Dossier zur Nutzenbewertung gemäß § 35a SGB V

Osimertinib (TAGRISSO®)

AstraZeneca GmbH

Modul 4 A – Anhang 4-G

Adjuvante Behandlung nach vollständiger Tumorresektion bei erwachsenen Patienten mit nichtkleinzelligem Lungenkarzinom (NSCLC) im Stadium IB-IIIA, deren Tumoren Mutationen des epidermalen Wachstumsfaktor-Rezeptors (Epidermal Growth Factor Receptor, EGFR) als Deletion im Exon 19 oder Substitutionsmutation im Exon 21 (L858R) aufweisen

Weitere Analysen und Kaplan-Meier-Plots zu den in Abschnitt 4.3.1.3 gezeigten Ergebnissen

Stand: 28.06.2024

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Table 2.6 ADAURA: Summary of status at time of first clinically meaningful deterioration in SF-36 physical and mental component scores
Full Analysis Set, DCO 11Apr2022

		Reason	AZD9291 (N=339)	Placebo (N=343)
Koerperliche Gesundheit PCS: 9.423	Verschlechterung	Gesamt	57 (16,8)	53 (15,5)
	Zensiert	Gesamt	282 (83,2)	290 (84,5)
		Keine Werte zur Baseline und/oder Folgevisiten (Tag 1)	29 (8,6)	32 (9,3)
		Ohne Verschlechterung am Leben	228 (67,3)	205 (59,8)
		Gestorben	4 (1,2)	14 (4,1)
		Zwei oder mehr verpasste Visiten vor auswertbarer Visite oder Tod*	21 (6,2)	39 (11,4)
Psychische Gesundheit MCS: 9.618	Verschlechterung	Gesamt	98 (28,9)	89 (25,9)
	Zensiert	Gesamt	241 (71,1)	254 (74,1)
		Keine Werte zur Baseline und/oder Folgevisiten (Tag 1)	29 (8,6)	32 (9,3)
		Ohne Verschlechterung am Leben	188 (55,5)	179 (52,2)
		Gestorben	5 (1,5)	11 (3,2)
		Zwei oder mehr verpasste Visiten vor auswertbarer Visite oder Tod*	19 (5,6)	32 (9,3)

Time to first deterioration is defined as time from date of randomisation to the date of first clinically important worsening (decrease of >=9.423 for PCS & >=9.618 for MCS) in the respective score. Death is not counted as an event.
Patients with evaluable baseline data and do not experience a clinically important deterioration are censored at the date of their last evaluable SF-36 assessment. Patients without evaluable baseline data for a score are censored at Day 1.
* If worsening happened prior to 2 missing (or more) visits it counts as deterioration event.
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Table 3.2.1 ADAURA: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
UE	337	330 (97,9)	0,4 [0,3; 0,5]	343	309 (90,1)	1,0 [0,7; 1,0]	1,85	[1,57; 2,18]	<0,0001*
SOC: Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	337	109 (32,3)	NE [NE; NE]	343	79 (23,0)	NE [NE; NE]	1,35	[1,01; 1,79]	0,0417*
PT: Asthenie	337	18 (5,3)	NE [NE; NE]	343	17 (5,0)	NE [NE; NE]	0,95	[0,49; 1,84]	0,8758
PT: Brustkorbbeschwerden	337	10 (3,0)	NE [NE; NE]	343	8 (2,3)	NE [NE; NE]	1,12	[0,44; 2,84]	0,8090
PT: Ermuedung	337	32 (9,5)	NE [NE; NE]	343	17 (5,0)	NE [NE; NE]	1,78	[1,02; 3,13]	0,0436*
PT: Fieber	337	17 (5,0)	NE [NE; NE]	343	10 (2,9)	NE [NE; NE]	1,61	[0,75; 3,43]	0,2185
PT: Oedem peripher	337	10 (3,0)	NE [NE; NE]	343	8 (2,3)	NE [NE; NE]	1,17	[0,46; 2,95]	0,7420
PT: Schleimhautentzuendung	337	10 (3,0)	NE [NE; NE]	343	1 (0,3)	NE [NE; NE]	4,97	[1,52; 16,25]	0,0079*
PT: Thoraxschmerz nicht kardialen Ursprungs	337	9 (2,7)	NE [NE; NE]	343	14 (4,1)	NE [NE; NE]	0,57	[0,25; 1,30]	0,1834
SOC: Augenerkrankungen	337	66 (19,6)	NE [NE; NE]	343	42 (12,2)	NE [NE; NE]	1,56	[1,07; 2,27]	0,0220*
PT: Sehen verschwommen	337	12 (3,6)	NE [NE; NE]	343	3 (0,9)	NE [NE; NE]	3,16	[1,15; 8,72]	0,0261*

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Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified log-rank test. Hazard ratio and 95% confidence interval derived from U and V statistics. Breslow method is used for handling ties. NC = not calculable. Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 3.2.1 ADAURA: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PT: Trockenes Auge	337	20 (5,9)	NE [NE; NE]	343	12 (3,5)	NE [NE; NE]	1,60	[0,80; 3,20]	0,1852
SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums	337	146 (43,3)	NE [NE; NE]	343	121 (35,3)	NE [NE; NE]	1,16	[0,91; 1,48]	0,2275
PT: Dyspnoe	337	13 (3,9)	NE [NE; NE]	343	16 (4,7)	NE [NE; NE]	0,71	[0,34; 1,47]	0,3564
PT: Epistaxis	337	21 (6,2)	NE [NE; NE]	343	5 (1,5)	NE [NE; NE]	3,03	[1,40; 6,57]	0,0049*
PT: Husten	337	66 (19,6)	NE [NE; NE]	343	61 (17,8)	NE [NE; NE]	1,01	[0,71; 1,44]	0,9424
PT: Nasenschleimhaut trocken	337	11 (3,3)	NE [NE; NE]	343	0	NE [NE; NE]	NC	NC	0,0011*
PT: Rhinorrhoe	337	11 (3,3)	NE [NE; NE]	343	6 (1,7)	NE [NE; NE]	1,65	[0,63; 4,27]	0,3057
PT: Schmerzen im Oropharynx	337	13 (3,9)	NE [NE; NE]	343	16 (4,7)	NE [NE; NE]	0,69	[0,33; 1,45]	0,3304
SOC: Erkrankungen der Geschlechtsorgane und der Brustdruese	337	20 (5,9)	NE [NE; NE]	343	14 (4,1)	NE [NE; NE]	1,25	[0,64; 2,46]	0,5161
SOC: Erkrankungen der Haut und des Unterhautgewebes	337	249 (73,9)	2,7 [1,8; 4,8]	343	130 (37,9)	NE [NE; NE]	2,71	[2,21; 3,33]	<0,0001*

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[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified log-rank test. Hazard ratio and 95% confidence interval derived from U and V statistics. Breslow method is used for handling ties. NC = not calculable. Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 3.2.1 ADAURA: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PT: Alopezie	337	21 (6,2)	NE [NE; NE]	343	8 (2,3)	NE [NE; NE]	2,39	[1,15; 4,95]	0,0195*
PT: Ausschlag	337	33 (9,8)	NE [NE; NE]	343	12 (3,5)	NE [NE; NE]	2,38	[1,32; 4,27]	0,0038*
PT: Ausschlag makulo-papuloes	337	23 (6,8)	NE [NE; NE]	343	14 (4,1)	NE [NE; NE]	1,64	[0,86; 3,12]	0,1349
PT: Ausschlag papuloes	337	17 (5,0)	NE [NE; NE]	343	3 (0,9)	NE [NE; NE]	3,90	[1,62; 9,40]	0,0024*
PT: Dermatitis akneiform	337	41 (12,2)	NE [NE; NE]	343	16 (4,7)	NE [NE; NE]	2,45	[1,46; 4,12]	0,0007*
PT: Erythem	337	11 (3,3)	NE [NE; NE]	343	6 (1,7)	NE [NE; NE]	1,75	[0,67; 4,53]	0,2498
PT: Hautfissuren	337	19 (5,6)	NE [NE; NE]	343	0	NE [NE; NE]	NC	NC	<0,0001*
PT: Nagelerkrankung	337	22 (6,5)	NE [NE; NE]	343	3 (0,9)	NE [NE; NE]	4,30	[1,96; 9,43]	0,0003*
PT: Onychoklasie	337	15 (4,5)	NE [NE; NE]	343	2 (0,6)	NE [NE; NE]	4,26	[1,64; 11,03]	0,0029*
PT: Pruritus	337	70 (20,8)	NE [NE; NE]	343	30 (8,7)	NE [NE; NE]	2,26	[1,53; 3,35]	<0,0001*
PT: Trockene Haut	337	84 (24,9)	NE [NE; NE]	343	23 (6,7)	NE [NE; NE]	3,36	[2,30; 4,91]	<0,0001*
SOC: Erkrankungen der Nieren und Harnwege	337	42 (12,5)	NE [NE; NE]	343	34 (9,9)	NE [NE; NE]	1,11	[0,71; 1,75]	0,6431

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Table 3.2.1 ADAURA: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PT: Haematurie	337	4 (1,2)	NE [NE; NE]	343	14 (4,1)	NE [NE; NE]	0,28	[0,11; 0,72]	0,0077*
PT: Proteinurie	337	14 (4,2)	NE [NE; NE]	343	4 (1,2)	NE [NE; NE]	2,82	[1,12; 7,12]	0,0282*
SOC: Erkrankungen des Blutes und des Lymphsystems	337	77 (22,8)	NE [NE; NE]	343	12 (3,5)	NE [NE; NE]	4,51	[2,98; 6,84]	<0,0001*
PT: Anaemie	337	28 (8,3)	NE [NE; NE]	343	7 (2,0)	NE [NE; NE]	3,08	[1,58; 5,98]	0,0009*
PT: Leukopenie	337	20 (5,9)	NE [NE; NE]	343	6 (1,7)	NE [NE; NE]	2,76	[1,28; 5,96]	0,0099*
PT: Neutropenie	337	21 (6,2)	NE [NE; NE]	343	1 (0,3)	NE [NE; NE]	5,97	[2,58; 13,80]	<0,0001*
PT: Thrombozytopenie	337	27 (8,0)	NE [NE; NE]	343	0	NE [NE; NE]	NC	NC	<0,0001*
SOC: Erkrankungen des Gastrointestinaltrakts	337	243 (72,1)	1,9 [1,1; 2,5]	343	157 (45,8)	25,0 [19,2; NE]	2,23	[1,82; 2,72]	<0,0001*
PT: Abdominalschmerz	337	20 (5,9)	NE [NE; NE]	343	5 (1,5)	NE [NE; NE]	3,22	[1,47; 7,06]	0,0036*
PT: Aphthoeses Ulkus	337	12 (3,6)	NE [NE; NE]	343	1 (0,3)	NE [NE; NE]	5,18	[1,74; 15,41]	0,0031*
PT: Bauch aufgetrieben	337	15 (4,5)	NE [NE; NE]	343	7 (2,0)	NE [NE; NE]	1,94	[0,84; 4,48]	0,1215
PT: Diarrhoe	337	159 (47,2)	NE [NE; NE]	343	70 (20,4)	NE [NE; NE]	2,64	[2,04; 3,43]	<0,0001*

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(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PT: Dyspepsie	337	15 (4,5)	NE [NE; NE]	343	5 (1,5)	NE [NE; NE]	2,42	[1,003; 5,84]	0,0492*
PT: Erbrechen	337	30 (8,9)	NE [NE; NE]	343	16 (4,7)	NE [NE; NE]	1,77	[0,99; 3,16]	0,0533
PT: Gastrooesophageale Refluxerkrankung	337	18 (5,3)	NE [NE; NE]	343	14 (4,1)	NE [NE; NE]	1,17	[0,58; 2,35]	0,6555
PT: Haemorrhoiden	337	10 (3,0)	NE [NE; NE]	343	4 (1,2)	NE [NE; NE]	2,12	[0,74; 6,08]	0,1601
PT: Mundtrockenheit	337	16 (4,7)	NE [NE; NE]	343	5 (1,5)	NE [NE; NE]	2,80	[1,19; 6,60]	0,0187*
PT: Mundulzeration	337	39 (11,6)	NE [NE; NE]	343	10 (2,9)	NE [NE; NE]	3,35	[1,91; 5,87]	<0,0001*
PT: Obstipation	337	21 (6,2)	NE [NE; NE]	343	18 (5,2)	NE [NE; NE]	1,07	[0,57; 2,01]	0,8380
PT: Schmerzen Oberbauch	337	16 (4,7)	NE [NE; NE]	343	15 (4,4)	NE [NE; NE]	1,01	[0,50; 2,04]	0,9795
PT: Stomatitis	337	59 (17,5)	NE [NE; NE]	343	15 (4,4)	NE [NE; NE]	3,55	[2,25; 5,60]	<0,0001*
PT: Uebelkeit	337	34 (10,1)	NE [NE; NE]	343	20 (5,8)	NE [NE; NE]	1,64	[0,96; 2,80]	0,0697
PT: Zahnschmerzen	337	8 (2,4)	NE [NE; NE]	343	18 (5,2)	NE [NE; NE]	0,41	[0,19; 0,89]	0,0232*
SOC: Erkrankungen des Nervensystems	337	92 (27,3)	NE [NE; NE]	343	92 (26,8)	NE [NE; NE]	0,93	[0,70; 1,25]	0,6332
PT: Dysgeusie	337	11 (3,3)	NE [NE; NE]	343	1 (0,3)	NE [NE; NE]	5,49	[1,77; 17,03]	0,0032*

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	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PT: Hypoaesthesie	337	14 (4,2)	NE [NE; NE]	343	11 (3,2)	NE [NE; NE]	1,18	[0,54; 2,59]	0,6771
PT: Kopfschmerzen	337	26 (7,7)	NE [NE; NE]	343	34 (9,9)	NE [NE; NE]	0,66	[0,39; 1,09]	0,1054
PT: Schwindelgefuehl	337	29 (8,6)	NE [NE; NE]	343	26 (7,6)	NE [NE; NE]	1,00	[0,59; 1,70]	0,9955
SOC: Erkrankungen des Ohrs und des Labyrinths	337	26 (7,7)	NE [NE; NE]	343	21 (6,1)	NE [NE; NE]	1,08	[0,61; 1,92]	0,7971
PT: Vertigo	337	11 (3,3)	NE [NE; NE]	343	7 (2,0)	NE [NE; NE]	1,35	[0,53; 3,42]	0,5278
SOC: Gefaesserkrankungen	337	31 (9,2)	NE [NE; NE]	343	28 (8,2)	NE [NE; NE]	0,98	[0,59; 1,64]	0,9398
PT: Hypertonie	337	15 (4,5)	NE [NE; NE]	343	19 (5,5)	NE [NE; NE]	0,65	[0,33; 1,28]	0,2116
SOC: Gutartige, boesartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)	337	13 (3,9)	NE [NE; NE]	343	14 (4,1)	NE [NE; NE]	0,78	[0,36; 1,66]	0,5143
SOC: Herzerkrankungen	337	42 (12,5)	NE [NE; NE]	343	28 (8,2)	NE [NE; NE]	1,27	[0,79; 2,03]	0,3238
SOC: Infektionen und parasitaere Erkrankungen	337	227 (67,4)	8,0 [5,8;10,9]	343	152 (44,3)	24,6 [18,5;33,3]	1,88	[1,53; 2,30]	<0,0001*

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	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PT: Bakterielle Harnwegsinfektion	337	10 (3,0)	NE [NE; NE]	343	5 (1,5)	NE [NE; NE]	1,82	[0,66; 5,03]	0,2456
PT: Bronchitis	337	12 (3,6)	NE [NE; NE]	343	18 (5,2)	NE [NE; NE]	0,57	[0,28; 1,17]	0,1227
PT: Gastroenteritis	337	10 (3,0)	NE [NE; NE]	343	2 (0,6)	NE [NE; NE]	3,24	[1,04; 10,11]	0,0429*
PT: Grippe	337	22 (6,5)	NE [NE; NE]	343	15 (4,4)	NE [NE; NE]	1,30	[0,68; 2,49]	0,4198
PT: Harnwegsinfektion	337	25 (7,4)	NE [NE; NE]	343	16 (4,7)	NE [NE; NE]	1,38	[0,74; 2,55]	0,3074
PT: Infektion der oberen Atemwege	337	53 (15,7)	NE [NE; NE]	343	37 (10,8)	NE [NE; NE]	1,24	[0,82; 1,87]	0,3151
PT: Konjunktivitis	337	18 (5,3)	NE [NE; NE]	343	10 (2,9)	NE [NE; NE]	1,65	[0,78; 3,46]	0,1881
PT: Nasopharyngitis	337	50 (14,8)	NE [NE; NE]	343	36 (10,5)	NE [NE; NE]	1,28	[0,84; 1,95]	0,2554
PT: Paronychie	337	92 (27,3)	NE [NE; NE]	343	5 (1,5)	NE [NE; NE]	6,84	[4,59; 10,19]	<0,0001*
PT: Pharyngitis	337	16 (4,7)	NE [NE; NE]	343	12 (3,5)	NE [NE; NE]	1,11	[0,53; 2,35]	0,7780
PT: Pneumonie	337	16 (4,7)	NE [NE; NE]	343	11 (3,2)	NE [NE; NE]	1,24	[0,58; 2,66]	0,5723
PT: Virale Infektion der oberen Atemwege	337	13 (3,9)	NE [NE; NE]	343	10 (2,9)	NE [NE; NE]	1,23	[0,54; 2,79]	0,6202

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1.
Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified log-rank test. Hazard ratio and 95% confidence interval derived from U and V statistics. Breslow method is used for handling ties. NC = not calculable. Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 3.2.1 ADAURA: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PT: Zystitis	337	10 (3,0)	NE [NE; NE]	343	6 (1,7)	NE [NE; NE]	1,45	[0,54; 3,89]	0,4565
SOC: Leber- und Gallenerkrankungen	337	9 (2,7)	NE [NE; NE]	343	17 (5,0)	NE [NE; NE]	0,46	[0,21; 0,99]	0,0465*
SOC: Psychiatrische Erkrankungen	337	29 (8,6)	NE [NE; NE]	343	27 (7,9)	NE [NE; NE]	0,96	[0,57; 1,62]	0,8747
PT: Schlaflosigkeit	337	18 (5,3)	NE [NE; NE]	343	17 (5,0)	NE [NE; NE]	0,92	[0,47; 1,79]	0,8022
SOC: Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	337	101 (30,0)	NE [NE; NE]	343	107 (31,2)	NE [NE; NE]	0,83	[0,63; 1,09]	0,1775
PT: Arthralgie	337	23 (6,8)	NE [NE; NE]	343	37 (10,8)	NE [NE; NE]	0,52	[0,31; 0,86]	0,0115*
PT: Brustschmerzen die Skelettmuskulatur betreffend	337	5 (1,5)	NE [NE; NE]	343	10 (2,9)	NE [NE; NE]	0,42	[0,15; 1,17]	0,0958
PT: Muskelspasmen	337	26 (7,7)	NE [NE; NE]	343	5 (1,5)	NE [NE; NE]	3,56	[1,76; 7,22]	0,0004*
PT: Myalgie	337	9 (2,7)	NE [NE; NE]	343	11 (3,2)	NE [NE; NE]	0,71	[0,29; 1,72]	0,4501
PT: Rueckenschmerzen	337	26 (7,7)	NE [NE; NE]	343	26 (7,6)	NE [NE; NE]	0,83	[0,48; 1,43]	0,5014
PT: Schmerz in einer Extremitaet	337	16 (4,7)	NE [NE; NE]	343	11 (3,2)	NE [NE; NE]	1,36	[0,64; 2,90]	0,4225

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1.
Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified log-rank test. Hazard ratio and 95% confidence interval derived from U and V statistics. Breslow method is used for handling ties. NC = not calculable. Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 3.2.1 ADAURA: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
SOC: Stoffwechsel- und Ernaehrungsstoerungen	337	95 (28,2)	NE [NE; NE]	343	45 (13,1)	NE [NE; NE]	2,03	[1,45; 2,82]	<0,0001*
PT: Appetit vermindert	337	48 (14,2)	NE [NE; NE]	343	13 (3,8)	NE [NE; NE]	3,26	[1,97; 5,39]	<0,0001*
PT: Hyperglykaemie	337	15 (4,5)	NE [NE; NE]	343	7 (2,0)	NE [NE; NE]	1,78	[0,77; 4,13]	0,1795
SOC: Untersuchungen	337	148 (43,9)	NE [NE; NE]	343	85 (24,8)	NE [NE; NE]	1,90	[1,47; 2,46]	<0,0001*
PT: Alaninaminotransferase erhoeht	337	22 (6,5)	NE [NE; NE]	343	26 (7,6)	NE [NE; NE]	0,76	[0,43; 1,34]	0,3435
PT: Aspartataminotransferase erhoeht	337	23 (6,8)	NE [NE; NE]	343	27 (7,9)	NE [NE; NE]	0,77	[0,44; 1,35]	0,3625
PT: Auswurffraktion verkleinert	337	15 (4,5)	NE [NE; NE]	343	9 (2,6)	NE [NE; NE]	1,43	[0,64; 3,19]	0,3874
PT: Blutharnstoff erhoeht	337	10 (3,0)	NE [NE; NE]	343	1 (0,3)	NE [NE; NE]	4,64	[1,42; 15,17]	0,0112*
PT: Elektrokardiogramm QT verlaengert	337	30 (8,9)	NE [NE; NE]	343	8 (2,3)	NE [NE; NE]	2,87	[1,51; 5,44]	0,0012*
PT: Gewicht erniedrigt	337	35 (10,4)	NE [NE; NE]	343	9 (2,6)	NE [NE; NE]	3,13	[1,73; 5,67]	0,0002*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1.
Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified log-rank test. Hazard ratio and 95% confidence interval derived from U and V statistics. Breslow method is used for handling ties. NC = not calculable. Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 3.2.1 ADAURA: Summary of analysis of time to first adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
PT: Kreatinin im Blut erhoeht	337	31 (9,2)	NE [NE; NE]	343	7 (2,0)	NE [NE; NE]	3,43	[1,81; 6,49]	0,0002*
PT: Kreatinphosphokinase im Blut erhoeht	337	11 (3,3)	NE [NE; NE]	343	5 (1,5)	NE [NE; NE]	1,80	[0,67; 4,82]	0,2441
PT: Leukozytenzahl erniedrigt	337	25 (7,4)	NE [NE; NE]	343	1 (0,3)	NE [NE; NE]	6,11	[2,83; 13,21]	<0,0001*
PT: Neutrophilenzahl erniedrigt	337	26 (7,7)	NE [NE; NE]	343	3 (0,9)	NE [NE; NE]	4,62	[2,23; 9,59]	<0,0001*
PT: Thrombozytenzahl vermindert	337	21 (6,2)	NE [NE; NE]	343	2 (0,6)	NE [NE; NE]	5,33	[2,35; 12,07]	<0,0001*
SOC: Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	337	46 (13,6)	NE [NE; NE]	343	35 (10,2)	NE [NE; NE]	1,13	[0,73; 1,76]	0,5778

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1.
Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified log-rank test. Hazard ratio and 95% confidence interval derived from U and V statistics. Breslow method is used for handling ties. NC = not calculable. Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 3.2.2 ADAURA: Summary of analysis of time to first serious adverse event
(total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
SUE	337	68 (20,2)	NE [NE; NE]	343	47 (13,7)	NE [NE; NE]	1,28	[0,88; 1,84]	0,1932
SUE SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums	337	12 (3,6)	NE [NE; NE]	343	4 (1,2)	NE [NE; NE]	2,34	[0,87; 6,28]	0,0920
SUE SOC: Infektionen und parasitaere Erkrankungen	337	16 (4,7)	NE [NE; NE]	343	7 (2,0)	NE [NE; NE]	1,95	[0,86; 4,43]	0,1105
SUE SOC: Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	337	11 (3,3)	NE [NE; NE]	343	6 (1,7)	NE [NE; NE]	1,52	[0,58; 3,96]	0,3923

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1.
Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified log-rank test. Hazard ratio and 95% confidence interval derived from U and V statistics. Breslow method is used for handling ties. NC = not calculable. Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 3.2.4 ADAURA: Summary of analysis of time to first adverse event with max. CTCAE grade 3 or higher (total, and by SOC and PT occurring with frequency >=10 patients and at least 1% in either treatment arm)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
UE mit CTCAE Grad >=3	337	79 (23,4)	NE [NE; NE]	343	48 (14,0)	NE [NE; NE]	1,55	[1,09; 2,19]	0,0142*
G>=3 SOC: Erkrankungen des Gastrointestinaltrakts	337	21 (6,2)	NE [NE; NE]	343	3 (0,9)	NE [NE; NE]	4,27	[1,91; 9,54]	0,0004*
G>=3 SOC: Infektionen und parasitaere Erkrankungen	337	17 (5,0)	NE [NE; NE]	343	7 (2,0)	NE [NE; NE]	2,13	[0,95; 4,74]	0,0656
G>=3 SOC: Untersuchungen	337	14 (4,2)	NE [NE; NE]	343	4 (1,2)	NE [NE; NE]	2,62	[1,03; 6,64]	0,0424*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1.
Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] p-value is estimated using unstratified log-rank test. Hazard ratio and 95% confidence interval derived from U and V statistics. Breslow method is used for handling ties. NC = not calculable. Hazard ratio <1 favours Osimertinib. * p<0.05.
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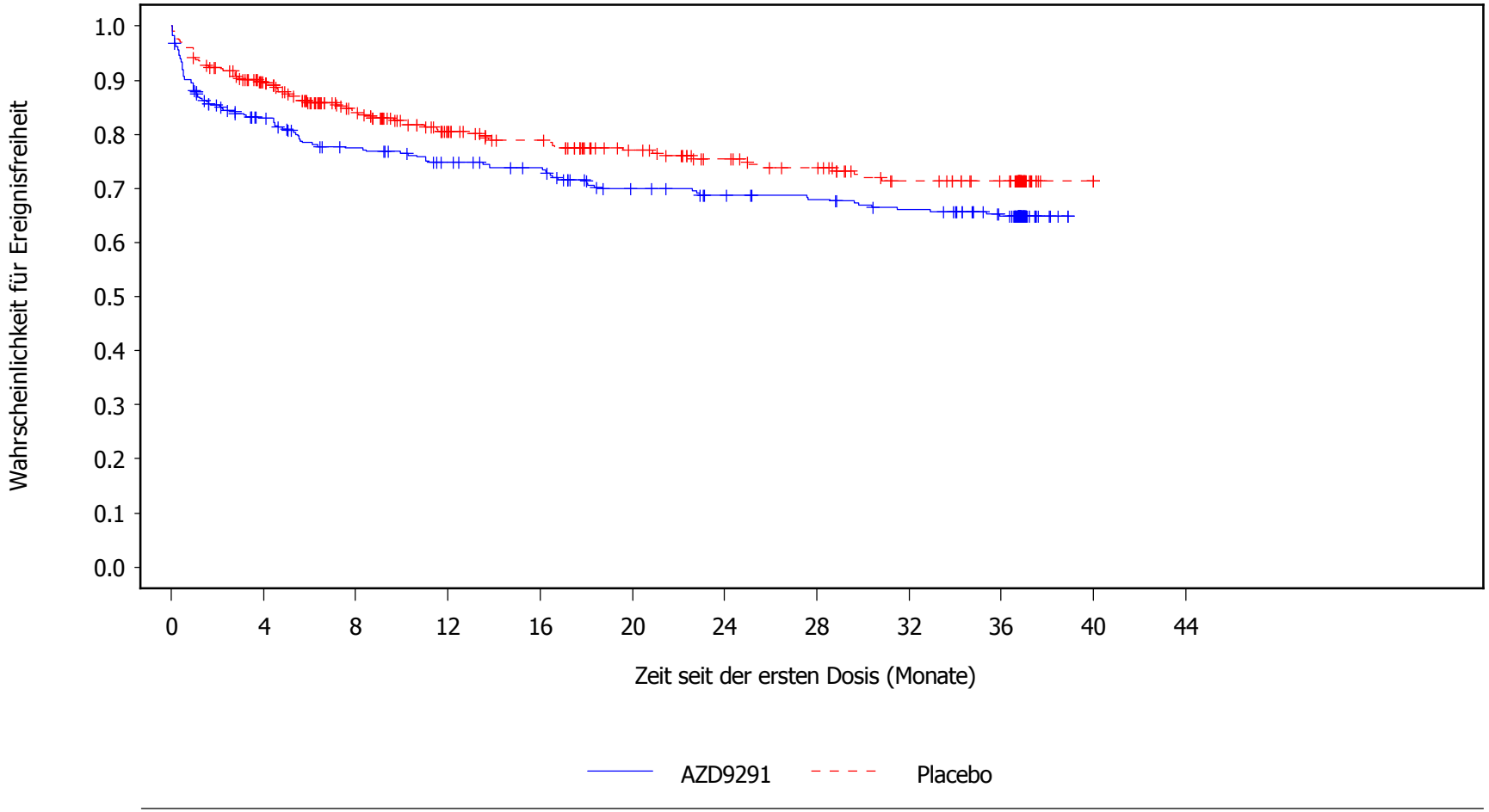
Figure 3.3.2 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Allgemeine Erkrankungen und Beschwerden am Verabreichungsort
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	262	237	222	213	191	183	178	170	155	0	0	AZD9291
343	286	235	194	177	155	139	130	114	105	0	0	Placebo

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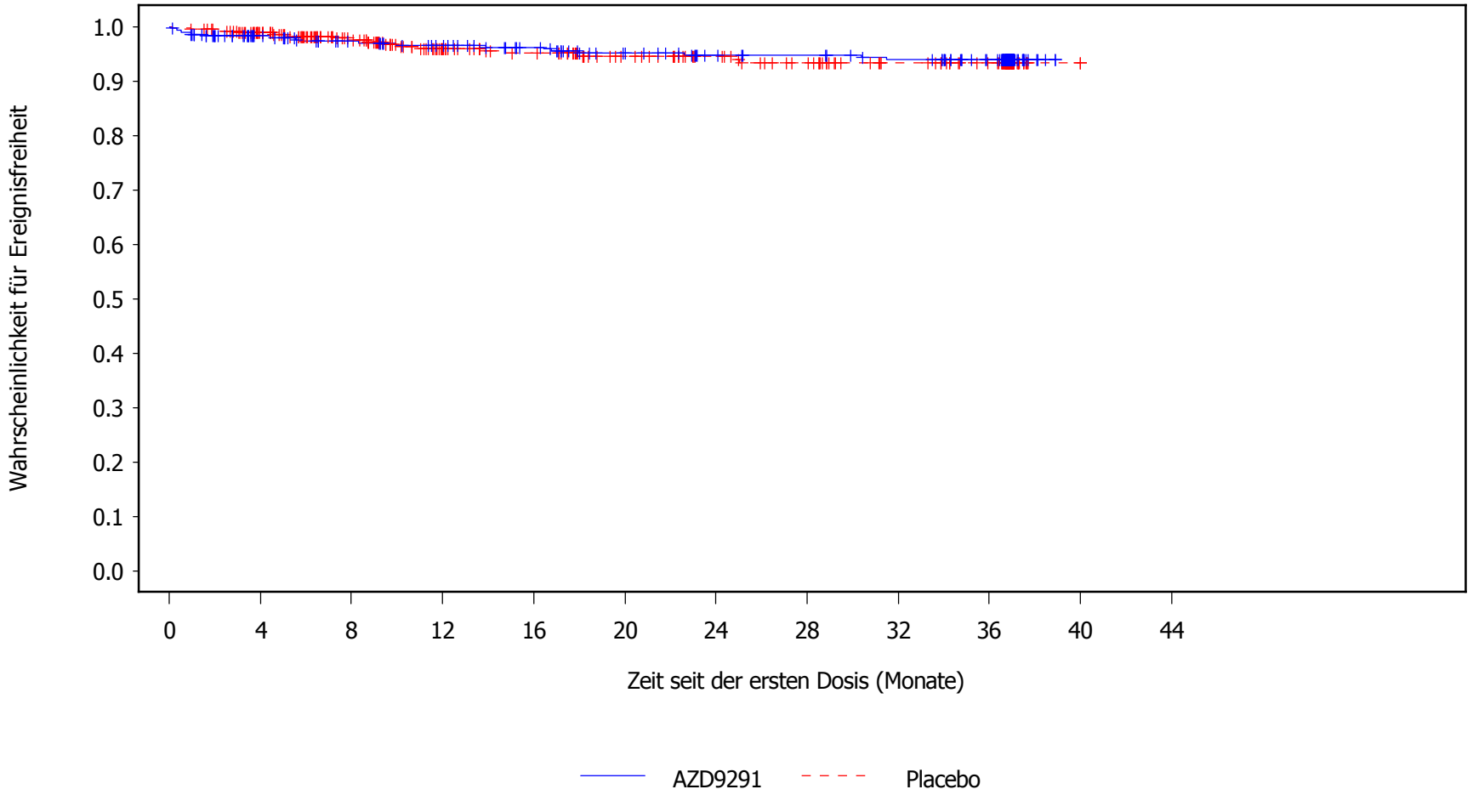
Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.3 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Asthenie
Safety Analysis Set, DCO 11Apr2022



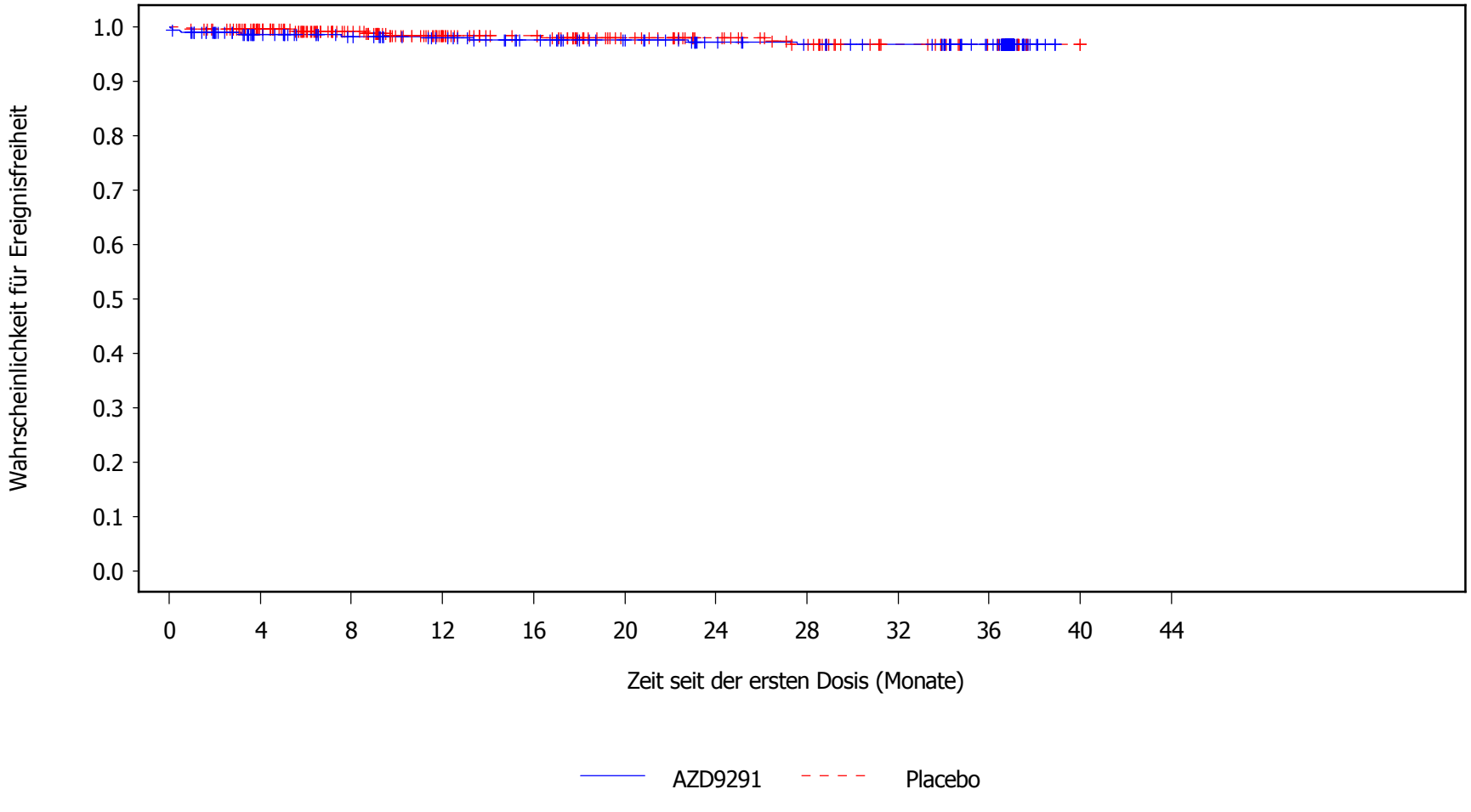
Anzahl an Patienten unter Risiko:

337	303	286	276	263	247	236	233	227	213	0	0	AZD9291
343	316	273	225	208	186	172	160	144	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bac 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.4 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Brustkorbbeschwerden
Safety Analysis Set, DCO 11Apr2022



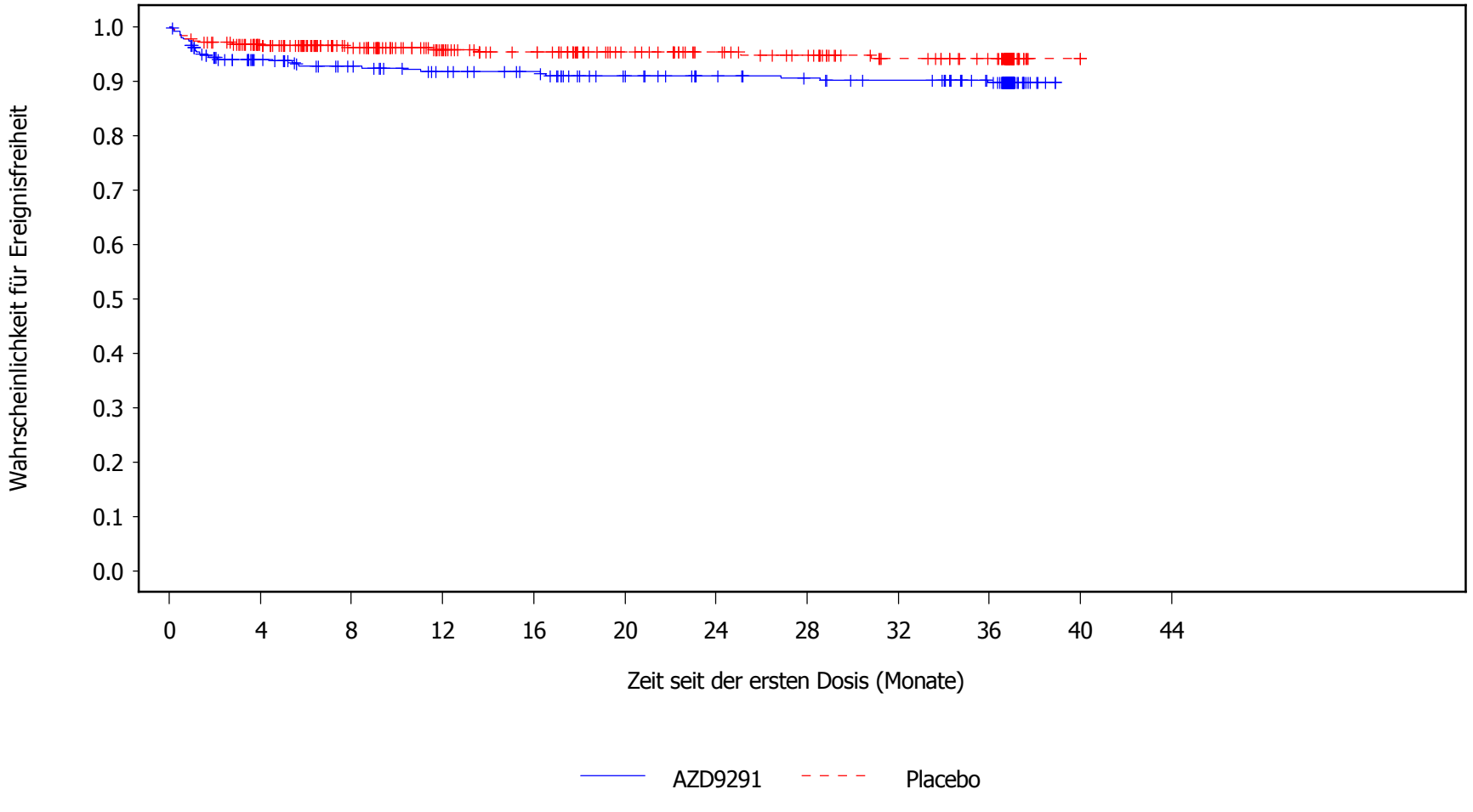
Anzahl an Patienten unter Risiko:

337	303	288	277	265	253	240	235	231	216	0	0	AZD9291
343	318	275	230	214	189	174	162	146	136	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bad 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.5 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Ermuedung
Safety Analysis Set, DCO 11Apr2022



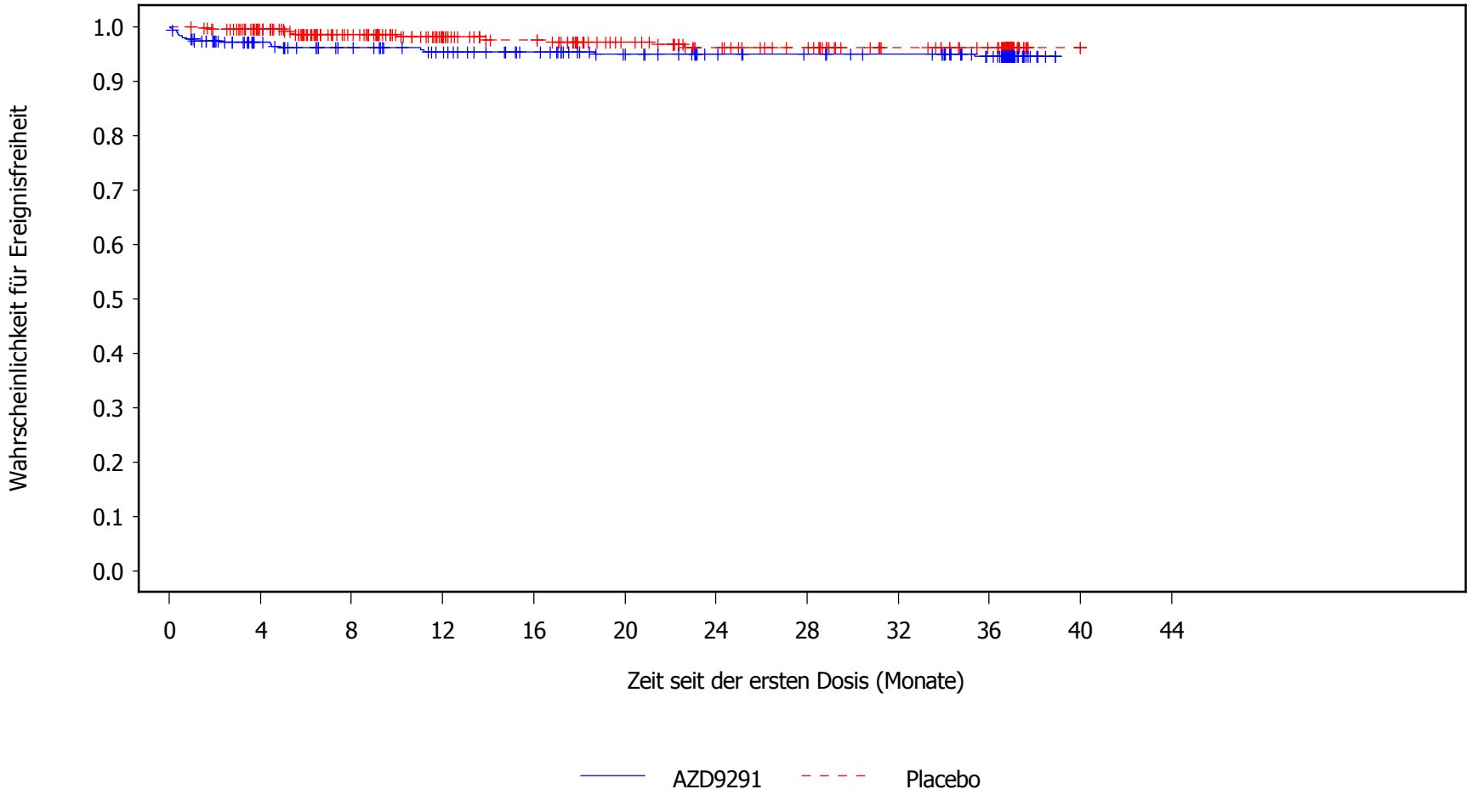
Anzahl an Patienten unter Risiko:

337	293	277	265	258	243	234	229	224	210	0	0	AZD9291
343	309	267	225	208	183	168	159	142	132	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bae 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.6 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Fieber
Safety Analysis Set, DCO 11Apr2022



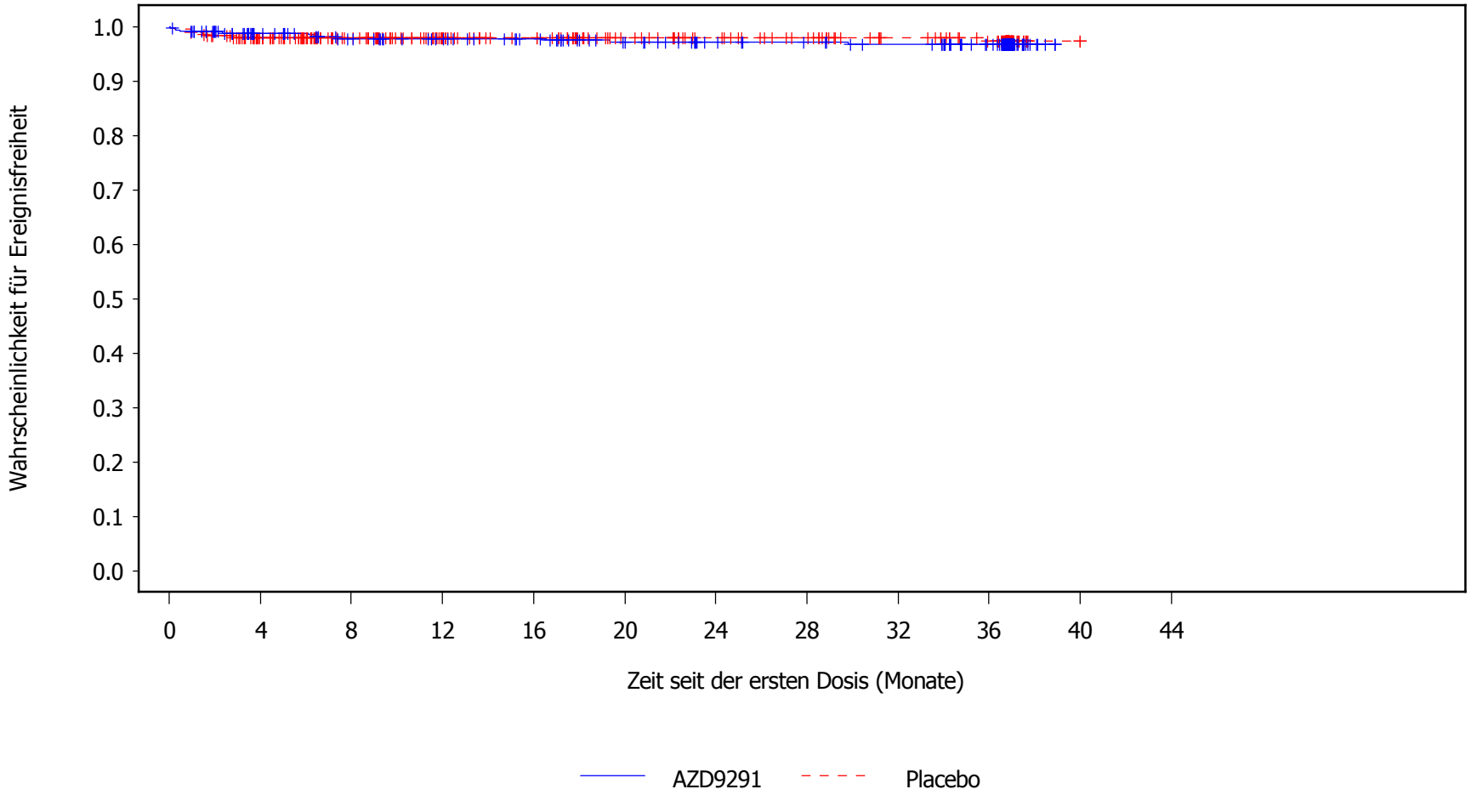
Anzahl an Patienten unter Risiko:

337	300	284	272	260	246	235	231	227	211	0	0	AZD9291
343	318	274	230	214	190	173	164	148	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2baf 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.7 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Oedem peripher
Safety Analysis Set, DCO 11Apr2022

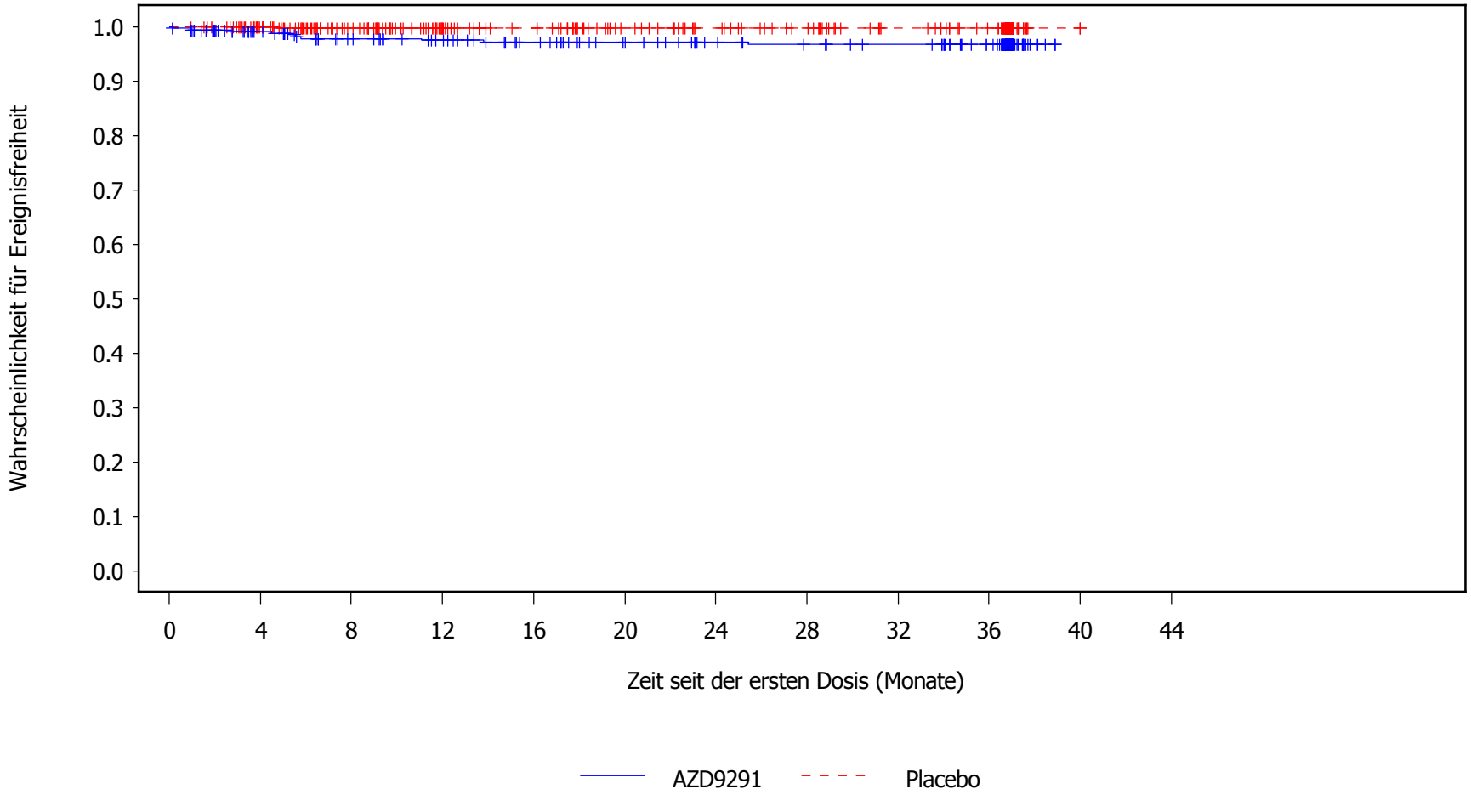


Anzahl an Patienten unter Risiko:

337	304	287	277	268	253	241	237	232	217	0	0	AZD9291
343	313	272	229	213	188	174	164	149	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bag 30JUN2023:09:36 kvbv306

Figure 3.3.8 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Schleimhautentzuendung
Safety Analysis Set, DCO 11Apr2022

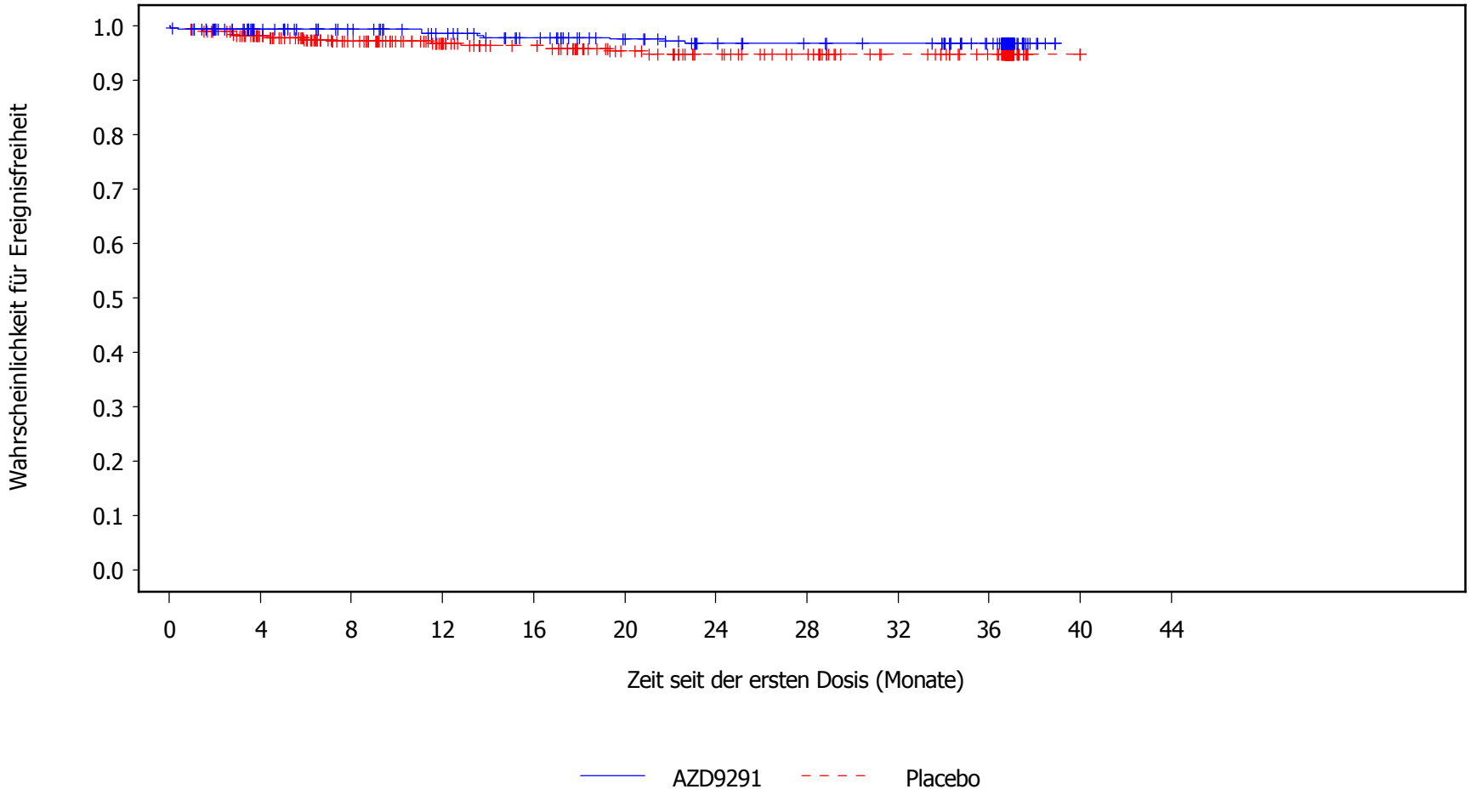


Anzahl an Patienten unter Risiko:

337	306	287	276	263	251	239	234	230	215	0	0	AZD9291
343	320	277	233	217	192	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bah 30JUN2023:09:36 kvbv306

Figure 3.3.9 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Thoraxschmerz nicht kardialen Ursprungs
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	307	292	280	267	253	240	236	233	218	0	0	AZD9291
343	315	271	230	214	187	171	161	146	135	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bai 30JUN2023:09:36 kvbv306

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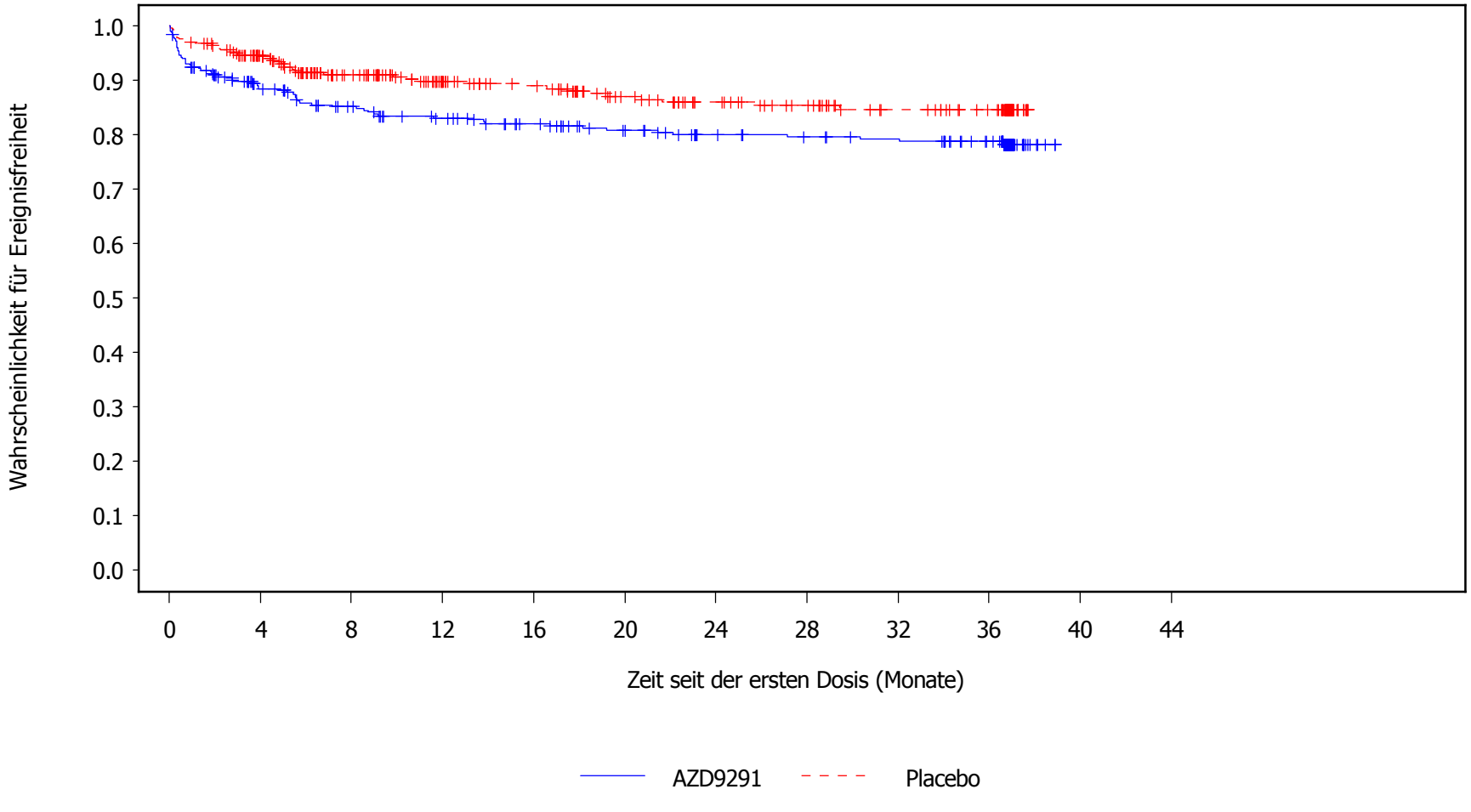
Figure 3.3.10 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Augenerkrankungen
Safety Analysis Set, DCO 11Apr2022

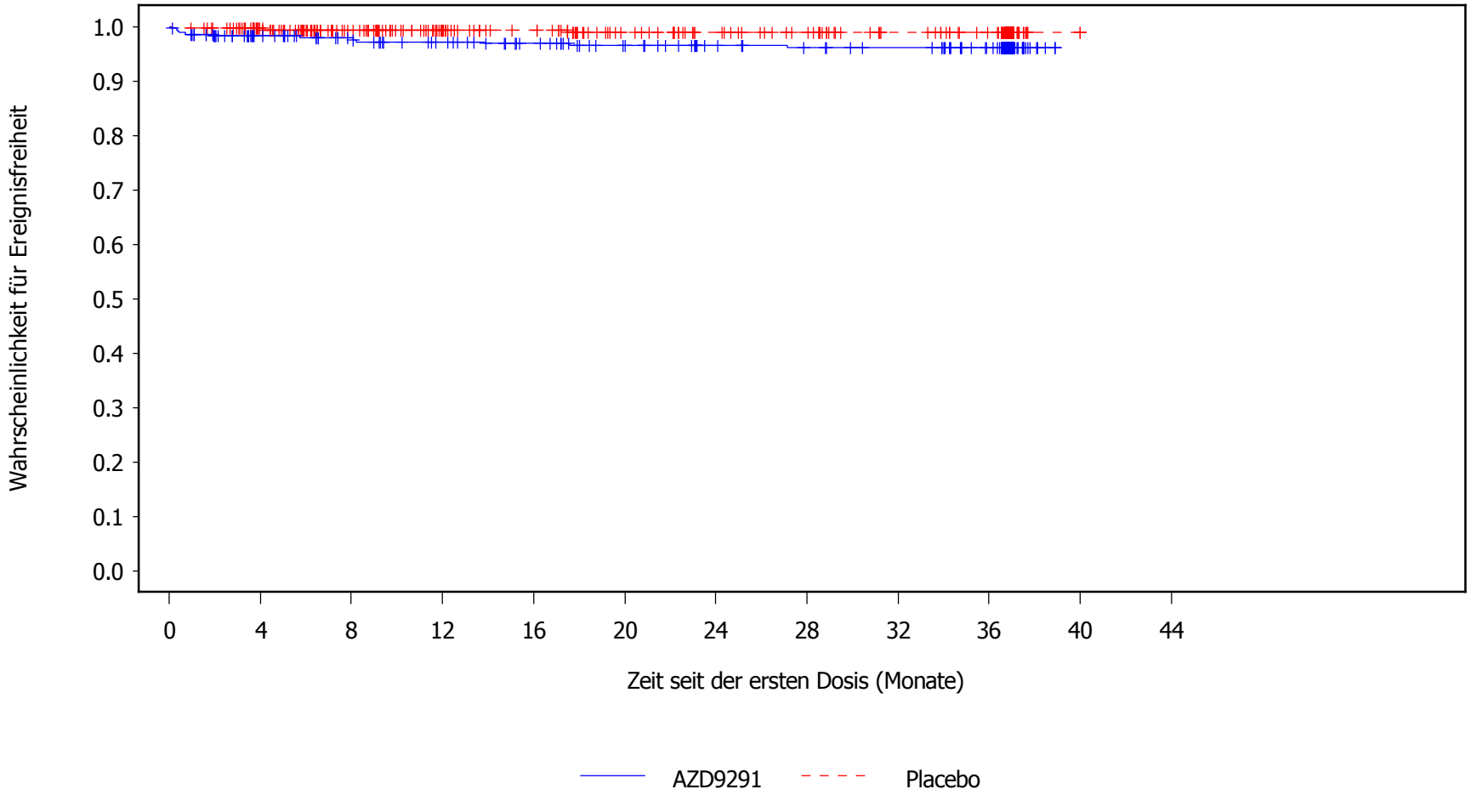


Anzahl an Patienten unter Risiko:

337	274	250	235	221	207	194	189	185	173	0	0	AZD9291
343	302	253	209	193	167	151	140	125	115	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2baj 30JUN2023:09:36 kvbv306

Figure 3.3.11 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Sehen verschwommen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	304	288	276	264	251	239	234	230	215	0	0	AZD9291
343	319	277	233	217	191	176	166	150	139	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bak 30JUN2023:09:36 kvbv306

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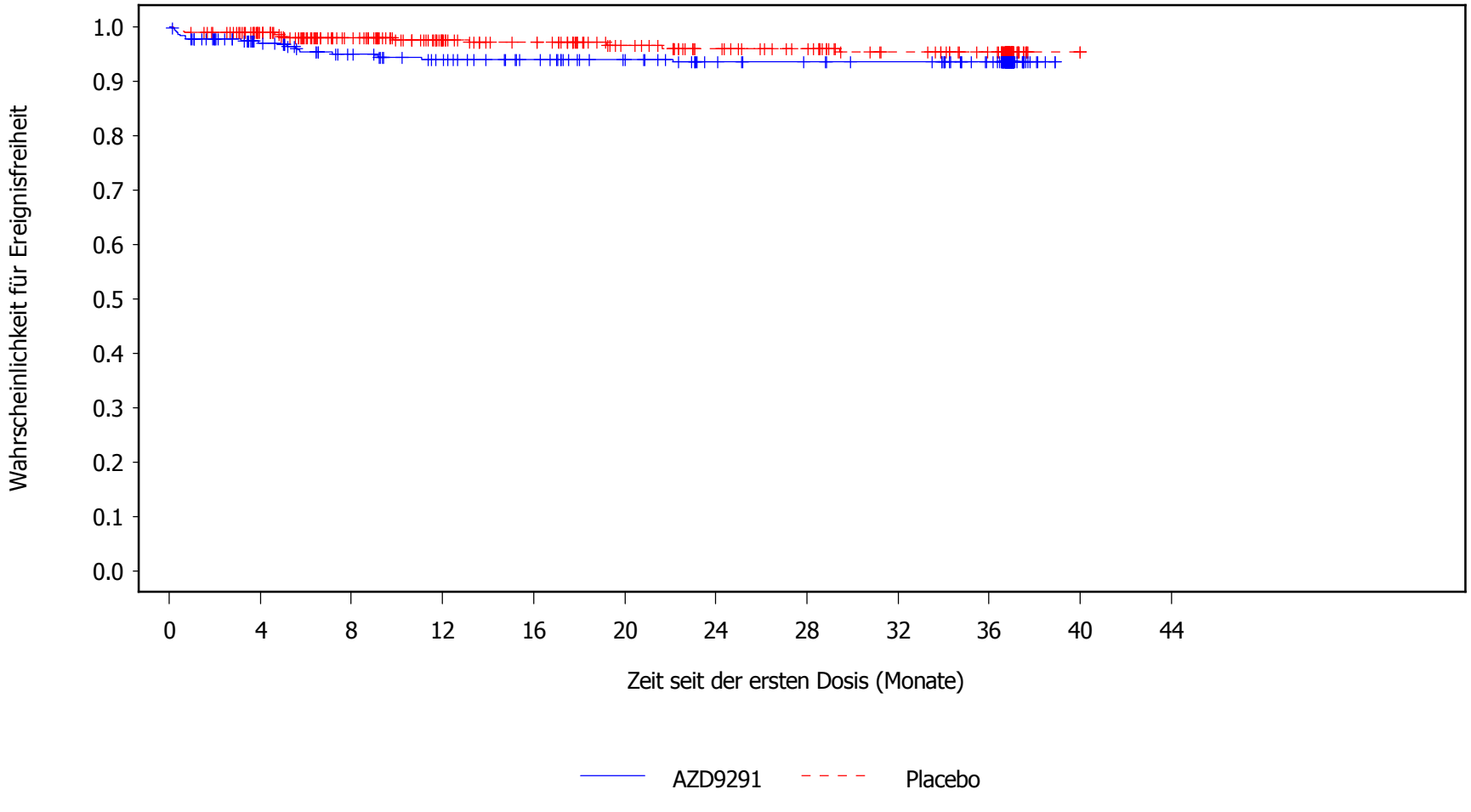
Figure 3.3.12 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Trockenes Auge
Safety Analysis Set, DCO 11Apr2022

