 5,26] 0,3017[2]	1,79 [0,59; 5,36] 0,2949[3]	0,6 [-0,6; 1,8] 0,2949[3]
G3	12/527 (2,3)	3/506 (0,6)	3,84 [1,09; 13,53] 0,0362[2]	3,91 [1,10; 13,93] 0,0237[3]	1,7 [0,2; 3,1] 0,0237[3]
GX	0/51 (0,0)	1/59 (1,7)	0,38 [0,02; 9,24] 0,5558[2]	0,38 [0,02; 9,50] 1,0000[4]	-1,7 [-5,0; 1,6] 1,0000[4]
Progesterone receptor status (Interaction p-value: 0,4887)					
Negative	5/156 (3,2)	3/169 (1,8)	1,81 [0,44; 7,43] 0,4130[2]	1,83 [0,43; 7,80] 0,4876[4]	1,4 [-2,0; 4,8] 0,4876[4]
Positive	18/1089 (1,7)	6/1067 (0,6)	2,94 [1,17; 7,38] 0,0216[2]	2,97 [1,18; 7,52] 0,0158[3]	1,1 [0,2; 2,0] 0,0158[3]
Unknown	0/10 (0,0)	0/7 (0,0)	NE	NE	NE
Race (Interaction p-value: 0,6138)					
White	17/958 (1,8)	9/944 (1,0)	1,86 [0,83; 4,15] 0,1294[2]	1,88 [0,83; 4,23] 0,1231[3]	0,8 [-0,2; 1,9] 0,1231[3]
Asian	6/250 (2,4)	1/242 (0,4)	5,81 [0,70; 47,89] 0,1022[2]	5,93 [0,71; 49,59] 0,1227[4]	2,0 [-0,1; 4,0] 0,1227[4]
Other	0/62 (0,0)	0/64 (0,0)	NE	NE	NE

Subgroup	Abemaciclib+ET[1] Pat. with event n/N (%)	ET[1] Pat. with event n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
ECOG-PS (Interaction p-value: 0,1224)					
ECOG-PS 0	15/1070 (1,4)	9/1020 (0,9)	1,59 [0,70; 3,61] 0,2696[2]	1,60 [0,70; 3,67] 0,2652[3]	0,5 [-0,4; 1,4] 0,2652[3]
ECOG-PS 1	8/213 (3,8)	1/245 (0,4)	9,20 [1,16; 72,98] 0,0357[2]	9,52 [1,18; 76,76] 0,0143[4]	3,3 [0,7; 6,0] 0,0143[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to appropriate comparator by GBA: Anastrozol, Letrozol; Anastrozol or Exemestan in sequence after Tamoxifen; 2: from Z-test; 3: from Chi^2-test; 4: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ECOG-PS: Eastern Cooperative Oncology Group - Performance Status; ET: endocrine therapy; mm: millimeter; n: number of patients with event; N: total number of patients in analysis; NE: not evaluated; OR: odds ratio; RR: relative risk; SOC: system organ class

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Anhang 4-G3: Sensitivitätsanalyse der Patienten, die initial eine der ZVT konformen Therapie erhielten - MONARCH-E

Anhang 4-G3.1: Charakterisierung der Population (Demographie und Baseline) - Sensitivitätsanalyse

Tabelle 4-136 (Anhang): Charakterisierung der Population (Demographie und Baseline) - Sensitivitätsanalyse

Tabelle: Charakterisierung der (Kohorte 1 Population - ITT - Prämenopausal) Studienpopulation (Demographie) - RCT mit dem zu bewertenden Arzneimittel - Monarch-E

	Abemaciclib+ET[1] (N = 630)	**ET[1] (N = 639)**	**Gesamt (N = 1269)**
Alter, Jahre, n	630	639	1269
Mittelwert (SD)	43,6 (6,1)	43,6 (6,1)	43,6 (6,1)
Median (Min-Max)	44,0 (23-57)	45,0 (24-59)	44,0 (23-59)
Altersgruppen, n (%)	630	639	1269
< 40 Jahre	141 (22,4)	153 (23,9)	294 (23,2)
≥ 40 bis < 50 Jahre	378 (60,0)	386 (60,4)	764 (60,2)
≥ 50 bis < 60 Jahre	111 (17,6)	100 (15,6)	211 (16,6)
< 65 Jahre	630 (100,0)	639 (100,0)	1269 (100,0)
≥ 60 bis < 70 Jahre	0 (0,0)	0 (0,0)	0 (0,0)
≥ 65 Jahre	0 (0,0)	0 (0,0)	0 (0,0)
≥ 70 bis < 80 Jahre	0 (0,0)	0 (0,0)	0 (0,0)
≥ 80 Jahre	0 (0,0)	0 (0,0)	0 (0,0)
Ethnische Zugehörigkeit 1, n (%)	617	626	1243
Amerikanische Ureinwohner/indigene Bevölkerung Alaskas	11 (1,8)	12 (1,9)	23 (1,9)
Asiatisch	209 (33,9)	200 (31,9)	409 (32,9)
Schwarz/afro-amerikanisch	8 (1,3)	9 (1,4)	17 (1,4)
Ureinwohner Hawaii oder Pazifik-Inseln	0 (0,0)	2 (0,3)	2 (0,2)
Weiß/kaukasisch	385 (62,4)	399 (63,7)	784 (63,1)
Multiple	4 (0,6)	4 (0,6)	8 (0,6)
Fehlend	13	13	26
Ethnische Zugehörigkeit 2, n (%)[2]	48	44	92
Hispanisch/Latino	4 (8,3)	2 (4,5)	6 (6,5)
Nicht hispanisch/Latino	44 (91,7)	42 (95,5)	86 (93,5)
Fehlend	0	0	0
Region, n (%)	630	639	1269
Nordamerika / Europa	301 (47,8)	298 (46,6)	599 (47,2)
Asien	175 (27,8)	182 (28,5)	357 (28,1)
Andere	154 (24,4)	159 (24,9)	313 (24,7)
ECOG PS, n (%)	630	639	1269
0	564 (89,5)	568 (88,9)	1132 (89,2)
1	66 (10,5)	71 (11,1)	137 (10,8)
2	0 (0,0)	0 (0,0)	0 (0,0)
3	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	0	0	0
Gewicht, kg, n	627	636	1263
Mittelwert (SD)	69,2 (16,4)	69,2 (16,2)	69,2 (16,3)
Median (Min-Max)	66,6 (40,0-165,2)	66,7 (35,3-153,2)	66,7 (35,3-165,2)
BMI (kg/m^2), n	617	631	1248
Mittelwert (SD)	26,3 (6,0)	26,2 (5,9)	26,3 (5,9)
Median (Min-Max)	25,2 (16,1-63,3)	25,2 (13,9-65,3)	25,2 (13,9-65,3)
< 18,5	20 (3,2)	21 (3,3)	41 (3,3)

	Abemaciclib+ET[1] (N = 630)	**ET[1] (N = 639)**	**Gesamt (N = 1269)**
≥ 18,5 bis < 25	274 (44,4)	288 (45,6)	562 (45,0)
≥ 25 bis < 30	194 (31,4)	183 (29,0)	377 (30,2)
≥ 30	129 (20,9)	139 (22,0)	268 (21,5)
Fehlend	13	8	21
Land, n (%)	630	639	1269
Argentinien	15 (2,4)	17 (2,7)	32 (2,5)
Australien	16 (2,5)	19 (3,0)	35 (2,8)
Belgien	5 (0,8)	5 (0,8)	10 (0,8)
Brasilien	31 (4,9)	37 (5,8)	68 (5,4)
China	2 (0,3)	2 (0,3)	4 (0,3)
Dänemark	22 (3,5)	24 (3,8)	46 (3,6)
Deutschland	49 (7,8)	42 (6,6)	91 (7,2)
Finnland	14 (2,2)	16 (2,5)	30 (2,4)
Frankreich	31 (4,9)	35 (5,5)	66 (5,2)
Griechenland	14 (2,2)	17 (2,7)	31 (2,4)
Großbritannien	32 (5,1)	32 (5,0)	64 (5,0)
Hongkong	4 (0,6)	5 (0,8)	9 (0,7)
Indien	23 (3,7)	13 (2,0)	36 (2,8)
Israel	6 (1,0)	3 (0,5)	9 (0,7)
Italien	4 (0,6)	2 (0,3)	6 (0,5)
Japan	81 (12,9)	81 (12,7)	162 (12,8)
Kanada	4 (0,6)	3 (0,5)	7 (0,6)
Republik Korea	65 (10,3)	64 (10,0)	129 (10,2)
Mexiko	14 (2,2)	16 (2,5)	30 (2,4)
Neuseeland	2 (0,3)	4 (0,6)	6 (0,5)
Niederlande	0 (0,0)	3 (0,5)	3 (0,2)
Österreich	2 (0,3)	0 (0,0)	2 (0,2)
Polen	11 (1,7)	13 (2,0)	24 (1,9)
Portugal	5 (0,8)	1 (0,2)	6 (0,5)
Puerto Rico	0 (0,0)	0 (0,0)	0 (0,0)
Rumänien	8 (1,3)	8 (1,3)	16 (1,3)
Russland	10 (1,6)	10 (1,6)	20 (1,6)
Saudi-Arabien	1 (0,2)	2 (0,3)	3 (0,2)
Schweden	2 (0,3)	2 (0,3)	4 (0,3)
Singapur	1 (0,2)	7 (1,1)	8 (0,6)
Spanien	42 (6,7)	39 (6,1)	81 (6,4)
Südafrika	0 (0,0)	1 (0,2)	1 (0,1)
Taiwan	22 (3,5)	23 (3,6)	45 (3,5)
Tschechien	2 (0,3)	3 (0,5)	5 (0,4)
Türkei	38 (6,0)	38 (5,9)	76 (6,0)
Ukraine	0 (0,0)	0 (0,0)	0 (0,0)
Ungarn	4 (0,6)	8 (1,3)	12 (0,9)
USA	48 (7,6)	44 (6,9)	92 (7,2)
Vorherige Chemotherapie, n (%)	630	639	1269
Adjuvante Chemotherapie	370 (58,7)	372 (58,2)	742 (58,5)

	Abemaciclib+ET[1] (N = 630)	**ET[1] (N = 639)**	**Gesamt (N = 1269)**
Neoadjuvante Chemotherapie	251 (39,8)	261 (40,8)	512 (40,3)
Keine Chemotherapie	9 (1,4)	6 (0,9)	15 (1,2)
Endokrine Therapie zu Beginn, n (%)	630	639	1269
Aromatase-Inhibitor	0 (0,0)	0 (0,0)	0 (0,0)
Tamoxifen	630 (100,0)	639 (100,0)	1269 (100,0)

1: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
2: Enthält nur Angaben der Zentren in USA, n ist die Anzahl der Patienten mit 'Hispanisch/Latino' oder 'Nicht hispanisch/Latino'
Abkürzungen: BMI: Body Mass Index; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; ITT: Intention to treat; kg: Kilogramm; m: Meter; Max: Maximum; Min: Minimum; n: Anzahl der Patienten; N: Gesamtzahl Population; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung; USA: Vereinigte Staaten von Amerika

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Tabelle: Charakterisierung der (Kohorte 1 Population - ITT - Postmenopausal) Studienpopulation (Demographie) - RCT mit dem zu bewertenden Arzneimittel - Monarch-E

	Abemaciclib+ET[1] (N = 1364)	**ET[1] (N = 1384)**	**Gesamt (N = 2748)**
Alter, Jahre, n	1364	1384	2748
Mittelwert (SD)	59,2 (9,0)	59,1 (9,1)	59,2 (9,0)
Median (Min-Max)	59,0 (32-89)	59,0 (27-86)	59,0 (27-89)
Altersgruppen, n (%)	1364	1384	2748
< 40 Jahre	17 (1,2)	28 (2,0)	45 (1,6)
≥ 40 bis < 50 Jahre	167 (12,2)	162 (11,7)	329 (12,0)
≥ 50 bis < 60 Jahre	535 (39,2)	522 (37,7)	1057 (38,5)
< 65 Jahre	984 (72,1)	1027 (74,2)	2011 (73,2)
≥ 60 bis < 70 Jahre	485 (35,6)	490 (35,4)	975 (35,5)
≥ 65 Jahre	380 (27,9)	357 (25,8)	737 (26,8)
≥ 70 bis < 80 Jahre	137 (10,0)	165 (11,9)	302 (11,0)
≥ 80 Jahre	23 (1,7)	17 (1,2)	40 (1,5)
Ethnische Zugehörigkeit 1, n (%)	1351	1365	2716
Amerikanische Ureinwohner/indigene Bevölkerung Alaskas	29 (2,1)	33 (2,4)	62 (2,3)
Asiatisch	259 (19,2)	251 (18,4)	510 (18,8)
Schwarz/afro-amerikanisch	24 (1,8)	24 (1,8)	48 (1,8)
Ureinwohner Hawaii oder Pazifik-Inseln	2 (0,1)	1 (0,1)	3 (0,1)
Weiß/kaukasisch	1028 (76,1)	1047 (76,7)	2075 (76,4)
Multiple	9 (0,7)	9 (0,7)	18 (0,7)
Fehlend	13	19	32
Ethnische Zugehörigkeit 2, n (%)[2]	217	226	443
Hispanisch/Latino	16 (7,4)	22 (9,7)	38 (8,6)
Nicht hispanisch/Latino	201 (92,6)	204 (90,3)	405 (91,4)
Fehlend	3	4	7
Region, n (%)	1364	1384	2748
Nordamerika / Europa	739 (54,2)	747 (54,0)	1486 (54,1)
Asien	209 (15,3)	207 (15,0)	416 (15,1)
Andere	416 (30,5)	430 (31,1)	846 (30,8)
ECOG PS, n (%)	1364	1384	2748
0	1135 (83,2)	1111 (80,3)	2246 (81,7)
1	229 (16,8)	273 (19,7)	502 (18,3)
2	0 (0,0)	0 (0,0)	0 (0,0)
3	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	0	0	0
Gewicht, kg, n	1357	1381	2738
Mittelwert (SD)	72,6 (16,0)	73,1 (15,7)	72,8 (15,9)
Median (Min-Max)	69,9 (34,0-158,0)	70,0 (36,1-137,6)	70,0 (34,0-158,0)
BMI (kg/m^2), n	1333	1370	2703
Mittelwert (SD)	28,0 (5,8)	28,2 (5,8)	28,1 (5,8)
Median (Min-Max)	27,0 (15,6-63,3)	27,3 (16,2-56,5)	27,2 (15,6-63,3)
< 18,5	16 (1,2)	19 (1,4)	35 (1,3)

	Abemaciclib+ET[1] (N = 1364)	**ET[1] (N = 1384)**	**Gesamt (N = 2748)**
≥ 18,5 bis < 25	431 (32,3)	436 (31,8)	867 (32,1)
≥ 25 bis < 30	476 (35,7)	451 (32,9)	927 (34,3)
≥ 30	410 (30,8)	464 (33,9)	874 (32,3)
Fehlend	31	14	45
Land, n (%)	1364	1384	2748
Argentinien	45 (3,3)	28 (2,0)	73 (2,7)
Australien	60 (4,4)	63 (4,6)	123 (4,5)
Belgien	45 (3,3)	33 (2,4)	78 (2,8)
Brasilien	82 (6,0)	82 (5,9)	164 (6,0)
China	43 (3,2)	40 (2,9)	83 (3,0)
Dänemark	28 (2,1)	26 (1,9)	54 (2,0)
Deutschland	58 (4,3)	85 (6,1)	143 (5,2)
Finnland	28 (2,1)	27 (2,0)	55 (2,0)
Frankreich	35 (2,6)	47 (3,4)	82 (3,0)
Griechenland	37 (2,7)	37 (2,7)	74 (2,7)
Großbritannien	47 (3,4)	43 (3,1)	90 (3,3)
Hongkong	3 (0,2)	4 (0,3)	7 (0,3)
Indien	34 (2,5)	34 (2,5)	68 (2,5)
Israel	13 (1,0)	21 (1,5)	34 (1,2)
Italien	31 (2,3)	24 (1,7)	55 (2,0)
Japan	83 (6,1)	86 (6,2)	169 (6,1)
Kanada	11 (0,8)	4 (0,3)	15 (0,5)
Republik Korea	42 (3,1)	38 (2,7)	80 (2,9)
Mexiko	55 (4,0)	72 (5,2)	127 (4,6)
Neuseeland	11 (0,8)	7 (0,5)	18 (0,7)
Niederlande	3 (0,2)	8 (0,6)	11 (0,4)
Österreich	11 (0,8)	11 (0,8)	22 (0,8)
Polen	36 (2,6)	26 (1,9)	62 (2,3)
Portugal	10 (0,7)	10 (0,7)	20 (0,7)
Puerto Rico	1 (0,1)	2 (0,1)	3 (0,1)
Rumänien	28 (2,1)	34 (2,5)	62 (2,3)
Russland	38 (2,8)	47 (3,4)	85 (3,1)
Saudi-Arabien	2 (0,1)	4 (0,3)	6 (0,2)
Schweden	4 (0,3)	2 (0,1)	6 (0,2)
Singapur	7 (0,5)	10 (0,7)	17 (0,6)
Spanien	63 (4,6)	58 (4,2)	121 (4,4)
Südafrika	2 (0,1)	3 (0,2)	5 (0,2)
Taiwan	30 (2,2)	29 (2,1)	59 (2,1)
Tschechien	10 (0,7)	6 (0,4)	16 (0,6)
Türkei	57 (4,2)	56 (4,0)	113 (4,1)
Ukraine	36 (2,6)	33 (2,4)	69 (2,5)
Ungarn	15 (1,1)	14 (1,0)	29 (1,1)
USA	220 (16,1)	230 (16,6)	450 (16,4)
Vorherige Chemotherapie, n (%)	1364	1384	2748
Adjuvante Chemotherapie	841 (61,7)	846 (61,1)	1687 (61,4)

	Abemaciclib+ET[1] (N = 1364)	**ET[1] (N = 1384)**	**Gesamt (N = 2748)**
Neoadjuvante Chemotherapie	449 (32,9)	454 (32,8)	903 (32,9)
Keine Chemotherapie	74 (5,4)	84 (6,1)	158 (5,7)
Endokrine Therapie zu Beginn, n (%)	1364	1384	2748
Aromatase-Inhibitor	1222 (89,6)	1230 (88,9)	2452 (89,2)
Tamoxifen	142 (10,4)	154 (11,1)	296 (10,8)

1: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
2: Enthält nur Angaben der Zentren in USA, n ist die Anzahl der Patienten mit 'Hispanisch/Latino' oder 'Nicht hispanisch/Latino'
Abkürzungen: BMI: Body Mass Index; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; ITT: Intention to treat; kg: Kilogramm; m: Meter; Max: Maximum; Min: Minimum; n: Anzahl der Patienten; N: Gesamtzahl Population; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung; USA: Vereinigte Staaten von Amerika

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Tabelle: Charakterisierung der (Kohorte 1 Population - ITT - Männer) Studienpopulation (Demographie) - RCT mit dem zu bewertenden Arzneimittel - Monarch-E

	Abemaciclib+ET[1] (N = 11)	**ET[1] (N = 11)**	**Gesamt (N = 22)**
Alter, Jahre, n	11	11	22
Mittelwert (SD)	61,5 (8,5)	66,4 (9,6)	63,9 (9,2)
Median (Min-Max)	59,0 (43-72)	65,0 (54-82)	64,0 (43-82)
Altersgruppen, n (%)	11	11	22
< 40 Jahre	0 (0,0)	0 (0,0)	0 (0,0)
≥ 40 bis < 50 Jahre	1 (9,1)	0 (0,0)	1 (4,5)
≥ 50 bis < 60 Jahre	5 (45,5)	3 (27,3)	8 (36,4)
< 65 Jahre	6 (54,5)	5 (45,5)	11 (50,0)
≥ 60 bis < 70 Jahre	3 (27,3)	5 (45,5)	8 (36,4)
≥ 65 Jahre	5 (45,5)	6 (54,5)	11 (50,0)
≥ 70 bis < 80 Jahre	2 (18,2)	1 (9,1)	3 (13,6)
≥ 80 Jahre	0 (0,0)	2 (18,2)	2 (9,1)
Ethnische Zugehörigkeit 1, n (%)	10	11	21
Amerikanische Ureinwohner/indigene Bevölkerung Alaskas	0 (0,0)	0 (0,0)	0 (0,0)
Asiatisch	2 (20,0)	2 (18,2)	4 (19,0)
Schwarz/afro-amerikanisch	0 (0,0)	0 (0,0)	0 (0,0)
Ureinwohner Hawaii oder Pazifik-Inseln	0 (0,0)	0 (0,0)	0 (0,0)
Weiß/kaukasisch	8 (80,0)	9 (81,8)	17 (81,0)
Multiple	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	1	0	1
Ethnische Zugehörigkeit 2, n (%)[2]	1	3	4
Hispanisch/Latino	0 (0,0)	0 (0,0)	0 (0,0)
Nicht hispanisch/Latino	1 (100,0)	3 (100,0)	4 (100,0)
Fehlend	0	0	0
Region, n (%)	11	11	22
Nordamerika / Europa	6 (54,5)	9 (81,8)	15 (68,2)
Asien	0 (0,0)	2 (18,2)	2 (9,1)
Andere	5 (45,5)	0 (0,0)	5 (22,7)
ECOG PS, n (%)	11	11	22
0	9 (81,8)	10 (90,9)	19 (86,4)
1	2 (18,2)	1 (9,1)	3 (13,6)
2	0 (0,0)	0 (0,0)	0 (0,0)
3	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	0	0	0
Gewicht, kg, n	11	11	22
Mittelwert (SD)	91,8 (18,4)	85,9 (17,9)	88,9 (18,0)
Median (Min-Max)	90,0 (71,0-136,8)	82,0 (53,7-109,3)	86,6 (53,7-136,8)
BMI (kg/m^2), n	10	11	21
Mittelwert (SD)	28,4 (4,8)	28,7 (6,4)	28,6 (5,6)
Median (Min-Max)	27,9 (21,7-38,2)	26,9 (19,0-42,2)	27,1 (19,0-42,2)
< 18,5	0 (0,0)	0 (0,0)	0 (0,0)

	Abemaciclib+ET[1] (N = 11)	**ET[1] (N = 11)**	**Gesamt (N = 22)**
≥ 18,5 bis < 25	3 (30,0)	3 (27,3)	6 (28,6)
≥ 25 bis < 30	4 (40,0)	3 (27,3)	7 (33,3)
≥ 30	3 (30,0)	5 (45,5)	8 (38,1)
Fehlend	1	0	1
Land, n (%)	11	11	22
Argentinien	2 (18,2)	0 (0,0)	2 (9,1)
Australien	1 (9,1)	1 (9,1)	2 (9,1)
Belgien	0 (0,0)	1 (9,1)	1 (4,5)
Brasilien	0 (0,0)	0 (0,0)	0 (0,0)
China	0 (0,0)	0 (0,0)	0 (0,0)
Dänemark	0 (0,0)	1 (9,1)	1 (4,5)
Deutschland	0 (0,0)	0 (0,0)	0 (0,0)
Finnland	1 (9,1)	0 (0,0)	1 (4,5)
Frankreich	0 (0,0)	0 (0,0)	0 (0,0)
Griechenland	0 (0,0)	0 (0,0)	0 (0,0)
Großbritannien	1 (9,1)	0 (0,0)	1 (4,5)
Hongkong	0 (0,0)	0 (0,0)	0 (0,0)
Indien	1 (9,1)	0 (0,0)	1 (4,5)
Israel	0 (0,0)	0 (0,0)	0 (0,0)
Italien	0 (0,0)	0 (0,0)	0 (0,0)
Japan	0 (0,0)	2 (18,2)	2 (9,1)
Kanada	1 (9,1)	0 (0,0)	1 (4,5)
Republik Korea	0 (0,0)	0 (0,0)	0 (0,0)
Mexiko	0 (0,0)	0 (0,0)	0 (0,0)
Neuseeland	0 (0,0)	0 (0,0)	0 (0,0)
Niederlande	0 (0,0)	0 (0,0)	0 (0,0)
Österreich	1 (9,1)	0 (0,0)	1 (4,5)
Polen	0 (0,0)	2 (18,2)	2 (9,1)
Portugal	0 (0,0)	0 (0,0)	0 (0,0)
Puerto Rico	0 (0,0)	0 (0,0)	0 (0,0)
Rumänien	0 (0,0)	0 (0,0)	0 (0,0)
Russland	0 (0,0)	0 (0,0)	0 (0,0)
Saudi-Arabien	0 (0,0)	0 (0,0)	0 (0,0)
Schweden	0 (0,0)	0 (0,0)	0 (0,0)
Singapur	0 (0,0)	0 (0,0)	0 (0,0)
Spanien	0 (0,0)	1 (9,1)	1 (4,5)
Südafrika	0 (0,0)	0 (0,0)	0 (0,0)
Taiwan	0 (0,0)	0 (0,0)	0 (0,0)
Tschechien	0 (0,0)	0 (0,0)	0 (0,0)
Türkei	2 (18,2)	0 (0,0)	2 (9,1)
Ukraine	0 (0,0)	0 (0,0)	0 (0,0)
Ungarn	0 (0,0)	0 (0,0)	0 (0,0)
USA	1 (9,1)	3 (27,3)	4 (18,2)
Vorherige Chemotherapie, n (%)	11	11	22
Adjuvante Chemotherapie	7 (63,6)	7 (63,6)	14 (63,6)

	Abemaciclib+ET[1] (N = 11)	**ET[1] (N = 11)**	**Gesamt (N = 22)**
Neoadjuvante Chemotherapie	2 (18,2)	3 (27,3)	5 (22,7)
Keine Chemotherapie	2 (18,2)	1 (9,1)	3 (13,6)
Endokrine Therapie zu Beginn, n (%)	11	11	22
Aromatase-Inhibitor	0 (0,0)	0 (0,0)	0 (0,0)
Tamoxifen	11 (100,0)	11 (100,0)	22 (100,0)

1: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
2: Enthält nur Angaben der Zentren in USA, n ist die Anzahl der Patienten mit 'Hispanisch/Latino' oder 'Nicht hispanisch/Latino'
Abkürzungen: BMI: Body Mass Index; ECOG-PS: Eastern Cooperative Oncology Group-Performance Status; ET: Endokrine Therapie; ITT: Intention to treat; kg: Kilogramm; m: Meter; Max: Maximum; Min: Minimum; n: Anzahl der Patienten; N: Gesamtzahl Population; RCT: Randomisierte kontrollierte Studie; SD: Standardabweichung; USA: Vereinigte Staaten von Amerika

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Tabelle: Charakterisierung der (Kohorte 1 Population - ITT - Prämenopausal) Studienpopulation (Baseline) - RCT mit dem zu bewertenden Arzneimittel - Monarch-E

	Abemaciclib+ET[1] (N = 630)	ET[1] (N = 639)	Gesamt (N = 1269)
Initiale pathologische Diagnose, n (%)			
Invasives duktales Karzinom	436 (69,2)	467 (73,1)	903 (71,2)
Brustkrebs	105 (16,7)	97 (15,2)	202 (15,9)
Invasives lobuläres Karzinom der Brust	78 (12,4)	66 (10,3)	144 (11,3)
Muzinöses Karzinom	6 (1,0)	2 (0,3)	8 (0,6)
Invasives papilläres Karzinom	2 (0,3)	0 (0,0)	2 (0,2)
Inflammatorische Karzinom	2 (0,3)	2 (0,3)	4 (0,3)
Medulläres Karzinom der Brust	1 (0,2)	3 (0,5)	4 (0,3)
Tubuläres Karzinom der Brust	0 (0,0)	1 (0,2)	1 (0,1)
Morbus Paget der Brustwarze	0 (0,0)	0 (0,0)	0 (0,0)
Metastasierter Brustkrebs	0 (0,0)	1 (0,2)	1 (0,1)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Primäre radiologisch bestimmte Tumorgröße vor der systemischen Therapie, n (%)	605	617	1222
< 20 mm	157 (24,9)	153 (23,9)	310 (24,4)
≥ 20 bis < 50 mm	298 (47,3)	317 (49,6)	615 (48,5)
≥ 50 mm	150 (23,8)	147 (23,0)	297 (23,4)
Fehlend	25 (4,0)	22 (3,4)	47 (3,7)
Primäre pathologisch bestimmte Tumorgröße nach der definitiven Chirurgie, n (%)	616	633	1249
< 20 mm	154 (24,4)	167 (26,1)	321 (25,3)
≥ 20 bis < 50 mm	292 (46,3)	293 (45,9)	585 (46,1)
≥ 50 mm	170 (27,0)	173 (27,1)	343 (27,0)
Fehlend	14 (2,2)	6 (0,9)	20 (1,6)
Beteiligung von ipsilateralen, supraklavikulären, ipsilateralen infraklavikulären oder ipsilateralen Mammaria interna Lymphknoten bei der initialen Diagnose, n (%)			
Ja	118 (18,7)	128 (20,0)	246 (19,4)
Nein	510 (81,0)	508 (79,5)	1018 (80,2)
Fehlend	2 (0,3)	3 (0,5)	5 (0,4)
Bewertung der axillären Lymphknoten, n (%)			
Positiv	626 (99,4)	639 (100,0)	1265 (99,7)
Negativ	4 (0,6)	0 (0,0)	4 (0,3)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Anzahl der positiven Lymphknoten, n (%)			
0	4 (0,6)	0 (0,0)	4 (0,3)
1 - 3	235 (37,3)	257 (40,2)	492 (38,8)
4 - 9	270 (42,9)	277 (43,3)	547 (43,1)
≥ 10	121 (19,2)	105 (16,4)	226 (17,8)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Histopathologisches Grading bei Diagnose, n (%)			
G1 - günstig	54 (8,6)	52 (8,1)	106 (8,4)
G2 – moderat günstig	274 (43,5)	285 (44,6)	559 (44,1)

	Abemaciclib+ET[1] (N = 630)	**ET[1] (N = 639)**	**Gesamt (N = 1269)**
G3 – ungünstig	271 (43,0)	264 (41,3)	535 (42,2)
Gx – kann nicht bewertet werden	31 (4,9)	37 (5,8)	68 (5,4)
Fehlend	0 (0,0)	1 (0,2)	1 (0,1)
Tumorstadium bei Erstdiagnose, n (%)			
Stadium IA	0 (0,0)	0 (0,0)	0 (0,0)
Stadium IIA	66 (10,5)	74 (11,6)	140 (11,0)
Stadium IIB	65 (10,3)	81 (12,7)	146 (11,5)
Stadium IIIA	266 (42,2)	255 (39,9)	521 (41,1)
Stadium IIIB	20 (3,2)	18 (2,8)	38 (3,0)
Stadium IIIC	211 (33,5)	209 (32,7)	420 (33,1)
Fehlend	2 (0,3)	2 (0,3)	4 (0,3)
Östrogenrezeptorstatus, n (%)			
Positiv	625 (99,2)	637 (99,7)	1262 (99,4)
Negativ	4 (0,6)	2 (0,3)	6 (0,5)
Unbekannt	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	1 (0,2)	0 (0,0)	1 (0,1)
Progesteronrezeptorstatus, n (%)			
Positiv	546 (86,7)	558 (87,3)	1104 (87,0)
Negativ	54 (8,6)	52 (8,1)	106 (8,4)
Unbekannt	5 (0,8)	9 (1,4)	14 (1,1)
Fehlend	25 (4,0)	20 (3,1)	45 (3,5)
HER2-Status zum Zeitpunkt der Erstdiagnose, n (%)			
Positiv	0 (0,0)	0 (0,0)	0 (0,0)
Negativ	630 (100,0)	639 (100,0)	1269 (100,0)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Ki-67 Zentrallaborergebnisse des nicht behandelten Tumors, n (%)			
< 20%	196 (31,1)	222 (34,7)	418 (32,9)
≥ 20%	267 (42,4)	276 (43,2)	543 (42,8)
Fehlend	138 (21,9)	114 (17,8)	252 (19,9)
Nicht zutreffend	18 (2,9)	14 (2,2)	32 (2,5)
Nicht bewertbar	11 (1,7)	13 (2,0)	24 (1,9)

1: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HER2: Humaner epidermaler Wachstumsfaktor-Rezeptor-2 (Human Epidermal Growth Factor Receptor 2); ITT: Intention to treat; Ki67: Antigen Ki (Kiel)-67; mm: Millimeter; n: Anzahl der Patienten; N: Gesamtzahl Population; RCT: Randomisierte kontrollierte Studie

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Tabelle: Charakterisierung der (Kohorte 1 Population - ITT - Postmenopausal) Studienpopulation (Baseline) - RCT mit dem zu bewertenden Arzneimittel - Monarch-E

	Abemaciclib+ET[1] (N = 1364)	ET[1] (N = 1384)	Gesamt (N = 2748)
Initiale pathologische Diagnose, n (%)			
Invasives duktales Karzinom	888 (65,1)	907 (65,5)	1795 (65,3)
Brustkrebs	218 (16,0)	240 (17,3)	458 (16,7)
Invasives lobuläres Karzinom der Brust	222 (16,3)	210 (15,2)	432 (15,7)
Muzinöses Karzinom	15 (1,1)	5 (0,4)	20 (0,7)
Invasives papilläres Karzinom	7 (0,5)	9 (0,7)	16 (0,6)
Inflammatorische Karzinom	6 (0,4)	6 (0,4)	12 (0,4)
Medulläres Karzinom der Brust	5 (0,4)	2 (0,1)	7 (0,3)
Tubuläres Karzinom der Brust	3 (0,2)	4 (0,3)	7 (0,3)
Morbus Paget der Brustwarze	0 (0,0)	1 (0,1)	1 (0,0)
Metastasierter Brustkrebs	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Primäre radiologisch bestimmte Tumorgröße vor der systemischen Therapie, n (%)	1306	1321	2627
< 20 mm	385 (28,2)	377 (27,2)	762 (27,7)
≥ 20 bis < 50 mm	695 (51,0)	746 (53,9)	1441 (52,4)
≥ 50 mm	226 (16,6)	198 (14,3)	424 (15,4)
Fehlend	58 (4,3)	63 (4,6)	121 (4,4)
Primäre pathologisch bestimmte Tumorgröße nach der definitiven Chirurgie, n (%)	1346	1372	2718
< 20 mm	359 (26,3)	360 (26,0)	719 (26,2)
≥ 20 bis < 50 mm	677 (49,6)	709 (51,2)	1386 (50,4)
≥ 50 mm	310 (22,7)	303 (21,9)	613 (22,3)
Fehlend	18 (1,3)	12 (0,9)	30 (1,1)
Beteiligung von ipsilateralen, supraklavikulären, ipsilateralen infraklavikulären oder ipsilateralen Mammaria interna Lymphknoten bei der initialen Diagnose, n (%)			
Ja	239 (17,5)	275 (19,9)	514 (18,7)
Nein	1122 (82,3)	1106 (79,9)	2228 (81,1)
Fehlend	3 (0,2)	3 (0,2)	6 (0,2)
Bewertung der axillären Lymphknoten, n (%)			
Positiv	1364 (100,0)	1379 (99,6)	2743 (99,8)
Negativ	0 (0,0)	5 (0,4)	5 (0,2)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Anzahl der positiven Lymphknoten, n (%)			
0	0 (0,0)	5 (0,4)	5 (0,2)
1 - 3	458 (33,6)	459 (33,2)	917 (33,4)
4 - 9	581 (42,6)	589 (42,6)	1170 (42,6)
≥ 10	325 (23,8)	331 (23,9)	656 (23,9)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Histopathologisches Grading bei Diagnose, n (%)			
G1 - günstig	94 (6,9)	105 (7,6)	199 (7,2)
G2 – moderat günstig	653 (47,9)	662 (47,8)	1315 (47,9)

	Abemaciclib+ET[1] (N = 1364)	**ET[1] (N = 1384)**	**Gesamt (N = 2748)**
G3 – ungünstig	562 (41,2)	551 (39,8)	1113 (40,5)
Gx – kann nicht bewertet werden	52 (3,8)	62 (4,5)	114 (4,1)
Fehlend	3 (0,2)	4 (0,3)	7 (0,3)
Tumorstadium bei Erstdiagnose, n (%)			
Stadium IA	0 (0,0)	0 (0,0)	0 (0,0)
Stadium IIA	119 (8,7)	124 (9,0)	243 (8,8)
Stadium IIB	160 (11,7)	147 (10,6)	307 (11,2)
Stadium IIIA	524 (38,4)	536 (38,7)	1060 (38,6)
Stadium IIIB	59 (4,3)	49 (3,5)	108 (3,9)
Stadium IIIC	500 (36,7)	526 (38,0)	1026 (37,3)
Fehlend	2 (0,1)	2 (0,1)	4 (0,1)
Östrogenrezeptorstatus, n (%)			
Positiv	1356 (99,4)	1370 (99,0)	2726 (99,2)
Negativ	6 (0,4)	13 (0,9)	19 (0,7)
Unbekannt	1 (0,1)	1 (0,1)	2 (0,1)
Fehlend	1 (0,1)	0 (0,0)	1 (0,0)
Progesteronrezeptorstatus, n (%)			
Positiv	1154 (84,6)	1169 (84,5)	2323 (84,5)
Negativ	170 (12,5)	179 (12,9)	349 (12,7)
Unbekannt	11 (0,8)	10 (0,7)	21 (0,8)
Fehlend	29 (2,1)	26 (1,9)	55 (2,0)
HER2-Status zum Zeitpunkt der Erstdiagnose, n (%)			
Positiv	0 (0,0)	1 (0,1)	1 (0,0)
Negativ	1364 (100,0)	1383 (99,9)	2747 (100,0)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Ki-67 Zentrallaborergebnisse des nicht behandelten Tumors, n (%)			
< 20%	546 (40,0)	559 (40,4)	1105 (40,2)
≥ 20%	525 (38,5)	511 (36,9)	1036 (37,7)
Fehlend	217 (15,9)	227 (16,4)	444 (16,2)
Nicht zutreffend	39 (2,9)	42 (3,0)	81 (2,9)
Nicht bewertbar	37 (2,7)	45 (3,3)	82 (3,0)

1: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HER2: Humaner epidermaler Wachstumsfaktor-Rezeptor-2 (Human Epidermal Growth Factor Receptor 2); ITT: Intention to treat; Ki67: Antigen Ki (Kiel)-67; mm: Millimeter; n: Anzahl der Patienten; N: Gesamtzahl Population; RCT: Randomisierte kontrollierte Studie

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Tabelle: Charakterisierung der (Kohorte 1 Population - ITT - Männer) Studienpopulation (Baseline) - RCT mit dem zu bewertenden Arzneimittel - Monarch-E

	Abemaciclib+ET[1] (N = 11)	ET[1] (N = 11)	Gesamt (N = 22)
Initiale pathologische Diagnose, n (%)			
Invasives duktales Karzinom	8 (72,7)	9 (81,8)	17 (77,3)
Brustkrebs	3 (27,3)	1 (9,1)	4 (18,2)
Invasives lobuläres Karzinom der Brust	0 (0,0)	0 (0,0)	0 (0,0)
Muzinöses Karzinom	0 (0,0)	0 (0,0)	0 (0,0)
Invasives papilläres Karzinom	0 (0,0)	0 (0,0)	0 (0,0)
Inflammatorische Karzinom	0 (0,0)	0 (0,0)	0 (0,0)
Medulläres Karzinom der Brust	0 (0,0)	0 (0,0)	0 (0,0)
Tubuläres Karzinom der Brust	0 (0,0)	0 (0,0)	0 (0,0)
Morbus Paget der Brustwarze	0 (0,0)	1 (9,1)	1 (4,5)
Metastasierter Brustkrebs	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Primäre radiologisch bestimmte Tumorgröße vor der systemischen Therapie, n (%)	9	11	20
< 20 mm	3 (27,3)	6 (54,5)	9 (40,9)
≥ 20 bis < 50 mm	5 (45,5)	5 (45,5)	10 (45,5)
≥ 50 mm	1 (9,1)	0 (0,0)	1 (4,5)
Fehlend	2 (18,2)	0 (0,0)	2 (9,1)
Primäre pathologisch bestimmte Tumorgröße nach der definitiven Chirurgie, n (%)	11	11	22
< 20 mm	2 (18,2)	3 (27,3)	5 (22,7)
≥ 20 bis < 50 mm	7 (63,6)	8 (72,7)	15 (68,2)
≥ 50 mm	2 (18,2)	0 (0,0)	2 (9,1)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Beteiligung von ipsilateralen, supraklavikulären, ipsilateralen infraklavikulären oder ipsilateralen Mammaria interna Lymphknoten bei der initialen Diagnose, n (%)			
Ja	2 (18,2)	4 (36,4)	6 (27,3)
Nein	9 (81,8)	7 (63,6)	16 (72,7)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Bewertung der axillären Lymphknoten, n (%)			
Positiv	11 (100,0)	11 (100,0)	22 (100,0)
Negativ	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Anzahl der positiven Lymphknoten, n (%)			
0	0 (0,0)	0 (0,0)	0 (0,0)
1 - 3	2 (18,2)	4 (36,4)	6 (27,3)
4 - 9	5 (45,5)	3 (27,3)	8 (36,4)
≥ 10	4 (36,4)	4 (36,4)	8 (36,4)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Histopathologisches Grading bei Diagnose, n (%)			
G1 - günstig	0 (0,0)	0 (0,0)	0 (0,0)
G2 – moderat günstig	7 (63,6)	4 (36,4)	11 (50,0)

	Abemaciclib+ET[1] (N = 11)	**ET[1] (N = 11)**	**Gesamt (N = 22)**
G3 – ungünstig	4 (36,4)	7 (63,6)	11 (50,0)
Gx – kann nicht bewertet werden	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Tumorstadium bei Erstdiagnose, n (%)			
Stadium IA	0 (0,0)	0 (0,0)	0 (0,0)
Stadium IIA	0 (0,0)	1 (9,1)	1 (4,5)
Stadium IIB	0 (0,0)	1 (9,1)	1 (4,5)
Stadium IIIA	5 (45,5)	1 (9,1)	6 (27,3)
Stadium IIIB	0 (0,0)	2 (18,2)	2 (9,1)
Stadium IIIC	6 (54,5)	6 (54,5)	12 (54,5)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Östrogenrezeptorstatus, n (%)			
Positiv	11 (100,0)	11 (100,0)	22 (100,0)
Negativ	0 (0,0)	0 (0,0)	0 (0,0)
Unbekannt	0 (0,0)	0 (0,0)	0 (0,0)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Progesteronrezeptorstatus, n (%)			
Positiv	8 (72,7)	9 (81,8)	17 (77,3)
Negativ	2 (18,2)	1 (9,1)	3 (13,6)
Unbekannt	1 (9,1)	0 (0,0)	1 (4,5)
Fehlend	0 (0,0)	1 (9,1)	1 (4,5)
HER2-Status zum Zeitpunkt der Erstdiagnose, n (%)			
Positiv	0 (0,0)	0 (0,0)	0 (0,0)
Negativ	11 (100,0)	11 (100,0)	22 (100,0)
Fehlend	0 (0,0)	0 (0,0)	0 (0,0)
Ki-67 Zentrallaborergebnisse des nicht behandelten Tumors, n (%)			
< 20%	5 (45,5)	3 (27,3)	8 (36,4)
≥ 20%	5 (45,5)	6 (54,5)	11 (50,0)
Fehlend	1 (9,1)	1 (9,1)	2 (9,1)
Nicht zutreffend	0 (0,0)	1 (9,1)	1 (4,5)
Nicht bewertbar	0 (0,0)	0 (0,0)	0 (0,0)

1: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HER2: Humaner epidermaler Wachstumsfaktor-Rezeptor-2 (Human Epidermal Growth Factor Receptor 2); ITT: Intention to treat; Ki67: Antigen Ki (Kiel)-67; mm: Millimeter; n: Anzahl der Patienten; N: Gesamtzahl Population; RCT: Randomisierte kontrollierte Studie

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Anhang 4-G3.2: Gesamtüberleben - Sensitivitätsanalyse

Tabelle 4-137 (Anhang): Gesamtüberleben - Sensitivitätsanalyse

Tabelle: Ergebnisse für Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel Kohorte 1 Population - ITT

Population	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
Gesamtüberleben					
Prämenopausal	19/630 (3,0)	NE [NE; NE]	15/639 (2,3)	NE [NE; NE]	1,28 [0,65; 2,53] 0,4672
Postmenopausal	57/1364 (4,2)	NE [NE; NE]	58/1384 (4,2)	NE [NE; NE]	1,02 [0,71; 1,48] 0,9000
Männer	2/11 (18,2)	NE [21,53; NE]	0/11 (0,0)	NE [NE; NE]	[4]

Datenschnitt: 01.04.2021
ITT-Population
1: Aus Log-rank-Test; 2: In Monaten; 3: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 4: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet.
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; n: Anzahl verstorbener Patienten; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht.