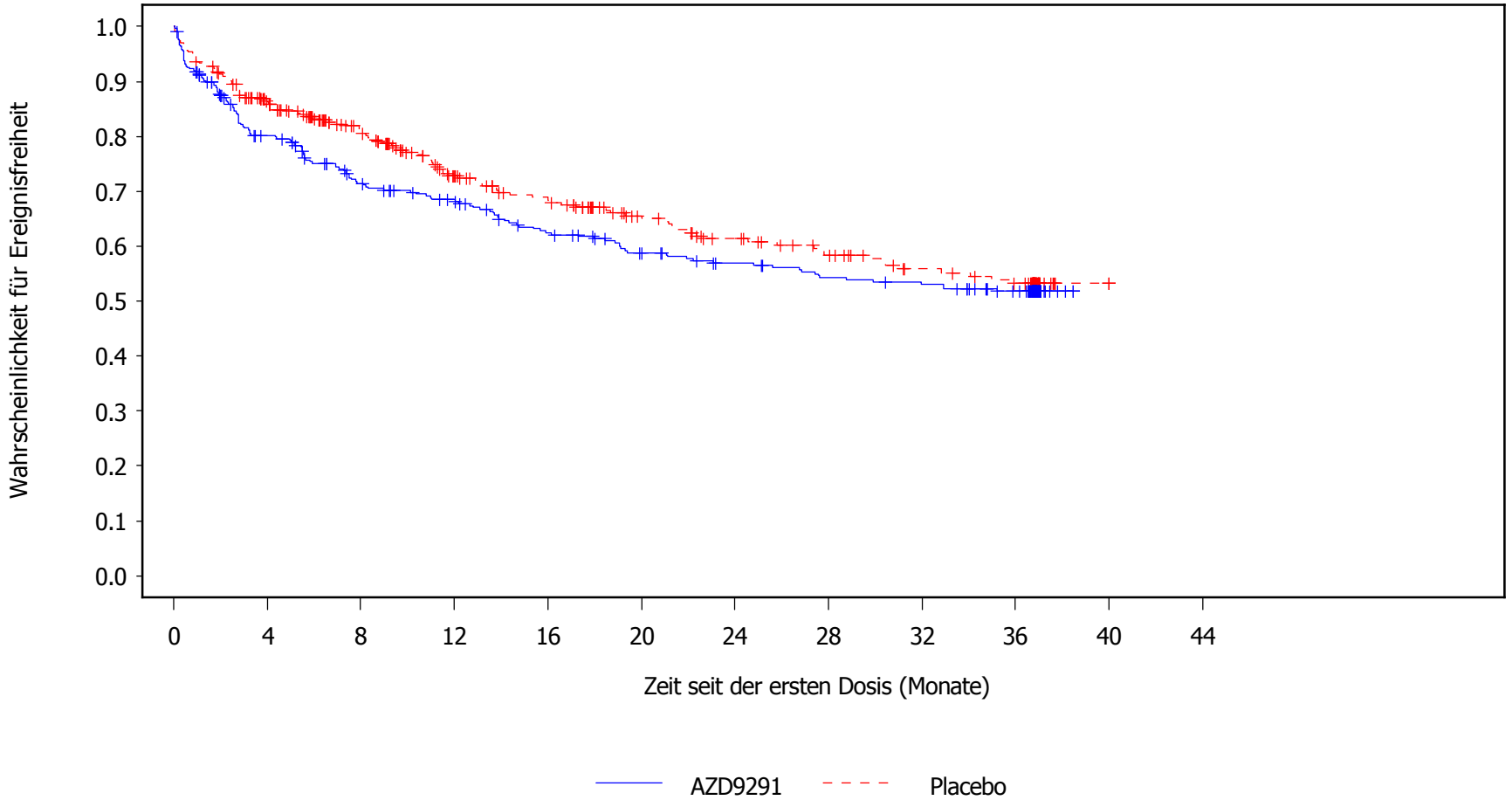


Anzahl an Patienten unter Risiko:

337	300	279	266	254	242	229	225	222	208	0	0	AZD9291
343	316	272	228	213	187	171	161	145	134	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bal 30JUN2023:09:36 kvbv306

Figure 3.3.13 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums
Safety Analysis Set, DCO 11Apr2022

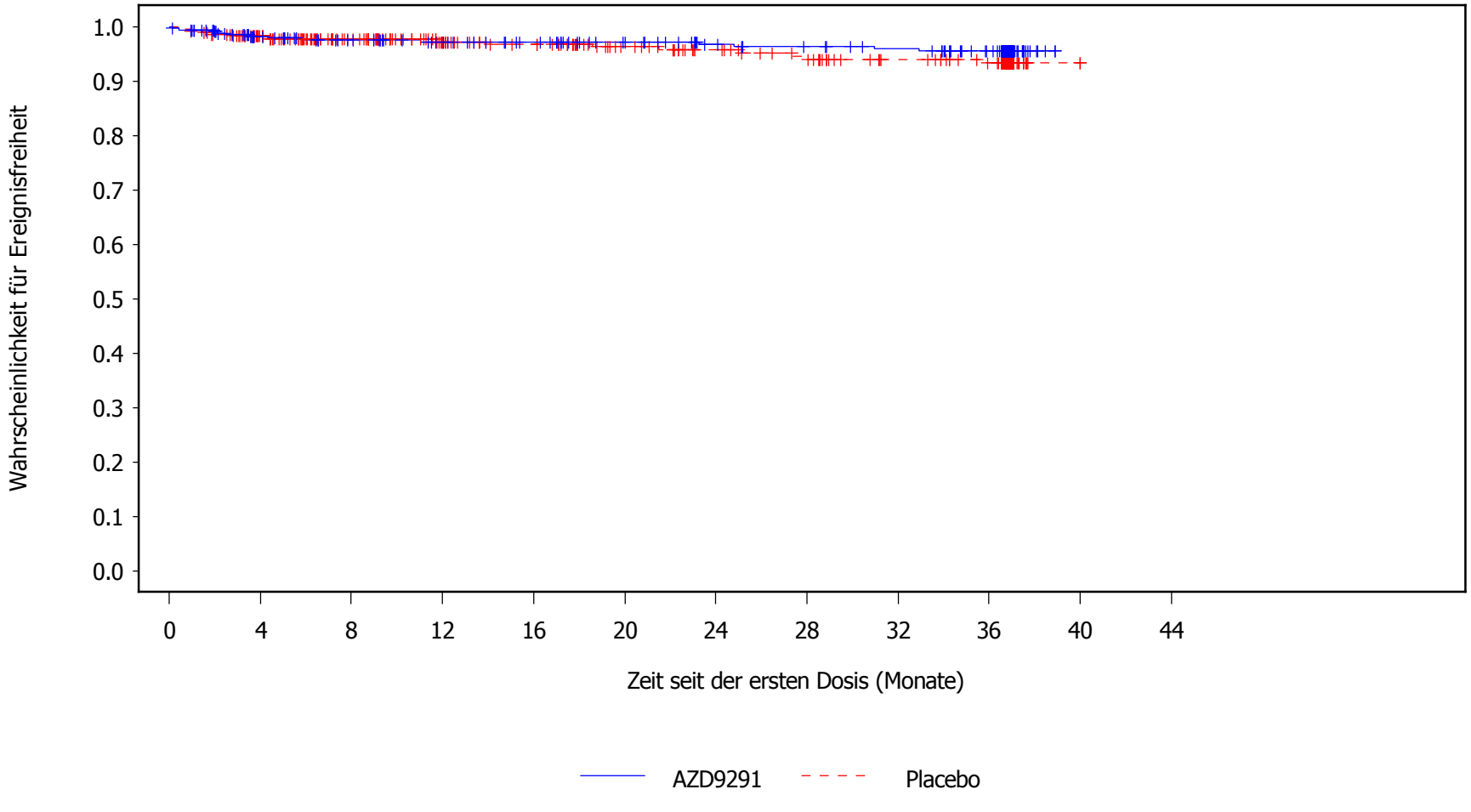


Anzahl an Patienten unter Risiko:

337	254	216	199	176	159	148	139	135	122	0	0 AZD9291
343	277	228	175	155	126	110	98	85	78	0	0 Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bam 30JUN2023:09:36 kvbv306

Figure 3.3.14 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Dyspnoe
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	287	276	266	253	240	235	230	215	0	0	AZD9291
343	314	271	227	211	186	170	159	144	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2ban 30JUN2023:09:36 kvbv306

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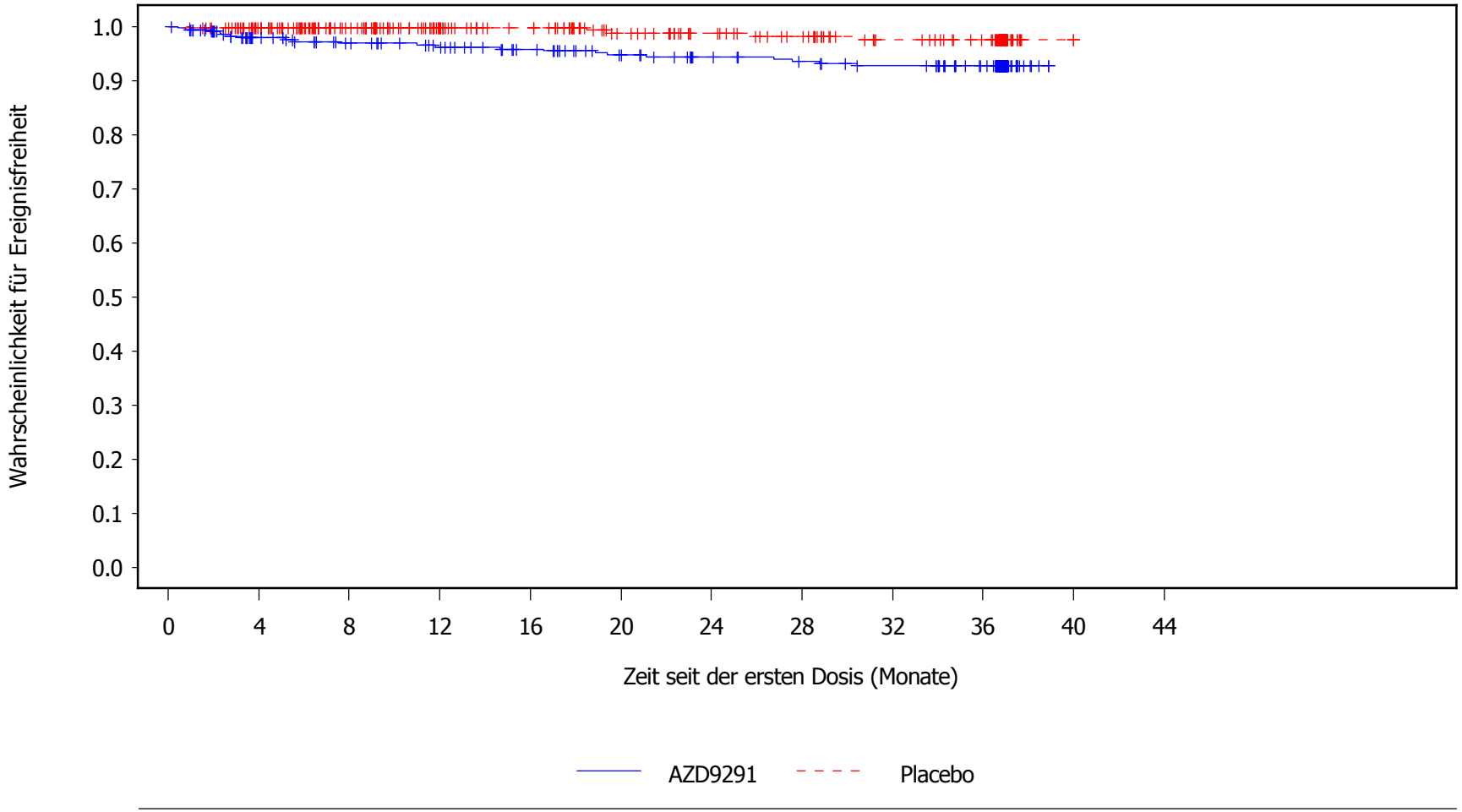
Figure 3.3.15 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Epistaxis
Safety Analysis Set, DCO 11Apr2022

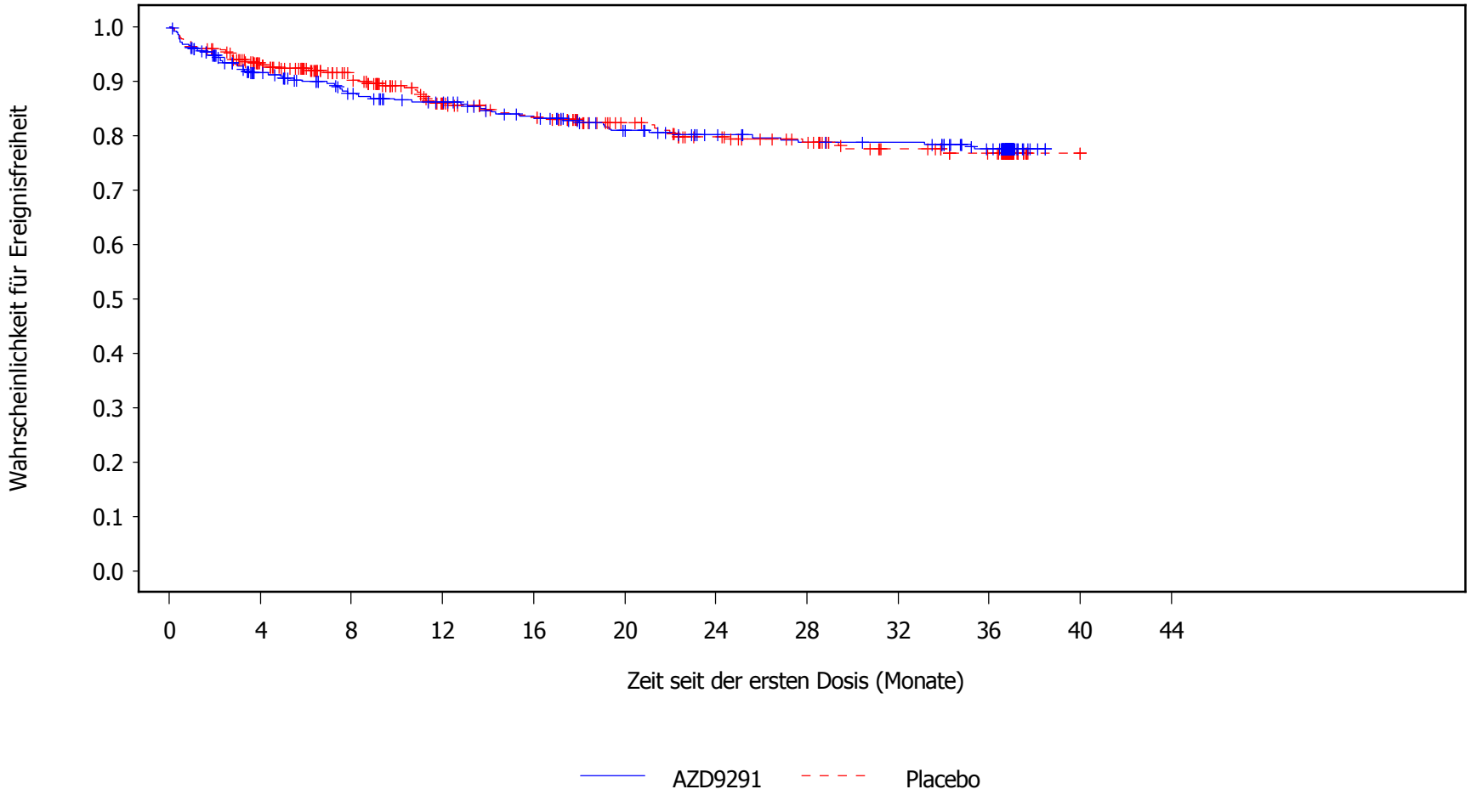


Anzahl an Patienten unter Risiko:

337	301	284	273	260	245	234	228	222	207	0	0	AZD9291
343	320	278	234	218	191	176	165	148	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bao 30JUN2023:09:36 kvbv306

Figure 3.3.16 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Husten
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	282	256	242	226	207	194	188	186	171	0	0	AZD9291
343	298	255	207	190	163	148	137	122	114	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bap 30JUN2023:09:36 kvbv306

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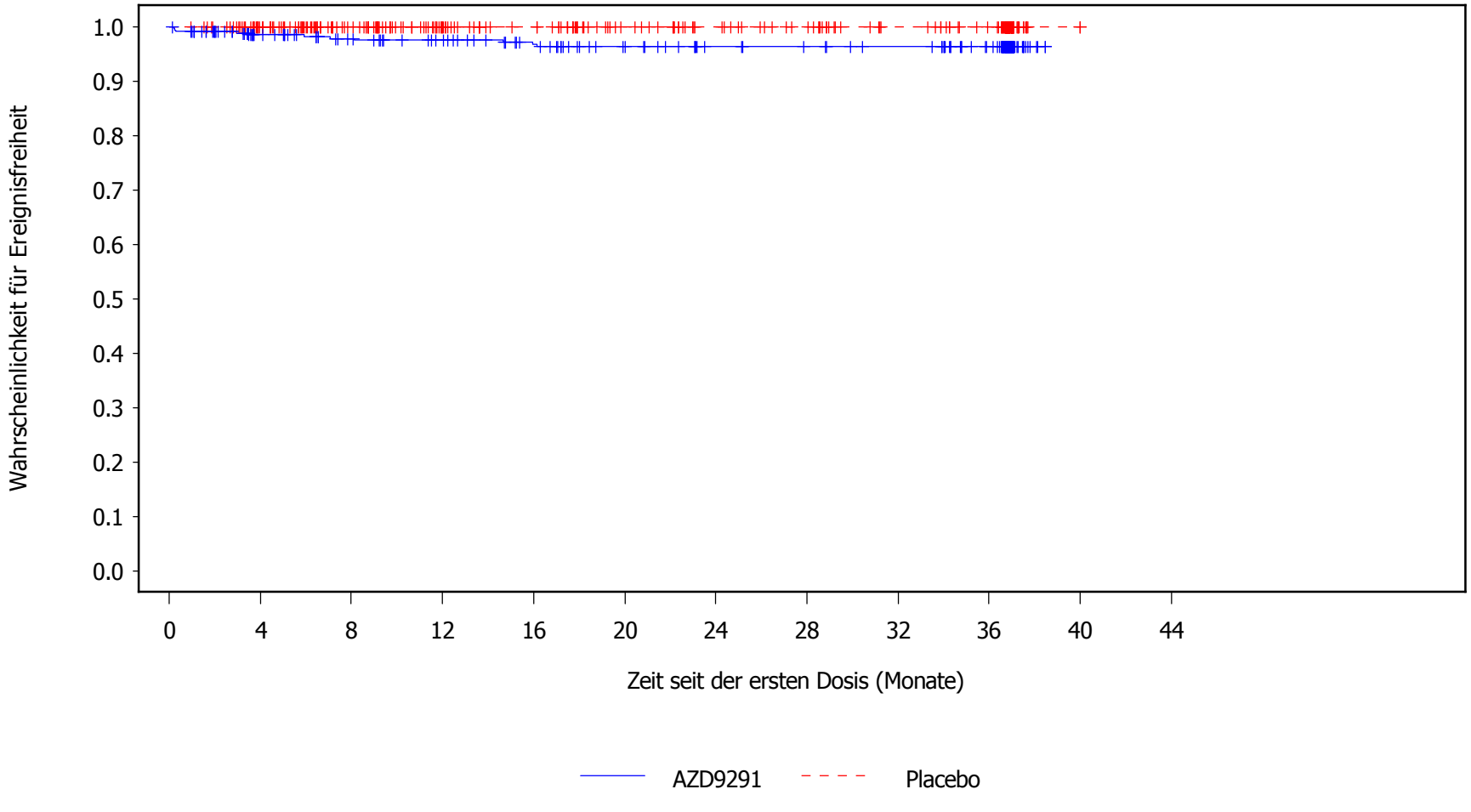
Figure 3.3.17 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Nasenschleimhaut trocken
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	286	275	261	247	236	233	229	214	0	0	AZD9291
343	320	278	234	218	193	178	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2baq 30JUN2023:09:36 kvbv306

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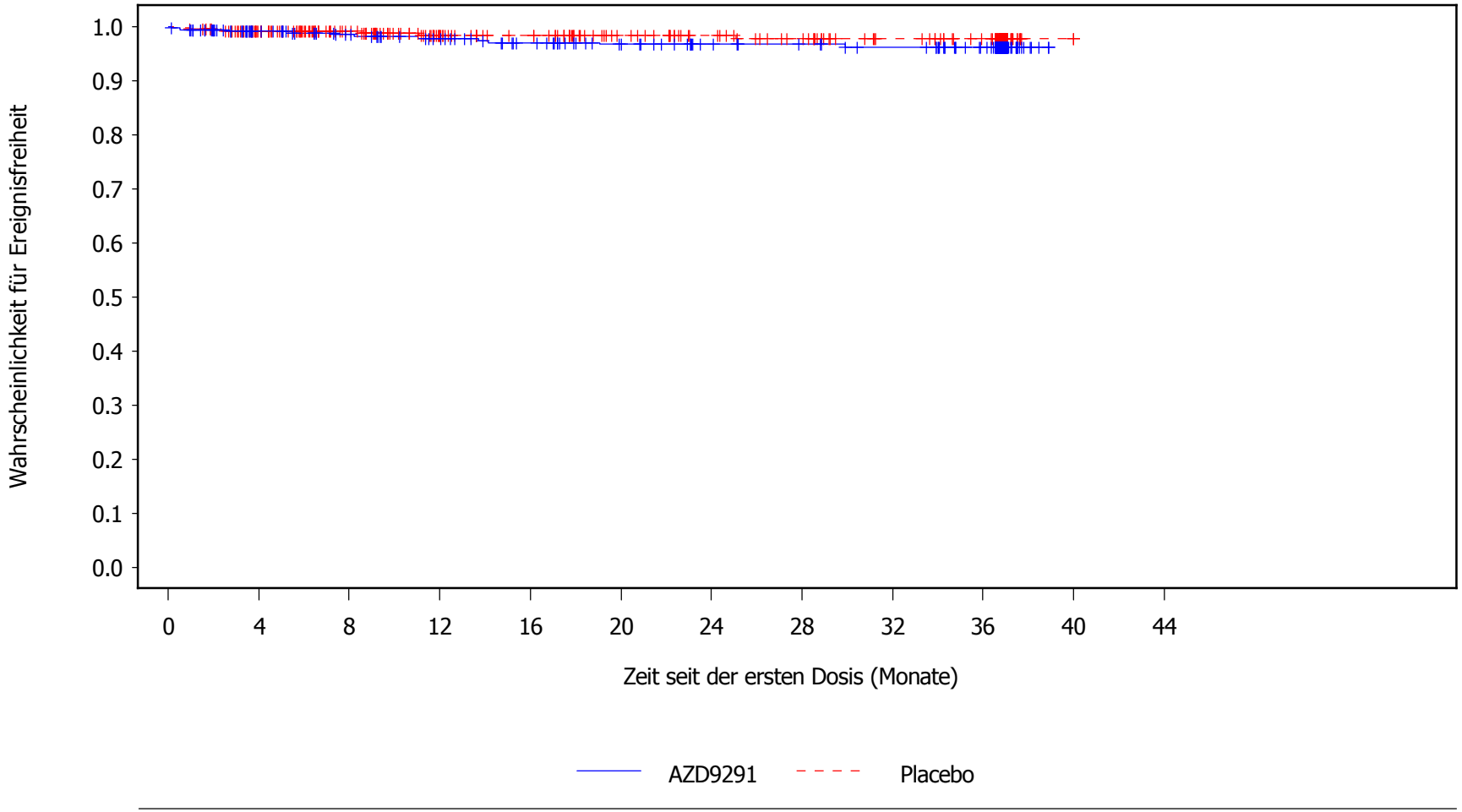
Figure 3.3.18 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Rhinorrhoe
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	305	288	276	262	248	236	232	227	212	0	0	AZD9291
343	317	276	230	215	190	176	165	149	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bar 30JUN2023:09:36 kvbv306

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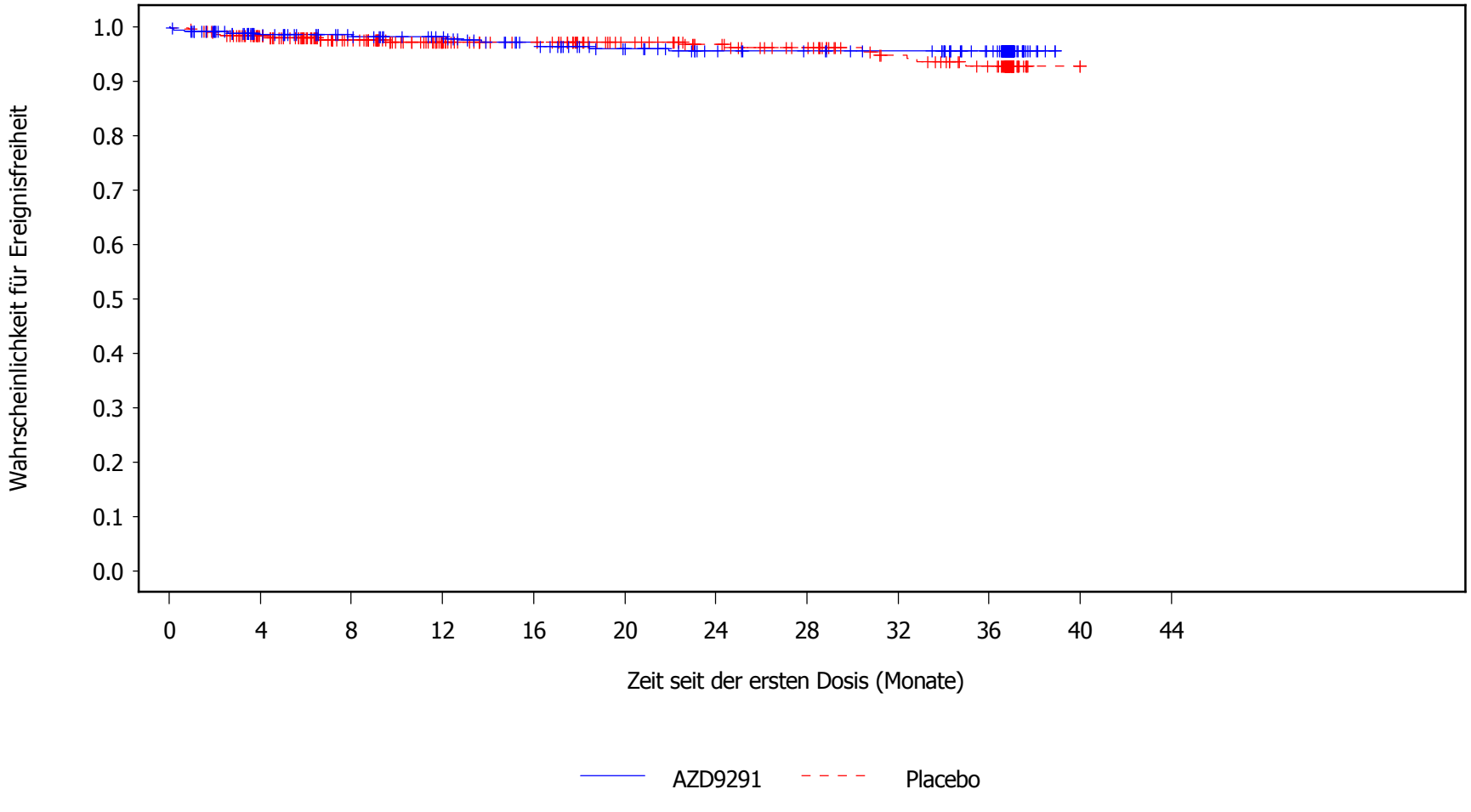
Figure 3.3.19 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Schmerzen im Oropharynx
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	288	277	262	247	235	231	227	212	0	0	AZD9291
343	314	271	226	210	185	170	159	142	129	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bas 30JUN2023:09:36 kvbv306

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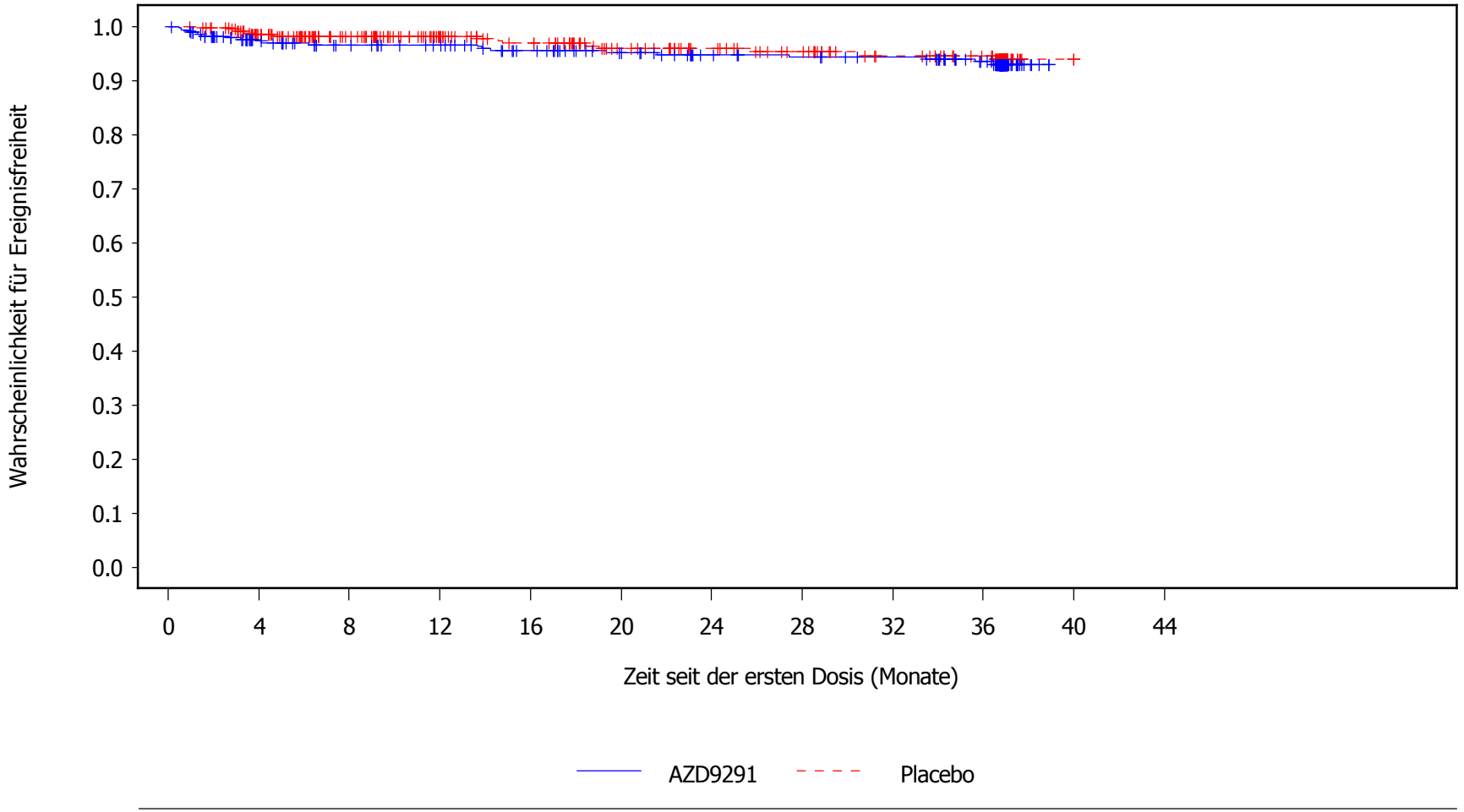
Figure 3.3.20 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen der Geschlechtsorgane und der Brustdruese
Safety Analysis Set, DCO 11Apr2022

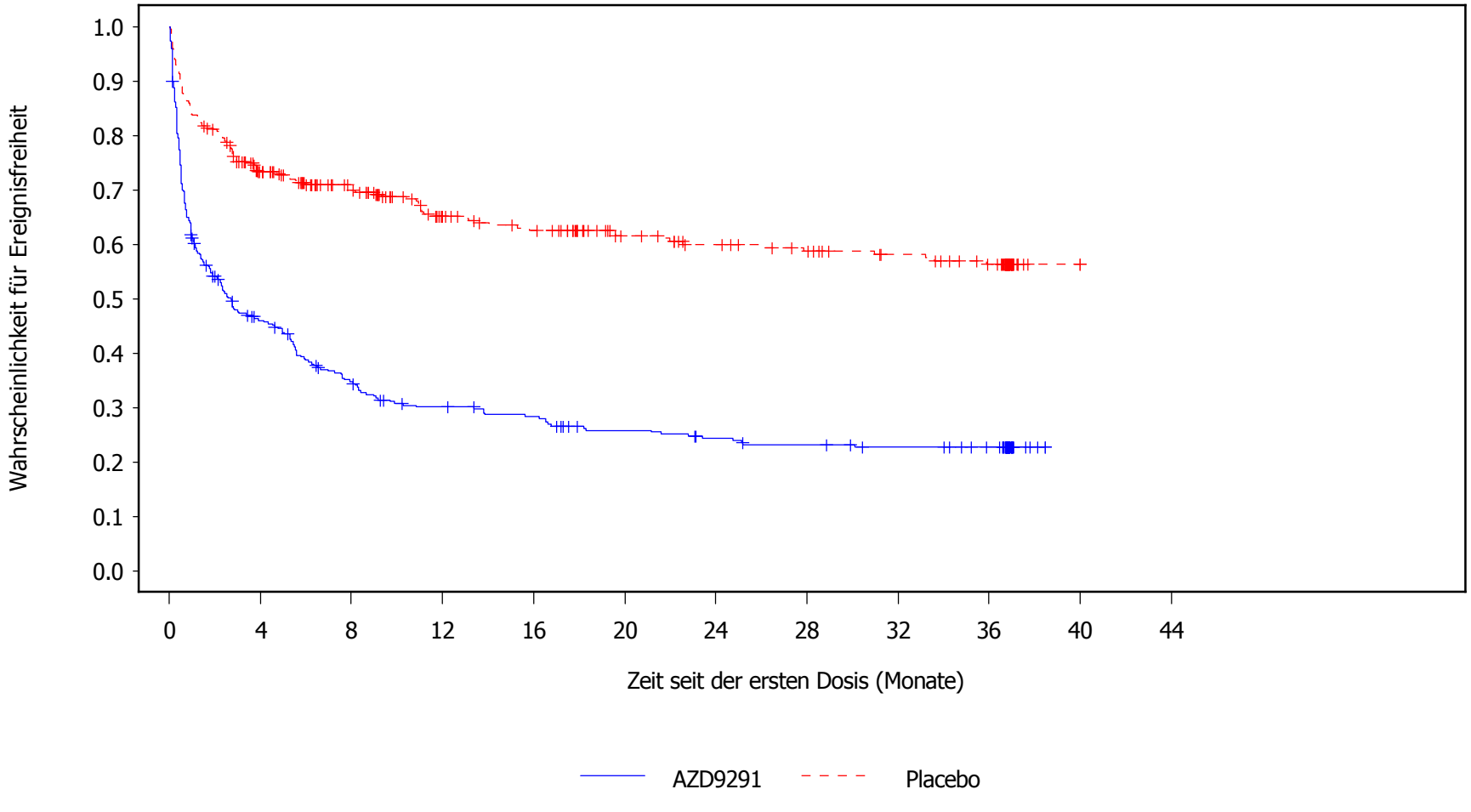


Anzahl an Patienten unter Risiko:

337	300	283	275	260	246	233	229	225	208	0	0	AZD9291
343	315	275	231	212	185	170	159	144	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bat 30JUN2023:09:36 kvbv306

Figure 3.3.21 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen der Haut und des Unterhautgewebes
Safety Analysis Set, DCO 11Apr2022

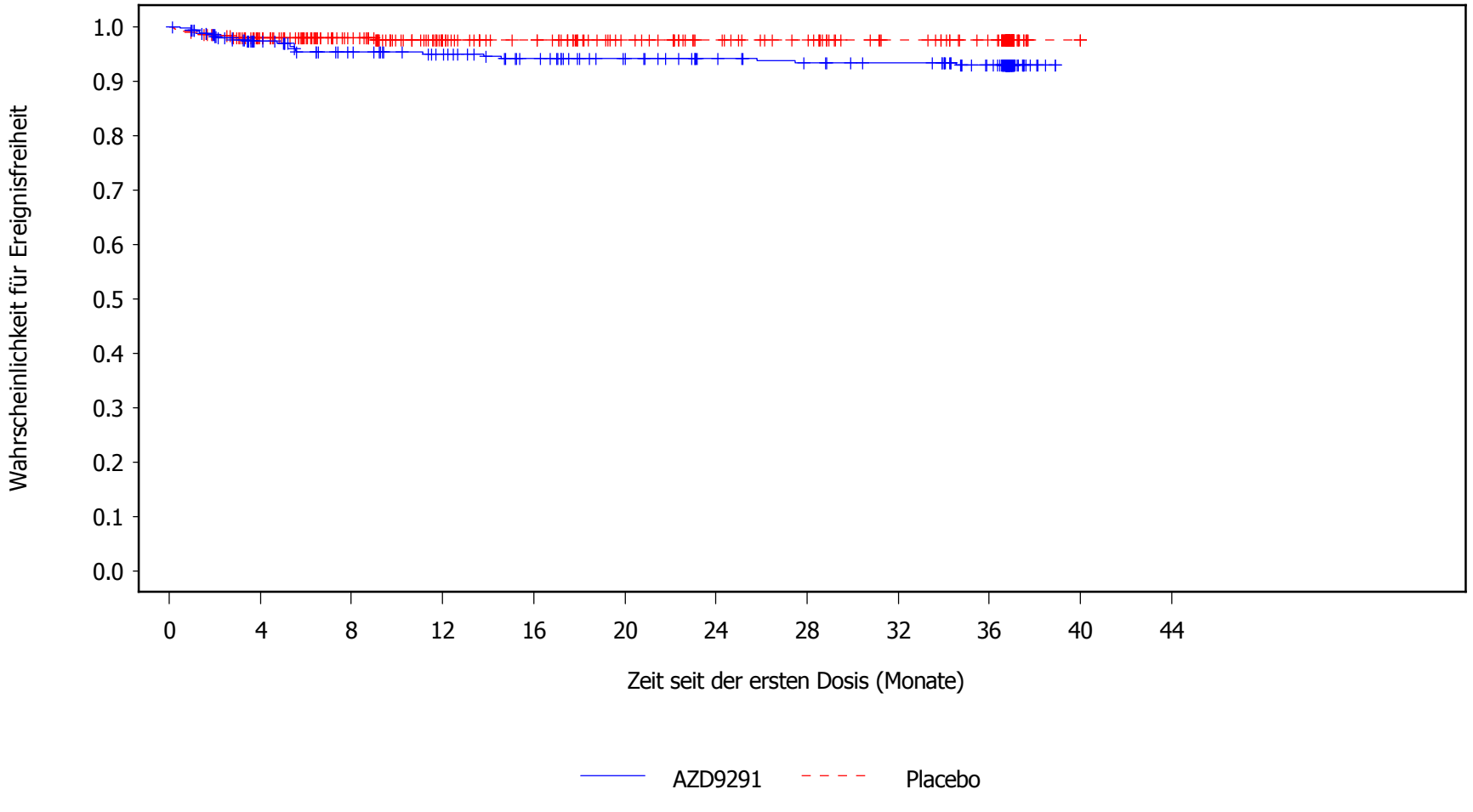


Anzahl an Patienten unter Risiko:

337	145	106	88	81	69	63	59	55	50	0	0 AZD9291
343	233	195	154	142	119	109	102	94	85	0	0 Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bau 30JUN2023:09:36 kvbv306

Figure 3.3.22 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Alopezie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	300	280	269	255	242	231	225	221	205	0	0	AZD9291
343	314	273	228	213	189	174	165	149	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bav 30JUN2023:09:36 kvbv306

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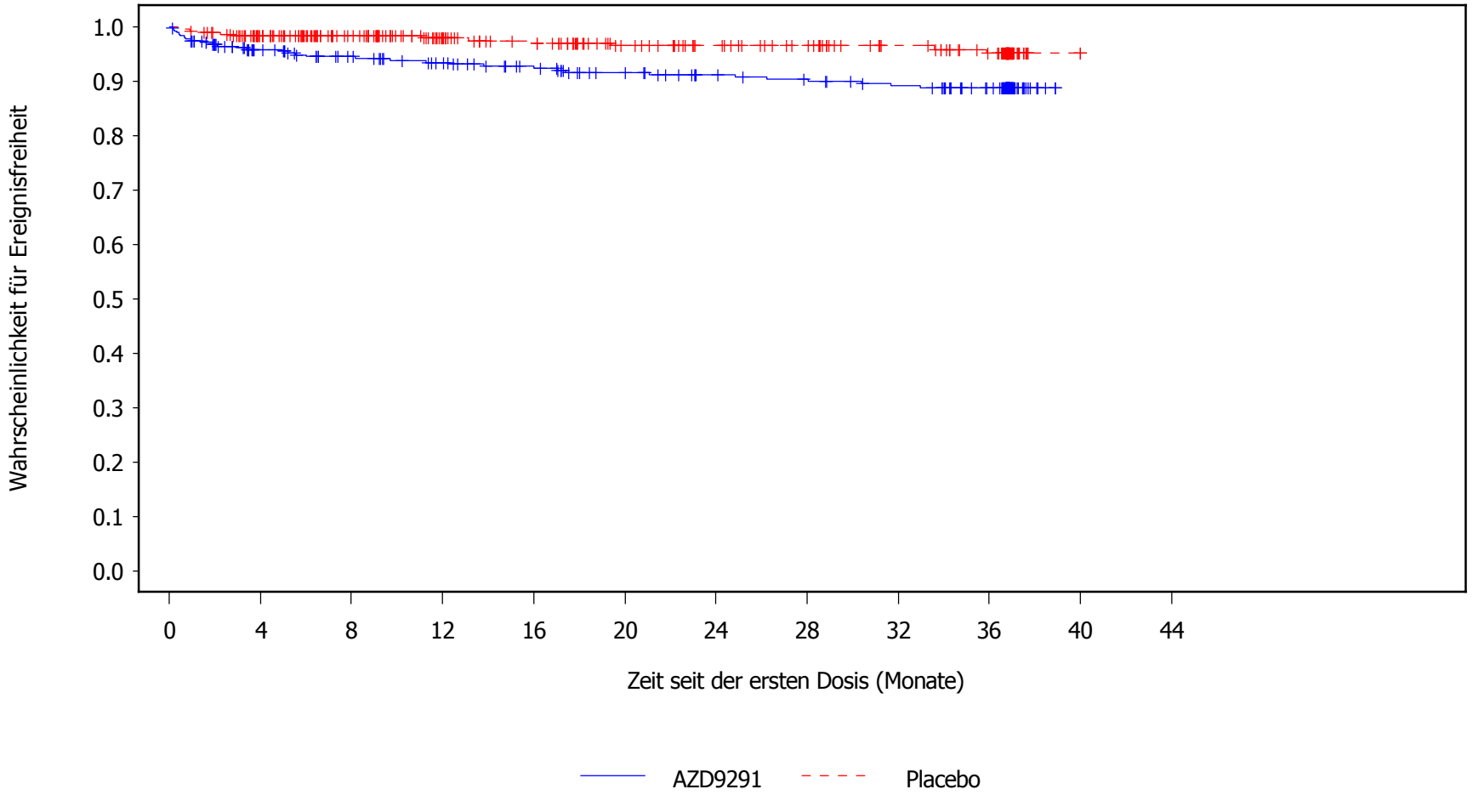
Figure 3.3.23 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Ausschlag
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	295	276	263	250	236	225	220	213	197	0	0	AZD9291
343	314	274	230	214	188	174	164	149	136	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2baw 30JUN2023:09:36 kvbv306

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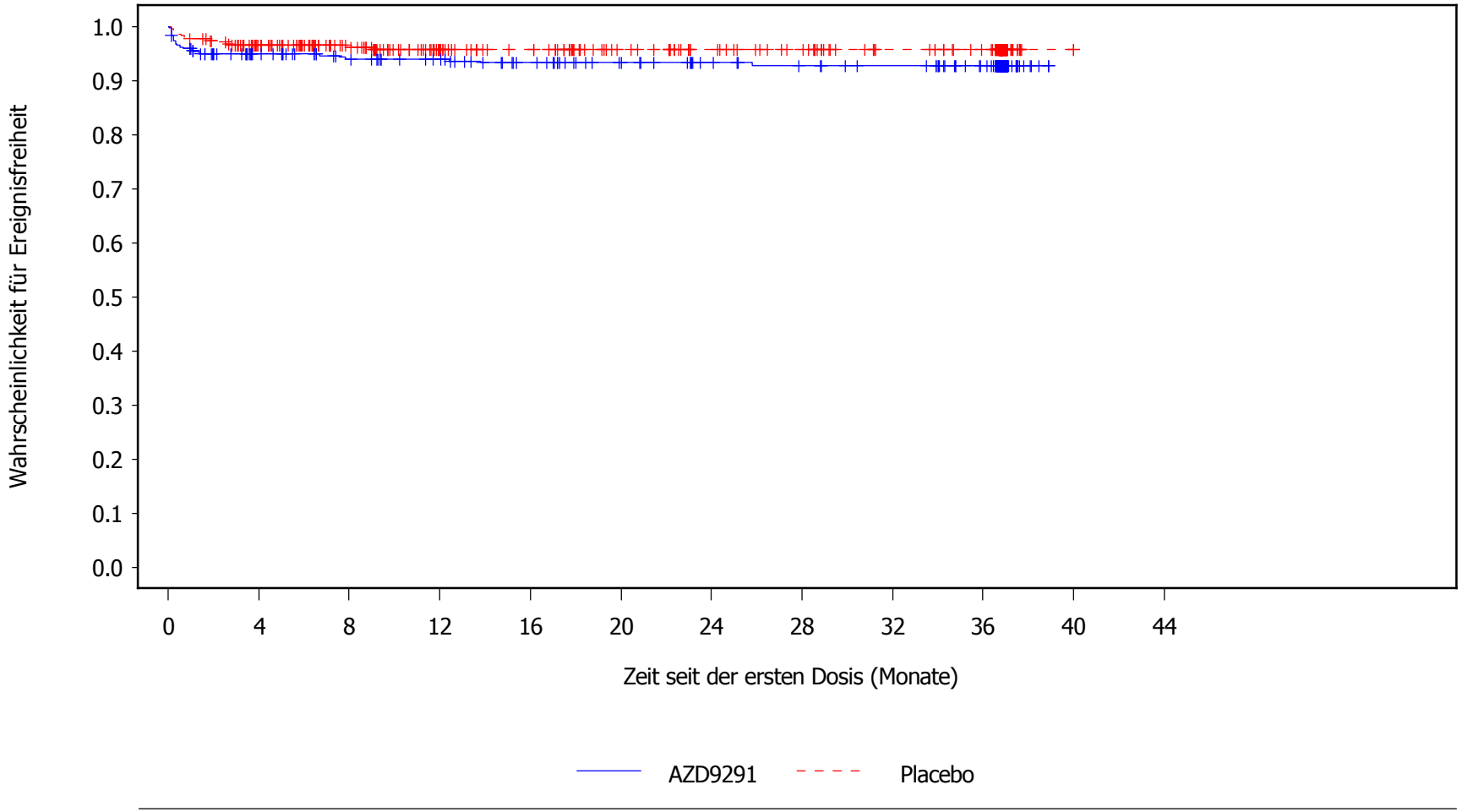
Figure 3.3.24 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Ausschlag makulo-papuloes
Safety Analysis Set, DCO 11Apr2022

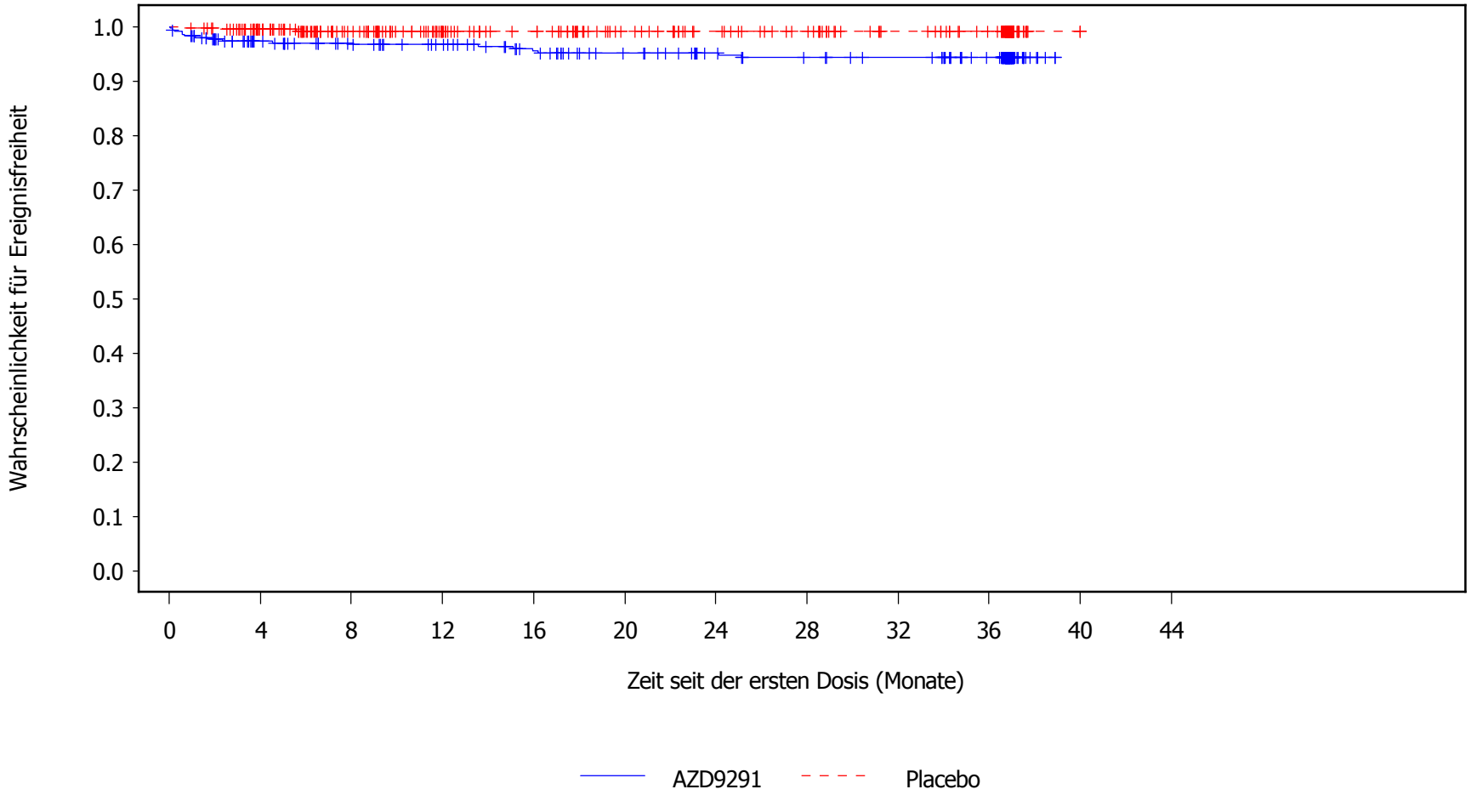


Anzahl an Patienten unter Risiko:

337	295	278	269	255	242	232	227	223	209	0	0	AZD9291
343	308	266	222	206	181	167	157	141	132	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bax 30JUN2023:09:36 kvbv306

Figure 3.3.25 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Ausschlag papuloes
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	300	286	275	260	246	235	229	225	211	0	0	AZD9291
343	318	275	232	216	191	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bay 30JUN2023:09:36 kvbv306

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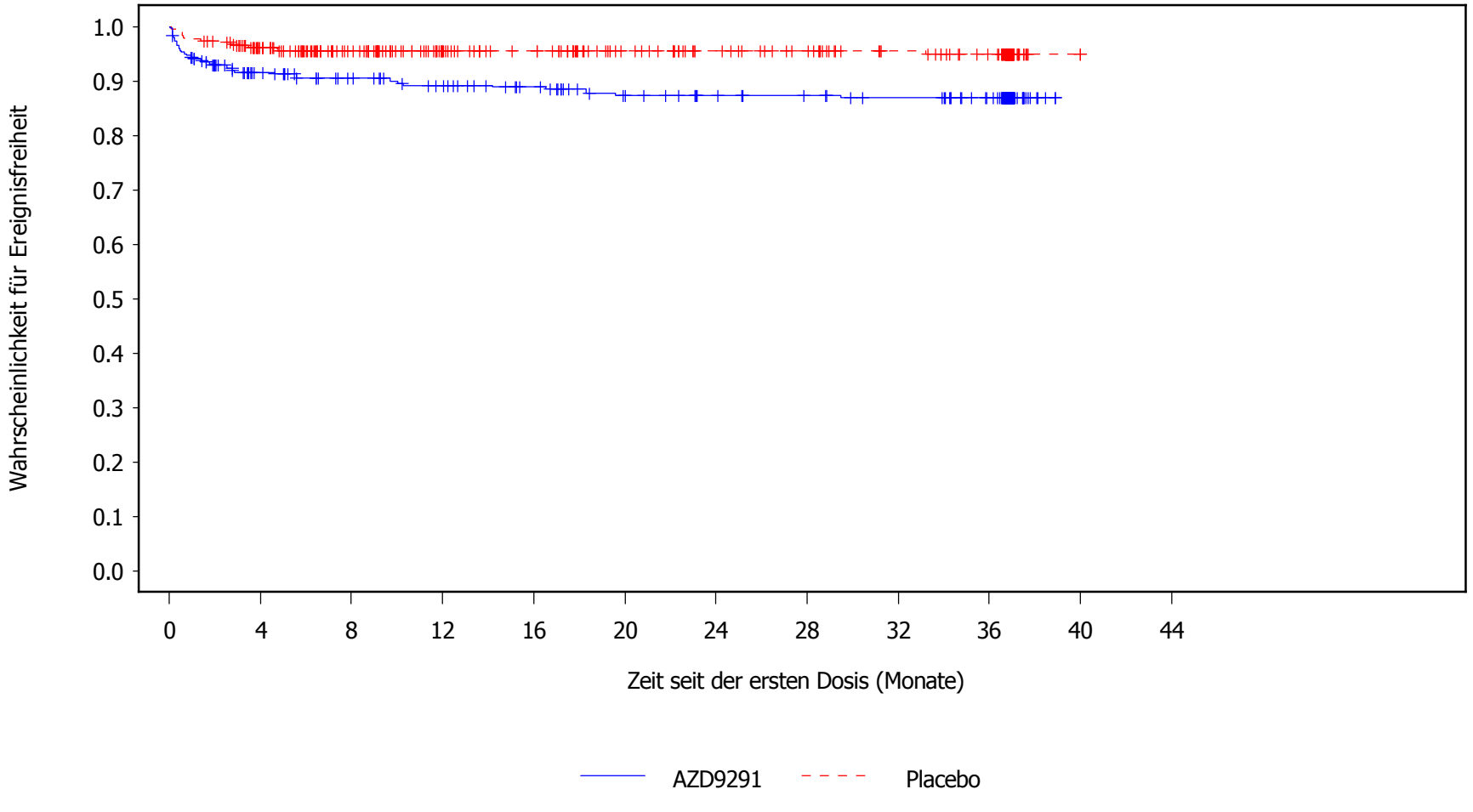
Figure 3.3.26 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Dermatitis akneiform
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	282	265	253	241	226	219	215	210	199	0	0	AZD9291
343	309	266	224	210	185	170	161	147	136	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2baz 30JUN2023:09:36 kvbv306

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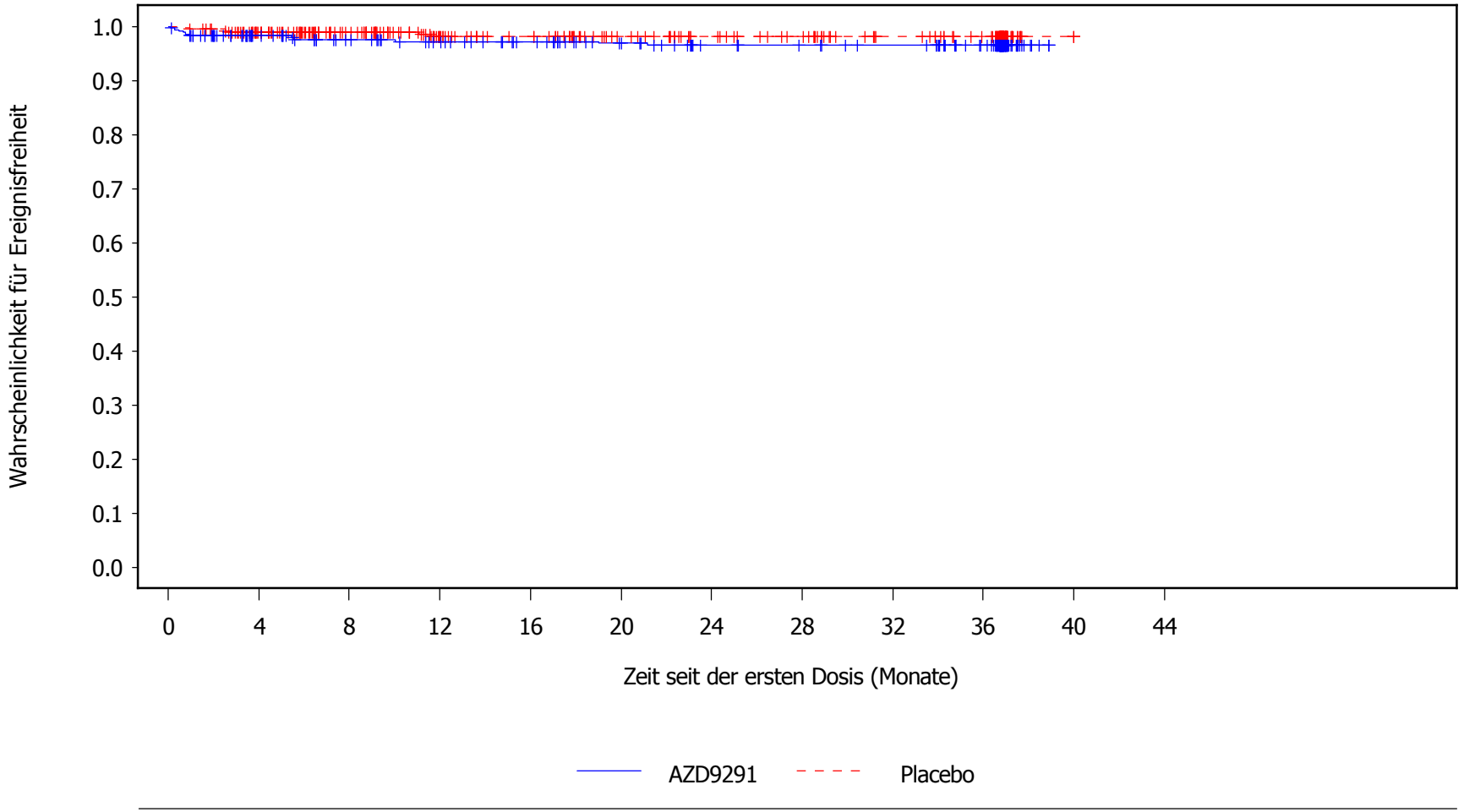
Figure 3.3.27 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Erythem
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	286	275	264	250	237	234	230	215	0	0	AZD9291
343	316	275	230	214	190	176	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bba 30JUN2023:09:36 kvbv306

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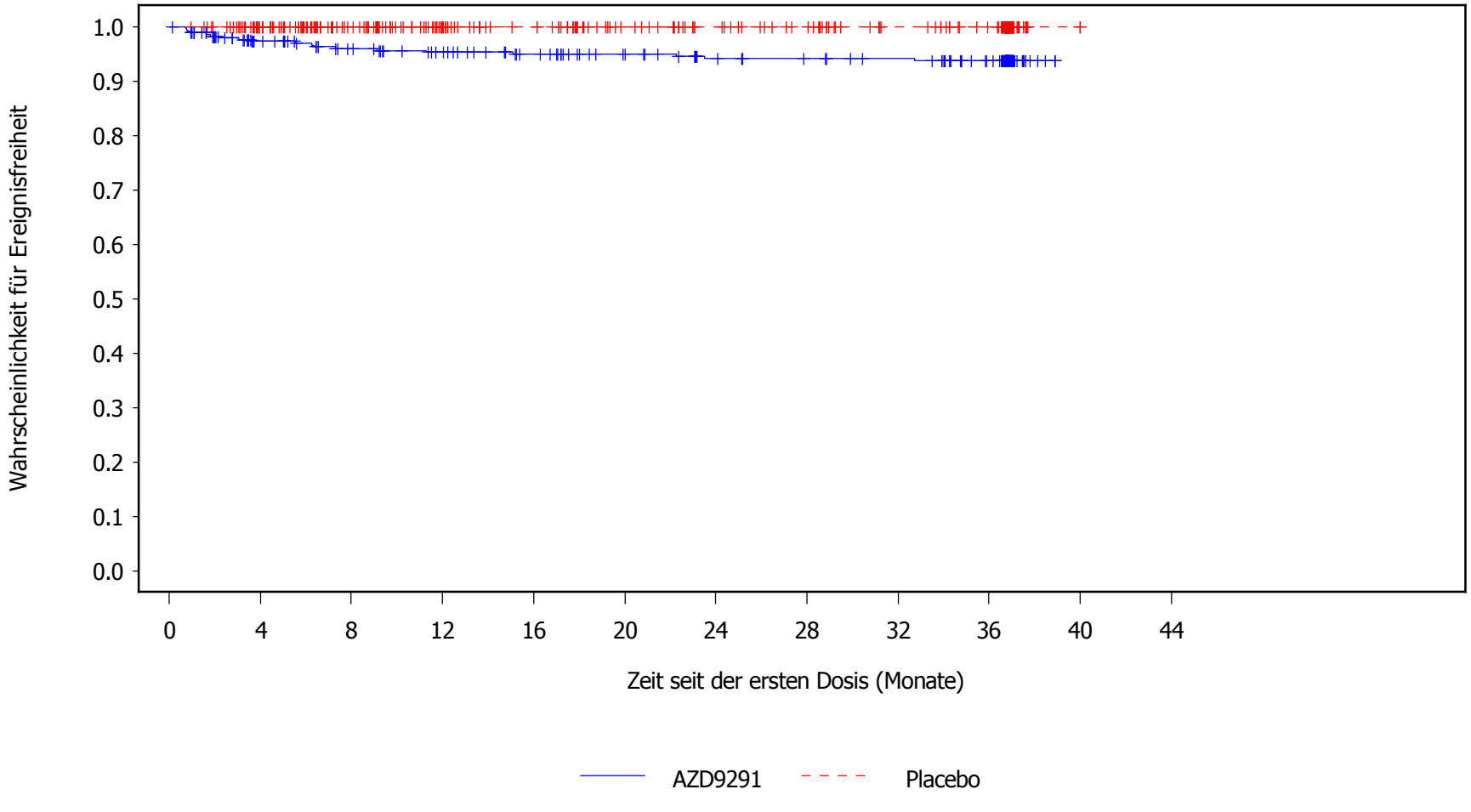
Figure 3.3.28 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Hautfissuren
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	300	281	269	256	243	232	228	224	208	0	0	AZD9291
343	320	278	234	218	193	178	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbb 30JUN2023:09:36 kvbv306

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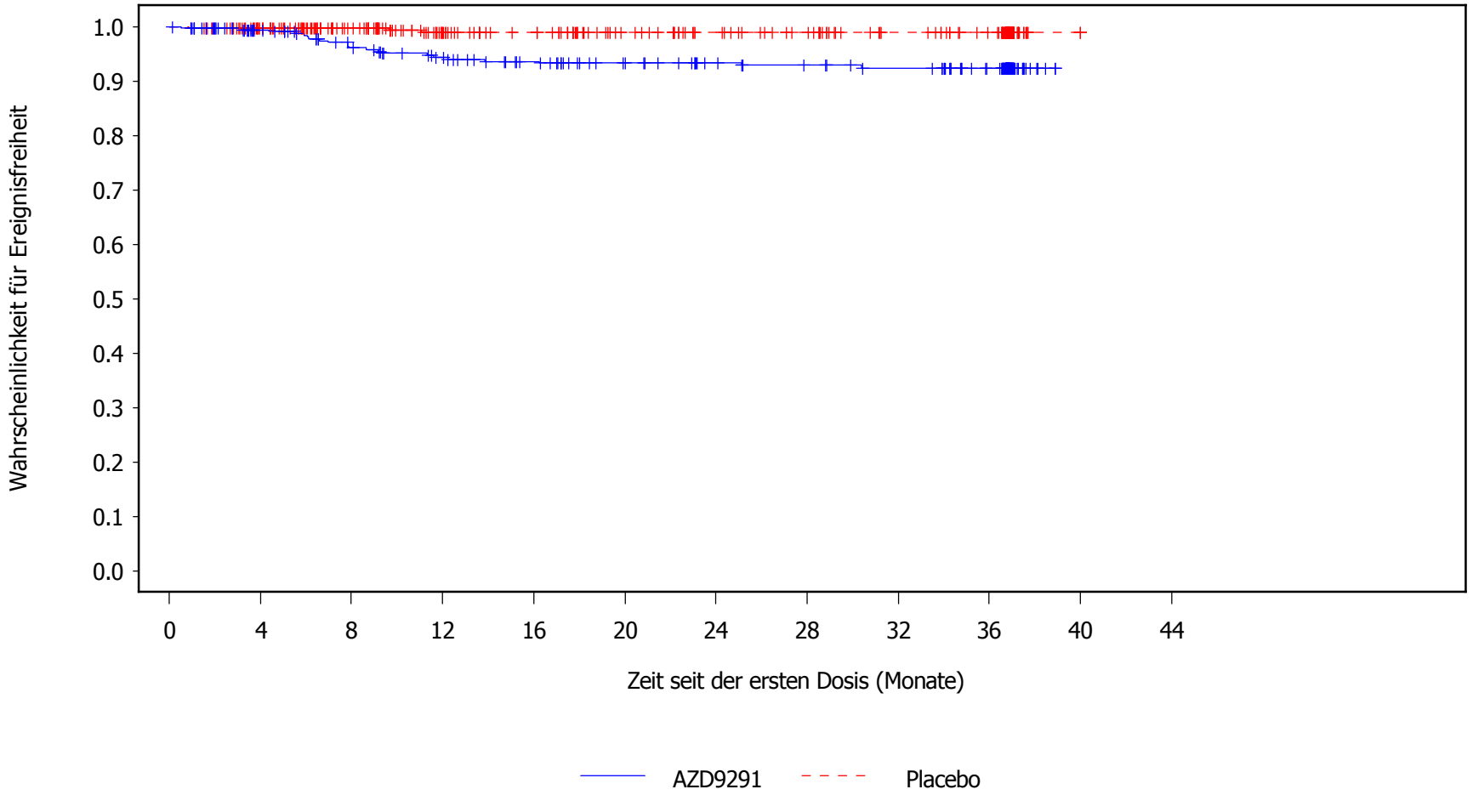
Figure 3.3.29 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Nagelerkrankung
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	306	283	268	254	240	229	224	219	204	0	0	AZD9291
343	319	277	232	216	191	176	166	150	139	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbc 30JUN2023:09:36 kvbv306

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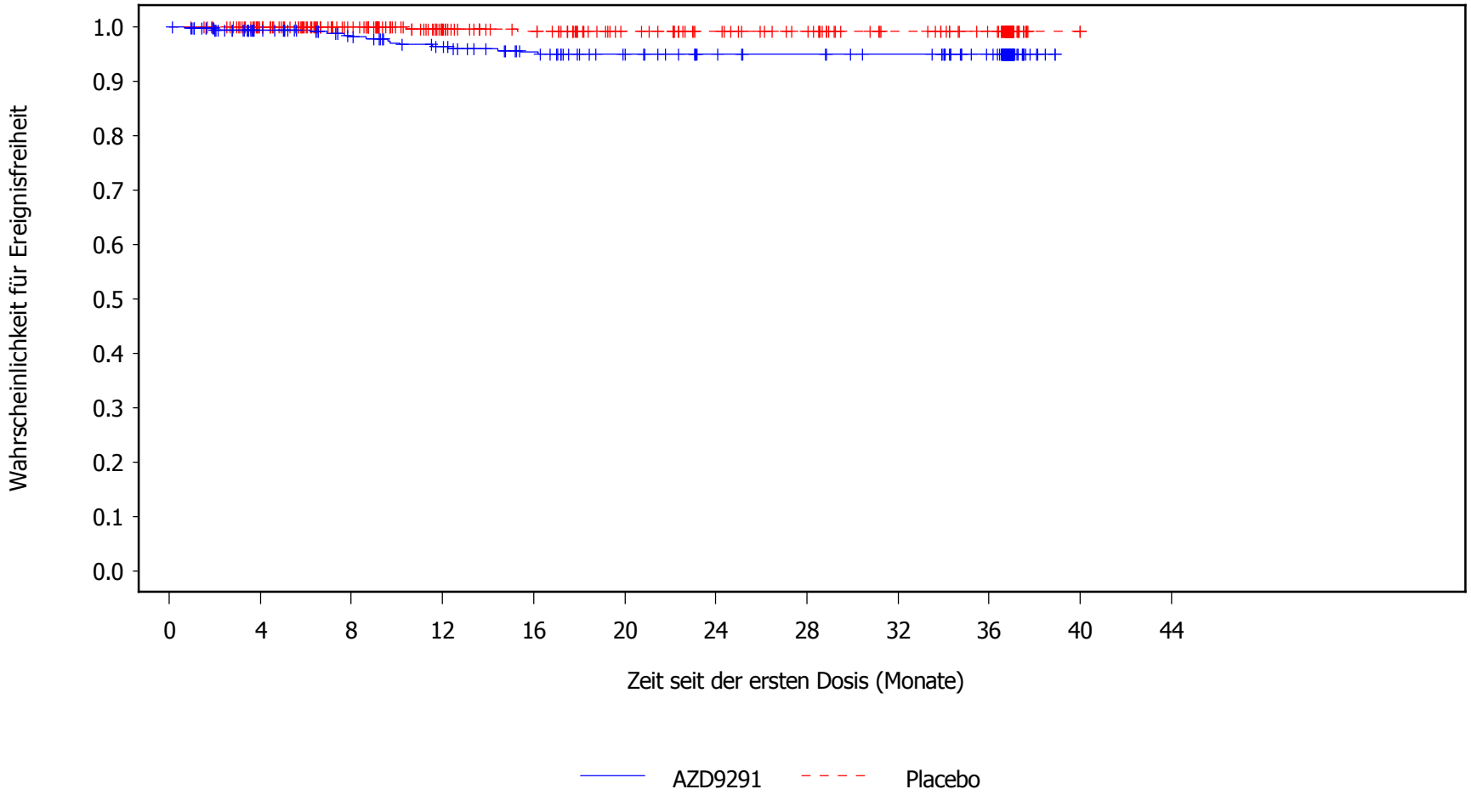
Figure 3.3.30 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Onychoklasie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	306	287	273	258	244	234	231	227	213	0	0	AZD9291
343	320	278	233	216	191	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbd 30JUN2023:09:36 kvbv306

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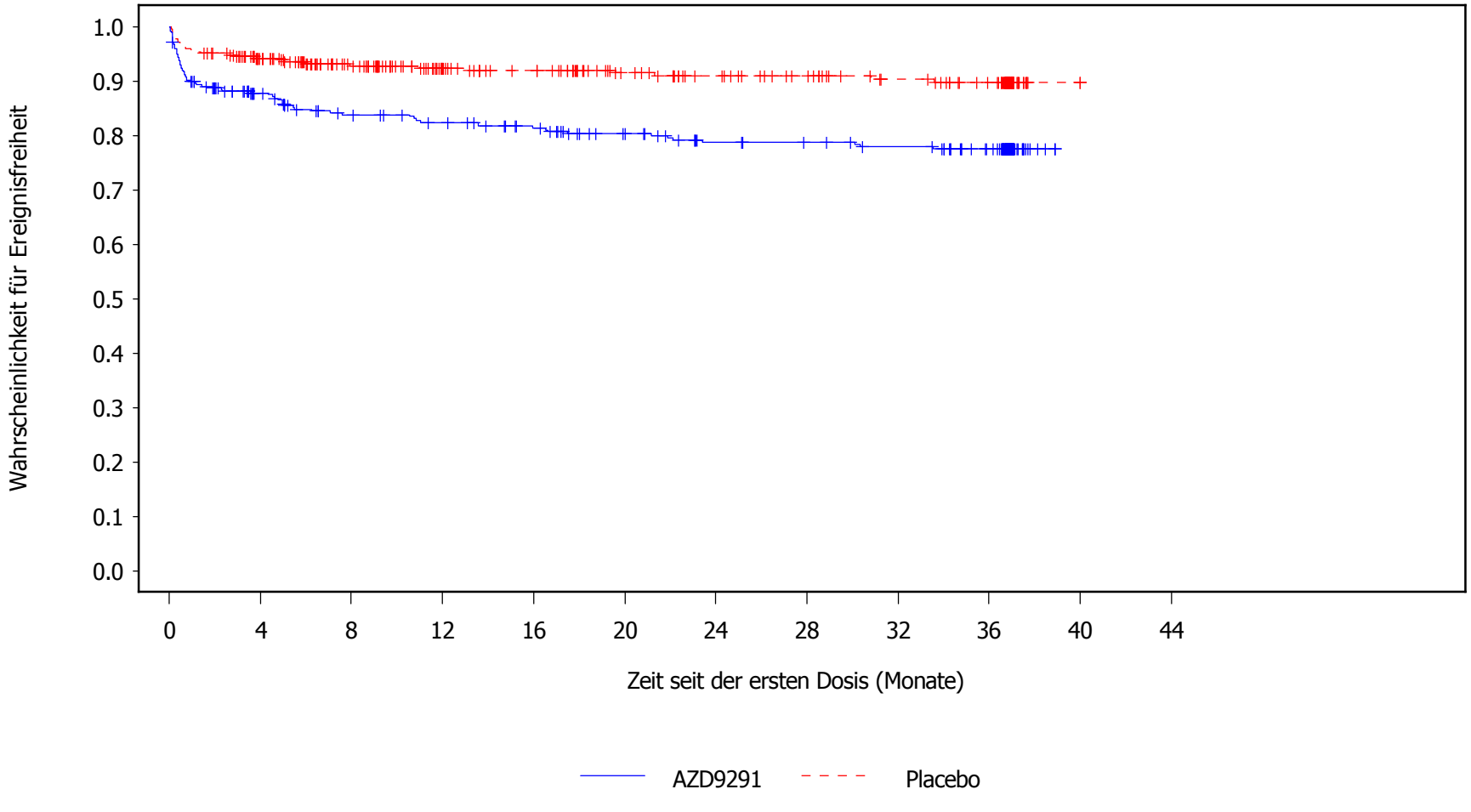
Figure 3.3.31 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Pruritus
Safety Analysis Set, DCO 11Apr2022

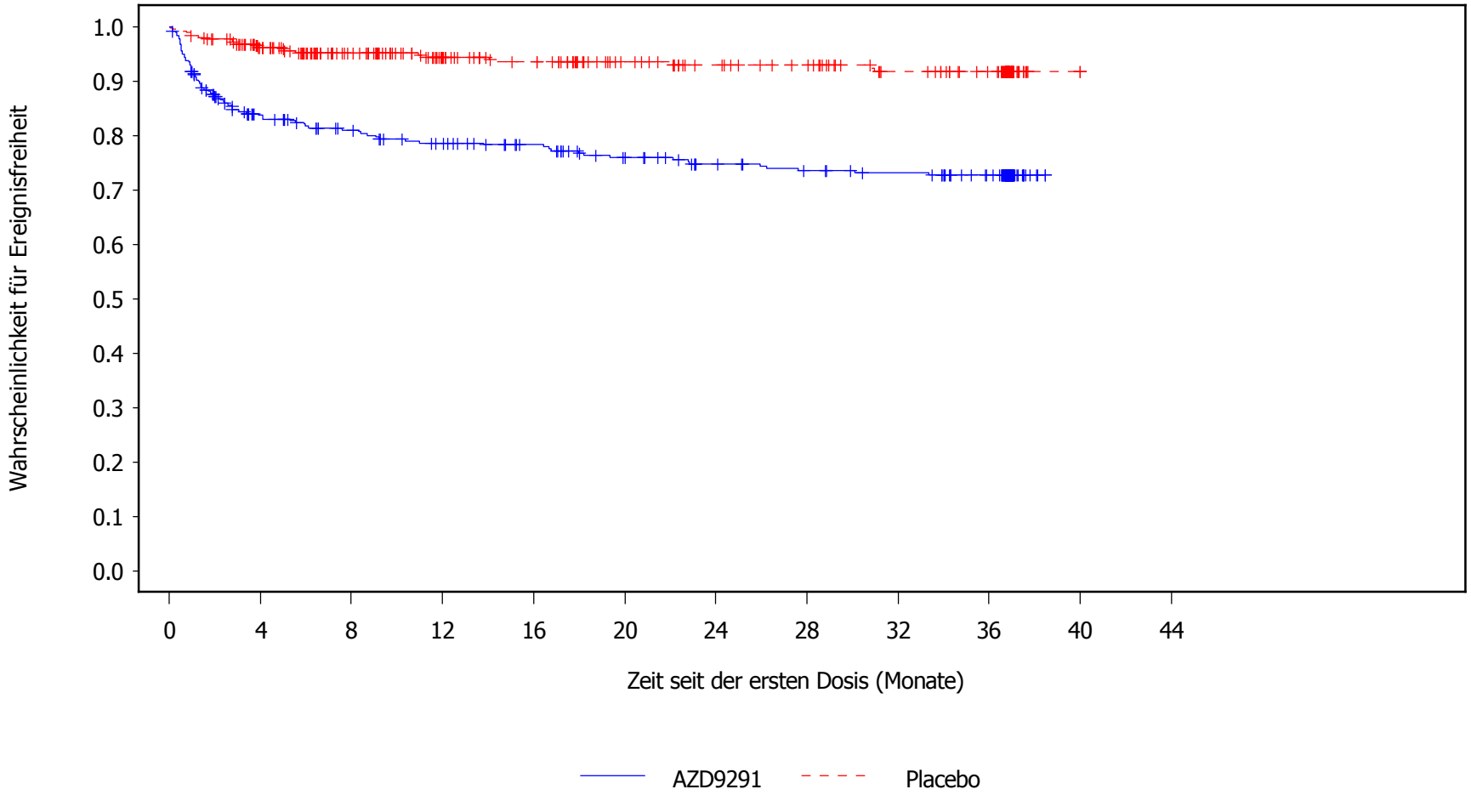


Anzahl an Patienten unter Risiko:

337	270	247	238	227	212	198	195	190	176	0	0 AZD9291
343	301	259	215	200	176	162	152	140	129	0	0 Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbe 30JUN2023:09:36 kvbv306

Figure 3.3.32 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Trockene Haut
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	257	238	224	211	195	182	175	170	156	0	0	AZD9291
343	307	264	220	203	178	165	158	142	131	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbf 30JUN2023:09:36 kvbv306

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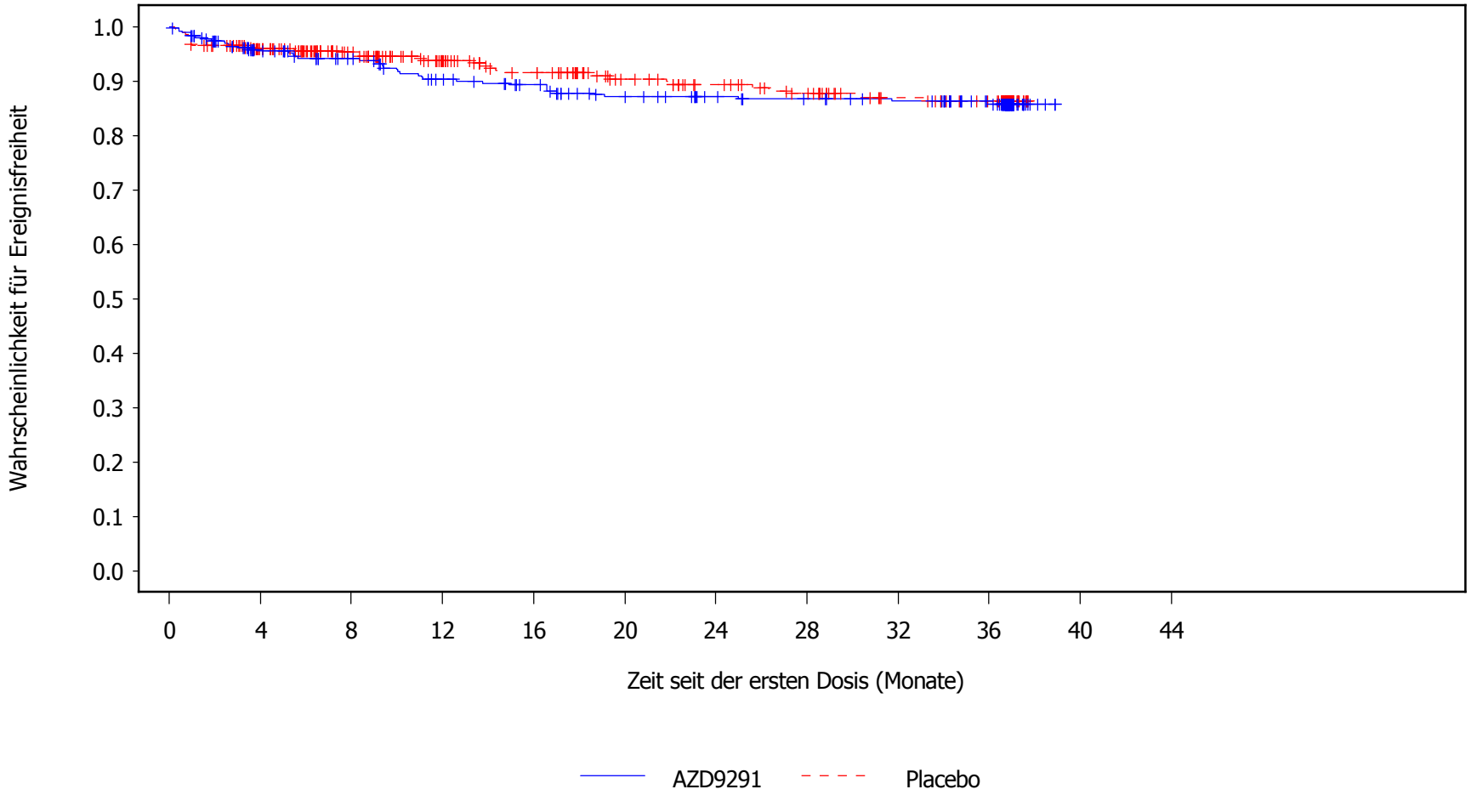
Figure 3.3.33 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen der Nieren und Harnwege
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	296	277	258	247	231	221	216	211	196	0	0	AZD9291
343	306	263	221	200	174	161	150	133	122	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbg 30JUN2023:09:36 kvbv306

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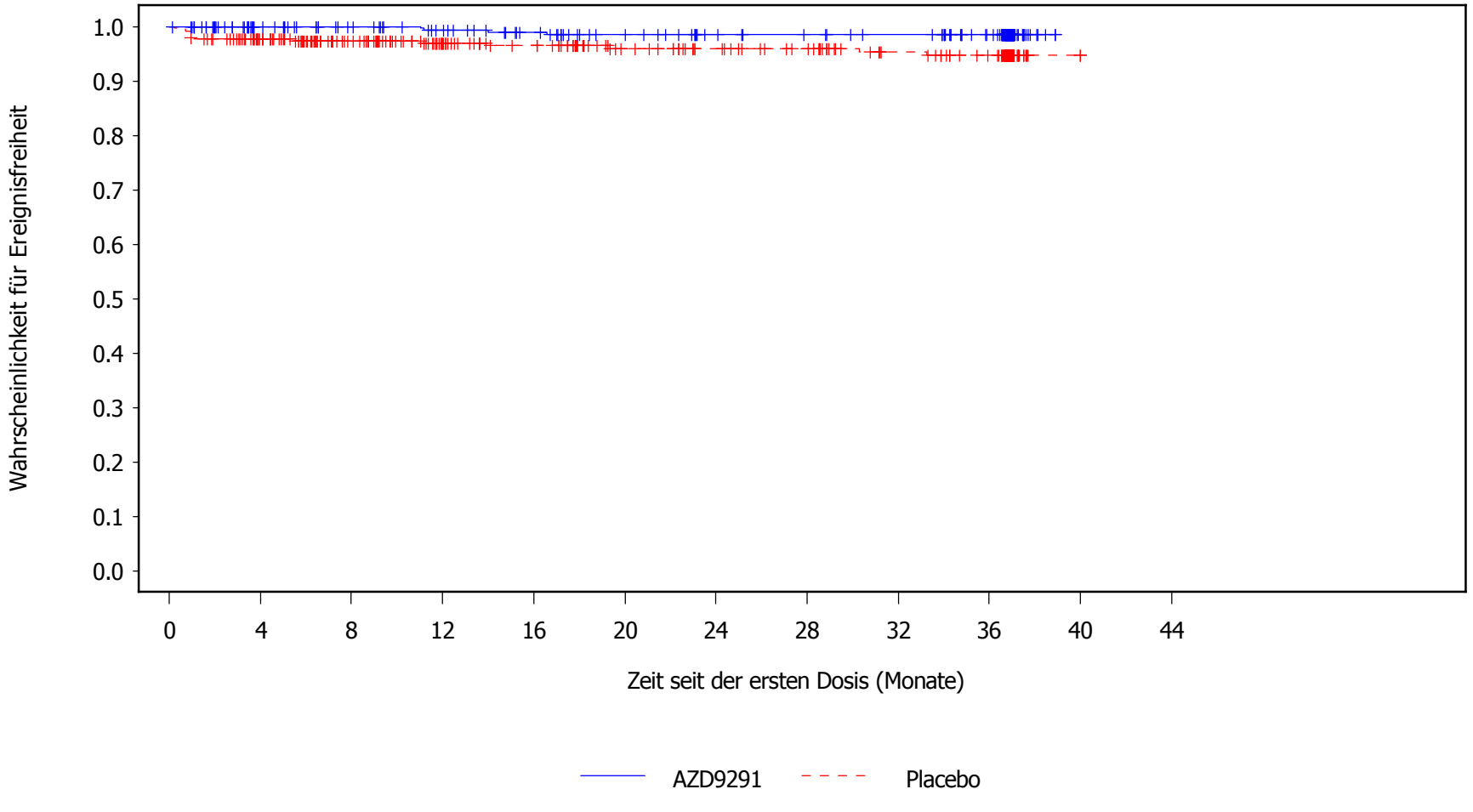
Figure 3.3.34 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Haematurie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	308	293	281	269	256	245	241	237	222	0	0	AZD9291
343	312	269	225	208	183	171	162	145	134	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbh 30JUN2023:09:36 kvbv306

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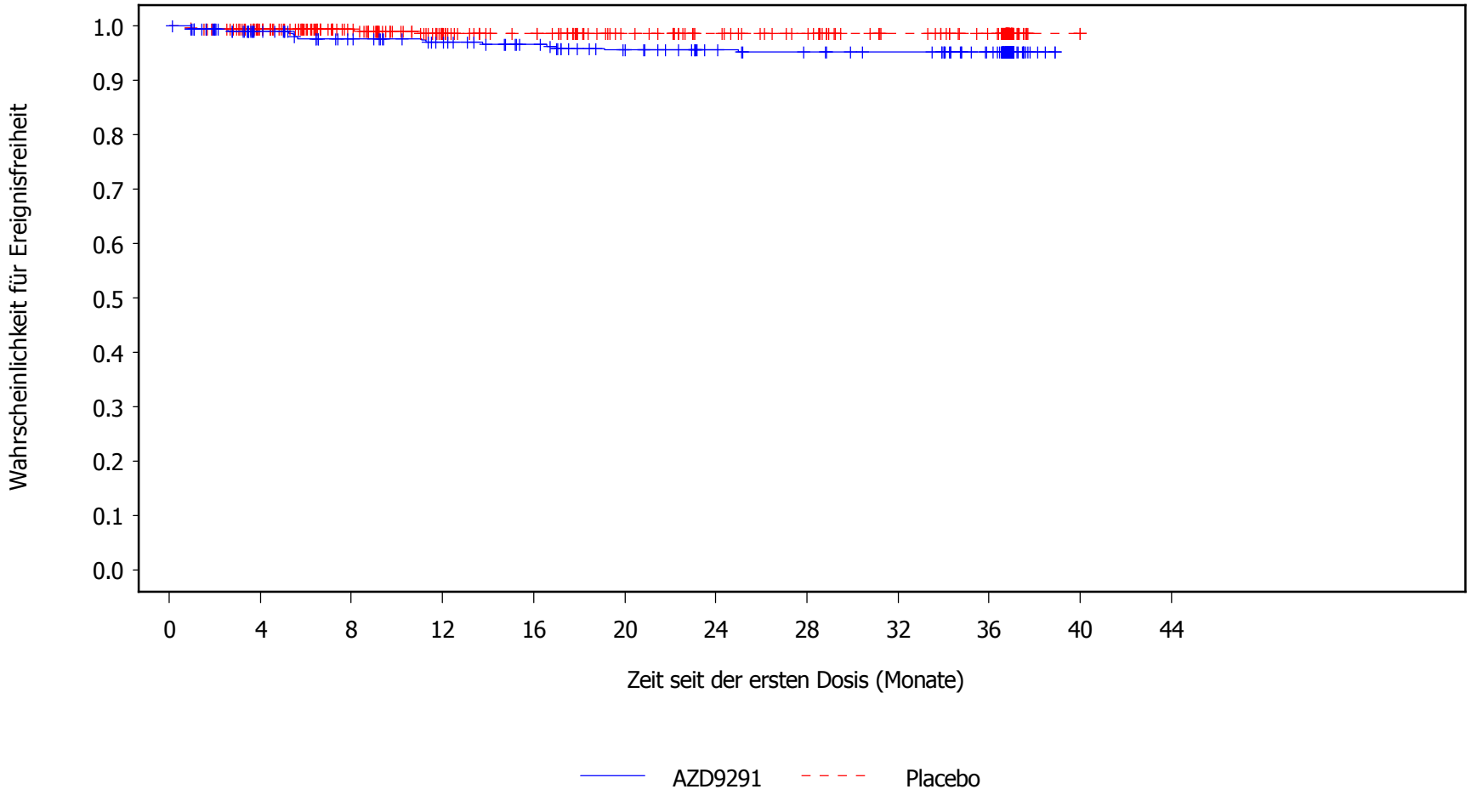
Figure 3.3.35 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Proteinurie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	306	288	276	264	250	238	233	229	214	0	0	AZD9291
343	318	276	232	216	191	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbi 30JUN2023:09:36 kvbv306

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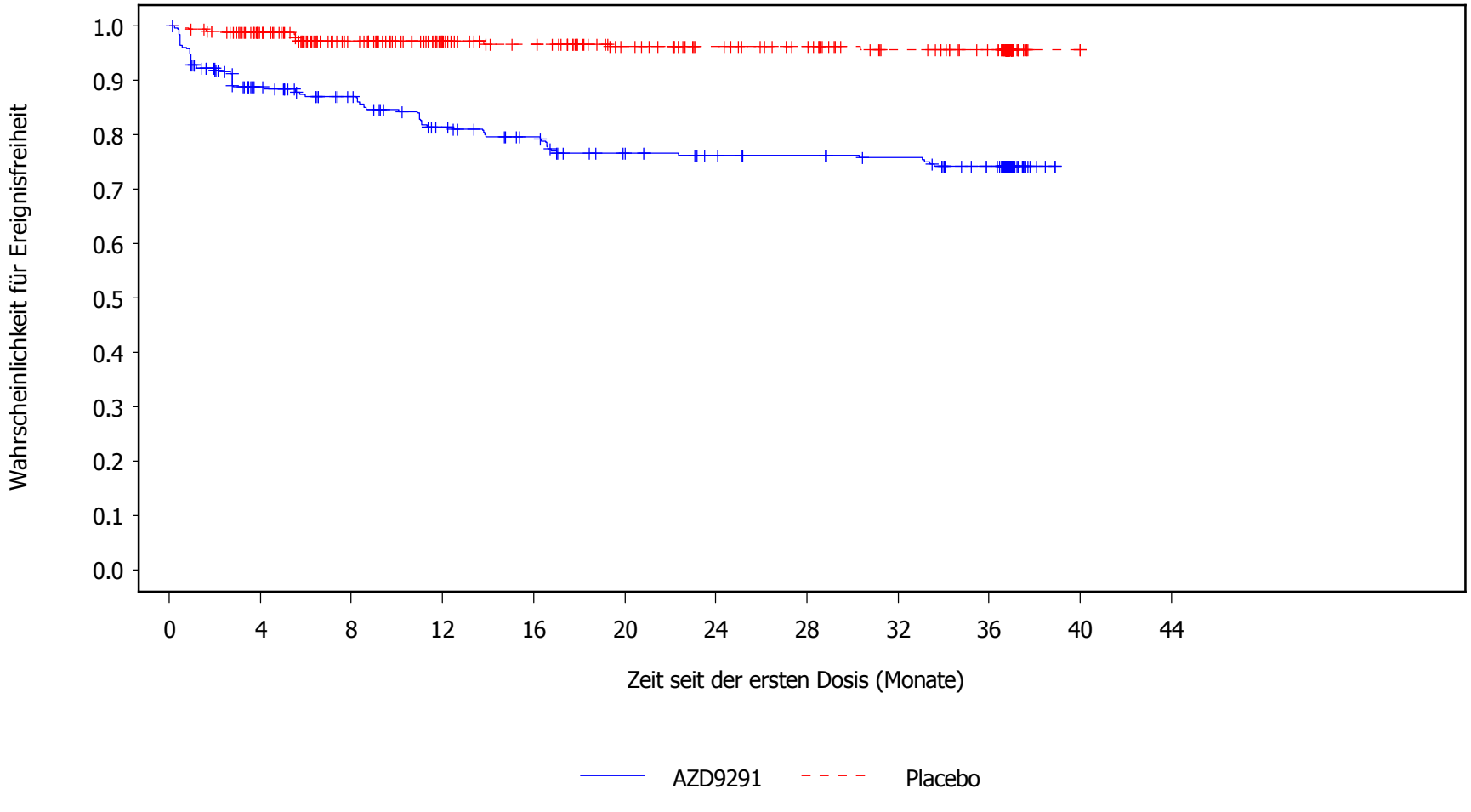
Figure 3.3.36 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen des Blutes und des Lymphsystems
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	272	252	227	214	198	190	187	183	169	0	0	AZD9291
343	316	270	229	212	187	172	163	148	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbj 30JUN2023:09:36 kvbv306

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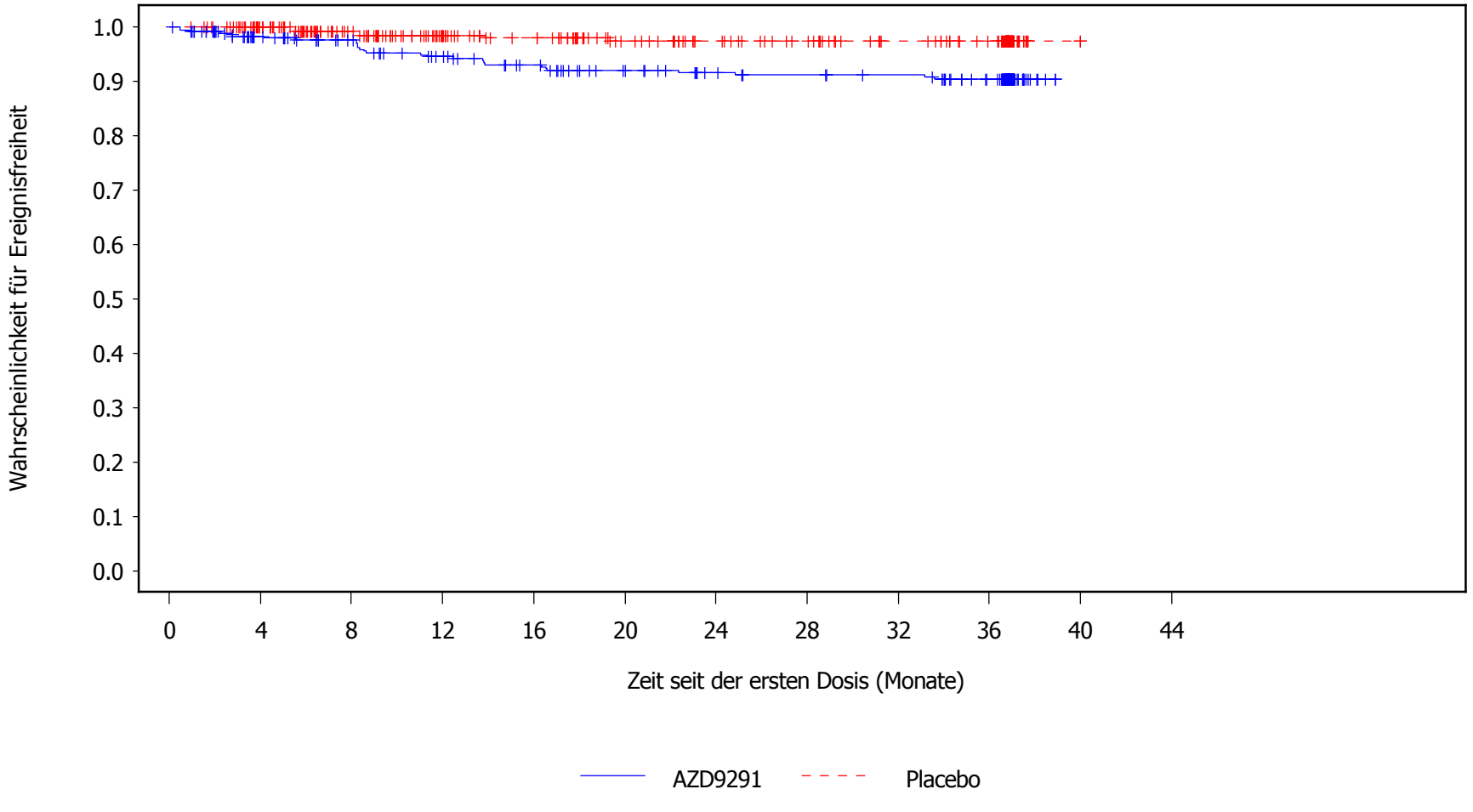
Figure 3.3.37 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Anaemie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	302	285	267	254	239	229	225	222	207	0	0	AZD9291
343	320	276	232	215	189	174	164	150	139	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbk 30JUN2023:09:36 kvbv306

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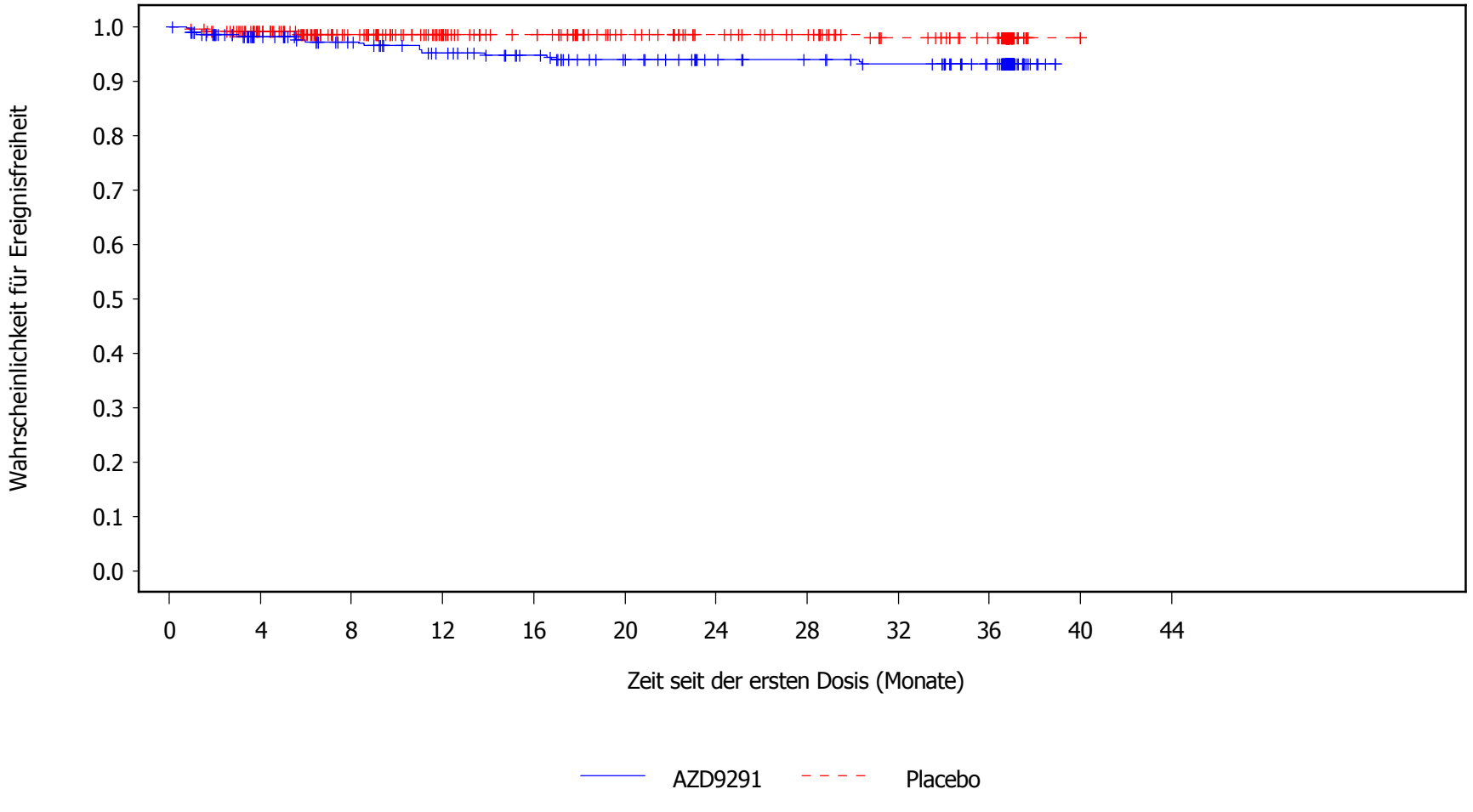
Figure 3.3.38 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Leukopenie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	302	284	268	256	242	230	226	220	205	0	0	AZD9291
343	317	273	231	215	190	175	166	150	139	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbl 30JUN2023:09:36 kvbv306

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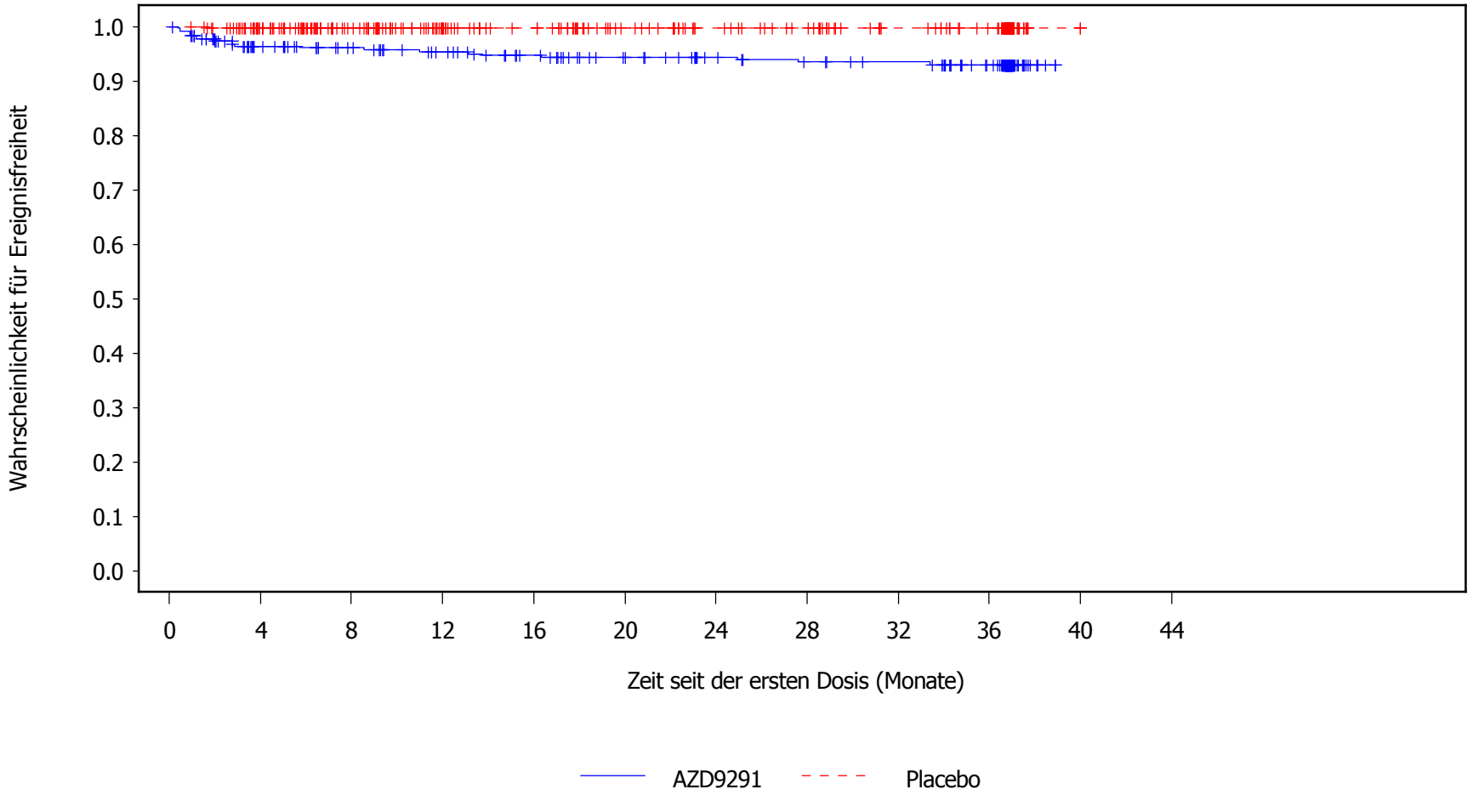
Figure 3.3.39 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Neutropenie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	296	280	268	255	242	231	225	221	205	0	0	AZD9291
343	319	277	233	217	192	177	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbm 30JUN2023:09:36 kvbv306

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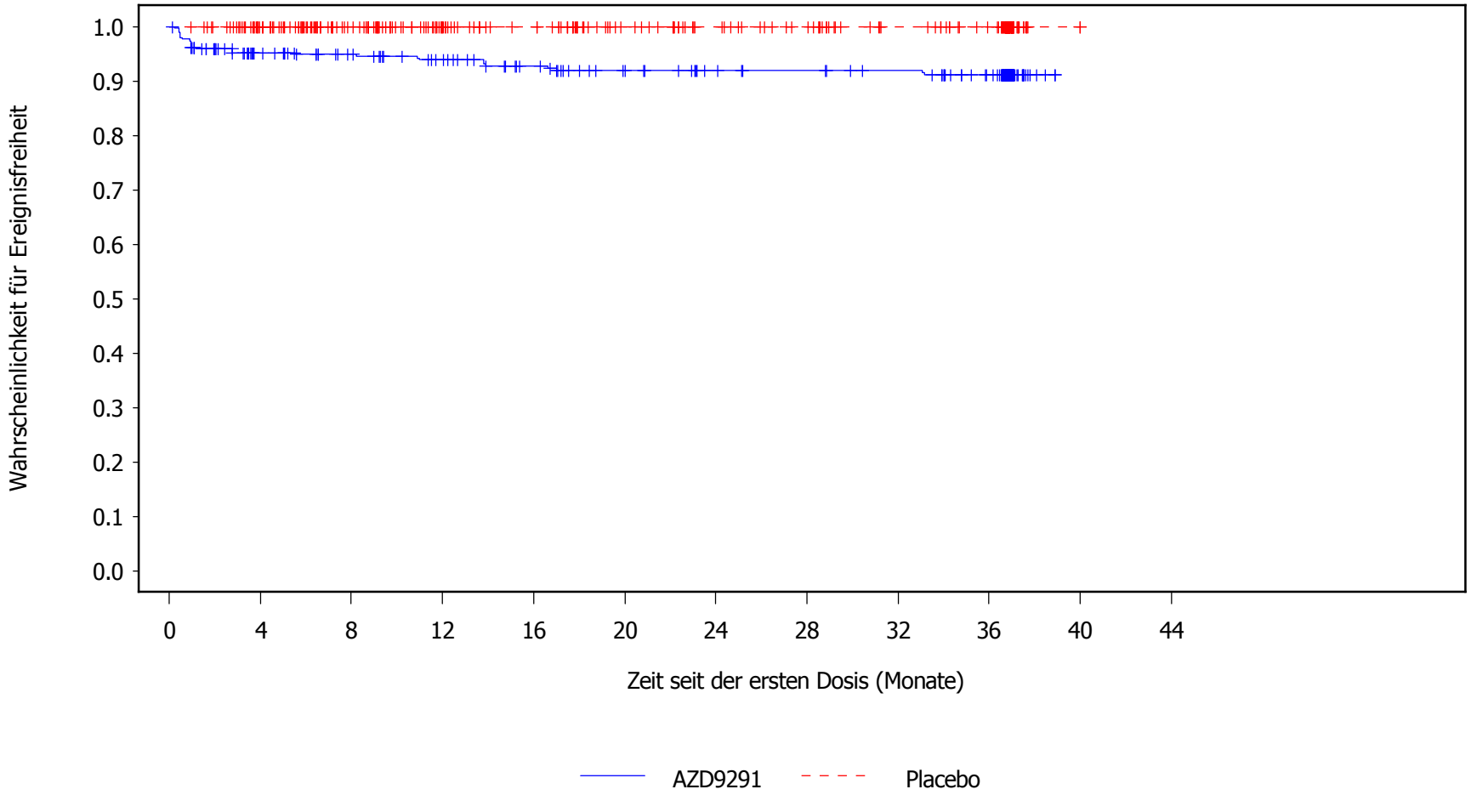
Figure 3.3.40 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Thrombozytopenie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	293	277	264	249	236	227	224	220	206	0	0	AZD9291
343	320	278	234	218	193	178	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbn 30JUN2023:09:36 kvbv306

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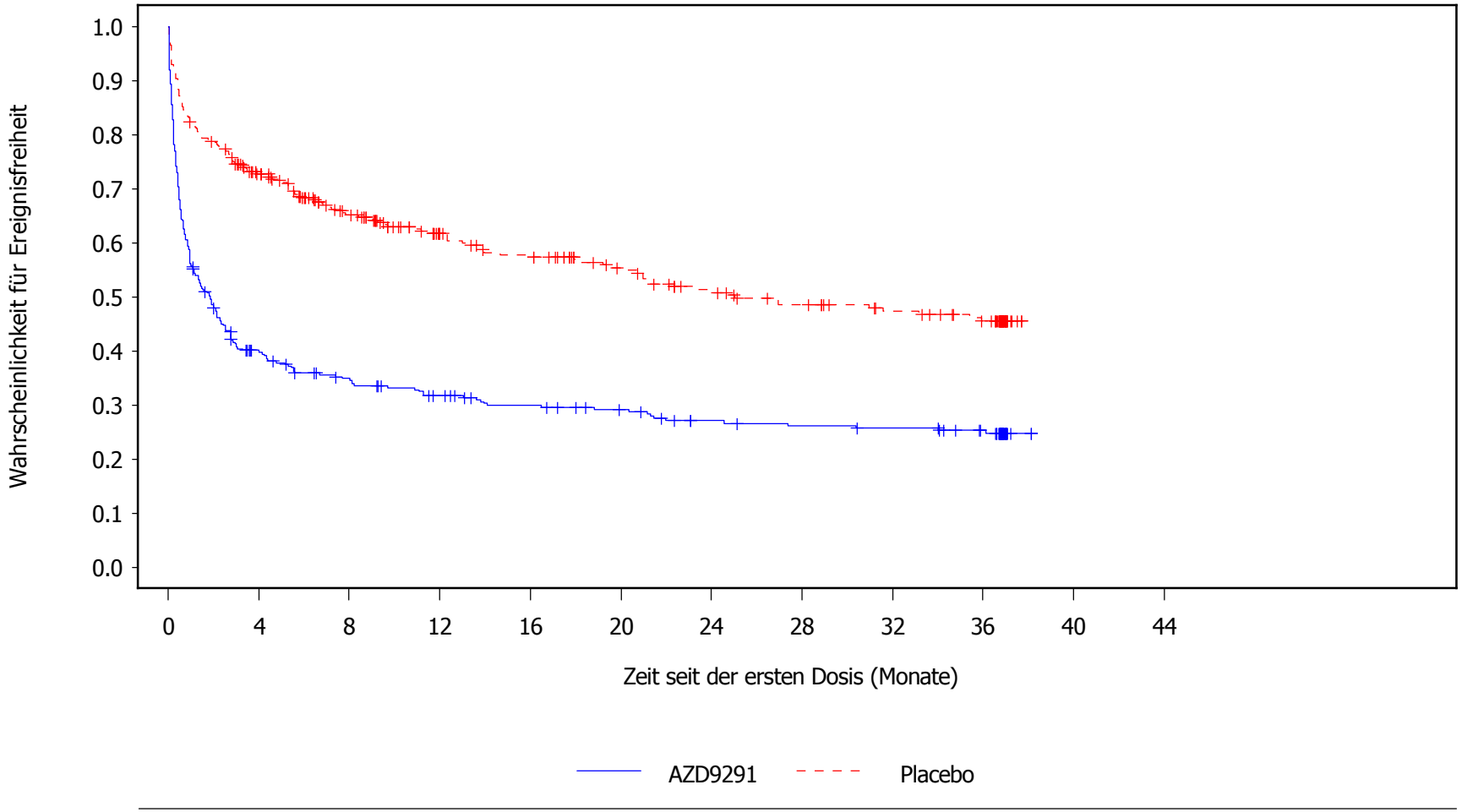
Figure 3.3.41 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen des Gastrointestinaltrakts
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	125	103	89	79	72	62	59	57	50	0	0	AZD9291
343	234	184	144	131	110	97	87	78	69	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbo 30JUN2023:09:36 kvbv306

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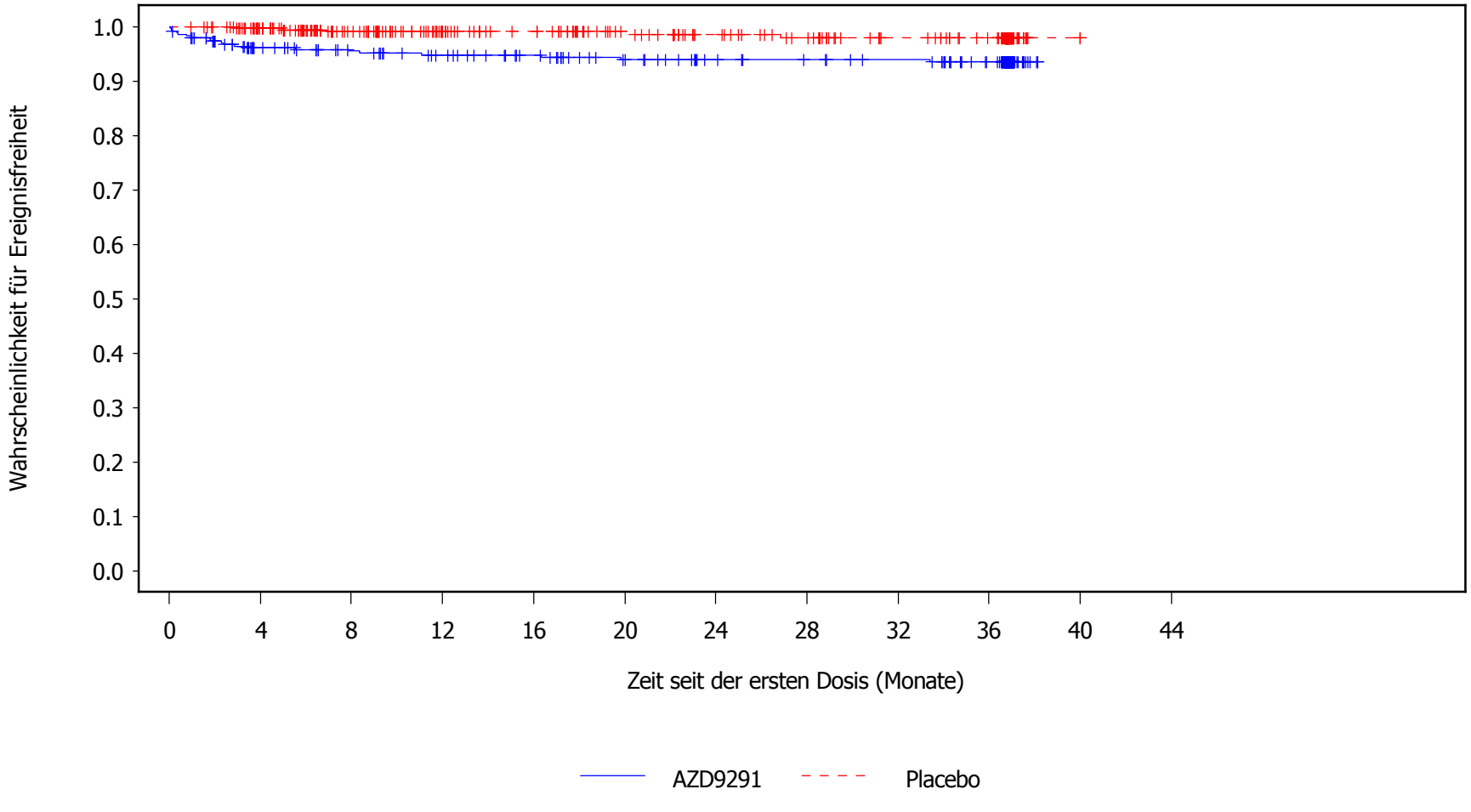
Figure 3.3.42 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Abdominalschmerz
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	299	283	272	261	247	235	231	227	211	0	0	AZD9291
343	319	275	231	216	191	175	164	148	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbp 30JUN2023:09:36 kvbv306

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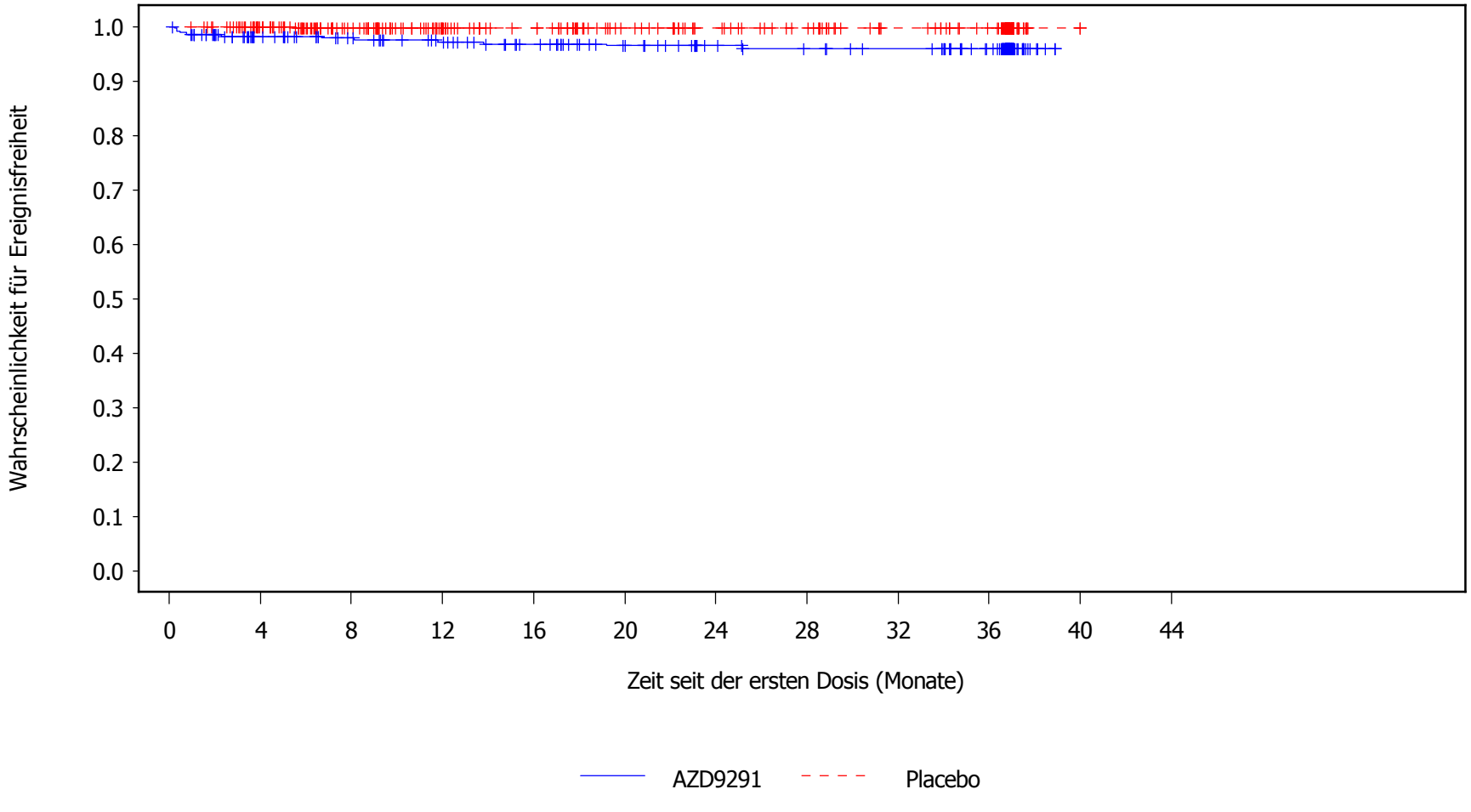
Figure 3.3.43 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Aphthoeses Ulkus
Safety Analysis Set, DCO 11Apr2022

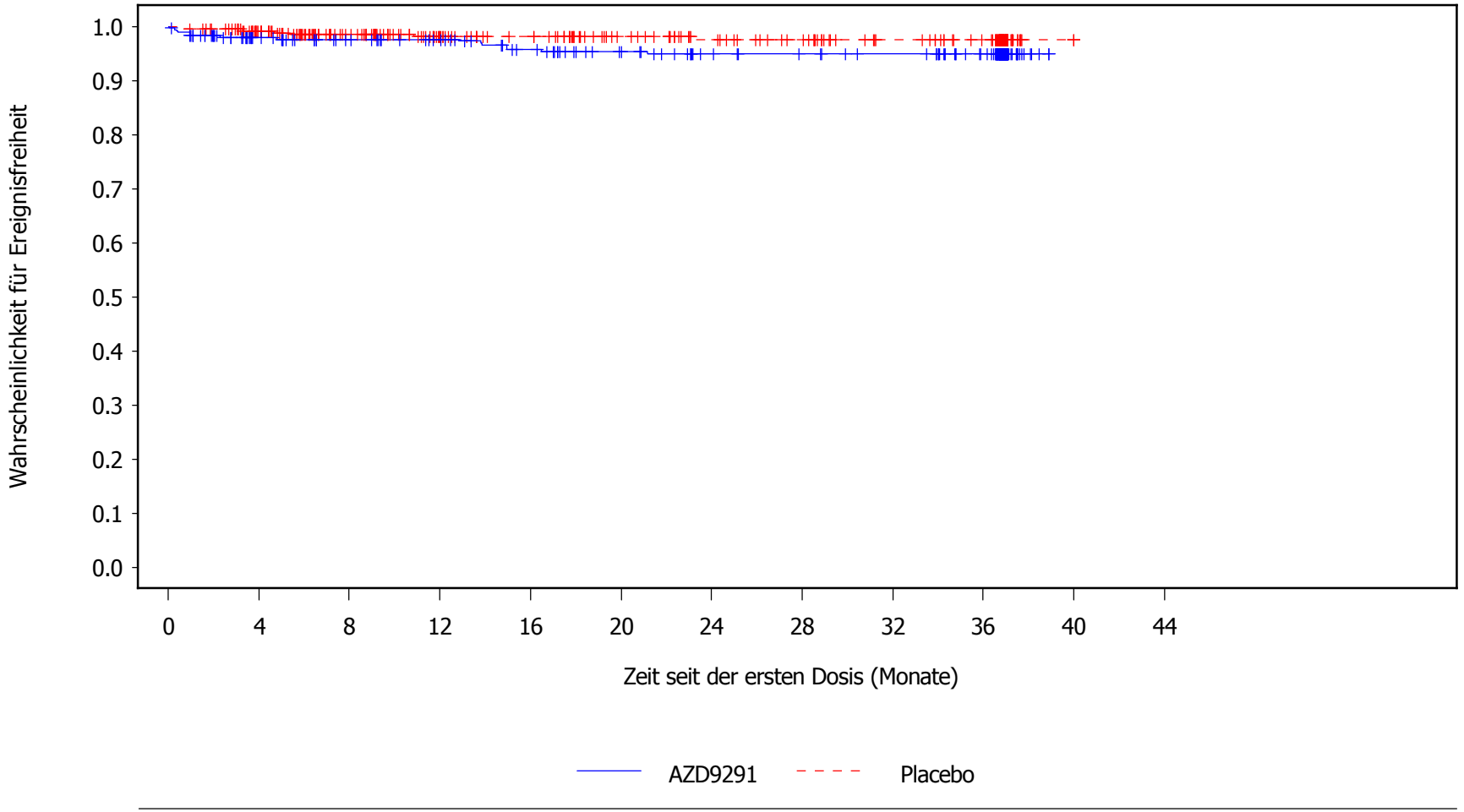


Anzahl an Patienten unter Risiko:

337	302	286	274	261	247	235	230	226	211	0	0	AZD9291
343	320	277	233	217	192	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbq 30JUN2023:09:36 kvbv306

Figure 3.3.44 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Bauch aufgetrieben
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	301	285	275	260	246	233	229	225	210	0	0	AZD9291
343	317	273	229	213	189	174	164	148	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbr 30JUN2023:09:36 kvbv306

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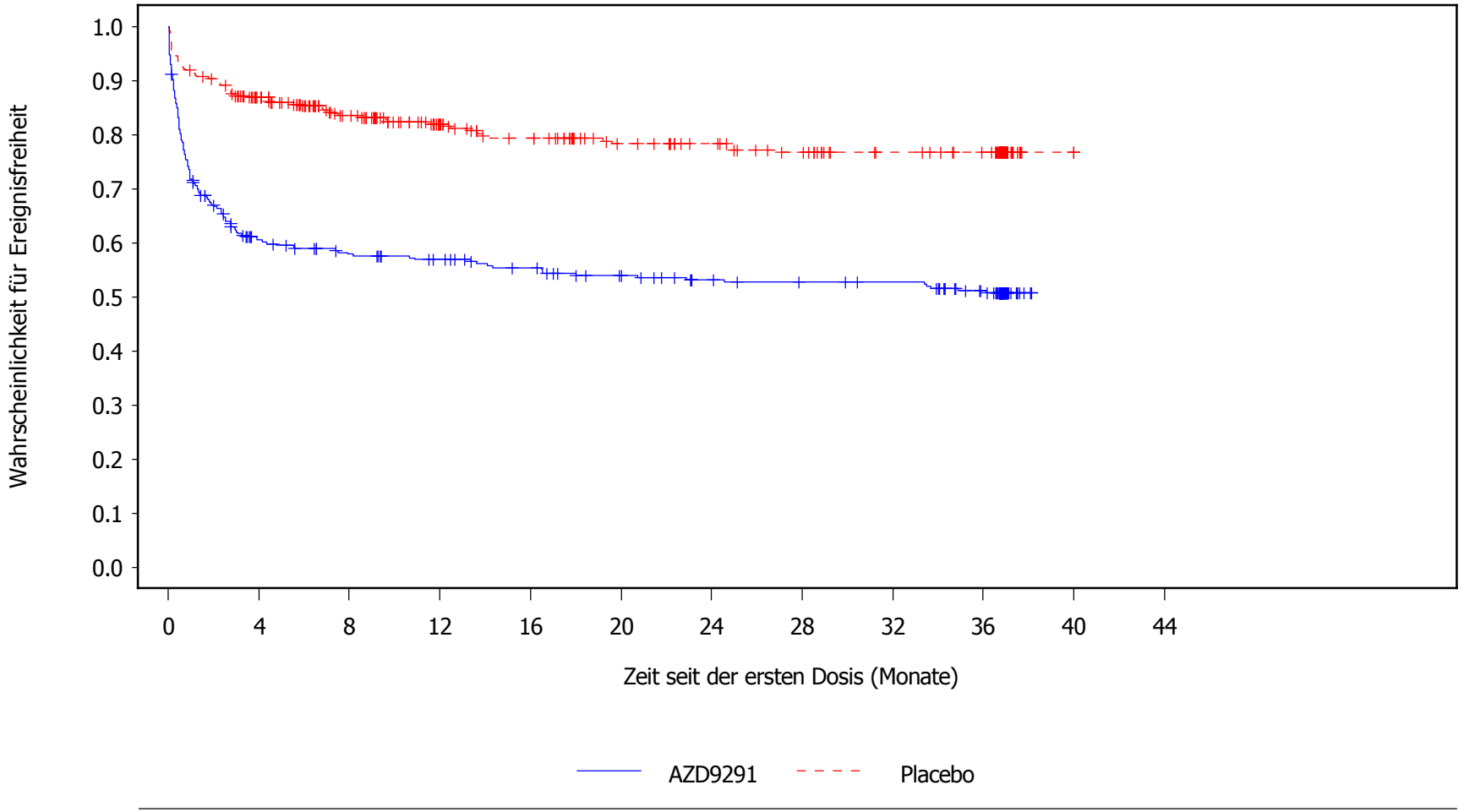
Figure 3.3.45 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Diarrhoe
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	189	174	165	155	144	134	130	128	113	0	0	AZD9291
343	280	235	192	175	154	145	134	122	116	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbs 30JUN2023:09:36 kvbv306

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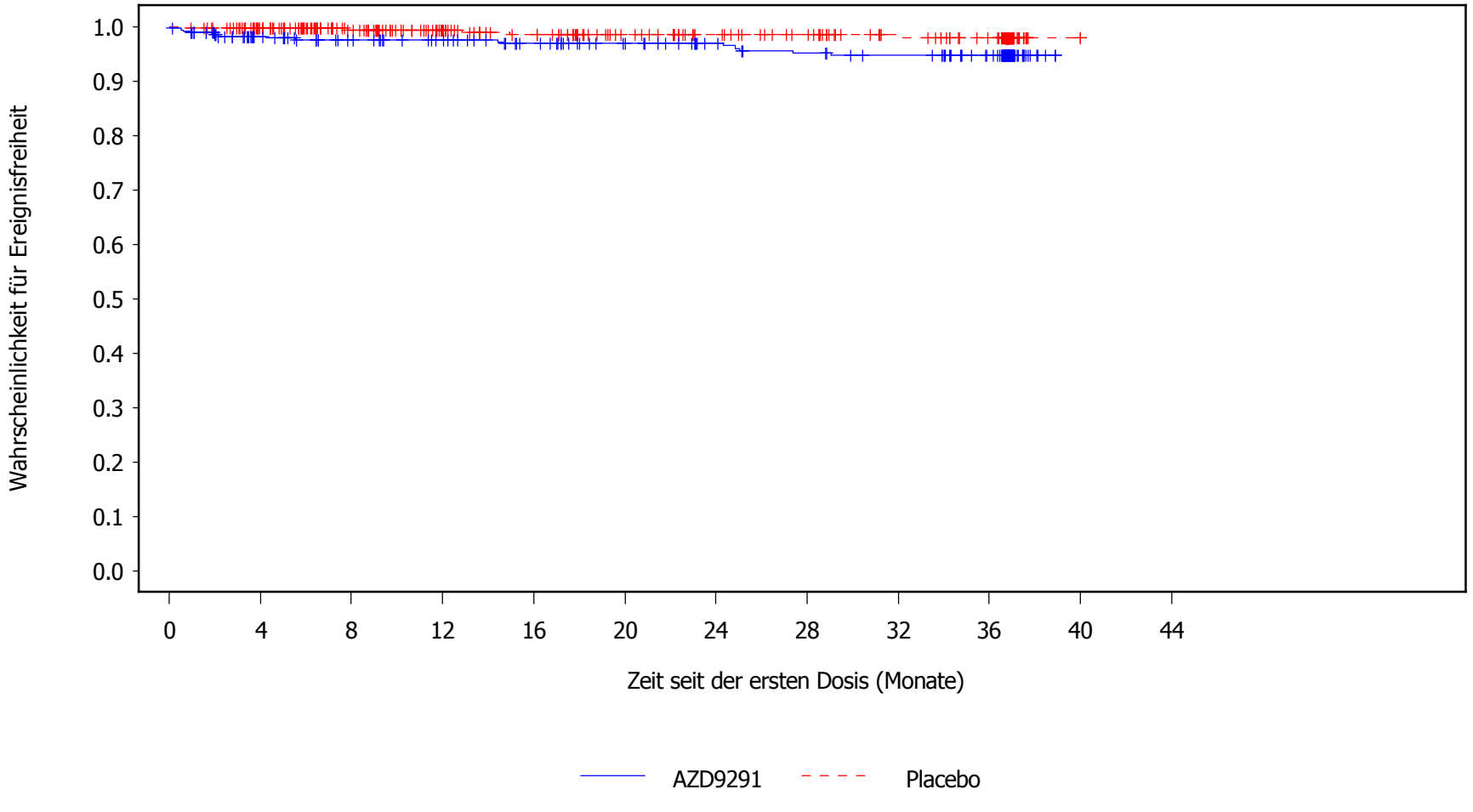
Figure 3.3.46 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Dyspepsie
Safety Analysis Set, DCO 11Apr2022

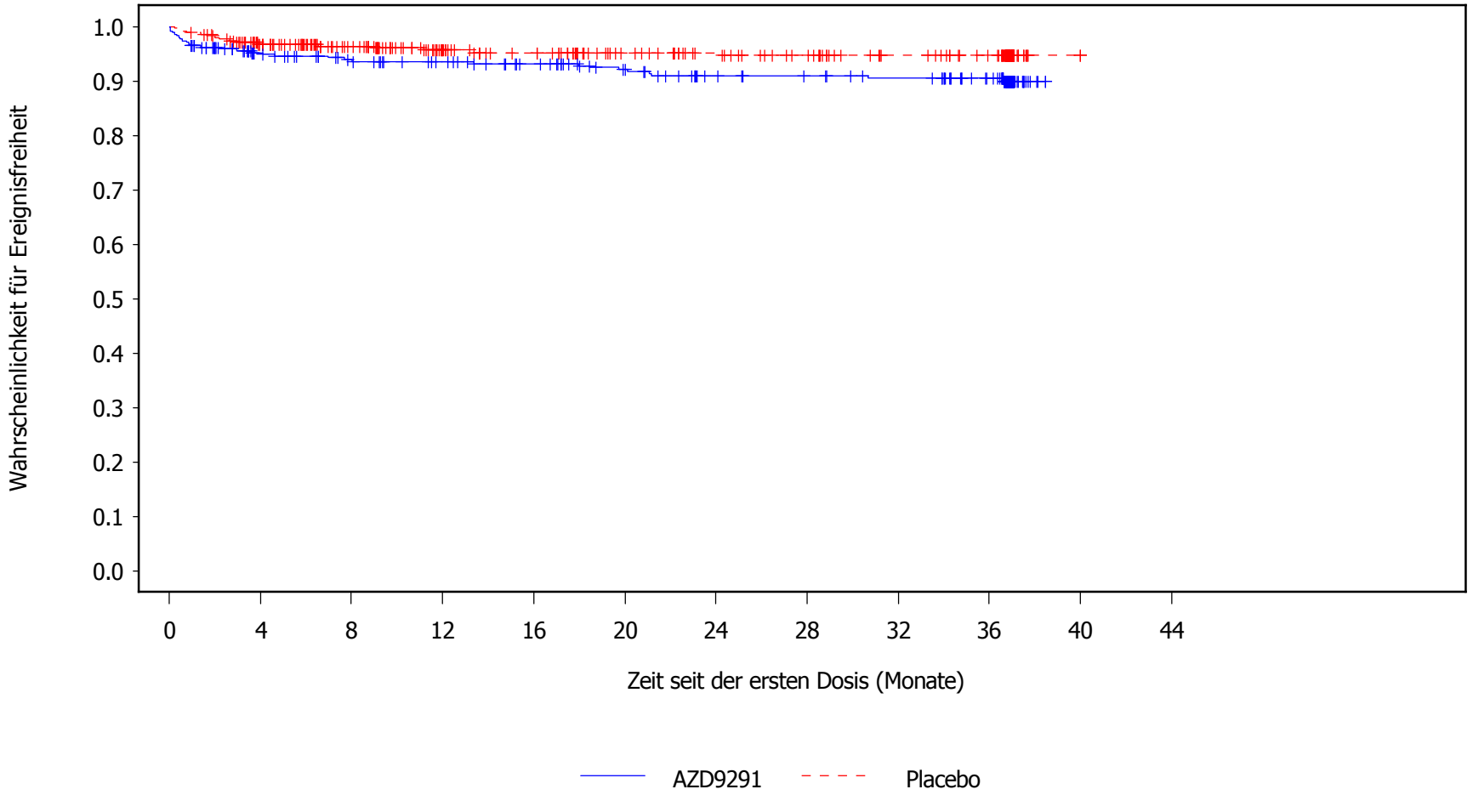


Anzahl an Patienten unter Risiko:

337	303	287	277	263	250	238	231	226	211	0	0	AZD9291
343	319	276	234	216	192	178	168	152	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbt 30JUN2023:09:36 kvbv306

Figure 3.3.47 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Erbrechen
Safety Analysis Set, DCO 11Apr2022