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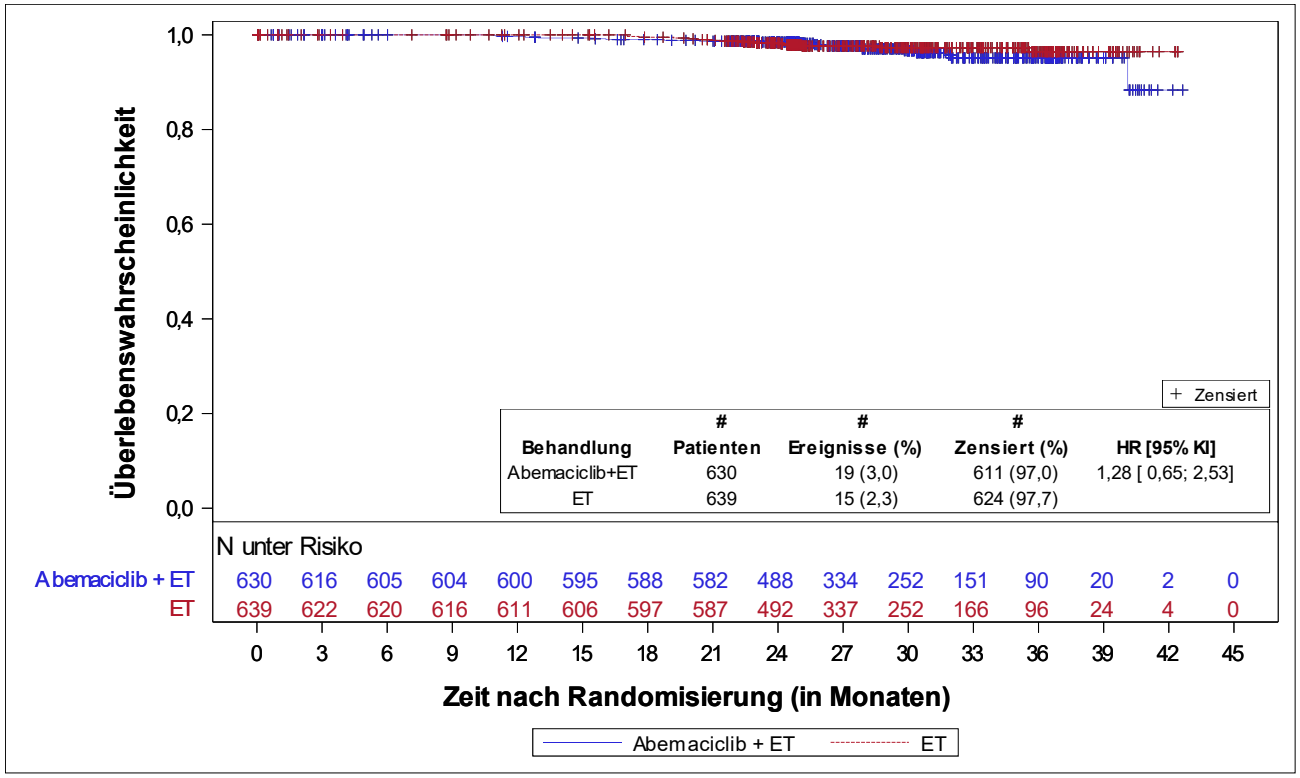
Abbildung 25 (Anhang): Kaplan-Meier-Kurven von Gesamtüberleben - Sensitivitätsanalyse

Kaplan-Meier-Kurven - Gesamtüberleben
Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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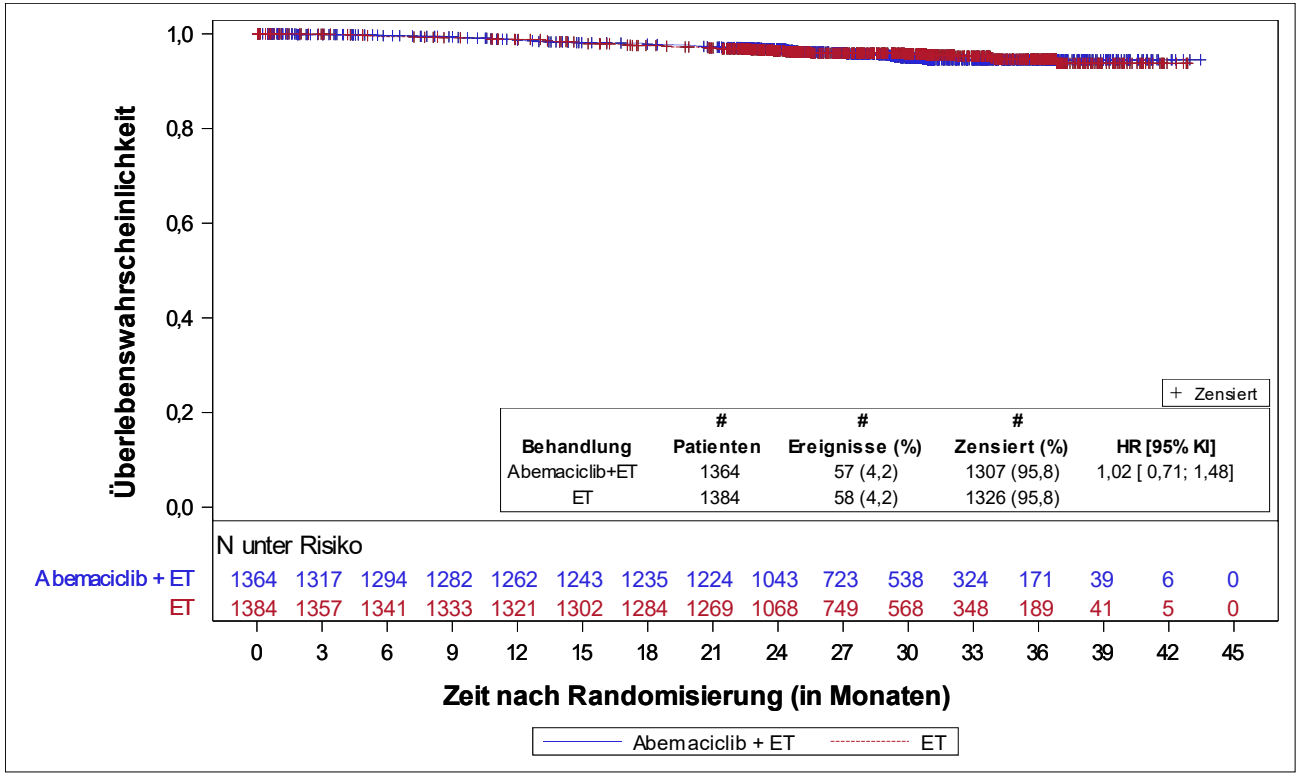
Kaplan-Meier-Kurven - Gesamtüberleben
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_km_eff.sas
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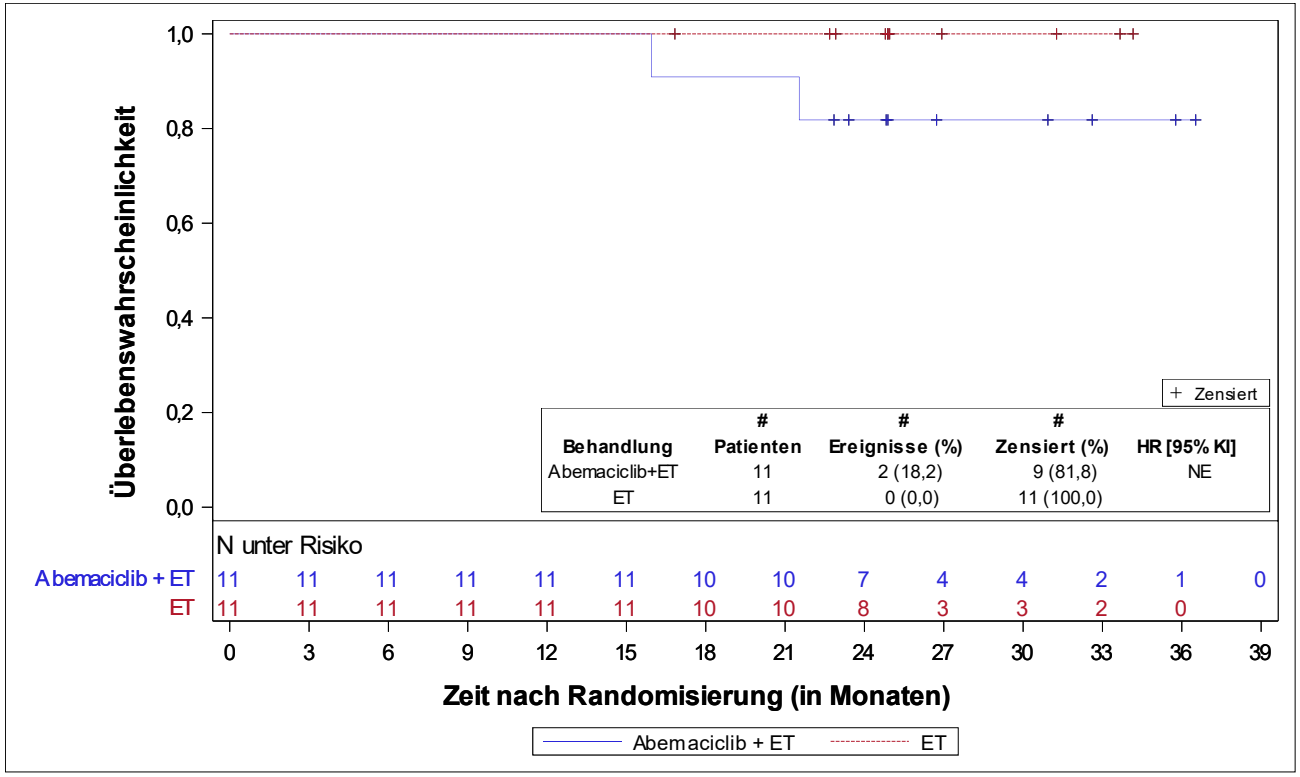
Kaplan-Meier-Kurven - Gesamtüberleben
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Männer: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_km_eff.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/f_km_os_men_itt2c1.rtf
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Anhang 4-G3.3: IDFS - Sensitivitätsanalyse

Tabelle 4-138 (Anhang): IDFS - Sensitivitätsanalyse

Tabelle: Ergebnisse für IDFS aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - ITT

Population	Abemaciclib+ET[3]		ET[3]		Abemaciclib+ET vs. ET[3]
	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	Pat. mit Ereignis n/N (%)	Mediane Ereigniszeit[2] [95% KI]	HR [95% KI] p-Wert[1]
IDFS					
Prämenopausal	48/630 (7,6)	NE [NE; NE]	90/639 (14,1)	NE [NE; NE]	0,53 [0,37; 0,75] 0,0003
Postmenopausal	130/1364 (9,5)	NE [NE; NE]	177/1384 (12,8)	NE [NE; NE]	0,76 [0,60; 0,95] 0,0157
Männer	2/11 (18,2)	NE [15,65; NE]	1/11 (9,1)	NE [21,76; NE]	[4]
lokales Brustkrebsrezidiv					
Prämenopausal	4/630 (0,6)	NE [NE; NE]	10/639 (1,6)	NE [NE; NE]	0,40 [0,12; 1,26] 0,1040
Postmenopausal	13/1364 (1,0)	NE [NE; NE]	14/1384 (1,0)	NE [NE; NE]	0,96 [0,45; 2,04] 0,9094
Männer	0/11 (0,0)	NE [NE; NE]	1/11 (9,1)	NE [21,76; NE]	[4]
regionäres invasives Brustkrebsrezidiv					
Prämenopausal	3/630 (0,5)	NE [NE; NE]	4/639 (0,6)	NE [NE; NE]	0,74 [0,16; 3,29] 0,6863
Postmenopausal	9/1364 (0,7)	NE [NE; NE]	12/1384 (0,9)	NE [NE; NE]	0,77 [0,33; 1,84] 0,5599
Männer	0/11 (0,0)	NE [NE; NE]	0/11 (0,0)	NE [NE; NE]	[4]
Fernrezidiv					
Prämenopausal	38/630 (6,0)	NE [NE; NE]	71/639 (11,1)	NE [NE; NE]	0,53 [0,36; 0,79] 0,0014
Postmenopausal	80/1364 (5,9)	NE [NE; NE]	126/1384 (9,1)	NE [NE; NE]	0,65 [0,49; 0,87] 0,0028
Männer	2/11 (18,2)	NE [15,65; NE]	0/11 (0,0)	NE [NE; NE]	[4]
Tod jeglicher Ursache					
Prämenopausal	0/630 (0,0)	NE [NE; NE]	0/639 (0,0)	NE [NE; NE]	[4]
Postmenopausal	14/1364 (1,0)	NE [NE; NE]	9/1384 (0,7)	NE [NE; NE]	1,60 [0,69; 3,70] 0,2648
Männer	0/11 (0,0)	NE [NE; NE]	0/11 (0,0)	NE [NE; NE]	[4]
kontralateraler invasiver Brustkrebs					

Population	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
Prämenopausal	1/630 (0,2)	NE [NE; NE]	4/639 (0,6)	NE [NE; NE]	0,25 [0,03; 2,24] 0,1806
Postmenopausal	3/1364 (0,2)	NE [NE; NE]	7/1384 (0,5)	NE [NE; NE]	0,44 [0,11; 1,71] 0,2236
Männer	0/11 (0,0)	NE [NE; NE]	0/11 (0,0)	NE [NE; NE]	[4]
Sekundäres Primärkarzinom (kein Brustkrebs)					
Prämenopausal	2/630 (0,3)	NE [NE; NE]	3/639 (0,5)	NE [NE; NE]	0,67 [0,11; 3,98] 0,6528
Postmenopausal	14/1364 (1,0)	NE [NE; NE]	13/1384 (0,9)	NE [NE; NE]	1,11 [0,52; 2,36] 0,7840
Männer	0/11 (0,0)	NE [NE; NE]	0/11 (0,0)	NE [NE; NE]	[4]

Datenschnitt: 01.04.2021
ITT-Population
1: Aus Log-rank-Test; 2: In Monaten; 3: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 4: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet.
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; IDFS: Invasives krankheitsfreies Überleben (invasive disease-free survival); ITT: Intention to Treat; KI: Konfidenzintervall; n: Anzahl Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht.

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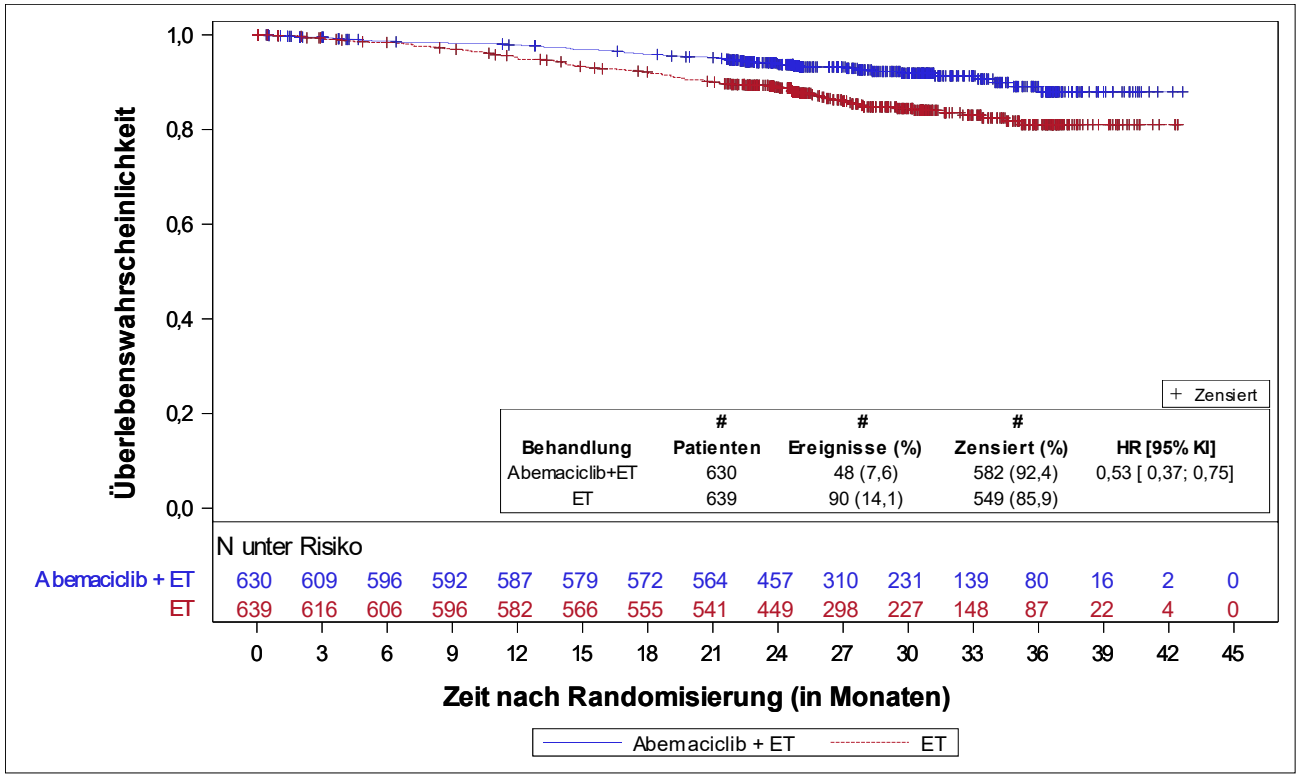
Abbildung 26 (Anhang): Kaplan-Meier-Kurven von IDFS - Sensitivitätsanalyse

Kaplan-Meier-Kurven - IDFS

Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021

Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)

Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl

Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende

Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten

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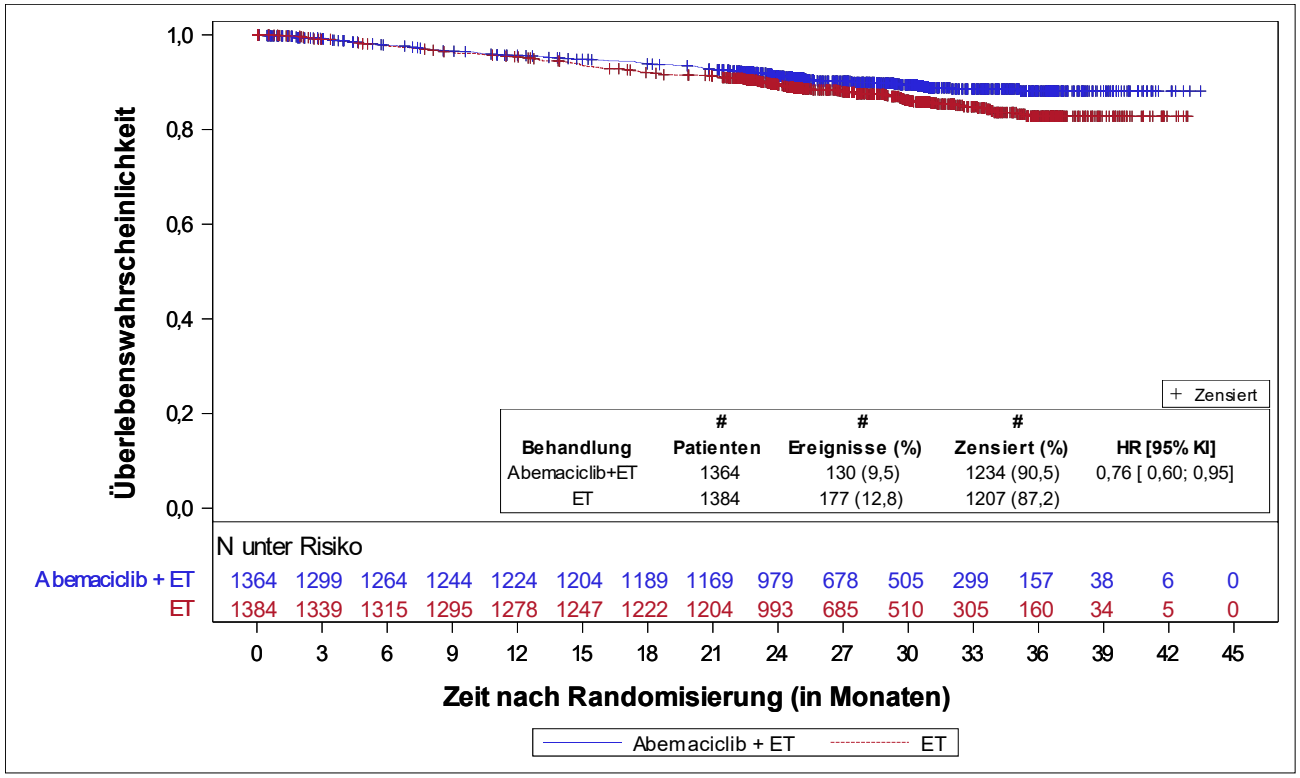
Kaplan-Meier-Kurven - IDFS
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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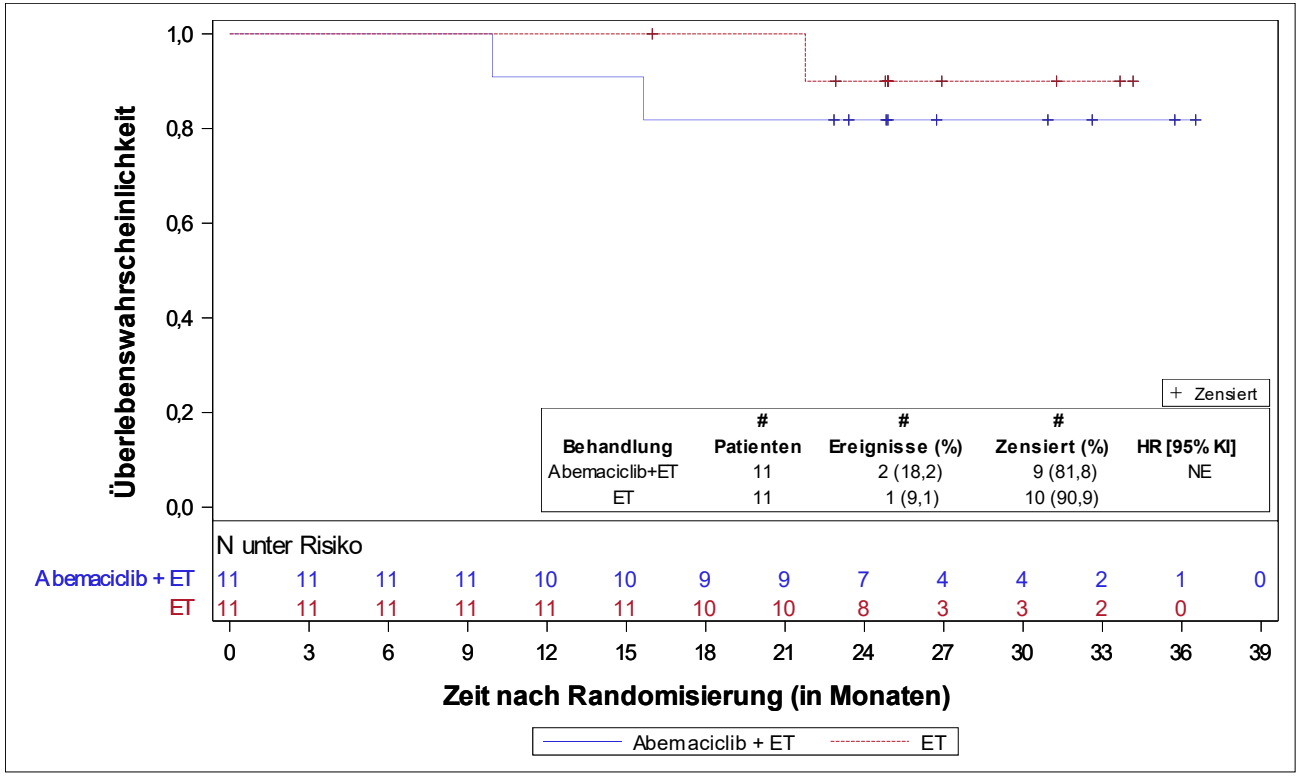
Kaplan-Meier-Kurven - IDFS
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Männer: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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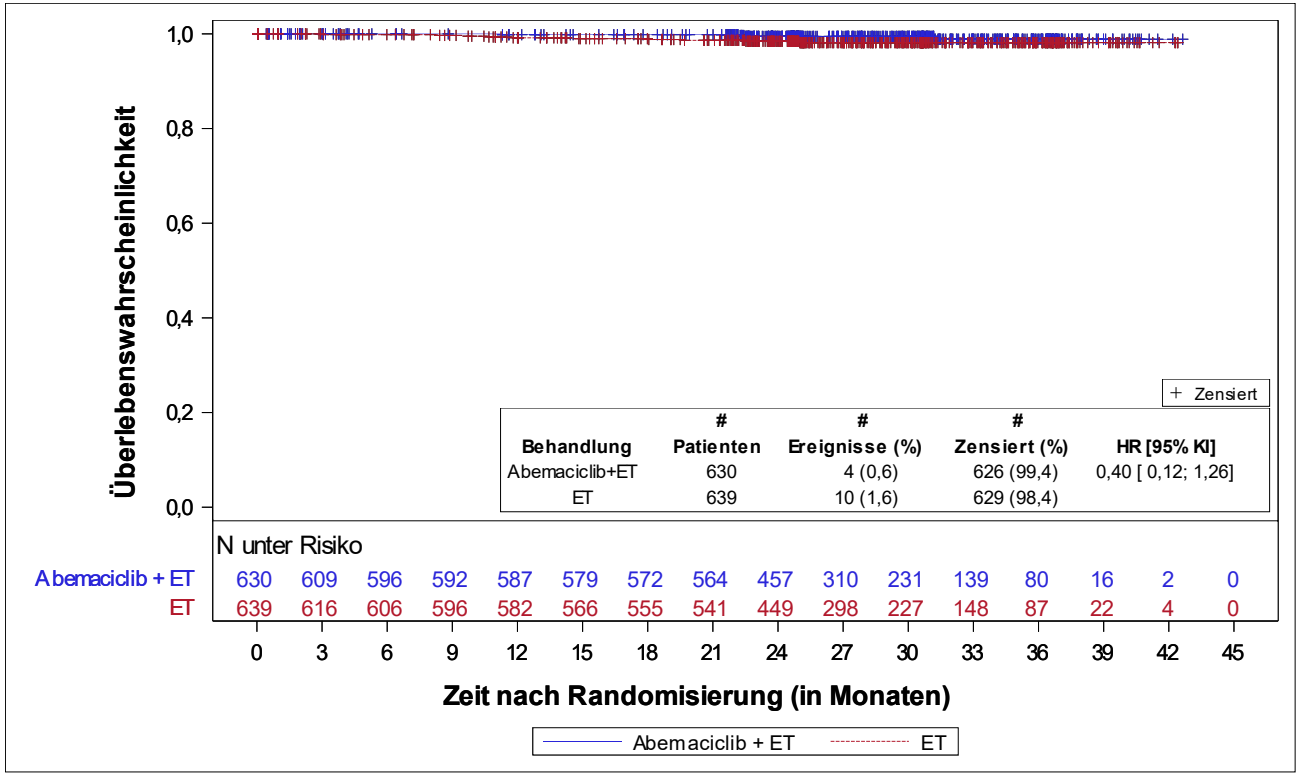
Kaplan-Meier-Kurven - lokales Brustkrebsrezidiv
Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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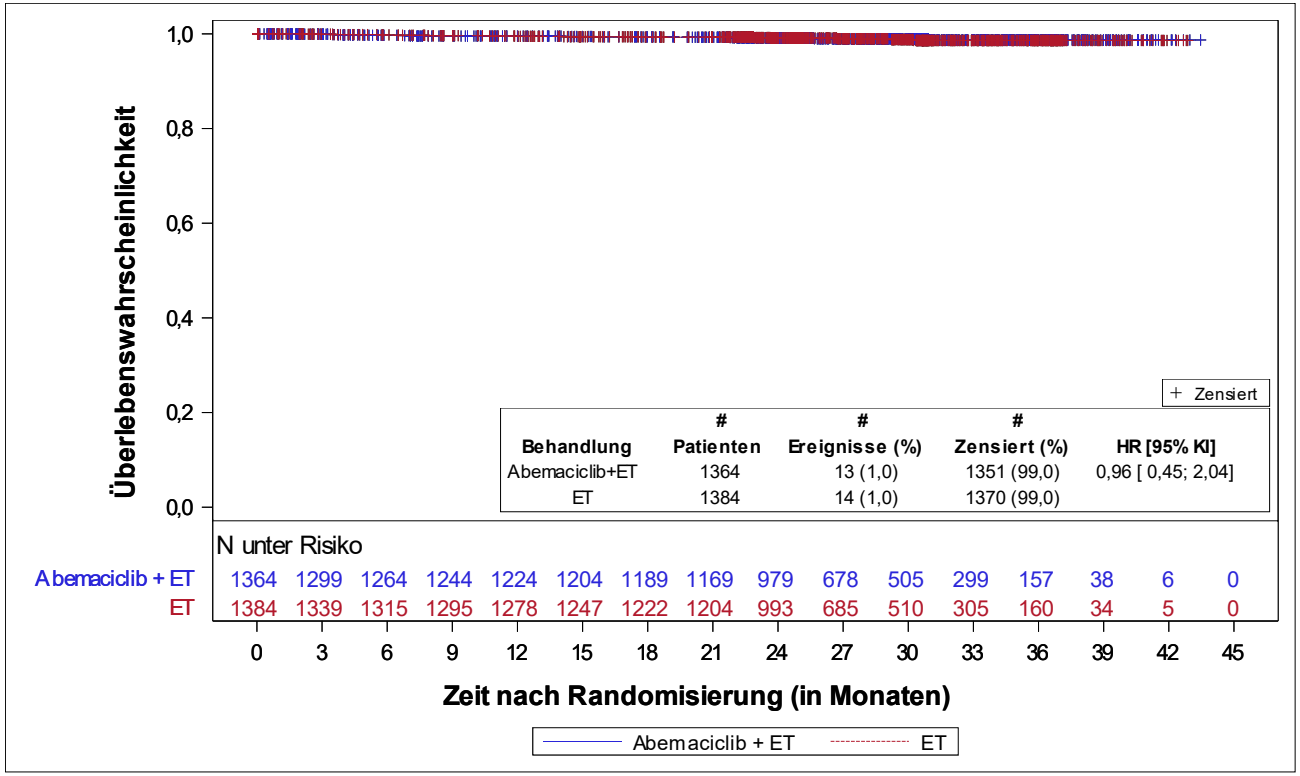
Kaplan-Meier-Kurven - lokales Brustkrebsrezidiv
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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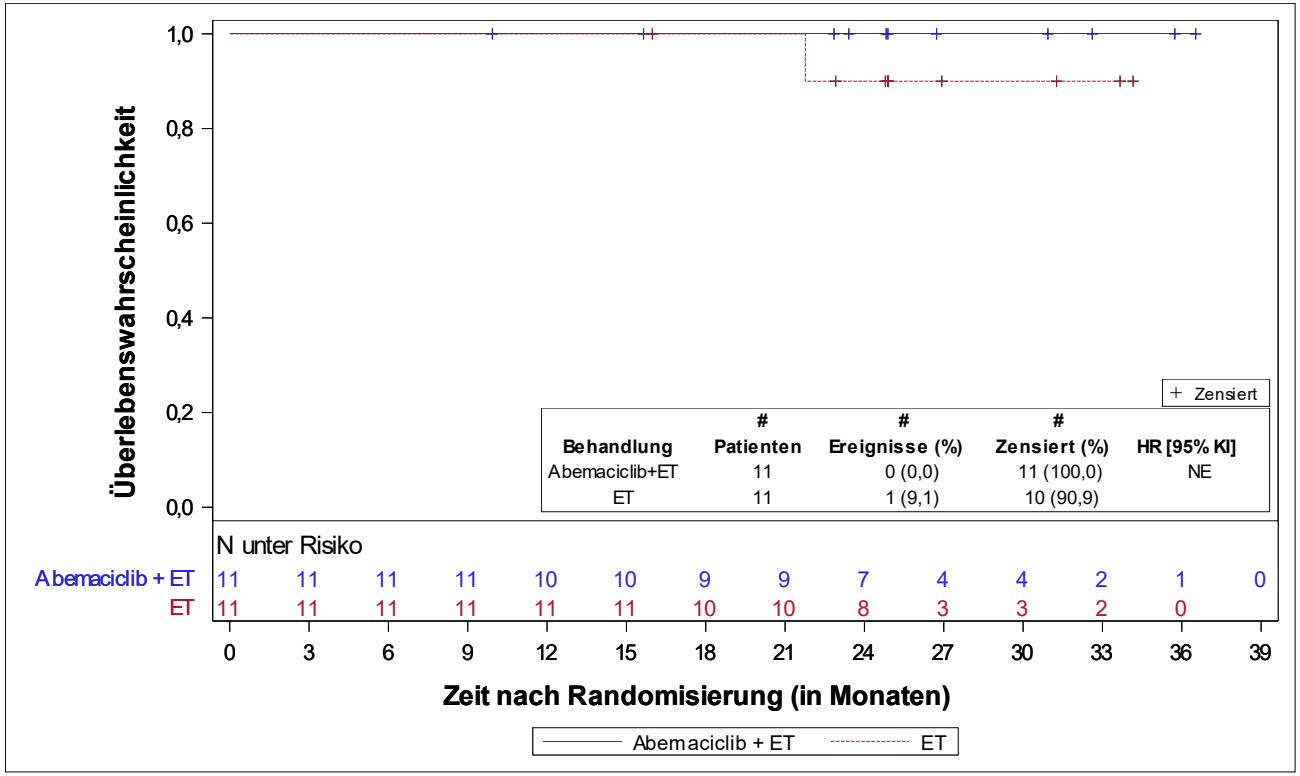
Kaplan-Meier-Kurven - lokales Brustkrebsrezidiv
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Männer: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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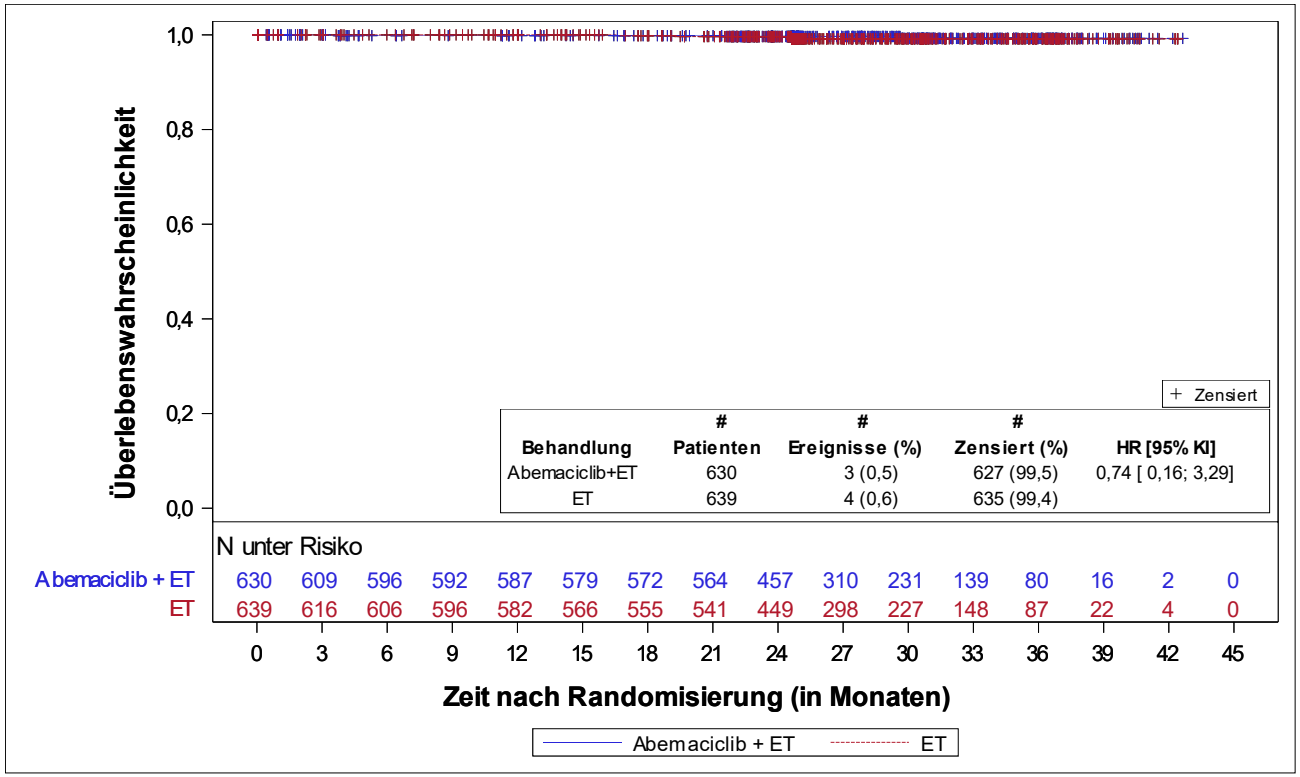
Kaplan-Meier-Kurven - regionäres invasives Brustkrebsrezidiv
Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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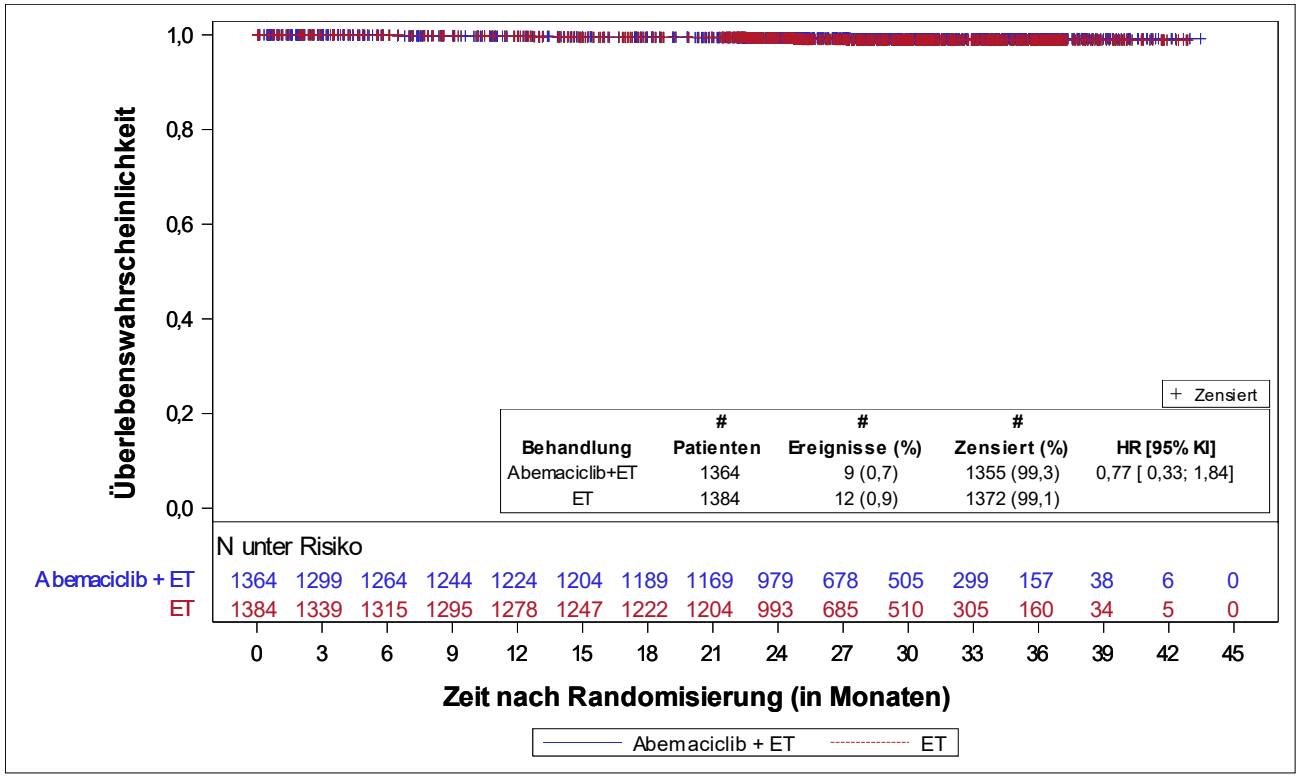
Kaplan-Meier-Kurven - regionäres invasives Brustkrebsrezidiv
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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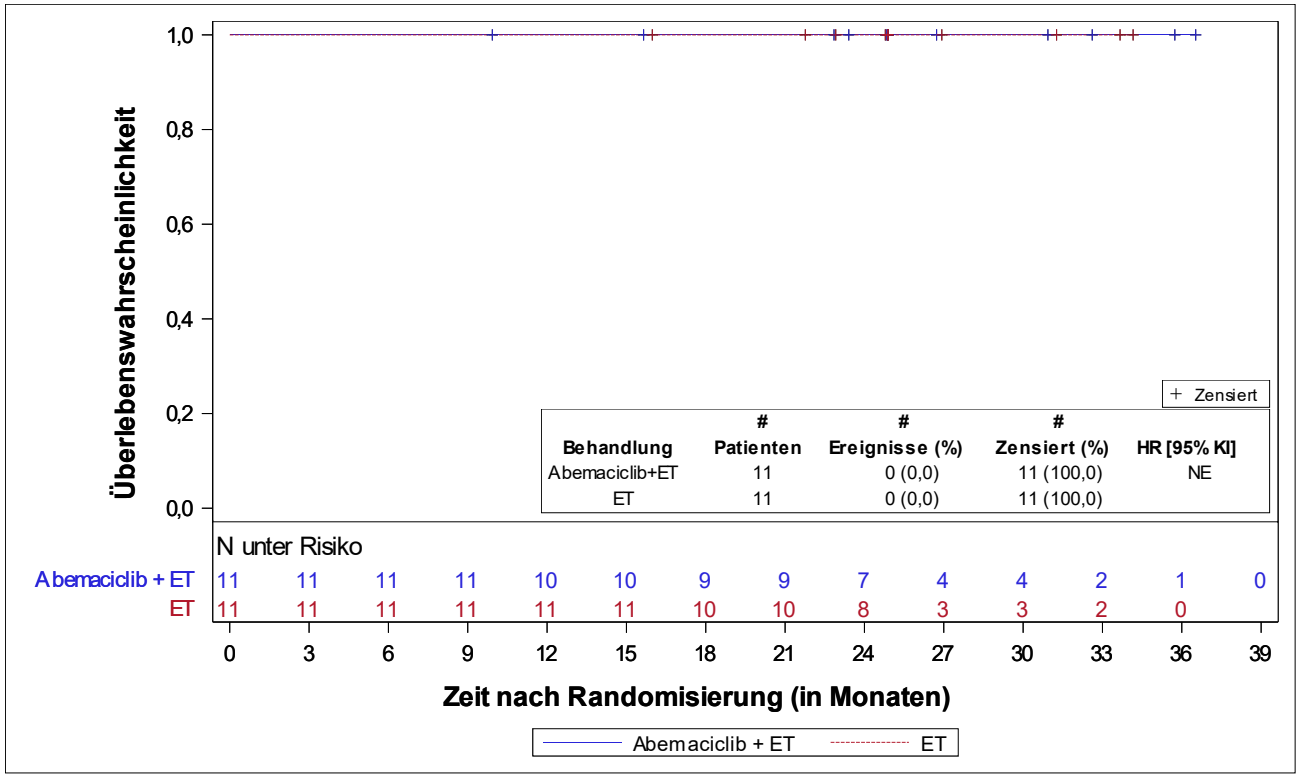
Kaplan-Meier-Kurven - regionäres invasives Brustkrebsrezidiv
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Männer: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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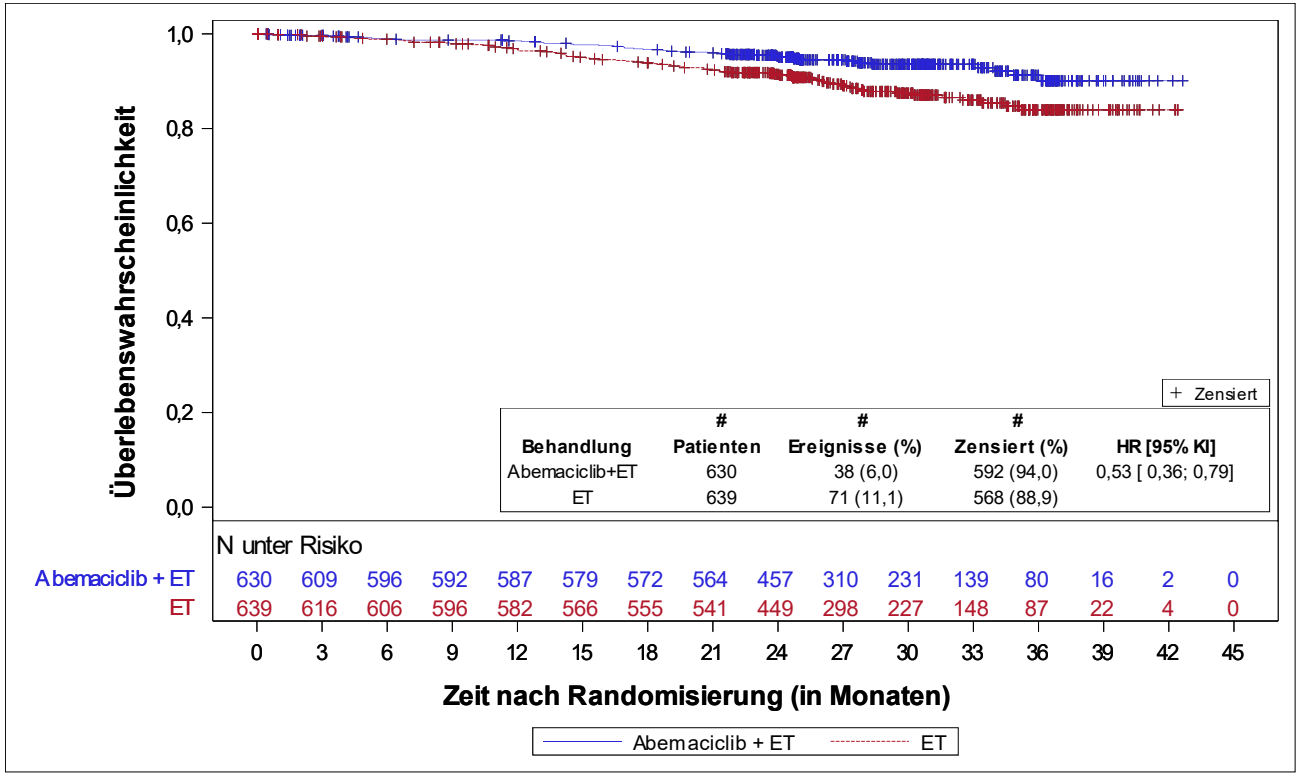
Kaplan-Meier-Kurven - Fernrezidiv
Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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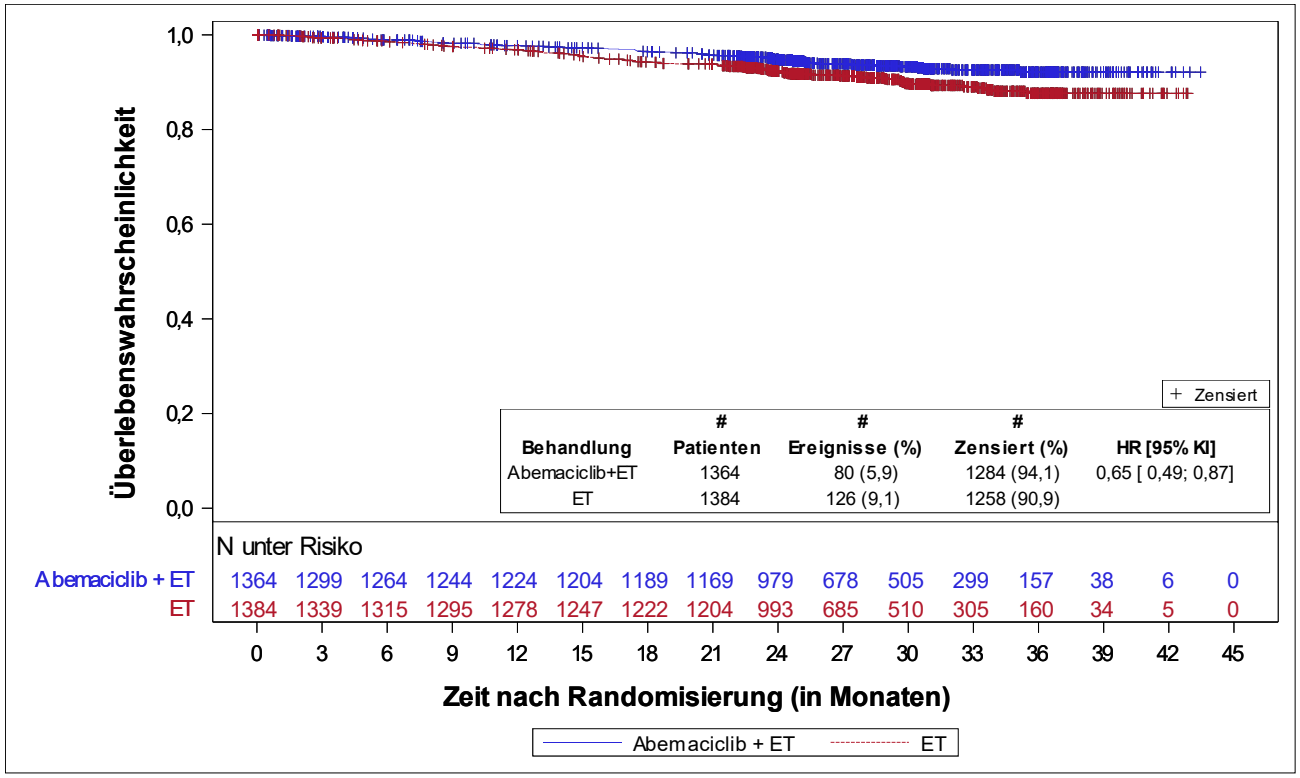
Kaplan-Meier-Kurven - Fernrezidiv
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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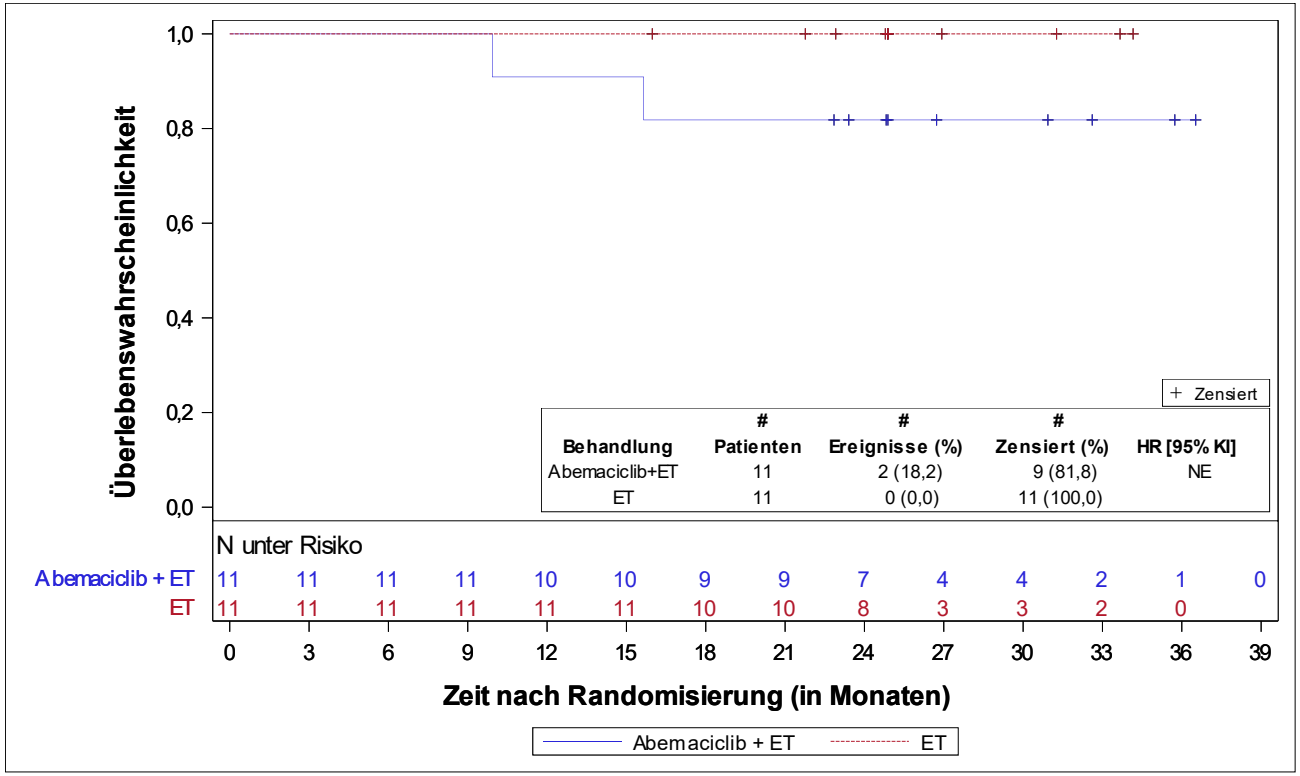
Kaplan-Meier-Kurven - Fernrezidiv
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
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Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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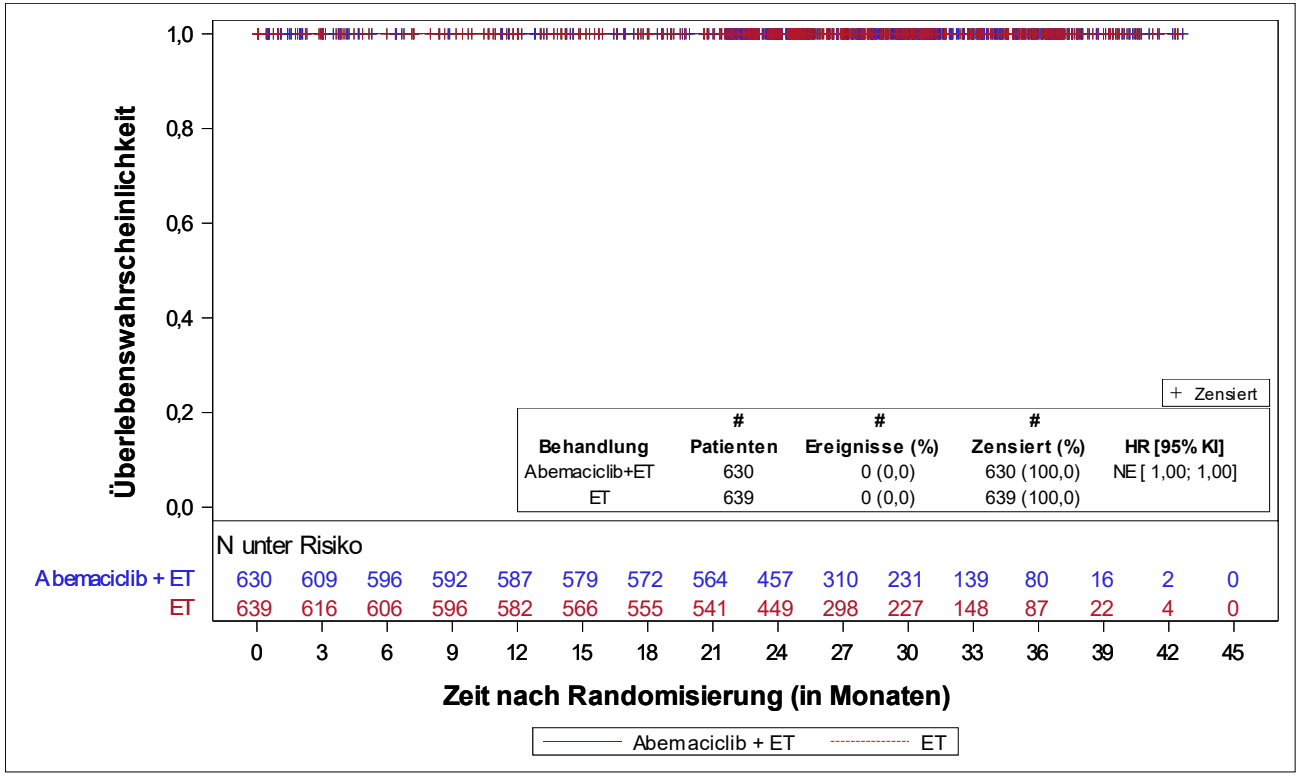
Kaplan-Meier-Kurven - Tod jeglicher Ursache
Kohorte 1 Population - ITT - Prämenopausal



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Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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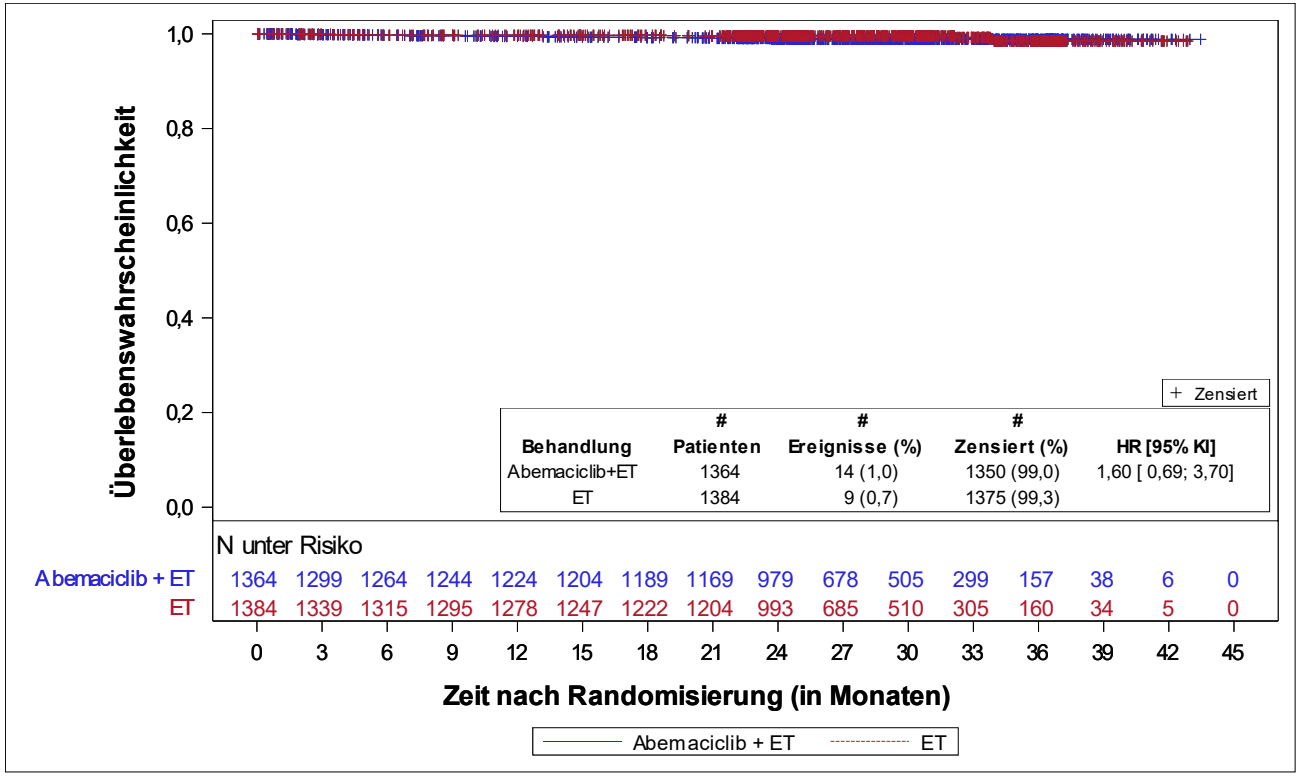
Kaplan-Meier-Kurven - Tod jeglicher Ursache
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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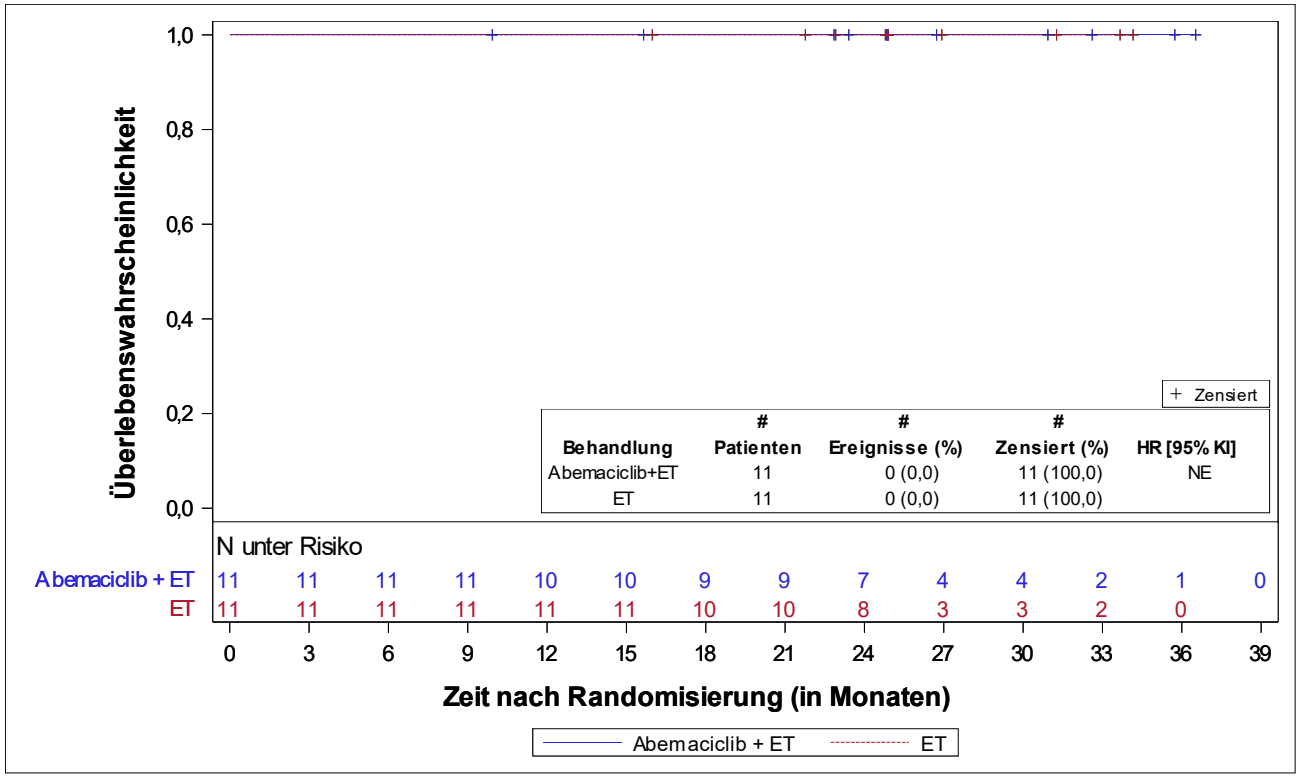
Kaplan-Meier-Kurven - Tod jeglicher Ursache
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Männer: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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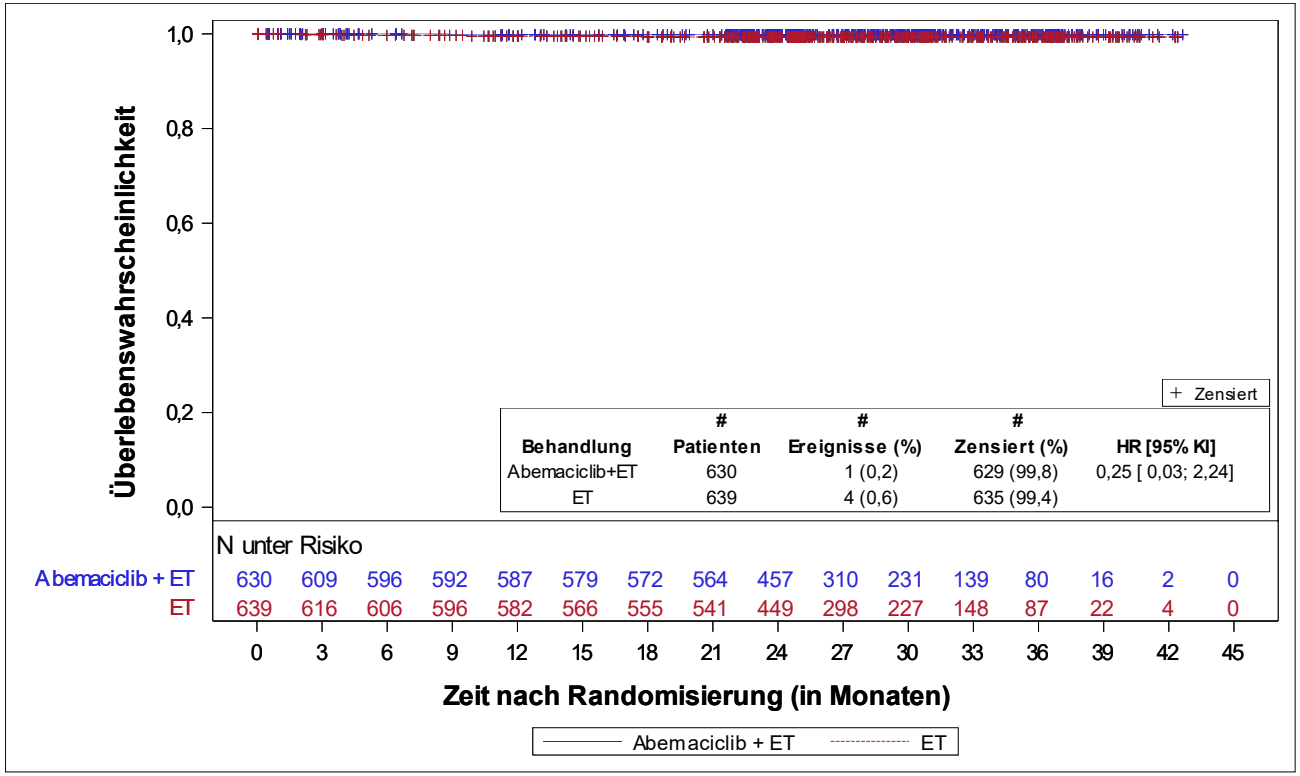
Kaplan-Meier-Kurven - kontralateraler invasiver Brustkrebs
Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
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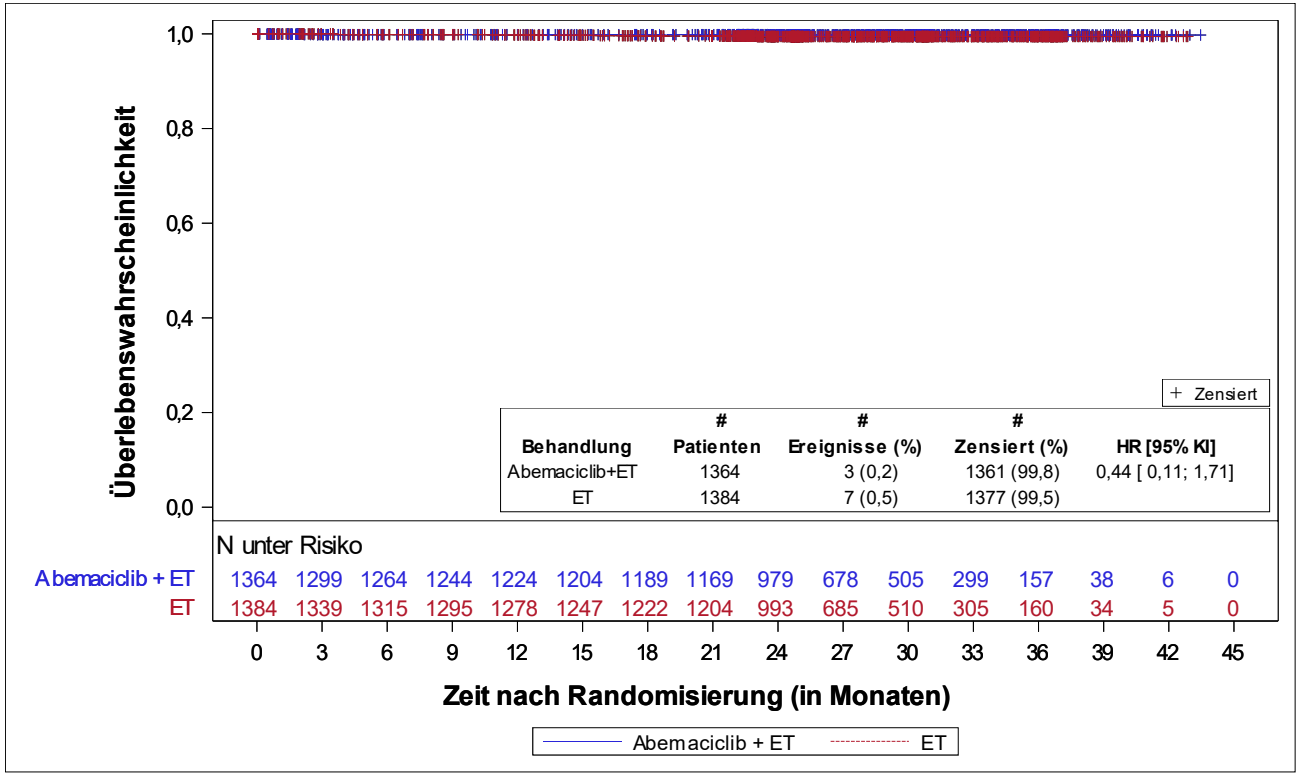
Kaplan-Meier-Kurven - kontralateraler invasiver Brustkrebs
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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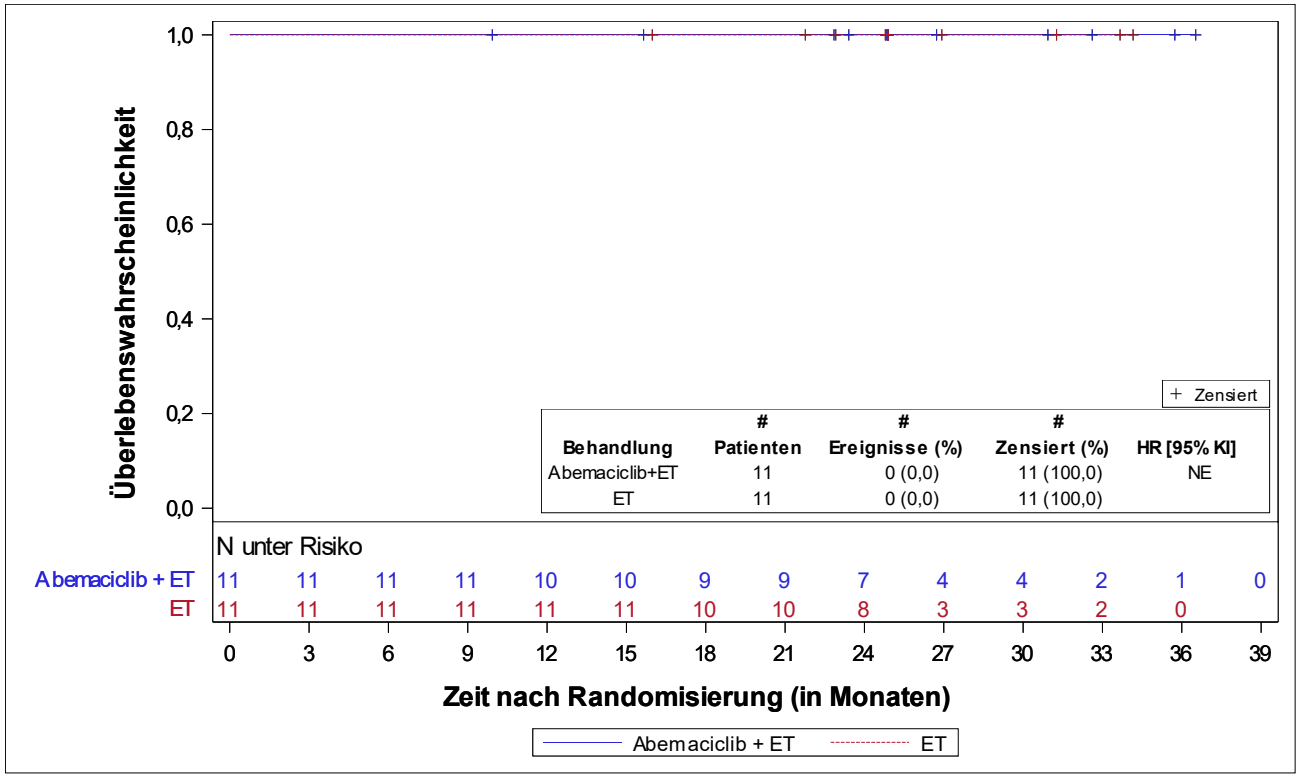
14FEB2022 / 04:13