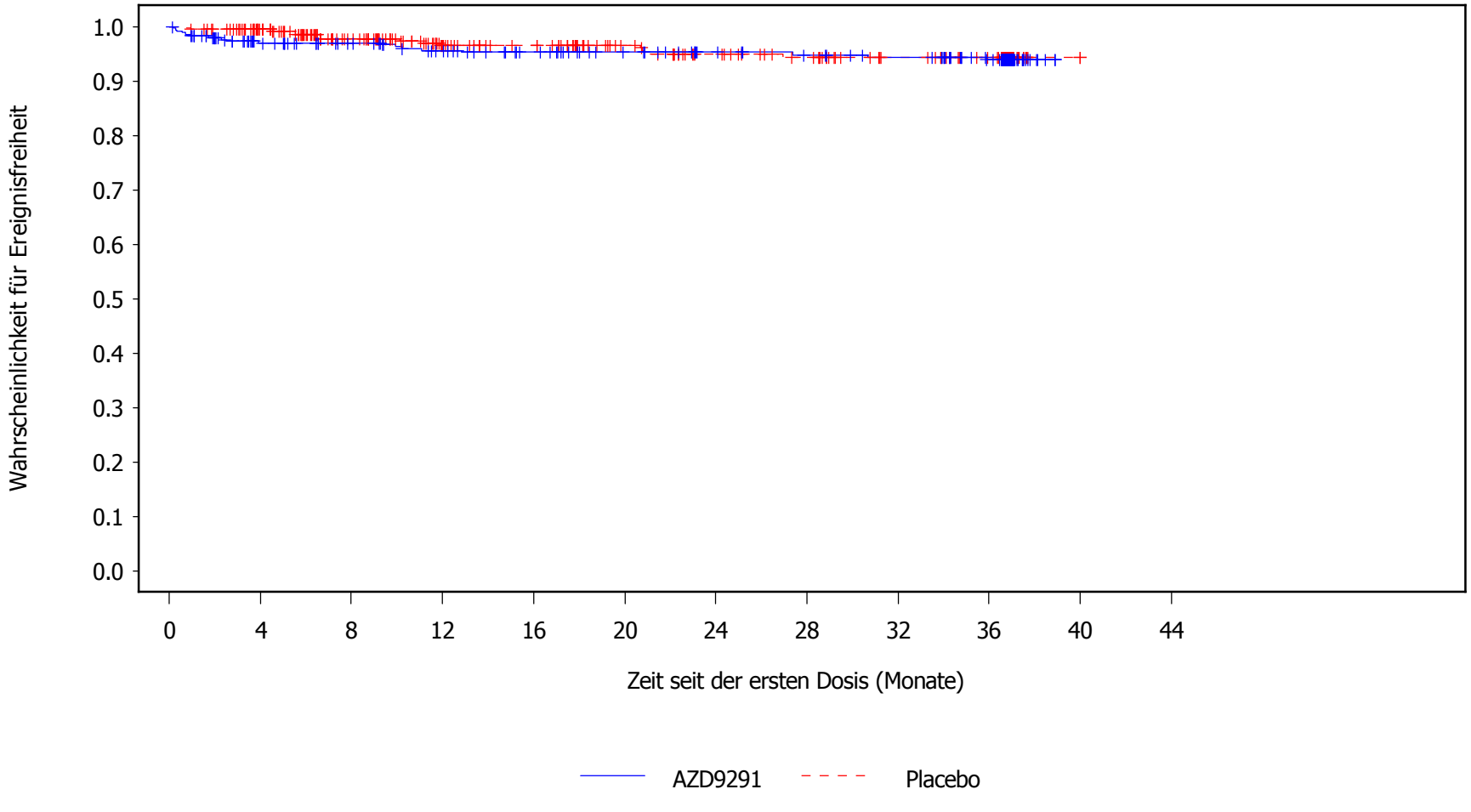


Anzahl an Patienten unter Risiko:

337	293	277	266	254	238	223	219	214	199	0	0	AZD9291
343	309	271	225	209	185	171	160	145	135	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbu 30JUN2023:09:36 kvbv306

Figure 3.3.48 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Gastrooesophageale Refluxerkrankung
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	299	284	270	257	245	235	230	225	209	0	0	AZD9291
343	318	271	225	210	185	168	158	143	132	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbv 30JUN2023:09:36 kvbv306

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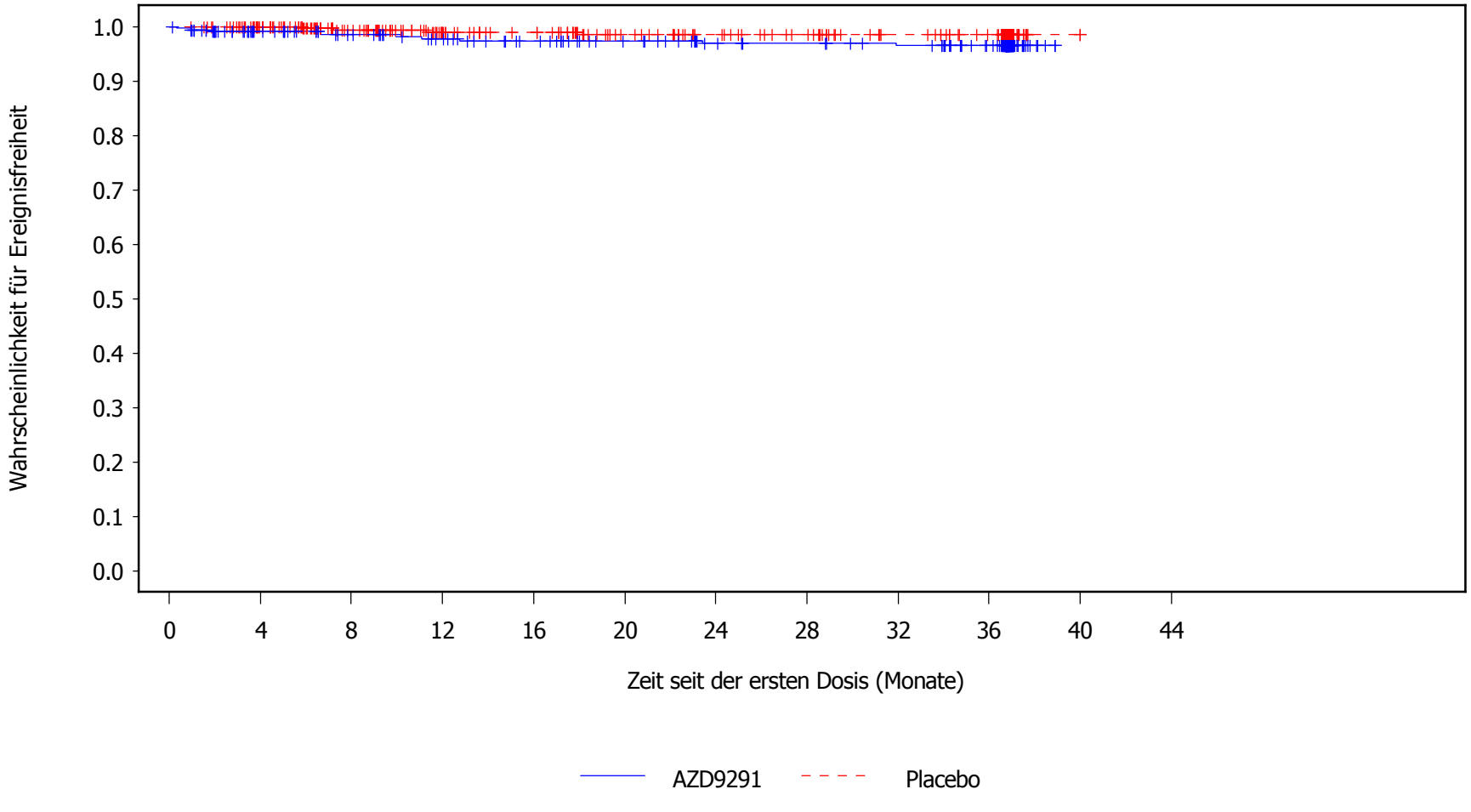
Figure 3.3.49 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Haemorrhoiden
Safety Analysis Set, DCO 11Apr2022

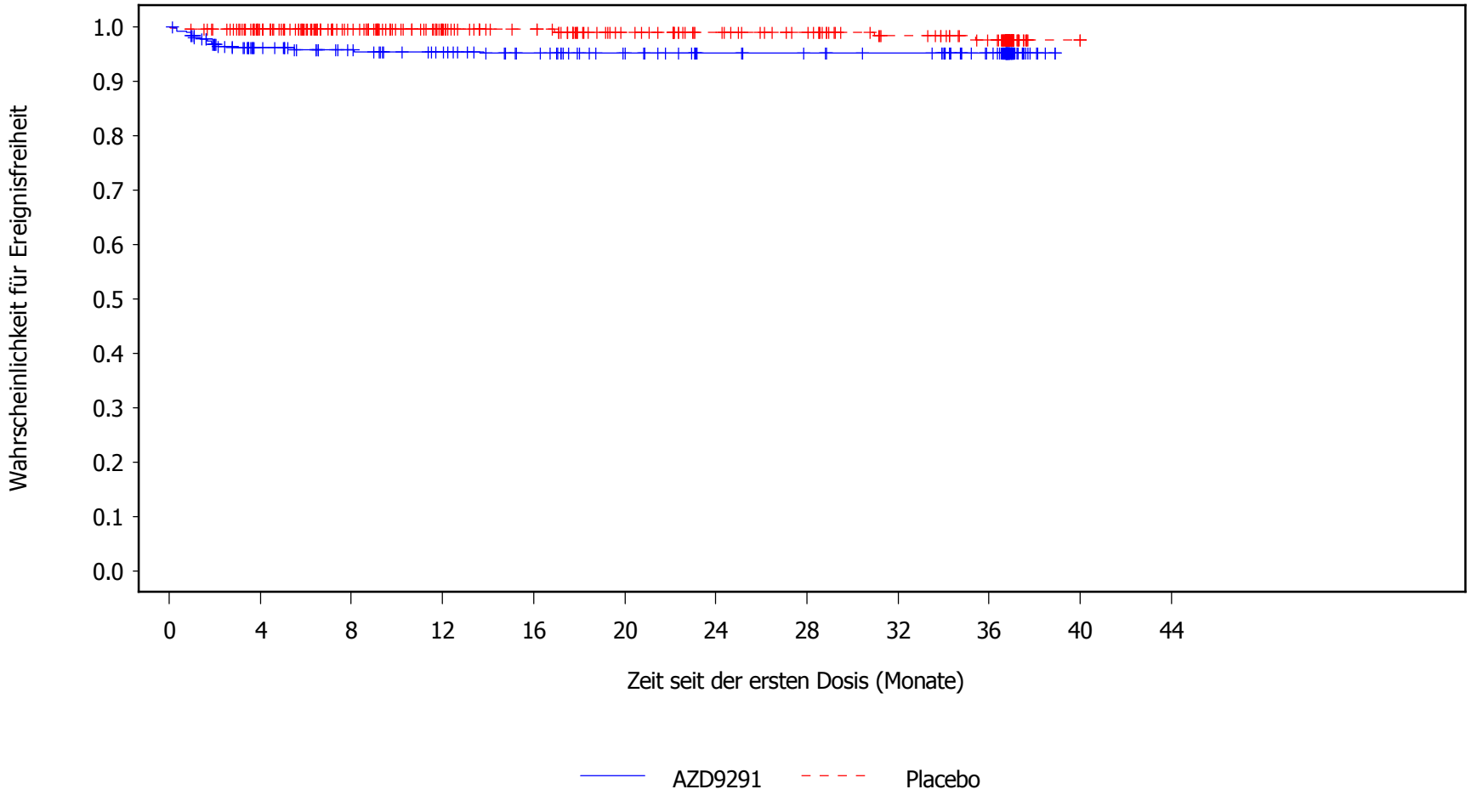


Anzahl an Patienten unter Risiko:

337	306	289	277	265	253	241	238	233	218	0	0	AZD9291
343	320	276	232	218	192	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbw 30JUN2023:09:36 kvbv306

Figure 3.3.50 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Mundtrockenheit
Safety Analysis Set, DCO 11Apr2022

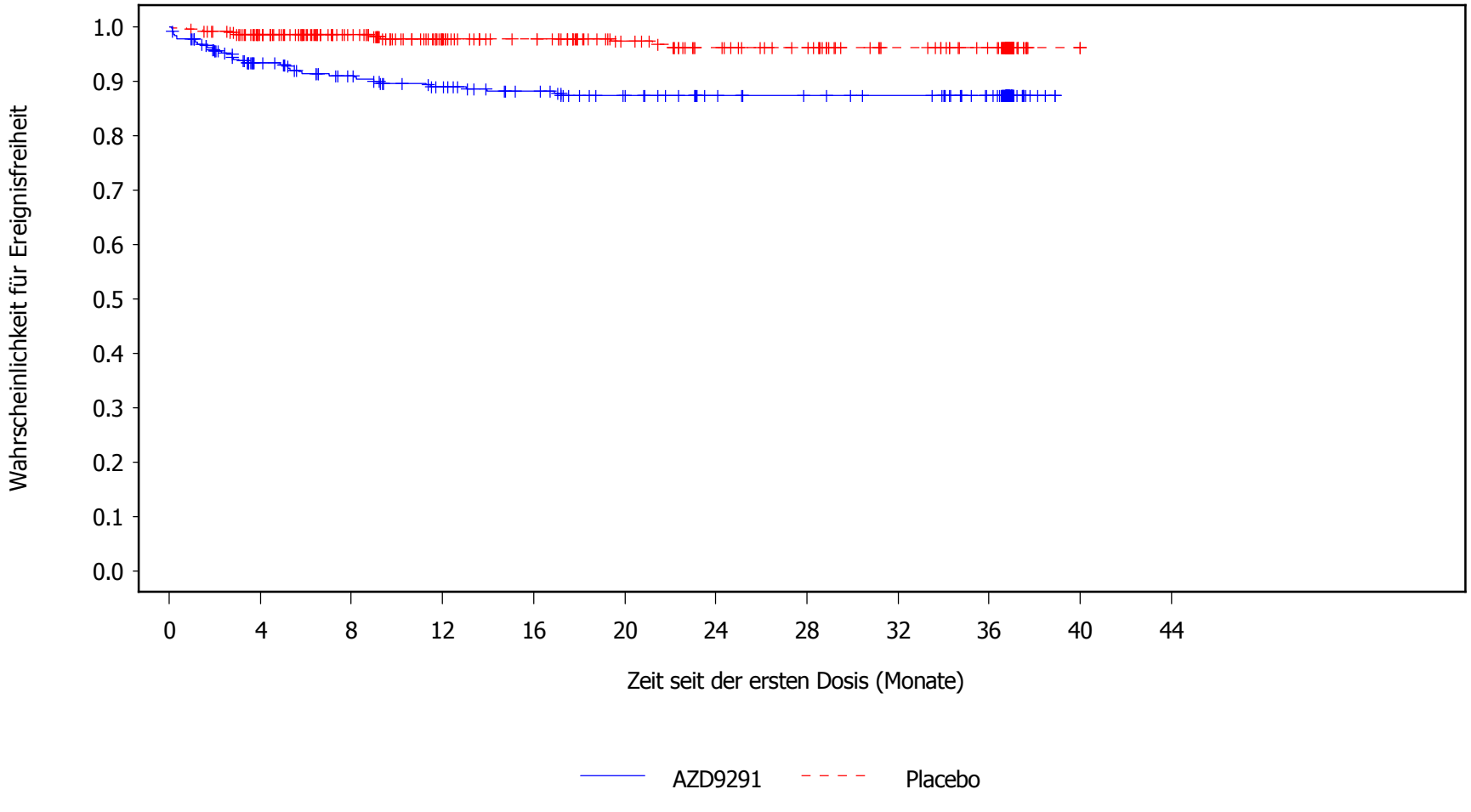


Anzahl an Patienten unter Risiko:

337	295	279	268	256	243	232	229	226	211	0	0	AZD9291
343	318	276	233	217	191	176	166	149	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbx 30JUN2023:09:36 kvbv306

Figure 3.3.51 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Mundulzeration
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	286	264	248	236	223	212	208	205	192	0	0	AZD9291
343	315	273	228	212	186	170	161	145	134	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bby 30JUN2023:09:36 kvbv306

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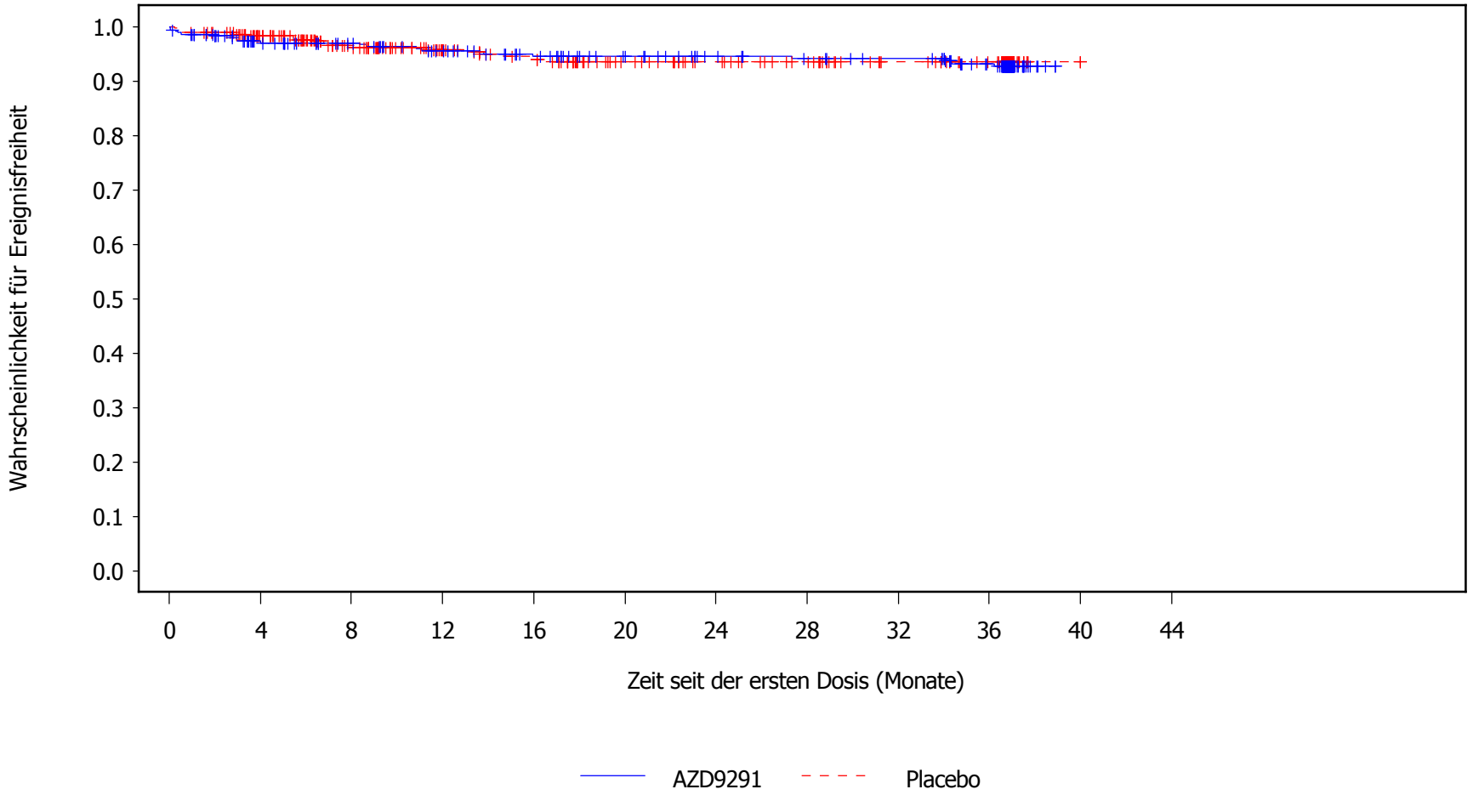
Figure 3.3.52 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Obstipation
Safety Analysis Set, DCO 11Apr2022

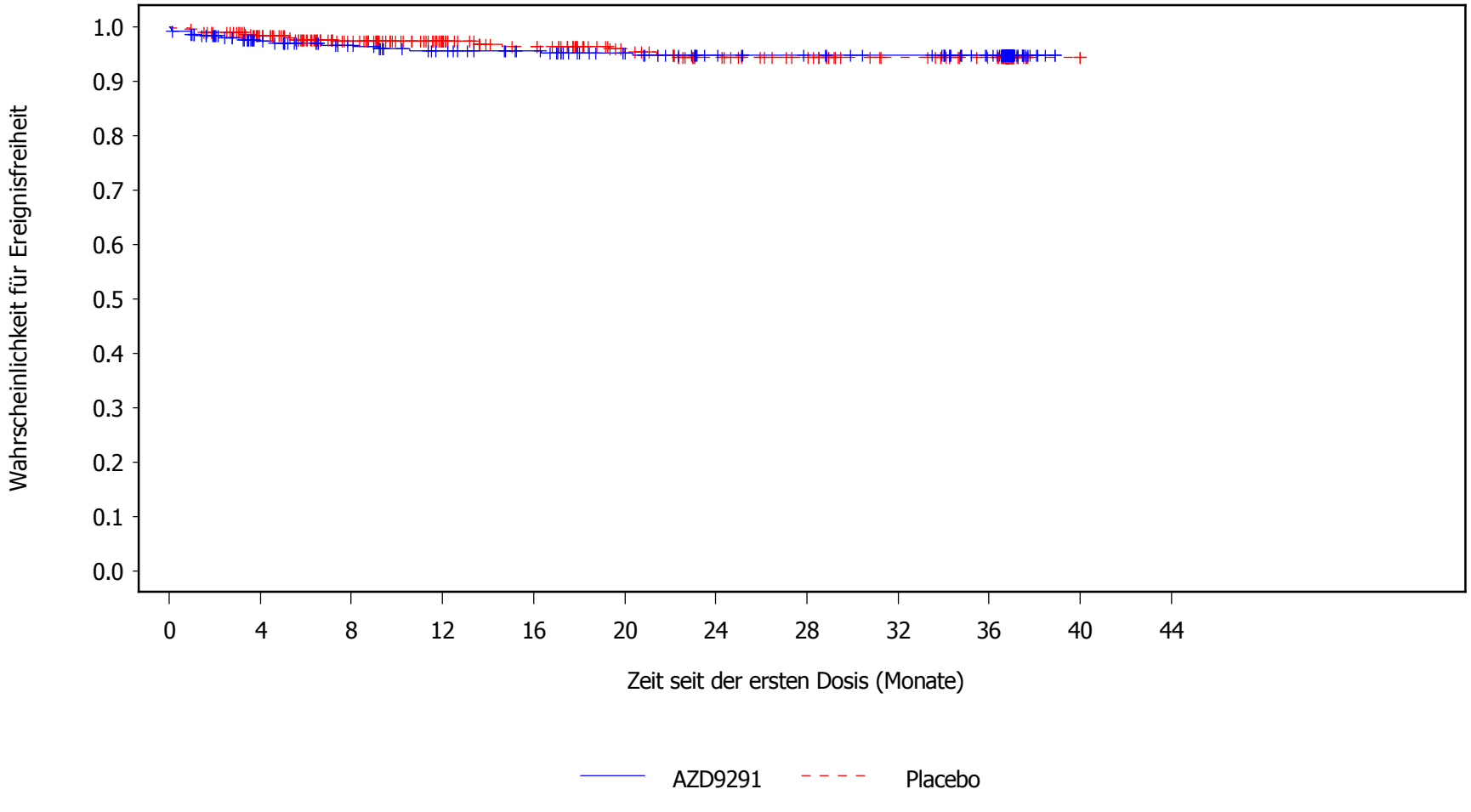


Anzahl an Patienten unter Risiko:

337	301	285	271	256	243	232	227	223	206	0	0	AZD9291
343	314	268	224	208	182	169	159	143	132	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bbz 30JUN2023:09:36 kvbv306

Figure 3.3.53 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Schmerzen Oberbauch
Safety Analysis Set, DCO 11Apr2022

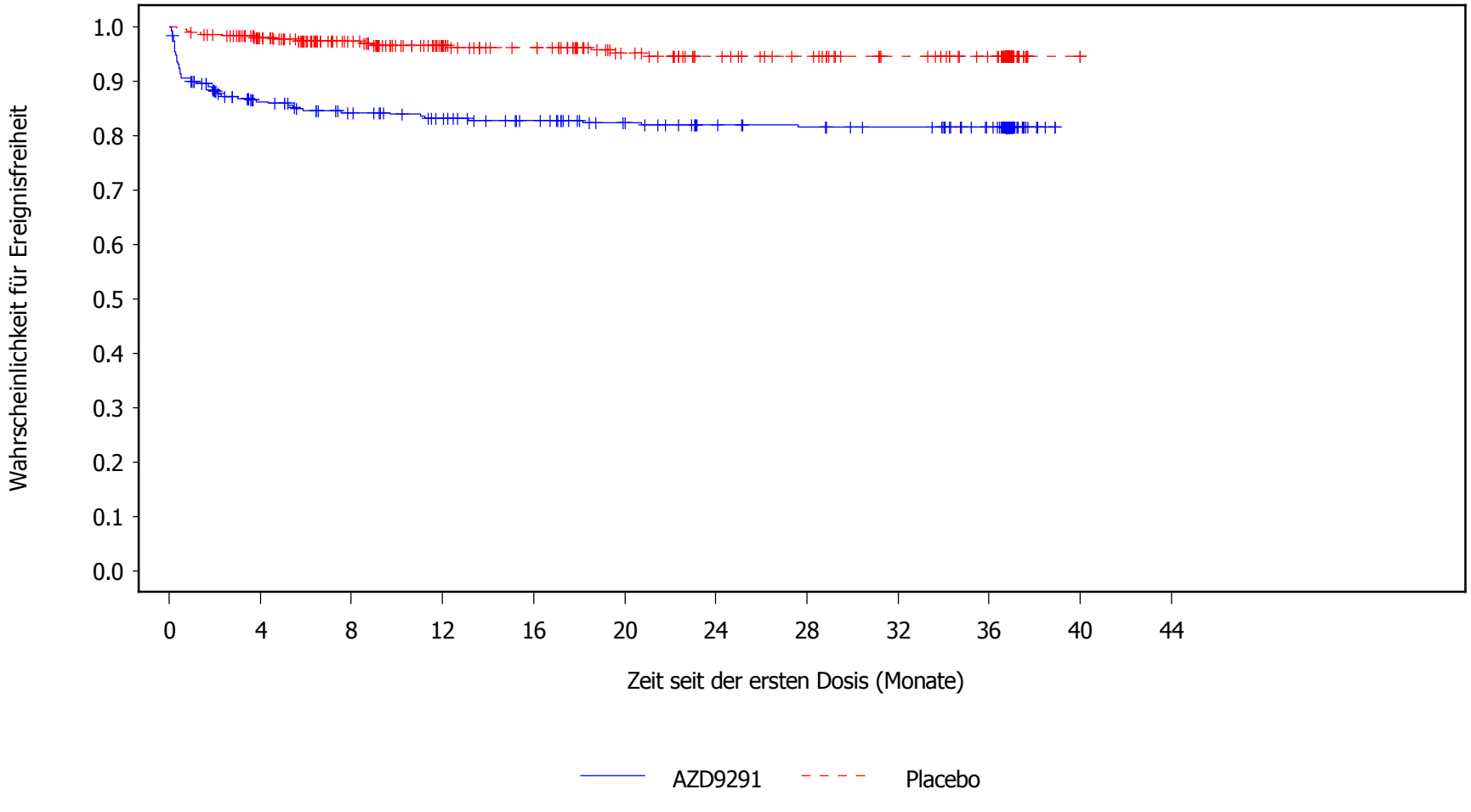


Anzahl an Patienten unter Risiko:

337	300	282	269	260	246	233	229	225	211	0	0	AZD9291
343	314	271	227	210	183	166	156	143	132	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bca 30JUN2023:09:36 kvbv306

Figure 3.3.54 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Stomatitis
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	265	247	235	223	209	198	194	190	177	0	0	AZD9291
343	314	270	225	210	184	168	160	148	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcb 30JUN2023:09:36 kvbv306

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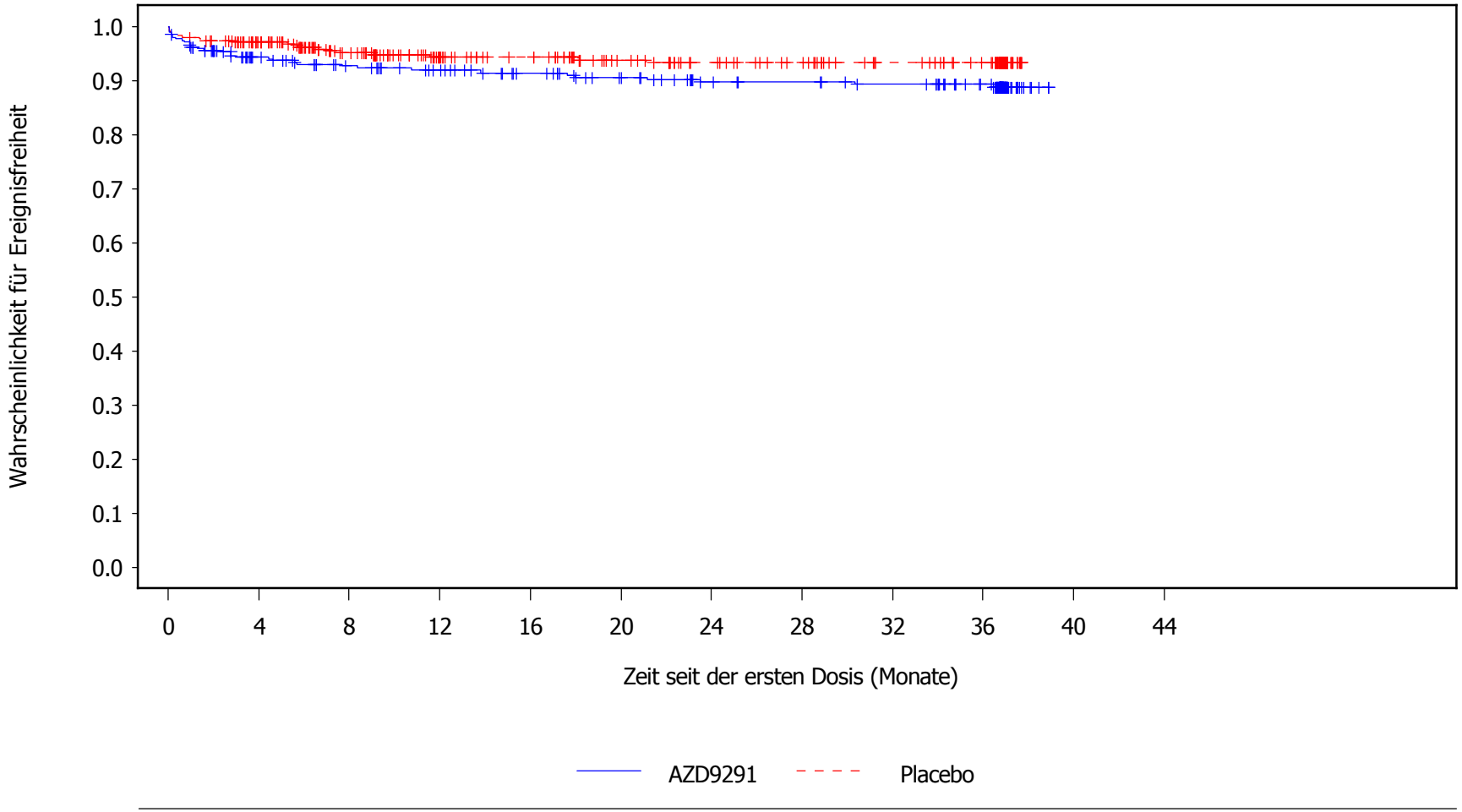
Figure 3.3.55 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Uebelkeit
Safety Analysis Set, DCO 11Apr2022

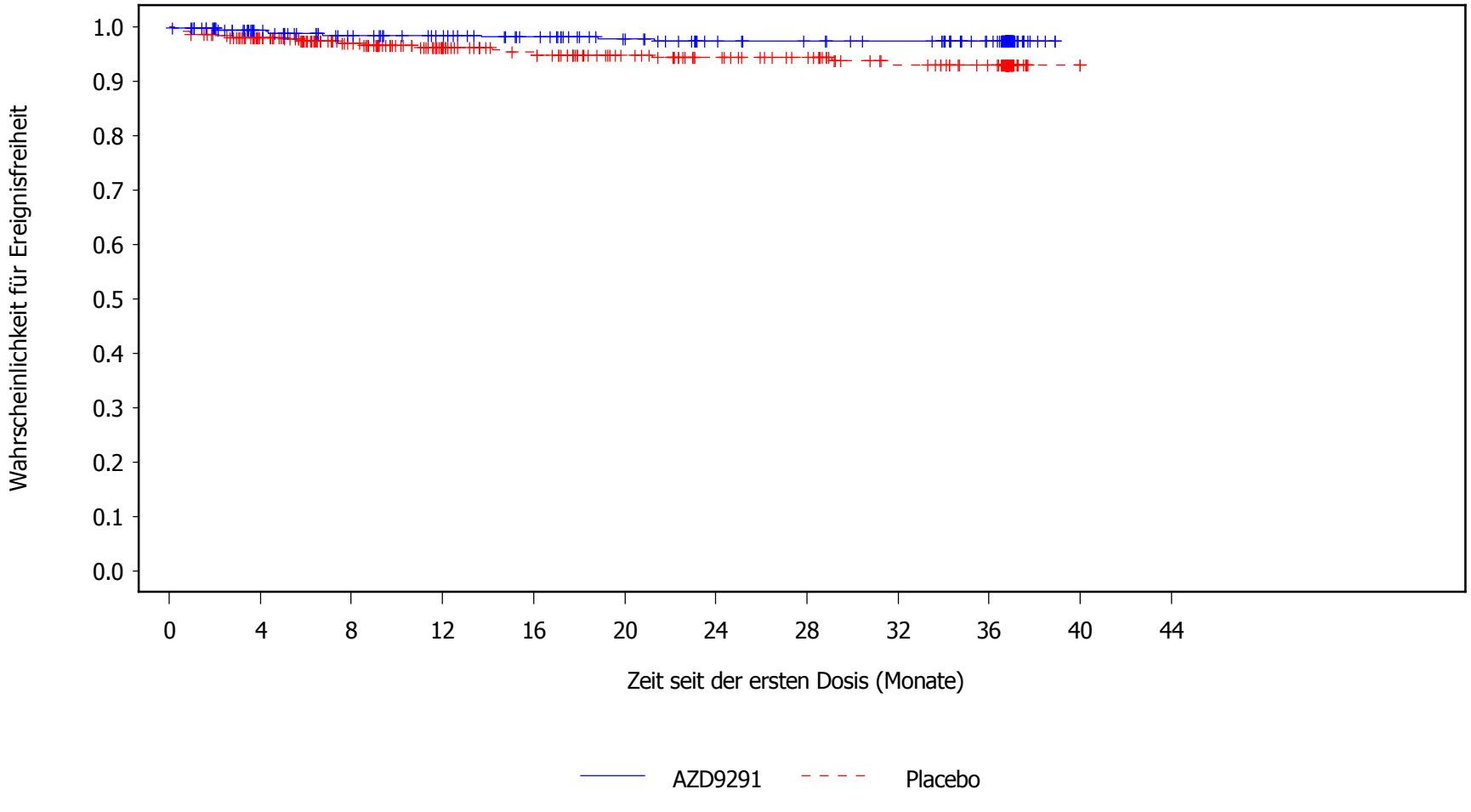


Anzahl an Patienten unter Risiko:

337	290	272	261	247	235	221	218	213	198	0	0	AZD9291
343	312	268	223	209	184	169	159	145	134	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcc 30JUN2023:09:36 kvbv306

Figure 3.3.56 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Zahnschmerzen
Safety Analysis Set, DCO 11Apr2022

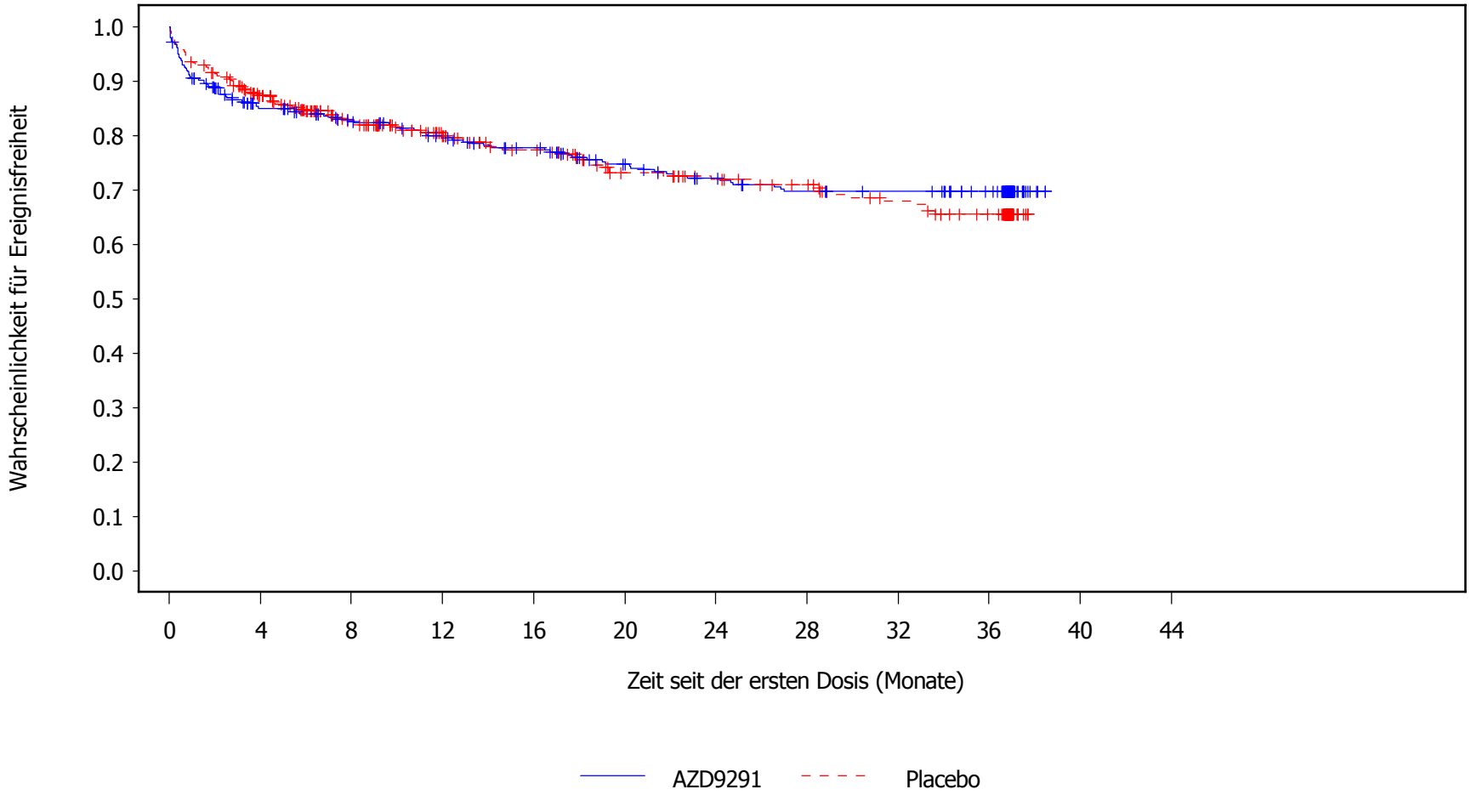


Anzahl an Patienten unter Risiko:

337	306	288	278	266	252	239	235	231	216	0	0	AZD9291
343	313	269	224	206	182	166	156	139	128	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcd 30JUN2023:09:36 kvbv306

Figure 3.3.57 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen des Nervensystems
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	264	244	229	216	197	184	175	172	161	0	0	AZD9291
343	281	232	191	171	145	134	126	112	100	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bce 30JUN2023:09:36 kvbv306

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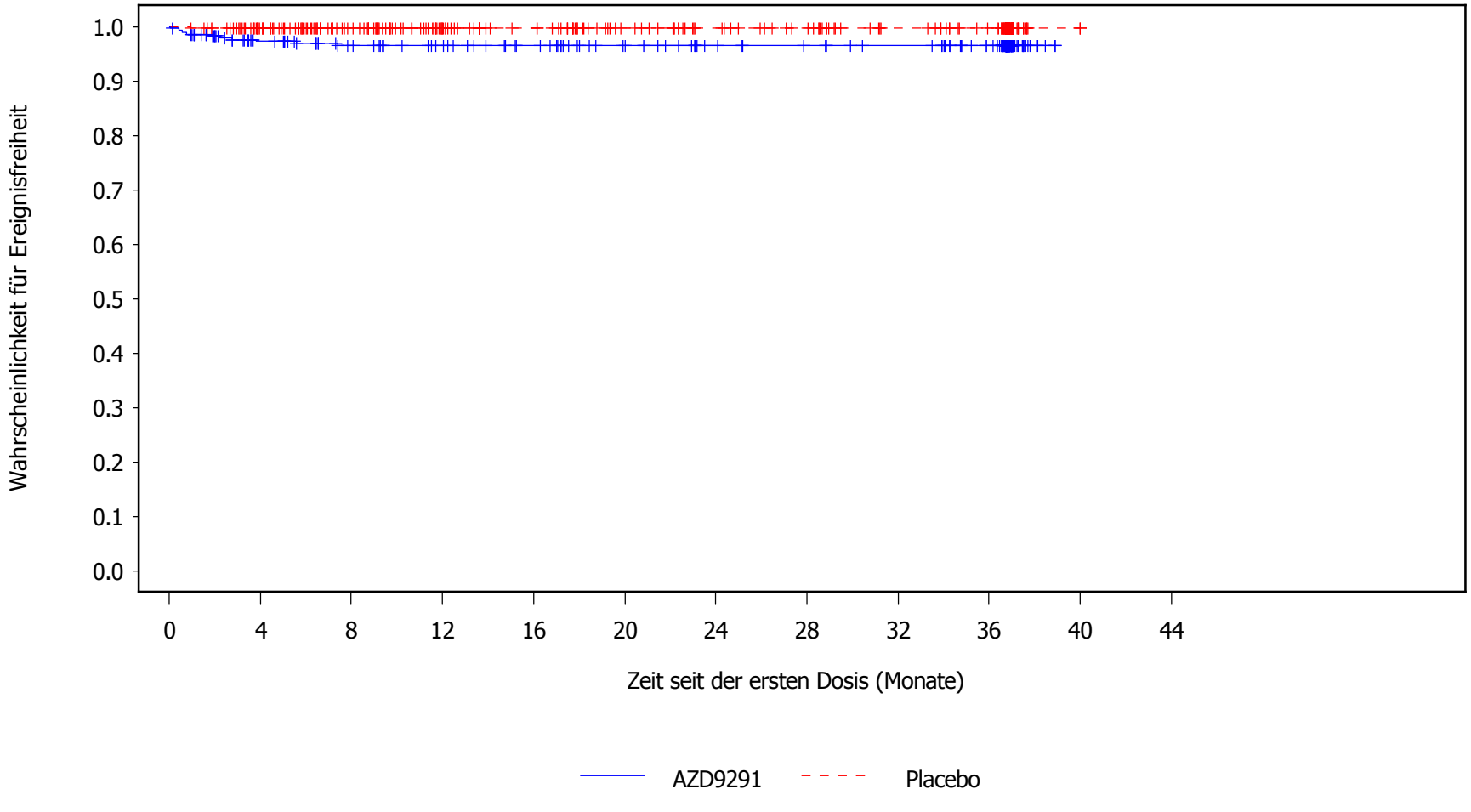
Figure 3.3.58 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Dysgeusie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	300	284	274	264	251	239	235	231	217	0	0	AZD9291
343	319	277	233	217	192	177	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcf 30JUN2023:09:36 kvbv306

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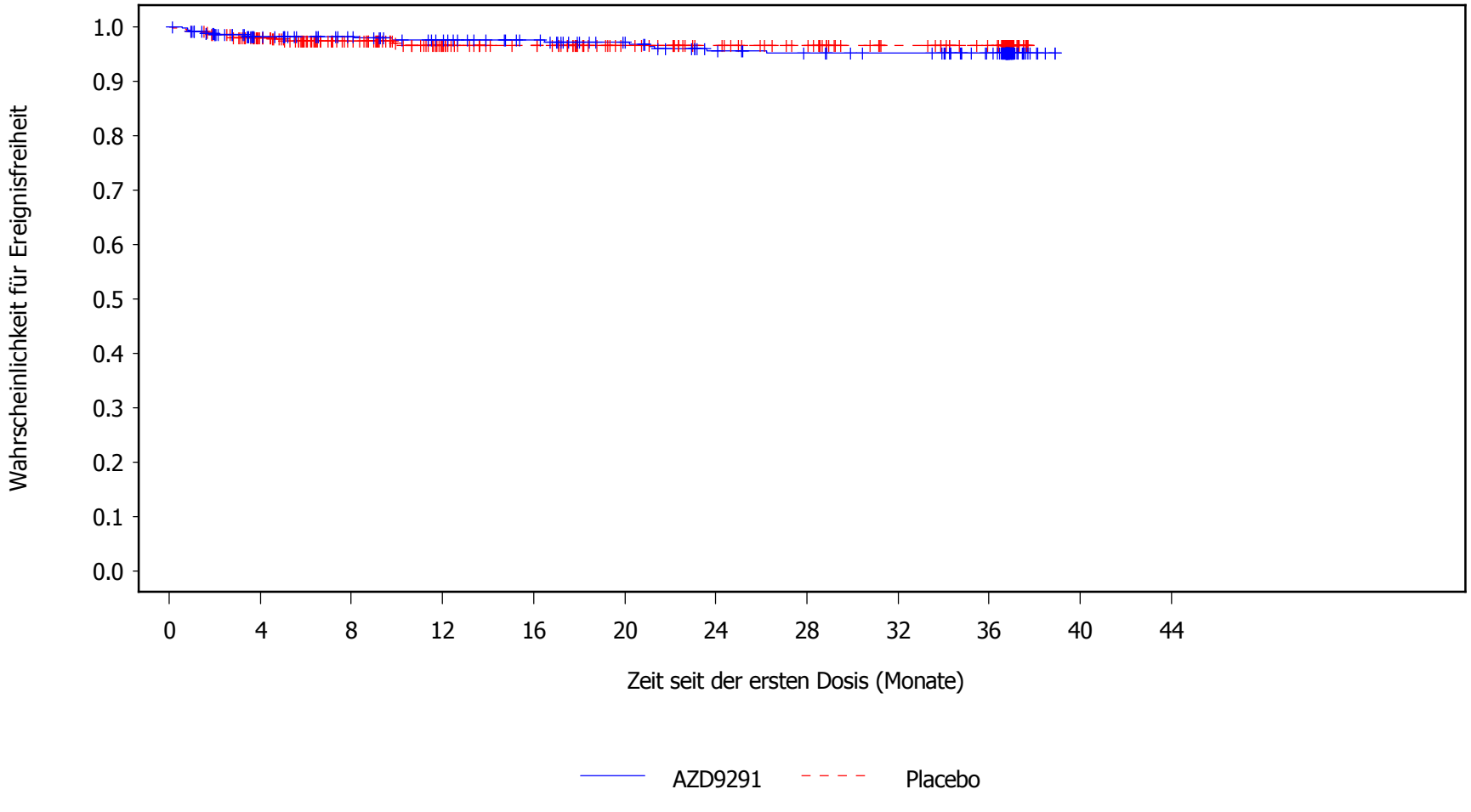
Figure 3.3.59 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Hypoaesthesie
Safety Analysis Set, DCO 11Apr2022

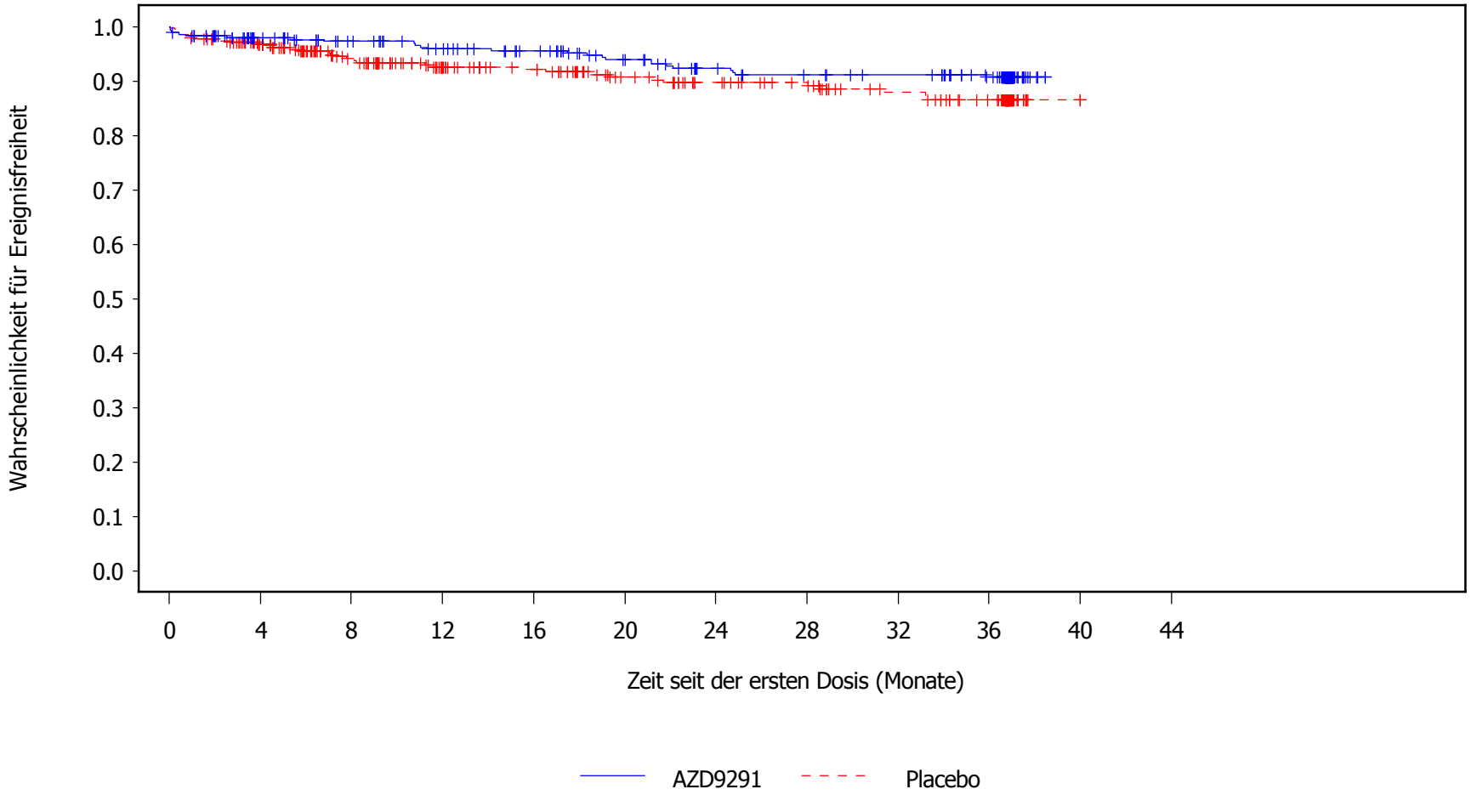


Anzahl an Patienten unter Risiko:

337	302	287	276	265	252	238	233	229	216	0	0	AZD9291
343	314	270	226	210	186	172	162	146	136	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcg 30JUN2023:09:36 kvbv306

Figure 3.3.60 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Kopfschmerzen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	286	273	261	244	229	222	218	204	0	0	AZD9291
343	310	264	220	204	179	163	154	138	125	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bch 30JUN2023:09:36 kvbv306

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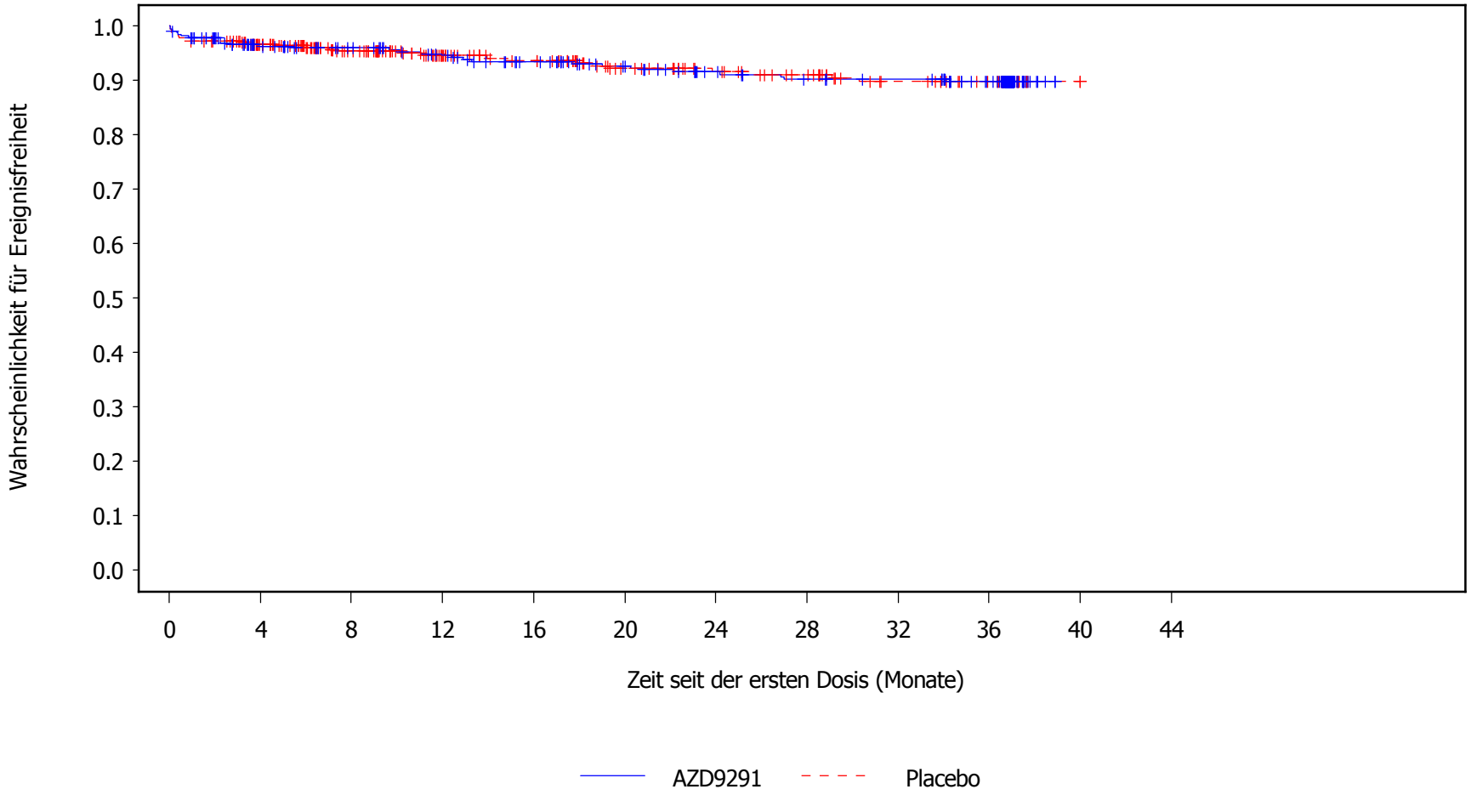
Figure 3.3.61 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Schwindelgefuehl
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	297	281	268	253	238	224	217	214	199	0	0	AZD9291
343	310	266	223	206	181	167	157	141	130	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bci 30JUN2023:09:36 kvbv306

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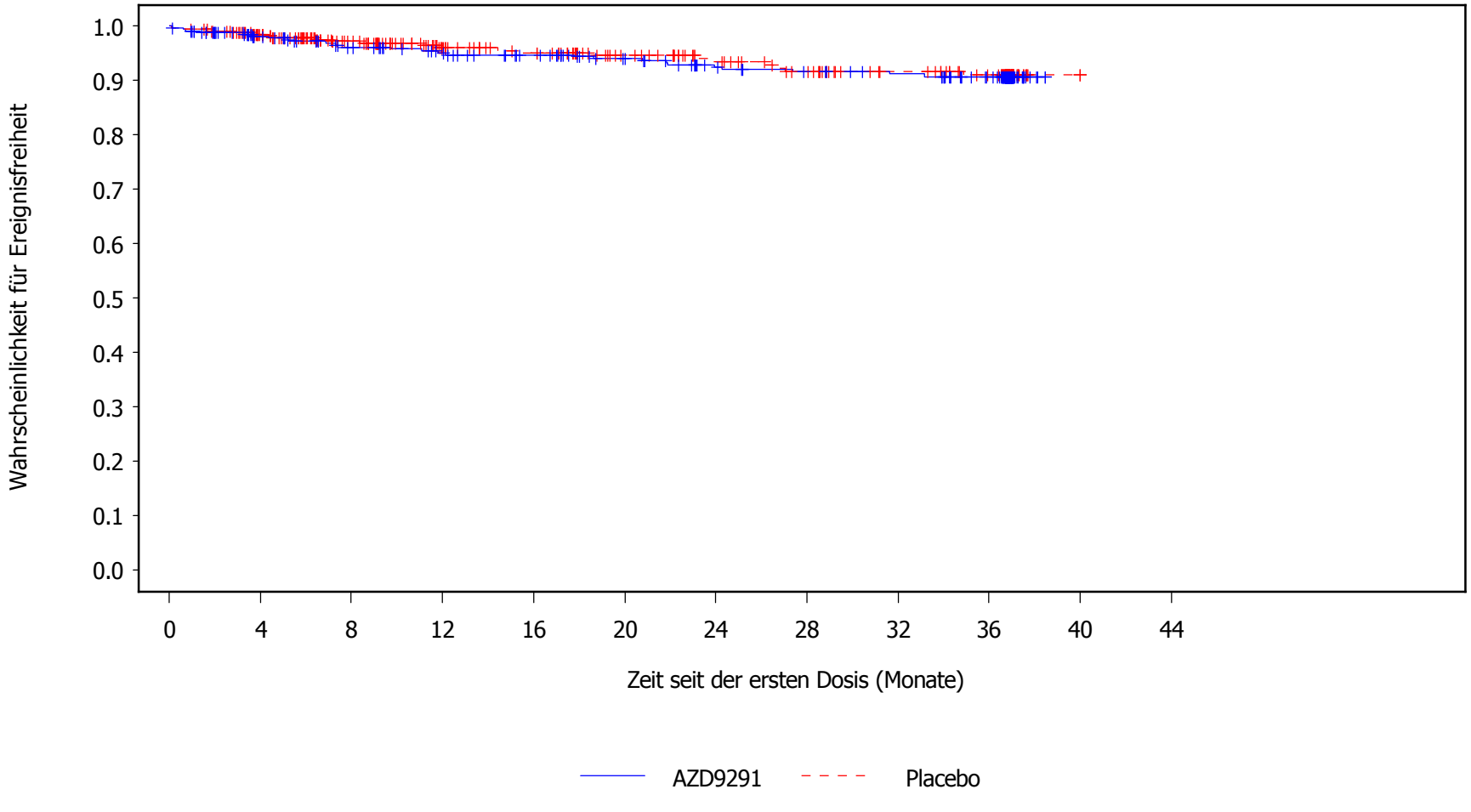
Figure 3.3.62 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Erkrankungen des Ohrs und des Labyrinths
Safety Analysis Set, DCO 11Apr2022

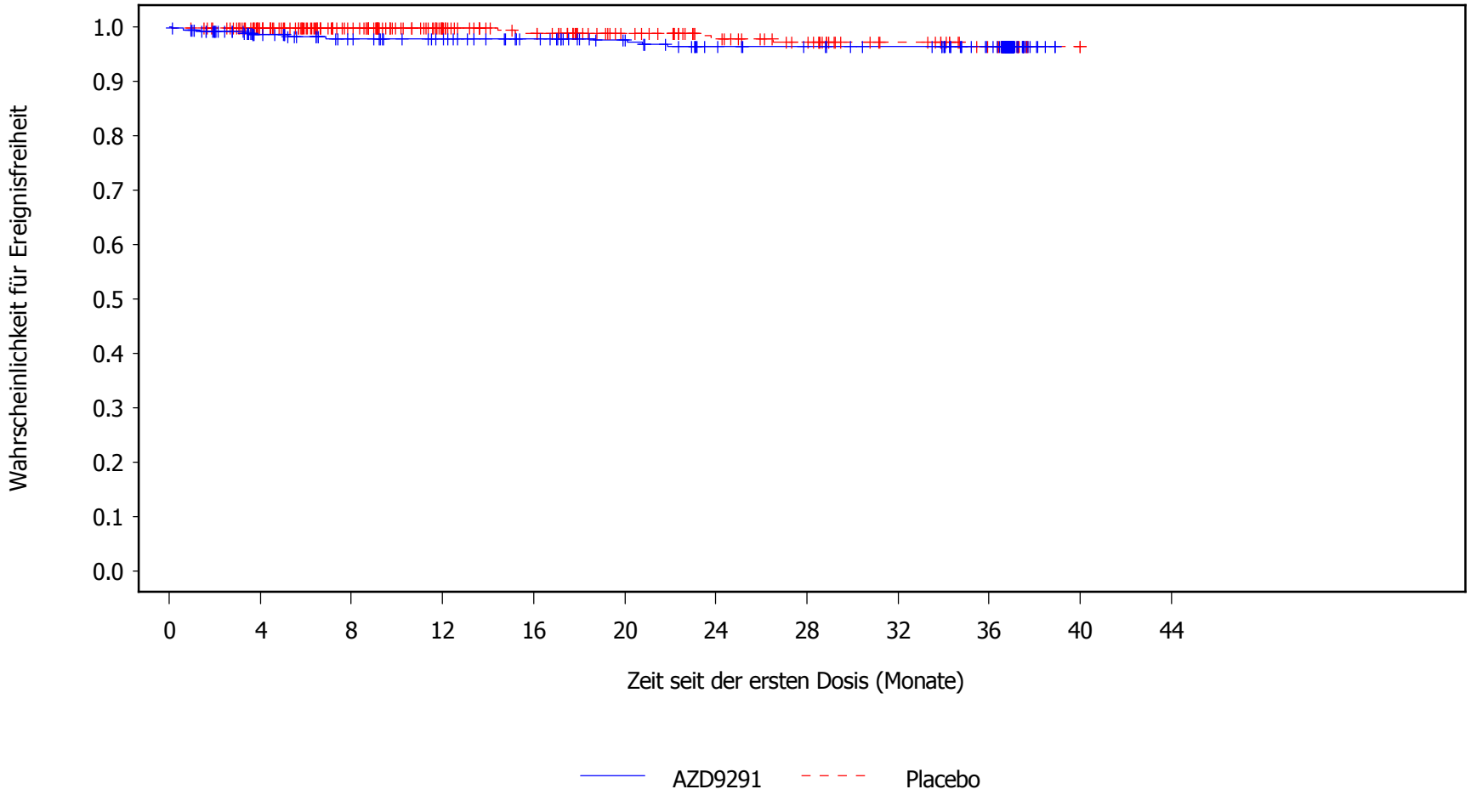


Anzahl an Patienten unter Risiko:

337	304	283	270	258	243	228	222	217	202	0	0	AZD9291
343	315	270	225	210	185	168	156	141	129	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcj 30JUN2023:09:36 kvbv306

Figure 3.3.63 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Vertigo
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	304	287	277	265	251	237	233	229	214	0	0	AZD9291
343	319	277	233	215	191	174	163	148	136	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bck 30JUN2023:09:36 kvbv306

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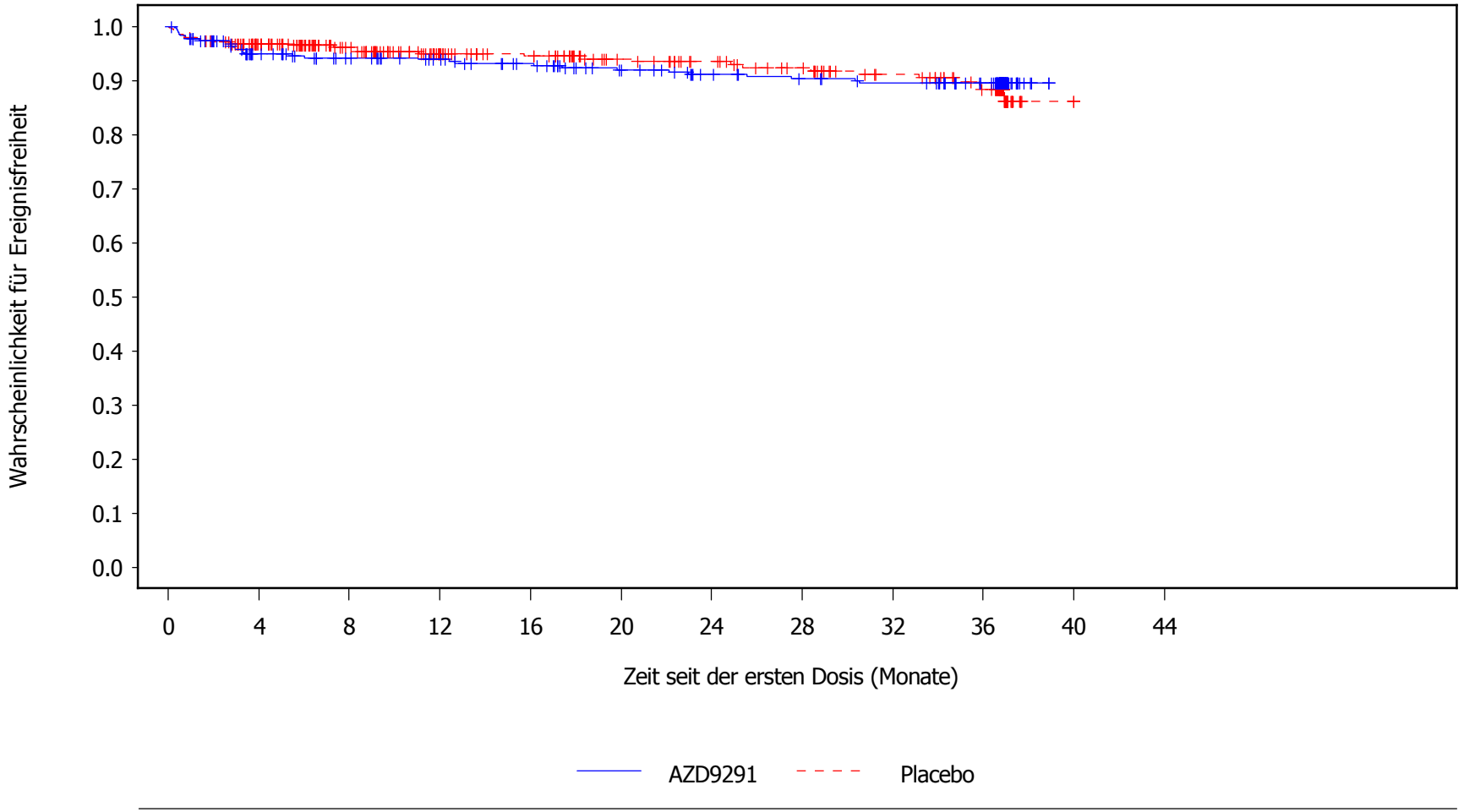
Figure 3.3.64 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Gefaesserkrankungen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	294	278	267	256	240	228	222	217	204	0	0	AZD9291
343	310	266	220	204	179	168	157	141	126	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcl 30JUN2023:09:36 kvbv306

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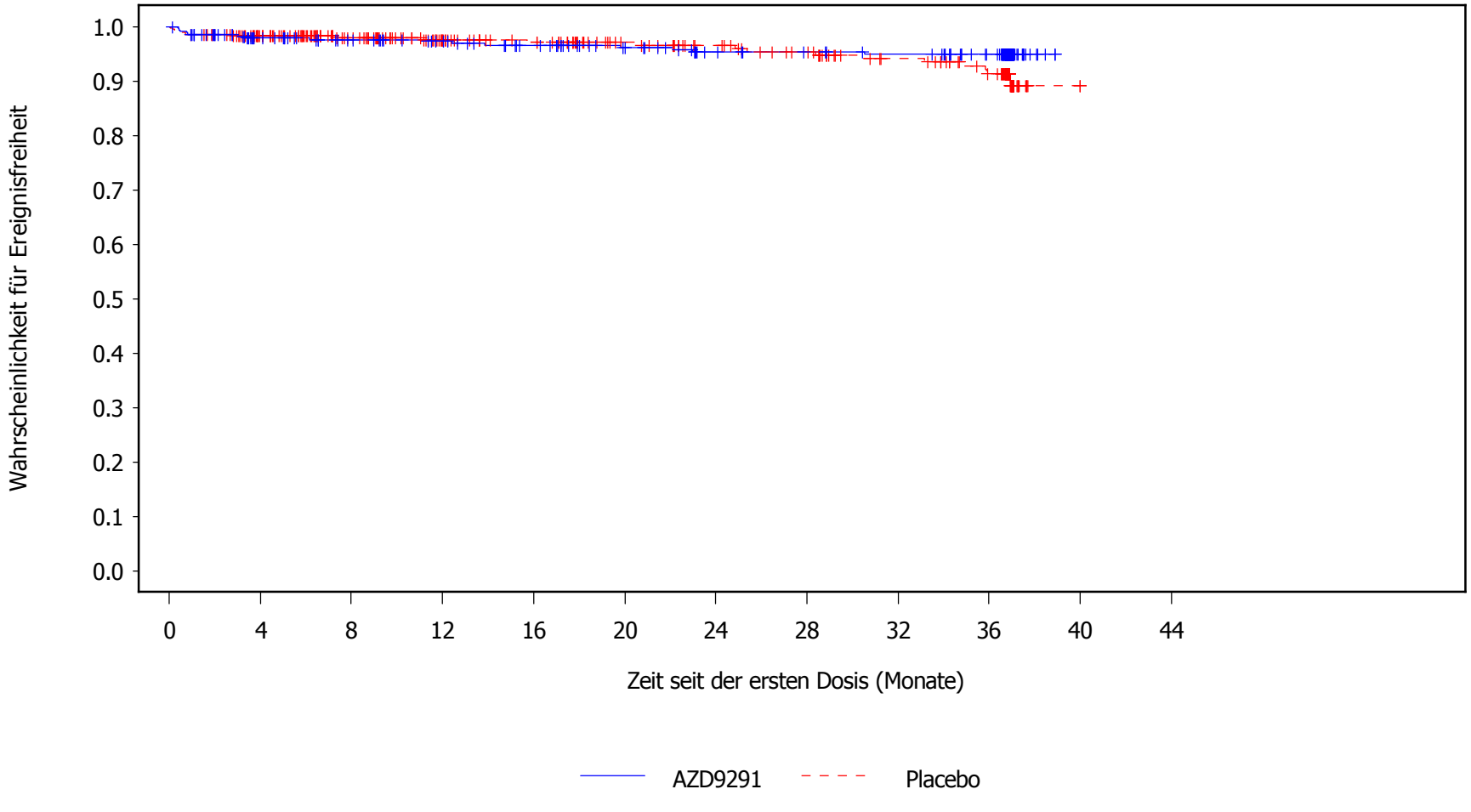
Figure 3.3.65 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Hypertonie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	288	277	265	251	237	233	229	216	0	0	AZD9291
343	314	271	227	210	185	171	160	143	128	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcm 30JUN2023:09:36 kvbv306

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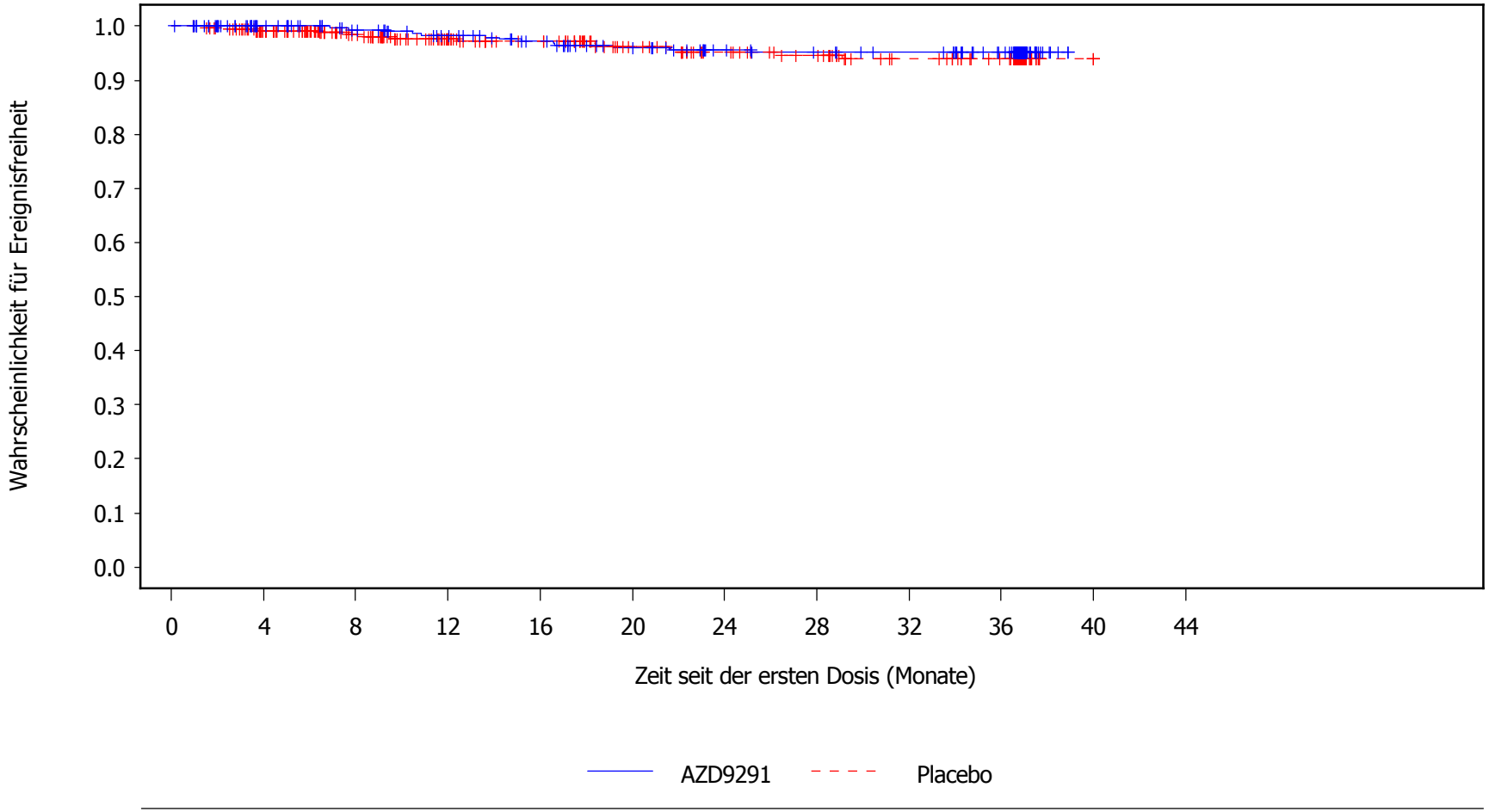
Figure 3.3.66 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Gutartige, boesartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	308	291	278	265	251	238	233	229	215	0	0	AZD9291
343	317	275	231	214	187	170	160	144	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcn 30JUN2023:09:36 kvbv306

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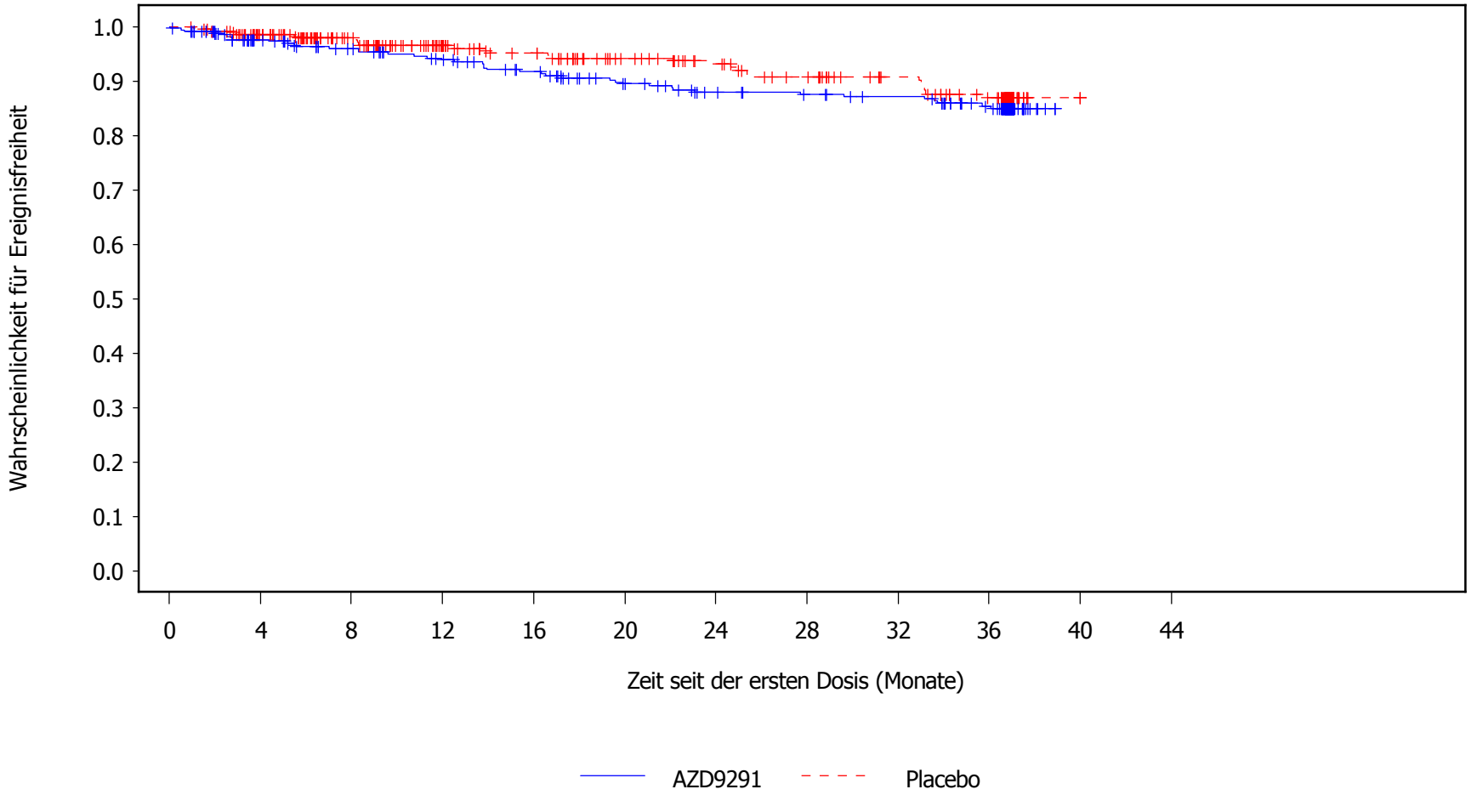
Figure 3.3.67 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Herzerkrankungen
Safety Analysis Set, DCO 11Apr2022

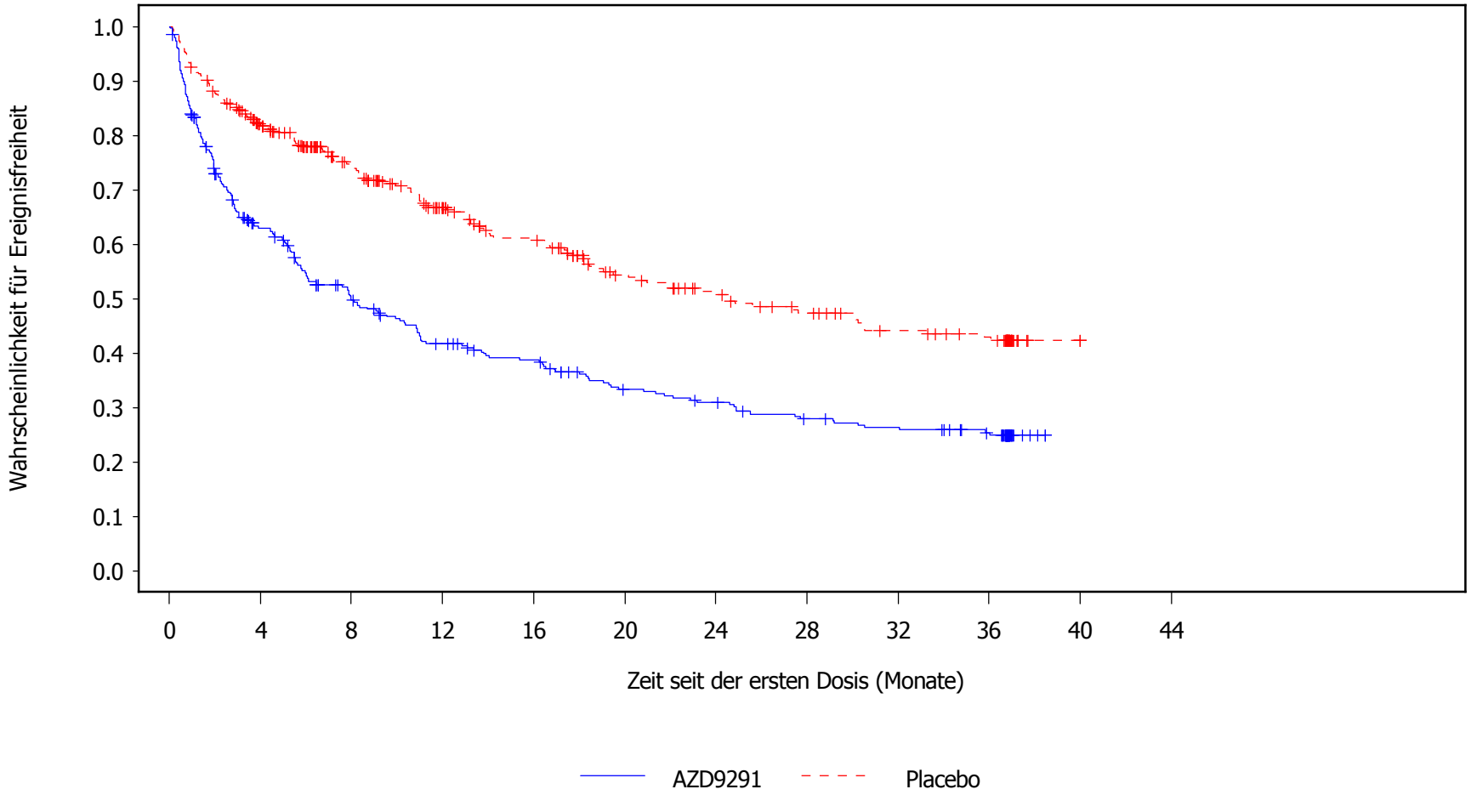


Anzahl an Patienten unter Risiko:

337	300	281	267	253	234	221	216	211	194	0	0	AZD9291
343	316	272	224	206	182	168	156	142	126	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bco 30JUN2023:09:36 kvbv306

Figure 3.3.68 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Infektionen und parasitaere Erkrankungen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	195	145	117	104	83	76	66	61	53	0	0	AZD9291
343	264	207	161	136	106	93	81	70	64	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcp 30JUN2023:09:36 kvbv306

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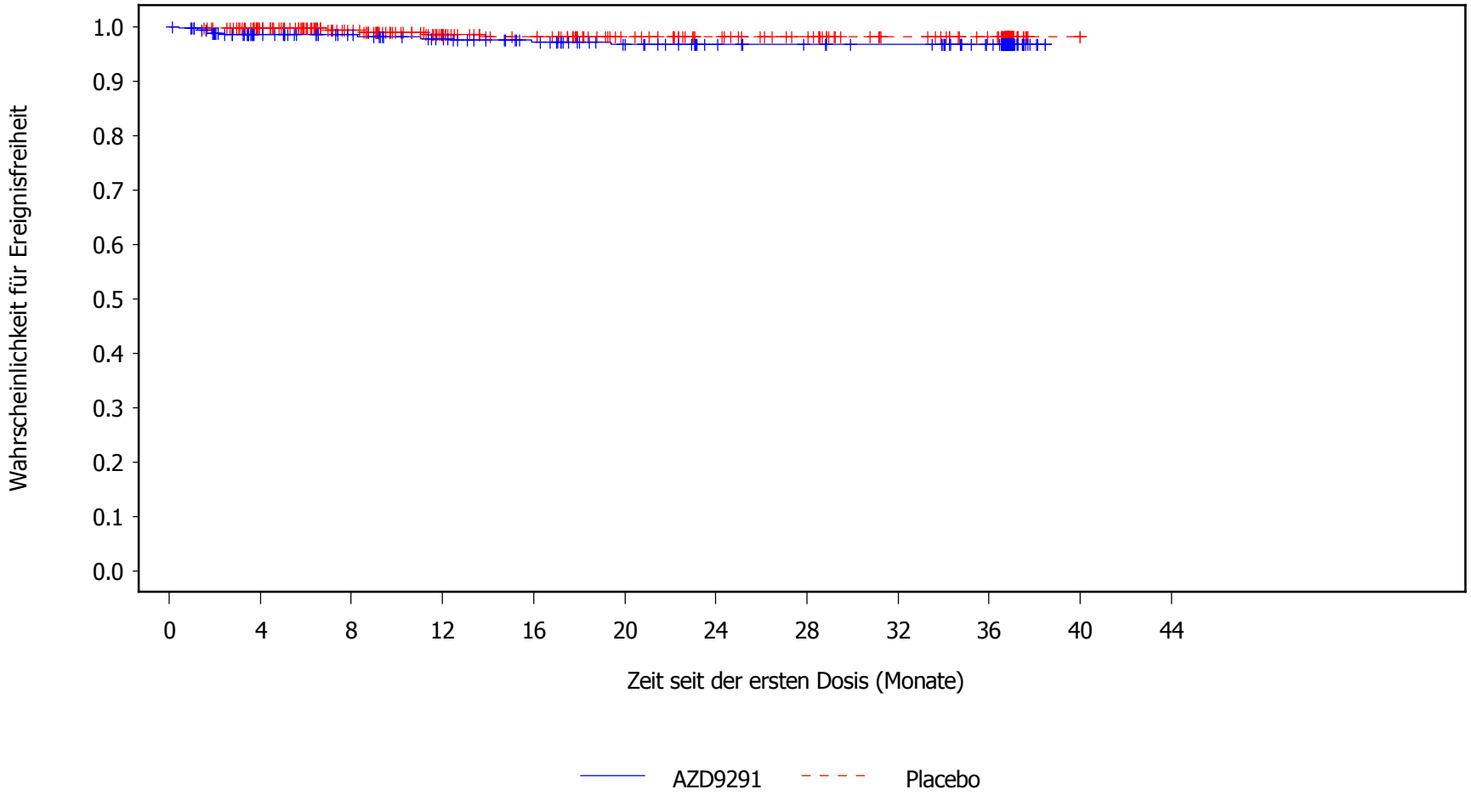
Figure 3.3.69 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Bakterielle Harnwegsinfektion
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	288	276	262	248	236	232	229	215	0	0	AZD9291
343	319	277	231	214	189	175	165	149	139	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcq 30JUN2023:09:36 kvbv306

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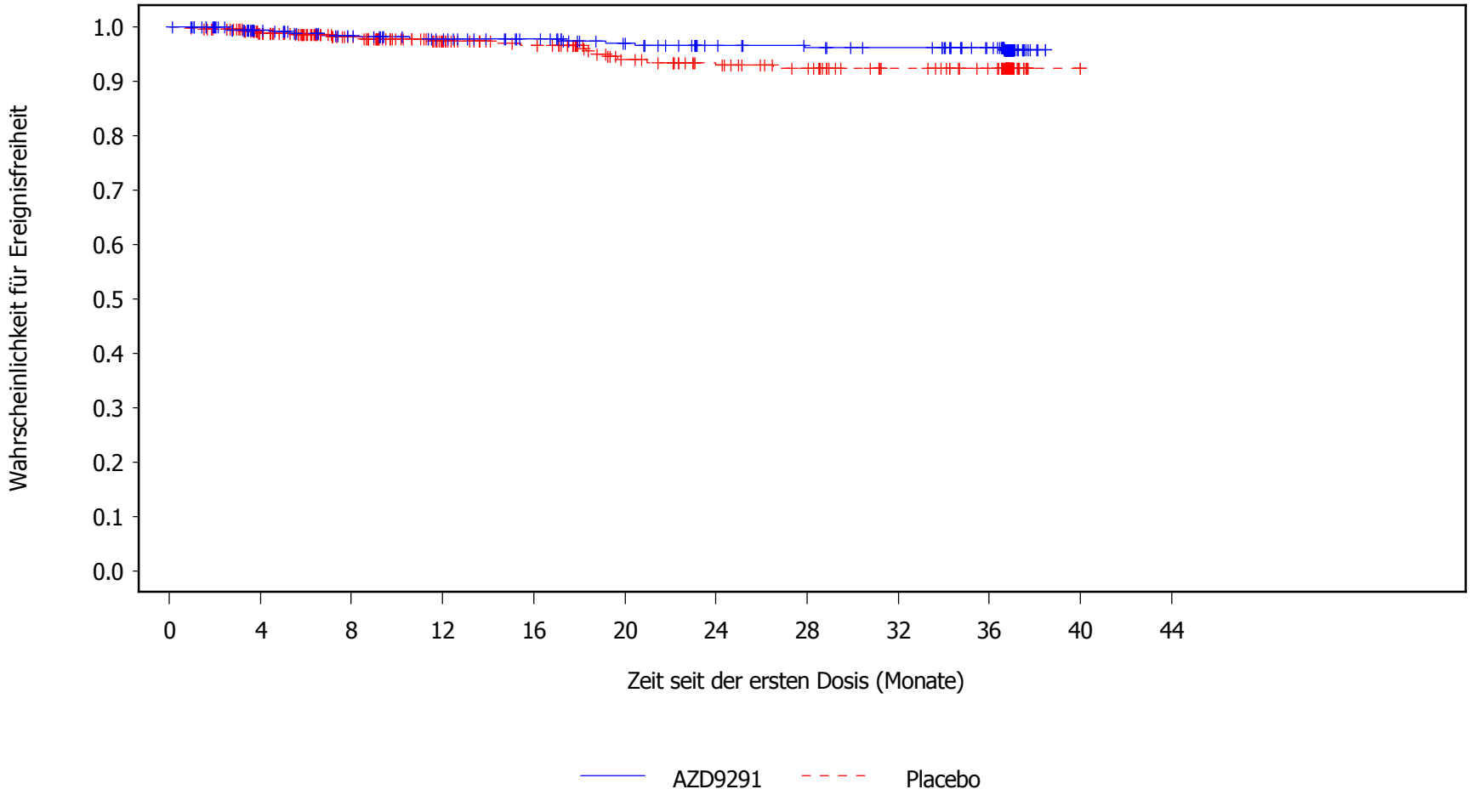
Figure 3.3.70 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Bronchitis
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	306	288	276	264	250	237	232	228	214	0	0	AZD9291
343	316	273	228	210	181	167	157	142	132	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcr 30JUN2023:09:36 kvbv306

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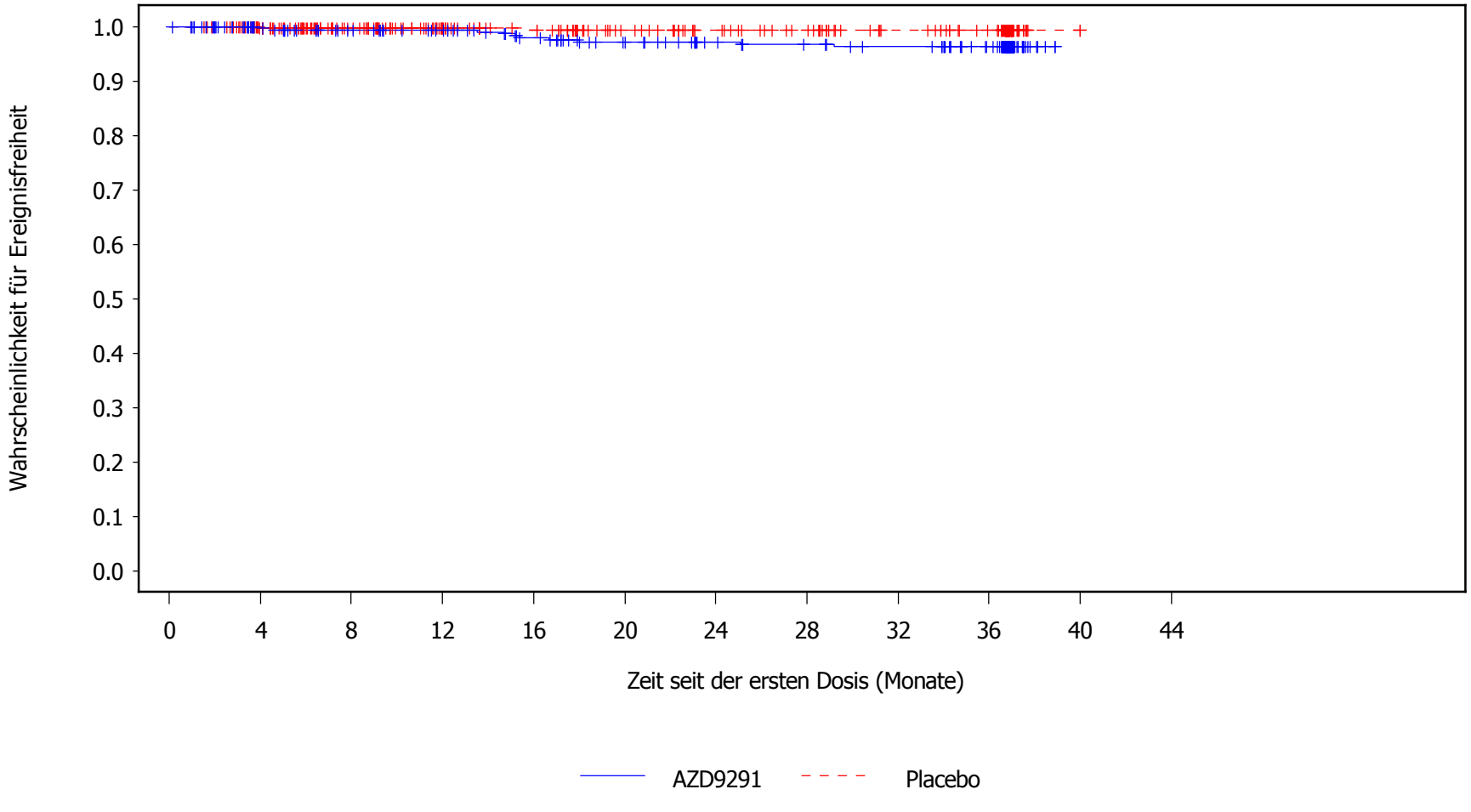
Figure 3.3.71 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Gastroenteritis
Safety Analysis Set, DCO 11Apr2022

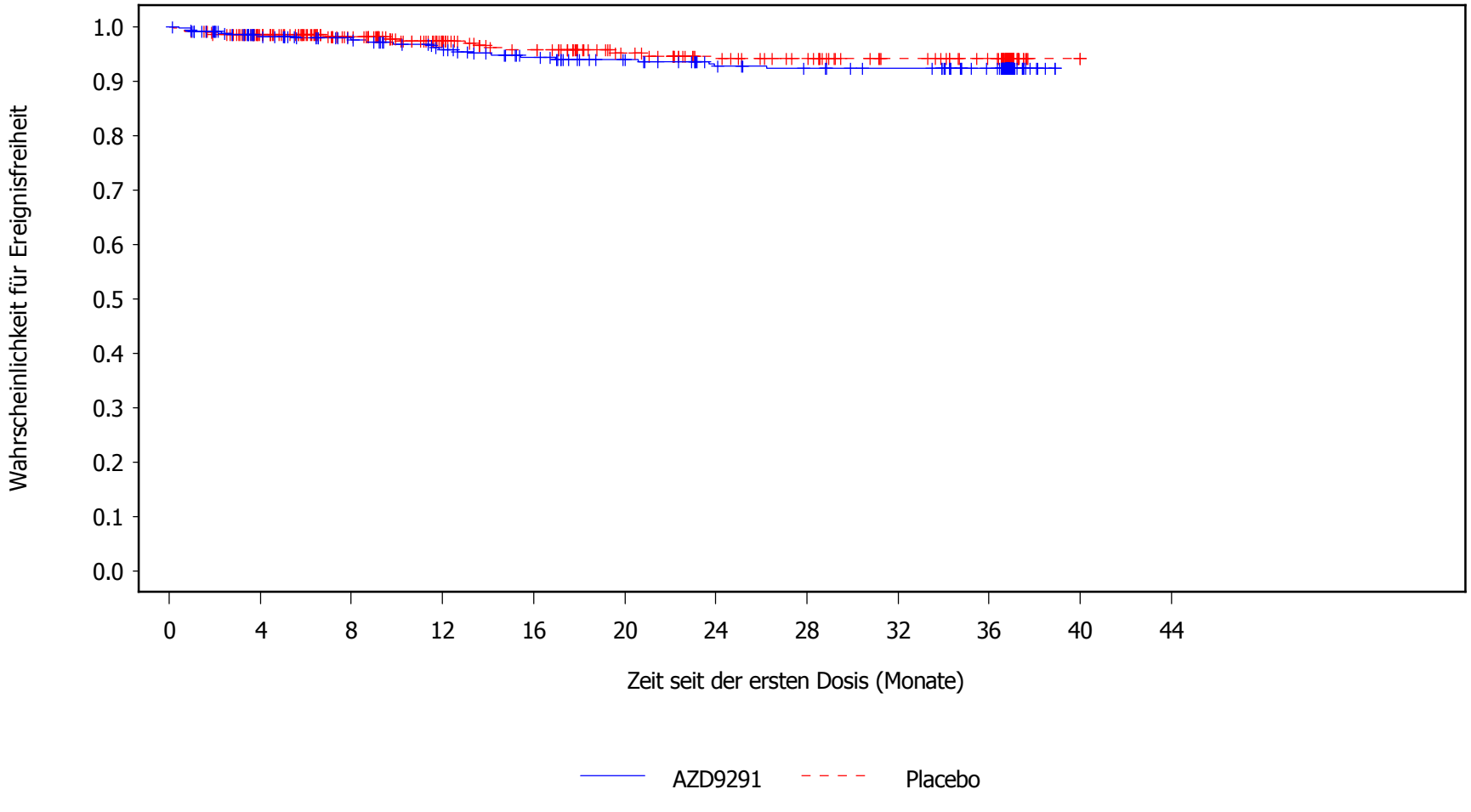


Anzahl an Patienten unter Risiko:

337	308	291	281	265	250	238	233	228	213	0	0	AZD9291
343	319	277	234	217	192	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcs 30JUN2023:09:36 kvbv306

Figure 3.3.72 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Grippe
Safety Analysis Set, DCO 11Apr2022

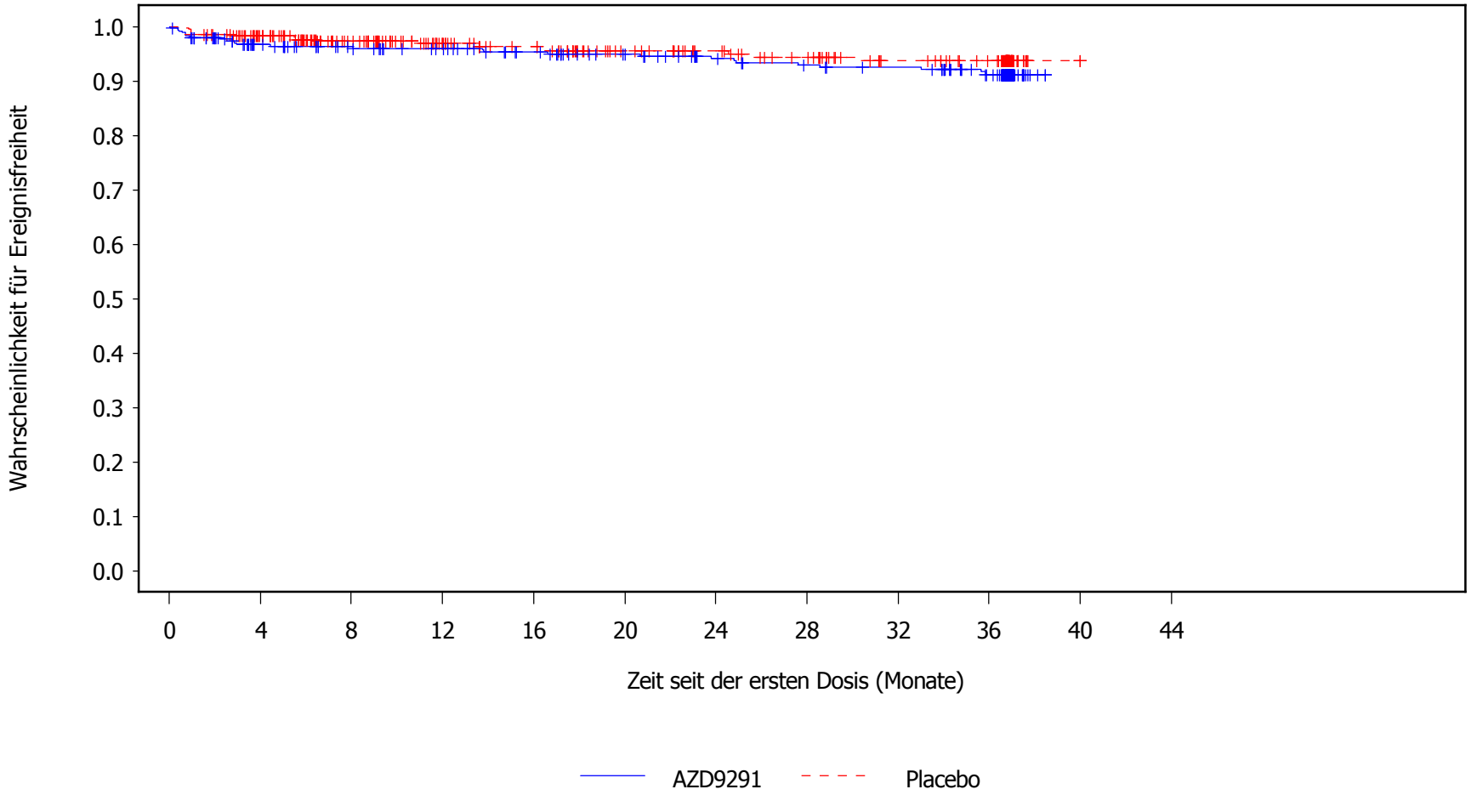


Anzahl an Patienten unter Risiko:

337	302	285	270	254	240	226	221	217	204	0	0	AZD9291
343	315	272	230	210	184	168	158	143	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bct 30JUN2023:09:36 kvbv306

Figure 3.3.73 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Harnwegsinfektion
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	298	282	272	259	246	233	226	222	204	0	0	AZD9291
343	315	270	227	211	184	171	160	143	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcu 30JUN2023:09:36 kvbv306

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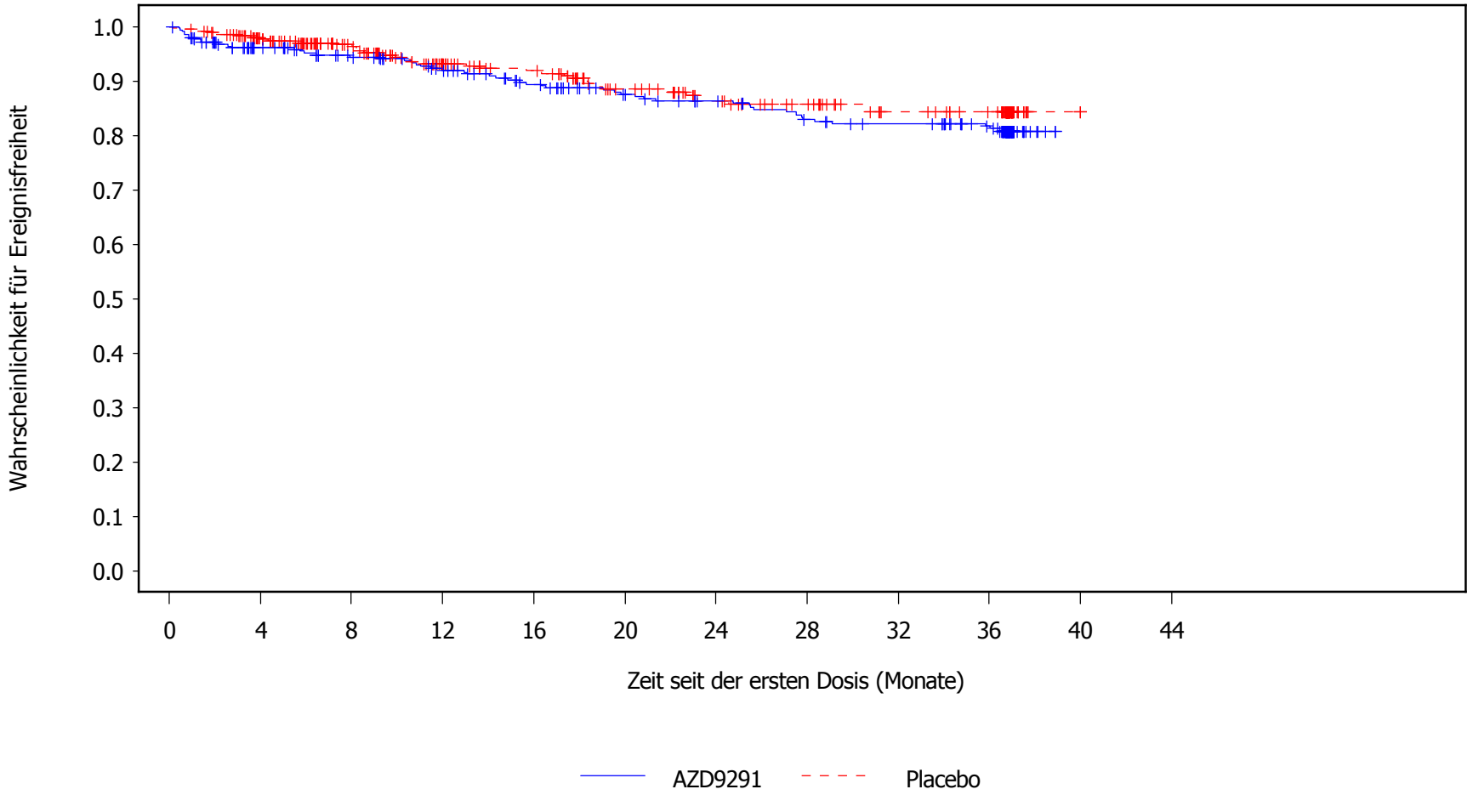
Figure 3.3.74 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Infektion der oberen Atemwege
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	296	276	259	240	222	212	200	194	180	0	0	AZD9291
343	313	268	218	200	172	153	142	126	119	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcv 30JUN2023:09:36 kvbv306

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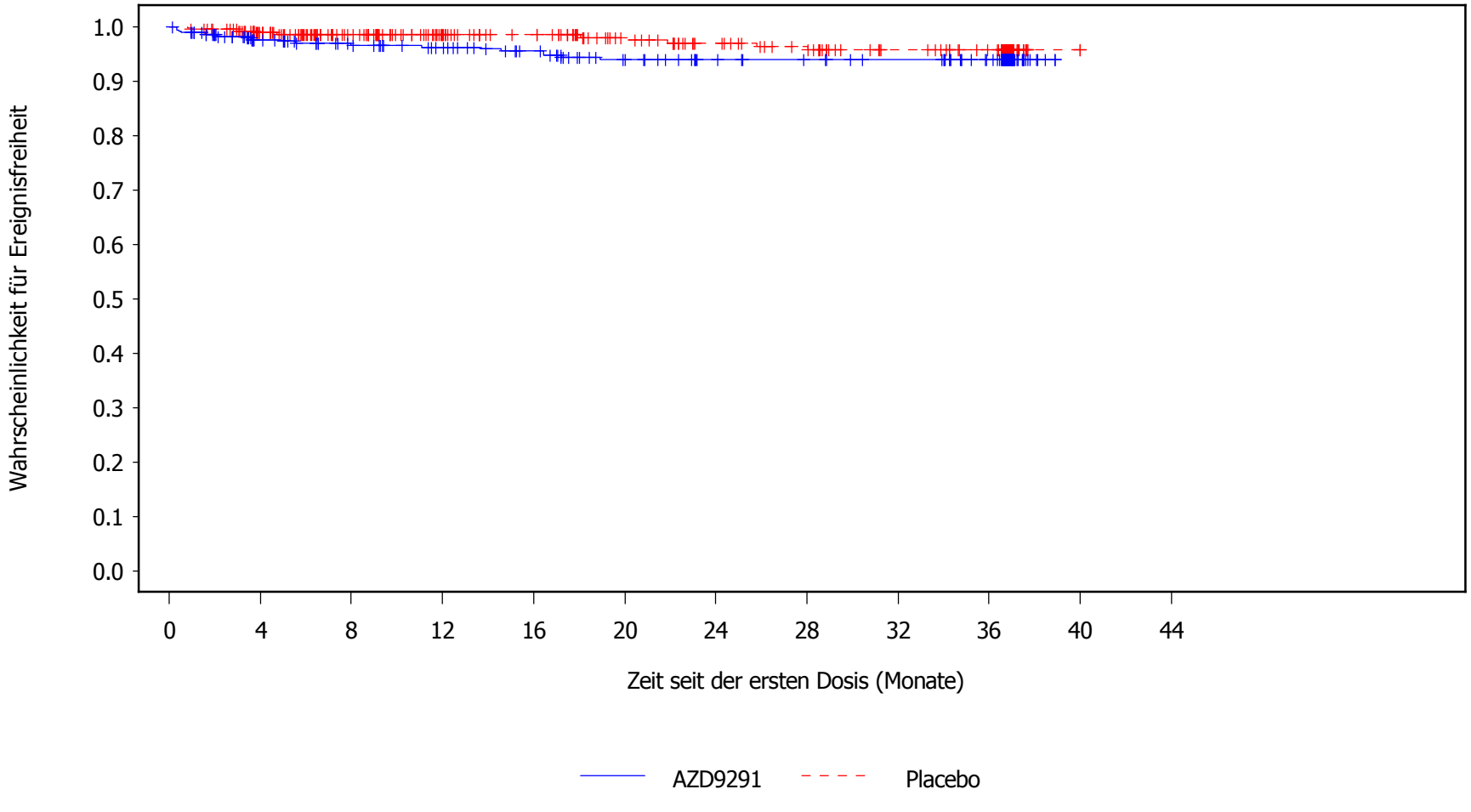
Figure 3.3.75 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Konjunktivitis
Safety Analysis Set, DCO 11Apr2022

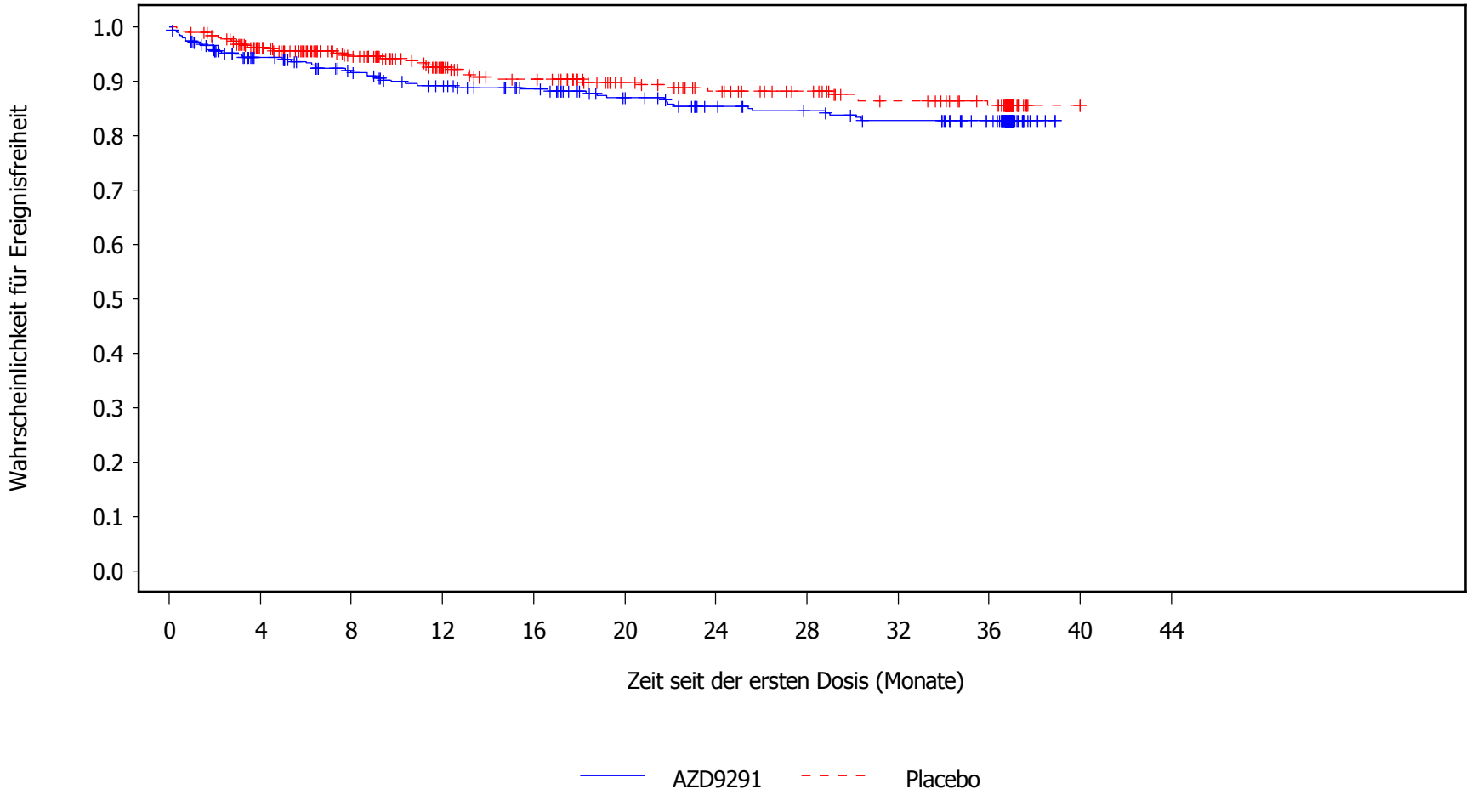


Anzahl an Patienten unter Risiko:

337	300	282	271	258	241	230	226	222	209	0	0	AZD9291
343	316	273	230	214	188	171	161	145	135	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcw 30JUN2023:09:36 kvbv306

Figure 3.3.76 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Nasopharyngitis
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	290	268	253	240	223	208	202	195	182	0	0 AZD9291
343	307	263	217	197	172	157	147	134	125	0	0 Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcx 30JUN2023:09:36 kvbv306

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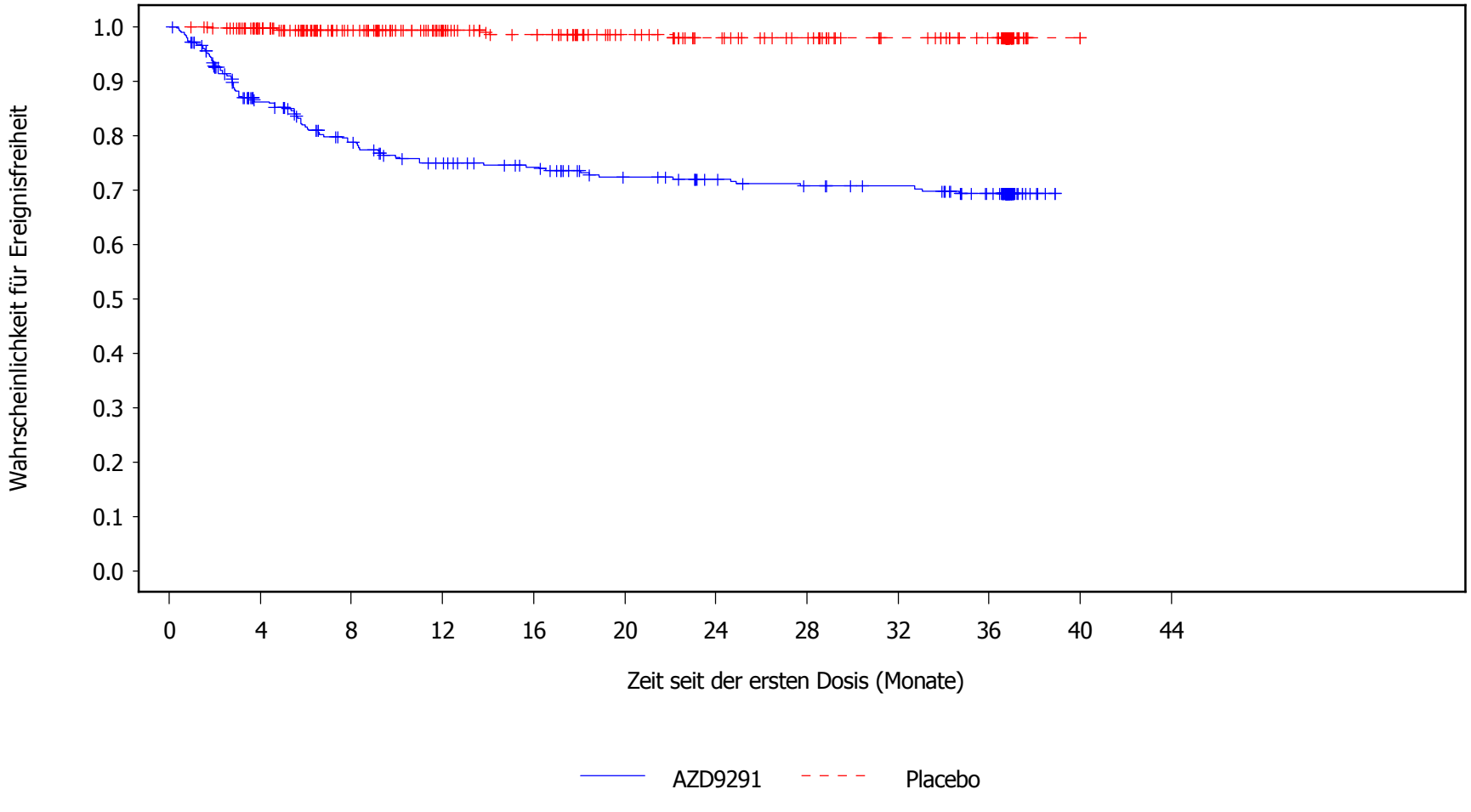
Figure 3.3.77 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Paronychie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	263	229	210	199	183	174	168	164	150	0	0	AZD9291
343	320	277	233	215	190	174	164	149	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcy 30JUN2023:09:36 kvbv306

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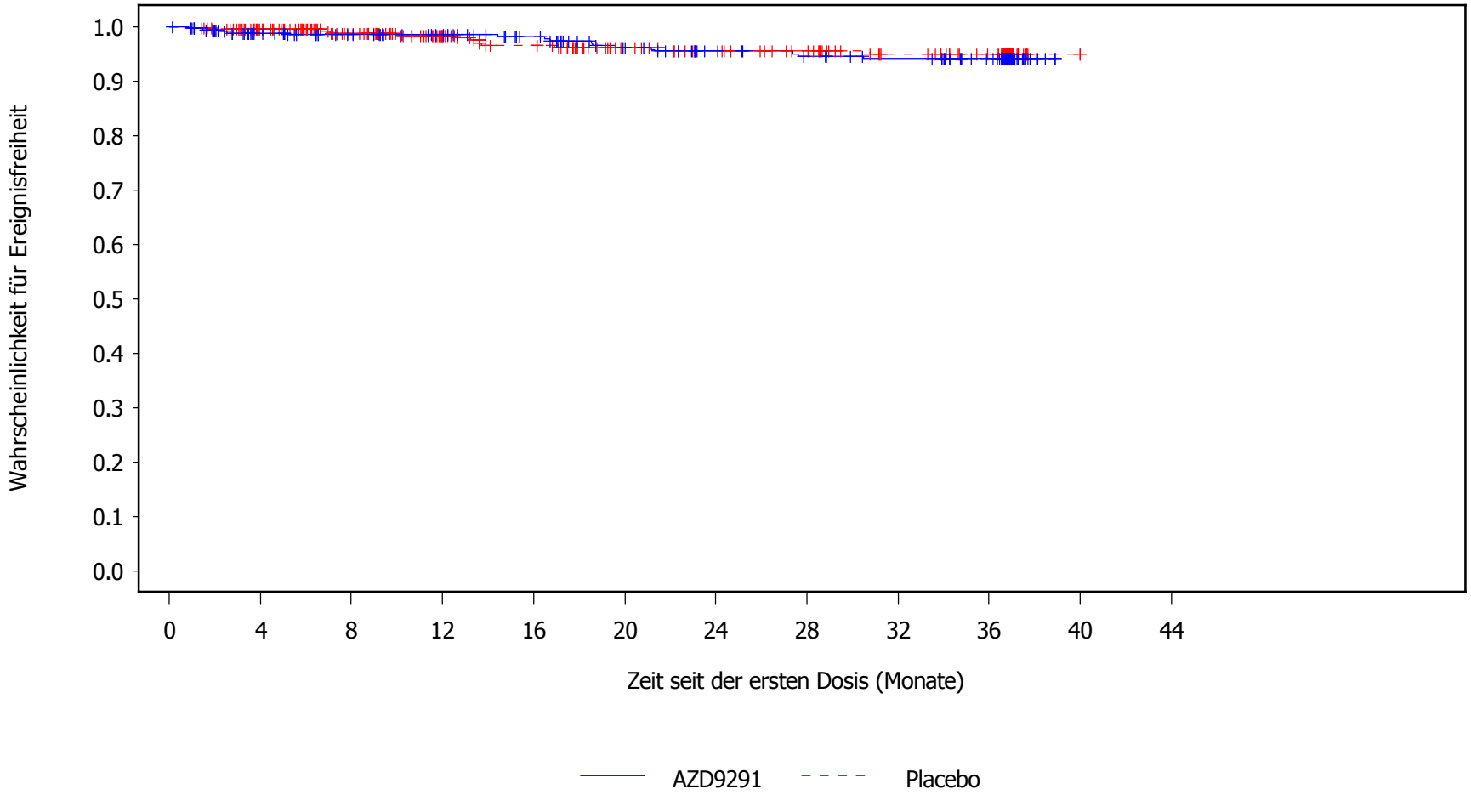
Figure 3.3.78 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Pharyngitis
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	305	289	279	266	249	235	229	224	210	0	0	AZD9291
343	318	274	229	210	185	172	163	147	136	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bcz 30JUN2023:09:36 kvbv306

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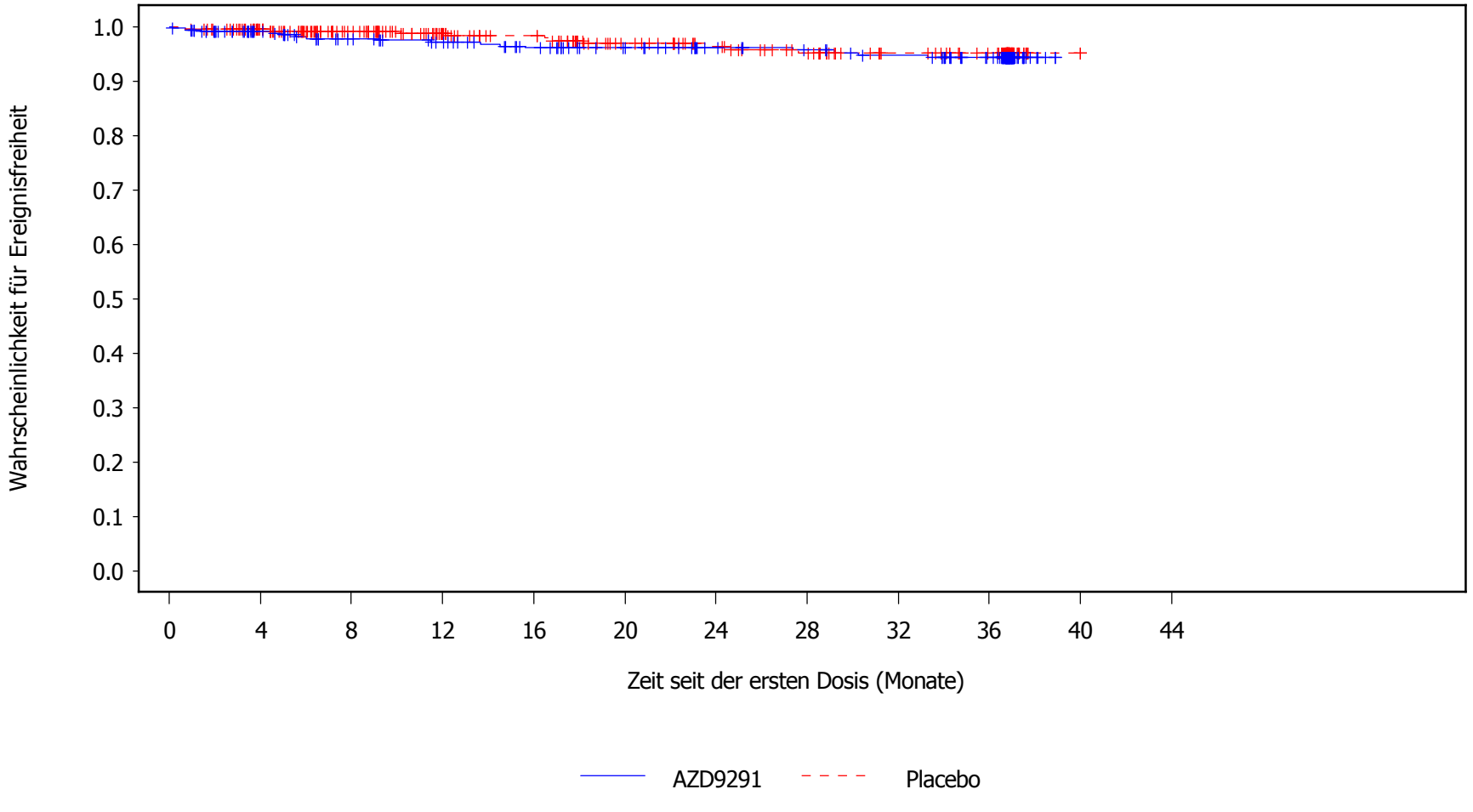
Figure 3.3.79 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Pneumonie
Safety Analysis Set, DCO 11Apr2022

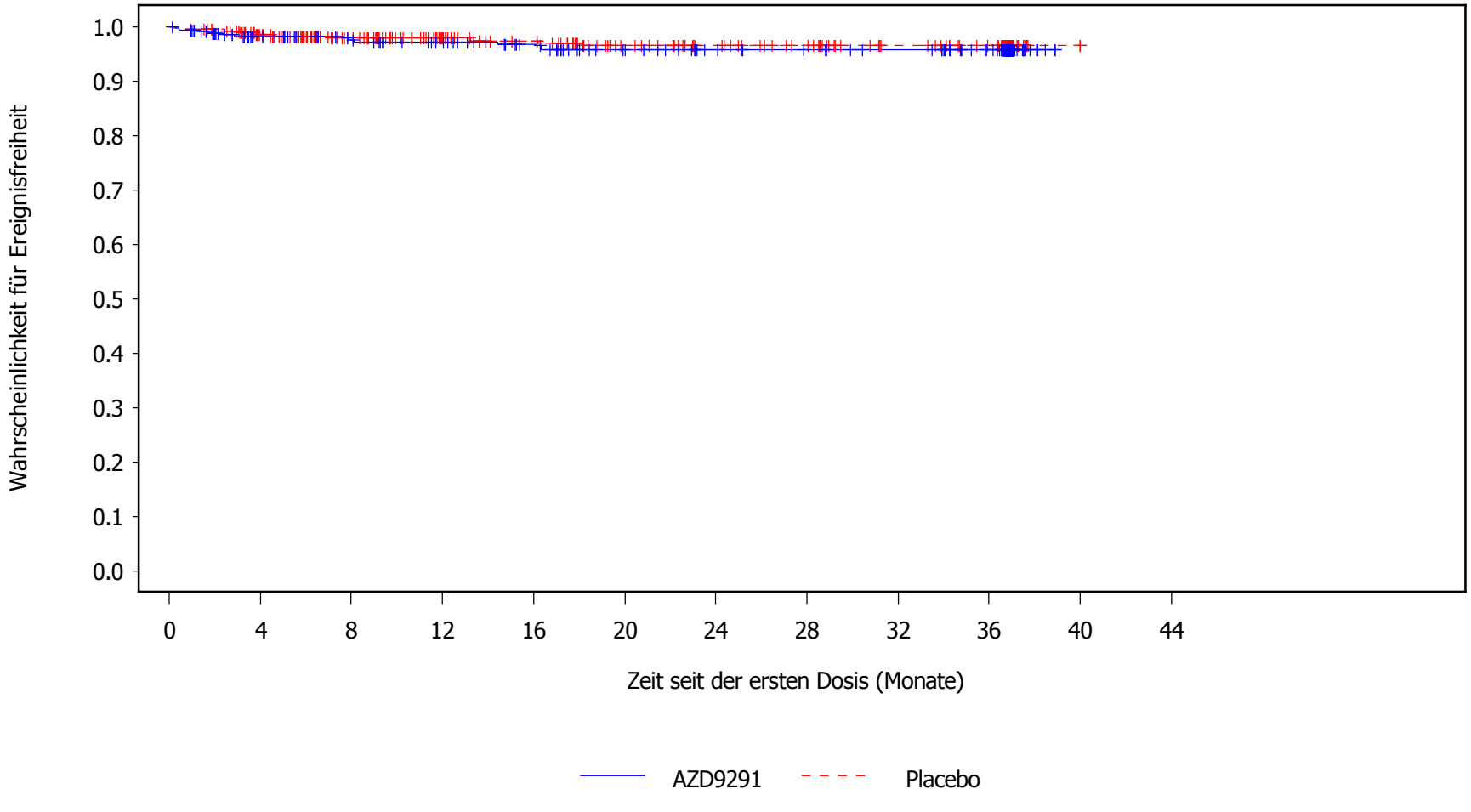


Anzahl an Patienten unter Risiko:

337	306	287	277	263	251	239	234	228	213	0	0	AZD9291
343	318	276	233	217	189	174	162	147	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bda 30JUN2023:09:36 kvbv306

Figure 3.3.80 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Virale Infektion der oberen Atemwege
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	286	275	262	246	234	230	226	211	0	0	AZD9291
343	316	272	229	212	185	170	160	144	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdb 30JUN2023:09:36 kvbv306

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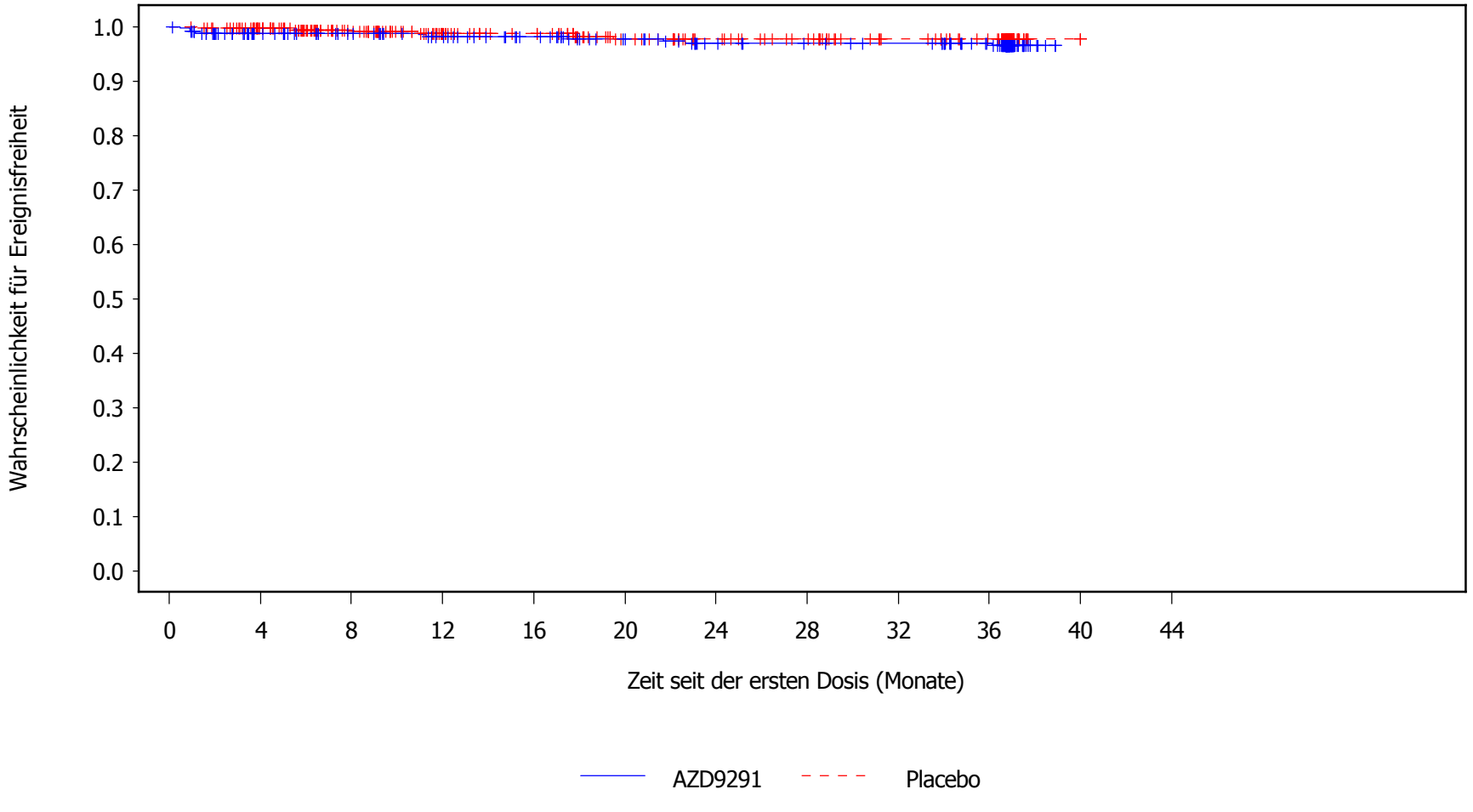
Figure 3.3.81 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Zystitis
Safety Analysis Set, DCO 11Apr2022

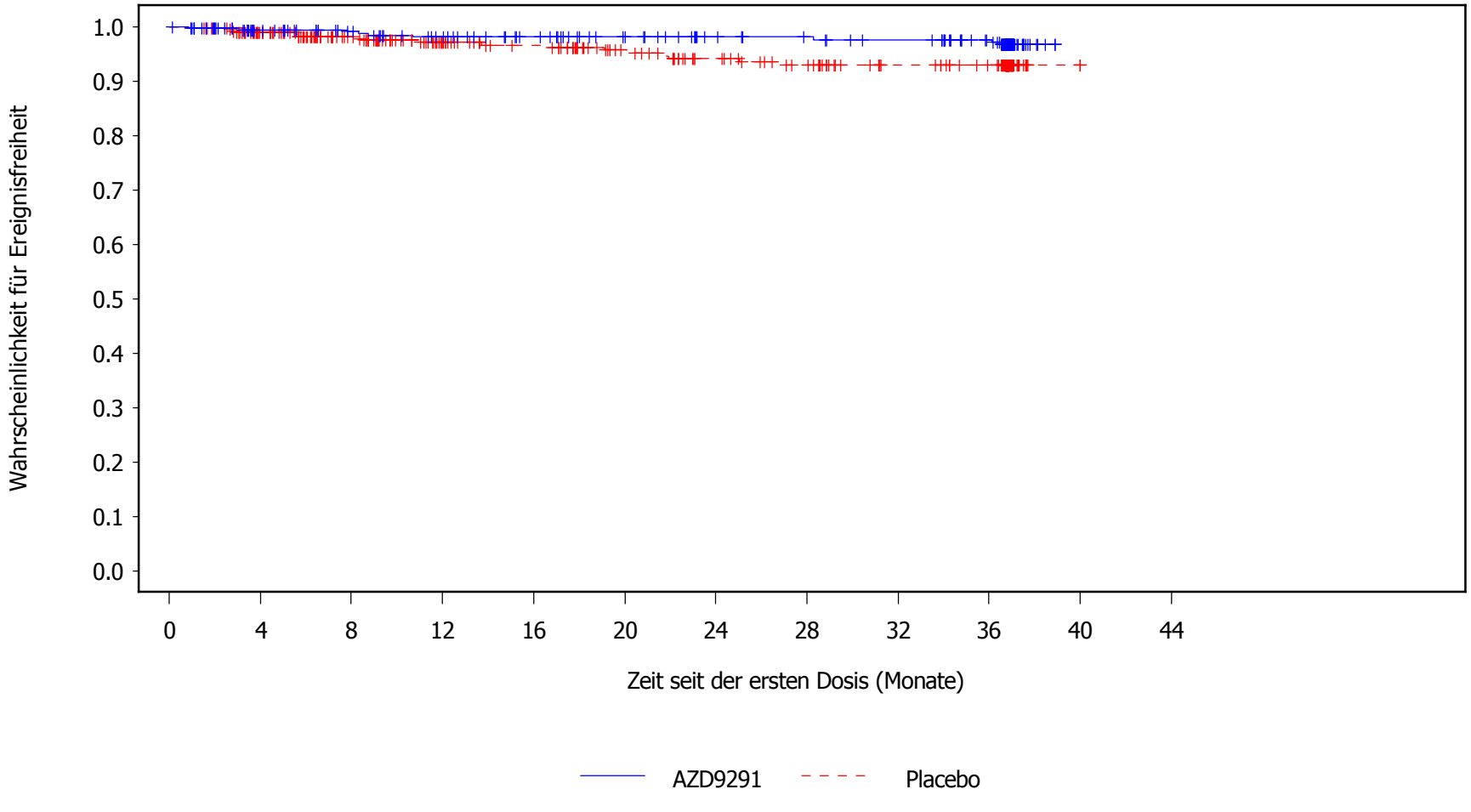


Anzahl an Patienten unter Risiko:

337	305	291	279	267	253	239	235	232	217	0	0	AZD9291
343	320	277	233	217	190	175	165	149	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdc 30JUN2023:09:36 kvbv306

Figure 3.3.82 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Leber- und Gallenerkrankungen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	306	290	277	265	253	241	237	232	217	0	0	AZD9291
343	316	274	229	212	187	169	157	141	132	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdd 30JUN2023:09:36 kvbv306