Kaplan-Meier-Kurven - kontralateraler invasiver Brustkrebs
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Männer: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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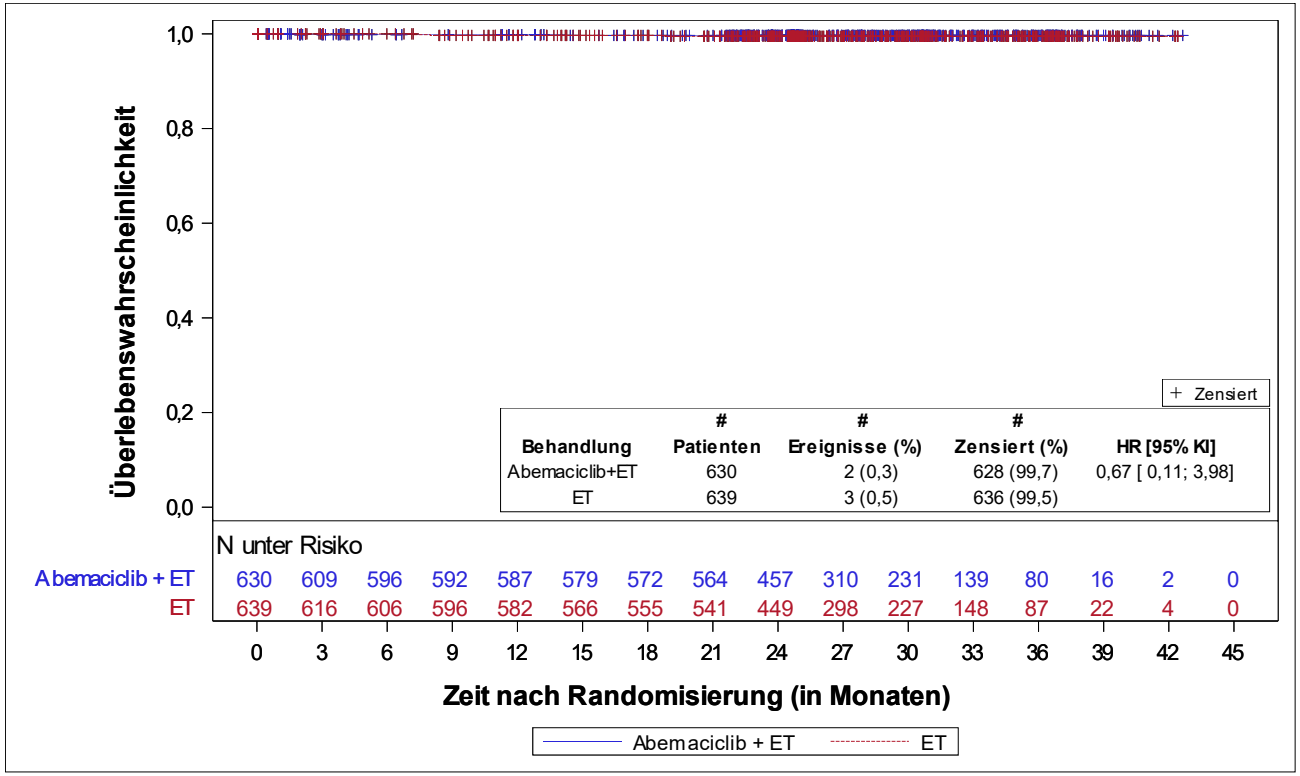
Kaplan-Meier-Kurven - Sekundäres Primärkarzinom (kein Brustkrebs)
Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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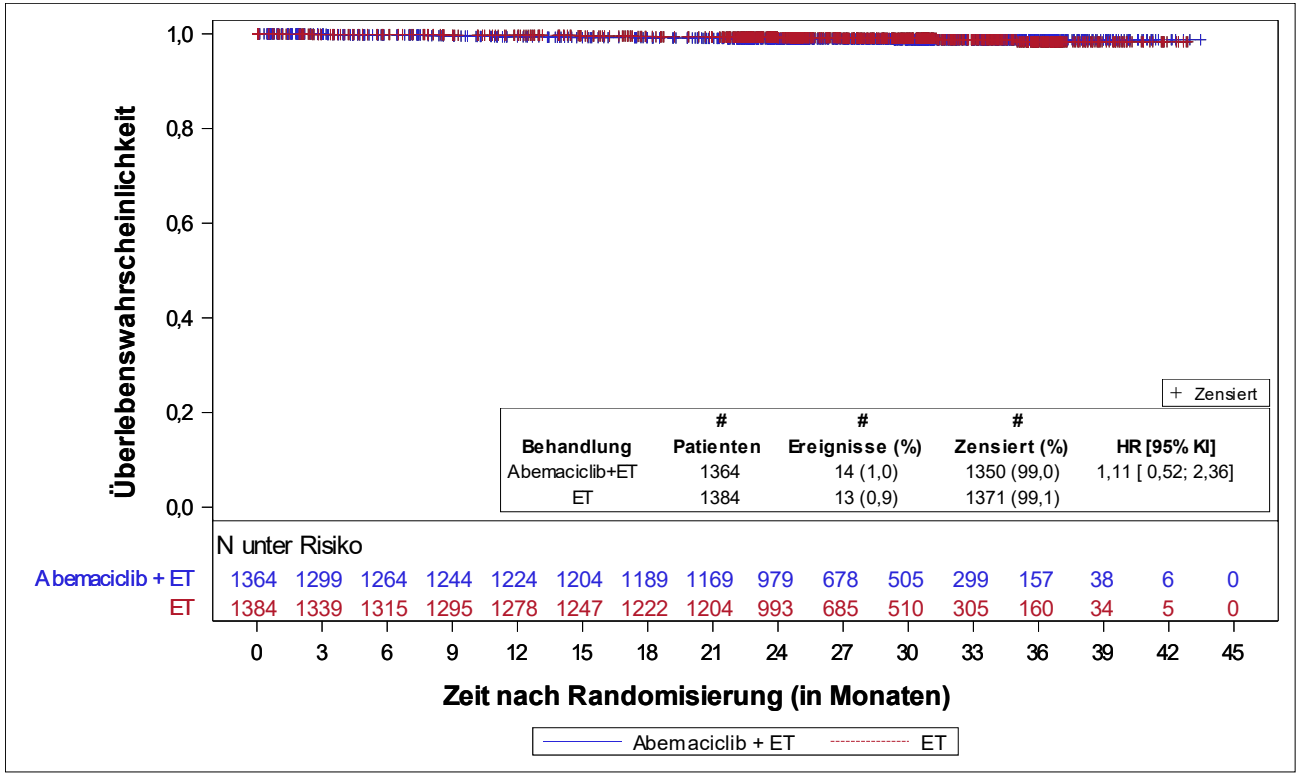
Kaplan-Meier-Kurven - Sekundäres Primärkarzinom (kein Brustkrebs)
Kohorte 1 Population - ITT - Postmenopausal



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Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
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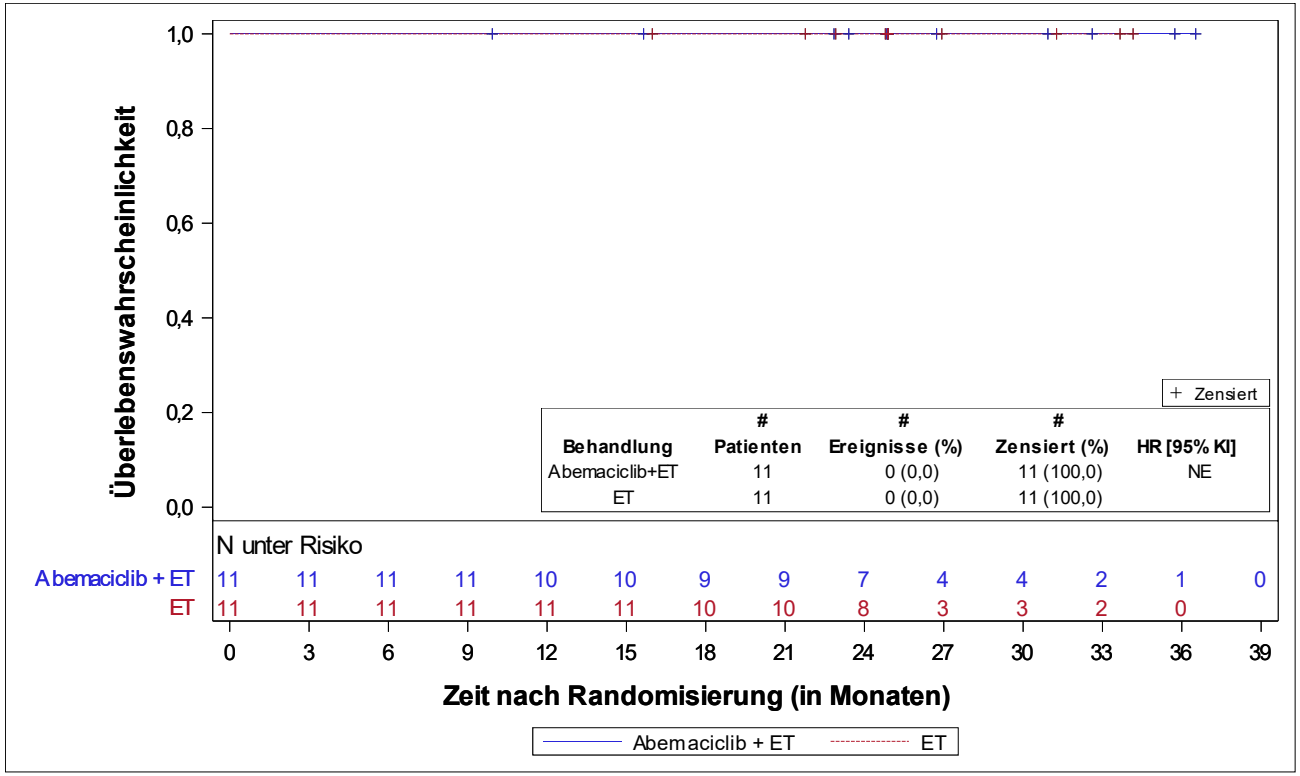
Kaplan-Meier-Kurven - Sekundäres Primärkarzinom (kein Brustkrebs)
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Männer: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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Anhang 4-G3.3.1: DRFS - Sensitivitätsanalyse

Tabelle 4-139 (Anhang): DRFS - Sensitivitätsanalyse

Tabelle: Ergebnisse für DRFS aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - ITT

Population	Abemaciclib+ET[3] Pat. mit Ereignis n/N (%)	Abemaciclib+ET[3] Mediane Ereigniszeit[2] [95% KI]	ET[3] Pat. mit Ereignis n/N (%)	ET[3] Mediane Ereigniszeit[2] [95% KI]	Abemaciclib+ET vs. ET[3] HR [95% KI] p-Wert[1]
DRFS					
Prämenopausal	40/630 (6,3)	NE [NE; NE]	75/639 (11,7)	NE [NE; NE]	0,53 [0,36; 0,78] 0,0010
Postmenopausal	106/1364 (7,8)	NE [NE; NE]	149/1384 (10,8)	NE [NE; NE]	0,73 [0,57; 0,94] 0,0145
Männer	2/11 (18,2)	NE [15,65; NE]	0/11 (0,0)	NE [NE; NE]	[4]

Datenschnitt: 01.04.2021
ITT-Population
1: Aus Log-rank-Test; 2: In Monaten; 3: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 4: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet.
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; DRFS: Fernmetastasenfreies Überleben (distant relapse-free survival); ITT: Intention to Treat; KI: Konfidenzintervall; n: Anzahl Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht.

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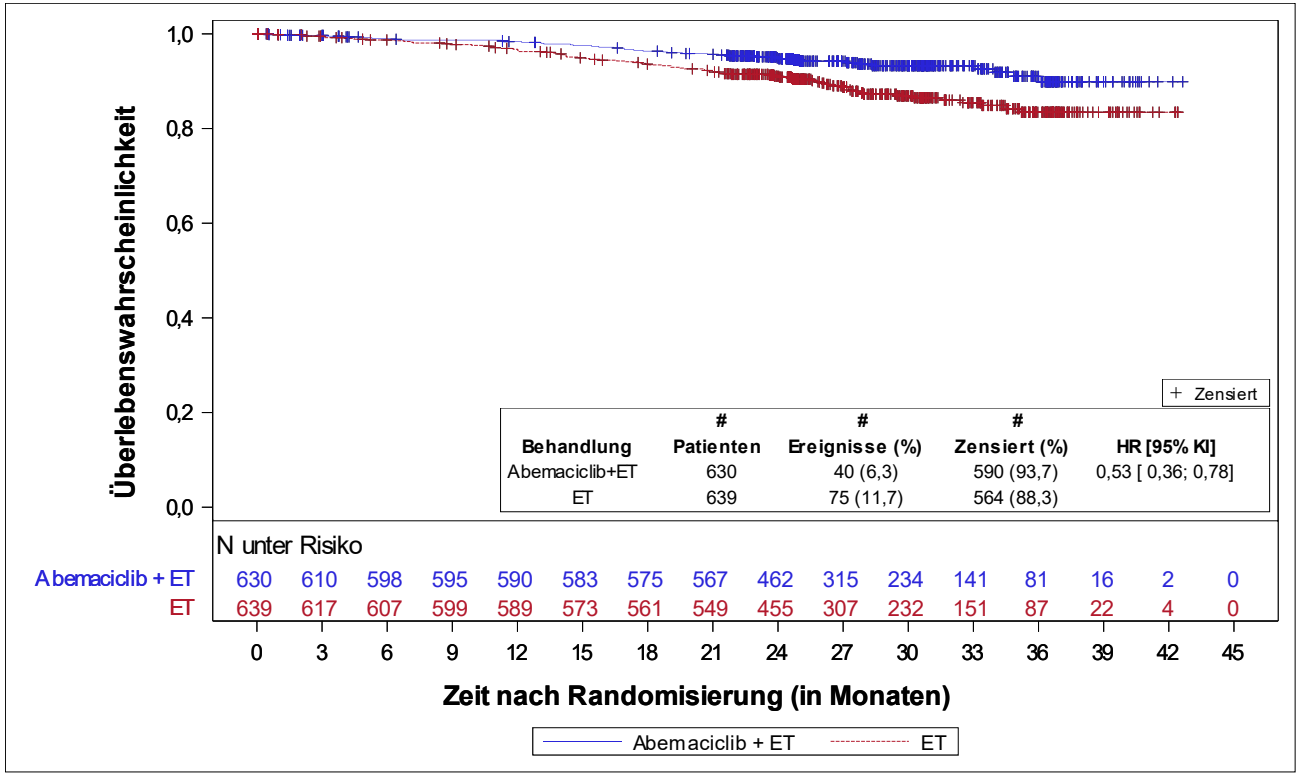
Abbildung 27 (Anhang): Kaplan-Meier-Kurven von DRFS - Sensitivitätsanalyse

Kaplan-Meier-Kurven - DRFS
Kohorte 1 Population - ITT - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
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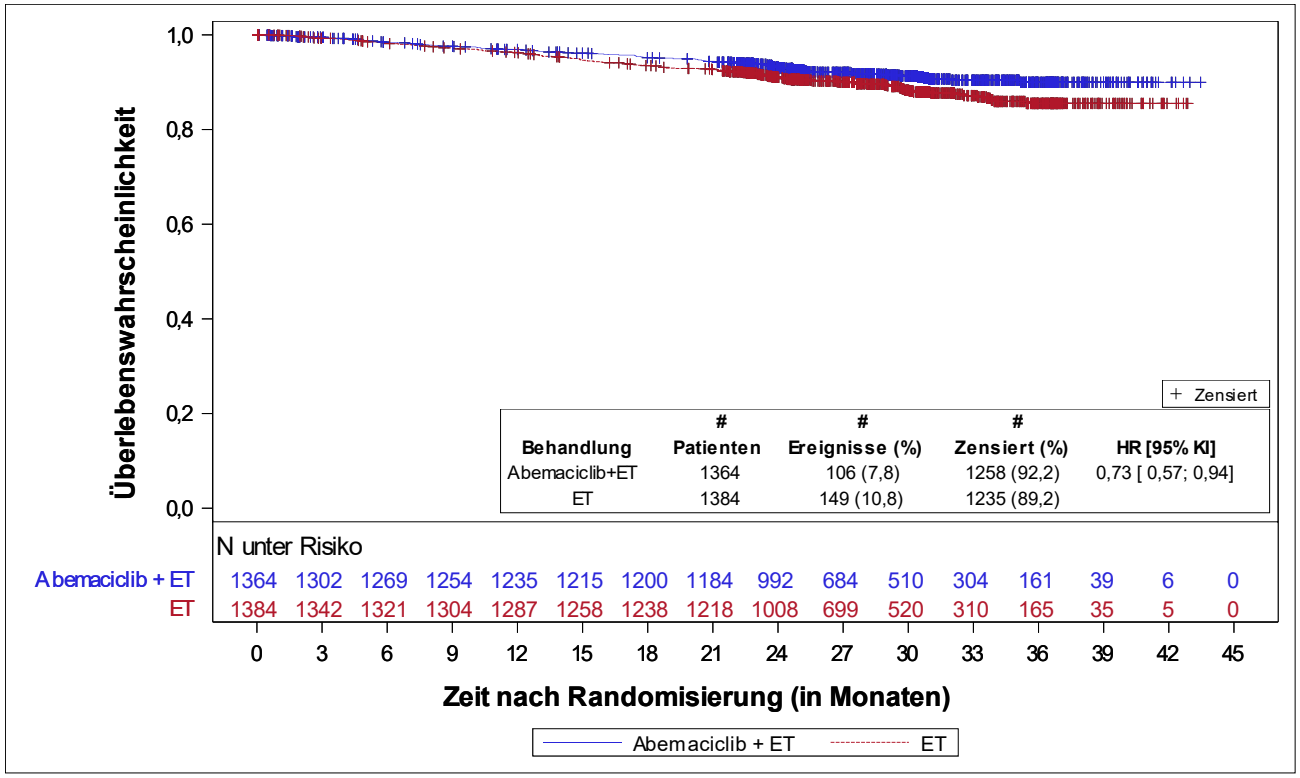
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/f_km_drfs_premp_itt2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
14FEB2022 / 04:13

Kaplan-Meier-Kurven - DRFS
Kohorte 1 Population - ITT - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_km_eff.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/f_km_drfs_posmp_itt2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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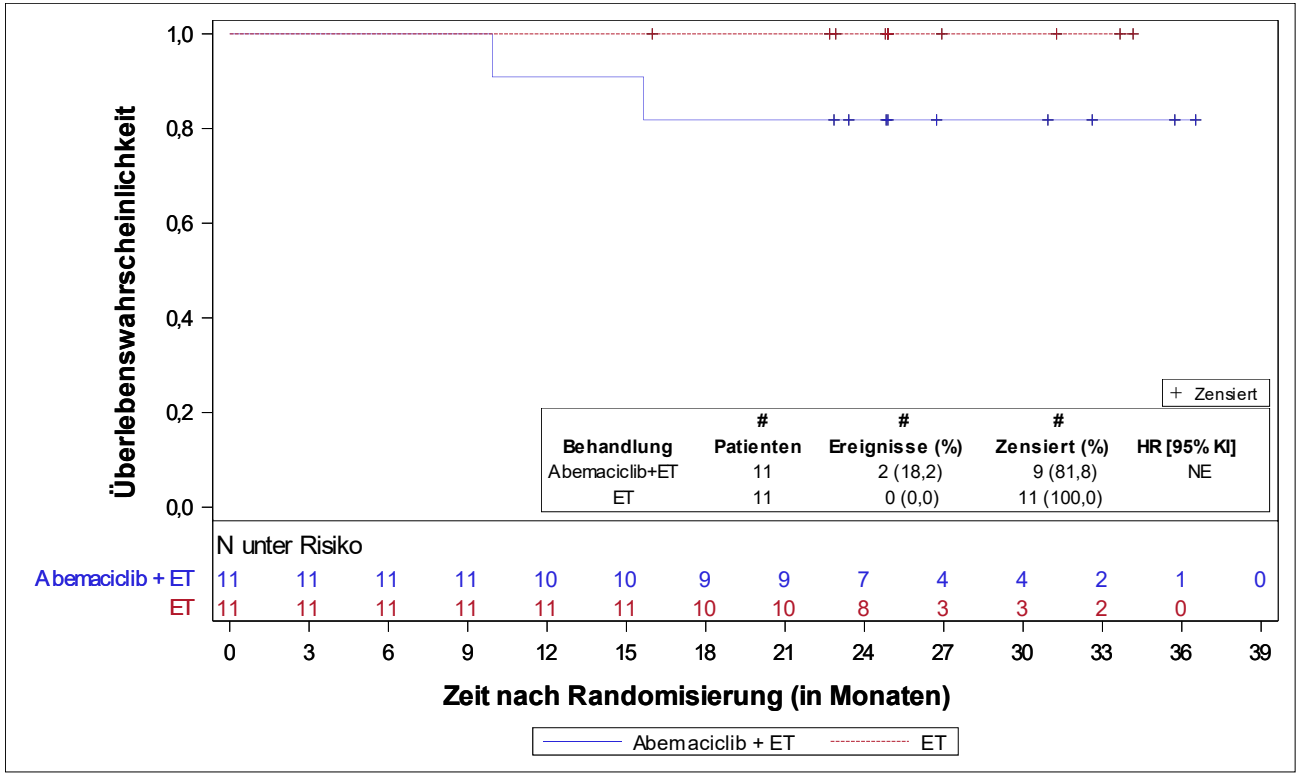
Kaplan-Meier-Kurven - DRFS
Kohorte 1 Population - ITT - Männer



Datenschnitt: 01.04.2021
Männer: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
Abkürzungen: ET: Endokrine Therapie; HR: Hazard Ratio; ITT: Intention to Treat; KI: Konfidenzintervall; N: Anzahl der Patienten; NE: Nicht errechenbar/nicht erreicht; #: Anzahl
Zensierte Patienten sind auf den Kaplan-Meier-Kurven gekennzeichnet anhand der Symbole in der Legende
Die Anzahl der Patienten unter der Abbildung beschreibt die Patienten unter Risiko zu den entsprechenden Zeitpunkten
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_km_eff.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/f_km_drfs_men_itt2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Anhang 4-G3.4: Gesundheitszustand anhand der EQ-5D VAS - Sensitivitätsanalyse

Tabelle 4-140 (Anhang): EQ-5D VAS - Sensitivitätsanalyse

Tabelle: Ergebnisse für die Veränderung Gesundheitszustand, EQ-5D aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Zeitpunkt	Abemaciclib+ET[1]										ET[1]										Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	M12 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Veränderung der EQ-5D VAS																				
Prämenopausal	547 77,34 (14,90)	515 77,66 (15,72)	503 78,39 (16,11)	491 78,81 (16,02)	461 79,46 (14,81)	407 80,23 (15,37)	390 80,35 (15,25)	221 80,77 (15,50)	[5]	1,46 (0,46)	558 78,16 (15,65)	522 79,42 (14,79)	520 80,97 (14,98)	484 81,53 (14,47)	448 81,40 (16,21)	399 81,48 (15,63)	410 80,95 (15,21)	234 81,29 (16,65)	2,30 (0,45)	-0,85 [-2,11;0,42] 0,1890 -0,08 [-0,20;0,04]
Postmenopausal	1159 77,65 (16,60)	1070 76,57 (16,04)	1039 78,13 (15,22)	983 78,62 (15,61)	937 78,16 (15,57)	838 78,68 (15,59)	835 79,12 (15,36)	452 79,43 (14,52)	[5]	-0,22 (0,31)	1187 78,00 (15,20)	1119 78,86 (15,46)	1109 79,81 (14,89)	1026 79,40 (15,24)	982 79,65 (15,42)	862 80,01 (15,65)	841 80,45 (15,35)	458 79,73 (16,27)	1,09 (0,30)	-1,30 [-2,15;-0,46] 0,0025 -0,12 [-0,21;-0,04]
Männer	10 79,70 (16,79)	9 81,89 (13,26)	9 83,89 (10,53)	7 79,29 (15,12)	6 74,17 (10,21)	5 76,00 (14,75)	6 79,17 (9,17)	5 82,00 (16,05)	3 86,67 (5,77)	[6]	9 75,00 (10,31)	9 84,44 (8,46)	9 85,33 (10,23)	9 80,67 (15,87)	9 78,33 (17,14)	5 79,80 (9,63)	8 79,00 (10,46)	3 73,33 (22,55)	[6]	[6]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: 30 Tage Follow-up; 3: 6 Monate Follow-up/12 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung der EQ-5D VAS = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung der EQ-5D VAS haben; 5: Visite wurde nicht in die Analyse einbezogen, da für weniger als 25% der Patienten Postbaseline-Werte vorlagen; 6: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet, dieses schließt den Verzicht auf die Darstellung der Postbaseline-Werte ein.
Abkürzungen: B: Baseline; ET: Endokrine Therapie; EQ-5D: European Quality of Life Questionnaire 5 Dimensions; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler; VAS: Visuelle Analogskala

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_mmrm_qol.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t1024_mmrm_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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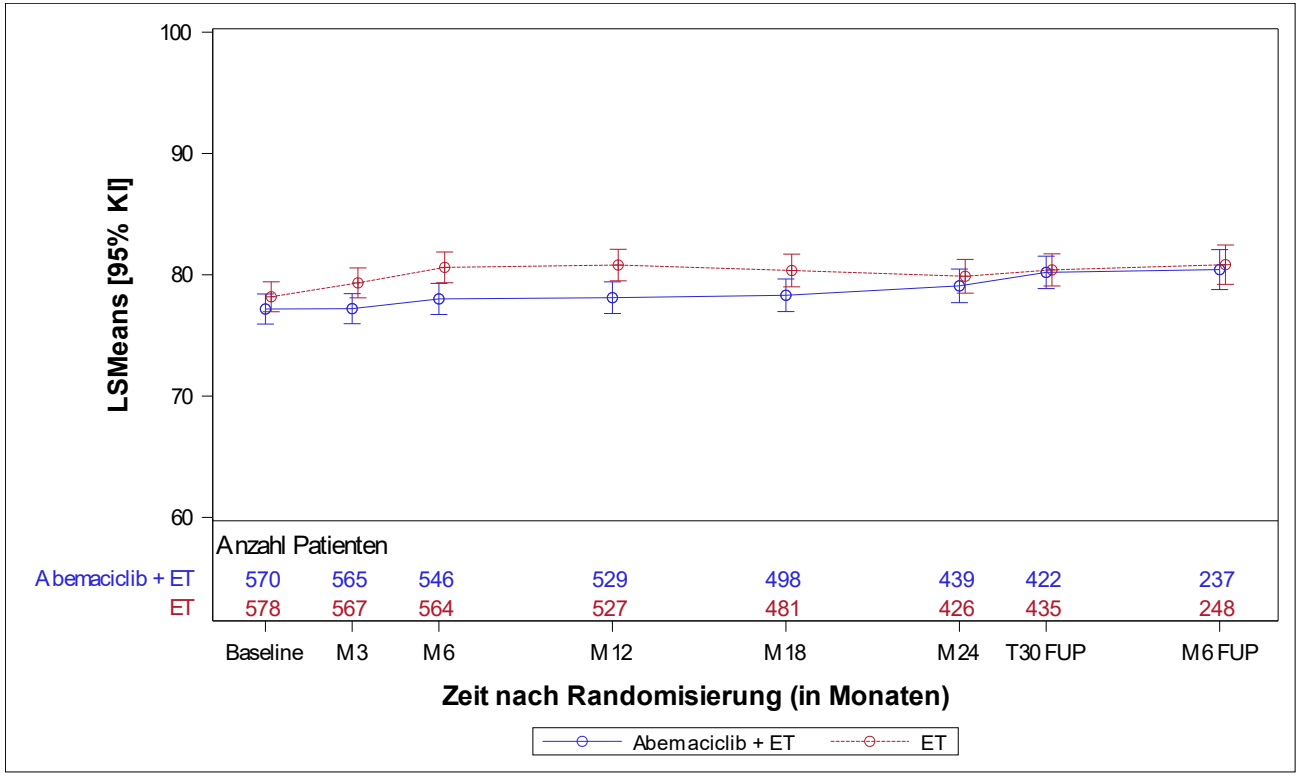
Abbildung 28 (Anhang): Verlaufskurven der EQ-5D VAS - Sensitivitätsanalyse

Verlaufskurven - EQ-5D VAS
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: EQ-5D VAS = Behandlung, Visite, Behandlung*Visite
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_lineplot_qol.sas
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Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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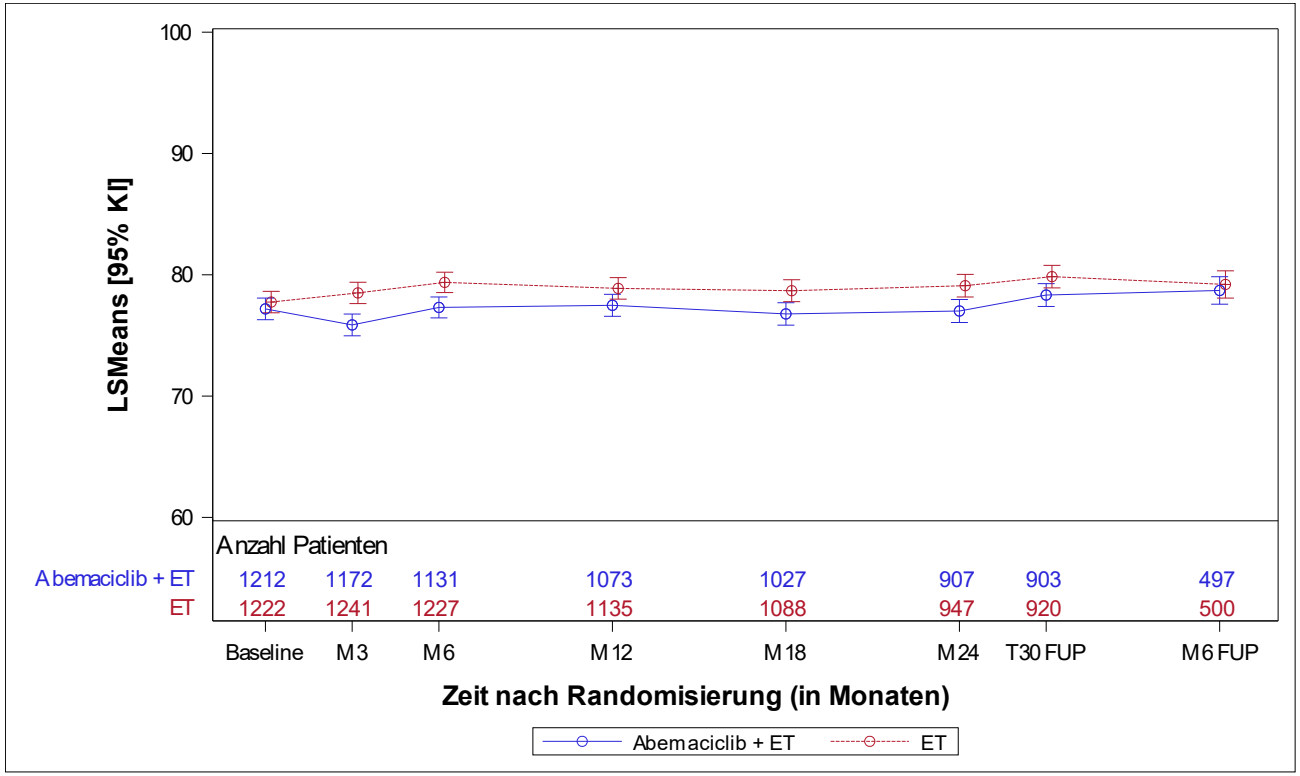
Verlaufskurven - EQ-5D VAS
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: EQ-5D VAS = Behandlung, Visite, Behandlung*Visite
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_lineplot_qol.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/f_lp_eq5dvas_posmp_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Anhang 4-G3.5: Symptomatik anhand FACIT-Fatigue - Sensitivitätsanalyse

Tabelle 4-141 (Anhang): FACIT-Fatigue - Sensitivitätsanalyse

Tabelle: Ergebnisse für die Veränderung FACIT-Fatigue aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Zeitpunkt	Abemaciclib+ET[1]										ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	M12 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Veränderung des FACIT-Fatigue																				
Prämenopausal	543 40,34 (9,03)	513 38,84 (9,86)	500 39,04 (10,13)	490 39,30 (9,79)	454 38,94 (10,11)	404 39,18 (10,77)	387 40,20 (10,10)	216 40,01 (9,78)	[5]	-1,17 (0,27)	555 40,20 (9,01)	522 40,73 (9,30)	508 41,51 (8,82)	480 41,33 (9,39)	449 41,51 (9,40)	403 41,10 (9,85)	404 41,25 (9,84)	235 41,17 (9,01)	0,52 (0,27)	-1,69 [-2,44;-0,94] <,0001 -0,27 [-0,39;-0,15]
Postmenopausal	1143 39,89 (9,61)	1053 38,02 (10,00)	1015 38,79 (9,88)	944 39,16 (9,53)	905 38,80 (9,97)	805 39,42 (9,36)	813 39,94 (9,50)	455 40,34 (9,12)	[5]	-1,16 (0,19)	1168 39,27 (9,69)	1081 39,84 (9,32)	1069 39,71 (9,63)	1006 40,04 (9,23)	959 40,11 (9,60)	843 40,41 (9,52)	831 40,18 (9,76)	446 40,06 (9,87)	0,34 (0,18)	-1,50 [-2,01;-0,99] <,0001 -0,24 [-0,32;-0,16]
Männer	10 43,10 (7,58)	9 41,11 (5,60)	9 46,44 (4,77)	6 39,83 (13,17)	6 43,67 (6,09)	5 41,80 (8,58)	6 48,00 (2,00)	5 43,00 (6,96)	3 42,67 (7,37)	[6]	10 44,90 (7,72)	10 43,00 (7,56)	9 47,33 (7,00)	10 44,40 (8,36)	10 42,30 (9,64)	6 42,67 (10,27)	8 43,00 (10,78)	3 45,67 (7,57)	[6]	[6]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: 30 Tage Follow-up; 3: 6 Monate Follow-up/12 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACIT-Fatigue Score = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACIT-Fatigue Score haben; 5: Visite wurde nicht in die Analyse einbezogen, da für weniger als 25% der Patienten Postbaseline-Werte vorlagen; 6: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet, dieses schließt den Verzicht auf die Darstellung der Postbaseline-Werte ein.
Abkürzungen: B: Baseline; ET: Endokrine Therapie; FACIT: Functional Assessment of Chronic Illness Therapy; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_mmrm_qol.sas
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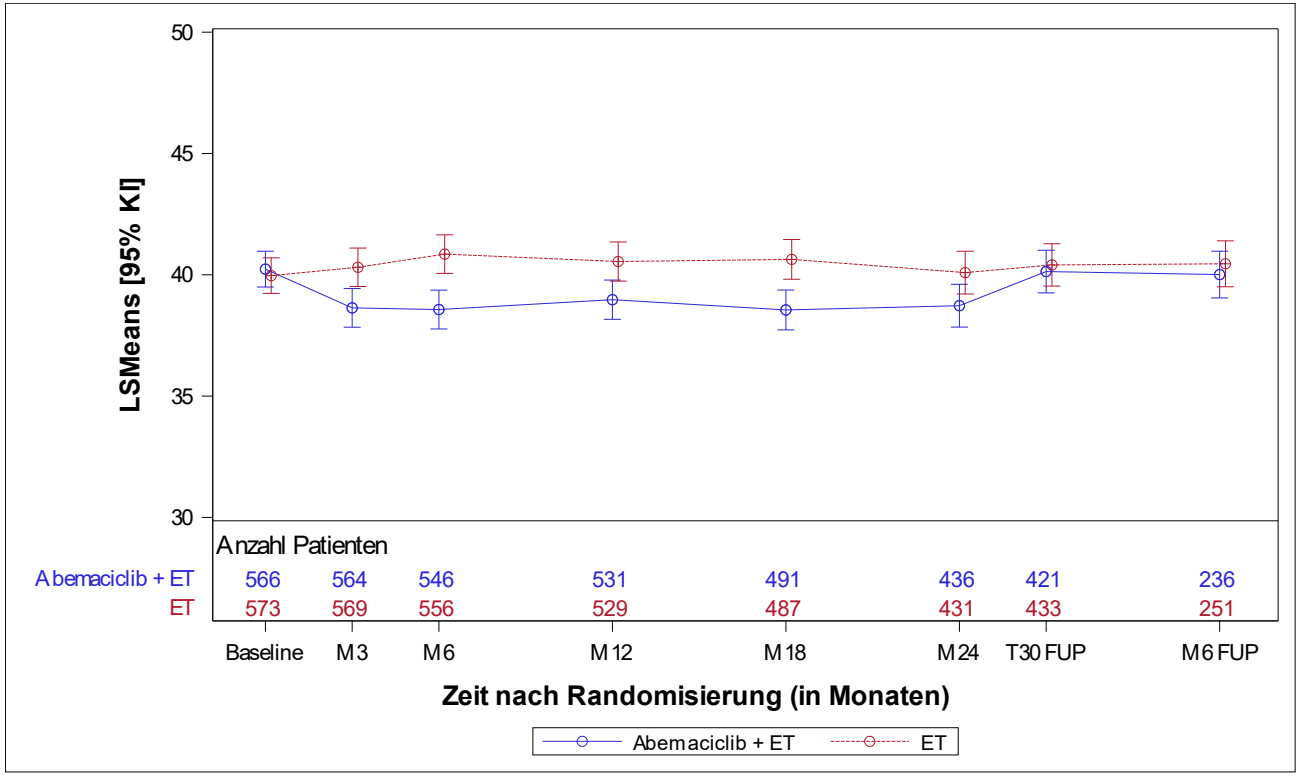
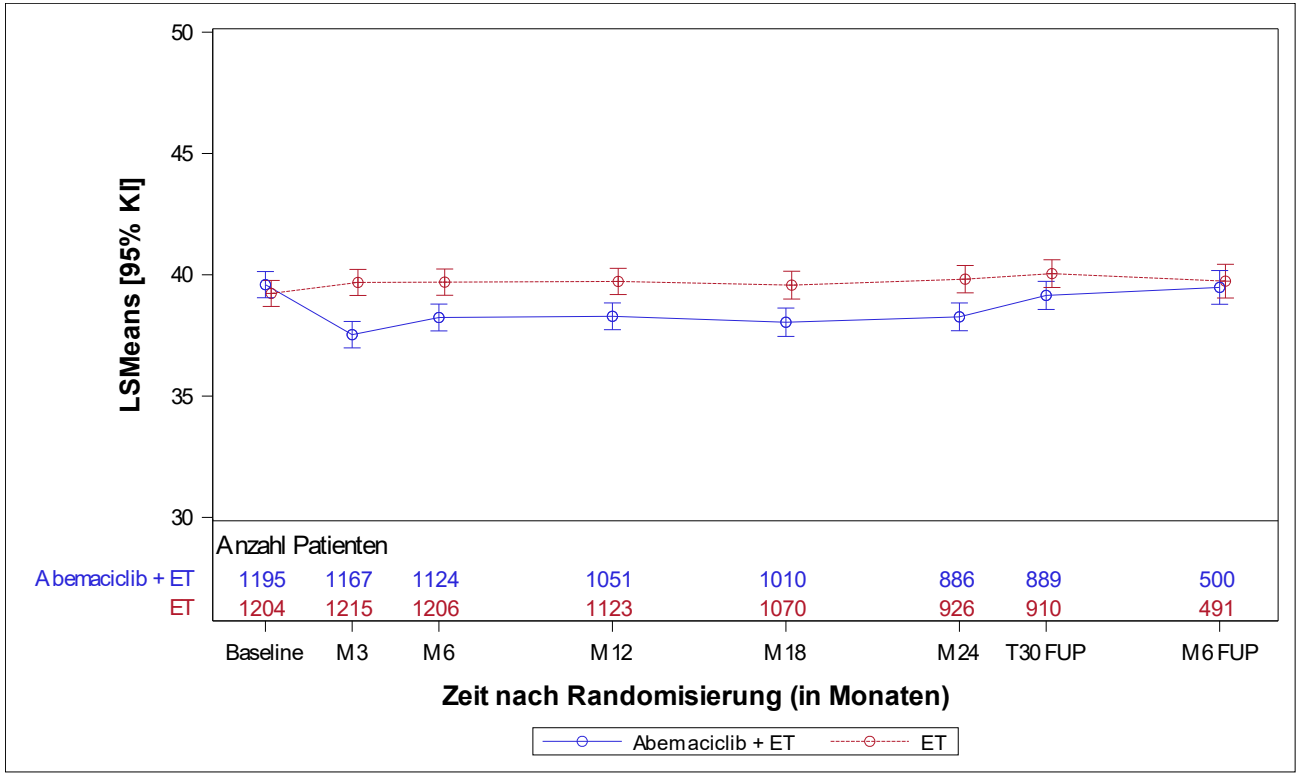
Abbildung 29 (Anhang): Verlaufskurven des FACIT-Fatigue - Sensitivitätsanalyse

Verlaufskurven - FACIT-Fatigue
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_lineplot_qol.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/f_lp_facitf_premp_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
14FEB2022 / 07:19