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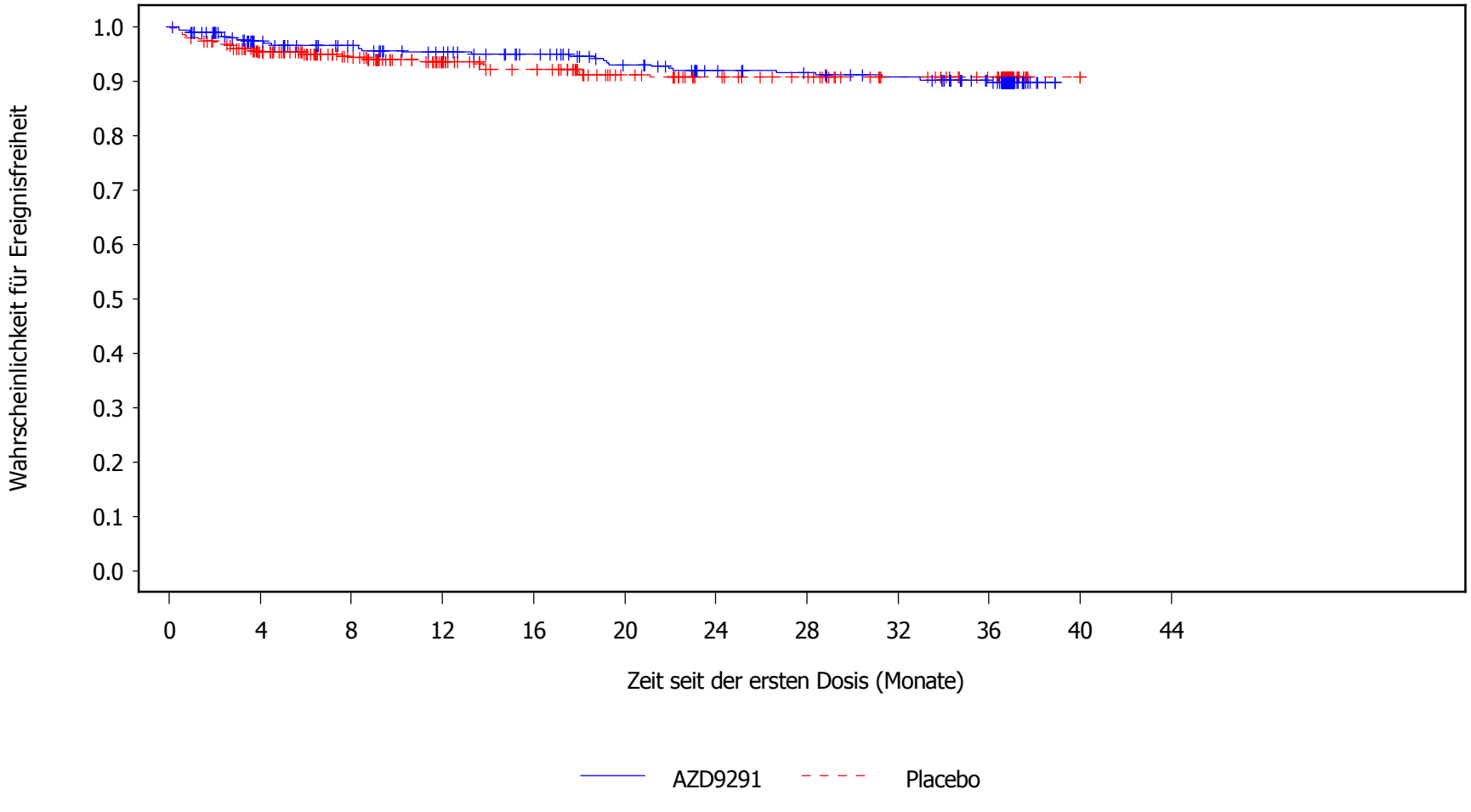
Figure 3.3.83 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Psychiatrische Erkrankungen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	301	285	272	260	244	231	226	220	204	0	0	AZD9291
343	305	264	223	205	179	165	158	144	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bde 30JUN2023:09:36 kvbv306

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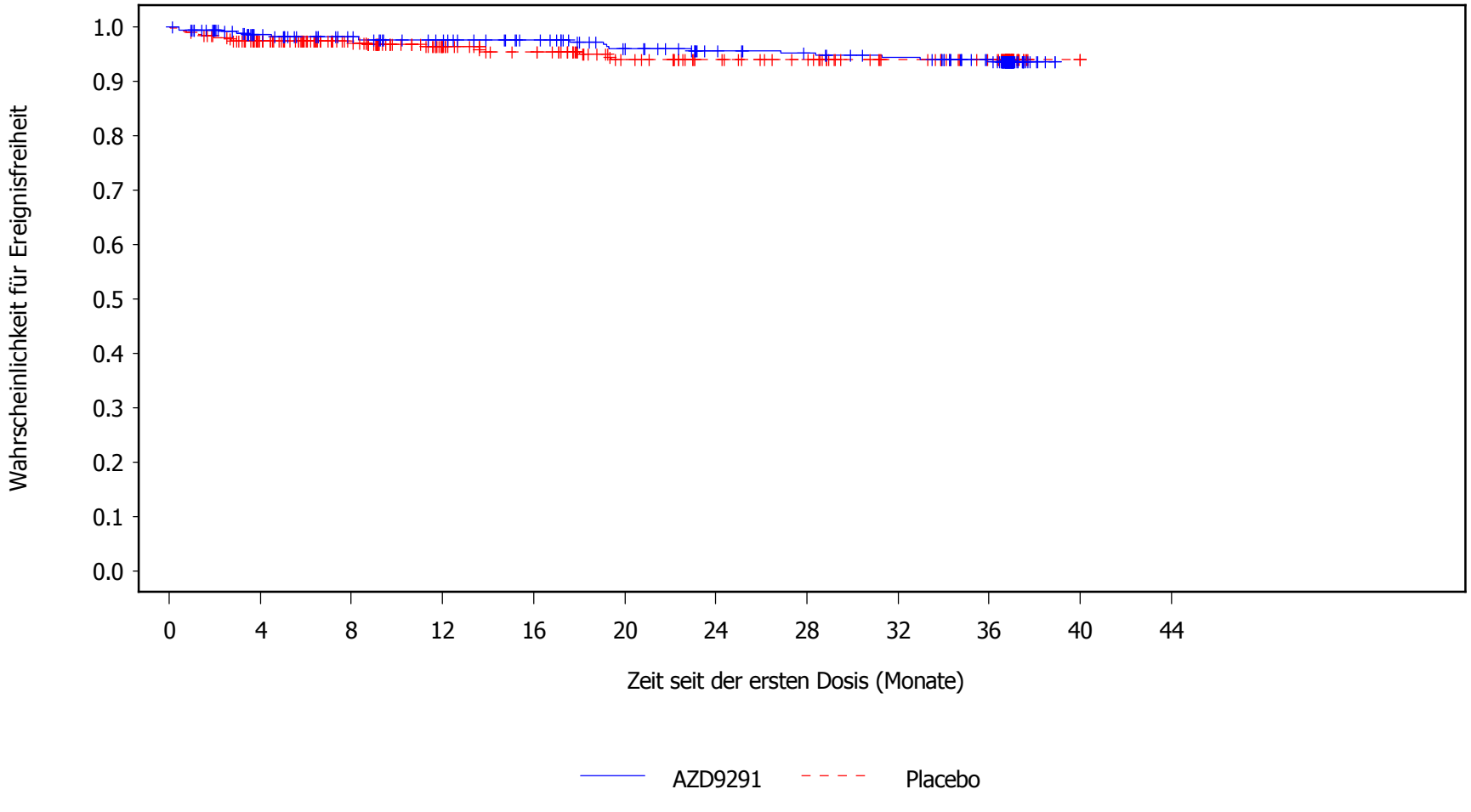
Figure 3.3.84 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Schlaflosigkeit
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	305	289	278	267	251	238	233	227	211	0	0	AZD9291
343	312	271	228	211	183	169	161	146	135	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdf 30JUN2023:09:36 kvbv306

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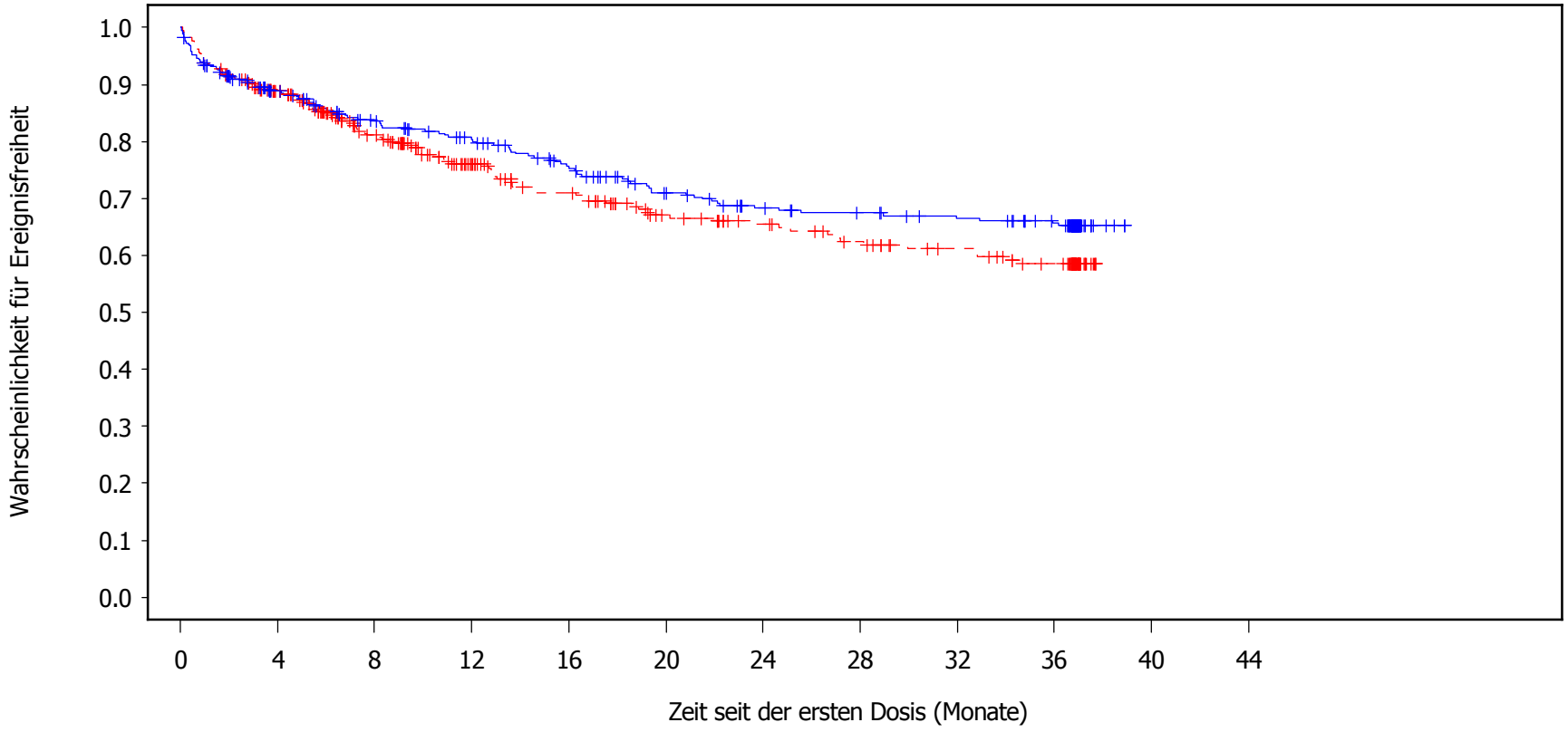
Figure 3.3.85 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	274	244	226	204	181	166	160	154	144	0	0 AZD9291
343	284	226	176	152	126	113	103	93	82	0	0 Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdg 30JUN2023:09:36 kvbv306

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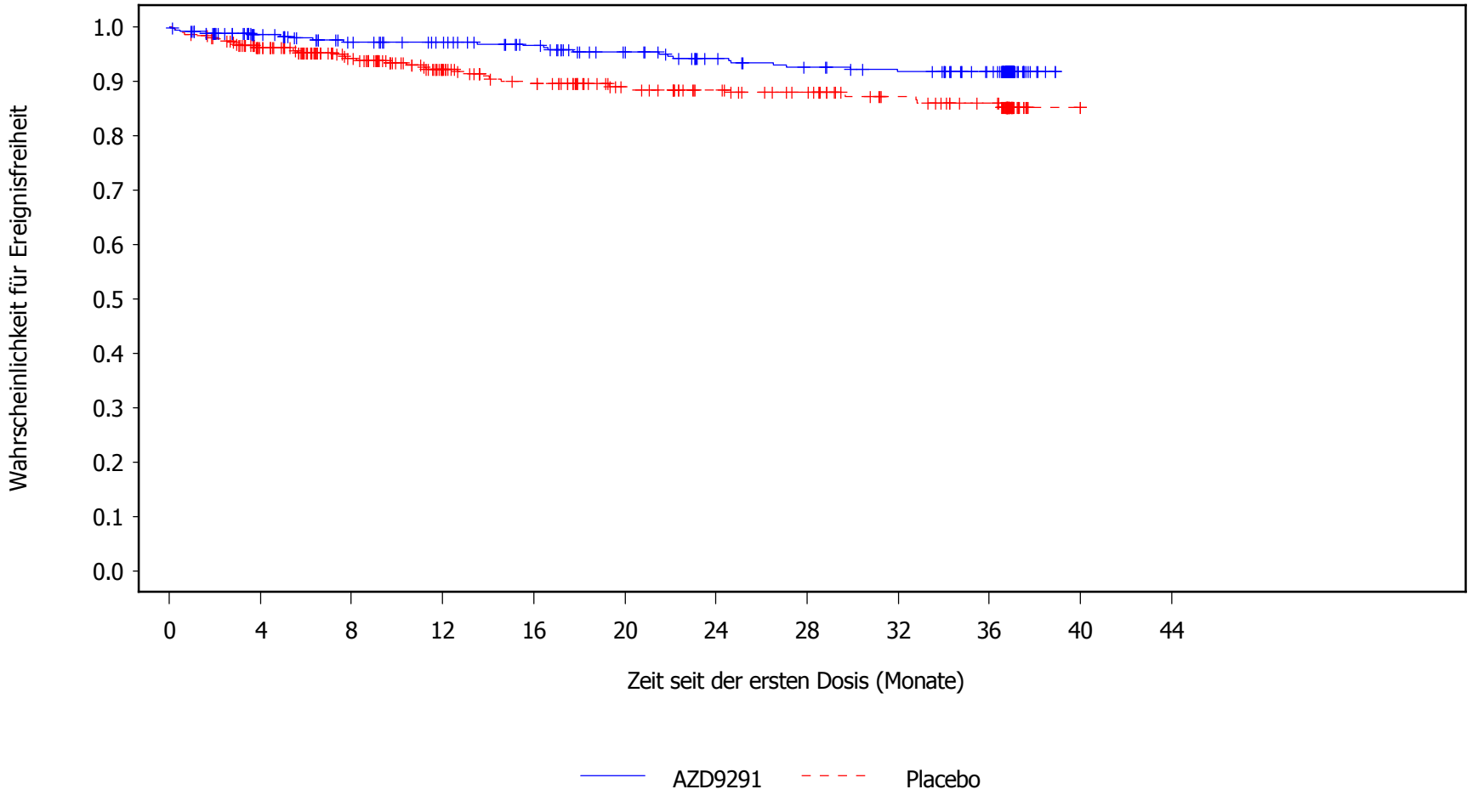
Figure 3.3.86 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Arthralgie
Safety Analysis Set, DCO 11Apr2022

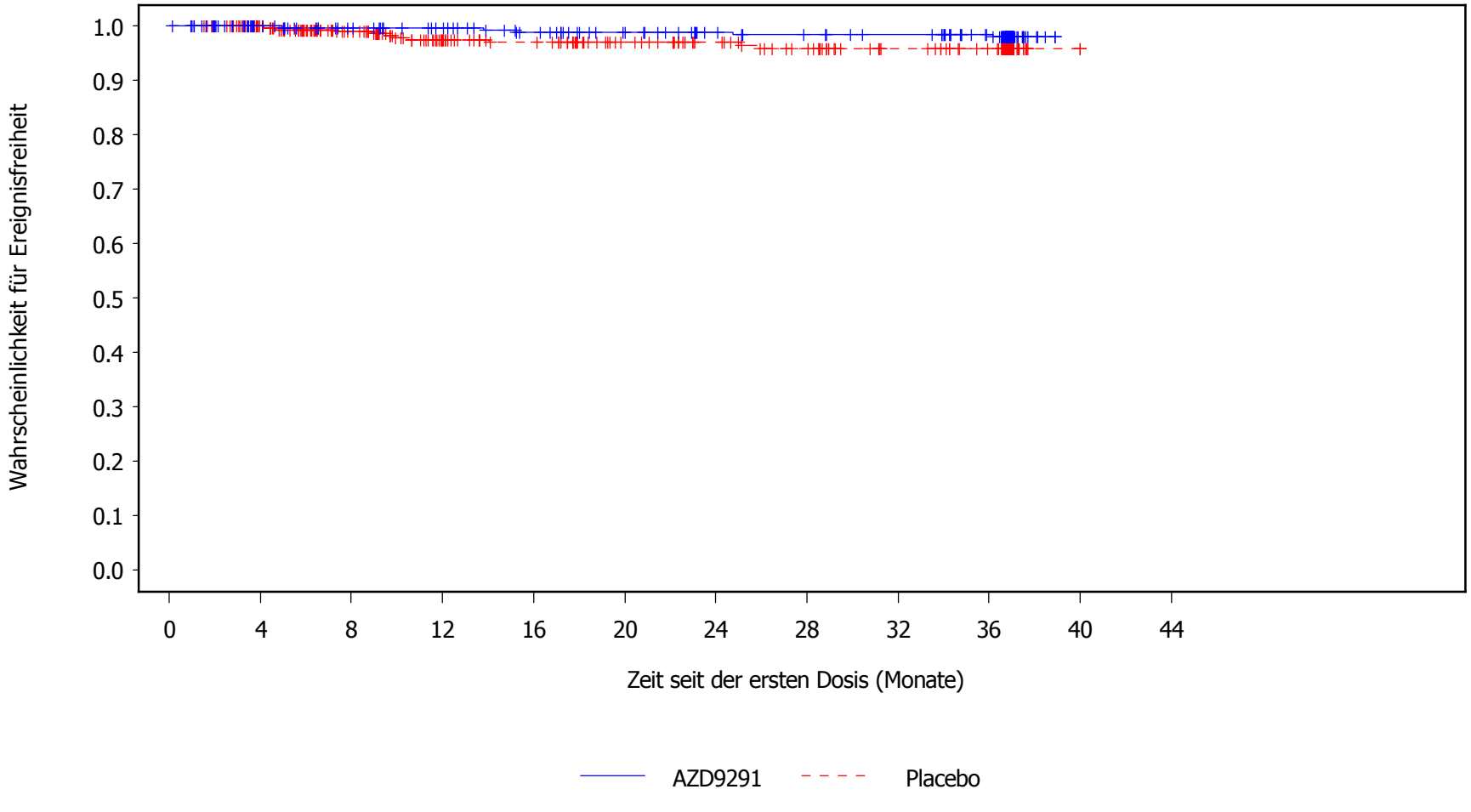


Anzahl an Patienten unter Risiko:

337	304	285	275	262	246	231	223	217	203	0	0	AZD9291
343	308	263	214	193	169	155	145	130	120	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdh 30JUN2023:09:36 kvbv306

Figure 3.3.87 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Brustschmerzen die Skelettmuskulatur betreffend
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	308	292	282	269	257	245	240	236	221	0	0	AZD9291
343	320	275	228	212	188	173	161	145	134	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdi 30JUN2023:09:36 kvbv306

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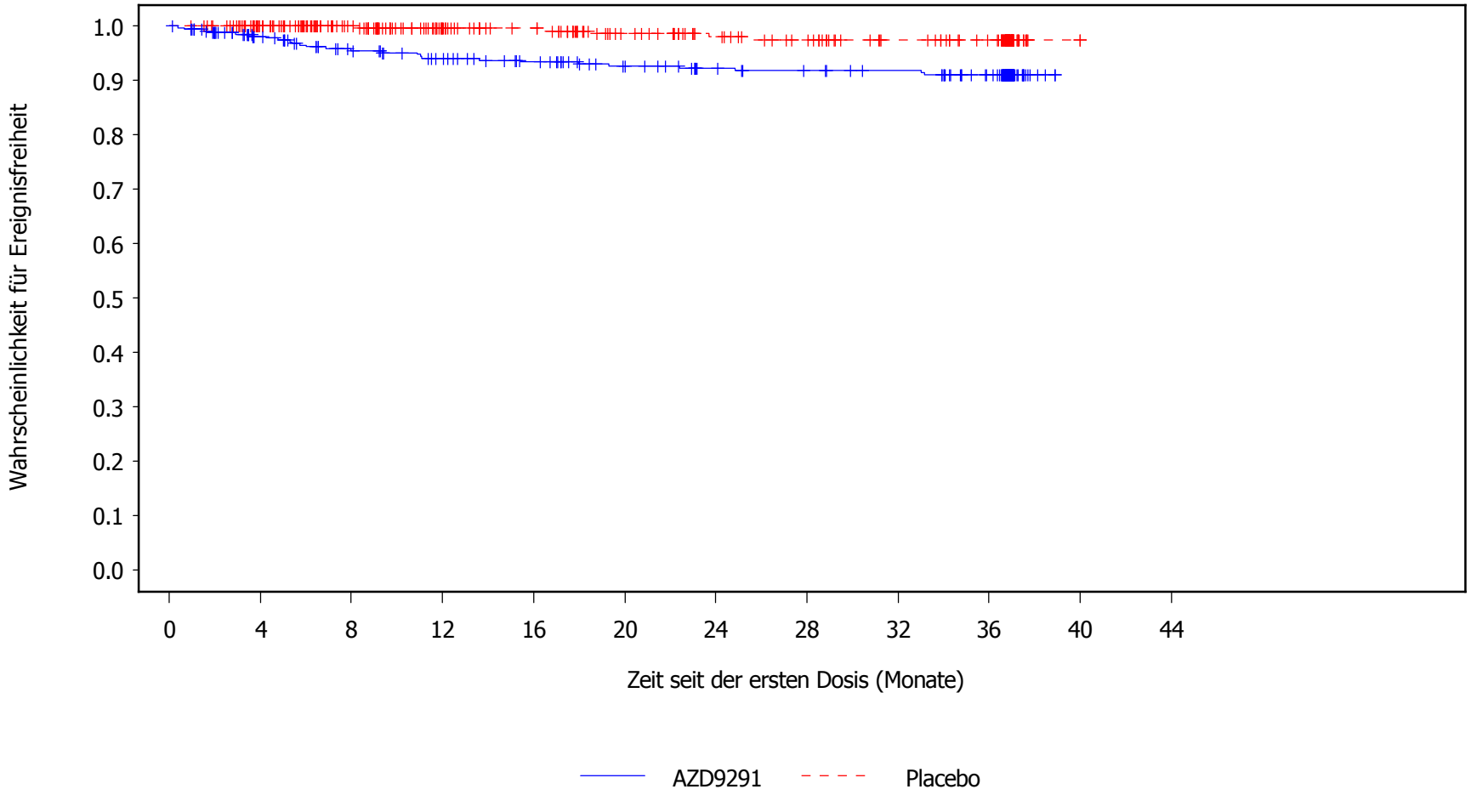
Figure 3.3.88 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Muskelspasmen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	304	281	268	255	240	229	224	220	205	0	0	AZD9291
343	320	278	233	217	190	174	164	149	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdj 30JUN2023:09:36 kvbv306

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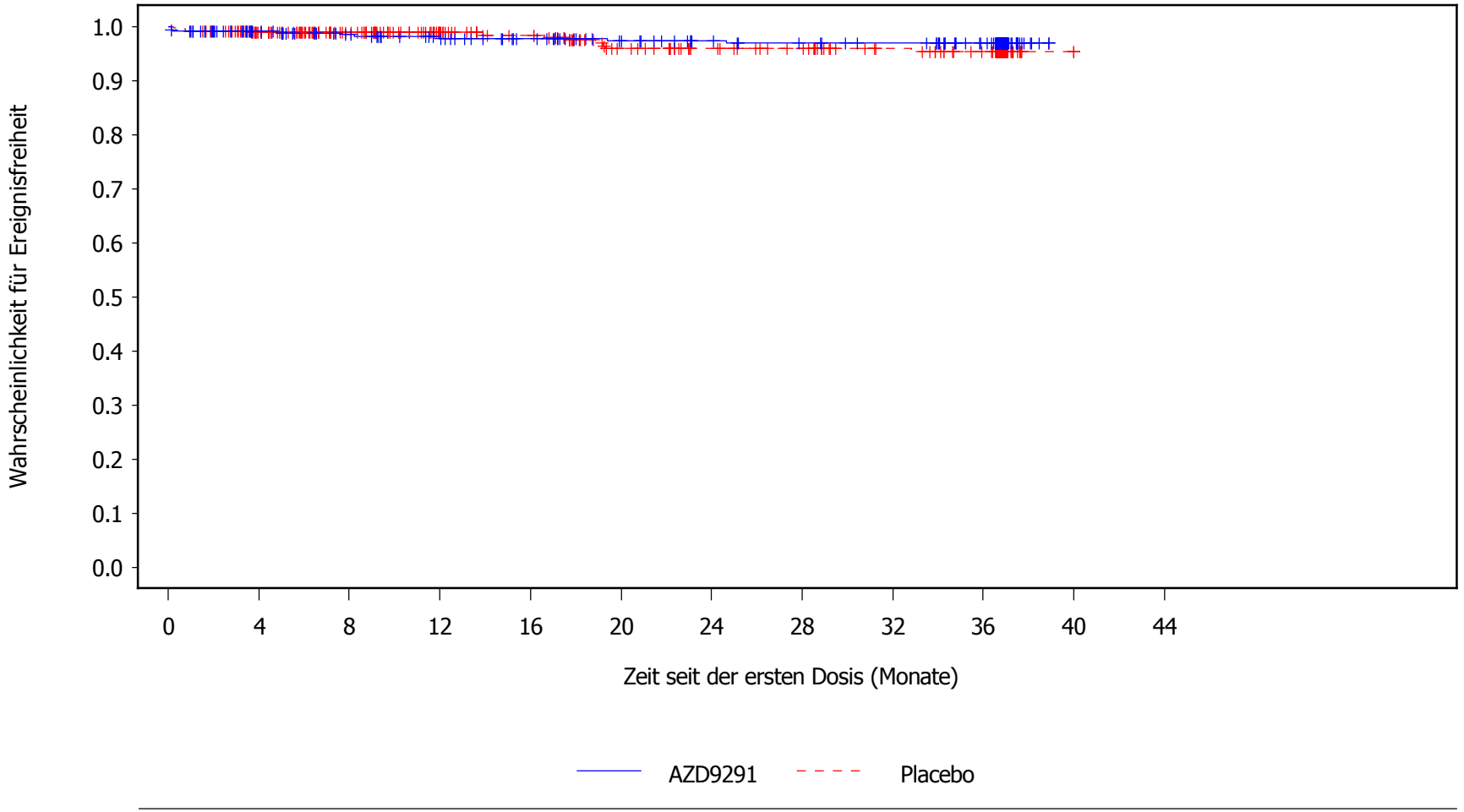
Figure 3.3.89 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Myalgie
Safety Analysis Set, DCO 11Apr2022

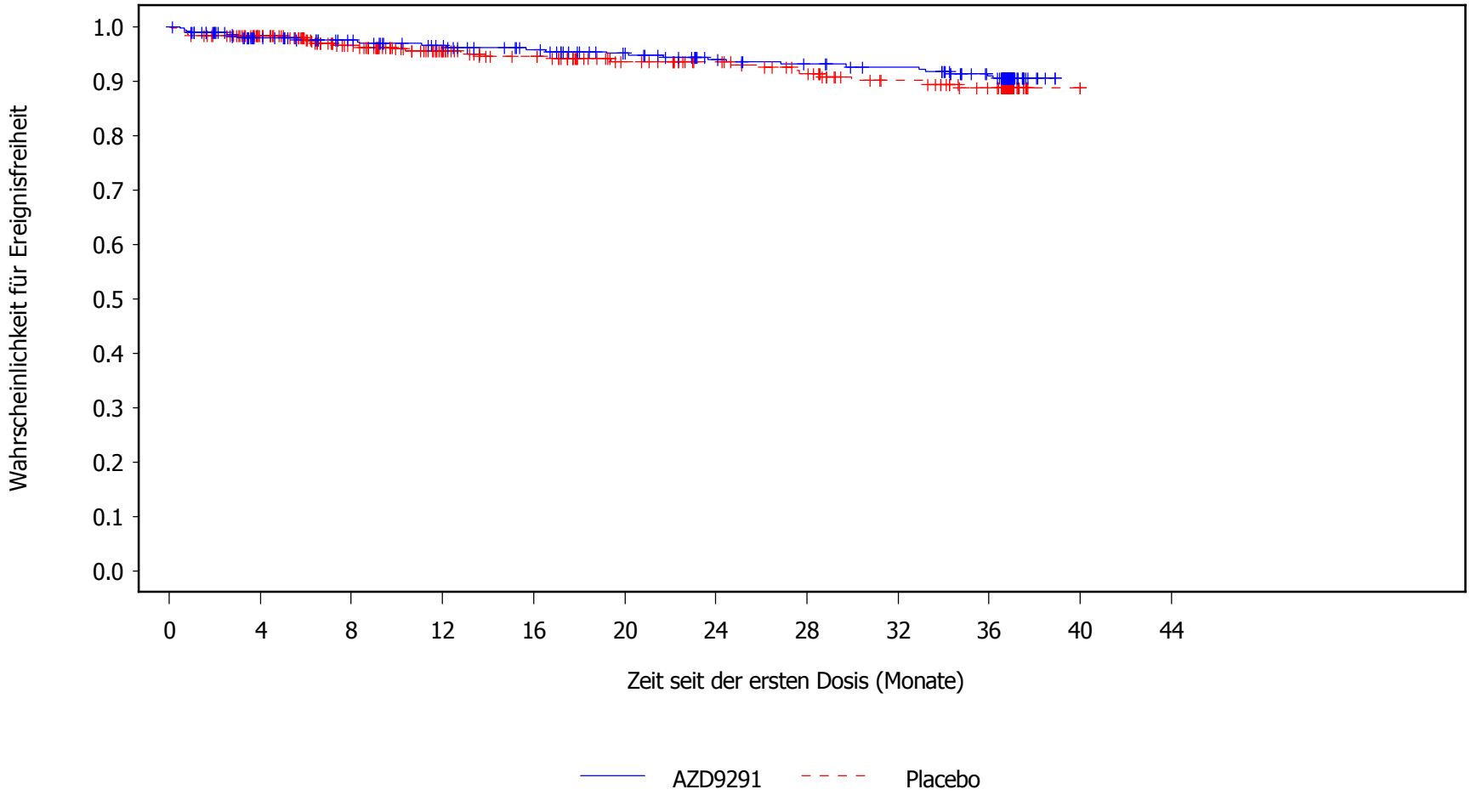


Anzahl an Patienten unter Risiko:

337	305	288	276	264	250	240	235	231	216	0	0	AZD9291
343	316	274	230	213	183	168	160	145	133	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdk 30JUN2023:09:36 kvbv306

Figure 3.3.90 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Rueckenschmerzen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	301	285	272	260	246	231	225	220	203	0	0	AZD9291
343	314	269	225	207	181	168	156	140	127	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdl 30JUN2023:09:36 kvbv306

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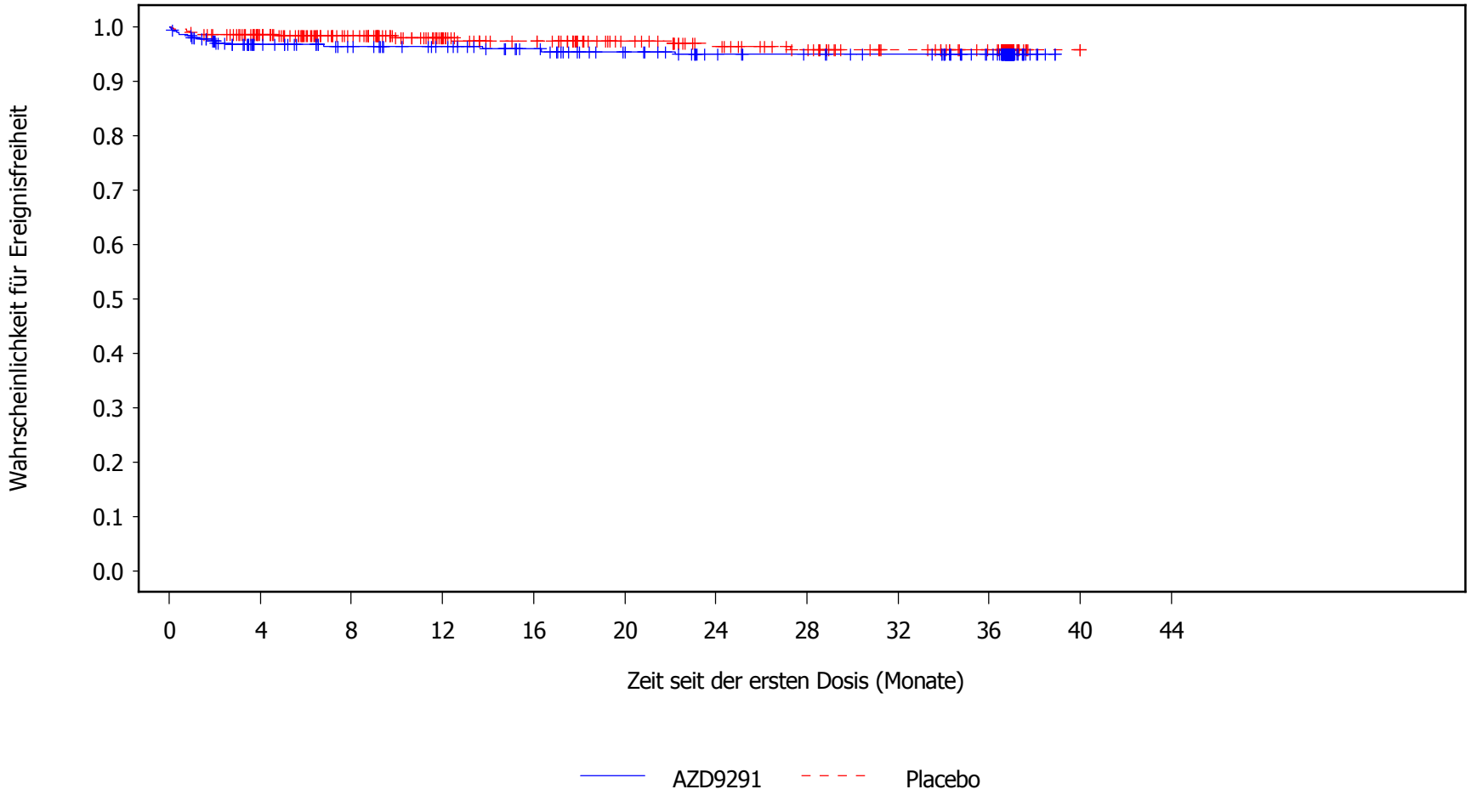
Figure 3.3.91 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Schmerz in einer Extremitaet
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	297	282	272	260	246	233	229	225	210	0	0	AZD9291
343	315	272	227	210	185	169	158	143	132	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdm 30JUN2023:09:36 kvbv306

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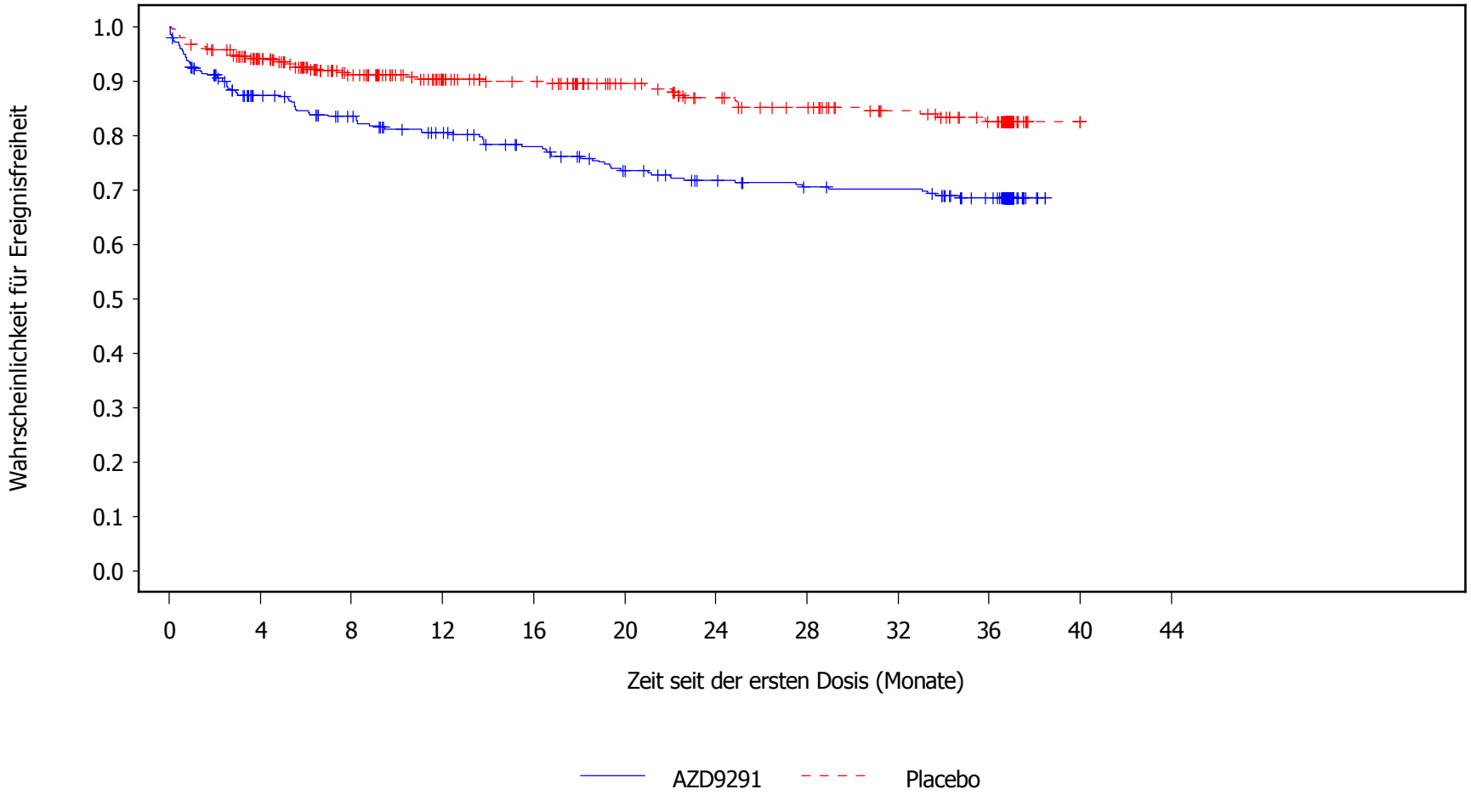
Figure 3.3.92 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Stoffwechsel- und Ernaehrungsstoerungen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	272	250	232	216	198	186	179	177	161	0	0	AZD9291
343	301	255	214	200	175	157	147	133	119	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdn 30JUN2023:09:36 kvbv306

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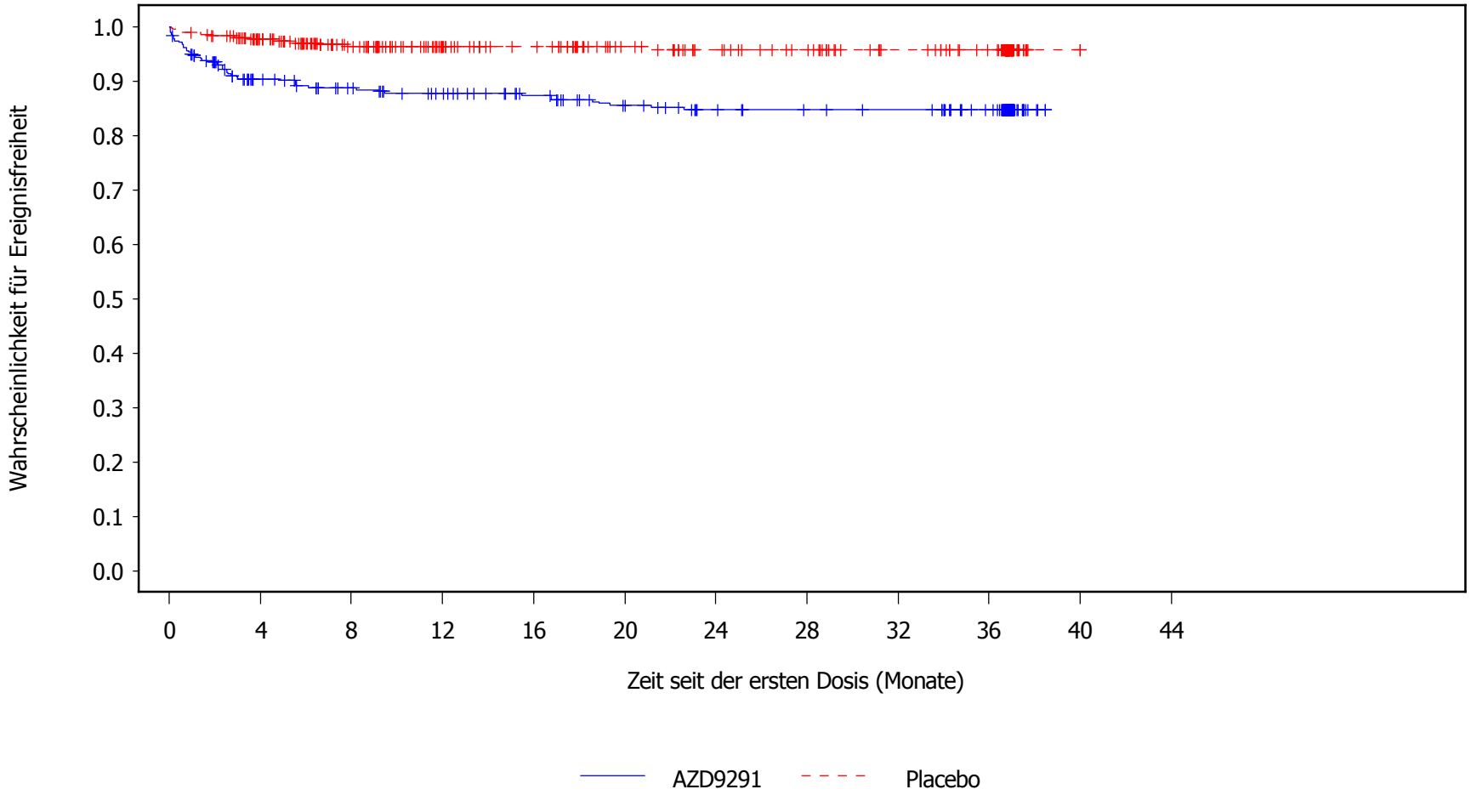
Figure 3.3.93 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Appetit vermindert
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	280	263	251	238	224	213	209	207	193	0	0	AZD9291
343	313	270	227	213	189	174	165	150	139	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdo 30JUN2023:09:36 kvbv306

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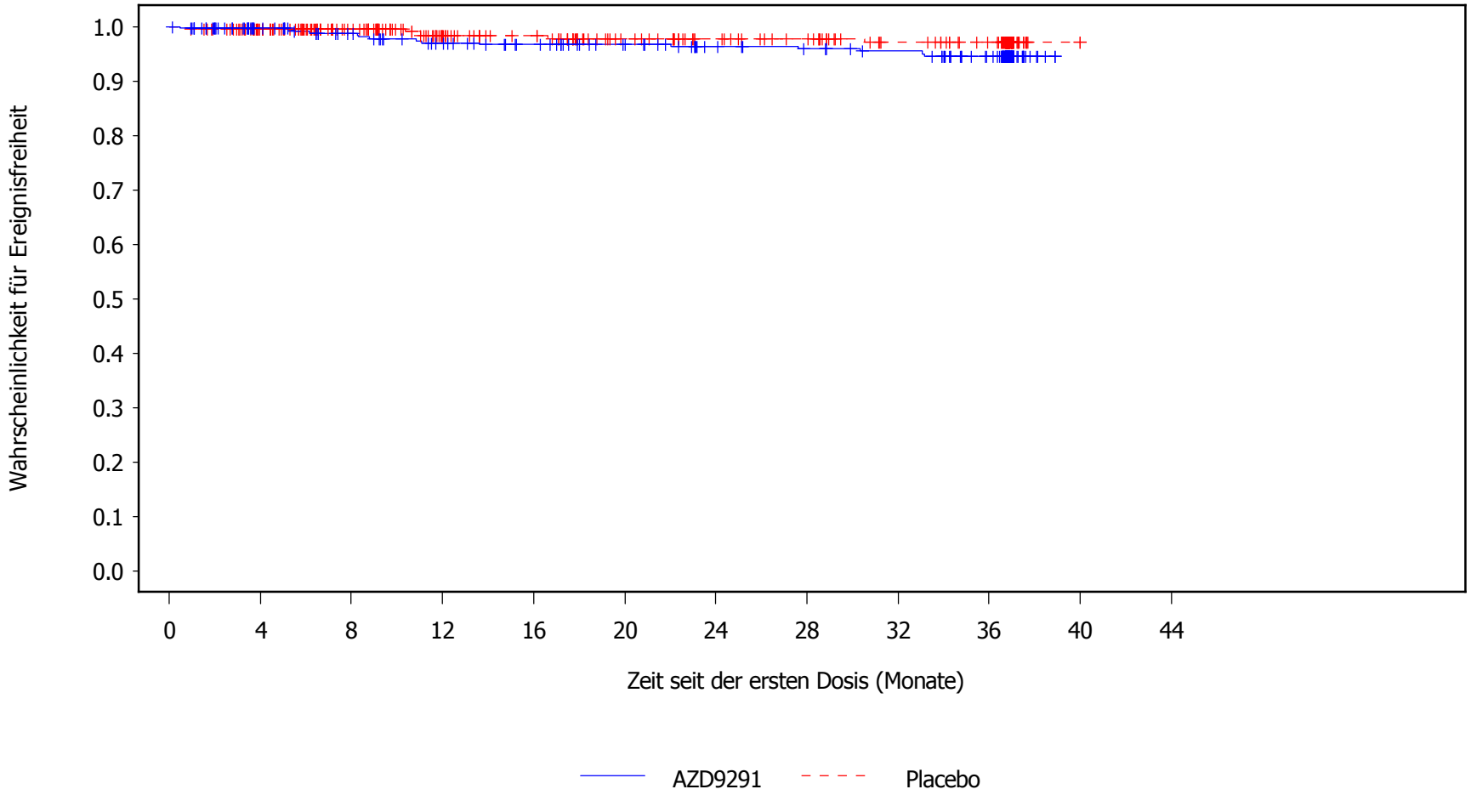
Figure 3.3.94 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Hyperglykaemie
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	307	290	275	264	252	239	234	229	212	0	0	AZD9291
343	318	276	230	214	188	173	164	147	136	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdp 30JUN2023:09:36 kvbv306

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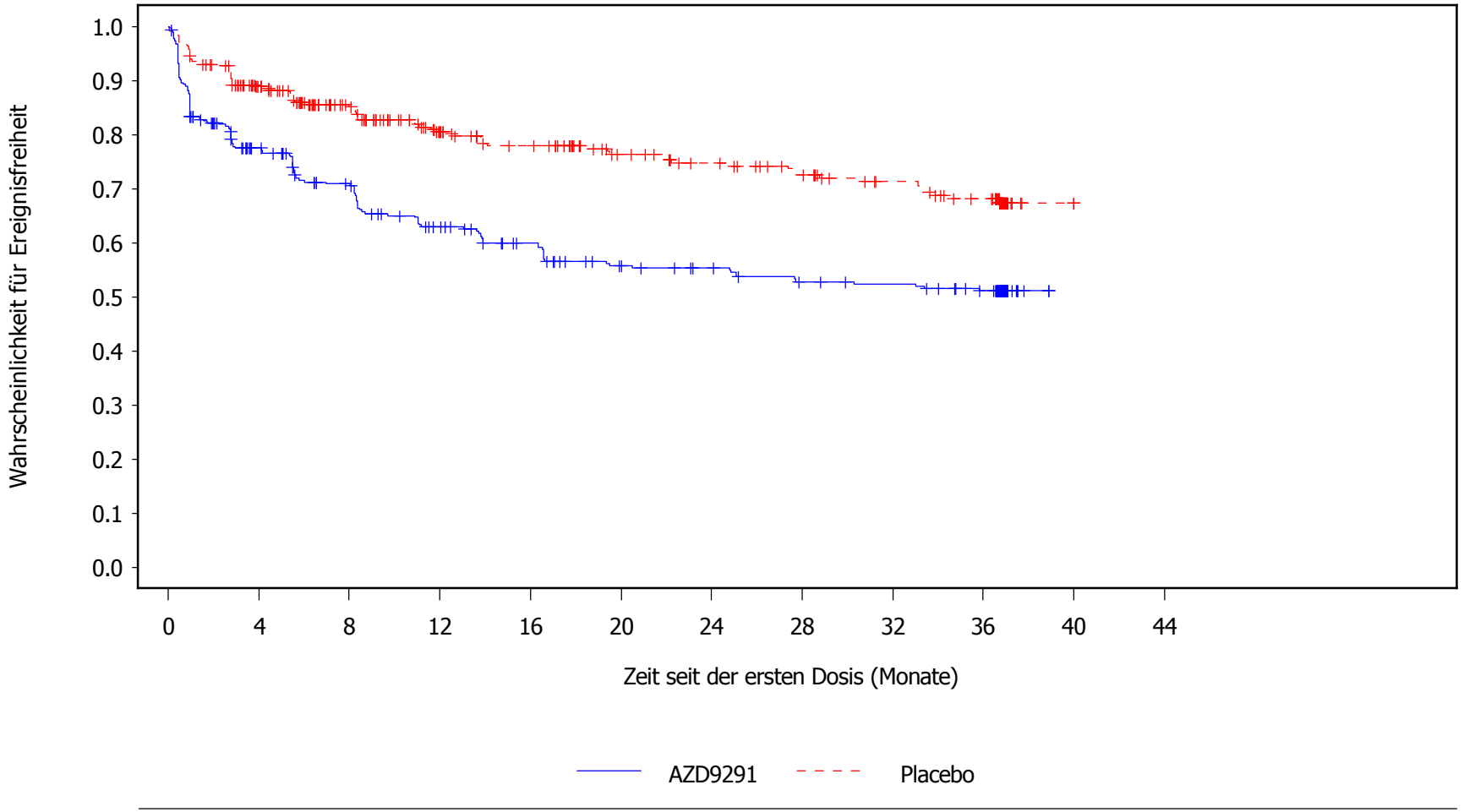
Figure 3.3.95 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Untersuchungen
Safety Analysis Set, DCO 11Apr2022

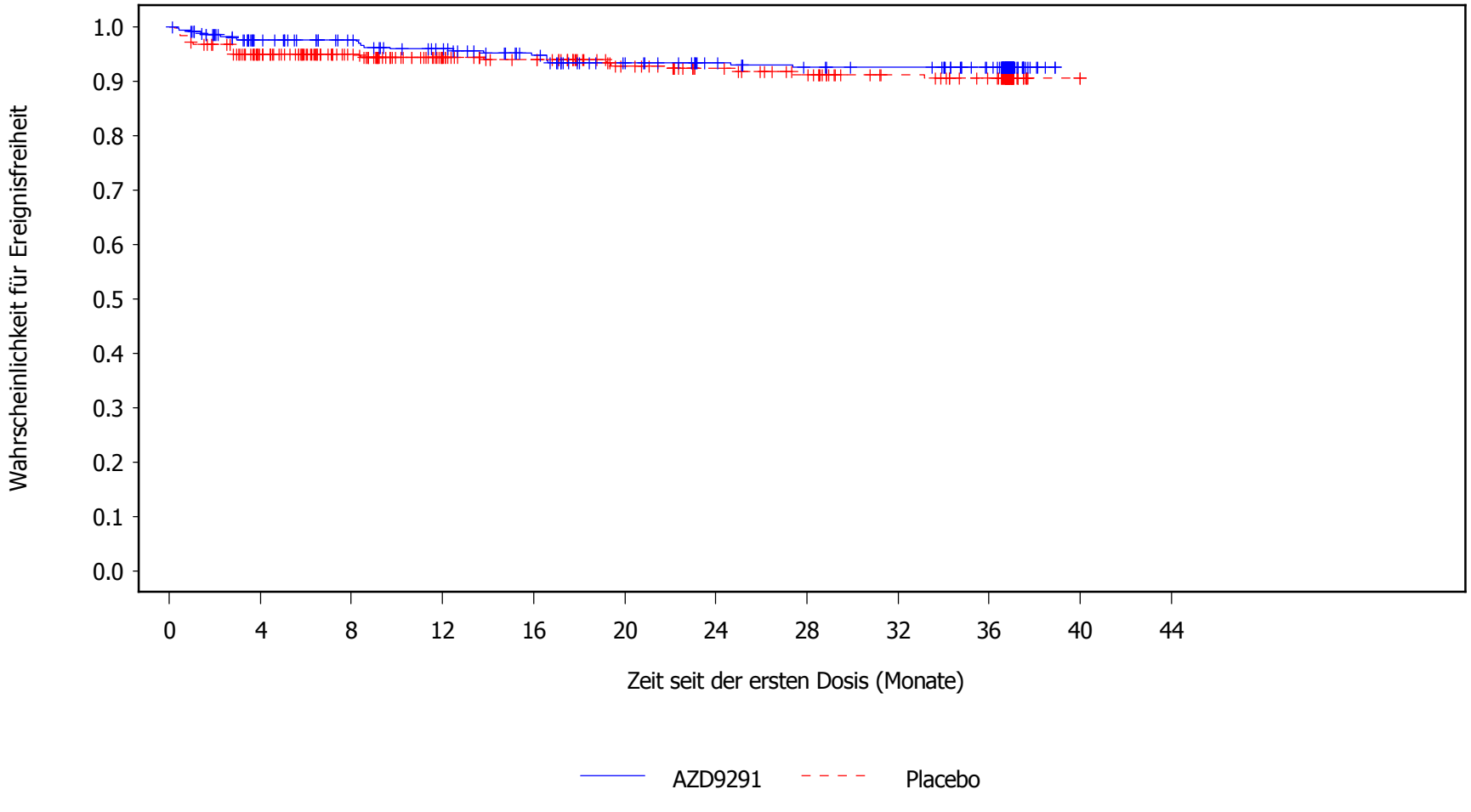


Anzahl an Patienten unter Risiko:

337	240	207	176	158	139	133	124	121	112	0	0	AZD9291
343	283	234	188	170	147	136	125	113	102	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdq 30JUN2023:09:36 kvbv306

Figure 3.3.96 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Alaninaminotransferase erhoeht
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	302	287	273	258	241	230	224	221	208	0	0	AZD9291
343	303	262	218	202	177	163	153	138	129	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdr 30JUN2023:09:36 kvbv306

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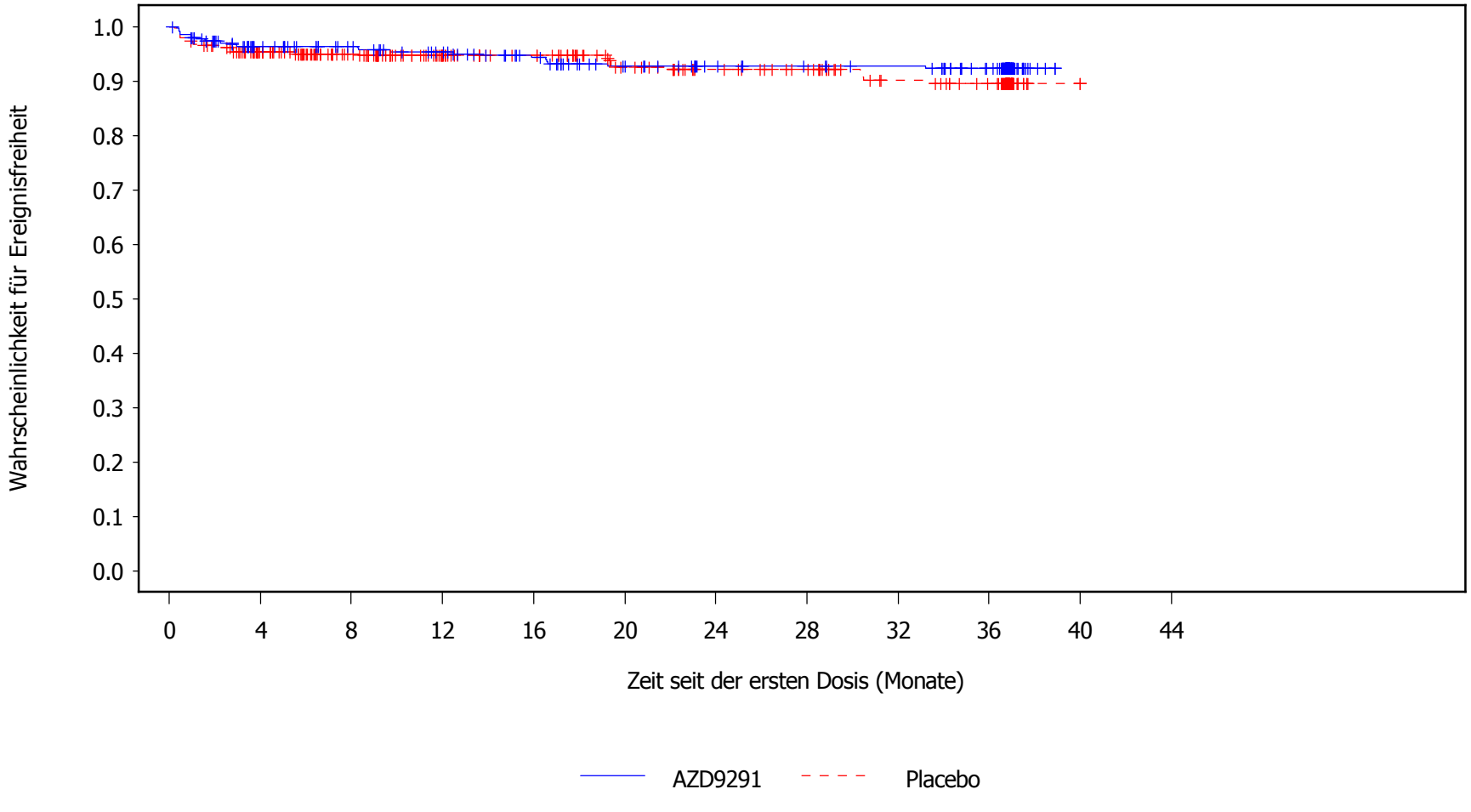
Figure 3.3.97 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Aspartataminotransferase erhoeht
Safety Analysis Set, DCO 11Apr2022

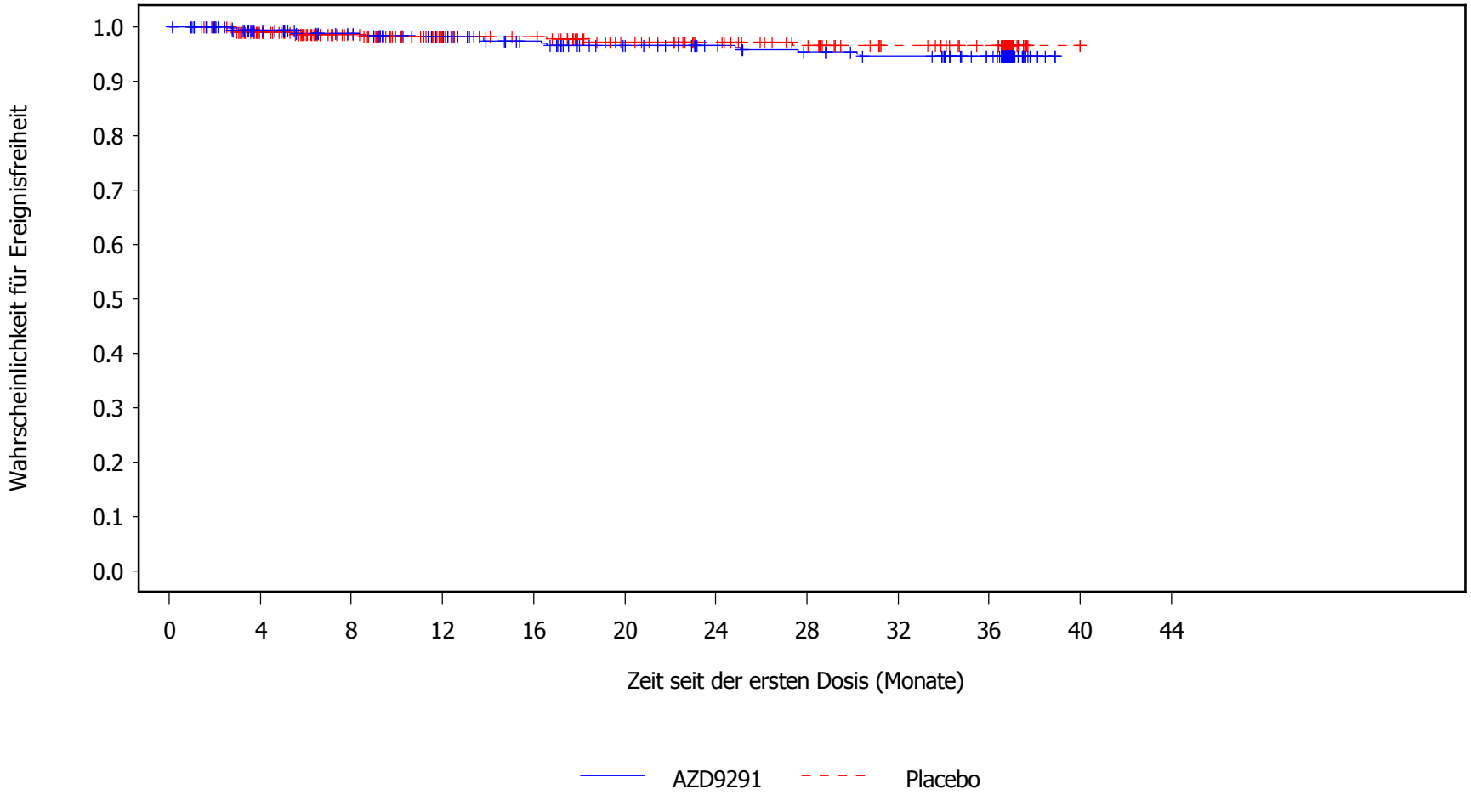


Anzahl an Patienten unter Risiko:

337	298	283	271	256	239	228	224	221	206	0	0	AZD9291
343	304	263	222	207	180	164	156	138	129	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bds 30JUN2023:09:36 kvbv306

Figure 3.3.98 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Auswurffraktion verkleinert
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	306	290	278	265	251	239	232	226	212	0	0	AZD9291
343	316	274	229	213	187	172	161	147	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdt 30JUN2023:09:36 kvbv306

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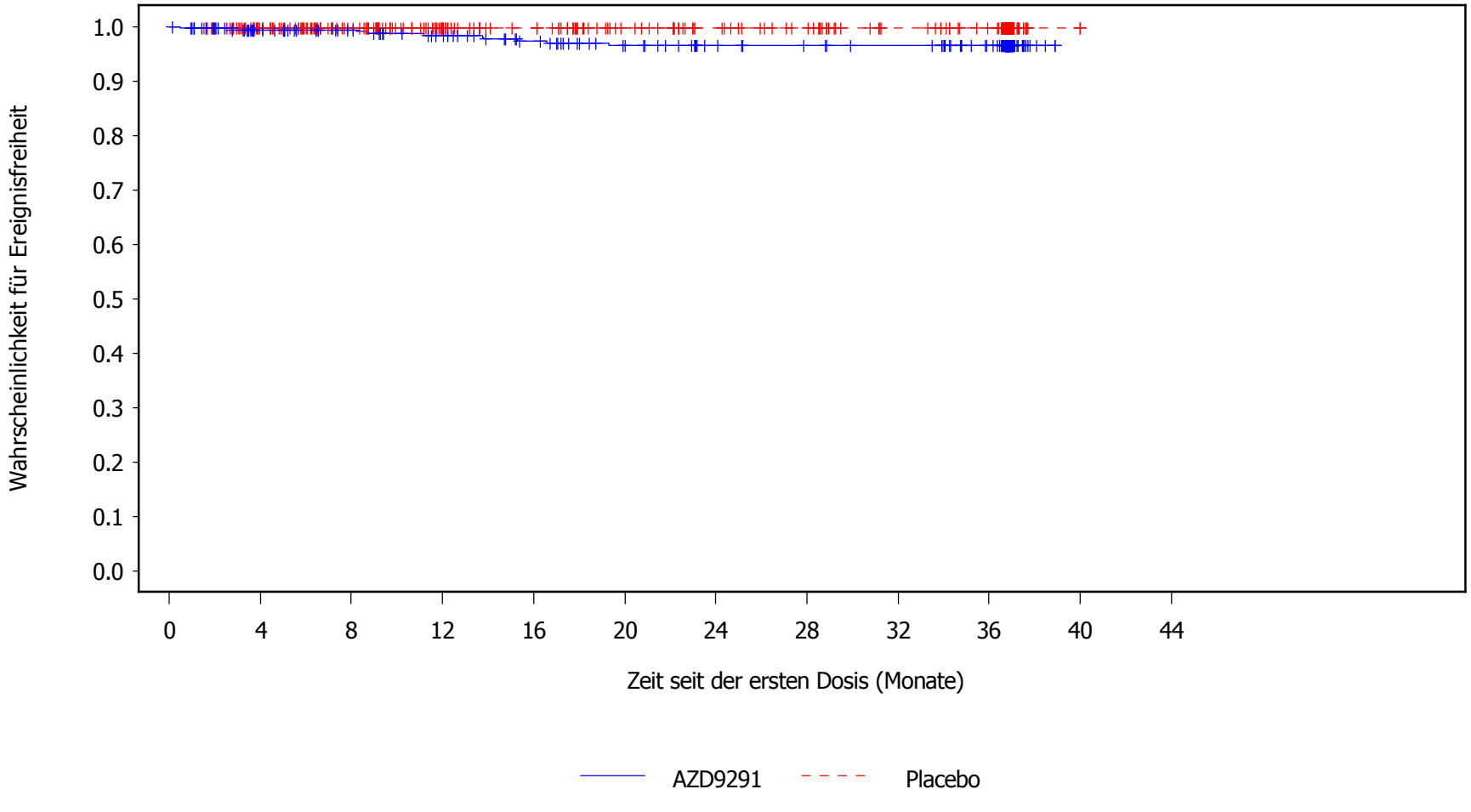
Figure 3.3.99 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Blutharnstoff erhoeht
Safety Analysis Set, DCO 11Apr2022

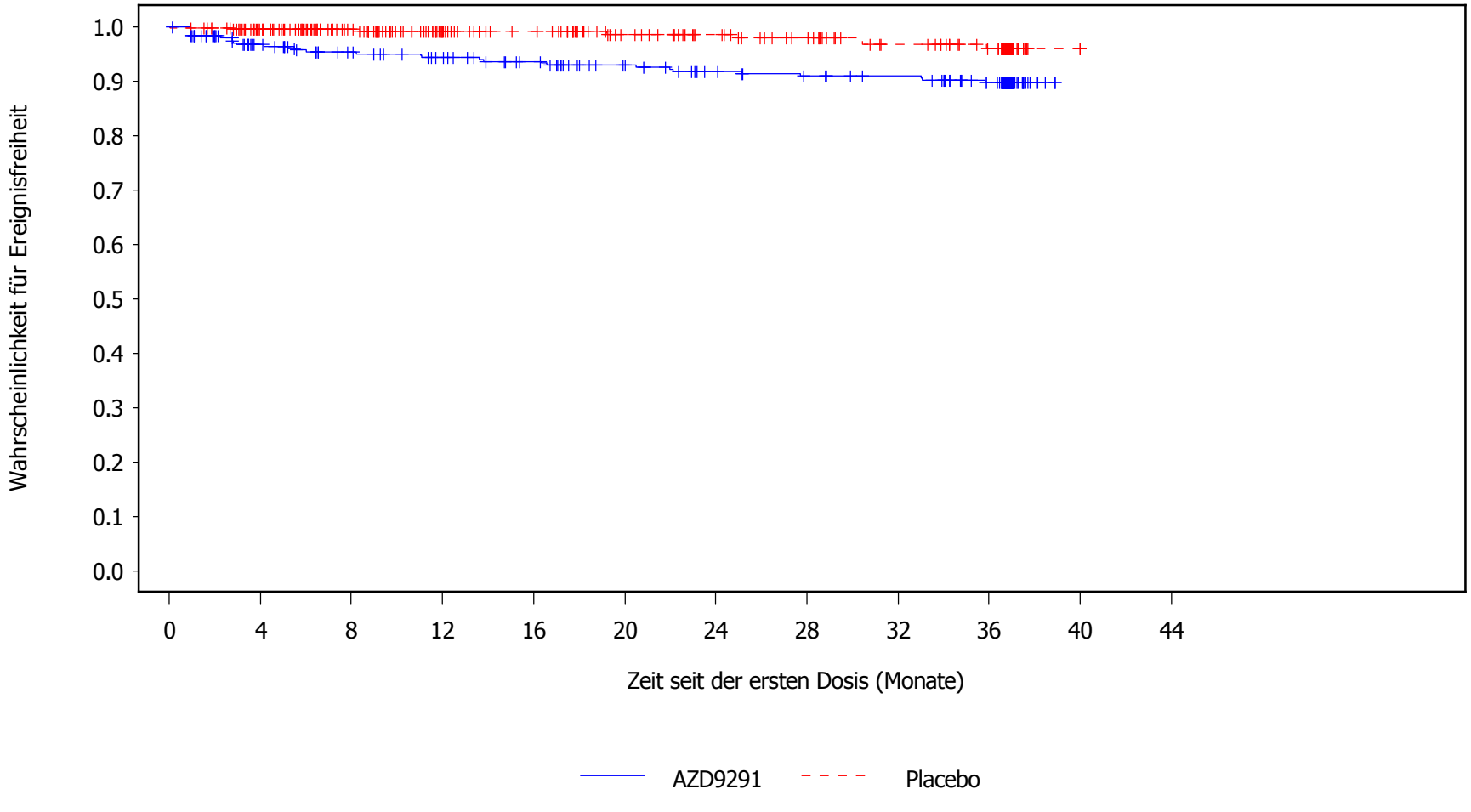


Anzahl an Patienten unter Risiko:

337	306	291	278	263	249	237	233	230	216	0	0	AZD9291
343	319	277	233	217	192	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdu 30JUN2023:09:36 kvbv306

Figure 3.3.100 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Elektrokardiogramm QT verlaengert
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	299	281	270	258	243	230	224	220	203	0	0	AZD9291
343	319	277	232	216	190	175	164	149	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdv 30JUN2023:09:36 kvbv306

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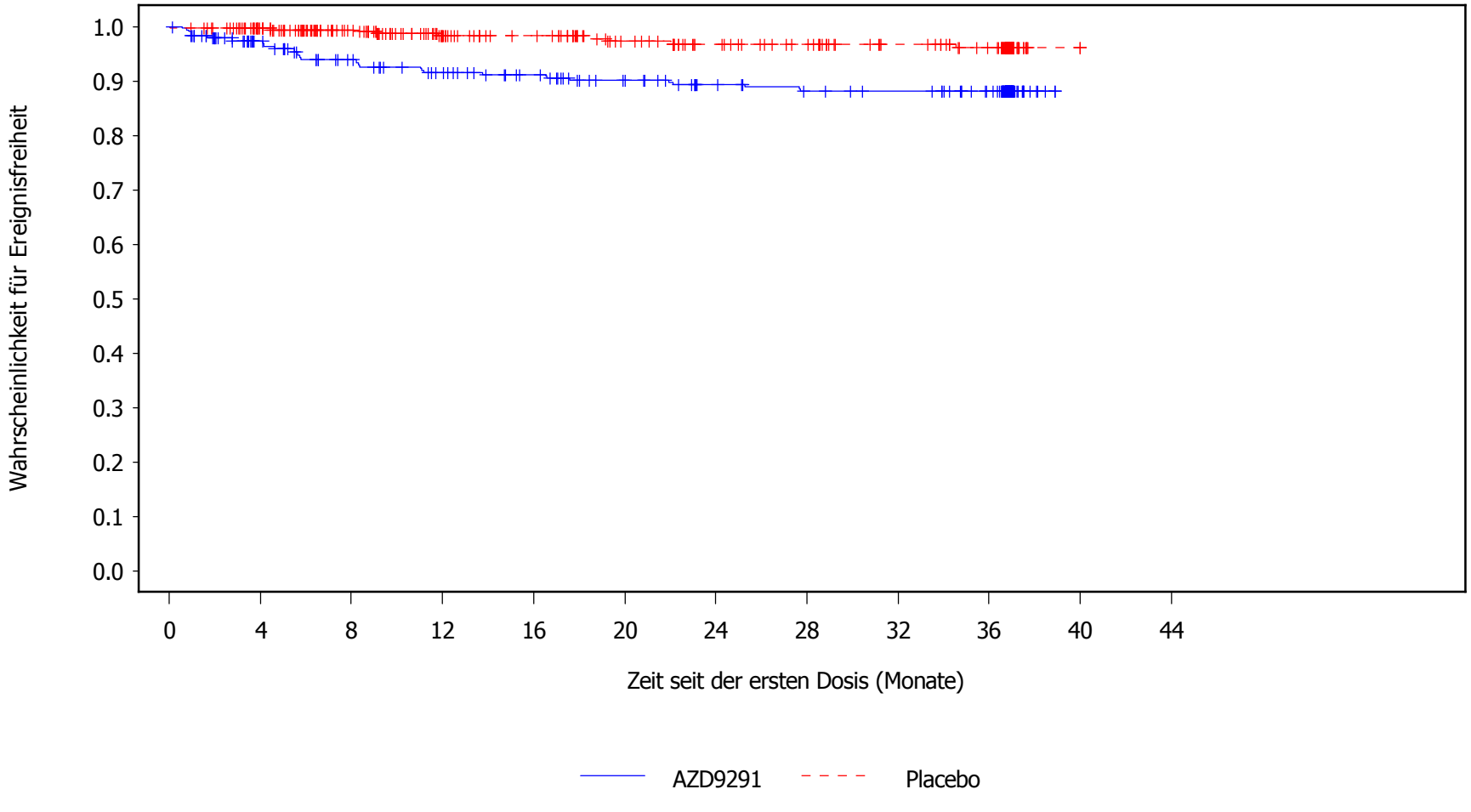
Figure 3.3.101 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Gewicht erniedrigt
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	299	274	258	246	231	218	211	208	197	0	0	AZD9291
343	319	276	230	214	189	173	163	148	136	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdw 30JUN2023:09:36 kvbv306

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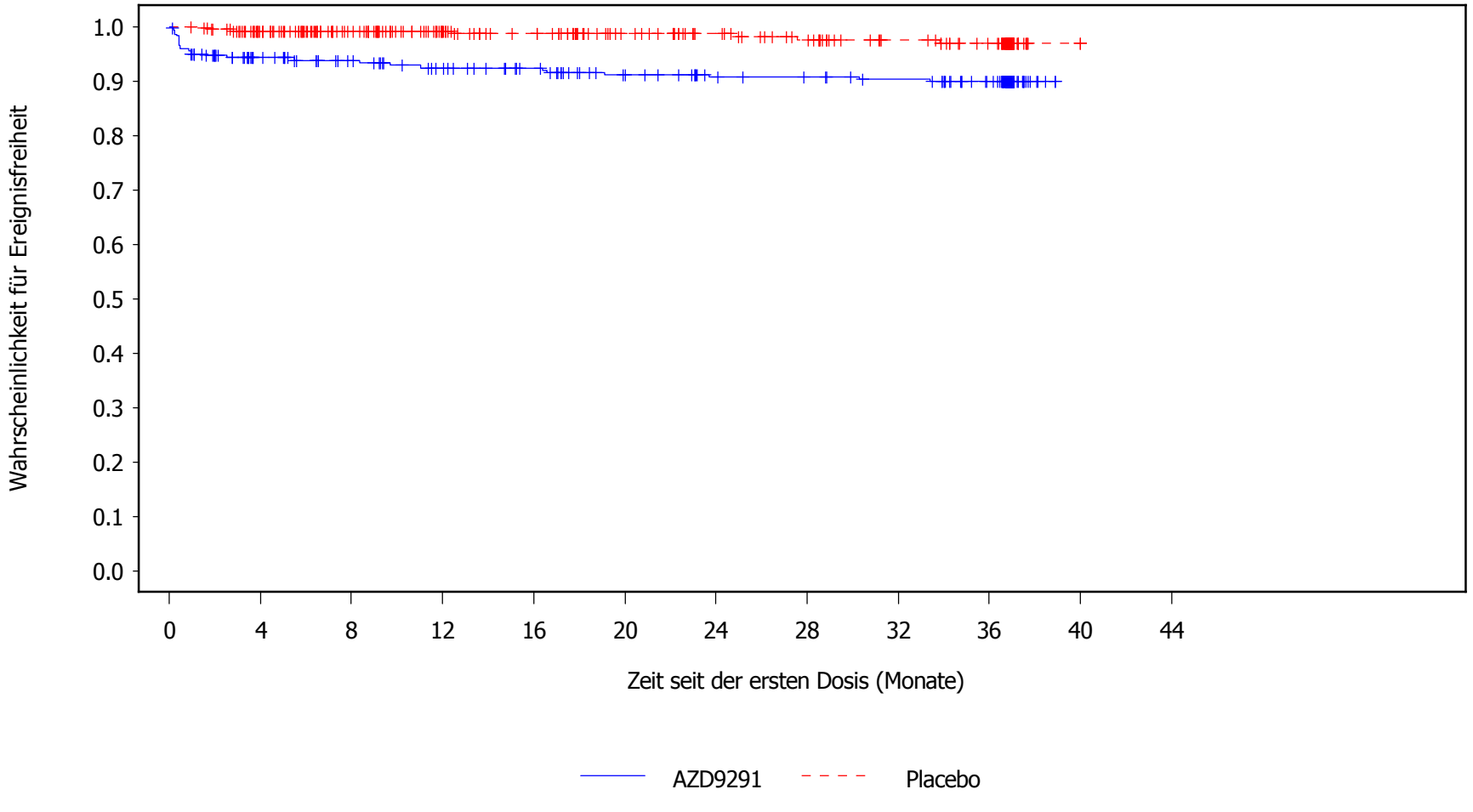
Figure 3.3.102 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Kreatinin im Blut erhoeht
Safety Analysis Set, DCO 11Apr2022

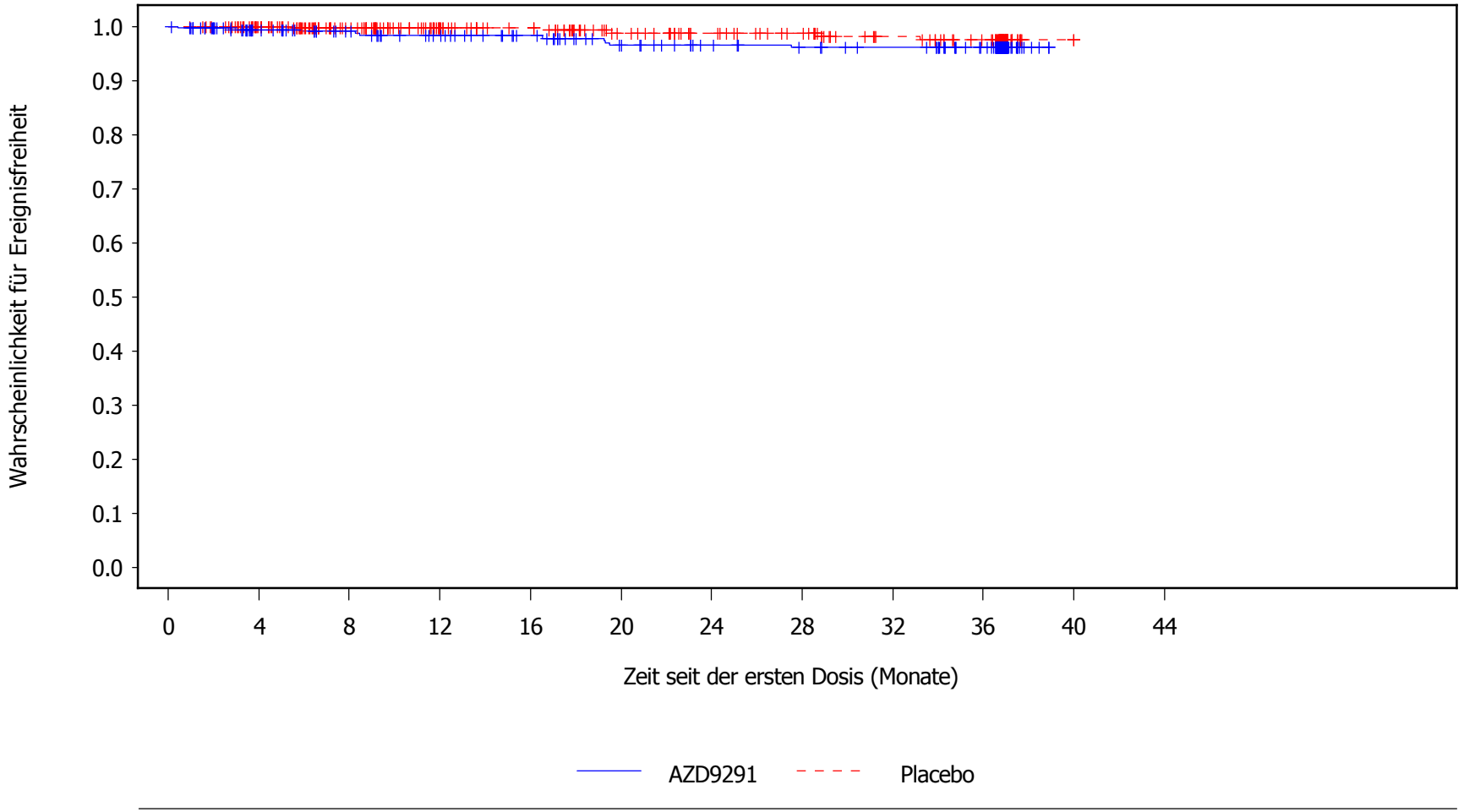


Anzahl an Patienten unter Risiko:

337	292	275	261	250	234	223	220	215	200	0	0	AZD9291
343	317	275	232	215	191	176	164	149	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdx 30JUN2023:09:36 kvbv306

Figure 3.3.103 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Kreatinphosphokinase im Blut erhoeht
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	306	290	278	266	248	238	233	229	214	0	0	AZD9291
343	320	277	233	218	191	176	166	149	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdy 30JUN2023:09:36 kvbv306

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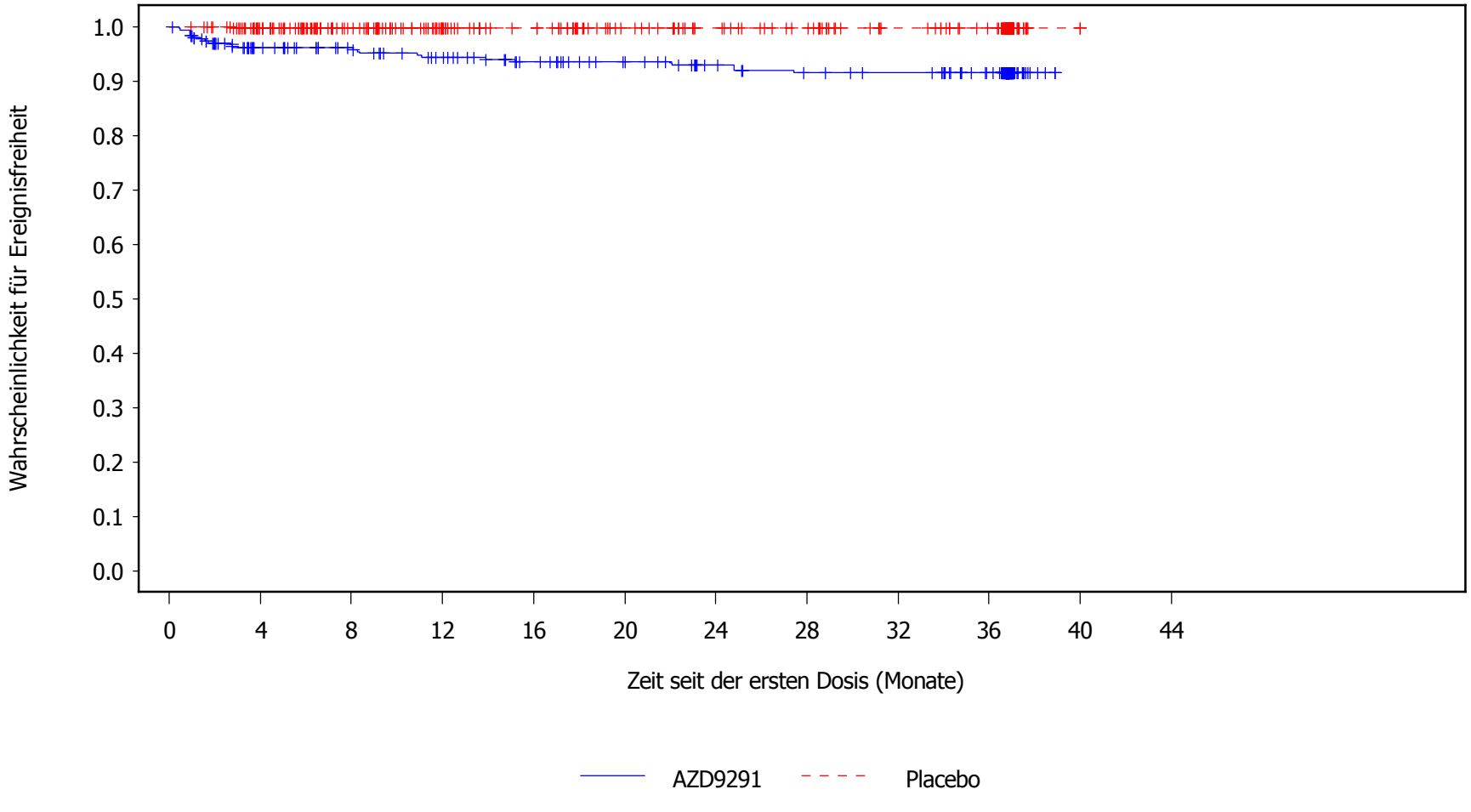
Figure 3.3.104 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Leukozytenzahl erniedrigt
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	295	280	266	252	241	228	221	218	204	0	0	AZD9291
343	319	277	233	217	192	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bdz 30JUN2023:09:36 kvbv306

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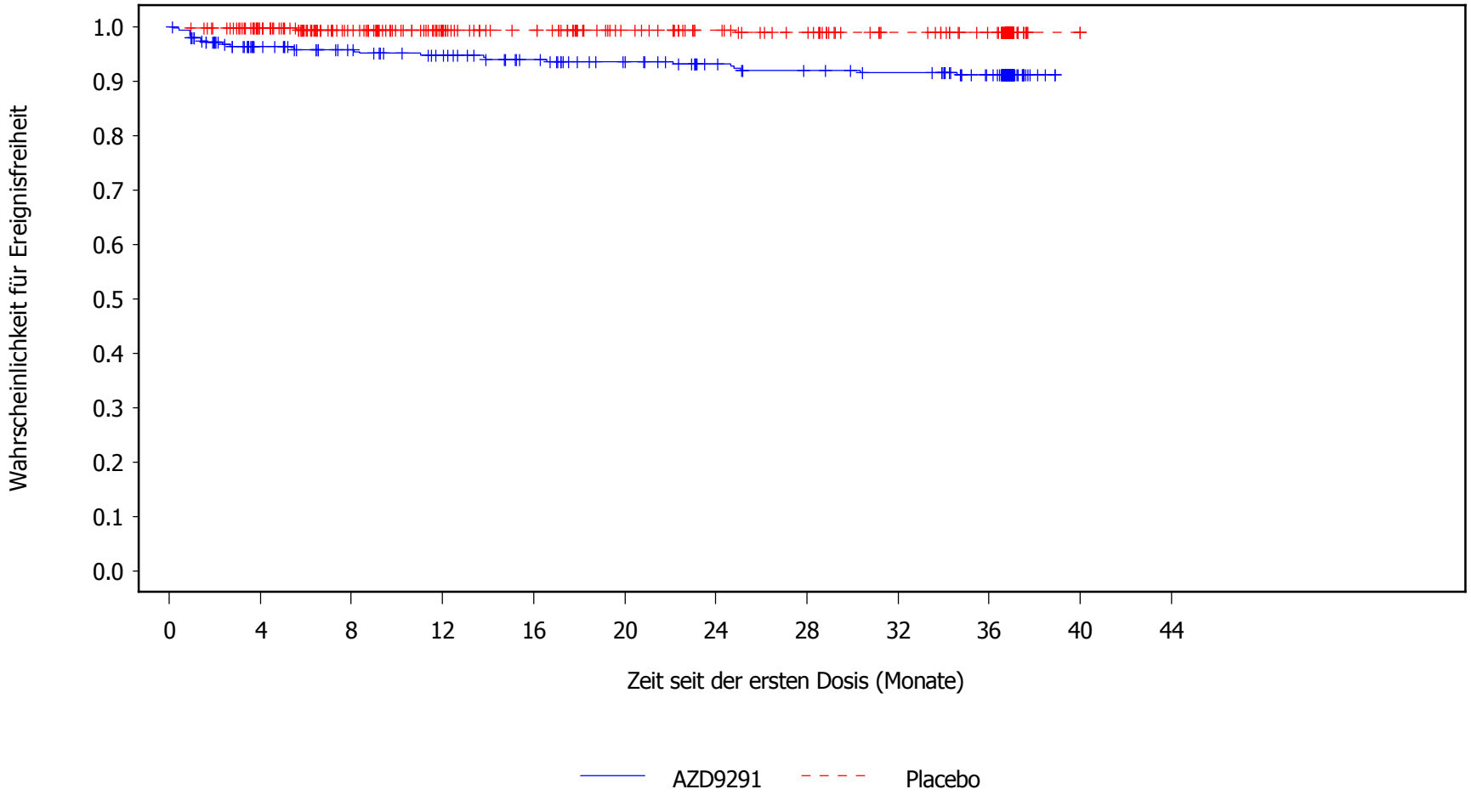
Figure 3.3.105 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Neutrophilenzahl erniedrigt
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	296	279	267	253	240	227	220	216	201	0	0	AZD9291
343	319	276	232	216	192	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bea 30JUN2023:09:36 kvbv306

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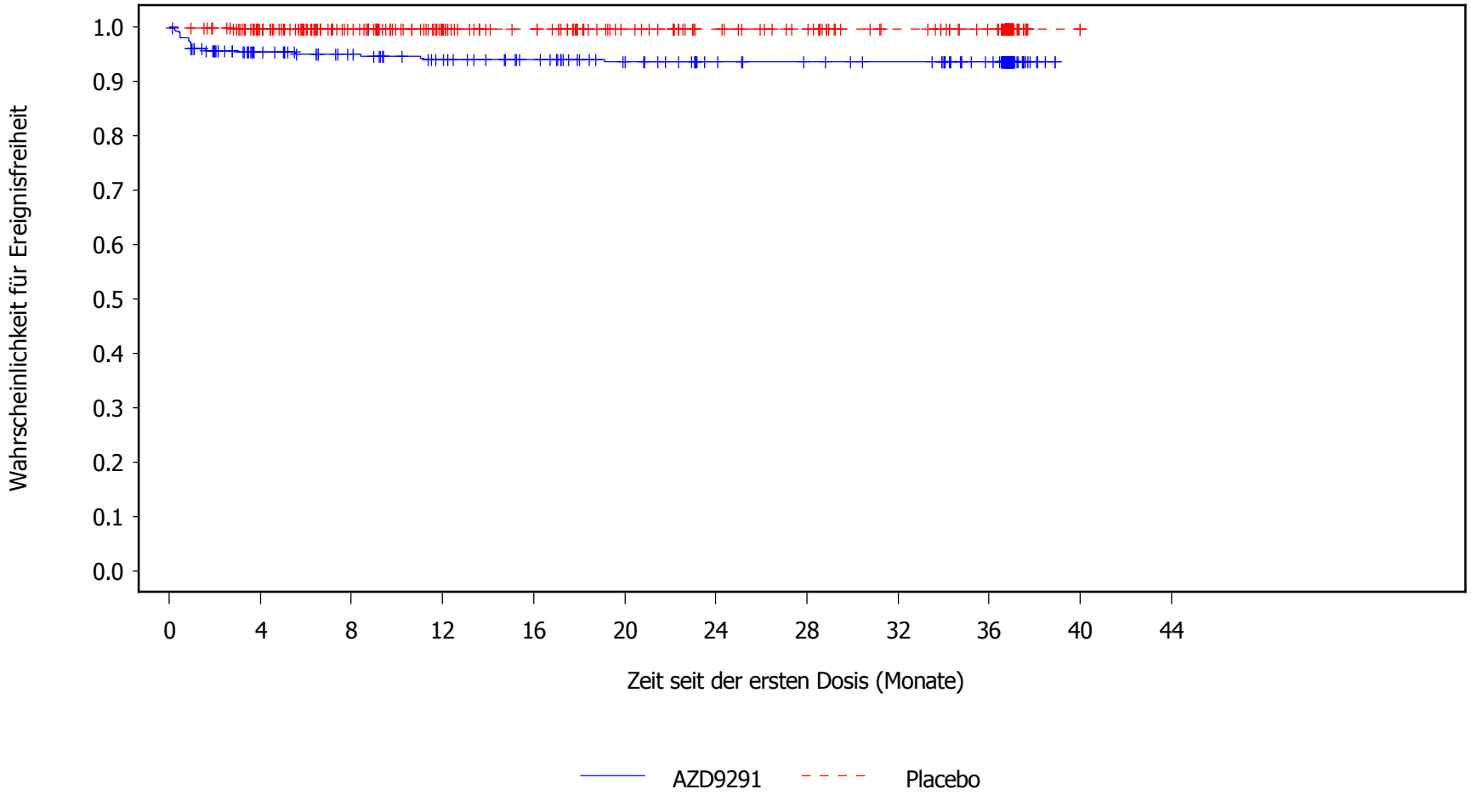
Figure 3.3.106 ADAURA: Kaplan-Meier plot of time to first occurrence of PT: Thrombozytenzahl vermindert
Safety Analysis Set, DCO 11Apr2022



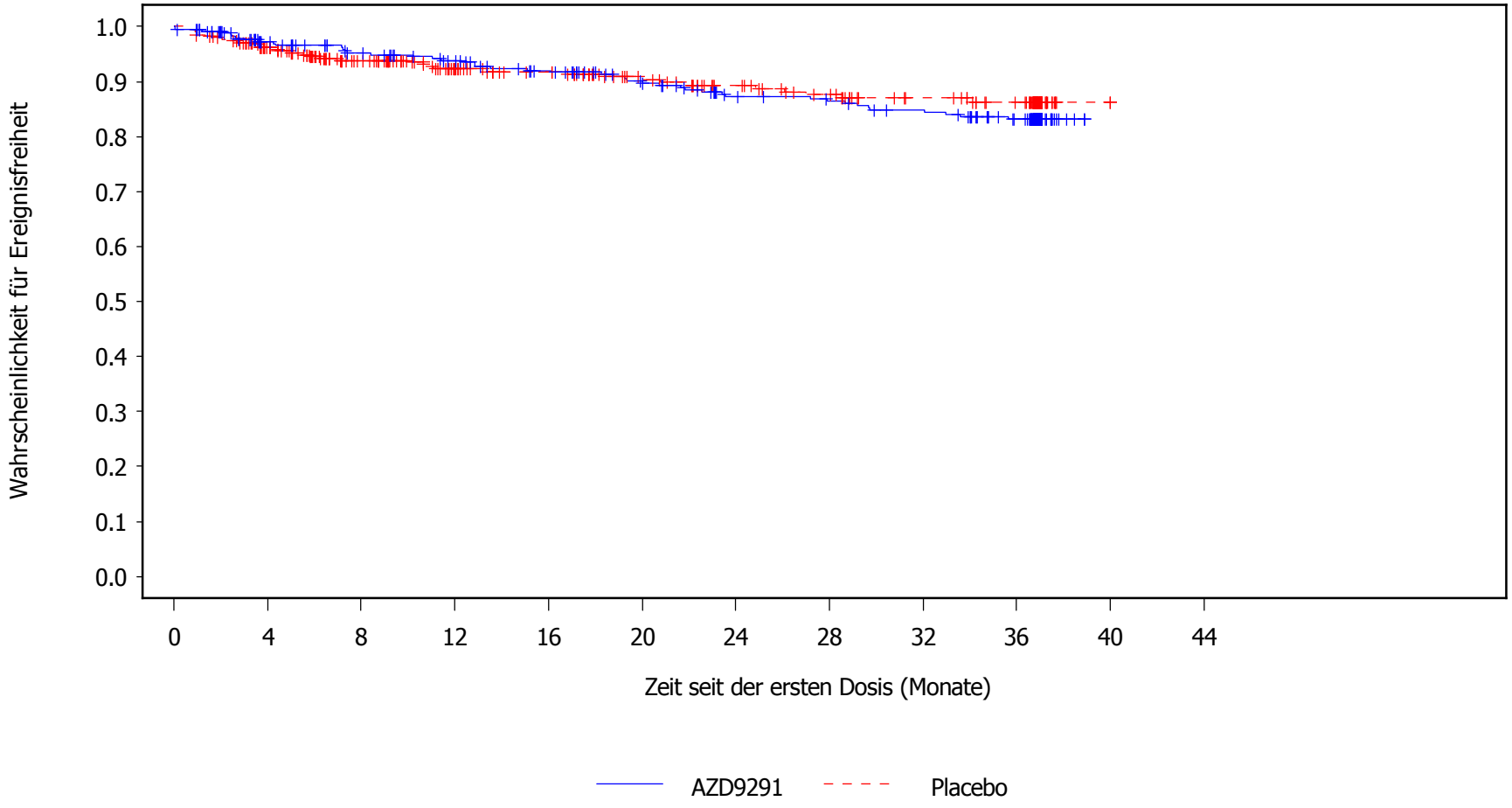
Anzahl an Patienten unter Risiko:

337	295	279	266	255	241	229	225	222	208	0	0	AZD9291
343	318	276	232	216	191	176	167	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2beb 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.107 ADAURA: Kaplan-Meier plot of time to first occurrence of SOC: Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen
Safety Analysis Set, DCO 11Apr2022

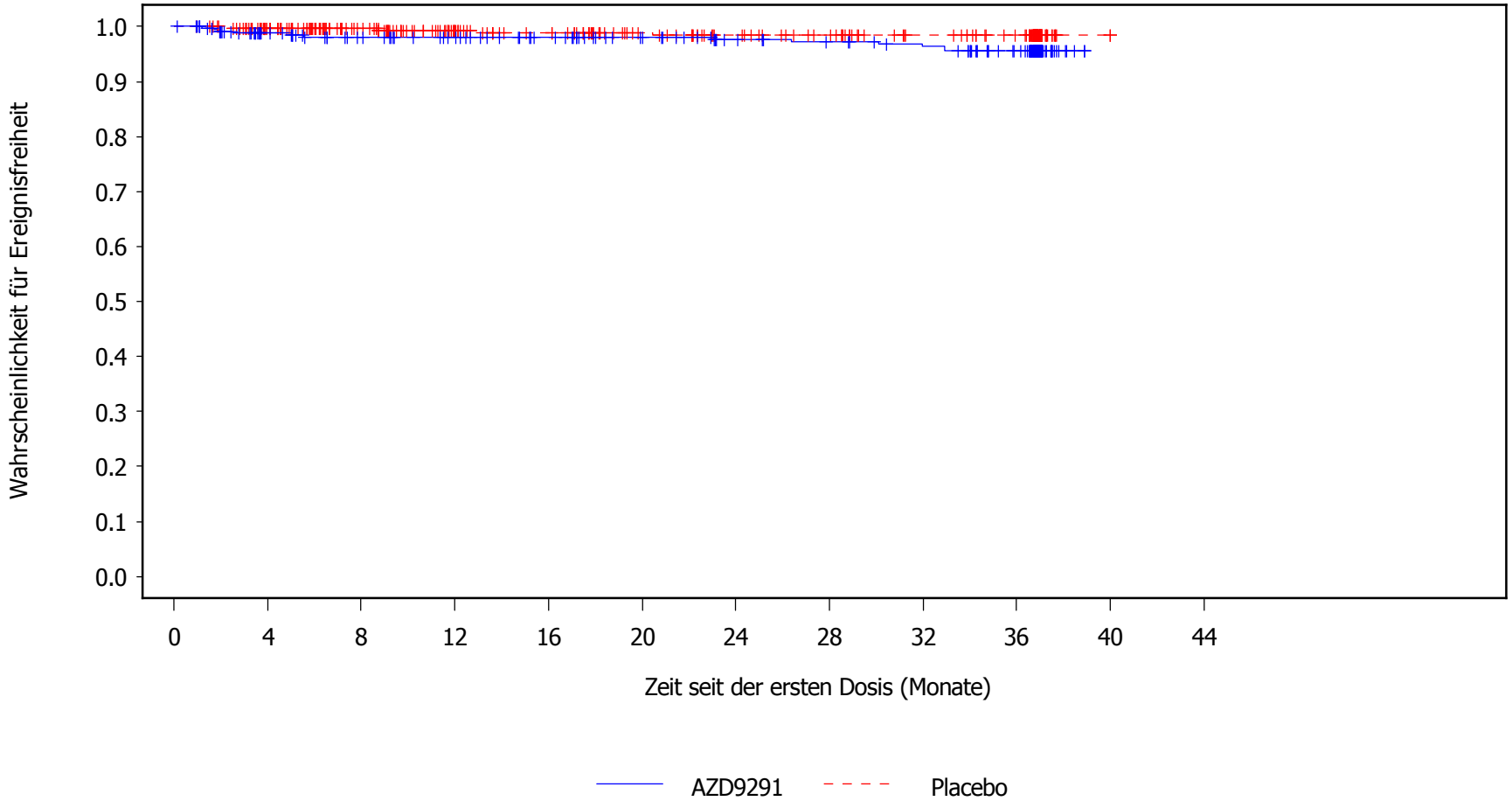


Anzahl an Patienten unter Risiko:

337	299	280	266	251	233	214	209	202	184	0	0 AZD9291
343	309	262	218	202	177	160	148	134	123	0	0 Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bec 30JUN2023:09:36 kvbv306

Figure 3.3.109 ADAURA: Kaplan-Meier plot of time to first occurrence of SUE SOC: Erkrankungen der Atemwege, des Brustraums und Mediastinums
Safety Analysis Set, DCO 11Apr2022

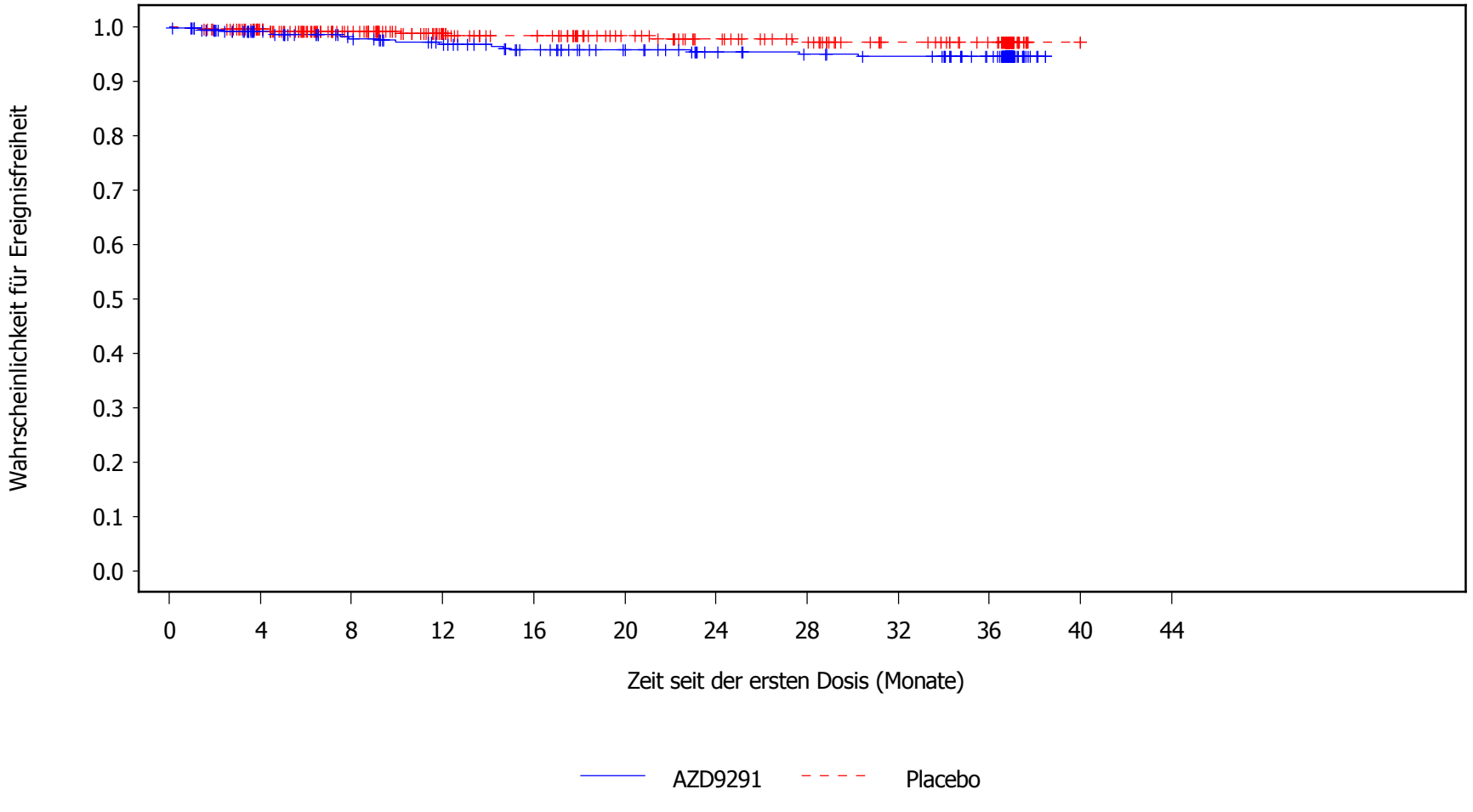


Anzahl an Patienten unter Risiko:

337	306	290	280	268	255	243	238	232	215	0	0	AZD9291
343	319	277	233	217	192	177	167	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bee 30JUN2023:09:36 kvbv306

Figure 3.3.110 ADAURA: Kaplan-Meier plot of time to first occurrence of SUE SOC: Infektionen und parasitaere Erkrankungen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	306	288	276	261	249	237	232	228	214	0	0	AZD9291
343	318	275	232	216	192	177	166	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bef 30JUN2023:09:36 kvbv306

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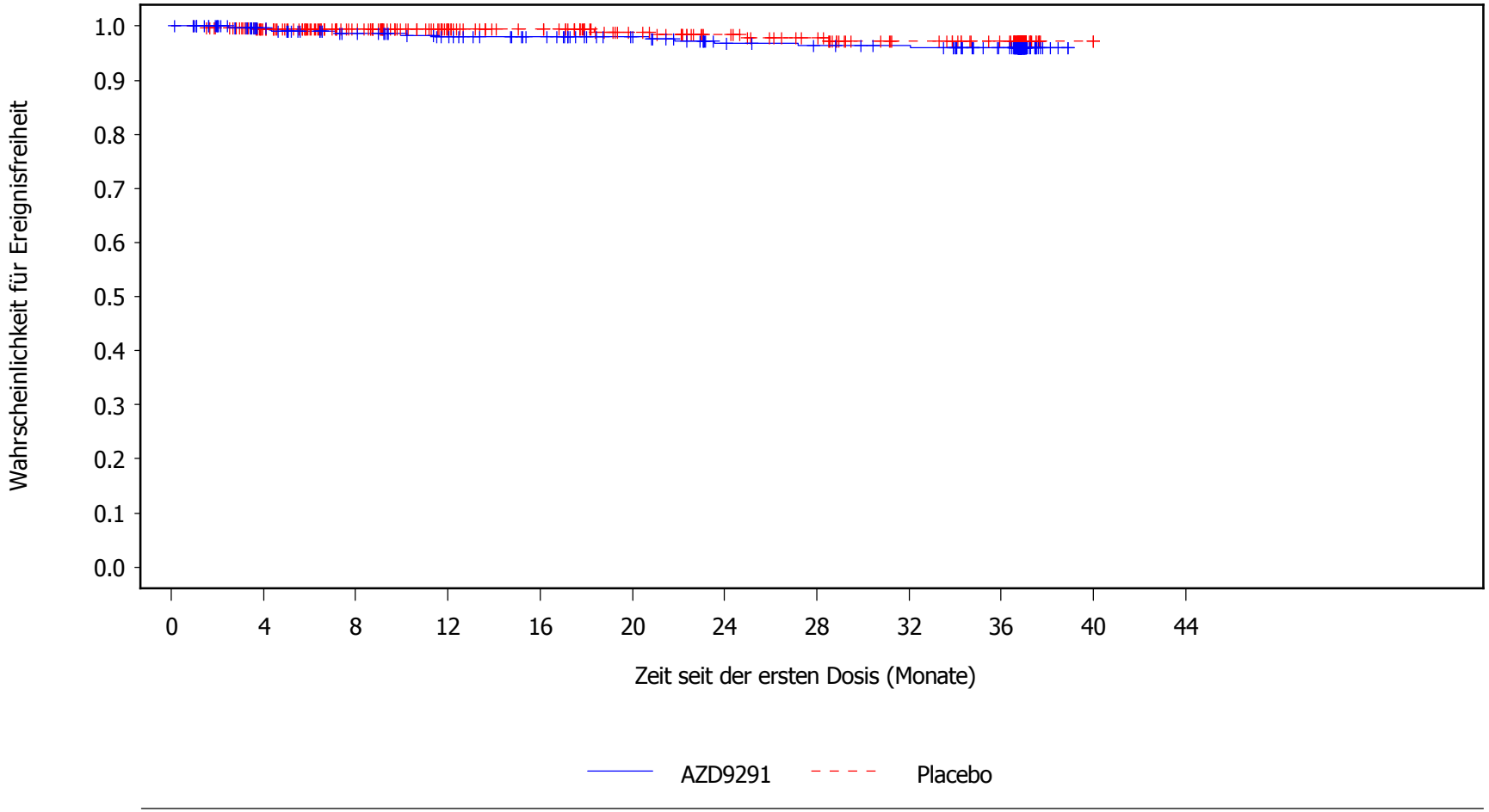
Figure 3.3.111 ADAURA: Kaplan-Meier plot of time to first occurrence of SUE SOC: Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	307	290	278	267	254	239	235	232	216	0	0	AZD9291
343	318	276	233	217	192	176	165	148	137	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2beg 30JUN2023:09:36 kvbv306

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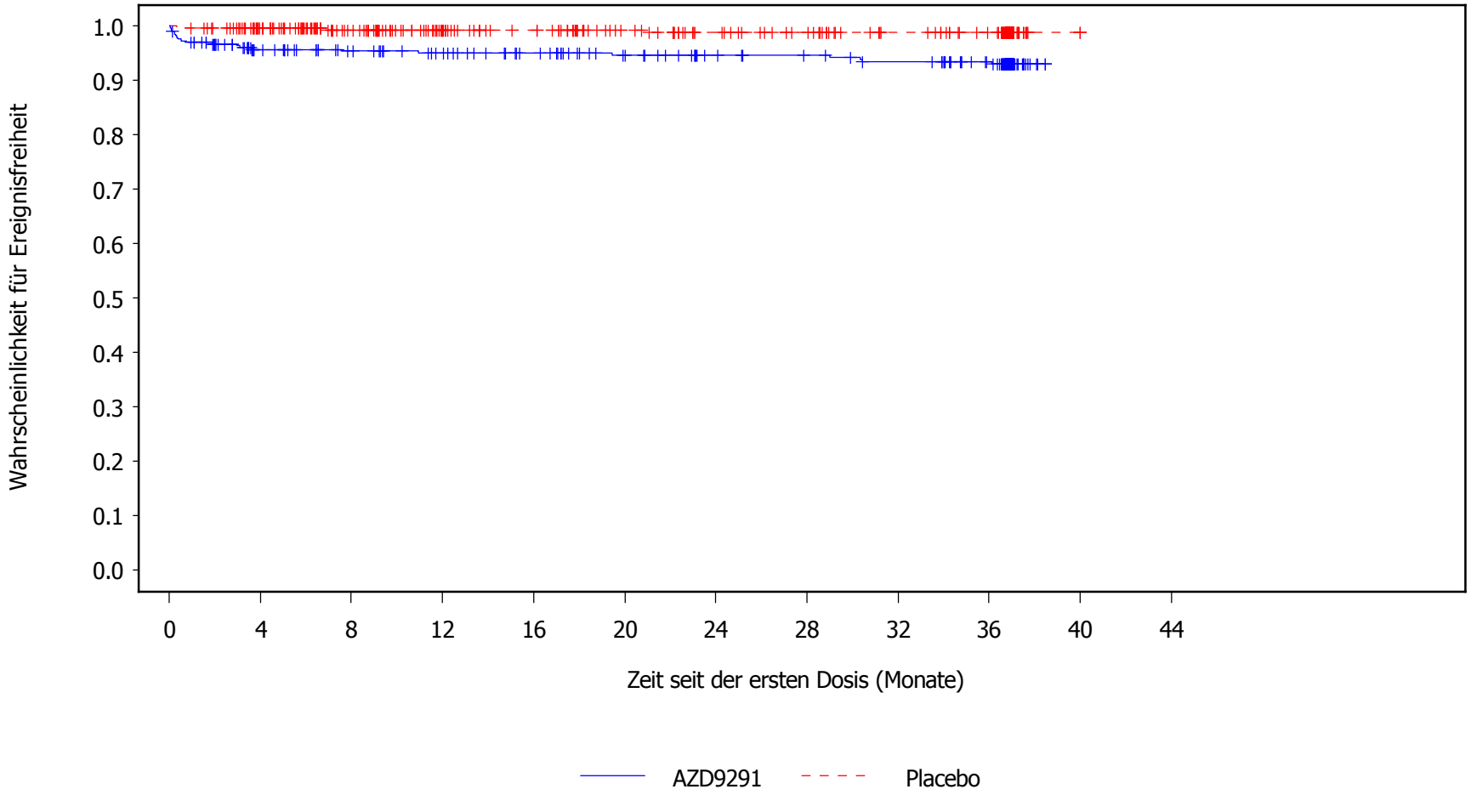
Figure 3.3.114 ADAURA: Kaplan-Meier plot of time to first occurrence of G>=3 SOC: Erkrankungen des Gastrointestinaltrakts
Safety Analysis Set, DCO 11Apr2022



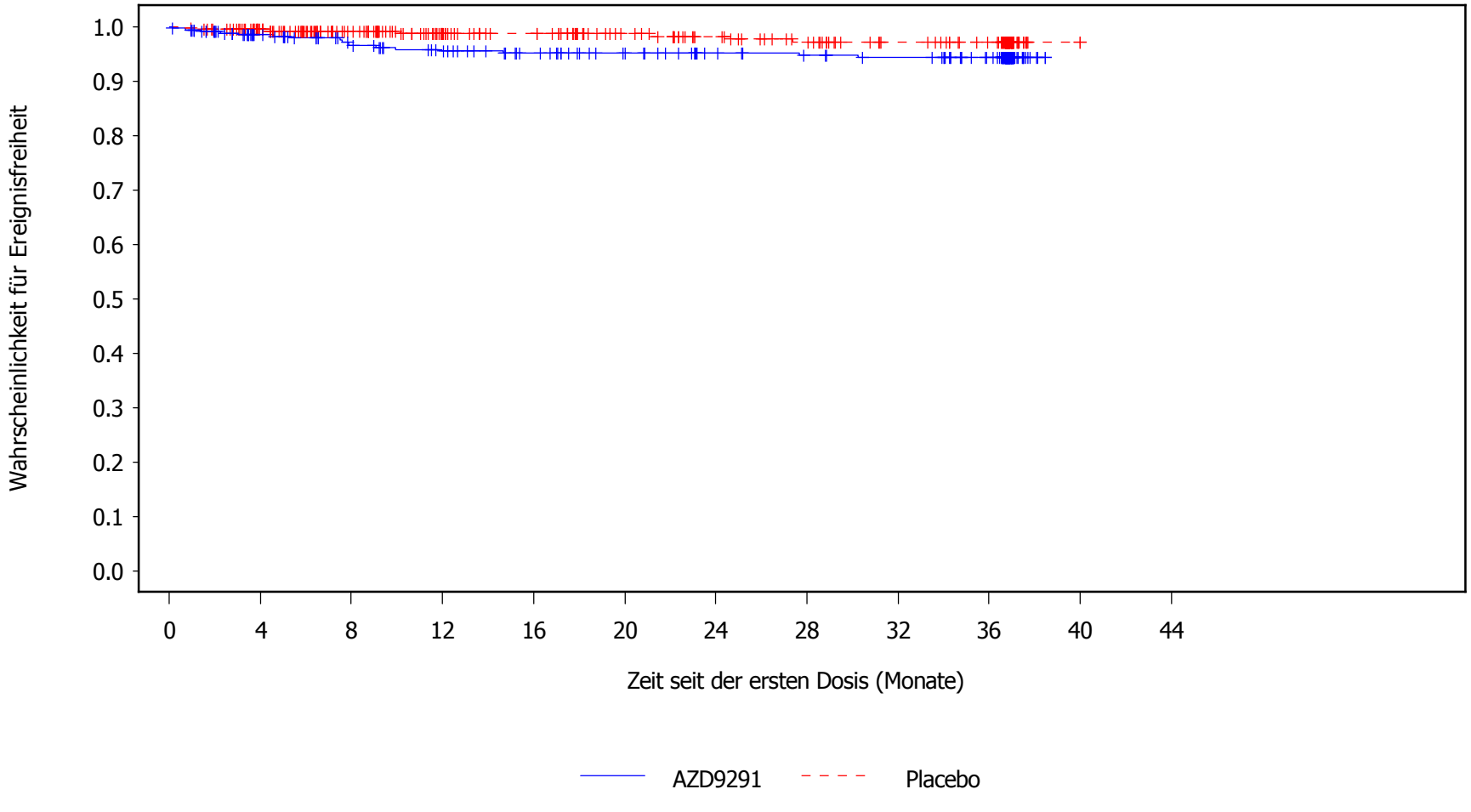
Anzahl an Patienten unter Risiko:

337	296	280	269	257	243	231	227	221	206	0	0	AZD9291
343	319	276	232	216	192	176	166	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bej 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.115 ADAURA: Kaplan-Meier plot of time to first occurrence of G>=3 SOC: Infektionen und parasitaere Erkrankungen
Safety Analysis Set, DCO 11Apr2022



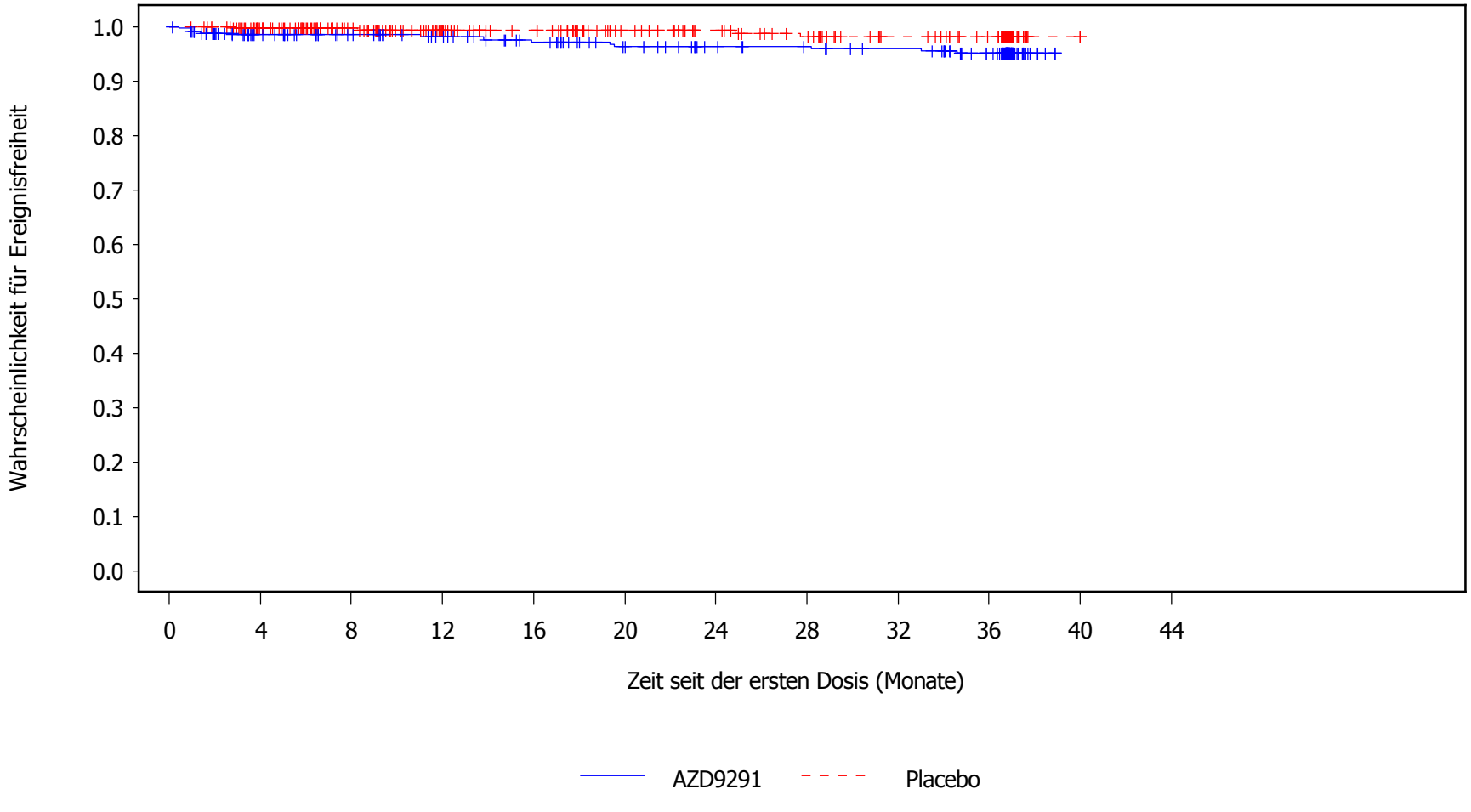
Anzahl an Patienten unter Risiko:

337	304	284	272	259	247	235	230	226	212	0	0	AZD9291
343	318	275	232	217	193	177	165	150	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bek 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.116 ADAURA: Kaplan-Meier plot of time to first occurrence of G>=3 SOC: Untersuchungen
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	303	288	277	264	250	238	234	229	213	0	0	AZD9291
343	319	278	233	217	192	177	166	151	140	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bel 30JUN2023:09:36 kvbv306

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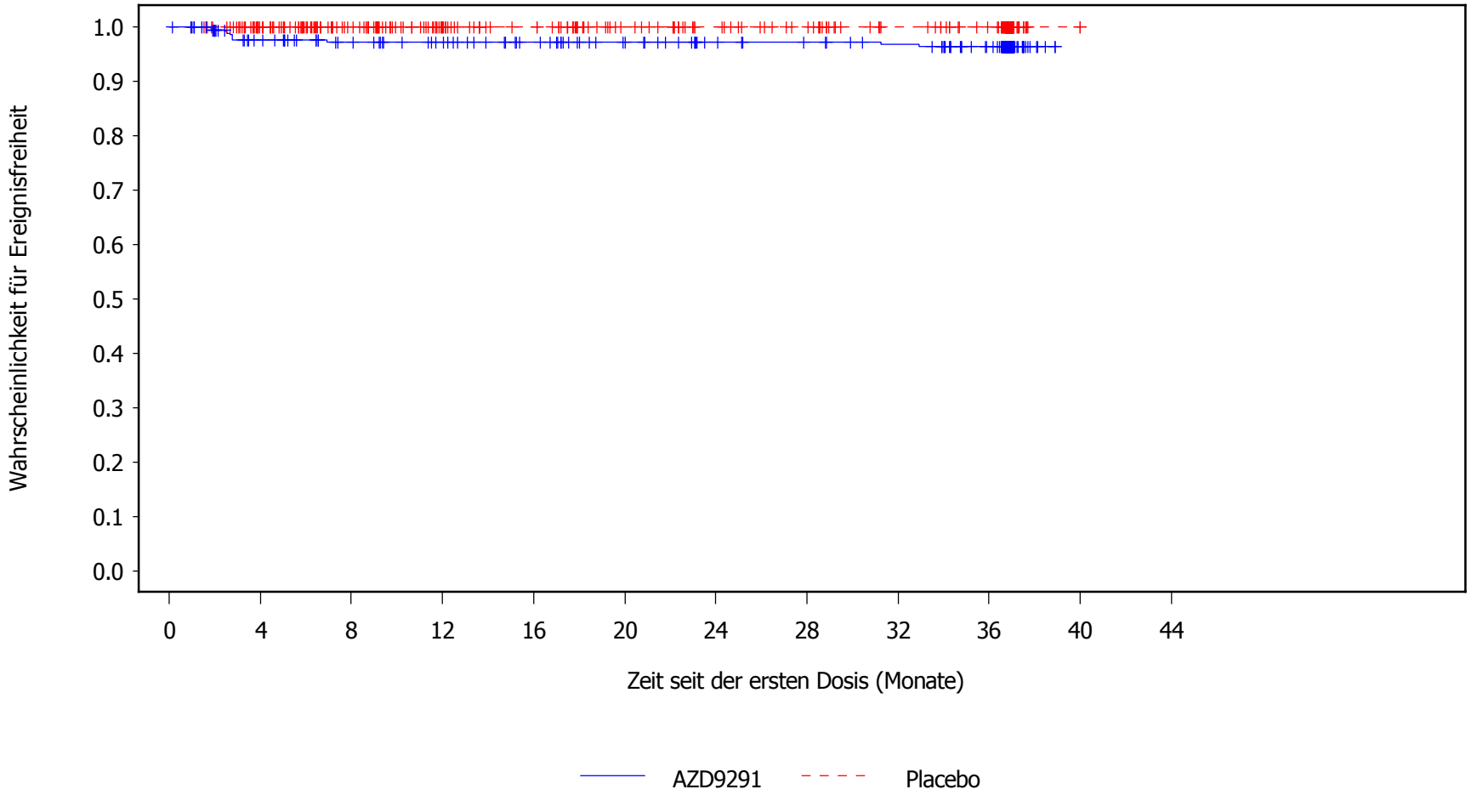
Figure 3.3.117 ADAURA: Kaplan-Meier plot of time to first occurrence of UESI GT: ILD UND PNEUMONITIS
Safety Analysis Set, DCO 11Apr2022

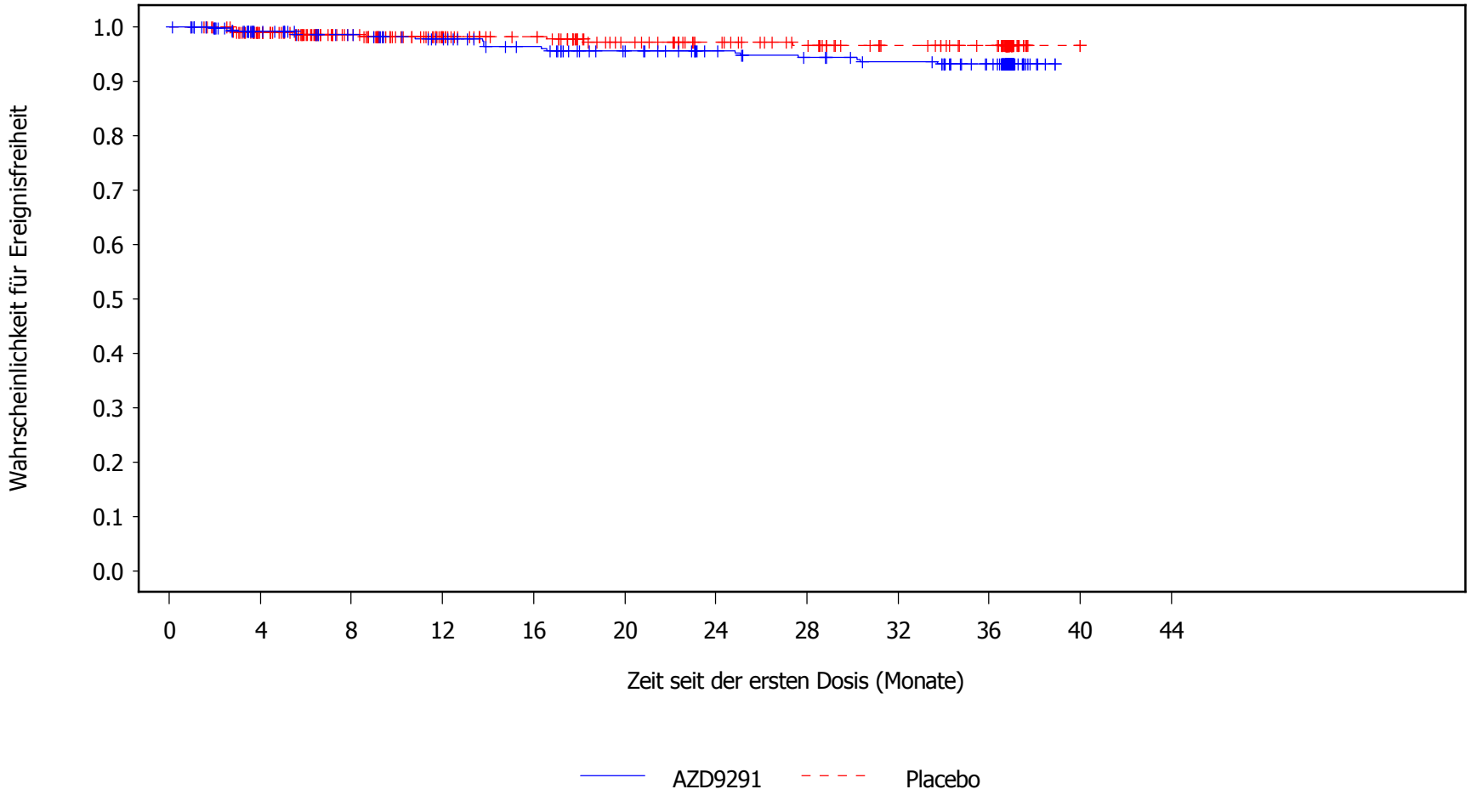


Anzahl an Patienten unter Risiko:

337	308	293	283	271	258	246	242	237	221	0	0	AZD9291
343	320	278	234	218	193	178	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bem 30JUN2023:09:36 kvbv306

Figure 3.3.118 ADAURA: Kaplan-Meier plot of time to first occurrence of UESI GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022



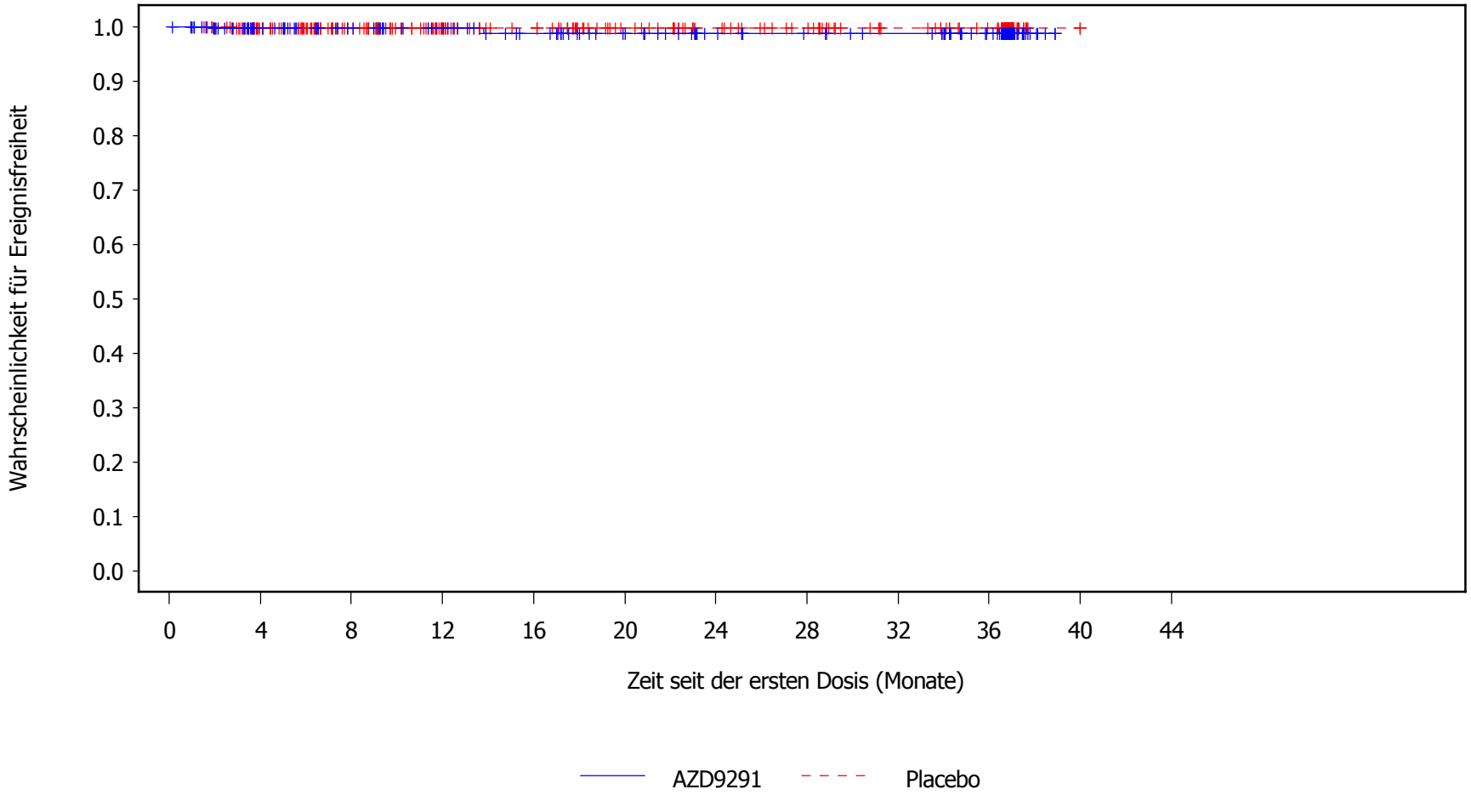
Anzahl an Patienten unter Risiko:

337	306	290	278	265	251	239	232	226	211	0	0	AZD9291
343	316	274	229	213	187	172	161	147	138	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2ben 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.119 ADAURA: Kaplan-Meier plot of time to first occurrence of UESI G>=3 GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022



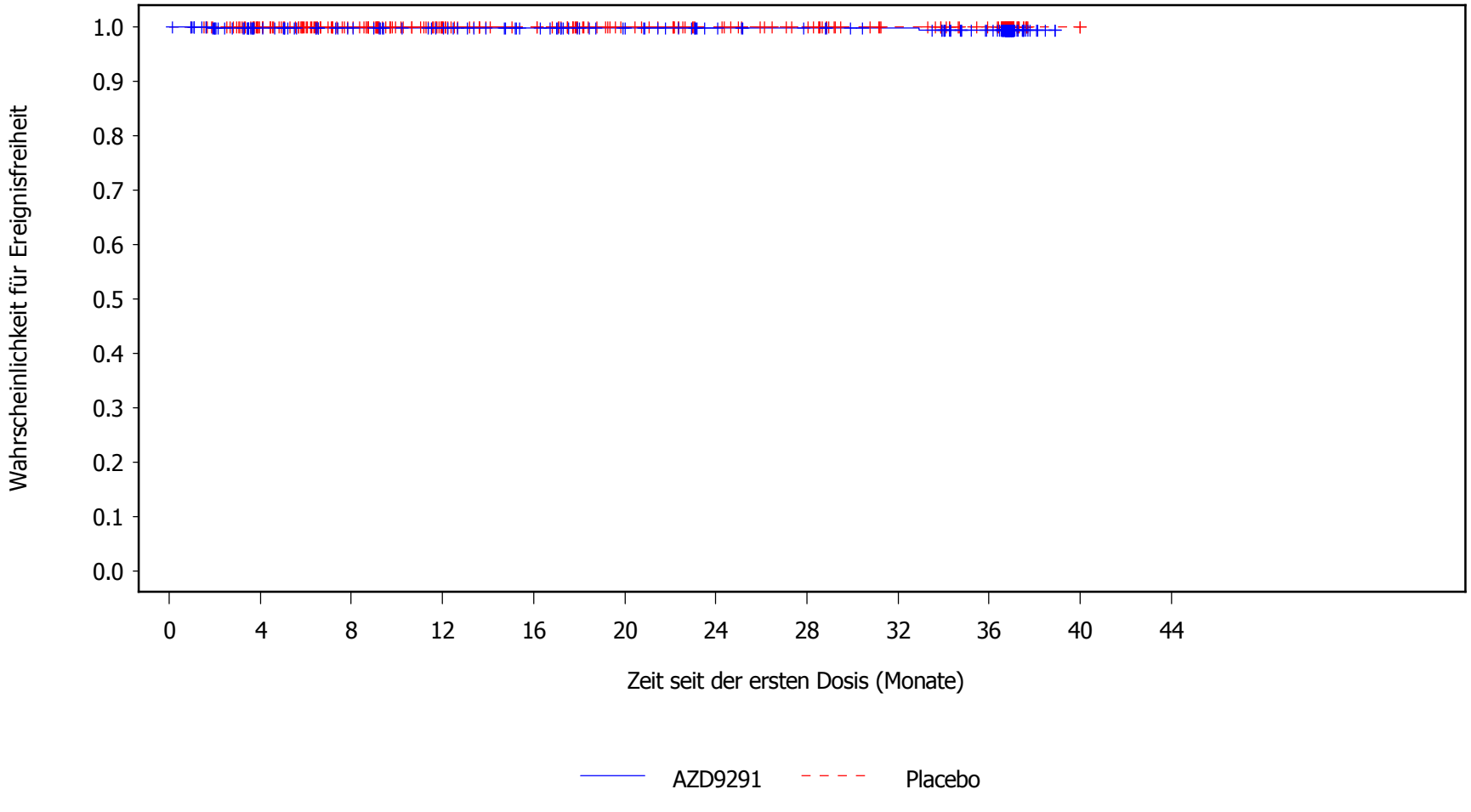
Anzahl an Patienten unter Risiko:

337	308	293	283	270	258	246	242	238	223	0	0	AZD9291
343	319	278	234	218	193	178	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2beo 30JUN2023:09:36 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 3.3.120 ADAURA: Kaplan-Meier plot of time to first occurrence of SUESI GT: ILD UND PNEUMONITIS
Safety Analysis Set, DCO 11Apr2022

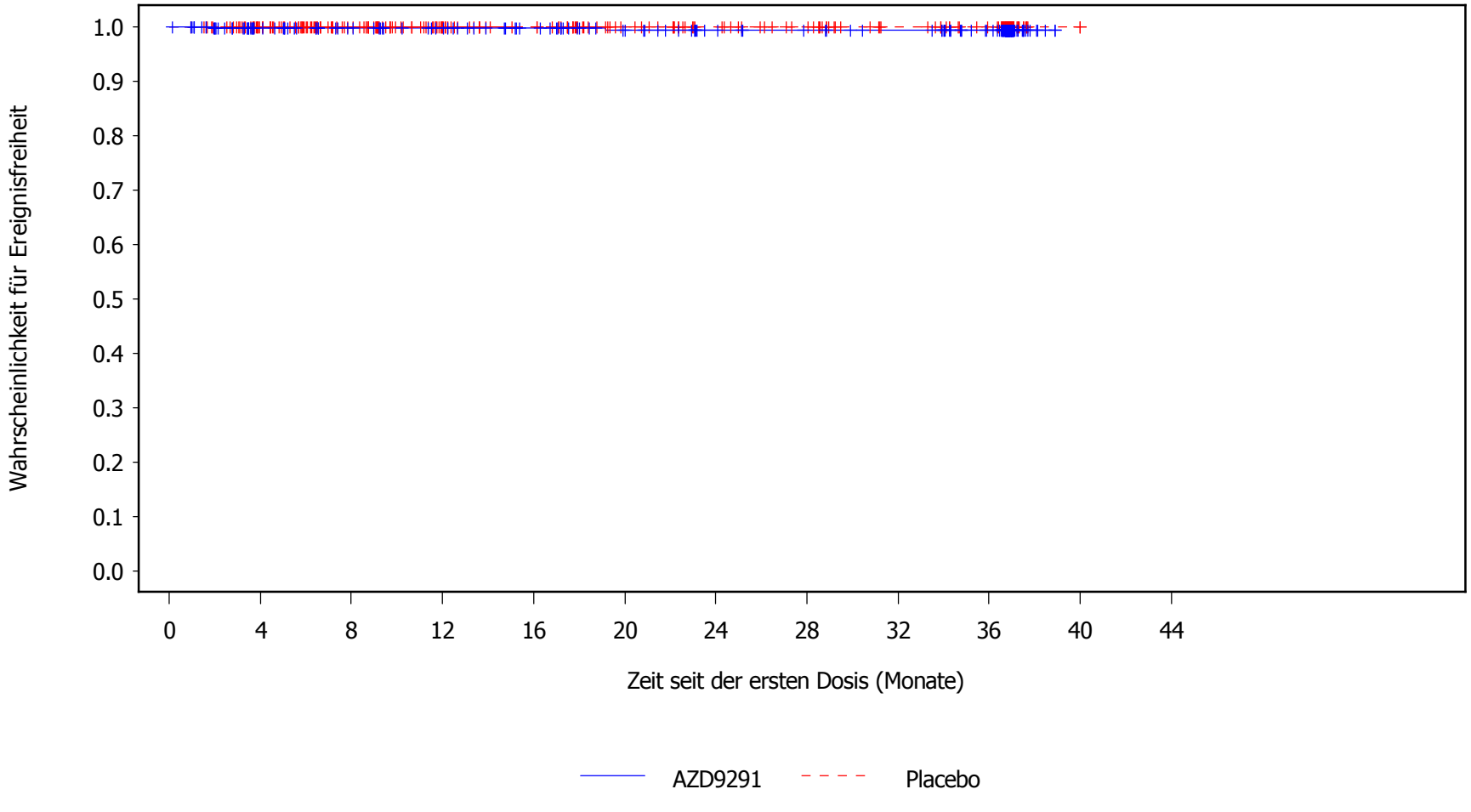


Anzahl an Patienten unter Risiko:

337	308	293	283	271	258	246	242	238	222	0	0	AZD9291
343	320	278	234	218	193	178	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2bep 30JUN2023:09:36 kvbv306

Figure 3.3.121 ADAURA: Kaplan-Meier plot of time to first occurrence of SUESI GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

337	308	293	283	271	257	245	241	237	222	0	0	AZD9291
343	320	278	234	218	193	178	168	152	141	0	0	Placebo

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttemae_v2.sas gttemae_v2beq 30JUN2023:09:36 kvbv306

Table 4.1.1.1 ADAURA: Summary of subgroup analysis of overall survival (OS)
Full Analysis Set, DCO 27Jan2023

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	18 (16,5)	NE [NE; NE]	95	24 (25,3)	NE [NE; NE]	0,62	[0,33; 1,13]	0,1204
Weiblich	230	24 (10,4)	NE [NE; NE]	248	58 (23,4)	NE [NE; NE]	0,41	[0,25; 0,66]	0,0001*
Interaktion p-Wert									0,3087
Alter									
<65 Jahre	185	22 (11,9)	NE [NE; NE]	195	38 (19,5)	NE [NE; NE]	0,56	[0,33; 0,94]	0,0276*
>=65 Jahre	154	20 (13,0)	NE [NE; NE]	148	44 (29,7)	NE [NE; NE]	0,42	[0,24; 0,69]	0,0007*
Interaktion p-Wert									0,4295
Abstammung									
Asiatisch	216	29 (13,4)	NE [NE; NE]	218	44 (20,2)	NE [NE; NE]	0,61	[0,38; 0,97]	0,0380*
Nicht-asiatisch	123	13 (10,6)	NE [NE; NE]	125	38 (30,4)	NE [NE; NE]	0,33	[0,17; 0,61]	0,0002*
Interaktion p-Wert									0,1213
EGFR-Mutation									
Exon 19 Deletion	187	18 (9,6)	NE [NE; NE]	191	47 (24,6)	NE [NE; NE]	0,35	[0,20; 0,59]	<0,0001*
L858R	152	24 (15,8)	NE [NE; NE]	152	35 (23,0)	78,7 [72,4; NE]	0,68	[0,40; 1,14]	0,1448
Interaktion p-Wert									0,0767
Krankheitsstadium Version 7									
Stadium IB	106	7 (6,6)	NE [NE; NE]	106	17 (16,0)	NE [NE; NE]	0,44	[0,17; 1,02]	0,0546
Stadium II	118	18 (15,3)	NE [NE; NE]	118	28 (23,7)	NE [NE; NE]	0,63	[0,34; 1,12]	0,1174
Stadium IIIA	115	17 (14,8)	NE [NE; NE]	119	37 (31,1)	NE [NE; NE]	0,37	[0,20; 0,64]	0,0003*
Interaktion p-Wert									0,4371
Krankheitsstadium Version 8									
Stadium IB	101	6 (5,9)	NE [NE; NE]	98	16 (16,3)	NE [NE; NE]	0,38	[0,14; 0,92]	0,0318*
Stadium II	113	18 (15,9)	NE [NE; NE]	119	27 (22,7)	NE [NE; NE]	0,70	[0,38; 1,25]	0,2298
Stadium IIIA	110	16 (14,5)	NE [NE; NE]	115	33 (28,7)	NE [NE; NE]	0,40	[0,22; 0,72]	0,0021*

OS is defined as the time from the date of randomisation until date of death due to any cause (regardless of subsequent anti-cancer therapy) or to the date patient was known to be alive. If patient dies immediately after >=2 consecutive missed visits, they will be censored at the date patient was known to be alive prior to the two missed visits. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms.
[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation. Hazard ratio <1 favours Osimertinib. * p<0.05.