Verlaufskurven - FACIT-Fatigue
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: FACIT-Fatigue Score = Behandlung, Visite, Behandlung*Visite.
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_lineplot_qol.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/f_lp_facitf_posmp_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Anhang 4-G3.6: Symptomatik anhand FACT-ES - Sensitivitätsanalyse

Tabelle 4-142 (Anhang): FACT-ES - Sensitivitätsanalyse

Tabelle: Ergebnisse für die Veränderung FACT-ES aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Zeitpunkt	Abemaciclib+ET[1]										ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	M12 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Veränderung des FACT-ES 19																				
Prämenopausal	559 60,11 (9,57)	536 57,38 (10,56)	522 56,83 (11,39)	513 56,43 (11,83)	482 55,69 (11,97)	420 55,98 (12,18)	403 58,12 (11,01)	227 56,71 (11,32)	[5]	-3,32 (0,30)	568 59,54 (9,82)	542 58,65 (9,91)	535 58,60 (10,02)	497 58,29 (10,66)	461 57,59 (11,23)	413 57,29 (11,66)	420 57,98 (11,30)	239 57,45 (11,60)	-1,81 (0,30)	-1,51 [-2,34;-0,67] 0,0004 -0,21 [-0,33;-0,09]
Postmenopausal	1176 63,45 (8,78)	1108 61,16 (9,60)	1071 61,22 (9,90)	1010 60,94 (9,73)	961 60,70 (9,94)	852 60,49 (10,04)	867 62,18 (9,33)	473 61,90 (9,00)	[5]	-2,37 (0,18)	1207 62,78 (8,96)	1150 62,00 (9,41)	1133 61,50 (9,61)	1065 61,20 (9,72)	1015 61,17 (9,82)	893 61,40 (9,72)	874 61,93 (9,51)	467 61,41 (9,22)	-1,46 (0,18)	-0,90 [-1,39;-0,41] 0,0003 -0,15 [-0,23;-0,07]
Männer	10 68,90 (6,51)	9 69,33 (2,69)	8 71,50 (3,30)	7 71,00 (3,37)	6 71,83 (3,66)	5 68,40 (8,26)	6 72,00 (5,83)	5 69,60 (8,38)	3 72,67 (3,51)	[6]	10 70,80 (5,16)	10 70,40 (4,14)	10 69,70 (7,32)	10 68,30 (9,10)	10 68,70 (6,25)	5 67,00 (7,18)	8 67,75 (7,09)	3 69,67 (2,31)	[6]	[6]
Veränderung des ESS 18																				
Prämenopausal	559 57,45 (8,93)	536 54,49 (9,96)	522 54,04 (10,73)	513 53,74 (11,05)	482 53,11 (11,19)	420 53,36 (11,35)	403 55,61 (10,22)	227 54,37 (10,61)	[5]	-3,29 (0,28)	568 56,93 (9,07)	542 55,97 (9,22)	535 55,98 (9,30)	497 55,70 (9,92)	461 55,00 (10,41)	413 54,78 (10,82)	420 55,39 (10,53)	239 54,95 (10,73)	-1,79 (0,28)	-1,50 [-2,28;-0,71] 0,0002 -0,22 [-0,34;-0,10]
Postmenopausal	1176 60,84 (8,07)	1108 58,51 (8,91)	1071 58,61 (9,19)	1010 58,42 (9,05)	961 58,25 (9,23)	852 58,12 (9,33)	867 59,78 (8,58)	473 59,71 (8,30)	[5]	-2,21 (0,17)	1207 60,31 (8,27)	1150 59,69 (8,68)	1133 59,27 (8,87)	1065 59,06 (9,00)	1015 59,00 (9,06)	893 59,18 (8,99)	874 59,61 (8,74)	467 59,12 (8,53)	-1,20 (0,16)	-1,01 [-1,46;-0,55] <,0001 -0,18 [-0,26;-0,10]
Männer	10 65,30 (6,34)	9 66,11 (2,20)	8 67,75 (3,33)	7 67,43 (3,05)	6 68,67 (3,14)	5 65,40 (8,76)	6 68,67 (5,47)	5 66,80 (7,40)	3 69,33 (3,06)	[6]	10 67,40 (4,12)	10 67,10 (3,38)	10 66,80 (6,11)	10 65,60 (7,68)	10 65,70 (5,58)	5 64,40 (6,23)	8 65,38 (5,95)	3 68,00 (1,73)	[6]	[6]

Zeitpunkt	Abemaciclib+ET[1]										ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	M12 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: 30 Tage Follow-up; 3: 6 Monate Follow-up/12 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT-ES Score = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT-ES Score haben; 5: Visite wurde nicht in die Analyse einbezogen, da für weniger als 25% der Patienten Postbaseline-Werte vorlagen; 6: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet, dieses schließt den Verzicht auf die Darstellung der Postbaseline-Werte ein. Abkürzungen: B: Baseline; ET: Endokrine Therapie; ESS: Endocrine symptom scale; FACT-ES: Functional Assessment of Cancer Therapy - Endokrine Symptome; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler																			

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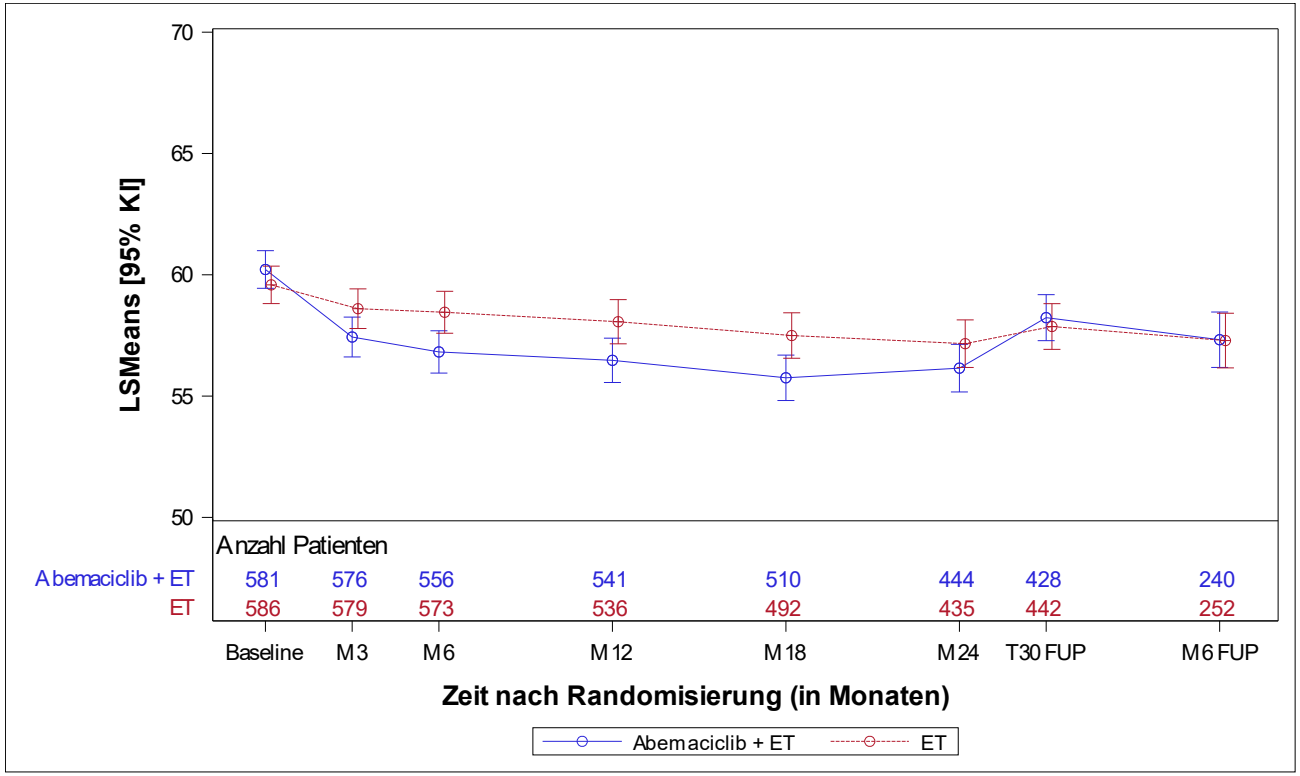
Abbildung 30 (Anhang): Verlaufskurven des FACT-ES - Sensitivitätsanalyse

Verlaufskurven - FACT-ES 19
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: FACT-ES 19 Score = Behandlung, Visite, Behandlung*Visite.
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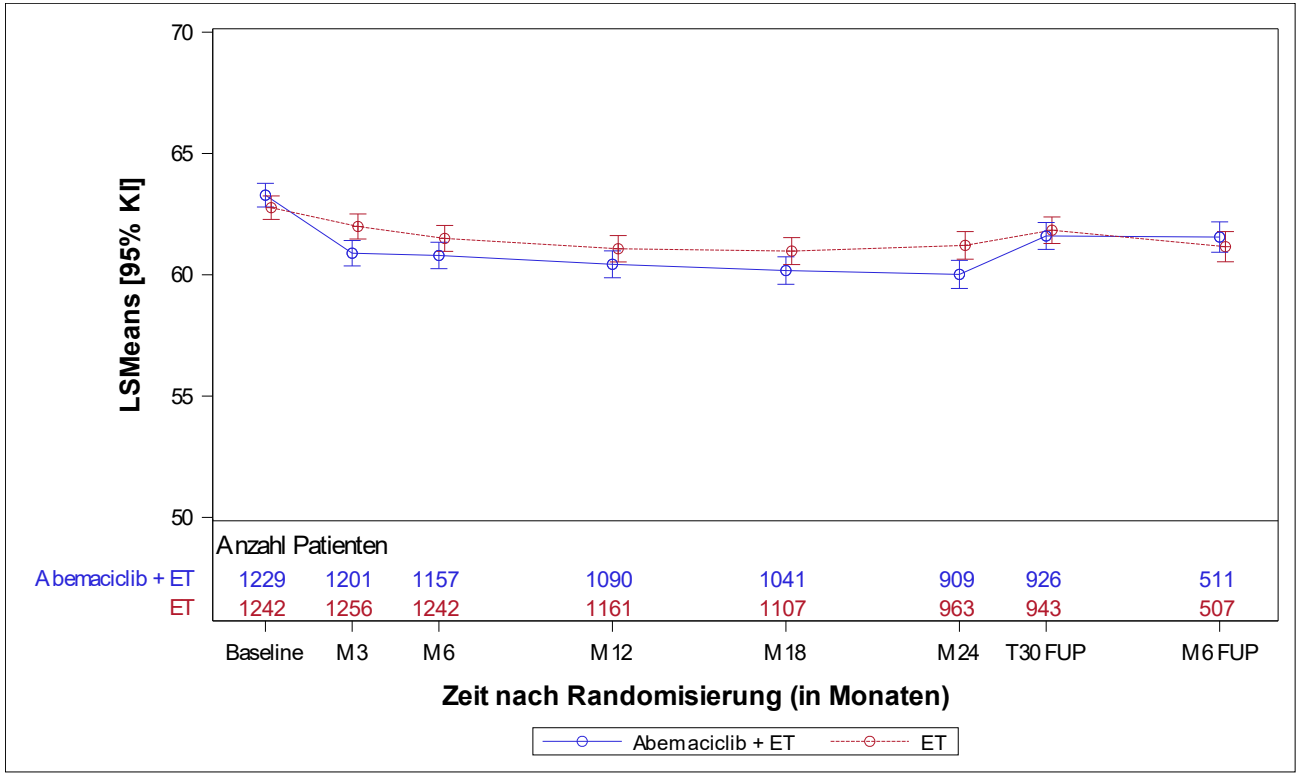
Verlaufskurven - FACT-ES 19
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: FACT-ES 19 Score = Behandlung, Visite, Behandlung*Visite.
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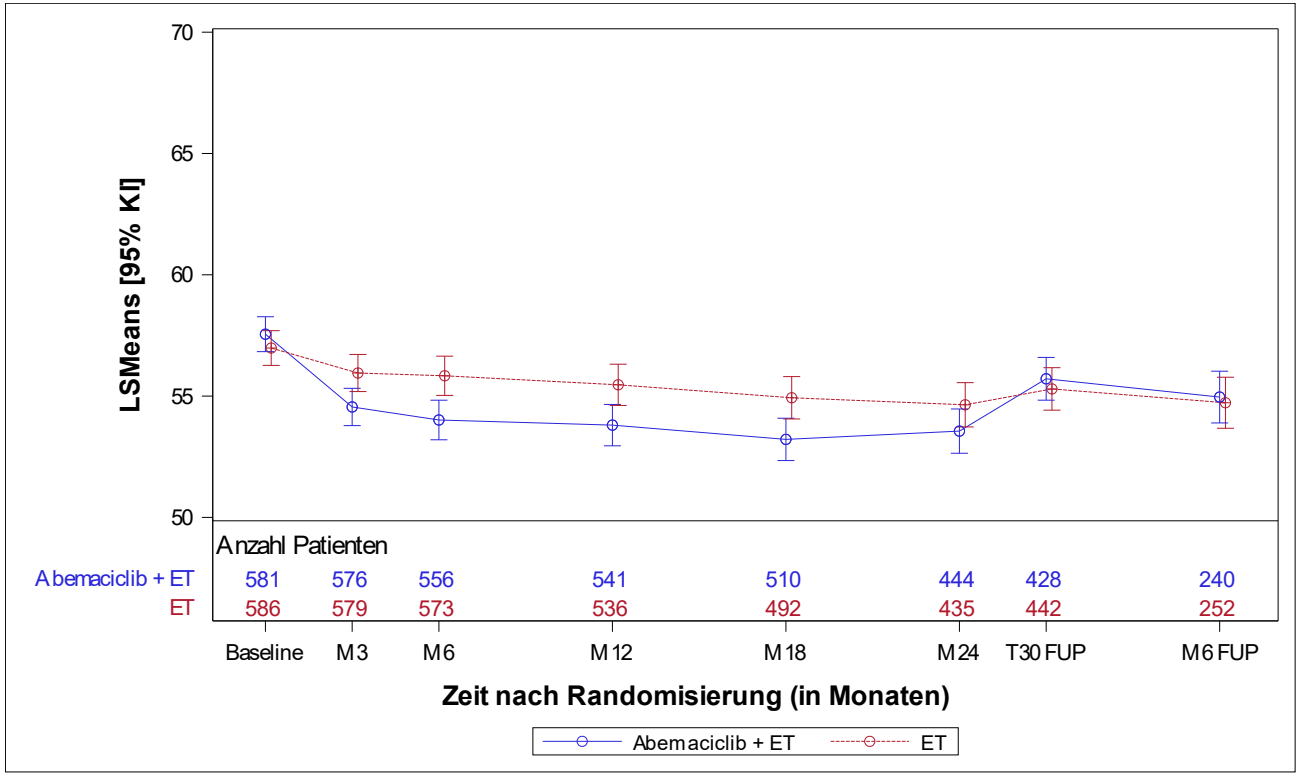
Verlaufskurven - ESS 18
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: ESS 18 Score = Behandlung, Visite, Behandlung*Visite.
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Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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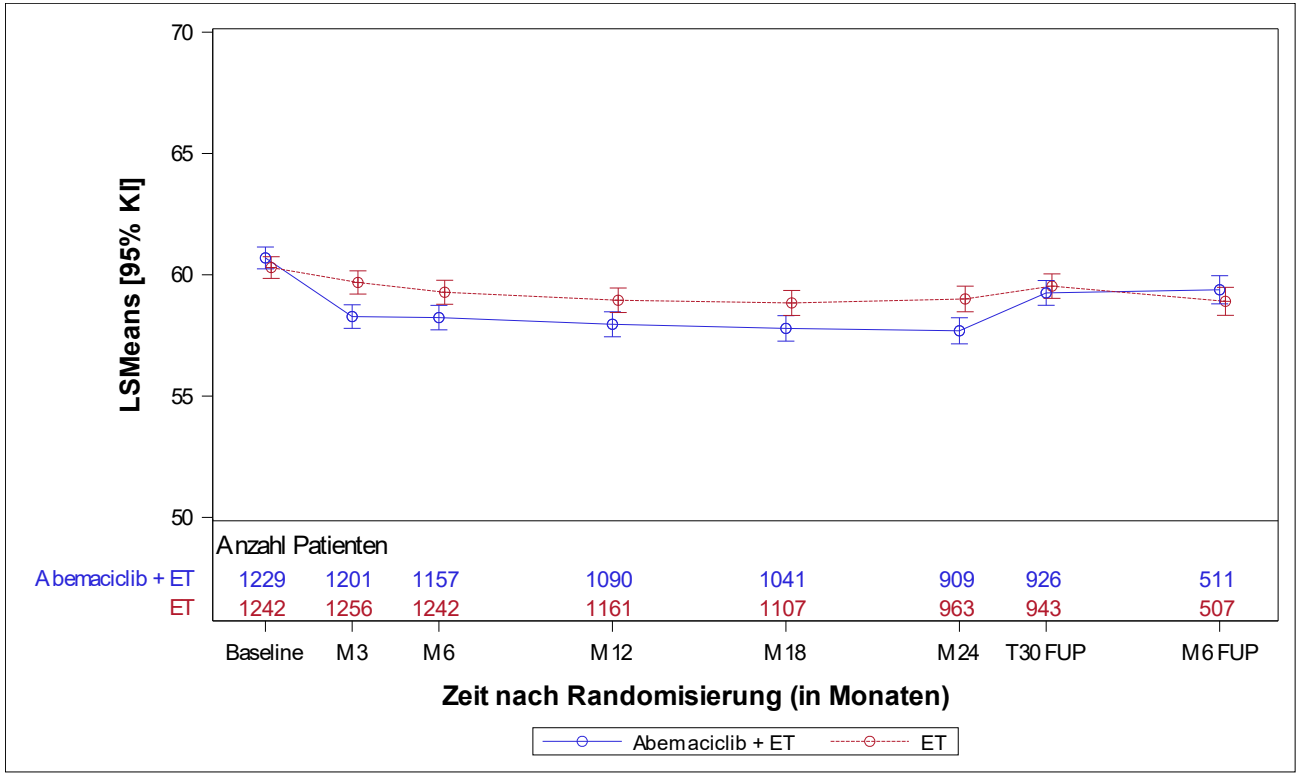
Verlaufskurven - ESS 18
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: ESS 18 Score = Behandlung, Visite, Behandlung*Visite.
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_lineplot_qol.sas
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Anhang 4-G3.7: Gesundheitsbezogene Lebensqualität anhand FACT-B - Sensitivitätsanalyse

Tabelle 4-143 (Anhang): FACT-B - Sensitivitätsanalyse

Tabelle: Ergebnisse für die Veränderung FACT aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Zeitpunkt	Abemaciclib+ET[1]										ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	M12 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Veränderung des FACT-B (Gesamtscore)																				
Prämenopausal	558 106,52 (16,96)	533 105,23 (17,98)	518 105,17 (19,37)	510 104,78 (19,47)	481 103,87 (19,34)	418 103,89 (20,32)	403 103,34 (19,94)	225 102,87 (19,07)	[5]	-2,13 (0,51)	566 105,63 (17,68)	541 106,39 (18,39)	530 107,23 (18,22)	495 107,96 (19,02)	455 108,30 (18,53)	413 107,24 (19,26)	415 105,92 (19,31)	236 105,77 (19,33)	0,88 (0,51)	-3,01 [-4,43;-1,59] <,0001 -0,25 [-0,37;-0,13]
Postmenopausal	1173 107,96 (18,38)	1102 106,60 (18,96)	1067 106,96 (19,10)	1005 106,54 (19,04)	953 106,20 (19,75)	851 105,87 (19,05)	863 105,99 (19,35)	470 106,38 (18,43)	[5]	-1,97 (0,35)	1208 107,34 (18,00)	1148 107,88 (18,15)	1130 107,89 (18,19)	1061 107,70 (18,19)	1015 107,82 (18,69)	896 107,82 (18,69)	873 107,01 (19,00)	470 106,51 (18,98)	-0,14 (0,34)	-1,83 [-2,79;-0,86] 0,0002 -0,15 [-0,23;-0,07]
Männer	10 111,80 (12,32)	9 112,56 (12,78)	9 120,22 (6,42)	7 110,43 (13,95)	6 113,00 (13,83)	5 116,40 (13,97)	6 117,00 (9,53)	5 114,40 (15,53)	3 118,67 (6,66)	[6]	9 112,67 (14,21)	9 113,78 (14,25)	9 115,44 (12,33)	9 116,67 (11,09)	9 115,00 (14,05)	6 117,50 (13,41)	7 108,29 (14,65)	3 106,67 (8,02)	[6]	[6]
Veränderung des FACT-G (Gesamtscore)																				
Prämenopausal	560 83,48 (13,22)	535 81,66 (14,31)	520 81,50 (15,19)	513 81,55 (15,23)	483 81,07 (14,89)	421 81,15 (15,98)	405 80,99 (15,90)	226 80,75 (14,94)	[5]	-2,16 (0,42)	566 82,77 (13,98)	541 82,91 (14,53)	531 83,43 (14,60)	495 84,02 (15,05)	458 84,40 (14,70)	415 83,52 (15,31)	417 82,15 (15,55)	237 81,63 (15,65)	0,03 (0,41)	-2,19 [-3,34;-1,04] 0,0002 -0,22 [-0,34;-0,10]
Postmenopausal	1175 84,11 (14,49)	1106 82,07 (15,21)	1070 82,42 (15,15)	1009 82,49 (15,01)	959 82,14 (15,44)	855 81,98 (15,08)	865 82,09 (15,47)	471 82,31 (15,04)	[5]	-2,24 (0,28)	1209 83,66 (14,21)	1151 83,66 (14,37)	1133 83,44 (14,44)	1063 83,40 (14,41)	1019 83,38 (14,73)	897 83,44 (14,88)	873 82,60 (14,99)	470 82,25 (15,01)	-0,79 (0,28)	-1,46 [-2,24;-0,68] 0,0002 -0,15 [-0,23;-0,07]
Männer	10 87,40 (10,51)	9 87,89 (9,43)	9 93,56 (5,25)	7 88,00 (9,42)	6 88,00 (13,31)	5 92,40 (6,66)	6 90,83 (9,28)	5 90,60 (12,76)	3 96,00 (7,94)	[6]	9 86,89 (11,40)	9 88,11 (12,15)	9 89,67 (8,67)	9 88,67 (8,67)	9 88,33 (10,89)	6 91,50 (7,09)	7 83,71 (12,85)	3 83,33 (4,93)	[6]	[6]

Zeitpunkt	Abemaciclib+ET[1]										ET[1]									Abemaciclib+ET vs. ET[1]
	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	M12 FUP[3] N MW (SD)	PB LSM (SE)	B N MW (SD)	M3 N MW (SD)	M6 N MW (SD)	M12 N MW (SD)	M18 N MW (SD)	M24 N MW (SD)	T30 FUP[2] N MW (SD)	M6 FUP[3] N MW (SD)	PB LSM (SE)	Differenz Δ [95% KI] p-Wert[4] Hedges'g [95% KI]
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: 30 Tage Follow-up; 3: 6 Monate Follow-up/12 Monate Follow-up; 4: p-Wert für Treatment Effekt aus dem MMRM Modell: Veränderung des FACT Score = Baseline, Behandlung, Visite, Behandlung*Visite. Die Analyse berücksichtigt alle Visiten, an denen mindestens 25% aller Patienten beider Behandlungsgruppen Werte für die Veränderung des FACT Score haben; 5: Visite wurde nicht in die Analyse einbezogen, da für weniger als 25% der Patienten Postbaseline-Werte vorlagen; 6: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet, dieses schließt den Verzicht auf die Darstellung der Postbaseline-Werte ein. Abkürzungen: B: Baseline; ET: Endokrine Therapie; FACT-B: Functional Assessment of Cancer Therapy - Breast Cancer; FACT-G: Functional Assessment of Cancer Therapy - General; KI: Konfidenzintervall; LSM: Least Squares Mean; M: Monat; MW: Mittelwert; N: Anzahl der Patienten mit Werten in der jeweiligen Visite; NE: Nicht errechenbar/nicht erreicht; PB: Post-Baseline; SD: Standardabweichung; SE: Standardfehler																			

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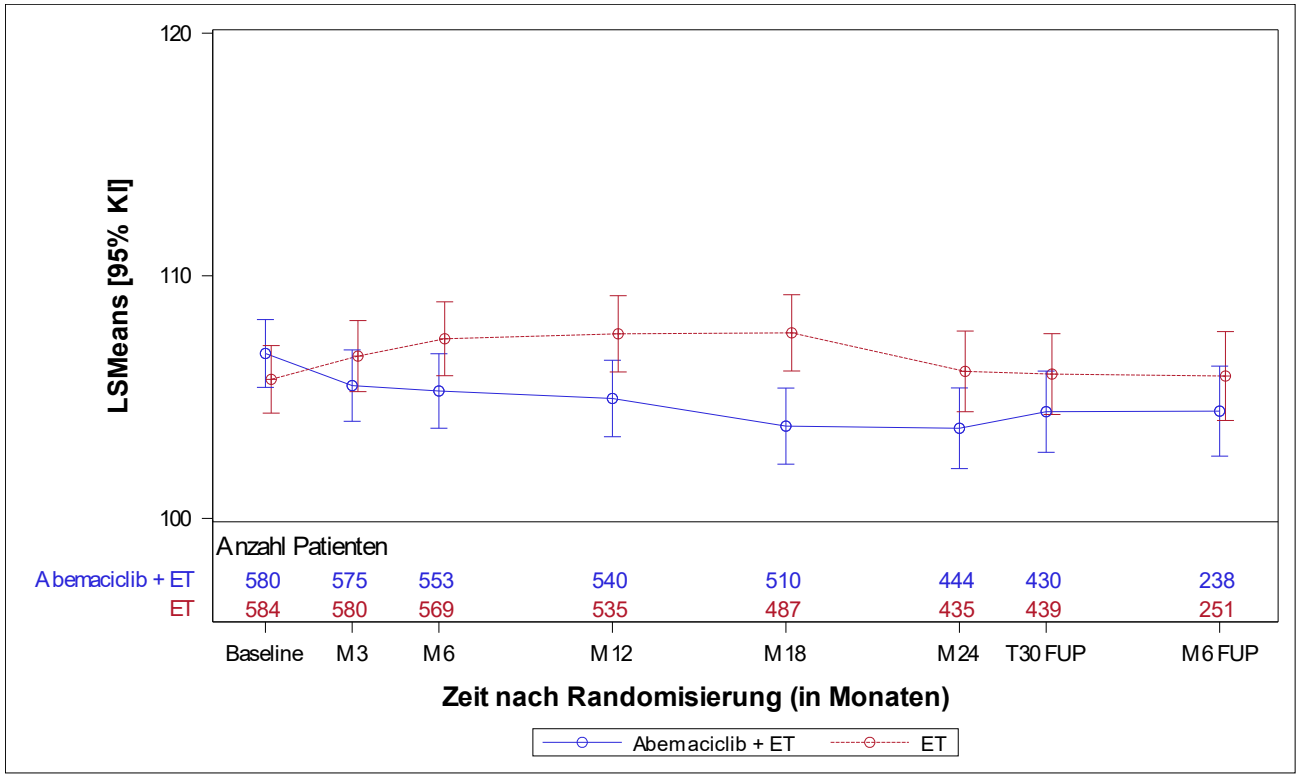
Abbildung 31 (Anhang): Verlaufskurven des FACT-B - Sensitivitätsanalyse

Verlaufskurven - FACT-B (Gesamtscore)
Kohorte 1 Population - Safety - Prämenopausal



Datenschnitt: 01.04.2021
Prämenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: FACT-B Gesamtscore = Behandlung, Visite, Behandlung*Visite.
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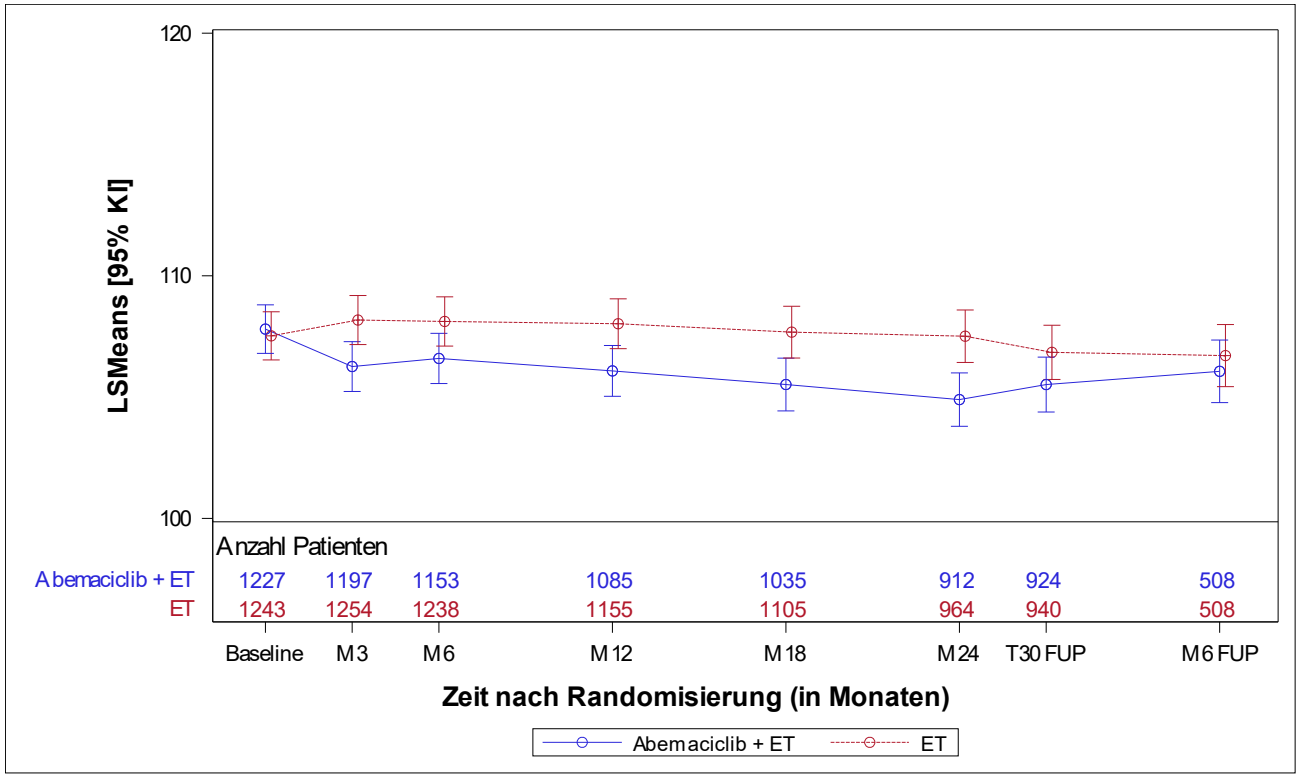
Verlaufskurven - FACT-B (Gesamtscore)
Kohorte 1 Population - Safety - Postmenopausal



Datenschnitt: 01.04.2021
Postmenopausal: gemäß ZVT des G-BA: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen)
LSMeans aus dem MMRM Modell: FACT-B Gesamtscore = Behandlung, Visite, Behandlung*Visite.
Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/f_gba2c1_lineplot_qol.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/f_lp_factbts_posmp_saf2c1.rtf
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Anhang 4-G3.8: Unerwünschte Ereignisse - Sensitivitätsanalyse

Anhang 4-G3.8.1: Unerwünschte Ereignisse (Gesamtraten) – Sensitivitätsanalyse

Tabelle 4-144 (Anhang): Unerwünschte Ereignisse (Gesamtraten) – Sensitivitätsanalyse

Tabelle: Ergebnisse für unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Unerwünschtes Ereignis (jeglicher Schweregrad)					
Prämenopausal	620/630 (98,4)	562/639 (87,9)	1,12 [1,09; 1,15] <,0001[3]	8,49 [4,35; 16,58] <,0001[4]	10,5 [7,8; 13,2] <,0001[4]
Postmenopausal	1339/1363 (98,2)	1237/1385 (89,3)	1,10 [1,08; 1,12] <,0001[3]	6,68 [4,31; 10,35] <,0001[4]	8,9 [7,2; 10,7] <,0001[4]
Männer	11/11 (100,0)	11/11 (100,0)	[2]	[2]	[2]
Schwerwiegendes unerwünschtes Ereignis					
Prämenopausal	83/630 (13,2)	56/639 (8,8)	1,50 [1,09; 2,07] 0,0127[3]	1,58 [1,10; 2,26] 0,0119[4]	4,4 [1,0; 7,8] 0,0119[4]
Postmenopausal	227/1363 (16,7)	136/1385 (9,8)	1,70 [1,39; 2,07] <,0001[3]	1,84 [1,46; 2,30] <,0001[4]	6,8 [4,3; 9,4] <,0001[4]
Männer	3/11 (27,3)	2/11 (18,2)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad ≥ 3					
Prämenopausal	287/630 (45,6)	102/639 (16,0)	2,85 [2,34; 3,48] <,0001[3]	4,41 [3,38; 5,73] <,0001[4]	29,6 [24,8; 34,4] <,0001[4]
Postmenopausal	691/1363 (50,7)	246/1385 (17,8)	2,85 [2,52; 3,23] <,0001[3]	4,76 [4,00; 5,67] <,0001[4]	32,9 [29,6; 36,3] <,0001[4]
Männer	5/11 (45,5)	3/11 (27,3)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad < 3					
Prämenopausal	617/630 (97,9)	558/639 (87,3)	1,12 [1,09; 1,16] <,0001[3]	6,89 [3,79; 12,51] <,0001[4]	10,6 [7,8; 13,4] <,0001[4]
Postmenopausal	1330/1363 (97,6)	1230/1385 (88,8)	1,10 [1,08; 1,12] <,0001[3]	5,08 [3,46; 7,45] <,0001[4]	8,8 [6,9; 10,6] <,0001[4]
Männer	11/11 (100,0)	11/11 (100,0)	[2]	[2]	[2]
Behandlungsabbruch aufgrund unerwünschter Ereignisse					
Prämenopausal	76/630 (12,1)	7/639 (1,1)	11,01 [5,12; 23,70] <,0001[3]	12,39 [5,66; 27,09] <,0001[4]	11,0 [8,3; 13,6] <,0001[4]
Postmenopausal	317/1363 (23,3)	17/1385 (1,2)	18,95 [11,70; 30,69] <,0001[3]	24,39 [14,87; 39,99] <,0001[4]	22,0 [19,7; 24,3] <,0001[4]
Männer	2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Datenschnitt: 01.04.2021 Safety-Population 1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet; 3: p-Wert basierend auf Z-Test; 4: p-Wert basierend auf Chi^2-Test. Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht; OR: Odds Ratio; RR: Relatives Risiko					

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_ae.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t1049_bp_ae_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
14FEB2022 / 07:19

Anhang 4-G3.8.2: Unerwünschte Ereignisse von speziellem Interesse - Sensitivitätsanalyse

Tabelle 4-145 (Anhang): Unerwünschte Ereignisse von speziellem Interesse - Sensitivitätsanalyse

Tabelle: Ergebnisse für unerwünschte Ereignisse: PT Neutropenie und erniedrigte Neutrophilenzahl aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Unerwünschtes Ereignis: PT Neutropenie und erniedrigte Neutrophilenzahl (jeglicher Schweregrad)					
Prämenopausal	271/630 (43,0)	45/639 (7,0)	6,11 [4,54; 8,21] <,0001[3]	9,96 [7,08; 14,02] <,0001[4]	36,0 [31,6; 40,3] <,0001[4]
Postmenopausal	586/1363 (43,0)	56/1385 (4,0)	10,63 [8,17; 13,84] <,0001[3]	17,90 [13,42; 23,87] <,0001[4]	39,0 [36,1; 41,8] <,0001[4]
Männer	3/11 (27,3)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad ≥ 3: PT Neutropenie und erniedrigte Neutrophilenzahl					
Prämenopausal	112/630 (17,8)	11/639 (1,7)	10,33 [5,61; 19,00] <,0001[3]	12,34 [6,57; 23,18] <,0001[4]	16,1 [12,9; 19,2] <,0001[4]
Postmenopausal	263/1363 (19,3)	7/1385 (0,5)	38,18 [18,09; 80,57] <,0001[3]	47,07 [22,13;100,12] <,0001[4]	18,8 [16,7; 20,9] <,0001[4]
Männer	2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad < 3: PT Neutropenie und erniedrigte Neutrophilenzahl					
Prämenopausal	225/630 (35,7)	39/639 (6,1)	5,85 [4,24; 8,07] <,0001[3]	8,55 [5,95; 12,28] <,0001[4]	29,6 [25,4; 33,8] <,0001[4]
Postmenopausal	523/1363 (38,4)	53/1385 (3,8)	10,03 [7,64; 13,17] <,0001[3]	15,65 [11,65; 21,03] <,0001[4]	34,5 [31,8; 37,3] <,0001[4]
Männer	2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Schwerwiegendes unerwünschtes Ereignis: PT Neutropenie und erniedrigte Neutrophilenzahl					
Prämenopausal	1/630 (0,2)	0/639 (0,0)	3,04 [0,12; 74,55] 0,4953[3]	3,05 [0,12; 74,95] 0,4965[5]	0,2 [-0,2; 0,5] 0,4965[5]
Postmenopausal	2/1363 (0,1)	0/1385 (0,0)	5,08 [0,24;105,73] 0,2939[3]	5,09 [0,24;106,08] 0,2459[5]	0,1 [-0,1; 0,3] 0,2459[5]
Männer	0/11 (0,0)	0/11 (0,0)	[2]	[2]	[2]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet; 3: p-Wert basierend auf Z-Test; 4: p-Wert basierend auf Chi^2-Test; 5: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

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Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t1050_bp_ae_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Tabelle: Ergebnisse für unerwünschte Ereignisse: Infektionen (SOC) aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Unerwünschtes Ereignis: SOC Infektionen (jeglicher Schweregrad)					
Prämenopausal	353/630 (56,0)	268/639 (41,9)	1,34 [1,19; 1,50] <,0001[3]	1,76 [1,41; 2,20] <,0001[4]	14,1 [8,6; 19,5] <,0001[4]
Postmenopausal	650/1363 (47,7)	521/1385 (37,6)	1,27 [1,16; 1,38] <,0001[3]	1,51 [1,30; 1,76] <,0001[4]	10,1 [6,4; 13,8] <,0001[4]
Männer	5/11 (45,5)	3/11 (27,3)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad ≥ 3: SOC Infektionen					
Prämenopausal	24/630 (3,8)	19/639 (3,0)	1,28 [0,71; 2,32] 0,4118[3]	1,29 [0,70; 2,38] 0,4105[4]	0,8 [-1,2; 2,8] 0,4105[4]
Postmenopausal	75/1363 (5,5)	40/1385 (2,9)	1,91 [1,31; 2,78] 0,0008[3]	1,96 [1,32; 2,90] 0,0006[4]	2,6 [1,1; 4,1] 0,0006[4]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad < 3: SOC Infektionen					
Prämenopausal	347/630 (55,1)	265/639 (41,5)	1,33 [1,18; 1,49] <,0001[3]	1,73 [1,39; 2,16] <,0001[4]	13,6 [8,2; 19,1] <,0001[4]
Postmenopausal	624/1363 (45,8)	513/1385 (37,0)	1,24 [1,13; 1,35] <,0001[3]	1,44 [1,23; 1,67] <,0001[4]	8,7 [5,1; 12,4] <,0001[4]
Männer	5/11 (45,5)	3/11 (27,3)	[2]	[2]	[2]
Schwerwiegendes unerwünschtes Ereignis: SOC Infektionen					
Prämenopausal	22/630 (3,5)	17/639 (2,7)	1,31 [0,70; 2,45] 0,3923[3]	1,32 [0,70; 2,52] 0,3908[4]	0,8 [-1,1; 2,7] 0,3908[4]
Postmenopausal	75/1363 (5,5)	39/1385 (2,8)	1,95 [1,34; 2,86] 0,0005[3]	2,01 [1,35; 2,98] 0,0004[4]	2,7 [1,2; 4,2] 0,0004[4]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet; 3: p-Wert basierend auf Z-Test; 4: p-Wert basierend auf Chi^2-Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_ae.sas
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Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
14FEB2022 / 07:19

Tabelle: Ergebnisse für unerwünschte Ereignisse: Diarrhoe (PT) aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Unerwünschtes Ereignis: PT Diarrhoe (jeglicher Schweregrad)					
Prämenopausal	514/630 (81,6)	45/639 (7,0)	11,59 [8,72; 15,39] <,0001[3]	58,49 [40,65; 84,16] <,0001[4]	74,5 [70,9; 78,2] <,0001[4]
Postmenopausal	1125/1363 (82,5)	131/1385 (9,5)	8,73 [7,40; 10,29] <,0001[3]	45,25 [36,03; 56,83] <,0001[4]	73,1 [70,5; 75,6] <,0001[4]
Männer	7/11 (63,6)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad ≥ 3: PT Diarrhoe					
Prämenopausal	33/630 (5,2)	2/639 (0,3)	16,74 [4,03; 69,45] 0,0001[3]	17,61 [4,21; 73,69] <,0001[4]	4,9 [3,1; 6,7] <,0001[4]
Postmenopausal	133/1363 (9,8)	2/1385 (0,1)	67,57 [16,76;272,46] <,0001[3]	74,77 [18,47;302,73] <,0001[4]	9,6 [8,0; 11,2] <,0001[4]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad < 3: PT Diarrhoe					
Prämenopausal	512/630 (81,3)	45/639 (7,0)	11,54 [8,69; 15,33] <,0001[3]	57,27 [39,83; 82,35] <,0001[4]	74,2 [70,6; 77,9] <,0001[4]
Postmenopausal	1119/1363 (82,1)	130/1385 (9,4)	8,75 [7,41; 10,32] <,0001[3]	44,27 [35,26; 55,59] <,0001[4]	72,7 [70,2; 75,3] <,0001[4]
Männer	7/11 (63,6)	0/11 (0,0)	[2]	[2]	[2]
Schwerwiegendes unerwünschtes Ereignis: PT Diarrhoe					
Prämenopausal	1/630 (0,2)	0/639 (0,0)	3,04 [0,12; 74,55] 0,4953[3]	3,05 [0,12; 74,95] 0,4965[5]	0,2 [-0,2; 0,5] 0,4965[5]
Postmenopausal	11/1363 (0,8)	0/1385 (0,0)	23,37 [1,38;396,20] 0,0291[3]	23,56 [1,39;400,22] 0,0008[4]	0,8 [0,3; 1,3] 0,0008[4]
Männer	0/11 (0,0)	0/11 (0,0)	[2]	[2]	[2]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet; 3: p-Wert basierend auf Z-Test; 4: p-Wert basierend auf Chi^2-Test; 5: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht; OR: Odds Ratio; PT: Preferred Term; RR: Relatives Risiko

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_ae.sas
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Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Tabelle: Ergebnisse für unerwünschte Ereignisse: Hepatische Ereignisse aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Unerwünschtes Ereignis: Hepatische Ereignisse (jeglicher Schweregrad)					
Prämenopausal	67/630 (10,6)	41/639 (6,4)	1,66 [1,14; 2,41] 0,0079[3]	1,74 [1,16; 2,60] 0,0071[4]	4,2 [1,2; 7,3] 0,0071[4]
Postmenopausal	203/1363 (14,9)	111/1385 (8,0)	1,86 [1,49; 2,31] <,0001[3]	2,01 [1,57; 2,57] <,0001[4]	6,9 [4,5; 9,2] <,0001[4]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad ≥ 3: Hepatische Ereignisse					
Prämenopausal	15/630 (2,4)	5/639 (0,8)	3,04 [1,11; 8,32] 0,0302[3]	3,09 [1,12; 8,56] 0,0223[4]	1,6 [0,2; 3,0] 0,0223[4]
Postmenopausal	46/1363 (3,4)	13/1385 (0,9)	3,60 [1,95; 6,62] <,0001[3]	3,69 [1,98; 6,85] <,0001[4]	2,4 [1,4; 3,5] <,0001[4]
Männer	0/11 (0,0)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad < 3: Hepatische Ereignisse					
Prämenopausal	66/630 (10,5)	40/639 (6,3)	1,67 [1,15; 2,44] 0,0074[3]	1,75 [1,16; 2,64] 0,0066[4]	4,2 [1,2; 7,3] 0,0066[4]
Postmenopausal	195/1363 (14,3)	107/1385 (7,7)	1,85 [1,48; 2,32] <,0001[3]	1,99 [1,55; 2,56] <,0001[4]	6,6 [4,3; 8,9] <,0001[4]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Schwerwiegendes unerwünschtes Ereignis: Hepatische Ereignisse					
Prämenopausal	2/630 (0,3)	0/639 (0,0)	5,07 [0,24;105,42] 0,2943[3]	5,09 [0,24;106,18] 0,2463[5]	0,3 [-0,1; 0,8] 0,2463[5]
Postmenopausal	4/1363 (0,3)	1/1385 (0,1)	4,06 [0,45; 36,32] 0,2095[3]	4,07 [0,45; 36,49] 0,2147[5]	0,2 [-0,1; 0,5] 0,2147[5]
Männer	0/11 (0,0)	0/11 (0,0)	[2]	[2]	[2]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet; 3: p-Wert basierend auf Z-Test; 4: p-Wert basierend auf Chi^2-Test; 5: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht; OR: Odds Ratio; RR: Relatives Risiko

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Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t1053_bp_ae_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
14FEB2022 / 07:19

Tabelle: Ergebnisse für unerwünschte Ereignisse: Venöse Thromboembolie aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Unerwünschtes Ereignis: Venöse Thromboembolie (jeglicher Schweregrad)					
Prämenopausal	17/630 (2,7)	4/639 (0,6)	4,31 [1,46; 12,74] 0,0082[3]	4,40 [1,47; 13,16] 0,0038[4]	2,1 [0,7; 3,5] 0,0038[4]
Postmenopausal	44/1363 (3,2)	11/1385 (0,8)	4,06 [2,11; 7,84] <,0001[3]	4,17 [2,14; 8,10] <,0001[4]	2,4 [1,4; 3,5] <,0001[4]
Männer	2/11 (18,2)	1/11 (9,1)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad ≥ 3: Venöse Thromboembolie					
Prämenopausal	10/630 (1,6)	3/639 (0,5)	3,38 [0,93; 12,23] 0,0633[3]	3,42 [0,94; 12,48] 0,0480[4]	1,1 [0,0; 2,2] 0,0480[4]
Postmenopausal	21/1363 (1,5)	4/1385 (0,3)	5,33 [1,84; 15,50] 0,0021[3]	5,40 [1,85; 15,78] 0,0005[4]	1,3 [0,5; 2,0] 0,0005[4]
Männer	1/11 (9,1)	1/11 (9,1)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad < 3: Venöse Thromboembolie					
Prämenopausal	11/630 (1,7)	1/639 (0,2)	11,16 [1,44; 86,16] 0,0207[3]	11,34 [1,46; 88,08] 0,0034[4]	1,6 [0,5; 2,7] 0,0034[4]
Postmenopausal	28/1363 (2,1)	9/1385 (0,6)	3,16 [1,50; 6,67] 0,0025[3]	3,21 [1,51; 6,82] 0,0014[4]	1,4 [0,5; 2,3] 0,0014[4]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Schwerwiegendes unerwünschtes Ereignis: Venöse Thromboembolie					
Prämenopausal	9/630 (1,4)	3/639 (0,5)	3,04 [0,83; 11,19] 0,0939[3]	3,07 [0,83; 11,40] 0,0776[4]	1,0 [-0,1; 2,0] 0,0776[4]
Postmenopausal	22/1363 (1,6)	4/1385 (0,3)	5,59 [1,93; 16,18] 0,0015[3]	5,66 [1,95; 16,48] 0,0003[4]	1,3 [0,6; 2,1] 0,0003[4]
Männer	1/11 (9,1)	1/11 (9,1)	[2]	[2]	[2]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet; 3: p-Wert basierend auf Z-Test; 4: p-Wert basierend auf Chi^2-Test; 5: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht; OR: Odds Ratio; RR: Relatives Risiko

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_ae.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t1054_bp_ae_saf2c1.rtf
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/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
14FEB2022 / 07:19

Tabelle: Ergebnisse für unerwünschte Ereignisse: ILD/Pneumonitis aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Unerwünschtes Ereignis: ILD/Pneumonitis (jeglicher Schweregrad)					
Prämenopausal	15/630 (2,4)	9/639 (1,4)	1,69 [0,75; 3,83] 0,2090[3]	1,71 [0,74; 3,93] 0,2035[4]	1,0 [-0,5; 2,5] 0,2035[4]
Postmenopausal	36/1363 (2,6)	18/1385 (1,3)	2,03 [1,16; 3,56] 0,0132[3]	2,06 [1,16; 3,65] 0,0113[4]	1,3 [0,3; 2,4] 0,0113[4]
Männer	2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad ≥ 3: ILD/Pneumonitis					
Prämenopausal	1/630 (0,2)	0/639 (0,0)	3,04 [0,12; 74,55] 0,4953[3]	3,05 [0,12; 74,95] 0,4965[5]	0,2 [-0,2; 0,5] 0,4965[5]
Postmenopausal	7/1363 (0,5)	1/1385 (0,1)	7,11 [0,88; 57,74] 0,0663[3]	7,14 [0,88; 58,15] 0,0374[5]	0,4 [0,0; 0,8] 0,0374[5]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad < 3: ILD/Pneumonitis					
Prämenopausal	15/630 (2,4)	9/639 (1,4)	1,69 [0,75; 3,83] 0,2090[3]	1,71 [0,74; 3,93] 0,2035[4]	1,0 [-0,5; 2,5] 0,2035[4]
Postmenopausal	33/1363 (2,4)	18/1385 (1,3)	1,86 [1,05; 3,29] 0,0322[3]	1,88 [1,06; 3,36] 0,0294[4]	1,1 [0,1; 2,1] 0,0294[4]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Schwerwiegendes unerwünschtes Ereignis: ILD/Pneumonitis					
Prämenopausal	2/630 (0,3)	0/639 (0,0)	5,07 [0,24;105,42] 0,2943[3]	5,09 [0,24;106,18] 0,2463[5]	0,3 [-0,1; 0,8] 0,2463[5]
Postmenopausal	8/1363 (0,6)	1/1385 (0,1)	8,13 [1,02; 64,91] 0,0481[3]	8,17 [1,02; 65,42] 0,0204[5]	0,5 [0,1; 0,9] 0,0204[5]
Männer	1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet; 3: p-Wert basierend auf Z-Test; 4: p-Wert basierend auf Chi^2-Test; 5: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; ILD: Interstitial Lung Disease; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht; OR: Odds Ratio; RR: Relatives Risiko

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Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t1055_bp_ae_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Tabelle: Ergebnisse für unerwünschte Ereignisse: Erkrankungen der Nieren und Harnwege (SOC) aus RCT mit dem zu bewertenden Arzneimittel
Kohorte 1 Population - Safety

Population	Abemaciclib+ET[1] Pat. mit Ereignis n/N (%)	ET[1] Pat. mit Ereignis n/N (%)	Abemaciclib+ET vs. ET[1] RR [95% KI] p-Wert	OR [95% KI] p-Wert	ARR [95% KI] p-Wert
Unerwünschtes Ereignis: Erkrankungen der Nieren und Harnwege (SOC) (jeglicher Schweregrad)					
Prämenopausal	49/630 (7,8)	32/639 (5,0)	1,55 [1,01; 2,39] 0,0456[3]	1,60 [1,01; 2,53] 0,0436[4]	2,8 [0,1; 5,5] 0,0436[4]
Postmenopausal	110/1363 (8,1)	78/1385 (5,6)	1,43 [1,08; 1,90] 0,0119[3]	1,47 [1,09; 1,99] 0,0113[4]	2,4 [0,6; 4,3] 0,0113[4]
Männer	0/11 (0,0)	2/11 (18,2)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad ≥ 3: Erkrankungen der Nieren und Harnwege (SOC)					
Prämenopausal	2/630 (0,3)	1/639 (0,2)	2,03 [0,18; 22,32] 0,5632[3]	2,03 [0,18; 22,46] 0,6221[5]	0,2 [-0,4; 0,7] 0,6221[5]
Postmenopausal	14/1363 (1,0)	3/1385 (0,2)	4,74 [1,37; 16,46] 0,0143[3]	4,78 [1,37; 16,67] 0,0067[4]	0,8 [0,2; 1,4] 0,0067[4]
Männer	0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Unerwünschtes Ereignis CTCAE Grad < 3: Erkrankungen der Nieren und Harnwege (SOC)					
Prämenopausal	47/630 (7,5)	31/639 (4,9)	1,54 [0,99; 2,39] 0,0552[3]	1,58 [0,99; 2,52] 0,0530[4]	2,6 [-0,0; 5,3] 0,0530[4]
Postmenopausal	107/1363 (7,9)	76/1385 (5,5)	1,43 [1,08; 1,90] 0,0136[3]	1,47 [1,08; 1,99] 0,0130[4]	2,4 [0,5; 4,2] 0,0130[4]
Männer	0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Schwerwiegendes unerwünschtes Ereignis: Erkrankungen der Nieren und Harnwege (SOC)					
Prämenopausal	2/630 (0,3)	0/639 (0,0)	5,07 [0,24;105,42] 0,2943[3]	5,09 [0,24;106,18] 0,2463[5]	0,3 [-0,1; 0,8] 0,2463[5]
Postmenopausal	8/1363 (0,6)	3/1385 (0,2)	2,71 [0,72; 10,19] 0,1403[3]	2,72 [0,72; 10,27] 0,1242[4]	0,4 [-0,1; 0,8] 0,1242[4]
Männer	0/11 (0,0)	0/11 (0,0)	[2]	[2]	[2]

Datenschnitt: 01.04.2021
Safety-Population
1: gemäß ZVT des G-BA: Prämenopausal: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Postmenopausal: Initiale Therapie mit Anastrozol, Letrozol; Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); Männer: Initiale Therapie mit Tamoxifen (mit jeglichen nachfolgenden Therapiesequenzen); 2: auf einen statistischen Test wurde aufgrund der geringen Patienten und Ereigniszahl verzichtet; 3: p-Wert basierend auf Z-Test; 4: p-Wert basierend auf Chi^2-Test; 5: p-Wert basierend auf exaktem Fisher Test.
Abkürzungen: ARR: Absolute Risikoreduktion; CTCAE: Common Terminology Criteria for Adverse Events; ET: Endokrine Therapie; KI: Konfidenzintervall; n: Anzahl der Patienten mit Ereignis; N: Gesamtzahl der Patienten in der Analyse; NE: Nicht errechenbar/nicht erreicht; OR: Odds Ratio; RR: Relatives Risiko; SOC: System Organ Class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_ae.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t1056_bp_ae_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Anhang 4-G3.8.3: Häufige unerwünschte Ereignisse nach SOC und PT - Sensitivitätsanalyse

Tabelle 4-146 (Anhang): Häufige unerwünschte Ereignisse nach SOC und PT - Sensitivitätsanalyse

Table: Results from binary analysis for adverse events according PT - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Abdominal discomfort				
10/630 (1,6)	5/639 (0,8)	2,03 [0,70; 5,90] 0,1942[3]	2,05 [0,70; 6,02] 0,1847[4]	0,8 [-0,4; 2,0] 0,1847[4]
Abdominal distension				
17/630 (2,7)	7/639 (1,1)	2,46 [1,03; 5,90] 0,0430[3]	2,50 [1,03; 6,08] 0,0361[4]	1,6 [0,1; 3,1] 0,0361[4]
Abdominal pain				
166/630 (26,3)	39/639 (6,1)	4,32 [3,10; 6,01] <,0001[3]	5,50 [3,80; 7,96] <,0001[4]	20,2 [16,3; 24,2] <,0001[4]
Abdominal pain upper				
83/630 (13,2)	26/639 (4,1)	3,24 [2,11; 4,96] <,0001[3]	3,58 [2,27; 5,64] <,0001[4]	9,1 [6,1; 12,2] <,0001[4]
Alanine aminotransferase increased				
53/630 (8,4)	35/639 (5,5)	1,54 [1,02; 2,32] 0,0414[3]	1,59 [1,02; 2,47] 0,0396[4]	2,9 [0,1; 5,7] 0,0396[4]
Alopecia				
58/630 (9,2)	13/639 (2,0)	4,53 [2,51; 8,17] <,0001[3]	4,88 [2,65; 9,00] <,0001[4]	7,2 [4,7; 9,7] <,0001[4]
Anaemia				
118/630 (18,7)	29/639 (4,5)	4,13 [2,79; 6,10] <,0001[3]	4,85 [3,18; 7,40] <,0001[4]	14,2 [10,7; 17,6] <,0001[4]
Anxiety				
31/630 (4,9)	35/639 (5,5)	0,90 [0,56; 1,44] 0,6554[3]	0,89 [0,54; 1,47] 0,6552[4]	-0,6 [-3,0; 1,9] 0,6552[4]
Arthralgia				
138/630 (21,9)	198/639 (31,0)	0,71 [0,59; 0,85] 0,0003[3]	0,62 [0,49; 0,80] 0,0002[4]	-9,1 [-13,9; -4,3] 0,0002[4]
Aspartate aminotransferase increased				
54/630 (8,6)	28/639 (4,4)	1,96 [1,26; 3,05] 0,0030[3]	2,05 [1,28; 3,27] 0,0024[4]	4,2 [1,5; 6,9] 0,0024[4]
Asthenia				
65/630 (10,3)	26/639 (4,1)	2,54 [1,63; 3,94] <,0001[3]	2,71 [1,70; 4,34] <,0001[4]	6,2 [3,4; 9,1] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Axillary pain				
11/630 (1,7)	8/639 (1,3)	1,39 [0,56; 3,44] 0,4708[3]	1,40 [0,56; 3,51] 0,4687[4]	0,5 [-0,8; 1,8] 0,4687[4]
Back pain				
77/630 (12,2)	83/639 (13,0)	0,94 [0,70; 1,26] 0,6808[3]	0,93 [0,67; 1,30] 0,6807[4]	-0,8 [-4,4; 2,9] 0,6807[4]
Blood alkaline phosphatase increased				
10/630 (1,6)	3/639 (0,5)	3,38 [0,93; 12,23] 0,0633[3]	3,42 [0,94; 12,48] 0,0480[4]	1,1 [0,0; 2,2] 0,0480[4]
Blood cholesterol increased				
10/630 (1,6)	9/639 (1,4)	1,13 [0,46; 2,75] 0,7932[3]	1,13 [0,46; 2,80] 0,7931[4]	0,2 [-1,2; 1,5] 0,7931[4]
Blood creatinine increased				
62/630 (9,8)	2/639 (0,3)	31,44 [7,72; 127,99] <,0001[3]	34,77 [8,47; 142,77] <,0001[4]	9,5 [7,2; 11,9] <,0001[4]
Bone pain				
11/630 (1,7)	19/639 (3,0)	0,59 [0,28; 1,22] 0,1554[3]	0,58 [0,27; 1,23] 0,1502[4]	-1,2 [-2,9; 0,4] 0,1502[4]
Breast pain				
30/630 (4,8)	27/639 (4,2)	1,13 [0,68; 1,87] 0,6447[3]	1,13 [0,67; 1,93] 0,6445[4]	0,5 [-1,7; 2,8] 0,6445[4]
Breast reconstruction				
8/630 (1,3)	11/639 (1,7)	0,74 [0,30; 1,82] 0,5095[3]	0,73 [0,29; 1,84] 0,5078[4]	-0,5 [-1,8; 0,9] 0,5078[4]
Cellulitis				
18/630 (2,9)	10/639 (1,6)	1,83 [0,85; 3,92] 0,1231[3]	1,85 [0,85; 4,04] 0,1172[4]	1,3 [-0,3; 2,9] 0,1172[4]
Chills				
18/630 (2,9)	2/639 (0,3)	9,13 [2,13; 39,18] 0,0029[3]	9,37 [2,16; 40,54] 0,0003[4]	2,5 [1,2; 3,9] 0,0003[4]
Conjunctivitis				
12/630 (1,9)	6/639 (0,9)	2,03 [0,77; 5,37] 0,1545[3]	2,05 [0,76; 5,49] 0,1458[4]	1,0 [-0,3; 2,3] 0,1458[4]
Constipation				
90/630 (14,3)	53/639 (8,3)	1,72 [1,25; 2,37] 0,0009[3]	1,84 [1,29; 2,64] 0,0007[4]	6,0 [2,5; 9,5] 0,0007[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Contusion				
12/630 (1,9)	9/639 (1,4)	1,35 [0,57; 3,19] 0,4901[3]	1,36 [0,57; 3,25] 0,4884[4]	0,5 [-0,9; 1,9] 0,4884[4]
Cough				
86/630 (13,7)	36/639 (5,6)	2,42 [1,67; 3,52] <,0001[3]	2,65 [1,76; 3,97] <,0001[4]	8,0 [4,8; 11,2] <,0001[4]
Cystitis				
22/630 (3,5)	11/639 (1,7)	2,03 [0,99; 4,15] 0,0526[3]	2,07 [0,99; 4,30] 0,0475[4]	1,8 [0,0; 3,5] 0,0475[4]
Decreased appetite				
60/630 (9,5)	10/639 (1,6)	6,09 [3,14; 11,78] <,0001[3]	6,62 [3,36; 13,06] <,0001[4]	8,0 [5,5; 10,4] <,0001[4]
Dental caries				
3/630 (0,5)	11/639 (1,7)	0,28 [0,08; 0,99] 0,0477[3]	0,27 [0,08; 0,98] 0,0337[4]	-1,2 [-2,4; -0,1] 0,0337[4]
Depressed mood				
10/630 (1,6)	11/639 (1,7)	0,92 [0,39; 2,16] 0,8515[3]	0,92 [0,39; 2,18] 0,8514[4]	-0,1 [-1,5; 1,3] 0,8514[4]
Depression				
35/630 (5,6)	26/639 (4,1)	1,37 [0,83; 2,24] 0,2179[3]	1,39 [0,82; 2,33] 0,2158[4]	1,5 [-0,9; 3,8] 0,2158[4]
Diarrhoea				
514/630 (81,6)	45/639 (7,0)	11,59 [8,72; 15,39] <,0001[3]	58,49 [40,65; 84,16] <,0001[4]	74,5 [70,9; 78,2] <,0001[4]
Dizziness				
55/630 (8,7)	37/639 (5,8)	1,51 [1,01; 2,25] 0,0453[3]	1,56 [1,01; 2,40] 0,0435[4]	2,9 [0,1; 5,8] 0,0435[4]
Dry eye				
24/630 (3,8)	11/639 (1,7)	2,21 [1,09; 4,48] 0,0272[3]	2,26 [1,10; 4,66] 0,0231[4]	2,1 [0,3; 3,9] 0,0231[4]
Dry mouth				
15/630 (2,4)	4/639 (0,6)	3,80 [1,27; 11,40] 0,0170[3]	3,87 [1,28; 11,73] 0,0101[4]	1,8 [0,4; 3,1] 0,0101[4]
Dry skin				
32/630 (5,1)	19/639 (3,0)	1,71 [0,98; 2,98] 0,0595[3]	1,75 [0,98; 3,11] 0,0562[4]	2,1 [-0,1; 4,3] 0,0562[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Dysgeusia				
19/630 (3,0)	1/639 (0,2)	19,27 [2,59; 143,52] 0,0039[3]	19,84 [2,65; 148,65] <,0001[4]	2,9 [1,5; 4,2] <,0001[4]
Dyspepsia				
61/630 (9,7)	19/639 (3,0)	3,26 [1,97; 5,39] <,0001[3]	3,50 [2,06; 5,93] <,0001[4]	6,7 [4,1; 9,4] <,0001[4]
Dyspnoea				
39/630 (6,2)	13/639 (2,0)	3,04 [1,64; 5,64] 0,0004[3]	3,18 [1,68; 6,01] 0,0002[4]	4,2 [2,0; 6,3] 0,0002[4]
Dysuria				
10/630 (1,6)	10/639 (1,6)	1,01 [0,43; 2,42] 0,9745[3]	1,01 [0,42; 2,45] 0,9745[4]	0,0 [-1,3; 1,4] 0,9745[4]
Eczema				
6/630 (1,0)	18/639 (2,8)	0,34 [0,14; 0,85] 0,0205[3]	0,33 [0,13; 0,84] 0,0148[4]	-1,9 [-3,4; -0,4] 0,0148[4]
Endometrial hyperplasia				
5/630 (0,8)	11/639 (1,7)	0,46 [0,16; 1,32] 0,1489[3]	0,46 [0,16; 1,32] 0,1386[4]	-0,9 [-2,2; 0,3] 0,1386[4]
Erythema				
14/630 (2,2)	4/639 (0,6)	3,55 [1,17; 10,73] 0,0247[3]	3,61 [1,18; 11,02] 0,0162[4]	1,6 [0,3; 2,9] 0,0162[4]
Fatigue				
181/630 (28,7)	86/639 (13,5)	2,13 [1,69; 2,69] <,0001[3]	2,59 [1,95; 3,45] <,0001[4]	15,3 [10,9; 19,7] <,0001[4]
Flatulence				
14/630 (2,2)	2/639 (0,3)	7,10 [1,62; 31,11] 0,0093[3]	7,24 [1,64; 31,98] 0,0023[4]	1,9 [0,7; 3,1] 0,0023[4]
Gamma-glutamyltransferase increased				
21/630 (3,3)	8/639 (1,3)	2,66 [1,19; 5,97] 0,0174[3]	2,72 [1,20; 6,19] 0,0131[4]	2,1 [0,4; 3,7] 0,0131[4]
Gastritis				
18/630 (2,9)	9/639 (1,4)	2,03 [0,92; 4,48] 0,0803[3]	2,06 [0,92; 4,62] 0,0738[4]	1,4 [-0,1; 3,0] 0,0738[4]
Gastroenteritis				
18/630 (2,9)	8/639 (1,3)	2,28 [1,00; 5,21] 0,0501[3]	2,32 [1,00; 5,37] 0,0436[4]	1,6 [0,0; 3,2] 0,0436[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Gastrooesophageal reflux disease				
23/630 (3,7)	14/639 (2,2)	1,67 [0,87; 3,21] 0,1266[3]	1,69 [0,86; 3,32] 0,1222[4]	1,5 [-0,4; 3,3] 0,1222[4]
Haemorrhoids				
25/630 (4,0)	10/639 (1,6)	2,54 [1,23; 5,24] 0,0119[3]	2,60 [1,24; 5,46] 0,0090[4]	2,4 [0,6; 4,2] 0,0090[4]
Headache				
129/630 (20,5)	109/639 (17,1)	1,20 [0,95; 1,51] 0,1196[3]	1,25 [0,94; 1,66] 0,1188[4]	3,4 [-0,9; 7,7] 0,1188[4]
Hepatic steatosis				
18/630 (2,9)	15/639 (2,3)	1,22 [0,62; 2,39] 0,5690[3]	1,22 [0,61; 2,45] 0,5684[4]	0,5 [-1,2; 2,3] 0,5684[4]
Herpes zoster				
7/630 (1,1)	12/639 (1,9)	0,59 [0,23; 1,49] 0,2665[3]	0,59 [0,23; 1,50] 0,2607[4]	-0,8 [-2,1; 0,6] 0,2607[4]
Hot flush				
119/630 (18,9)	158/639 (24,7)	0,76 [0,62; 0,94] 0,0123[3]	0,71 [0,54; 0,93] 0,0118[4]	-5,8 [-10,4; -1,3] 0,0118[4]
Hyperglycaemia				
6/630 (1,0)	11/639 (1,7)	0,55 [0,21; 1,49] 0,2406[3]	0,55 [0,20; 1,49] 0,2335[4]	-0,8 [-2,0; 0,5] 0,2335[4]
Hypertension				
34/630 (5,4)	23/639 (3,6)	1,50 [0,89; 2,52] 0,1251[3]	1,53 [0,89; 2,62] 0,1222[4]	1,8 [-0,5; 4,1] 0,1222[4]
Hypertriglyceridaemia				
16/630 (2,5)	10/639 (1,6)	1,62 [0,74; 3,55] 0,2252[3]	1,64 [0,74; 3,64] 0,2204[4]	1,0 [-0,6; 2,5] 0,2204[4]
Hypokalaemia				
20/630 (3,2)	2/639 (0,3)	10,14 [2,38; 43,21] 0,0017[3]	10,44 [2,43; 44,87] <,0001[4]	2,9 [1,4; 4,3] <,0001[4]
Hypothyroidism				
10/630 (1,6)	15/639 (2,3)	0,68 [0,31; 1,49] 0,3332[3]	0,67 [0,30; 1,51] 0,3300[4]	-0,8 [-2,3; 0,8] 0,3300[4]
Influenza				
34/630 (5,4)	29/639 (4,5)	1,19 [0,73; 1,93] 0,4821[3]	1,20 [0,72; 1,99] 0,4815[4]	0,9 [-1,5; 3,2] 0,4815[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Influenza like illness				
50/630 (7,9)	27/639 (4,2)	1,88 [1,19; 2,96] 0,0066[3]	1,95 [1,21; 3,16] 0,0056[4]	3,7 [1,1; 6,3] 0,0056[4]
Insomnia				
58/630 (9,2)	62/639 (9,7)	0,95 [0,67; 1,33] 0,7626[3]	0,94 [0,65; 1,37] 0,7626[4]	-0,5 [-3,7; 2,7] 0,7626[4]
Lacrimation increased				
33/630 (5,2)	1/639 (0,2)	33,47 [4,59; 243,98] 0,0005[3]	35,27 [4,81; 258,66] <,0001[4]	5,1 [3,3; 6,8] <,0001[4]
Leukopenia				
62/630 (9,8)	11/639 (1,7)	5,72 [3,04; 10,75] <,0001[3]	6,23 [3,25; 11,95] <,0001[4]	8,1 [5,6; 10,7] <,0001[4]
Lymphocyte count decreased				
67/630 (10,6)	17/639 (2,7)	4,00 [2,37; 6,73] <,0001[3]	4,35 [2,53; 7,50] <,0001[4]	8,0 [5,3; 10,7] <,0001[4]
Lymphoedema				
92/630 (14,6)	69/639 (10,8)	1,35 [1,01; 1,81] 0,0428[3]	1,41 [1,01; 1,97] 0,0417[4]	3,8 [0,1; 7,5] 0,0417[4]
Lymphopenia				
22/630 (3,5)	9/639 (1,4)	2,48 [1,15; 5,34] 0,0204[3]	2,53 [1,16; 5,54] 0,0162[4]	2,1 [0,4; 3,8] 0,0162[4]
Malaise				
25/630 (4,0)	10/639 (1,6)	2,54 [1,23; 5,24] 0,0119[3]	2,60 [1,24; 5,46] 0,0090[4]	2,4 [0,6; 4,2] 0,0090[4]
Mastitis				
9/630 (1,4)	14/639 (2,2)	0,65 [0,28; 1,50] 0,3126[3]	0,65 [0,28; 1,51] 0,3087[4]	-0,8 [-2,2; 0,7] 0,3087[4]
Mouth ulceration				
10/630 (1,6)	0/639 (0,0)	21,30 [1,25; 362,70] 0,0345[3]	21,64 [1,27; 370,14] 0,0009[5]	1,6 [0,6; 2,6] 0,0009[5]
Mucosal inflammation				
14/630 (2,2)	6/639 (0,9)	2,37 [0,92; 6,12] 0,0755[3]	2,40 [0,92; 6,28] 0,0665[4]	1,3 [-0,1; 2,7] 0,0665[4]
Muscle spasms				
47/630 (7,5)	34/639 (5,3)	1,40 [0,91; 2,15] 0,1211[3]	1,43 [0,91; 2,26] 0,1190[4]	2,1 [-0,6; 4,8] 0,1190[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Musculoskeletal chest pain				
19/630 (3,0)	18/639 (2,8)	1,07 [0,57; 2,02] 0,8332[3]	1,07 [0,56; 2,06] 0,8332[4]	0,2 [-1,7; 2,1] 0,8332[4]
Musculoskeletal pain				
10/630 (1,6)	10/639 (1,6)	1,01 [0,43; 2,42] 0,9745[3]	1,01 [0,42; 2,45] 0,9745[4]	0,0 [-1,3; 1,4] 0,9745[4]
Musculoskeletal stiffness				
10/630 (1,6)	6/639 (0,9)	1,69 [0,62; 4,62] 0,3064[3]	1,70 [0,61; 4,71] 0,3007[4]	0,6 [-0,6; 1,9] 0,3007[4]
Myalgia				
56/630 (8,9)	38/639 (5,9)	1,49 [1,01; 2,22] 0,0472[3]	1,54 [1,01; 2,37] 0,0454[4]	2,9 [0,1; 5,8] 0,0454[4]
Nail disorder				
15/630 (2,4)	2/639 (0,3)	7,61 [1,75; 33,13] 0,0069[3]	7,77 [1,77; 34,11] 0,0014[4]	2,1 [0,8; 3,3] 0,0014[4]
Nasopharyngitis				
92/630 (14,6)	58/639 (9,1)	1,61 [1,18; 2,19] 0,0026[3]	1,71 [1,21; 2,43] 0,0023[4]	5,5 [2,0; 9,1] 0,0023[4]
Nausea				
182/630 (28,9)	57/639 (8,9)	3,24 [2,46; 4,27] <,0001[3]	4,15 [3,01; 5,72] <,0001[4]	20,0 [15,8; 24,1] <,0001[4]
Neck pain				
15/630 (2,4)	7/639 (1,1)	2,17 [0,89; 5,29] 0,0875[3]	2,20 [0,89; 5,44] 0,0794[4]	1,3 [-0,2; 2,7] 0,0794[4]
Neuropathy peripheral				
15/630 (2,4)	13/639 (2,0)	1,17 [0,56; 2,44] 0,6747[3]	1,17 [0,55; 2,49] 0,6744[4]	0,3 [-1,3; 2,0] 0,6744[4]
Neutropenia				
123/630 (19,5)	20/639 (3,1)	6,24 [3,94; 9,88] <,0001[3]	7,51 [4,61; 12,22] <,0001[4]	16,4 [13,0; 19,8] <,0001[4]
Neutrophil count decreased				
155/630 (24,6)	25/639 (3,9)	6,29 [4,18; 9,46] <,0001[3]	8,01 [5,17; 12,43] <,0001[4]	20,7 [17,0; 24,4] <,0001[4]
Oedema				
11/630 (1,7)	2/639 (0,3)	5,58 [1,24; 25,07] 0,0250[3]	5,66 [1,25; 25,64] 0,0113[4]	1,4 [0,3; 2,5] 0,0113[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Oedema peripheral				
50/630 (7,9)	31/639 (4,9)	1,64 [1,06; 2,53] 0,0263[3]	1,69 [1,06; 2,68] 0,0246[4]	3,1 [0,4; 5,8] 0,0246[4]
Onychoclasis				
17/630 (2,7)	5/639 (0,8)	3,45 [1,28; 9,29] 0,0144[3]	3,52 [1,29; 9,59] 0,0089[4]	1,9 [0,5; 3,4] 0,0089[4]
Oropharyngeal pain				
31/630 (4,9)	19/639 (3,0)	1,65 [0,94; 2,90] 0,0781[3]	1,69 [0,94; 3,02] 0,0746[4]	1,9 [-0,2; 4,1] 0,0746[4]
Osteopenia				
10/630 (1,6)	4/639 (0,6)	2,54 [0,80; 8,04] 0,1141[3]	2,56 [0,80; 8,21] 0,1012[4]	1,0 [-0,2; 2,1] 0,1012[4]
Osteoporosis				
12/630 (1,9)	13/639 (2,0)	0,94 [0,43; 2,04] 0,8680[3]	0,94 [0,42; 2,07] 0,8680[4]	-0,1 [-1,7; 1,4] 0,8680[4]
Pain				
18/630 (2,9)	12/639 (1,9)	1,52 [0,74; 3,13] 0,2547[3]	1,54 [0,73; 3,22] 0,2510[4]	1,0 [-0,7; 2,7] 0,2510[4]
Pain in extremity				
68/630 (10,8)	67/639 (10,5)	1,03 [0,75; 1,42] 0,8586[3]	1,03 [0,72; 1,48] 0,8585[4]	0,3 [-3,1; 3,7] 0,8585[4]
Palpitations				
12/630 (1,9)	0/639 (0,0)	25,36 [1,50; 427,35] 0,0249[3]	25,85 [1,53; 437,52] 0,0005[4]	1,9 [0,8; 3,0] 0,0005[4]
Paraesthesia				
7/630 (1,1)	15/639 (2,3)	0,47 [0,19; 1,15] 0,0997[3]	0,47 [0,19; 1,15] 0,0916[4]	-1,2 [-2,7; 0,2] 0,0916[4]
Peripheral sensory neuropathy				
15/630 (2,4)	12/639 (1,9)	1,27 [0,60; 2,69] 0,5357[3]	1,27 [0,59; 2,74] 0,5347[4]	0,5 [-1,1; 2,1] 0,5347[4]
Peripheral swelling				
15/630 (2,4)	14/639 (2,2)	1,09 [0,53; 2,23] 0,8209[3]	1,09 [0,52; 2,27] 0,8208[4]	0,2 [-1,5; 1,8] 0,8208[4]
Platelet count decreased				
39/630 (6,2)	8/639 (1,3)	4,94 [2,33; 10,50] <,0001[3]	5,20 [2,41; 11,23] <,0001[4]	4,9 [2,9; 7,0] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Pneumonia				
14/630 (2,2)	8/639 (1,3)	1,78 [0,75; 4,20] 0,1918[3]	1,79 [0,75; 4,30] 0,1855[4]	1,0 [-0,5; 2,4] 0,1855[4]
Procedural pain				
23/630 (3,7)	14/639 (2,2)	1,67 [0,87; 3,21] 0,1266[3]	1,69 [0,86; 3,32] 0,1222[4]	1,5 [-0,4; 3,3] 0,1222[4]
Productive cough				
13/630 (2,1)	5/639 (0,8)	2,64 [0,95; 7,35] 0,0638[3]	2,67 [0,95; 7,54] 0,0537[4]	1,3 [-0,0; 2,6] 0,0537[4]
Pruritus				
61/630 (9,7)	26/639 (4,1)	2,38 [1,52; 3,72] 0,0001[3]	2,53 [1,57; 4,06] <,0001[4]	5,6 [2,8; 8,4] <,0001[4]
Pyrexia				
66/630 (10,5)	33/639 (5,2)	2,03 [1,36; 3,04] 0,0006[3]	2,15 [1,39; 3,31] 0,0004[4]	5,3 [2,4; 8,3] 0,0004[4]
Rash				
51/630 (8,1)	30/639 (4,7)	1,72 [1,11; 2,67] 0,0146[3]	1,79 [1,12; 2,85] 0,0132[4]	3,4 [0,7; 6,1] 0,0132[4]
Rectal haemorrhage				
11/630 (1,7)	2/639 (0,3)	5,58 [1,24; 25,07] 0,0250[3]	5,66 [1,25; 25,64] 0,0113[4]	1,4 [0,3; 2,5] 0,0113[4]
Rhinitis allergic				
18/630 (2,9)	12/639 (1,9)	1,52 [0,74; 3,13] 0,2547[3]	1,54 [0,73; 3,22] 0,2510[4]	1,0 [-0,7; 2,7] 0,2510[4]
Rhinorrhoea				
12/630 (1,9)	5/639 (0,8)	2,43 [0,86; 6,87] 0,0928[3]	2,46 [0,86; 7,03] 0,0821[4]	1,1 [-0,1; 2,4] 0,0821[4]
Sinusitis				
24/630 (3,8)	11/639 (1,7)	2,21 [1,09; 4,48] 0,0272[3]	2,26 [1,10; 4,66] 0,0231[4]	2,1 [0,3; 3,9] 0,0231[4]
Skin infection				
12/630 (1,9)	7/639 (1,1)	1,74 [0,69; 4,39] 0,2415[3]	1,75 [0,69; 4,48] 0,2353[4]	0,8 [-0,5; 2,1] 0,2353[4]
Stomatitis				
52/630 (8,3)	11/639 (1,7)	4,79 [2,53; 9,10] <,0001[3]	5,14 [2,65; 9,94] <,0001[4]	6,5 [4,2; 8,9] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Taste disorder				
10/630 (1,6)	2/639 (0,3)	5,07 [1,12; 23,05] 0,0356[3]	5,14 [1,12; 23,54] 0,0190[4]	1,3 [0,2; 2,3] 0,0190[4]
Thrombocytopenia				
21/630 (3,3)	8/639 (1,3)	2,66 [1,19; 5,97] 0,0174[3]	2,72 [1,20; 6,19] 0,0131[4]	2,1 [0,4; 3,7] 0,0131[4]
Tinnitus				
3/630 (0,5)	10/639 (1,6)	0,30 [0,08; 1,10] 0,0697[3]	0,30 [0,08; 1,10] 0,0541[4]	-1,1 [-2,2; 0,0] 0,0541[4]
Toothache				
18/630 (2,9)	8/639 (1,3)	2,28 [1,00; 5,21] 0,0501[3]	2,32 [1,00; 5,37] 0,0436[4]	1,6 [0,0; 3,2] 0,0436[4]
Upper respiratory tract infection				
57/630 (9,0)	53/639 (8,3)	1,09 [0,76; 1,56] 0,6335[3]	1,10 [0,74; 1,63] 0,6334[4]	0,8 [-2,3; 3,9] 0,6334[4]
Urinary tract infection				
55/630 (8,7)	31/639 (4,9)	1,80 [1,18; 2,76] 0,0069[3]	1,88 [1,19; 2,96] 0,0060[4]	3,9 [1,1; 6,6] 0,0060[4]
Urticaria				
11/630 (1,7)	4/639 (0,6)	2,79 [0,89; 8,71] 0,0776[3]	2,82 [0,89; 8,91] 0,0649[4]	1,1 [-0,1; 2,3] 0,0649[4]
Vaginal discharge				
9/630 (1,4)	22/639 (3,4)	0,41 [0,19; 0,89] 0,0247[3]	0,41 [0,19; 0,89] 0,0201[4]	-2,0 [-3,7; -0,3] 0,0201[4]
Vaginal haemorrhage				
11/630 (1,7)	12/639 (1,9)	0,93 [0,41; 2,09] 0,8602[3]	0,93 [0,41; 2,12] 0,8602[4]	-0,1 [-1,6; 1,3] 0,8602[4]
Vaginal infection				
16/630 (2,5)	10/639 (1,6)	1,62 [0,74; 3,55] 0,2252[3]	1,64 [0,74; 3,64] 0,2204[4]	1,0 [-0,6; 2,5] 0,2204[4]
Vertigo				
16/630 (2,5)	11/639 (1,7)	1,48 [0,69; 3,15] 0,3158[3]	1,49 [0,68; 3,23] 0,3125[4]	0,8 [-0,8; 2,4] 0,3125[4]
Viral infection				
12/630 (1,9)	5/639 (0,8)	2,43 [0,86; 6,87] 0,0928[3]	2,46 [0,86; 7,03] 0,0821[4]	1,1 [-0,1; 2,4] 0,0821[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Vitamin D deficiency				
9/630 (1,4)	17/639 (2,7)	0,54 [0,24; 1,20] 0,1279[3]	0,53 [0,23; 1,20] 0,1214[4]	-1,2 [-2,8; 0,3] 0,1214[4]
Vomiting				
100/630 (15,9)	27/639 (4,2)	3,76 [2,49; 5,66] <,0001[3]	4,28 [2,75; 6,65] <,0001[4]	11,6 [8,4; 14,9] <,0001[4]
Vulvovaginal dryness				
30/630 (4,8)	25/639 (3,9)	1,22 [0,72; 2,05] 0,4582[3]	1,23 [0,71; 2,11] 0,4574[4]	0,8 [-1,4; 3,1] 0,4574[4]
Weight decreased				
14/630 (2,2)	6/639 (0,9)	2,37 [0,92; 6,12] 0,0755[3]	2,40 [0,92; 6,28] 0,0665[4]	1,3 [-0,1; 2,7] 0,0665[4]
Weight increased				
15/630 (2,4)	15/639 (2,3)	1,01 [0,50; 2,06] 0,9686[3]	1,01 [0,49; 2,09] 0,9686[4]	0,0 [-1,6; 1,7] 0,9686[4]
White blood cell count decreased				
161/630 (25,6)	33/639 (5,2)	4,95 [3,46; 7,08] <,0001[3]	6,30 [4,25; 9,34] <,0001[4]	20,4 [16,6; 24,2] <,0001[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test; 5: from Fisher's exact test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttiraep_premp_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
14FEB2022 / 08:38

Table: Results from binary analysis for adverse events according PT - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Abdominal discomfort				
21/1363 (1,5)	7/1385 (0,5)	3,05 [1,30; 7,15] 0,0104[3]	3,08 [1,31; 7,27] 0,0069[4]	1,0 [0,3; 1,8] 0,0069[4]
Abdominal distension				
37/1363 (2,7)	14/1385 (1,0)	2,69 [1,46; 4,94] 0,0015[3]	2,73 [1,47; 5,08] 0,0009[4]	1,7 [0,7; 2,7] 0,0009[4]
Abdominal pain				
334/1363 (24,5)	73/1385 (5,3)	4,65 [3,65; 5,92] <,0001[3]	5,83 [4,47; 7,61] <,0001[4]	19,2 [16,7; 21,8] <,0001[4]
Abdominal pain upper				
130/1363 (9,5)	50/1385 (3,6)	2,64 [1,92; 3,63] <,0001[3]	2,82 [2,01; 3,94] <,0001[4]	5,9 [4,1; 7,8] <,0001[4]
Alanine aminotransferase increased				
166/1363 (12,2)	78/1385 (5,6)	2,16 [1,67; 2,80] <,0001[3]	2,32 [1,76; 3,08] <,0001[4]	6,5 [4,4; 8,7] <,0001[4]
Alopecia				
157/1363 (11,5)	41/1385 (3,0)	3,89 [2,78; 5,44] <,0001[3]	4,27 [3,00; 6,07] <,0001[4]	8,6 [6,6; 10,5] <,0001[4]
Anaemia				
344/1363 (25,2)	49/1385 (3,5)	7,13 [5,34; 9,53] <,0001[3]	9,20 [6,75; 12,55] <,0001[4]	21,7 [19,2; 24,2] <,0001[4]
Anxiety				
42/1363 (3,1)	63/1385 (4,5)	0,68 [0,46; 0,99] 0,0464[3]	0,67 [0,45; 0,99] 0,0448[4]	-1,5 [-2,9; -0,0] 0,0448[4]
Arthralgia				
381/1363 (28,0)	575/1385 (41,5)	0,67 [0,61; 0,75] <,0001[3]	0,55 [0,47; 0,64] <,0001[4]	-13,6 [-17,1; -10,0] <,0001[4]
Arthritis				
12/1363 (0,9)	25/1385 (1,8)	0,49 [0,25; 0,97] 0,0397[3]	0,48 [0,24; 0,97] 0,0355[4]	-0,9 [-1,8; -0,1] 0,0355[4]
Aspartate aminotransferase increased				
155/1363 (11,4)	73/1385 (5,3)	2,16 [1,65; 2,82] <,0001[3]	2,31 [1,73; 3,08] <,0001[4]	6,1 [4,0; 8,2] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Asthenia				
154/1363 (11,3)	78/1385 (5,6)	2,01 [1,54; 2,61] <,0001[3]	2,13 [1,61; 2,83] <,0001[4]	5,7 [3,6; 7,7] <,0001[4]
Axillary pain				
24/1363 (1,8)	21/1385 (1,5)	1,16 [0,65; 2,08] 0,6138[3]	1,16 [0,65; 2,10] 0,6135[4]	0,2 [-0,7; 1,2] 0,6135[4]
Back pain				
124/1363 (9,1)	169/1385 (12,2)	0,75 [0,60; 0,93] 0,0087[3]	0,72 [0,56; 0,92] 0,0084[4]	-3,1 [-5,4; -0,8] 0,0084[4]
Blood alkaline phosphatase increased				
63/1363 (4,6)	42/1385 (3,0)	1,52 [1,04; 2,24] 0,0311[3]	1,55 [1,04; 2,31] 0,0297[4]	1,6 [0,2; 3,0] 0,0297[4]
Blood bilirubin increased				
18/1363 (1,3)	10/1385 (0,7)	1,83 [0,85; 3,95] 0,1240[3]	1,84 [0,85; 4,00] 0,1182[4]	0,6 [-0,2; 1,4] 0,1182[4]
Blood cholesterol increased				
14/1363 (1,0)	25/1385 (1,8)	0,57 [0,30; 1,09] 0,0891[3]	0,56 [0,29; 1,09] 0,0848[4]	-0,8 [-1,7; 0,1] 0,0848[4]
Blood creatinine increased				
162/1363 (11,9)	17/1385 (1,2)	9,68 [5,91; 15,87] <,0001[3]	10,85 [6,55; 18,00] <,0001[4]	10,7 [8,8; 12,5] <,0001[4]
Bone pain				
40/1363 (2,9)	57/1385 (4,1)	0,71 [0,48; 1,06] 0,0953[3]	0,70 [0,47; 1,06] 0,0935[4]	-1,2 [-2,6; 0,2] 0,0935[4]
Breast pain				
46/1363 (3,4)	65/1385 (4,7)	0,72 [0,50; 1,04] 0,0808[3]	0,71 [0,48; 1,04] 0,0793[4]	-1,3 [-2,8; 0,2] 0,0793[4]
Bronchitis				
26/1363 (1,9)	31/1385 (2,2)	0,85 [0,51; 1,43] 0,5435[3]	0,85 [0,50; 1,44] 0,5431[4]	-0,3 [-1,4; 0,7] 0,5431[4]
COVID-19				
34/1363 (2,5)	10/1385 (0,7)	3,45 [1,71; 6,96] 0,0005[3]	3,52 [1,73; 7,15] 0,0002[4]	1,8 [0,8; 2,7] 0,0002[4]
Cataract				
26/1363 (1,9)	12/1385 (0,9)	2,20 [1,12; 4,35] 0,0229[3]	2,23 [1,12; 4,43] 0,0195[4]	1,0 [0,2; 1,9] 0,0195[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Cellulitis				
31/1363 (2,3)	21/1385 (1,5)	1,50 [0,87; 2,60] 0,1476[3]	1,51 [0,86; 2,64] 0,1447[4]	0,8 [-0,3; 1,8] 0,1447[4]
Chest pain				
30/1363 (2,2)	29/1385 (2,1)	1,05 [0,63; 1,74] 0,8464[3]	1,05 [0,63; 1,76] 0,8463[4]	0,1 [-1,0; 1,2] 0,8463[4]
Chills				
20/1363 (1,5)	13/1385 (0,9)	1,56 [0,78; 3,13] 0,2072[3]	1,57 [0,78; 3,17] 0,2033[4]	0,5 [-0,3; 1,3] 0,2033[4]
Conjunctivitis				
22/1363 (1,6)	13/1385 (0,9)	1,72 [0,87; 3,40] 0,1190[3]	1,73 [0,87; 3,45] 0,1144[4]	0,7 [-0,2; 1,5] 0,1144[4]
Constipation				
164/1363 (12,0)	81/1385 (5,8)	2,06 [1,59; 2,66] <,0001[3]	2,20 [1,67; 2,91] <,0001[4]	6,2 [4,1; 8,3] <,0001[4]
Contusion				
21/1363 (1,5)	19/1385 (1,4)	1,12 [0,61; 2,08] 0,7119[3]	1,13 [0,60; 2,10] 0,7117[4]	0,2 [-0,7; 1,1] 0,7117[4]
Cough				
206/1363 (15,1)	125/1385 (9,0)	1,67 [1,36; 2,06] <,0001[3]	1,79 [1,42; 2,27] <,0001[4]	6,1 [3,7; 8,5] <,0001[4]
Cystitis				
38/1363 (2,8)	35/1385 (2,5)	1,10 [0,70; 1,74] 0,6708[3]	1,11 [0,69; 1,76] 0,6707[4]	0,3 [-0,9; 1,5] 0,6707[4]
Decreased appetite				
173/1363 (12,7)	45/1385 (3,2)	3,91 [2,84; 5,38] <,0001[3]	4,33 [3,09; 6,06] <,0001[4]	9,4 [7,4; 11,4] <,0001[4]
Deep vein thrombosis				
31/1363 (2,3)	5/1385 (0,4)	6,30 [2,46; 16,15] 0,0001[3]	6,42 [2,49; 16,57] <,0001[4]	1,9 [1,1; 2,8] <,0001[4]
Dehydration				
26/1363 (1,9)	5/1385 (0,4)	5,28 [2,04; 13,72] 0,0006[3]	5,37 [2,05; 14,02] 0,0001[4]	1,5 [0,8; 2,3] 0,0001[4]
Depression				
60/1363 (4,4)	58/1385 (4,2)	1,05 [0,74; 1,50] 0,7817[3]	1,05 [0,73; 1,52] 0,7817[4]	0,2 [-1,3; 1,7] 0,7817[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Dermatitis				
19/1363 (1,4)	8/1385 (0,6)	2,41 [1,06; 5,49] 0,0358[3]	2,43 [1,06; 5,58] 0,0301[4]	0,8 [0,1; 1,6] 0,0301[4]
Diarrhoea				
1125/1363 (82,5)	131/1385 (9,5)	8,73 [7,40; 10,29] <,0001[3]	45,25 [36,03; 56,83] <,0001[4]	73,1 [70,5; 75,6] <,0001[4]
Dizziness				
147/1363 (10,8)	97/1385 (7,0)	1,54 [1,21; 1,97] 0,0006[3]	1,61 [1,23; 2,10] 0,0005[4]	3,8 [1,7; 5,9] 0,0005[4]
Dry eye				
41/1363 (3,0)	13/1385 (0,9)	3,20 [1,73; 5,95] 0,0002[3]	3,27 [1,75; 6,14] <,0001[4]	2,1 [1,0; 3,1] <,0001[4]
Dry mouth				
55/1363 (4,0)	20/1385 (1,4)	2,79 [1,68; 4,64] <,0001[3]	2,87 [1,71; 4,81] <,0001[4]	2,6 [1,4; 3,8] <,0001[4]
Dry skin				
54/1363 (4,0)	29/1385 (2,1)	1,89 [1,21; 2,95] 0,0050[3]	1,93 [1,22; 3,05] 0,0042[4]	1,9 [0,6; 3,1] 0,0042[4]
Dysgeusia				
63/1363 (4,6)	5/1385 (0,4)	12,80 [5,17; 31,73] <,0001[3]	13,38 [5,36; 33,35] <,0001[4]	4,3 [3,1; 5,4] <,0001[4]
Dyspepsia				
100/1363 (7,3)	37/1385 (2,7)	2,75 [1,90; 3,97] <,0001[3]	2,88 [1,96; 4,24] <,0001[4]	4,7 [3,0; 6,3] <,0001[4]
Dyspnoea				
99/1363 (7,3)	62/1385 (4,5)	1,62 [1,19; 2,21] 0,0021[3]	1,67 [1,21; 2,32] 0,0019[4]	2,8 [1,0; 4,5] 0,0019[4]
Dyspnoea exertional				
14/1363 (1,0)	9/1385 (0,6)	1,58 [0,69; 3,64] 0,2820[3]	1,59 [0,68; 3,68] 0,2777[4]	0,4 [-0,3; 1,1] 0,2777[4]
Dysuria				
24/1363 (1,8)	15/1385 (1,1)	1,63 [0,86; 3,09] 0,1371[3]	1,64 [0,86; 3,13] 0,1331[4]	0,7 [-0,2; 1,6] 0,1331[4]
Eczema				
14/1363 (1,0)	16/1385 (1,2)	0,89 [0,44; 1,81] 0,7468[3]	0,89 [0,43; 1,83] 0,7466[4]	-0,1 [-0,9; 0,6] 0,7466[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Epistaxis				
24/1363 (1,8)	3/1385 (0,2)	8,13 [2,45; 26,93] 0,0006[3]	8,26 [2,48; 27,48] <,0001[4]	1,5 [0,8; 2,3] <,0001[4]
Erythema				
17/1363 (1,2)	17/1385 (1,2)	1,02 [0,52; 1,98] 0,9625[3]	1,02 [0,52; 2,00] 0,9625[4]	0,0 [-0,8; 0,8] 0,9625[4]
Fall				
47/1363 (3,4)	34/1385 (2,5)	1,40 [0,91; 2,17] 0,1257[3]	1,42 [0,91; 2,22] 0,1237[4]	1,0 [-0,3; 2,3] 0,1237[4]
Fatigue				
423/1363 (31,0)	180/1385 (13,0)	2,39 [2,04; 2,80] <,0001[3]	3,01 [2,48; 3,66] <,0001[4]	18,0 [15,0; 21,1] <,0001[4]
Flatulence				
44/1363 (3,2)	8/1385 (0,6)	5,59 [2,64; 11,83] <,0001[3]	5,74 [2,69; 12,24] <,0001[4]	2,7 [1,6; 3,7] <,0001[4]
Gamma-glutamyltransferase increased				
45/1363 (3,3)	16/1385 (1,2)	2,86 [1,62; 5,03] 0,0003[3]	2,92 [1,64; 5,19] 0,0001[4]	2,1 [1,0; 3,2] 0,0001[4]
Gastritis				
33/1363 (2,4)	25/1385 (1,8)	1,34 [0,80; 2,24] 0,2631[3]	1,35 [0,80; 2,28] 0,2613[4]	0,6 [-0,5; 1,7] 0,2613[4]
Gastroenteritis				
22/1363 (1,6)	15/1385 (1,1)	1,49 [0,78; 2,86] 0,2304[3]	1,50 [0,77; 2,90] 0,2272[4]	0,5 [-0,3; 1,4] 0,2272[4]
Gastrointestinal pain				
17/1363 (1,2)	0/1385 (0,0)	35,56 [2,14; 590,80] 0,0127[3]	36,01 [2,16; 599,46] <,0001[4]	1,2 [0,7; 1,8] <,0001[4]
Gastrooesophageal reflux disease				
45/1363 (3,3)	28/1385 (2,0)	1,63 [1,02; 2,60] 0,0390[3]	1,65 [1,03; 2,67] 0,0370[4]	1,3 [0,1; 2,5] 0,0370[4]
Haemorrhoids				
31/1363 (2,3)	16/1385 (1,2)	1,97 [1,08; 3,58] 0,0266[3]	1,99 [1,08; 3,66] 0,0237[4]	1,1 [0,1; 2,1] 0,0237[4]
Headache				
241/1363 (17,7)	173/1385 (12,5)	1,42 [1,18; 1,70] 0,0002[3]	1,50 [1,22; 1,86] 0,0001[4]	5,2 [2,5; 7,9] 0,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Hepatic steatosis				
24/1363 (1,8)	22/1385 (1,6)	1,11 [0,62; 1,97] 0,7248[3]	1,11 [0,62; 1,99] 0,7247[4]	0,2 [-0,8; 1,1] 0,7247[4]
Herpes zoster				
25/1363 (1,8)	27/1385 (1,9)	0,94 [0,55; 1,61] 0,8245[3]	0,94 [0,54; 1,63] 0,8245[4]	-0,1 [-1,1; 0,9] 0,8245[4]
Hot flush				
167/1363 (12,3)	259/1385 (18,7)	0,66 [0,55; 0,78] <,0001[3]	0,61 [0,49; 0,75] <,0001[4]	-6,4 [-9,1; -3,8] <,0001[4]
Hypercalcaemia				
27/1363 (2,0)	18/1385 (1,3)	1,52 [0,84; 2,75] 0,1627[3]	1,53 [0,84; 2,80] 0,1594[4]	0,7 [-0,3; 1,6] 0,1594[4]
Hypercholesterolaemia				
15/1363 (1,1)	26/1385 (1,9)	0,59 [0,31; 1,10] 0,0972[3]	0,58 [0,31; 1,10] 0,0931[4]	-0,8 [-1,7; 0,1] 0,0931[4]
Hyperglycaemia				
20/1363 (1,5)	31/1385 (2,2)	0,66 [0,38; 1,14] 0,1374[3]	0,65 [0,37; 1,15] 0,1344[4]	-0,8 [-1,8; 0,2] 0,1344[4]
Hyperhidrosis				
19/1363 (1,4)	27/1385 (1,9)	0,72 [0,40; 1,28] 0,2588[3]	0,71 [0,39; 1,28] 0,2565[4]	-0,6 [-1,5; 0,4] 0,2565[4]
Hyperkalaemia				
14/1363 (1,0)	7/1385 (0,5)	2,03 [0,82; 5,02] 0,1242[3]	2,04 [0,82; 5,08] 0,1164[4]	0,5 [-0,1; 1,2] 0,1164[4]
Hypersensitivity				
14/1363 (1,0)	12/1385 (0,9)	1,19 [0,55; 2,55] 0,6639[3]	1,19 [0,55; 2,58] 0,6635[4]	0,2 [-0,6; 0,9] 0,6635[4]
Hypertension				
61/1363 (4,5)	83/1385 (6,0)	0,75 [0,54; 1,03] 0,0755[3]	0,73 [0,52; 1,03] 0,0743[4]	-1,5 [-3,2; 0,1] 0,0743[4]
Hypertriglyceridaemia				
24/1363 (1,8)	29/1385 (2,1)	0,84 [0,49; 1,44] 0,5262[3]	0,84 [0,49; 1,45] 0,5256[4]	-0,3 [-1,4; 0,7] 0,5256[4]
Hyperuricaemia				
20/1363 (1,5)	10/1385 (0,7)	2,03 [0,95; 4,33] 0,0658[3]	2,05 [0,95; 4,39] 0,0601[4]	0,7 [-0,0; 1,5] 0,0601[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Hypoalbuminaemia				
16/1363 (1,2)	6/1385 (0,4)	2,71 [1,06; 6,90] 0,0367[3]	2,73 [1,07; 7,00] 0,0294[4]	0,7 [0,1; 1,4] 0,0294[4]
Hypokalaemia				
62/1363 (4,5)	18/1385 (1,3)	3,50 [2,08; 5,88] <,0001[3]	3,62 [2,13; 6,15] <,0001[4]	3,2 [2,0; 4,5] <,0001[4]
Hyponatraemia				
20/1363 (1,5)	9/1385 (0,6)	2,26 [1,03; 4,94] 0,0415[3]	2,28 [1,03; 5,02] 0,0360[4]	0,8 [0,1; 1,6] 0,0360[4]
Hypotension				
25/1363 (1,8)	9/1385 (0,6)	2,82 [1,32; 6,02] 0,0073[3]	2,86 [1,33; 6,14] 0,0050[4]	1,2 [0,4; 2,0] 0,0050[4]
Hypothyroidism				
18/1363 (1,3)	22/1385 (1,6)	0,83 [0,45; 1,54] 0,5584[3]	0,83 [0,44; 1,55] 0,5578[4]	-0,3 [-1,2; 0,6] 0,5578[4]
Influenza				
50/1363 (3,7)	49/1385 (3,5)	1,04 [0,70; 1,53] 0,8544[3]	1,04 [0,70; 1,55] 0,8544[4]	0,1 [-1,3; 1,5] 0,8544[4]
Influenza like illness				
61/1363 (4,5)	47/1385 (3,4)	1,32 [0,91; 1,92] 0,1459[3]	1,33 [0,90; 1,97] 0,1445[4]	1,1 [-0,4; 2,5] 0,1445[4]
Insomnia				
105/1363 (7,7)	115/1385 (8,3)	0,93 [0,72; 1,20] 0,5626[3]	0,92 [0,70; 1,21] 0,5625[4]	-0,6 [-2,6; 1,4] 0,5625[4]
Joint stiffness				
13/1363 (1,0)	36/1385 (2,6)	0,37 [0,20; 0,69] 0,0018[3]	0,36 [0,19; 0,68] 0,0011[4]	-1,6 [-2,6; -0,7] 0,0011[4]
Lacrimation increased				
80/1363 (5,9)	6/1385 (0,4)	13,55 [5,93; 30,95] <,0001[3]	14,33 [6,23; 32,97] <,0001[4]	5,4 [4,1; 6,7] <,0001[4]
Leukopenia				
195/1363 (14,3)	25/1385 (1,8)	7,93 [5,26; 11,94] <,0001[3]	9,08 [5,95; 13,87] <,0001[4]	12,5 [10,5; 14,5] <,0001[4]
Lymphocyte count decreased				
118/1363 (8,7)	29/1385 (2,1)	4,13 [2,77; 6,16] <,0001[3]	4,43 [2,93; 6,70] <,0001[4]	6,6 [4,9; 8,2] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Lymphoedema				
163/1363 (12,0)	118/1385 (8,5)	1,40 [1,12; 1,76] 0,0031[3]	1,46 [1,14; 1,87] 0,0029[4]	3,4 [1,2; 5,7] 0,0029[4]
Lymphopenia				
70/1363 (5,1)	11/1385 (0,8)	6,47 [3,44; 12,16] <,0001[3]	6,76 [3,56; 12,83] <,0001[4]	4,3 [3,1; 5,6] <,0001[4]
Malaise				
36/1363 (2,6)	14/1385 (1,0)	2,61 [1,42; 4,82] 0,0021[3]	2,66 [1,43; 4,95] 0,0014[4]	1,6 [0,6; 2,6] 0,0014[4]
Mastitis				
12/1363 (0,9)	19/1385 (1,4)	0,64 [0,31; 1,32] 0,2265[3]	0,64 [0,31; 1,32] 0,2226[4]	-0,5 [-1,3; 0,3] 0,2226[4]
Memory impairment				
21/1363 (1,5)	12/1385 (0,9)	1,78 [0,88; 3,60] 0,1097[3]	1,79 [0,88; 3,65] 0,1047[4]	0,7 [-0,1; 1,5] 0,1047[4]
Mouth ulceration				
14/1363 (1,0)	2/1385 (0,1)	7,11 [1,62; 31,24] 0,0094[3]	7,18 [1,63; 31,64] 0,0024[4]	0,9 [0,3; 1,5] 0,0024[4]
Mucosal inflammation				
42/1363 (3,1)	11/1385 (0,8)	3,88 [2,01; 7,50] <,0001[3]	3,97 [2,04; 7,75] <,0001[4]	2,3 [1,3; 3,3] <,0001[4]
Muscle spasms				
79/1363 (5,8)	63/1385 (4,5)	1,27 [0,92; 1,76] 0,1408[3]	1,29 [0,92; 1,81] 0,1397[4]	1,2 [-0,4; 2,9] 0,1397[4]
Muscular weakness				
20/1363 (1,5)	10/1385 (0,7)	2,03 [0,95; 4,33] 0,0658[3]	2,05 [0,95; 4,39] 0,0601[4]	0,7 [-0,0; 1,5] 0,0601[4]
Musculoskeletal chest pain				
41/1363 (3,0)	35/1385 (2,5)	1,19 [0,76; 1,86] 0,4426[3]	1,20 [0,76; 1,89] 0,4420[4]	0,5 [-0,7; 1,7] 0,4420[4]
Musculoskeletal pain				
16/1363 (1,2)	25/1385 (1,8)	0,65 [0,35; 1,21] 0,1759[3]	0,65 [0,34; 1,22] 0,1724[4]	-0,6 [-1,5; 0,3] 0,1724[4]
Musculoskeletal stiffness				
18/1363 (1,3)	22/1385 (1,6)	0,83 [0,45; 1,54] 0,5584[3]	0,83 [0,44; 1,55] 0,5578[4]	-0,3 [-1,2; 0,6] 0,5578[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Myalgia				
81/1363 (5,9)	99/1385 (7,1)	0,83 [0,63; 1,10] 0,2025[3]	0,82 [0,61; 1,11] 0,2017[4]	-1,2 [-3,1; 0,6] 0,2017[4]
Nail disorder				
25/1363 (1,8)	2/1385 (0,1)	12,70 [3,01; 53,52] 0,0005[3]	12,92 [3,05; 54,66] <,0001[4]	1,7 [0,9; 2,4] <,0001[4]
Nasal congestion				
21/1363 (1,5)	15/1385 (1,1)	1,42 [0,74; 2,75] 0,2940[3]	1,43 [0,73; 2,78] 0,2914[4]	0,5 [-0,4; 1,3] 0,2914[4]
Nasopharyngitis				
112/1363 (8,2)	96/1385 (6,9)	1,19 [0,91; 1,54] 0,2033[3]	1,20 [0,91; 1,60] 0,2026[4]	1,3 [-0,7; 3,3] 0,2026[4]
Nausea				
417/1363 (30,6)	119/1385 (8,6)	3,56 [2,95; 4,30] <,0001[3]	4,69 [3,76; 5,85] <,0001[4]	22,0 [19,1; 24,9] <,0001[4]
Neck pain				
27/1363 (2,0)	35/1385 (2,5)	0,78 [0,48; 1,29] 0,3364[3]	0,78 [0,47; 1,30] 0,3351[4]	-0,5 [-1,7; 0,6] 0,3351[4]
Neuropathy peripheral				
42/1363 (3,1)	46/1385 (3,3)	0,93 [0,61; 1,40] 0,7211[3]	0,93 [0,60; 1,42] 0,7210[4]	-0,2 [-1,6; 1,1] 0,7210[4]
Neutropenia				
309/1363 (22,7)	31/1385 (2,2)	10,13 [7,06; 14,54] <,0001[3]	12,80 [8,77; 18,69] <,0001[4]	20,4 [18,1; 22,8] <,0001[4]
Neutrophil count decreased				
297/1363 (21,8)	25/1385 (1,8)	12,07 [8,08; 18,03] <,0001[3]	15,16 [10,00; 22,97] <,0001[4]	20,0 [17,7; 22,3] <,0001[4]
Night sweats				
11/1363 (0,8)	18/1385 (1,3)	0,62 [0,29; 1,31] 0,2109[3]	0,62 [0,29; 1,31] 0,2064[4]	-0,5 [-1,3; 0,3] 0,2064[4]
Non-cardiac chest pain				
14/1363 (1,0)	12/1385 (0,9)	1,19 [0,55; 2,55] 0,6639[3]	1,19 [0,55; 2,58] 0,6635[4]	0,2 [-0,6; 0,9] 0,6635[4]
Oedema				
18/1363 (1,3)	10/1385 (0,7)	1,83 [0,85; 3,95] 0,1240[3]	1,84 [0,85; 4,00] 0,1182[4]	0,6 [-0,2; 1,4] 0,1182[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Oedema peripheral				
102/1363 (7,5)	62/1385 (4,5)	1,67 [1,23; 2,27] 0,0010[3]	1,73 [1,25; 2,39] 0,0009[4]	3,0 [1,2; 4,8] 0,0009[4]
Onychoclasis				
24/1363 (1,8)	3/1385 (0,2)	8,13 [2,45; 26,93] 0,0006[3]	8,26 [2,48; 27,48] <,0001[4]	1,5 [0,8; 2,3] <,0001[4]
Oral herpes				
18/1363 (1,3)	7/1385 (0,5)	2,61 [1,09; 6,24] 0,0304[3]	2,63 [1,10; 6,33] 0,0244[4]	0,8 [0,1; 1,5] 0,0244[4]
Oropharyngeal pain				
53/1363 (3,9)	38/1385 (2,7)	1,42 [0,94; 2,14] 0,0954[3]	1,43 [0,94; 2,19] 0,0936[4]	1,1 [-0,2; 2,5] 0,0936[4]
Osteoarthritis				
16/1363 (1,2)	27/1385 (1,9)	0,60 [0,33; 1,11] 0,1053[3]	0,60 [0,32; 1,11] 0,1014[4]	-0,8 [-1,7; 0,2] 0,1014[4]
Osteopenia				
22/1363 (1,6)	28/1385 (2,0)	0,80 [0,46; 1,39] 0,4252[3]	0,80 [0,45; 1,40] 0,4241[4]	-0,4 [-1,4; 0,6] 0,4241[4]
Osteoporosis				
31/1363 (2,3)	50/1385 (3,6)	0,63 [0,41; 0,98] 0,0404[3]	0,62 [0,39; 0,98] 0,0385[4]	-1,3 [-2,6; -0,1] 0,0385[4]
Pain				
32/1363 (2,3)	35/1385 (2,5)	0,93 [0,58; 1,49] 0,7606[3]	0,93 [0,57; 1,51] 0,7606[4]	-0,2 [-1,3; 1,0] 0,7606[4]
Pain in extremity				
137/1363 (10,1)	158/1385 (11,4)	0,88 [0,71; 1,09] 0,2512[3]	0,87 [0,68; 1,11] 0,2507[4]	-1,4 [-3,7; 1,0] 0,2507[4]
Palpitations				
32/1363 (2,3)	15/1385 (1,1)	2,17 [1,18; 3,98] 0,0127[3]	2,20 [1,18; 4,07] 0,0106[4]	1,3 [0,3; 2,2] 0,0106[4]
Paraesthesia				
37/1363 (2,7)	39/1385 (2,8)	0,96 [0,62; 1,50] 0,8714[3]	0,96 [0,61; 1,52] 0,8714[4]	-0,1 [-1,3; 1,1] 0,8714[4]
Paronychia				
15/1363 (1,1)	4/1385 (0,3)	3,81 [1,27; 11,45] 0,0172[3]	3,84 [1,27; 11,60] 0,0102[4]	0,8 [0,2; 1,4] 0,0102[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Peripheral sensory neuropathy				
17/1363 (1,2)	14/1385 (1,0)	1,23 [0,61; 2,49] 0,5581[3]	1,24 [0,61; 2,52] 0,5574[4]	0,2 [-0,6; 1,0] 0,5574[4]
Peripheral swelling				
32/1363 (2,3)	25/1385 (1,8)	1,30 [0,77; 2,18] 0,3197[3]	1,31 [0,77; 2,22] 0,3183[4]	0,5 [-0,5; 1,6] 0,3183[4]
Pharyngitis				
10/1363 (0,7)	15/1385 (1,1)	0,68 [0,31; 1,50] 0,3380[3]	0,68 [0,30; 1,51] 0,3348[4]	-0,3 [-1,1; 0,4] 0,3348[4]
Platelet count decreased				
121/1363 (8,9)	9/1385 (0,6)	13,66 [6,97; 26,78] <,0001[3]	14,89 [7,53; 29,45] <,0001[4]	8,2 [6,7; 9,8] <,0001[4]
Pneumonia				
34/1363 (2,5)	20/1385 (1,4)	1,73 [1,00; 2,99] 0,0502[3]	1,75 [1,00; 3,05] 0,0473[4]	1,1 [0,0; 2,1] 0,0473[4]
Pneumonitis				
21/1363 (1,5)	4/1385 (0,3)	5,33 [1,84; 15,50] 0,0021[3]	5,40 [1,85; 15,78] 0,0005[4]	1,3 [0,5; 2,0] 0,0005[4]
Procedural pain				
38/1363 (2,8)	29/1385 (2,1)	1,33 [0,83; 2,15] 0,2399[3]	1,34 [0,82; 2,19] 0,2382[4]	0,7 [-0,5; 1,8] 0,2382[4]
Productive cough				
22/1363 (1,6)	16/1385 (1,2)	1,40 [0,74; 2,65] 0,3054[3]	1,40 [0,73; 2,68] 0,3031[4]	0,5 [-0,4; 1,3] 0,3031[4]
Pruritus				
115/1363 (8,4)	62/1385 (4,5)	1,88 [1,40; 2,54] <,0001[3]	1,97 [1,43; 2,70] <,0001[4]	4,0 [2,1; 5,8] <,0001[4]
Pyrexia				
108/1363 (7,9)	53/1385 (3,8)	2,07 [1,50; 2,85] <,0001[3]	2,16 [1,54; 3,03] <,0001[4]	4,1 [2,3; 5,9] <,0001[4]
Rash				
125/1363 (9,2)	44/1385 (3,2)	2,89 [2,06; 4,04] <,0001[3]	3,08 [2,16; 4,38] <,0001[4]	6,0 [4,2; 7,8] <,0001[4]
Rash maculo-papular				
23/1363 (1,7)	5/1385 (0,4)	4,67 [1,78; 12,26] 0,0017[3]	4,74 [1,80; 12,50] 0,0005[4]	1,3 [0,6; 2,1] 0,0005[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Respiratory tract infection				
16/1363 (1,2)	10/1385 (0,7)	1,63 [0,74; 3,57] 0,2259[3]	1,63 [0,74; 3,61] 0,2212[4]	0,5 [-0,3; 1,2] 0,2212[4]
Rhinitis allergic				
23/1363 (1,7)	25/1385 (1,8)	0,93 [0,53; 1,64] 0,8140[3]	0,93 [0,53; 1,65] 0,8140[4]	-0,1 [-1,1; 0,9] 0,8140[4]
Sciatica				
12/1363 (0,9)	17/1385 (1,2)	0,72 [0,34; 1,50] 0,3757[3]	0,71 [0,34; 1,50] 0,3734[4]	-0,3 [-1,1; 0,4] 0,3734[4]
Seroma				
20/1363 (1,5)	7/1385 (0,5)	2,90 [1,23; 6,84] 0,0148[3]	2,93 [1,24; 6,96] 0,0106[4]	1,0 [0,2; 1,7] 0,0106[4]
Sinusitis				
33/1363 (2,4)	36/1385 (2,6)	0,93 [0,58; 1,48] 0,7654[3]	0,93 [0,58; 1,50] 0,7654[4]	-0,2 [-1,3; 1,0] 0,7654[4]
Skin infection				
13/1363 (1,0)	15/1385 (1,1)	0,88 [0,42; 1,84] 0,7360[3]	0,88 [0,42; 1,86] 0,7359[4]	-0,1 [-0,9; 0,6] 0,7359[4]
Stomatitis				
70/1363 (5,1)	12/1385 (0,9)	5,93 [3,23; 10,89] <,0001[3]	6,19 [3,34; 11,48] <,0001[4]	4,3 [3,0; 5,5] <,0001[4]
Syncope				
15/1363 (1,1)	11/1385 (0,8)	1,39 [0,64; 3,01] 0,4091[3]	1,39 [0,64; 3,04] 0,4070[4]	0,3 [-0,4; 1,0] 0,4070[4]
Taste disorder				
23/1363 (1,7)	2/1385 (0,1)	11,69 [2,76; 49,47] 0,0008[3]	11,87 [2,79; 50,44] <,0001[4]	1,5 [0,8; 2,3] <,0001[4]
Tendonitis				
11/1363 (0,8)	21/1385 (1,5)	0,53 [0,26; 1,10] 0,0885[3]	0,53 [0,25; 1,10] 0,0832[4]	-0,7 [-1,5; 0,1] 0,0832[4]
Thrombocytopenia				
90/1363 (6,6)	9/1385 (0,6)	10,16 [5,14; 20,08] <,0001[3]	10,81 [5,42; 21,54] <,0001[4]	6,0 [4,6; 7,3] <,0001[4]
Thrombophlebitis superficial				
14/1363 (1,0)	1/1385 (0,1)	14,23 [1,87; 108,03] 0,0103[3]	14,36 [1,89; 109,38] 0,0007[4]	1,0 [0,4; 1,5] 0,0007[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Tooth extraction				
10/1363 (0,7)	14/1385 (1,0)	0,73 [0,32; 1,63] 0,4370[3]	0,72 [0,32; 1,64] 0,4350[4]	-0,3 [-1,0; 0,4] 0,4350[4]
Toothache				
19/1363 (1,4)	19/1385 (1,4)	1,02 [0,54; 1,91] 0,9604[3]	1,02 [0,54; 1,93] 0,9604[4]	0,0 [-0,9; 0,9] 0,9604[4]
Tremor				
18/1363 (1,3)	8/1385 (0,6)	2,29 [1,00; 5,24] 0,0507[3]	2,30 [1,00; 5,32] 0,0443[4]	0,7 [0,0; 1,5] 0,0443[4]
Trigger finger				
13/1363 (1,0)	19/1385 (1,4)	0,70 [0,34; 1,40] 0,3098[3]	0,69 [0,34; 1,41] 0,3071[4]	-0,4 [-1,2; 0,4] 0,3071[4]
Upper respiratory tract infection				
116/1363 (8,5)	102/1385 (7,4)	1,16 [0,90; 1,49] 0,2669[3]	1,17 [0,89; 1,54] 0,2664[4]	1,1 [-0,9; 3,2] 0,2664[4]
Urinary tract infection				
129/1363 (9,5)	80/1385 (5,8)	1,64 [1,25; 2,14] 0,0003[3]	1,71 [1,28; 2,28] 0,0003[4]	3,7 [1,7; 5,7] 0,0003[4]
Vaginal haemorrhage				
5/1363 (0,4)	14/1385 (1,0)	0,36 [0,13; 1,00] 0,0511[3]	0,36 [0,13; 1,00] 0,0417[4]	-0,6 [-1,3; -0,0] 0,0417[4]
Vertigo				
41/1363 (3,0)	30/1385 (2,2)	1,39 [0,87; 2,21] 0,1662[3]	1,40 [0,87; 2,26] 0,1642[4]	0,8 [-0,3; 2,0] 0,1642[4]
Viral infection				
15/1363 (1,1)	2/1385 (0,1)	7,62 [1,75; 33,26] 0,0069[3]	7,69 [1,76; 33,71] 0,0014[4]	1,0 [0,4; 1,5] 0,0014[4]
Vision blurred				
33/1363 (2,4)	14/1385 (1,0)	2,40 [1,29; 4,46] 0,0058[3]	2,43 [1,29; 4,56] 0,0044[4]	1,4 [0,4; 2,4] 0,0044[4]
Vitamin B12 deficiency				
16/1363 (1,2)	4/1385 (0,3)	4,06 [1,36; 12,13] 0,0119[3]	4,10 [1,37; 12,30] 0,0064[4]	0,9 [0,2; 1,5] 0,0064[4]
Vitamin D deficiency				
17/1363 (1,2)	15/1385 (1,1)	1,15 [0,58; 2,30] 0,6885[3]	1,15 [0,57; 2,32] 0,6883[4]	0,2 [-0,6; 1,0] 0,6883[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Vomiting				
245/1363 (18,0)	68/1385 (4,9)	3,66 [2,83; 4,74] <,0001[3]	4,24 [3,21; 5,62] <,0001[4]	13,1 [10,7; 15,4] <,0001[4]
Vulvovaginal dryness				
29/1363 (2,1)	44/1385 (3,2)	0,67 [0,42; 1,06] 0,0896[3]	0,66 [0,41; 1,07] 0,0872[4]	-1,0 [-2,2; 0,2] 0,0872[4]
Weight decreased				
56/1363 (4,1)	20/1385 (1,4)	2,85 [1,72; 4,71] <,0001[3]	2,92 [1,75; 4,90] <,0001[4]	2,7 [1,4; 3,9] <,0001[4]
Weight increased				
25/1363 (1,8)	34/1385 (2,5)	0,75 [0,45; 1,25] 0,2635[3]	0,74 [0,44; 1,25] 0,2617[4]	-0,6 [-1,7; 0,5] 0,2617[4]
White blood cell count decreased				
301/1363 (22,1)	54/1385 (3,9)	5,66 [4,28; 7,49] <,0001[3]	6,99 [5,17; 9,44] <,0001[4]	18,2 [15,8; 20,6] <,0001[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Anastrozol, Letrozol; Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Results from binary analysis for adverse events according PT - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Anxiety				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Arthralgia				
1/11 (9,1)	5/11 (45,5)	[2]	[2]	[2]
Atrial fibrillation				
0/11 (0,0)	2/11 (18,2)	[2]	[2]	[2]
Blood creatinine increased				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Constipation				
3/11 (27,3)	0/11 (0,0)	[2]	[2]	[2]
Cough				
4/11 (36,4)	1/11 (9,1)	[2]	[2]	[2]
Decreased appetite				
3/11 (27,3)	0/11 (0,0)	[2]	[2]	[2]
Diarrhoea				
7/11 (63,6)	0/11 (0,0)	[2]	[2]	[2]
Dry mouth				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Dyspnoea				
2/11 (18,2)	1/11 (9,1)	[2]	[2]	[2]
Fatigue				
6/11 (54,5)	3/11 (27,3)	[2]	[2]	[2]
Hot flush				
1/11 (9,1)	3/11 (27,3)	[2]	[2]	[2]
Hypoalbuminaemia				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Hyponatraemia				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Lymphoedema				
2/11 (18,2)	2/11 (18,2)	[2]	[2]	[2]
Musculoskeletal chest pain				
0/11 (0,0)	2/11 (18,2)	[2]	[2]	[2]
Nausea				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Neutropenia				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Palpitations				
1/11 (9,1)	2/11 (18,2)	[2]	[2]	[2]
Platelet count decreased				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Pneumonitis				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Polyneuropathy				
0/11 (0,0)	2/11 (18,2)	[2]	[2]	[2]
Vomiting				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Weight decreased				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
White blood cell count decreased				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]

Data cut-off: 01.04.2021
Safety Population - Men
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
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Table: Results from binary analysis for adverse events according SOC - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
215/630 (34,1)	66/639 (10,3)	3,30 [2,57; 4,25] <,0001[3]	4,50 [3,32; 6,09] <,0001[4]	23,8 [19,4; 28,2] <,0001[4]
Cardiac disorders				
30/630 (4,8)	18/639 (2,8)	1,69 [0,95; 3,00] 0,0730[3]	1,73 [0,95; 3,13] 0,0694[4]	1,9 [-0,2; 4,0] 0,0694[4]
Ear and labyrinth disorders				
30/630 (4,8)	34/639 (5,3)	0,89 [0,55; 1,44] 0,6494[3]	0,89 [0,54; 1,47] 0,6492[4]	-0,6 [-3,0; 1,8] 0,6492[4]
Endocrine disorders				
12/630 (1,9)	22/639 (3,4)	0,55 [0,28; 1,11] 0,0949[3]	0,54 [0,27; 1,11] 0,0898[4]	-1,5 [-3,3; 0,2] 0,0898[4]
Eye disorders				
94/630 (14,9)	43/639 (6,7)	2,22 [1,57; 3,13] <,0001[3]	2,43 [1,66; 3,55] <,0001[4]	8,2 [4,8; 11,6] <,0001[4]
Gastrointestinal disorders				
573/630 (91,0)	227/639 (35,5)	2,56 [2,30; 2,85] <,0001[3]	18,25 [13,29; 25,05] <,0001[4]	55,4 [51,1; 59,8] <,0001[4]
General disorders and administration site conditions				
364/630 (57,8)	213/639 (33,3)	1,73 [1,52; 1,97] <,0001[3]	2,74 [2,18; 3,44] <,0001[4]	24,4 [19,1; 29,8] <,0001[4]
Hepatobiliary disorders				
39/630 (6,2)	22/639 (3,4)	1,80 [1,08; 3,00] 0,0244[3]	1,85 [1,08; 3,16] 0,0222[4]	2,7 [0,4; 5,1] 0,0222[4]
Immune system disorders				
15/630 (2,4)	17/639 (2,7)	0,89 [0,45; 1,78] 0,7510[3]	0,89 [0,44; 1,80] 0,7509[4]	-0,3 [-2,0; 1,4] 0,7509[4]
Infections and infestations				
353/630 (56,0)	268/639 (41,9)	1,34 [1,19; 1,50] <,0001[3]	1,76 [1,41; 2,20] <,0001[4]	14,1 [8,6; 19,5] <,0001[4]
Injury, poisoning and procedural complications				
102/630 (16,2)	86/639 (13,5)	1,20 [0,92; 1,57] 0,1717[3]	1,24 [0,91; 1,69] 0,1708[4]	2,7 [-1,2; 6,6] 0,1708[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Investigations				
311/630 (49,4)	120/639 (18,8)	2,63 [2,20; 3,15] <,0001[3]	4,22 [3,28; 5,43] <,0001[4]	30,6 [25,6; 35,5] <,0001[4]
Metabolism and nutrition disorders				
138/630 (21,9)	70/639 (11,0)	2,00 [1,53; 2,61] <,0001[3]	2,28 [1,67; 3,11] <,0001[4]	11,0 [6,9; 15,0] <,0001[4]
Musculoskeletal and connective tissue disorders				
305/630 (48,4)	348/639 (54,5)	0,89 [0,80; 0,99] 0,0316[3]	0,78 [0,63; 0,98] 0,0312[4]	-6,0 [-11,5; -0,6] 0,0312[4]
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
19/630 (3,0)	20/639 (3,1)	0,96 [0,52; 1,79] 0,9063[3]	0,96 [0,51; 1,82] 0,9063[4]	-0,1 [-2,0; 1,8] 0,9063[4]
Nervous system disorders				
235/630 (37,3)	189/639 (29,6)	1,26 [1,08; 1,48] 0,0037[3]	1,42 [1,12; 1,79] 0,0035[4]	7,7 [2,5; 12,9] 0,0035[4]
Psychiatric disorders				
140/630 (22,2)	135/639 (21,1)	1,05 [0,85; 1,30] 0,6359[3]	1,07 [0,82; 1,39] 0,6358[4]	1,1 [-3,4; 5,6] 0,6358[4]
Renal and urinary disorders				
49/630 (7,8)	32/639 (5,0)	1,55 [1,01; 2,39] 0,0456[3]	1,60 [1,01; 2,53] 0,0436[4]	2,8 [0,1; 5,5] 0,0436[4]
Reproductive system and breast disorders				
117/630 (18,6)	141/639 (22,1)	0,84 [0,68; 1,05] 0,1229[3]	0,81 [0,61; 1,06] 0,1220[4]	-3,5 [-7,9; 0,9] 0,1220[4]
Respiratory, thoracic and mediastinal disorders				
191/630 (30,3)	95/639 (14,9)	2,04 [1,64; 2,54] <,0001[3]	2,49 [1,89; 3,28] <,0001[4]	15,5 [10,9; 20,0] <,0001[4]
Skin and subcutaneous tissue disorders				
258/630 (41,0)	143/639 (22,4)	1,83 [1,54; 2,17] <,0001[3]	2,41 [1,88; 3,07] <,0001[4]	18,6 [13,6; 23,6] <,0001[4]
Surgical and medical procedures				
39/630 (6,2)	49/639 (7,7)	0,81 [0,54; 1,21] 0,3013[3]	0,79 [0,51; 1,23] 0,3002[4]	-1,5 [-4,3; 1,3] 0,3002[4]
Vascular disorders				
232/630 (36,8)	239/639 (37,4)	0,98 [0,85; 1,14] 0,8316[3]	0,98 [0,78; 1,23] 0,8316[4]	-0,6 [-5,9; 4,7] 0,8316[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class				

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Table: Results from binary analysis for adverse events according SOC - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
617/1363 (45,3)	121/1385 (8,7)	5,18 [4,33; 6,20] <,0001[3]	8,64 [6,97; 10,71] <,0001[4]	36,5 [33,5; 39,6] <,0001[4]
Cardiac disorders				
99/1363 (7,3)	66/1385 (4,8)	1,52 [1,13; 2,06] 0,0063[3]	1,57 [1,14; 2,16] 0,0059[4]	2,5 [0,7; 4,3] 0,0059[4]
Ear and labyrinth disorders				
56/1363 (4,1)	63/1385 (4,5)	0,90 [0,64; 1,28] 0,5711[3]	0,90 [0,62; 1,30] 0,5709[4]	-0,4 [-2,0; 1,1] 0,5709[4]
Endocrine disorders				
26/1363 (1,9)	35/1385 (2,5)	0,75 [0,46; 1,25] 0,2721[3]	0,75 [0,45; 1,25] 0,2704[4]	-0,6 [-1,7; 0,5] 0,2704[4]
Eye disorders				
212/1363 (15,6)	77/1385 (5,6)	2,80 [2,18; 3,59] <,0001[3]	3,13 [2,38; 4,11] <,0001[4]	10,0 [7,7; 12,3] <,0001[4]
Gastrointestinal disorders				
1215/1363 (89,1)	474/1385 (34,2)	2,60 [2,42; 2,81] <,0001[3]	15,78 [12,87; 19,34] <,0001[4]	54,9 [51,9; 57,9] <,0001[4]
General disorders and administration site conditions				
767/1363 (56,3)	474/1385 (34,2)	1,64 [1,51; 1,79] <,0001[3]	2,47 [2,12; 2,89] <,0001[4]	22,0 [18,4; 25,7] <,0001[4]
Hepatobiliary disorders				
63/1363 (4,6)	58/1385 (4,2)	1,10 [0,78; 1,56] 0,5791[3]	1,11 [0,77; 1,60] 0,5789[4]	0,4 [-1,1; 2,0] 0,5789[4]
Immune system disorders				
32/1363 (2,3)	34/1385 (2,5)	0,96 [0,59; 1,54] 0,8545[3]	0,96 [0,59; 1,56] 0,8545[4]	-0,1 [-1,3; 1,0] 0,8545[4]
Infections and infestations				
650/1363 (47,7)	521/1385 (37,6)	1,27 [1,16; 1,38] <,0001[3]	1,51 [1,30; 1,76] <,0001[4]	10,1 [6,4; 13,8] <,0001[4]
Injury, poisoning and procedural complications				
238/1363 (17,5)	212/1385 (15,3)	1,14 [0,96; 1,35] 0,1274[3]	1,17 [0,96; 1,43] 0,1270[4]	2,2 [-0,6; 4,9] 0,1270[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Investigations				
660/1363 (48,4)	306/1385 (22,1)	2,19 [1,96; 2,45] <,0001[3]	3,31 [2,81; 3,91] <,0001[4]	26,3 [22,9; 29,8] <,0001[4]
Metabolism and nutrition disorders				
380/1363 (27,9)	226/1385 (16,3)	1,71 [1,48; 1,98] <,0001[3]	1,98 [1,65; 2,39] <,0001[4]	11,6 [8,5; 14,6] <,0001[4]
Musculoskeletal and connective tissue disorders				
681/1363 (50,0)	852/1385 (61,5)	0,81 [0,76; 0,87] <,0001[3]	0,62 [0,54; 0,73] <,0001[4]	-11,6 [-15,2; -7,9] <,0001[4]
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
40/1363 (2,9)	40/1385 (2,9)	1,02 [0,66; 1,56] 0,9421[3]	1,02 [0,65; 1,59] 0,9421[4]	0,0 [-1,2; 1,3] 0,9421[4]
Nervous system disorders				
539/1363 (39,5)	405/1385 (29,2)	1,35 [1,22; 1,50] <,0001[3]	1,58 [1,35; 1,86] <,0001[4]	10,3 [6,8; 13,8] <,0001[4]
Psychiatric disorders				
229/1363 (16,8)	259/1385 (18,7)	0,90 [0,76; 1,06] 0,1931[3]	0,88 [0,72; 1,07] 0,1927[4]	-1,9 [-4,8; 1,0] 0,1927[4]
Renal and urinary disorders				
110/1363 (8,1)	78/1385 (5,6)	1,43 [1,08; 1,90] 0,0119[3]	1,47 [1,09; 1,99] 0,0113[4]	2,4 [0,6; 4,3] 0,0113[4]
Reproductive system and breast disorders				
137/1363 (10,1)	194/1385 (14,0)	0,72 [0,58; 0,88] 0,0016[3]	0,69 [0,54; 0,87] 0,0014[4]	-4,0 [-6,4; -1,5] 0,0014[4]
Respiratory, thoracic and mediastinal disorders				
406/1363 (29,8)	286/1385 (20,6)	1,44 [1,26; 1,65] <,0001[3]	1,63 [1,37; 1,94] <,0001[4]	9,1 [5,9; 12,4] <,0001[4]
Skin and subcutaneous tissue disorders				
544/1363 (39,9)	322/1385 (23,2)	1,72 [1,53; 1,93] <,0001[3]	2,19 [1,86; 2,59] <,0001[4]	16,7 [13,2; 20,1] <,0001[4]
Surgical and medical procedures				
77/1363 (5,6)	85/1385 (6,1)	0,92 [0,68; 1,24] 0,5873[3]	0,92 [0,67; 1,26] 0,5872[4]	-0,5 [-2,2; 1,3] 0,5872[4]
Vascular disorders				
429/1363 (31,5)	436/1385 (31,5)	1,00 [0,90; 1,12] 0,9975[3]	1,00 [0,85; 1,17] 0,9975[4]	-0,0 [-3,5; 3,5] 0,9975[4]

Abemaciclib+ET[1]	**ET[1]**	**Abemaciclib+ET vs. ET[1]**		
Pat. with event n/N (%)	**Pat. with event n/N (%)**	**RR [95% CI] p-value**	**OR [95% CI] p-value**	**ARR [95% CI] p-value**
Data cut-off: 01.04.2021 Safety Population - Postmenopausal 1: According to acceptable comparator by G-BA: Initial therapy with Anastrozol, Letrozol; Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class				

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Table: Results from binary analysis for adverse events according SOC - events occurring in ≥10% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
3/11 (27,3)	1/11 (9,1)	[2]	[2]	[2]
Cardiac disorders				
1/11 (9,1)	2/11 (18,2)	[2]	[2]	[2]
Eye disorders				
2/11 (18,2)	1/11 (9,1)	[2]	[2]	[2]
Gastrointestinal disorders				
8/11 (72,7)	1/11 (9,1)	[2]	[2]	[2]
General disorders and administration site conditions				
6/11 (54,5)	5/11 (45,5)	[2]	[2]	[2]
Infections and infestations				
5/11 (45,5)	3/11 (27,3)	[2]	[2]	[2]
Injury, poisoning and procedural complications				
0/11 (0,0)	3/11 (27,3)	[2]	[2]	[2]
Investigations				
5/11 (45,5)	1/11 (9,1)	[2]	[2]	[2]
Metabolism and nutrition disorders				
4/11 (36,4)	0/11 (0,0)	[2]	[2]	[2]
Musculoskeletal and connective tissue disorders				
3/11 (27,3)	7/11 (63,6)	[2]	[2]	[2]
Nervous system disorders				
3/11 (27,3)	4/11 (36,4)	[2]	[2]	[2]
Psychiatric disorders				
2/11 (18,2)	2/11 (18,2)	[2]	[2]	[2]
Renal and urinary disorders				
0/11 (0,0)	2/11 (18,2)	[2]	[2]	[2]
Respiratory, thoracic and mediastinal disorders				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
7/11 (63,6)	2/11 (18,2)	2	2	2
Skin and subcutaneous tissue disorders				
4/11 (36,4)	1/11 (9,1)	2	2	2
Vascular disorders				
3/11 (27,3)	7/11 (63,6)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Results from binary analysis for serious adverse events according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
No events in category				
-	-	-	-	-

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences).
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
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Table: Results from binary analysis for serious adverse events according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Deep vein thrombosis				
15/1363 (1,1)	2/1385 (0,1)	7,62 [1,75; 33,26] 0,0069[3]	7,69 [1,76; 33,71] 0,0014[4]	1,0 [0,4; 1,5] 0,0014[4]
Pneumonia				
15/1363 (1,1)	8/1385 (0,6)	1,91 [0,81; 4,48] 0,1394[3]	1,92 [0,81; 4,53] 0,1325[4]	0,5 [-0,2; 1,2] 0,1325[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Anastrozol, Letrozol; Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
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Table: Results from binary analysis for serious adverse events according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aortic stenosis				
0/11 (0,0)	1/11 (9,1)	2	2	2
Cellulitis streptococcal				
1/11 (9,1)	0/11 (0,0)	2	2	2
Coronary artery disease				
0/11 (0,0)	1/11 (9,1)	2	2	2
Deep vein thrombosis				
0/11 (0,0)	1/11 (9,1)	2	2	2
Hyponatraemia				
1/11 (9,1)	0/11 (0,0)	2	2	2
Pneumonitis				
1/11 (9,1)	0/11 (0,0)	2	2	2
Pulmonary embolism				
1/11 (9,1)	0/11 (0,0)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttirsaep_men_saf2c1.rtf
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Tabl: Results from binary analysis for serious adverse events according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
General disorders and administration site conditions				
10/630 (1,6)	3/639 (0,5)	3,38 [0,93; 12,23] 0,0633[3]	3,42 [0,94; 12,48] 0,0480[4]	1,1 [0,0; 2,2] 0,0480[4]
Infections and infestations				
22/630 (3,5)	17/639 (2,7)	1,31 [0,70; 2,45] 0,3923[3]	1,32 [0,70; 2,52] 0,3908[4]	0,8 [-1,1; 2,7] 0,3908[4]
Reproductive system and breast disorders				
5/630 (0,8)	12/639 (1,9)	0,42 [0,15; 1,19] 0,1037[3]	0,42 [0,15; 1,19] 0,0930[4]	-1,1 [-2,3; 0,2] 0,0930[4]
Respiratory, thoracic and mediastinal disorders				
10/630 (1,6)	2/639 (0,3)	5,07 [1,12; 23,05] 0,0356[3]	5,14 [1,12; 23,54] 0,0190[4]	1,3 [0,2; 2,3] 0,0190[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttirsaes_premp_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Results from binary analysis for serious adverse events according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Cardiac disorders				
17/1363 (1,2)	9/1385 (0,6)	1,92 [0,86; 4,29] 0,1122[3]	1,93 [0,86; 4,35] 0,1058[4]	0,6 [-0,1; 1,3] 0,1058[4]
Gastrointestinal disorders				
33/1363 (2,4)	15/1385 (1,1)	2,24 [1,22; 4,10] 0,0092[3]	2,27 [1,23; 4,19] 0,0074[4]	1,3 [0,4; 2,3] 0,0074[4]
Infections and infestations				
75/1363 (5,5)	39/1385 (2,8)	1,95 [1,34; 2,86] 0,0005[3]	2,01 [1,35; 2,98] 0,0004[4]	2,7 [1,2; 4,2] 0,0004[4]
Injury, poisoning and procedural complications				
20/1363 (1,5)	17/1385 (1,2)	1,20 [0,63; 2,27] 0,5859[3]	1,20 [0,63; 2,30] 0,5853[4]	0,2 [-0,6; 1,1] 0,5853[4]
Nervous system disorders				
16/1363 (1,2)	15/1385 (1,1)	1,08 [0,54; 2,18] 0,8217[3]	1,08 [0,53; 2,20] 0,8216[4]	0,1 [-0,7; 0,9] 0,8216[4]
Respiratory, thoracic and mediastinal disorders				
20/1363 (1,5)	10/1385 (0,7)	2,03 [0,95; 4,33] 0,0658[3]	2,05 [0,95; 4,39] 0,0601[4]	0,7 [-0,0; 1,5] 0,0601[4]
Vascular disorders				
22/1363 (1,6)	6/1385 (0,4)	3,73 [1,52; 9,16] 0,0042[3]	3,77 [1,52; 9,33] 0,0021[4]	1,2 [0,4; 1,9] 0,0021[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Anastrozol, Letrozol; Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Results from binary analysis for serious adverse events according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Cardiac disorders				
0/11 (0,0)	1/11 (9,1)	2	2	2
Infections and infestations				
1/11 (9,1)	0/11 (0,0)	2	2	2
Metabolism and nutrition disorders				
1/11 (9,1)	0/11 (0,0)	2	2	2
Respiratory, thoracic and mediastinal disorders				
2/11 (18,2)	0/11 (0,0)	2	2	2
Vascular disorders				
0/11 (0,0)	2/11 (18,2)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
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Tabl: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Alanine aminotransferase increased				
12/630 (1,9)	5/639 (0,8)	2,43 [0,86; 6,87] 0,0928[3]	2,46 [0,86; 7,03] 0,0821[4]	1,1 [-0,1; 2,4] 0,0821[4]
Aspartate aminotransferase increased				
10/630 (1,6)	4/639 (0,6)	2,54 [0,80; 8,04] 0,1141[3]	2,56 [0,80; 8,21] 0,1012[4]	1,0 [-0,2; 2,1] 0,1012[4]
Diarrhoea				
33/630 (5,2)	2/639 (0,3)	16,74 [4,03; 69,45] 0,0001[3]	17,61 [4,21; 73,69] <,0001[4]	4,9 [3,1; 6,7] <,0001[4]
Hypertriglyceridaemia				
10/630 (1,6)	3/639 (0,5)	3,38 [0,93; 12,23] 0,0633[3]	3,42 [0,94; 12,48] 0,0480[4]	1,1 [0,0; 2,2] 0,0480[4]
Leukopenia				
14/630 (2,2)	0/639 (0,0)	29,41 [1,76; 492,01] 0,0186[3]	30,08 [1,79; 505,37] 0,0002[4]	2,2 [1,1; 3,4] 0,0002[4]
Lymphocyte count decreased				
28/630 (4,4)	0/639 (0,0)	57,81 [3,54; 944,89] 0,0044[3]	60,50 [3,69; 993,15] <,0001[4]	4,4 [2,8; 6,1] <,0001[4]
Neutropenia				
48/630 (7,6)	6/639 (0,9)	8,11 [3,50; 18,82] <,0001[3]	8,70 [3,70; 20,48] <,0001[4]	6,7 [4,5; 8,9] <,0001[4]
Neutrophil count decreased				
64/630 (10,2)	5/639 (0,8)	12,98 [5,26; 32,04] <,0001[3]	14,34 [5,73; 35,88] <,0001[4]	9,4 [6,9; 11,8] <,0001[4]
White blood cell count decreased				
49/630 (7,8)	5/639 (0,8)	9,94 [3,99; 24,78] <,0001[3]	10,69 [4,23; 27,02] <,0001[4]	7,0 [4,8; 9,2] <,0001[4]

Data cut-off: 01.04.2021
Safety Population - Premenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Alanine aminotransferase increased				
36/1363 (2,6)	8/1385 (0,6)	4,57 [2,13; 9,80] <,0001[3]	4,67 [2,16; 10,08] <,0001[4]	2,1 [1,1; 3,0] <,0001[4]
Anaemia				
38/1363 (2,8)	5/1385 (0,4)	7,72 [3,05; 19,56] <,0001[3]	7,92 [3,11; 20,17] <,0001[4]	2,4 [1,5; 3,4] <,0001[4]
Arthralgia				
5/1363 (0,4)	20/1385 (1,4)	0,25 [0,10; 0,67] 0,0060[3]	0,25 [0,09; 0,67] 0,0029[4]	-1,1 [-1,8; -0,4] 0,0029[4]
Aspartate aminotransferase increased				
23/1363 (1,7)	5/1385 (0,4)	4,67 [1,78; 12,26] 0,0017[3]	4,74 [1,80; 12,50] 0,0005[4]	1,3 [0,6; 2,1] 0,0005[4]
Diarrhoea				
133/1363 (9,8)	2/1385 (0,1)	67,57 [16,76; 272,46] <,0001[3]	74,77 [18,47; 302,73] <,0001[4]	9,6 [8,0; 11,2] <,0001[4]
Fatigue				
36/1363 (2,6)	3/1385 (0,2)	12,19 [3,76; 39,50] <,0001[3]	12,50 [3,84; 40,68] <,0001[4]	2,4 [1,5; 3,3] <,0001[4]
Gamma-glutamyltransferase increased				
21/1363 (1,5)	5/1385 (0,4)	4,27 [1,61; 11,29] 0,0034[3]	4,32 [1,62; 11,49] 0,0014[4]	1,2 [0,5; 1,9] 0,0014[4]
Hypertension				
17/1363 (1,2)	25/1385 (1,8)	0,69 [0,37; 1,27] 0,2362[3]	0,69 [0,37; 1,28] 0,2334[4]	-0,6 [-1,5; 0,4] 0,2334[4]
Hypokalaemia				
20/1363 (1,5)	5/1385 (0,4)	4,06 [1,53; 10,80] 0,0049[3]	4,11 [1,54; 10,98] 0,0023[4]	1,1 [0,4; 1,8] 0,0023[4]
Leukopenia				
48/1363 (3,5)	2/1385 (0,1)	24,39 [5,94; 100,14] <,0001[3]	25,24 [6,12; 104,06] <,0001[4]	3,4 [2,4; 4,4] <,0001[4]
Lymphocyte count decreased				
47/1363 (3,4)	5/1385 (0,4)	9,55 [3,81; 23,94] <,0001[3]	9,86 [3,91; 24,86] <,0001[4]	3,1 [2,1; 4,1] <,0001[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Lymphopenia				
22/1363 (1,6)	2/1385 (0,1)	11,18 [2,63; 47,44] 0,0011[3]	11,34 [2,66; 48,34] <,0001[4]	1,5 [0,8; 2,2] <,0001[4]
Neutropenia				
142/1363 (10,4)	4/1385 (0,3)	36,07 [13,39; 97,17] <,0001[3]	40,15 [14,82; 108,78] <,0001[4]	10,1 [8,5; 11,8] <,0001[4]
Neutrophil count decreased				
131/1363 (9,6)	3/1385 (0,2)	44,37 [14,16; 139,02] <,0001[3]	48,98 [15,56; 154,24] <,0001[4]	9,4 [7,8; 11,0] <,0001[4]
White blood cell count decreased				
100/1363 (7,3)	3/1385 (0,2)	33,87 [10,77; 106,54] <,0001[3]	36,47 [11,54; 115,30] <,0001[4]	7,1 [5,7; 8,5] <,0001[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Anastrozol, Letrozol; Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttirgr3p_posmp_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam, /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according PT - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Aortic stenosis				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Atrial fibrillation				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Cellulitis streptococcal				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Coronary artery disease				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Deep vein thrombosis				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Diarrhoea				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Finger amputation				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Gastrointestinal pain				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Haematuria				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Headache				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Hypoalbuminaemia				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Hyponatraemia				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Lymphocyte count decreased				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Neutropenia				

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
2/11 (18,2)	0/11 (0,0)	2	2	2
Platelet count decreased				
2/11 (18,2)	0/11 (0,0)	2	2	2
Pneumonitis				
1/11 (9,1)	0/11 (0,0)	2	2	2
Postoperative respiratory failure				
0/11 (0,0)	1/11 (9,1)	2	2	2
Pulmonary embolism				
1/11 (9,1)	0/11 (0,0)	2	2	2
Radius fracture				
0/11 (0,0)	1/11 (9,1)	2	2	2
Tendon injury				
0/11 (0,0)	1/11 (9,1)	2	2	2

Data cut-off: 01.04.2021
Safety Population - Men
1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 2: No statistical test is performed due to low number of patients and events.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; PT: preferred term; RR: relative risk

Program Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/programs/primary/tfl/german_dossier/t_gba2c1_bp_aesocpt.sas
Output Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/output/restricted/tfl/german_dossier/t_gba_bp_ttirgr3p_men_saf2c1.rtf
Dataset Location: /lillyce/prd/ly2835219/i3y_mc_jpcf/csr3/data/analysis/shared/adam,
/lillyce/prd/ly2835219/i3y_mc_jpcf/misc8/data/analysis/restricted/adamgba
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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Premenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
68/630 (10,8)	8/639 (1,3)	8,62 [4,18; 17,79] <,0001[3]	9,54 [4,55; 20,03] <,0001[4]	9,5 [7,0; 12,1] <,0001[4]
Gastrointestinal disorders				
46/630 (7,3)	5/639 (0,8)	9,33 [3,73; 23,33] <,0001[3]	9,99 [3,94; 25,31] <,0001[4]	6,5 [4,4; 8,7] <,0001[4]
General disorders and administration site conditions				
14/630 (2,2)	7/639 (1,1)	2,03 [0,82; 4,99] 0,1237[3]	2,05 [0,82; 5,12] 0,1157[4]	1,1 [-0,3; 2,5] 0,1157[4]
Infections and infestations				
24/630 (3,8)	19/639 (3,0)	1,28 [0,71; 2,32] 0,4118[3]	1,29 [0,70; 2,38] 0,4105[4]	0,8 [-1,2; 2,8] 0,4105[4]
Investigations				
121/630 (19,2)	13/639 (2,0)	9,44 [5,39; 16,55] <,0001[3]	11,45 [6,38; 20,52] <,0001[4]	17,2 [13,9; 20,4] <,0001[4]
Metabolism and nutrition disorders				
14/630 (2,2)	6/639 (0,9)	2,37 [0,92; 6,12] 0,0755[3]	2,40 [0,92; 6,28] 0,0665[4]	1,3 [-0,1; 2,7] 0,0665[4]
Reproductive system and breast disorders				
3/630 (0,5)	12/639 (1,9)	0,25 [0,07; 0,89] 0,0329[3]	0,25 [0,07; 0,89] 0,0209[4]	-1,4 [-2,6; -0,2] 0,0209[4]
Respiratory, thoracic and mediastinal disorders				
11/630 (1,7)	2/639 (0,3)	5,58 [1,24; 25,07] 0,0250[3]	5,66 [1,25; 25,64] 0,0113[4]	1,4 [0,3; 2,5] 0,0113[4]
Surgical and medical procedures				
6/630 (1,0)	10/639 (1,6)	0,61 [0,22; 1,66] 0,3333[3]	0,60 [0,22; 1,67] 0,3282[4]	-0,6 [-1,8; 0,6] 0,3282[4]
Vascular disorders				
10/630 (1,6)	11/639 (1,7)	0,92 [0,39; 2,16] 0,8515[3]	0,92 [0,39; 2,18] 0,8514[4]	-0,1 [-1,5; 1,3] 0,8514[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Premenopausal 1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class				

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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Postmenopausal

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
214/1363 (15,7)	14/1385 (1,0)	15,53 [9,09; 26,53] <,0001[3]	18,24 [10,56; 31,50] <,0001[4]	14,7 [12,7; 16,7] <,0001[4]
Cardiac disorders				
15/1363 (1,1)	12/1385 (0,9)	1,27 [0,60; 2,70] 0,5349[3]	1,27 [0,59; 2,73] 0,5339[4]	0,2 [-0,5; 1,0] 0,5339[4]
Eye disorders				
14/1363 (1,0)	6/1385 (0,4)	2,37 [0,91; 6,15] 0,0759[3]	2,39 [0,91; 6,23] 0,0670[4]	0,6 [-0,0; 1,2] 0,0670[4]
Gastrointestinal disorders				
159/1363 (11,7)	21/1385 (1,5)	7,69 [4,91; 12,05] <,0001[3]	8,58 [5,41; 13,61] <,0001[4]	10,1 [8,3; 12,0] <,0001[4]
General disorders and administration site conditions				
60/1363 (4,4)	9/1385 (0,6)	6,77 [3,38; 13,60] <,0001[3]	7,04 [3,48; 14,24] <,0001[4]	3,8 [2,6; 4,9] <,0001[4]
Infections and infestations				
75/1363 (5,5)	40/1385 (2,9)	1,91 [1,31; 2,78] 0,0008[3]	1,96 [1,32; 2,90] 0,0006[4]	2,6 [1,1; 4,1] 0,0006[4]
Injury, poisoning and procedural complications				
18/1363 (1,3)	19/1385 (1,4)	0,96 [0,51; 1,83] 0,9073[3]	0,96 [0,50; 1,84] 0,9073[4]	-0,1 [-0,9; 0,8] 0,9073[4]
Investigations				
256/1363 (18,8)	32/1385 (2,3)	8,13 [5,67; 11,65] <,0001[3]	9,78 [6,71; 14,24] <,0001[4]	16,5 [14,3; 18,7] <,0001[4]
Metabolism and nutrition disorders				
68/1363 (5,0)	23/1385 (1,7)	3,00 [1,88; 4,79] <,0001[3]	3,11 [1,93; 5,02] <,0001[4]	3,3 [2,0; 4,7] <,0001[4]
Musculoskeletal and connective tissue disorders				
15/1363 (1,1)	37/1385 (2,7)	0,41 [0,23; 0,75] 0,0035[3]	0,41 [0,22; 0,74] 0,0025[4]	-1,6 [-2,6; -0,6] 0,0025[4]
Nervous system disorders				
29/1363 (2,1)	21/1385 (1,5)	1,40 [0,80; 2,45] 0,2329[3]	1,41 [0,80; 2,49] 0,2305[4]	0,6 [-0,4; 1,6] 0,2305[4]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Renal and urinary disorders				
14/1363 (1,0)	3/1385 (0,2)	4,74 [1,37; 16,46] 0,0143[3]	4,78 [1,37; 16,67] 0,0067[4]	0,8 [0,2; 1,4] 0,0067[4]
Respiratory, thoracic and mediastinal disorders				
27/1363 (2,0)	12/1385 (0,9)	2,29 [1,16; 4,49] 0,0165[3]	2,31 [1,17; 4,58] 0,0135[4]	1,1 [0,2; 2,0] 0,0135[4]
Surgical and medical procedures				
15/1363 (1,1)	13/1385 (0,9)	1,17 [0,56; 2,45] 0,6730[3]	1,17 [0,56; 2,48] 0,6727[4]	0,2 [-0,6; 0,9] 0,6727[4]
Vascular disorders				
34/1363 (2,5)	36/1385 (2,6)	0,96 [0,60; 1,52] 0,8616[3]	0,96 [0,60; 1,54] 0,8616[4]	-0,1 [-1,3; 1,1] 0,8616[4]

Data cut-off: 01.04.2021
Safety Population - Postmenopausal
1: According to acceptable comparator by G-BA: Initial therapy with Anastrozol, Letrozol; Tamoxifen (with all following sequences); 3: from Z-test; 4: from Chi^2-test.
Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class

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Table: Results from binary analysis for adverse events with CTCAE Grade ≥ 3 according SOC - events occurring in ≥5% of patients in one treatment arm, and events occurring in ≥10 patients and ≥1% of patients in one treatment arm – from RCT with medical drug to be assessed - Cohort 1 Population - Safety - Men

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Blood and lymphatic system disorders				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Cardiac disorders				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Gastrointestinal disorders				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Infections and infestations				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Injury, poisoning and procedural complications				
0/11 (0,0)	2/11 (18,2)	[2]	[2]	[2]
Investigations				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Metabolism and nutrition disorders				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Nervous system disorders				
1/11 (9,1)	0/11 (0,0)	[2]	[2]	[2]
Renal and urinary disorders				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Respiratory, thoracic and mediastinal disorders				
2/11 (18,2)	0/11 (0,0)	[2]	[2]	[2]
Surgical and medical procedures				
0/11 (0,0)	1/11 (9,1)	[2]	[2]	[2]
Vascular disorders				
0/11 (0,0)	2/11 (18,2)	[2]	[2]	[2]

Abemaciclib+ET[1]	ET[1]	Abemaciclib+ET vs. ET[1]		
Pat. with event n/N (%)	Pat. with event n/N (%)	RR [95% CI] p-value	OR [95% CI] p-value	ARR [95% CI] p-value
Data cut-off: 01.04.2021 Safety Population - Men 1: According to acceptable comparator by G-BA: Initial therapy with Tamoxifen (with all following sequences); 2: No statistical test is performed due to low number of patients and events. Abbreviations: ARR: absolute risk reduction; CI: confidence interval; CTCAE: common terminology criteria for adverse events; ET: endocrine therapy; n: number of patients with event; N: total number of patients in analysis; NE: not evaluable/not reached; OR: odds ratio; RR: relative risk; SOC: system organ class				

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