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Table 4.1.1.1 ADAURA: Summary of subgroup analysis of overall survival (OS)
Full Analysis Set, DCO 27Jan2023

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktion p-Wert									0,3692
Adjuvante Chemotherapie									
Ja	203	26 (12,8)	NE [NE; NE]	207	48 (23,2)	NE [NE; NE]	0,49	[0,30; 0,79]	0,0029*
Nein	136	16 (11,8)	NE [NE; NE]	136	34 (25,0)	NE [NE; NE]	0,47	[0,25; 0,83]	0,0094*
Interaktion p-Wert									0,8901
Raucherstatus									
Ja	108	13 (12,0)	NE [NE; NE]	86	21 (24,4)	NE [NE; NE]	0,45	[0,22; 0,89]	0,0212*
Nein	231	29 (12,6)	NE [NE; NE]	257	61 (23,7)	NE [NE; NE]	0,49	[0,31; 0,76]	0,0013*
Interaktion p-Wert									0,8221
Region									
Asien	205	27 (13,2)	NE [NE; NE]	209	41 (19,6)	NE [NE; NE]	0,62	[0,38; 1,01]	0,0539
Europa	62	4 (6,5)	NE [NE; NE]	69	14 (20,3)	NE [NE; NE]	0,32	[0,09; 0,89]	0,0287*
Nordamerika	14	2 (14,3)	70,1 [70,1; NE]	11	3 (27,3)	NE [NE; NE]	0,42	[0,06; 2,53]	0,3333
Rest der Welt	58	9 (15,5)	NE [NE; NE]	54	24 (44,4)	72,4 [60,2; NE]	0,31	[0,14; 0,65]	0,0014*
Interaktion p-Wert									0,3976

OS is defined as the time from the date of randomisation until date of death due to any cause (regardless of subsequent anti-cancer therapy) or to the date patient was known to be alive. If patient dies immediately after >=2 consecutive missed visits, they will be censored at the date patient was known to be alive prior to the two missed visits. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms.
[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation. Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 4.1.1.2 ADAURA: Summary of subgroup analysis of time to first disease-free survival (DFS)
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	33 (30,3)	NE [NE; NE]	95	62 (65,3)	23,3 [12,9;38,8]	0,31	[0,20; 0,48]	<0,0001*
Weiblich	230	61 (26,5)	65,8 [61,7; NE]	248	149 (60,1)	30,8 [23,4;38,8]	0,31	[0,23; 0,42]	<0,0001*
Interaktion p-Wert									0,9955
Alter									
<65 Jahre	185	53 (28,6)	65,8 [57,0; NE]	195	123 (63,1)	27,7 [19,4;36,1]	0,31	[0,22; 0,42]	<0,0001*
>=65 Jahre	154	41 (26,6)	61,7 [61,7; NE]	148	88 (59,5)	30,8 [22,1;41,1]	0,33	[0,23; 0,48]	<0,0001*
Interaktion p-Wert									0,7529
Abstammung									
Asiatisch	216	66 (30,6)	NE [NE; NE]	218	136 (62,4)	29,4 [22,3;36,1]	0,34	[0,25; 0,45]	<0,0001*
Nicht-asiatisch	123	28 (22,8)	65,8 [61,7; NE]	125	75 (60,0)	26,4 [18,8;41,6]	0,28	[0,18; 0,43]	<0,0001*
Interaktion p-Wert									0,4860
EGFR-Mutation									
Exon 19 Deletion	187	48 (25,7)	65,8 [61,7; NE]	191	127 (66,5)	22,6 [17,5;33,0]	0,24	[0,17; 0,33]	<0,0001*
L858R	152	46 (30,3)	NE [NE; NE]	152	84 (55,3)	38,9 [27,4;50,2]	0,45	[0,31; 0,64]	<0,0001*
Interaktion p-Wert									0,0114*
Krankheitsstadium Version 7									
Stadium IB	106	19 (17,9)	NE [NE; NE]	106	44 (41,5)	NE [NE; NE]	0,41	[0,23; 0,69]	0,0006*
Stadium II	118	33 (28,0)	65,8 [55,0; NE]	118	69 (58,5)	31,5 [22,1;49,7]	0,34	[0,23; 0,52]	<0,0001*
Stadium IIIA	115	42 (36,5)	55,1 [49,5; NE]	119	98 (82,4)	12,9 [11,0;19,0]	0,20	[0,14; 0,29]	<0,0001*
Interaktion p-Wert									0,0549
Krankheitsstadium Version 8									
Stadium IB	101	19 (18,8)	NE [NE; NE]	98	40 (40,8)	NE [NE; NE]	0,44	[0,25; 0,76]	0,0025*

DFS is defined as the time from the date of randomisation until the date of disease recurrence or death (by any cause in the absence of recurrence) regardless of whether the patient withdraws from randomised therapy or receives another anti-cancer therapy prior to recurrence. If patient experience recurrence or dies immediately after >=2 consecutive missed visits, they will be censored at the time of the latest evaluable assessment for disease recurrence prior to the two missed visits. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms.

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).

[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation. Hazard ratio <1 favours Osimertinib. * p<0.05.

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Table 4.1.1.2 ADAURA: Summary of subgroup analysis of time to first disease-free survival (DFS)
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium II	113	29 (25,7)	65,8 [54,4; NE]	119	69 (58,0)	33,1 [24,5;49,8]	0,33	[0,21; 0,50]	<0,0001*
Stadium IIIA	110	41 (37,3)	55,1 [49,5; NE]	115	92 (80,0)	14,4 [11,0;21,3]	0,22	[0,15; 0,31]	<0,0001*
Interaktion p-Wert									0,0890
Adjuvante Chemotherapie									
Ja	203	62 (30,5)	65,8 [54,4; NE]	207	140 (67,6)	24,6 [18,4;32,9]	0,29	[0,21; 0,39]	<0,0001*
Nein	136	32 (23,5)	NE [NE; NE]	136	71 (52,2)	41,6 [27,6; NE]	0,36	[0,24; 0,55]	<0,0001*
Interaktion p-Wert									0,3902
Raucherstatus									
Ja	108	27 (25,0)	NE [NE; NE]	86	57 (66,3)	24,9 [17,5;38,5]	0,26	[0,16; 0,40]	<0,0001*
Nein	231	67 (29,0)	65,8 [61,7; NE]	257	154 (59,9)	30,8 [22,3;38,9]	0,34	[0,26; 0,45]	<0,0001*
Interaktion p-Wert									0,3002
Region									
Asien	205	63 (30,7)	NE [NE; NE]	209	132 (63,2)	29,4 [22,1;36,1]	0,34	[0,25; 0,45]	<0,0001*
Europa	62	11 (17,7)	65,8 [65,8; NE]	69	37 (53,6)	34,7 [16,8; NE]	0,25	[0,12; 0,48]	<0,0001*
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	7 (63,6)	27,8 [2,8; NE]	0,06	[0,00; 0,33]	0,0006*
Rest der Welt	58	19 (32,8)	NE [NE; NE]	54	35 (64,8)	21,9 [16,8;39,5]	0,36	[0,20; 0,62]	0,0002*
Interaktion p-Wert									0,2261

DFS is defined as the time from the date of randomisation until the date of disease recurrence or death (by any cause in the absence of recurrence) regardless of whether the patient withdraws from randomised therapy or receives another anti-cancer therapy prior to recurrence. If patient experience recurrence or dies immediately after >=2 consecutive missed visits, they will be censored at the time of the latest evaluable assessment for disease recurrence prior to the two missed visits. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms.

[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).

[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation. Hazard ratio <1 favours Osimertinib. * p<0.05.

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Table 4.1.1.3 ADAURA: Summary of subgroup analysis of time to first subsequent anti-cancer therapy (TFST)
Full Analysis Set, DCO 27Jan2023

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	35 (32,1)	NE [NE; NE]	95	60 (63,2)	25,0 [14,6;44,6]	0,34	[0,22; 0,52]	<0,0001*
Weiblich	230	54 (23,5)	NE [NE; NE]	248	141 (56,9)	38,4 [29,0;48,2]	0,29	[0,21; 0,40]	<0,0001*
Interaktion p-Wert									0,5651
Alter									
<65 Jahre	185	51 (27,6)	NE [NE; NE]	195	118 (60,5)	33,9 [23,0;44,6]	0,30	[0,22; 0,42]	<0,0001*
>=65 Jahre	154	38 (24,7)	NE [NE; NE]	148	83 (56,1)	36,5 [28,8;66,2]	0,33	[0,22; 0,48]	<0,0001*
Interaktion p-Wert									0,7474
Abstammung									
Asiatisch	216	63 (29,2)	NE [NE; NE]	218	126 (57,8)	35,4 [28,9;46,0]	0,35	[0,26; 0,47]	<0,0001*
Nicht-asiatisch	123	26 (21,1)	NE [NE; NE]	125	75 (60,0)	34,5 [22,1;48,4]	0,25	[0,16; 0,39]	<0,0001*
Interaktion p-Wert									0,2489
EGFR-Mutation									
Exon 19 Deletion	187	44 (23,5)	NE [NE; NE]	191	121 (63,4)	28,7 [22,1;39,0]	0,23	[0,16; 0,32]	<0,0001*
L858R	152	45 (29,6)	NE [NE; NE]	152	80 (52,6)	48,4 [31,1; NE]	0,46	[0,32; 0,66]	<0,0001*
Interaktion p-Wert									0,0063*
Krankheitsstadium Version 7									
Stadium IB	106	16 (15,1)	NE [NE; NE]	106	42 (39,6)	NE [NE; NE]	0,34	[0,19; 0,59]	<0,0001*
Stadium II	118	34 (28,8)	NE [NE; NE]	118	67 (56,8)	35,6 [24,6; NE]	0,37	[0,24; 0,55]	<0,0001*
Stadium IIIA	115	39 (33,9)	NE [NE; NE]	119	92 (77,3)	18,2 [12,0;23,2]	0,21	[0,14; 0,30]	<0,0001*
Interaktion p-Wert									0,1020
Krankheitsstadium Version 8									
Stadium IB	101	16 (15,8)	NE [NE; NE]	98	36 (36,7)	NE [NE; NE]	0,39	[0,21; 0,69]	0,0011*
Stadium II	113	30 (26,5)	NE [NE; NE]	119	67 (56,3)	39,8 [28,9; NE]	0,35	[0,22; 0,53]	<0,0001*
Stadium IIIA	110	39 (35,5)	NE [NE; NE]	115	87 (75,7)	18,2 [12,3;23,2]	0,23	[0,15; 0,33]	<0,0001*

TFST is defined as the time from the date of randomisation to the earlier of the date of first subsequent anti-cancer therapy/procedure start date following study treatment discontinuation, or death. If a patient did not receive anti-cancer therapy, they are censored at the last time known not to have received TFST. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms.
[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation. Hazard ratio <1 favours Osimertinib. * p<0.05.

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Table 4.1.1.3 ADAURA: Summary of subgroup analysis of time to first subsequent anti-cancer therapy (TFST)
Full Analysis Set, DCO 27Jan2023

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Interaktion p-Wert									0,1937
Adjuvante Chemotherapie									
Ja	203	57 (28,1)	NE [NE; NE]	207	133 (64,3)	29,0 [22,3;36,5]	0,28	[0,20; 0,38]	<0,0001*
Nein	136	32 (23,5)	NE [NE; NE]	136	68 (50,0)	55,2 [31,2; NE]	0,37	[0,24; 0,56]	<0,0001*
Interaktion p-Wert									0,2871
Raucherstatus									
Ja	108	29 (26,9)	NE [NE; NE]	86	52 (60,5)	33,3 [22,3;45,1]	0,30	[0,19; 0,47]	<0,0001*
Nein	231	60 (26,0)	NE [NE; NE]	257	149 (58,0)	35,4 [28,9;47,3]	0,32	[0,23; 0,43]	<0,0001*
Interaktion p-Wert									0,8651
Region									
Asien	205	59 (28,8)	NE [NE; NE]	209	120 (57,4)	36,4 [28,9;46,0]	0,35	[0,25; 0,47]	<0,0001*
Europa	62	9 (14,5)	NE [NE; NE]	69	35 (50,7)	46,2 [19,6; NE]	0,22	[0,10; 0,43]	<0,0001*
Nordamerika	14	2 (14,3)	70,1 [70,1; NE]	11	8 (72,7)	30,4 [5,8; NE]	0,11	[0,02; 0,44]	0,0012*
Rest der Welt	58	19 (32,8)	NE [NE; NE]	54	38 (70,4)	22,3 [17,7;43,5]	0,32	[0,18; 0,55]	<0,0001*
Interaktion p-Wert									0,3130

TFST is defined as the time from the date of randomisation to the earlier of the date of first subsequent anti-cancer therapy/procedure start date following study treatment discontinuation, or death. If a patient did not receive anti-cancer therapy, they are censored at the last time known not to have received TFST. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms.
[a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached).
[b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation. Hazard ratio <1 favours Osimertinib. * p<0.05.
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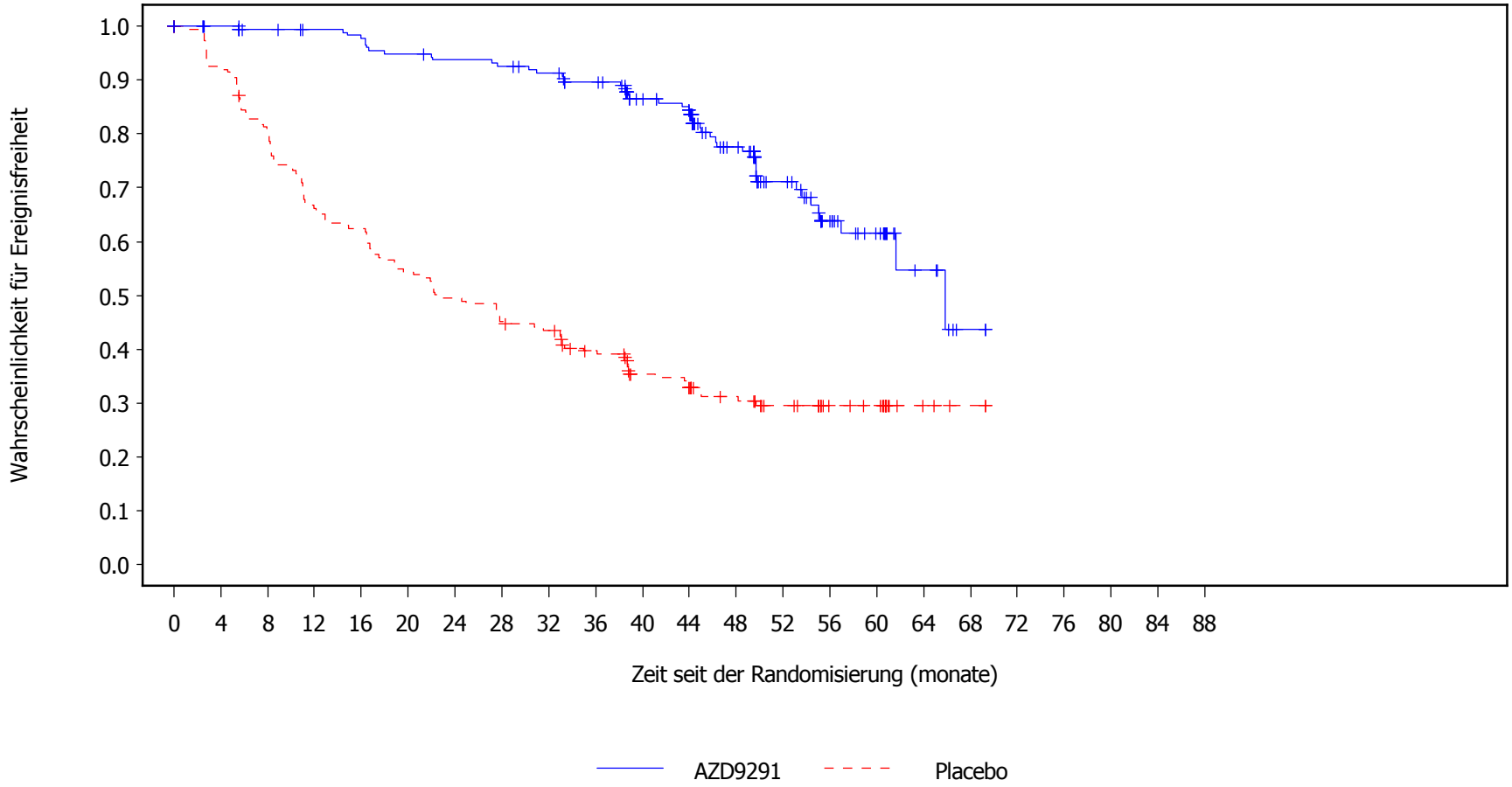
Figure 4.1.2.1 ADAURA Subgroup Analysis: Kaplan-Meier plot of disease-free survival for EGFR Mutation Status = Exon 19 Deletion
Full Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

187	182	176	173	170	165	162	160	156	149	128	119	83	54	33	23	7	1	0	0	0	0	AZD9291
191	173	150	123	116	101	92	84	80	68	55	49	38	30	19	17	3	1	0	0	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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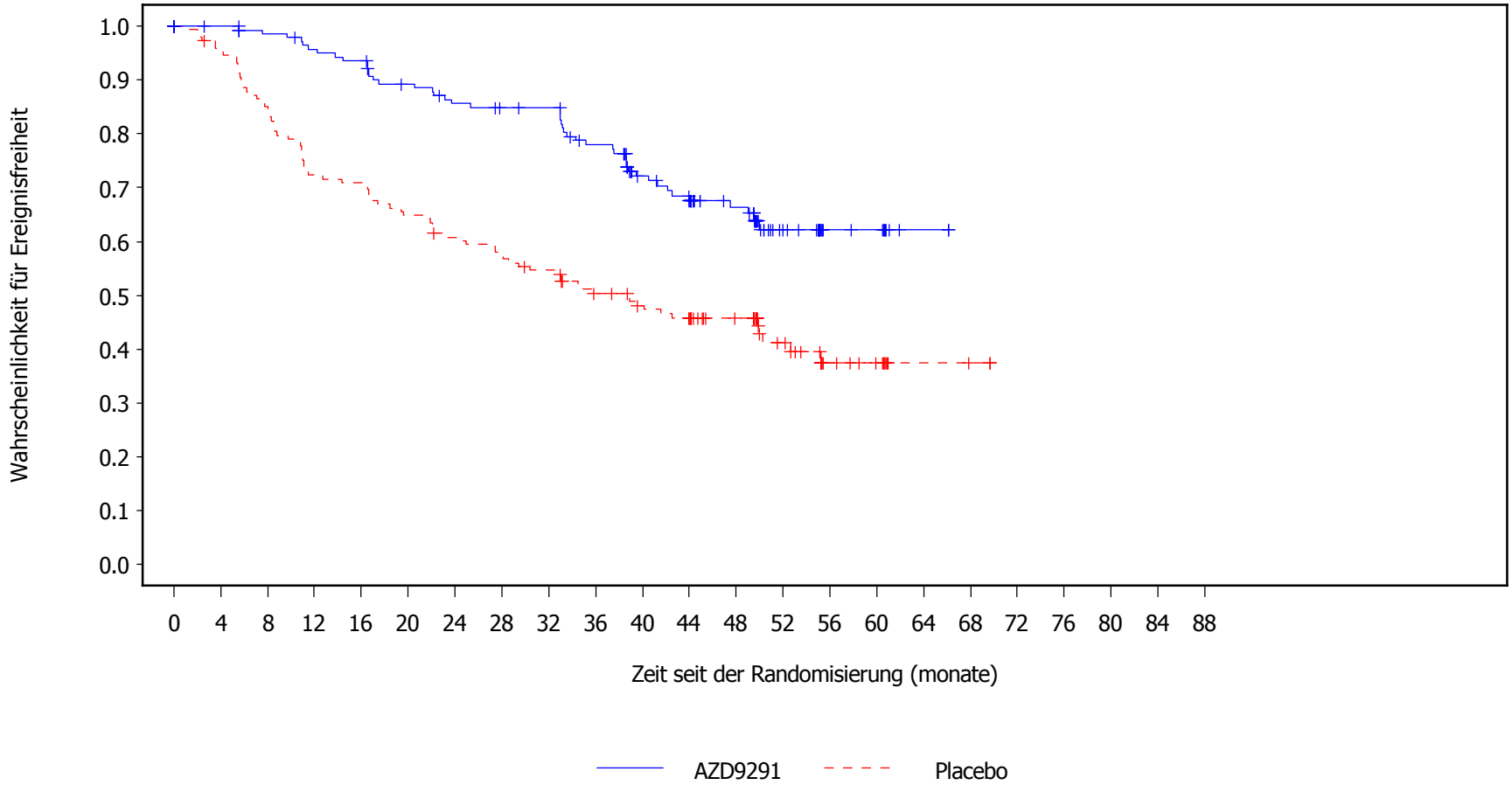
Figure 4.1.2.2 ADAURA Subgroup Analysis: Kaplan-Meier plot of disease-free survival for EGFR Mutation Status = L858R
Full Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

152	144	139	134	131	122	116	113	112	100	80	72	56	27	11	10	1	0	0	0	0	0	AZD9291
152	142	126	107	105	96	89	84	79	69	63	58	46	25	12	8	2	1	0	0	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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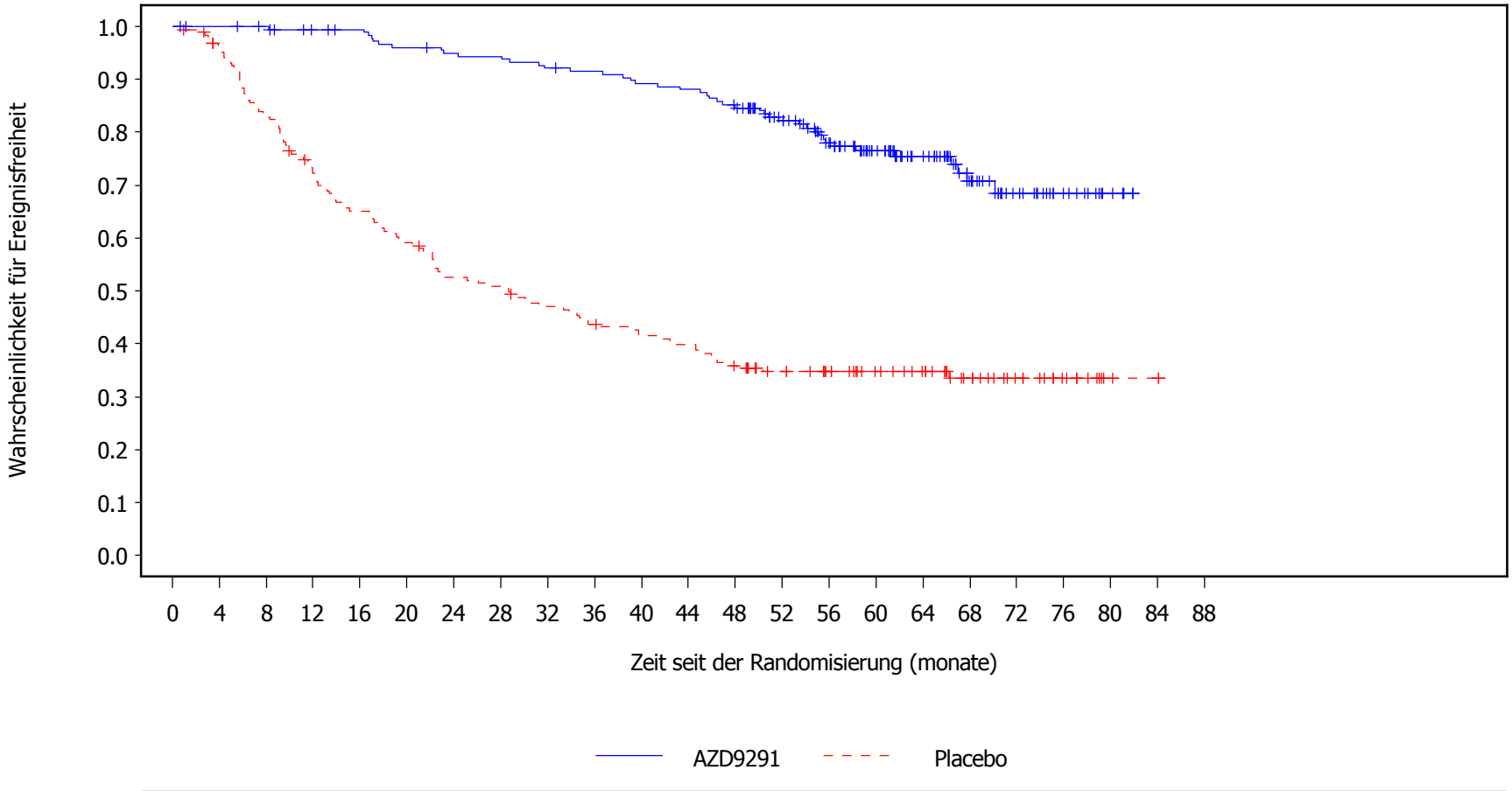
Figure 4.1.2.3 ADAURA Subgroup Analysis: Kaplan-Meier plot of time to first subsequent therapy for EGFR Mutation Status = Exon 19 Deletion
Full Analysis Set, DCO 27Jan2023



Anzahl an Patienten unter Risiko:

187	185	183	178	176	170	167	166	162	160	156	154	148	128	109	84	64	40	23	12	4	0	0	AZD9291
191	179	156	133	120	109	96	93	85	79	74	71	63	55	48	40	35	25	17	10	2	1	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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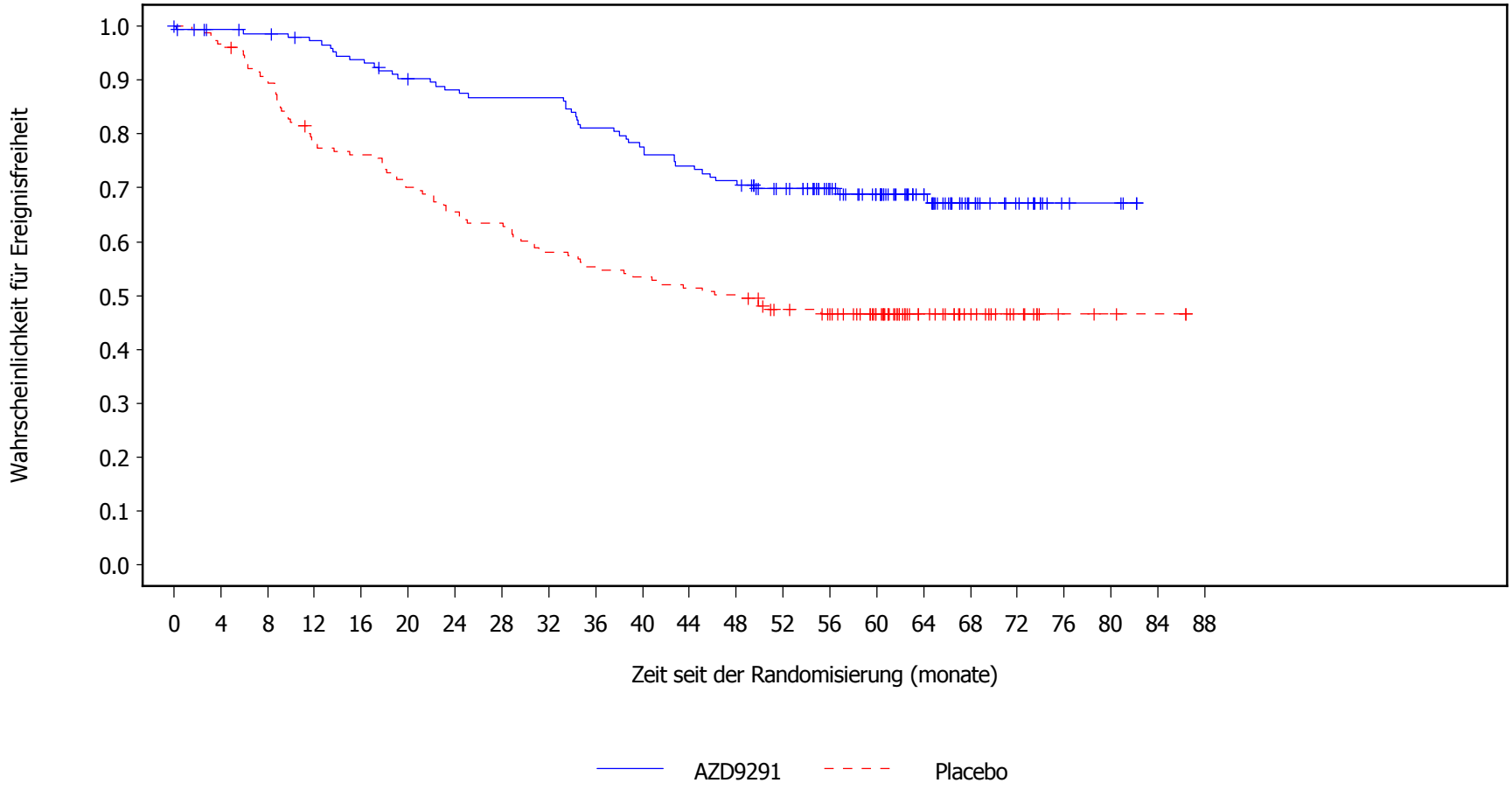
Figure 4.1.2.4 ADAURA Subgroup Analysis: Kaplan-Meier plot of time to first subsequent therapy for EGFR Mutation Status = L858R
Full Analysis Set, DCO 27Jan2023



Anzahl an Patienten unter Risiko:

152	146	144	140	135	128	125	123	123	115	110	105	101	91	77	63	43	22	14	4	3	0	0	AZD9291
152	147	136	117	114	105	98	95	87	83	80	77	75	66	61	49	28	19	10	3	2	1	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
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Table 4.1.3 ADAURA: Summary of subgroup analysis of overall recurrence rate
(odds ratio, relative risk and risk difference)
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)		Placebo (N=343)		Behandlungseffekt					
					Odds Ratio		Relatives Risiko		Risikodifferenz	
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	n	Anzahl (%) der Patienten mit Ereignis	Schätzer [95%-KI]	2-seitiger p-Wert	Schätzer [95%-KI]	2-seitiger p-Wert	Schätzer [95%-KI]	2-seitiger p-Wert
Geschlecht										
Maennlich [a][d][g]	109	33(30,3)	95	62(65,3)	0,23[0,13; 0,41]	<0,0001 *	0,46[0,33; 0,63]	<0,0001 *	-0,35[-0,47; -0,22]	<0,0001 *
Weiblich [a][d][g]	230	61(26,5)	248	149(60,1)	0,24[0,16; 0,35]	<0,0001 *	0,44[0,34; 0,56]	<0,0001 *	-0,34[-0,42; -0,25]	<0,0001 *
Int. p-Wert [a][d][g]						0,9179		0,8079		0,8555
Alter										
<65 Jahre [a][d][g]	185	53(28,6)	195	123(63,1)	0,24[0,15; 0,36]	<0,0001 *	0,45[0,35; 0,58]	<0,0001 *	-0,34[-0,44; -0,25]	<0,0001 *
>=65 Jahre [a][d][g]	154	41(26,6)	148	88(59,5)	0,25[0,15; 0,40]	<0,0001 *	0,45[0,33; 0,59]	<0,0001 *	-0,33[-0,43; -0,22]	<0,0001 *
Int. p-Wert [a][d][g]						0,8771		0,9424		0,8251
Abstammung										
Asiatisch [a][d][g]	216	66(30,6)	218	136(62,4)	0,27[0,18; 0,39]	<0,0001 *	0,49[0,39; 0,61]	<0,0001 *	-0,32[-0,41; -0,23]	<0,0001 *
Nicht-asiatisch [a][d][g]	123	28(22,8)	125	75(60,0)	0,20[0,11; 0,34]	<0,0001 *	0,38[0,26; 0,53]	<0,0001 *	-0,37[-0,48; -0,26]	<0,0001 *
Int. p-Wert [a][d][g]						0,3863		0,2271		0,4640
EGFR-Mutation										

Includes disease recurrence or death reported regardless of subsequent anti-cancer therapy. Deaths reported after >=2 missed visits are censored at the time of latest evaluable assessment for disease recurrence. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms. NC=Not calculable. CI=Confidence interval. PL=Profile likelihood. LR=Likelihood ratio test. Separate models fitted to subgroup levels including the response and a term for treatment as a factor.

[a] Odds ratio (OR), 95% PL CI, LR p-value using logistic regression.
[d] Relative risk (RR), 95% PL CI and LR p-value estimated using log-binomial regression.
[g] Risk difference (RD), 95% PL CI and LR p-value estimated using binomial regression. OR <1, RR <1 or RD <0 favours Osi.
* p<0.05.

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Table 4.1.3 ADAURA: Summary of subgroup analysis of overall recurrence rate
(odds ratio, relative risk and risk difference)
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)		Placebo (N=343)		Behandlungseffekt					
					Odds Ratio		Relatives Risiko		Risikodifferenz	
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	n	Anzahl (%) der Patienten mit Ereignis	Schätzer [95%-KI]	2-seitiger p-Wert	Schätzer [95%-KI]	2-seitiger p-Wert	Schätzer [95%-KI]	2-seitiger p-Wert
Exon 19 Deletion [a][d][g]	187	48(25,7)	191	127(66,5)	0,17[0,11; 0,27]	<0,0001 *	0,39[0,29; 0,50]	<0,0001 *	-0,41[-0,50; -0,31]	<0,0001 *
L858R [a][d][g]	152	46(30,3)	152	84(55,3)	0,35[0,22; 0,56]	<0,0001 *	0,55[0,41; 0,72]	<0,0001 *	-0,25[-0,36; -0,14]	<0,0001 *
Int. p-Wert [a][d][g]						0,0336 *		0,0758		0,0281 *
Krankheitsstadium Version 7										
Stadium IB [a][d][g]	106	19(17,9)	106	44(41,5)	0,31[0,16; 0,57]	0,0001 *	0,43[0,26; 0,67]	0,0001 *	-0,24[-0,35; -0,12]	0,0001 *
Stadium II [a][d][g]	118	33(28,0)	118	69(58,5)	0,28[0,16; 0,47]	<0,0001 *	0,48[0,34; 0,65]	<0,0001 *	-0,31[-0,42; -0,18]	<0,0001 *
Stadium IIIA [a][d][g]	115	42(36,5)	119	98(82,4)	0,12[0,07; 0,22]	<0,0001 *	0,44[0,34; 0,56]	<0,0001 *	-0,46[-0,56; -0,34]	<0,0001 *
Int. p-Wert [a][d][g]						0,0668		0,9178		0,0256 *
Krankheitsstadium Version 8										
Stadium IB [a][d][g]	101	19(18,8)	98	40(40,8)	0,34[0,17; 0,63]	0,0006 *	0,46[0,28; 0,72]	0,0006 *	-0,22[-0,34; -0,10]	0,0006 *
Stadium II [a][d][g]	113	29(25,7)	119	69(58,0)	0,25[0,14; 0,43]	<0,0001 *	0,44[0,31; 0,62]	<0,0001 *	-0,32[-0,44; -0,20]	<0,0001 *
Stadium IIIA [a][d][g]	110	41(37,3)	115	92(80,0)	0,15[0,08; 0,27]	<0,0001 *	0,47[0,35; 0,59]	<0,0001 *	-0,43[-0,54; -0,31]	<0,0001 *
Int. p-Wert [a][d][g]						0,1733		0,9731		0,0596
Adjuvante Chemotherapie										

Includes disease recurrence or death reported regardless of subsequent anti-cancer therapy. Deaths reported after >=2 missed visits are censored at the time of latest evaluable assessment for disease recurrence. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms. NC=Not calculable. CI=Confidence interval. PL=Profile likelihood. LR=Likelihood ratio test. Separate models fitted to subgroup levels including the response and a term for treatment as a factor.

[a] Odds ratio (OR), 95% PL CI, LR p-value using logistic regression.
[d] Relative risk (RR), 95% PL CI and LR p-value estimated using log-binomial regression.
[g] Risk difference (RD), 95% PL CI and LR p-value estimated using binomial regression. OR <1, RR <1 or RD <0 favours Osi.
* p<0.05.

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Table 4.1.3 ADAURA: Summary of subgroup analysis of overall recurrence rate
(odds ratio, relative risk and risk difference)
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)		Placebo (N=343)		Behandlungseffekt								
					Odds Ratio			Relatives Risiko			Risikodifferenz		
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	n	Anzahl (%) der Patienten mit Ereignis	Schätzer [95%-KI]		2-seitiger p-Wert	Schätzer [95%-KI]		2-seitiger p-Wert	Schätzer [95%-KI]		2-seitiger p-Wert
Ja [a][d][g]	203	62(30,5)	207	140(67,6)	0,21[0,14;	0,32]	<0,0001 *	0,45[0,36;	0,56]	<0,0001 *	-0,37[-0,46;	-0,28]	<0,0001 *
Nein [a][d][g]	136	32(23,5)	136	71(52,2)	0,28[0,17;	0,47]	<0,0001 *	0,45[0,31;	0,63]	<0,0001 *	-0,29[-0,39;	-0,17]	<0,0001 *
Int. p-Wert [a][d][g]							0,3921			0,9926			0,2449
Raucherstatus													
Ja [a][d][g]	108	27(25,0)	86	57(66,3)	0,17[0,09;	0,31]	<0,0001 *	0,38[0,26;	0,53]	<0,0001 *	-0,41[-0,54;	-0,28]	<0,0001 *
Nein [a][d][g]	231	67(29,0)	257	154(59,9)	0,27[0,19;	0,40]	<0,0001 *	0,48[0,38;	0,60]	<0,0001 *	-0,31[-0,39;	-0,22]	<0,0001 *
Int. p-Wert [a][d][g]							0,1970			0,2420			0,1926
Region													
Asien [a][d][g]	205	63(30,7)	209	132(63,2)	0,26[0,17;	0,39]	<0,0001 *	0,49[0,38;	0,61]	<0,0001 *	-0,32[-0,41;	-0,23]	<0,0001 *
Europa [a][d][g]	62	11(17,7)	69	37(53,6)	0,19[0,08;	0,41]	<0,0001 *	0,33[0,17;	0,56]	<0,0001 *	-0,36[-0,50;	-0,20]	<0,0001 *
Nordamerika [a][d][g]	14	1(7,1)	11	7(63,6)	0,04[0,00;	0,35]	0,0018 *	0,11[0,01;	0,50]	0,0018 *	-0,56[-0,83;	-0,22]	0,0018 *
Rest der Welt [a][d][g]	58	19(32,8)	54	35(64,8)	0,26[0,12;	0,57]	0,0006 *	0,51[0,32;	0,75]	0,0006 *	-0,32[-0,49;	-0,14]	0,0006 *
Int. p-Wert [a][d][g]							0,3844			0,1621			0,5835

Includes disease recurrence or death reported regardless of subsequent anti-cancer therapy. Deaths reported after >=2 missed visits are censored at the time of latest evaluable assessment for disease recurrence. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms. NC=Not calculable. CI=Confidence interval. PL=Profile likelihood. LR=Likelihood ratio test. Separate models fitted to subgroup levels including the response and a term for treatment as a factor.

[a] Odds ratio (OR), 95% PL CI, LR p-value using logistic regression.
[d] Relative risk (RR), 95% PL CI and LR p-value estimated using log-binomial regression.
[g] Risk difference (RD), 95% PL CI and LR p-value estimated using binomial regression. OR <1, RR <1 or RD <0 favours Osi.
* p<0.05.

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Table 4.2.1.1 ADAURA: Summary of subgroup analysis of time to first deterioration (decrease of >=9.423) in SF-36 physical component
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	16 (14,7)	NE [NE; NE]	95	13 (13,7)	NE [NE; NE]	0,91	[0,44; 1,93]	0,8045
Weiblich	230	41 (17,8)	NE [NE; NE]	248	40 (16,1)	NE [NE; NE]	1,03	[0,66; 1,59]	0,9012
Interaktion p-Wert									0,7821
Alter									
<65 Jahre	185	22 (11,9)	NE [NE; NE]	195	31 (15,9)	NE [NE; NE]	0,64	[0,37; 1,10]	0,1089
>=65 Jahre	154	35 (22,7)	NE [NE; NE]	148	22 (14,9)	NE [NE; NE]	1,48	[0,88; 2,57]	0,1422
Interaktion p-Wert									0,0296*
Abstammung									
Asiatisch	216	32 (14,8)	NE [NE; NE]	218	30 (13,8)	NE [NE; NE]	0,94	[0,57; 1,56]	0,8099
Nicht-asiatisch	123	25 (20,3)	NE [NE; NE]	125	23 (18,4)	36,4 [36,4; NE]	1,07	[0,61; 1,90]	0,8066
Interaktion p-Wert									0,7315
EGFR-Mutation									
Exon 19 Deletion	187	27 (14,4)	NE [NE; NE]	191	26 (13,6)	NE [NE; NE]	0,89	[0,52; 1,54]	0,6803
L858R	152	30 (19,7)	NE [NE; NE]	152	27 (17,8)	NE [NE; NE]	1,10	[0,66; 1,87]	0,7122
Interaktion p-Wert									0,5801
Krankheitsstadium Version 7									
Stadium IB	106	15 (14,2)	NE [NE; NE]	106	19 (17,9)	NE [NE; NE]	0,86	[0,43; 1,68]	0,6530
Stadium II	118	21 (17,8)	NE [NE; NE]	118	20 (16,9)	NE [NE; NE]	0,91	[0,49; 1,70]	0,7722
Stadium IIIA	115	21 (18,3)	NE [NE; NE]	119	14 (11,8)	NE [NE; NE]	1,22	[0,63; 2,47]	0,5567
Interaktion p-Wert									0,7323
Krankheitsstadium Version 8									
Stadium IB	101	17 (16,8)	NE [NE; NE]	98	16 (16,3)	NE [NE; NE]	1,11	[0,56; 2,21]	0,7689
Stadium II	113	17 (15,0)	NE [NE; NE]	119	23 (19,3)	NE [NE; NE]	0,70	[0,37; 1,30]	0,2611

Time to first deterioration is defined as time from date of randomisation to the date of first clinically important worsening (decrease of >=9.423) in the respective score. Death is not counted as an event. Patients with evaluable baseline data and do not experience a clinically important deterioration are censored at the date of their last evaluable SF-36 assessment. Patients without evaluable baseline data for a score are censored at Day 1. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms. [a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached). [b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 4.2.1.1 ADAURA: Summary of subgroup analysis of time to first deterioration (decrease of >=9.423) in SF-36 physical component
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	110	22 (20,0)	NE [NE; NE]	115	11 (9,6)	NE [NE; NE]	1,69	[0,83; 3,63]	0,1473
Interaktion p-Wert									0,1840
Adjuvante Chemotherapie									
Ja	203	30 (14,8)	NE [NE; NE]	207	37 (17,9)	NE [NE; NE]	0,70	[0,43; 1,13]	0,1459
Nein	136	27 (19,9)	NE [NE; NE]	136	16 (11,8)	NE [NE; NE]	1,69	[0,92; 3,20]	0,0914
Interaktion p-Wert									0,0259*
Raucherstatus									
Ja	108	17 (15,7)	NE [NE; NE]	86	15 (17,4)	NE [NE; NE]	0,80	[0,40; 1,61]	0,5201
Nein	231	40 (17,3)	NE [NE; NE]	257	38 (14,8)	NE [NE; NE]	1,07	[0,68; 1,67]	0,7681
Interaktion p-Wert									0,4827
Region									
Asien	205	31 (15,1)	NE [NE; NE]	209	29 (13,9)	NE [NE; NE]	0,94	[0,57; 1,57]	0,8205
Europa	62	14 (22,6)	NE [NE; NE]	69	18 (26,1)	36,4 [28,0; NE]	0,90	[0,44; 1,80]	0,7645
Nordamerika	14	3 (21,4)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	2,04	[0,26; 41,37]	0,5149
Rest der Welt	58	9 (15,5)	NE [NE; NE]	54	5 (9,3)	NE [NE; NE]	1,53	[0,53; 4,97]	0,4398
Interaktion p-Wert									0,7629

Time to first deterioration is defined as time from date of randomisation to the date of first clinically important worsening (decrease of >=9.423) in the respective score. Death is not counted as an event. Patients with evaluable baseline data and do not experience a clinically important deterioration are censored at the date of their last evaluable SF-36 assessment. Patients without evaluable baseline data for a score are censored at Day 1. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms. [a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached). [b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Osimertinib. * p<0.05.
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Table 4.2.1.2 ADAURA: Summary of subgroup analysis of time to first deterioration (decrease of >=9.618) in SF-36 mental component score
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	29 (26,6)	NE [NE; NE]	95	16 (16,8)	NE [NE; NE]	1,43	[0,79; 2,70]	0,2411
Weiblich	230	69 (30,0)	NE [NE; NE]	248	73 (29,4)	36,4 [35,9; NE]	0,93	[0,67; 1,29]	0,6615
Interaktion p-Wert									0,2156
Alter									
<65 Jahre	185	51 (27,6)	NE [NE; NE]	195	43 (22,1)	NE [NE; NE]	1,13	[0,75; 1,70]	0,5575
>=65 Jahre	154	47 (30,5)	NE [NE; NE]	148	46 (31,1)	NE [NE; NE]	0,89	[0,59; 1,35]	0,5932
Interaktion p-Wert									0,4276
Abstammung									
Asiatisch	216	64 (29,6)	NE [NE; NE]	218	49 (22,5)	NE [NE; NE]	1,21	[0,84; 1,76]	0,3151
Nicht-asiatisch	123	34 (27,6)	NE [NE; NE]	125	40 (32,0)	36,4 [22,2; NE]	0,77	[0,48; 1,21]	0,2580
Interaktion p-Wert									0,1302
EGFR-Mutation									
Exon 19 Deletion	187	53 (28,3)	NE [NE; NE]	191	51 (26,7)	NE [NE; NE]	0,87	[0,59; 1,28]	0,4688
L858R	152	45 (29,6)	NE [NE; NE]	152	38 (25,0)	36,4 [36,4; NE]	1,22	[0,80; 1,89]	0,3586
Interaktion p-Wert									0,2429
Krankheitsstadium Version 7									
Stadium IB	106	29 (27,4)	NE [NE; NE]	106	31 (29,2)	NE [NE; NE]	1,04	[0,62; 1,72]	0,8852
Stadium II	118	35 (29,7)	NE [NE; NE]	118	30 (25,4)	NE [NE; NE]	1,06	[0,65; 1,73]	0,8283
Stadium IIIA	115	34 (29,6)	NE [NE; NE]	119	28 (23,5)	36,4 [31,7; NE]	0,95	[0,57; 1,57]	0,8269
Interaktion p-Wert									0,9471
Krankheitsstadium Version 8									
Stadium IB	101	28 (27,7)	NE [NE; NE]	98	30 (30,6)	NE [NE; NE]	0,99	[0,59; 1,66]	0,9703

Time to first deterioration is defined as time from date of randomisation to the date of first clinically important worsening (decrease of >=9.618) in the respective score. Death is not counted as an event. Patients with evaluable baseline data and do not experience a clinically important deterioration are censored at the date of their last evaluable SF-36 assessment. Patients without evaluable baseline data for a score are censored at Day 1. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms. [a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached). [b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Osimertinib. * p<0.05.
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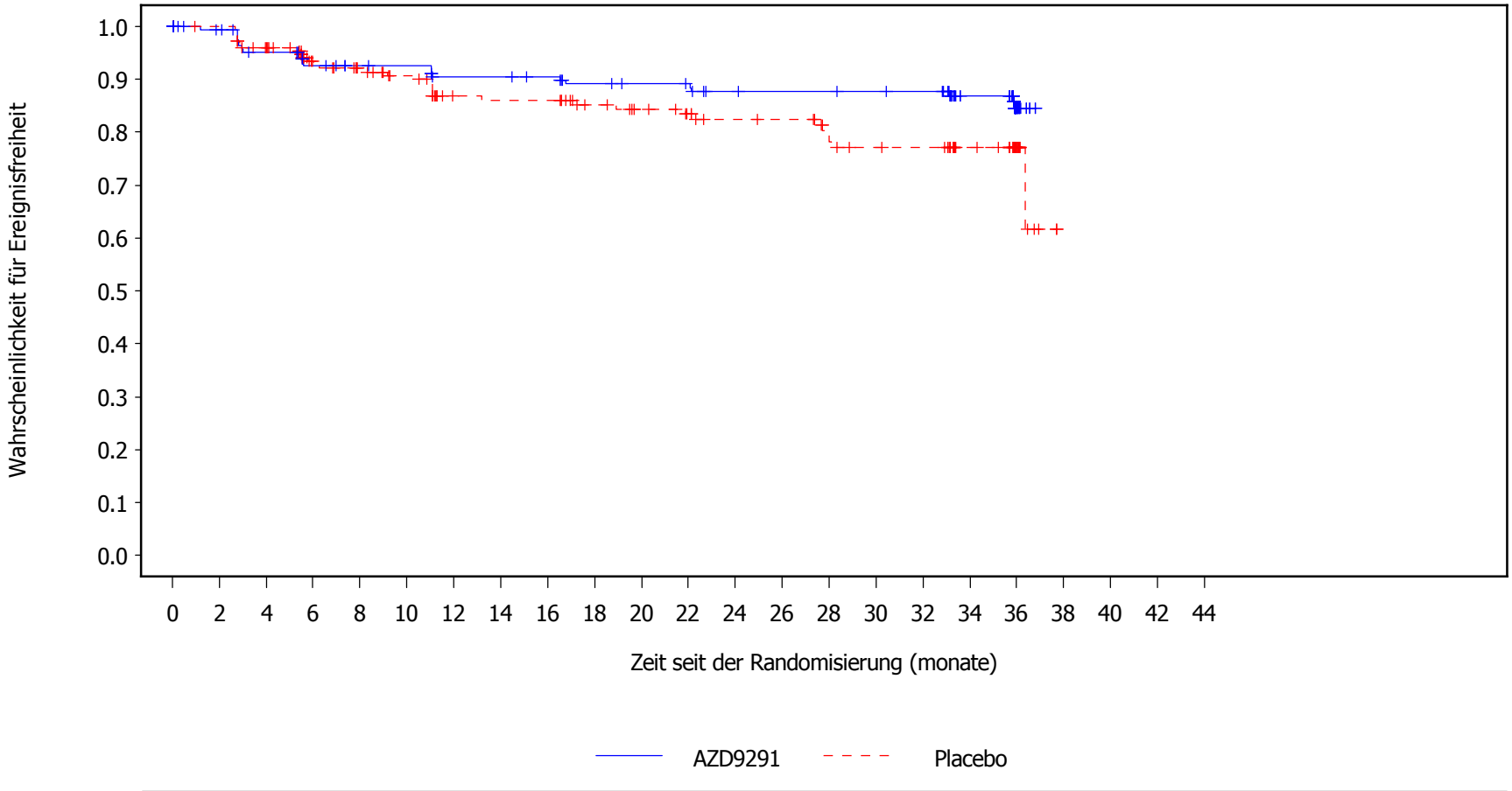
Table 4.2.1.2 ADAURA: Summary of subgroup analysis of time to first deterioration (decrease of >=9.618) in SF-36 mental component score
Full Analysis Set, DCO 11Apr2022

	AZD9291 (N=339)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium II	113	34 (30,1)	NE [NE; NE]	119	29 (24,4)	NE [NE; NE]	1,16	[0,71; 1,92]	0,5515
Stadium IIIA	110	35 (31,8)	NE [NE; NE]	115	28 (24,3)	36,4 [31,7; NE]	0,99	[0,60; 1,63]	0,9543
Interaktion p-Wert									0,8727
Adjuvante Chemotherapie									
Ja	203	57 (28,1)	NE [NE; NE]	207	48 (23,2)	NE [NE; NE]	1,07	[0,73; 1,58]	0,7310
Nein	136	41 (30,1)	NE [NE; NE]	136	41 (30,1)	NE [NE; NE]	0,95	[0,62; 1,47]	0,8197
Interaktion p-Wert									0,6898
Raucherstatus									
Ja	108	33 (30,6)	NE [NE; NE]	86	16 (18,6)	NE [NE; NE]	1,57	[0,88; 2,92]	0,1328
Nein	231	65 (28,1)	NE [NE; NE]	257	73 (28,4)	NE [NE; NE]	0,88	[0,63; 1,23]	0,4655
Interaktion p-Wert									0,0954
Region									
Asien	205	63 (30,7)	NE [NE; NE]	209	48 (23,0)	NE [NE; NE]	1,22	[0,84; 1,78]	0,2997
Europa	62	17 (27,4)	35,9 [27,6; NE]	69	23 (33,3)	36,4 [11,7; NE]	0,78	[0,41; 1,46]	0,4434
Nordamerika	14	2 (14,3)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	1,01	[0,10; 21,75]	0,9939
Rest der Welt	58	16 (27,6)	NE [NE; NE]	54	17 (31,5)	33,1 [20,3; NE]	0,74	[0,37; 1,48]	0,3945
Interaktion p-Wert									0,4964

Time to first deterioration is defined as time from date of randomisation to the date of first clinically important worsening (decrease of >=9.618) in the respective score. Death is not counted as an event. Patients with evaluable baseline data and do not experience a clinically important deterioration are censored at the date of their last evaluable SF-36 assessment. Patients without evaluable baseline data for a score are censored at Day 1. Analysis is performed if there are >= 10 patients at each subgroup level and >= 10 events in at least one subgroup level combined for both arms. [a] Median time to event (95% CL) based on the Kaplan Meier estimate. NE=Not estimable (e.g. median is not reached). [b] Estimated from the main effects of an unstratified Cox proportional hazard model including treatment, subgroup and subgroup-by-treatment interaction. Ties are handled using Efron method and 95% CI derived from profile likelihood estimation.
Hazard ratio <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesubpr2.sas gttesubpr2b 13JUL2023:08:56 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 4.2.2.1 ADAURA: Kaplan-Meier plot of SF-36 Zeit bis zur ersten Verschlechterung - Koerperliche Gesundheit PCS: 9.423 for Alter = <65 Jahre
Full Analysis Set, DCO 11Apr2022

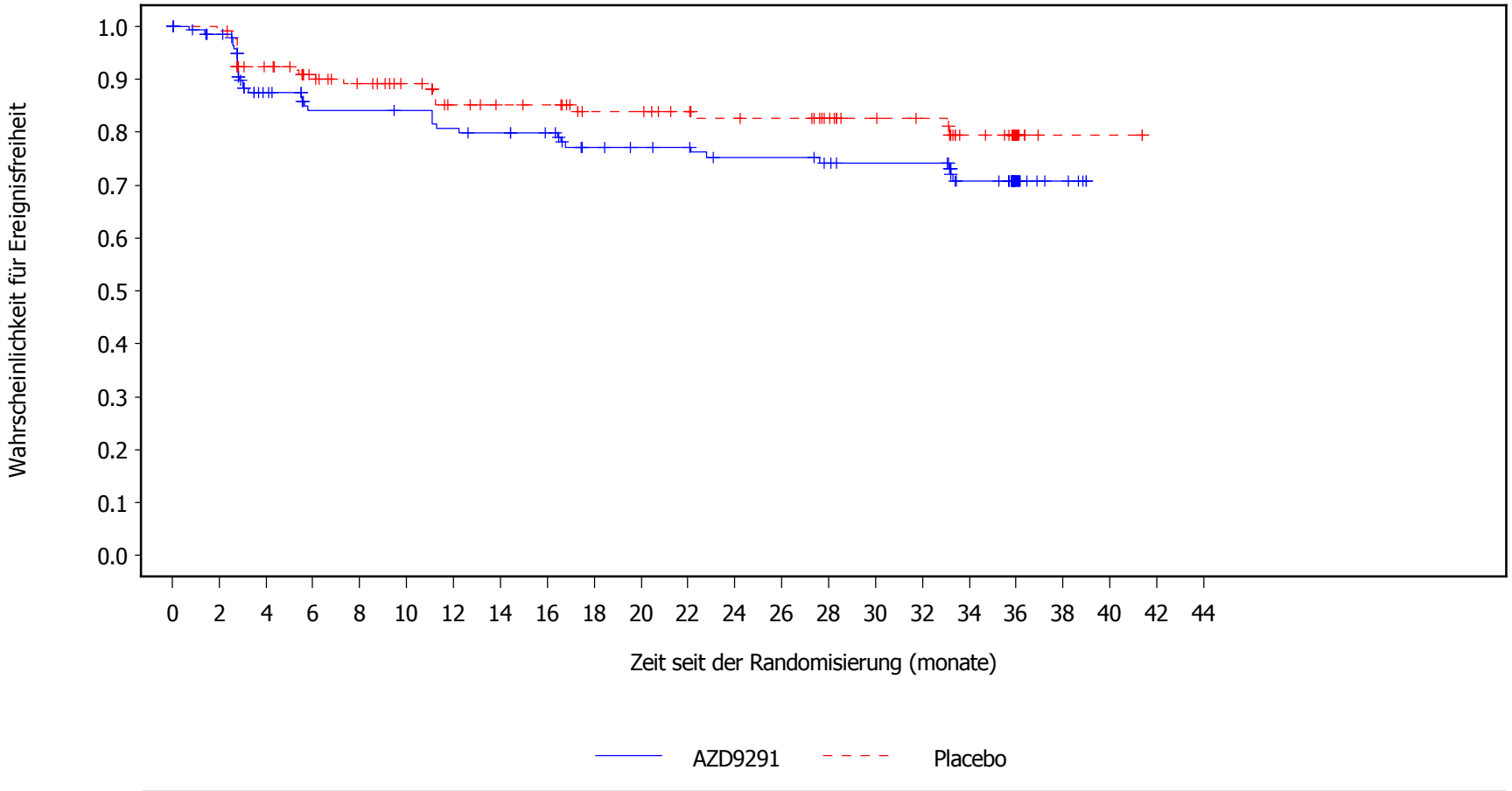


Anzahl an Patienten unter Risiko:

185	163	153	144	140	139	133	133	131	126	124	123	118	117	117	116	115	94	24	0	0	0	0	AZD9291
195	176	164	138	130	122	107	106	106	97	92	87	82	81	73	70	69	54	16	0	0	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in unstratified Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesubpr2.sas gttesubpr2baa 13JUL2023:08:56 kvbv306

Figure 4.2.2.2 ADAURA: Kaplan-Meier plot of SF-36 Zeit bis zur ersten Verschlechterung - Koerperliche Gesundheit PCS: 9.423 for Alter = >=65 Jahre
Full Analysis Set, DCO 11Apr2022



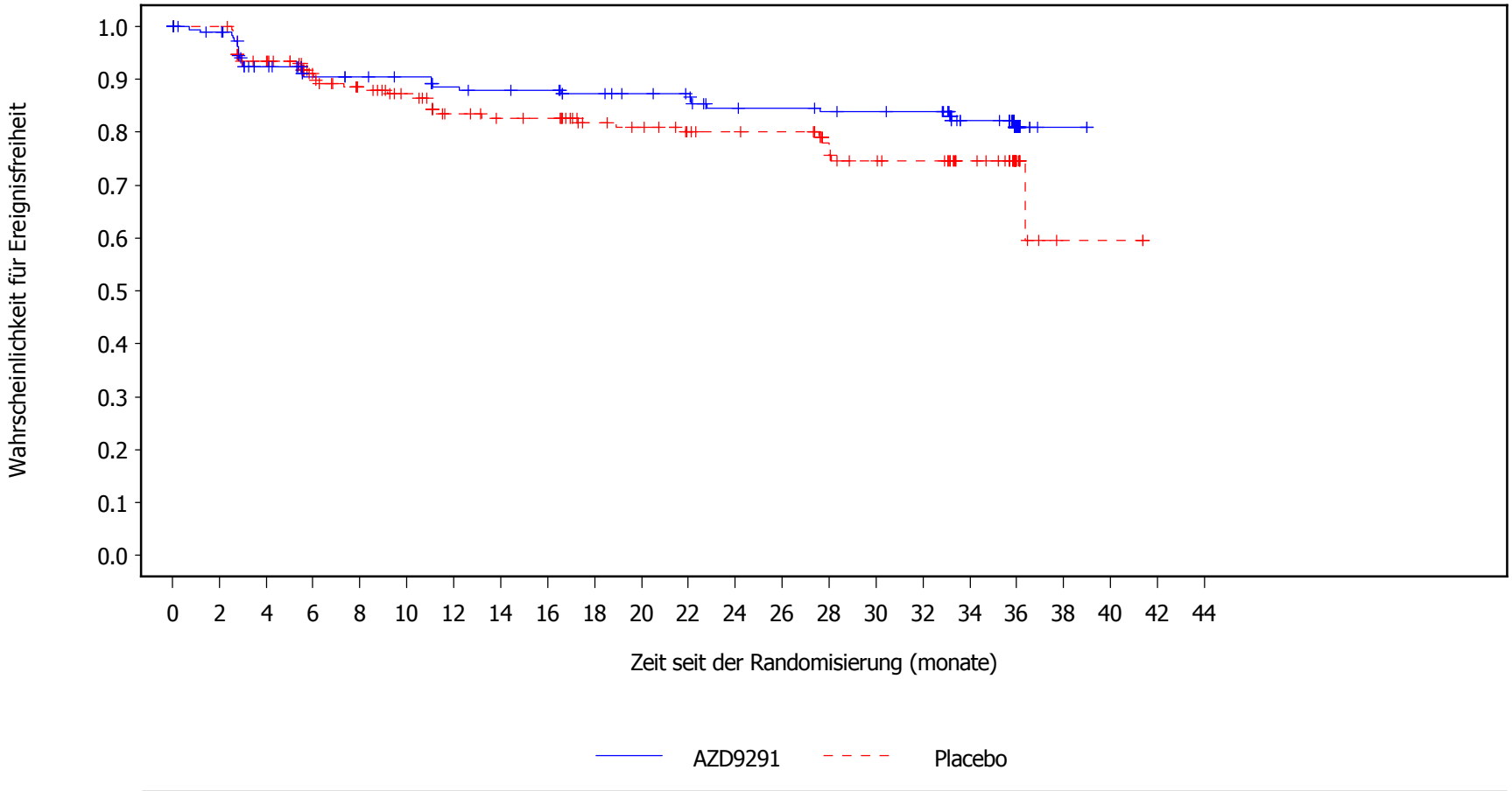
Anzahl an Patienten unter Risiko:

154	138	110	100	100	99	95	93	90	82	80	79	75	75	72	70	70	59	22	4	0	0	0	AZD9291
148	133	117	106	99	93	83	80	79	72	72	68	65	64	59	54	52	43	10	1	1	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in unstratified Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesubpr2.sas gttesubpr2bab 13JUL2023:08:56 kvbv306

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 4.2.2.3 ADAURA: Kaplan-Meier plot of SF-36 Zeit bis zur ersten Verschlechterung - Koerperliche Gesundheit PCS: 9.423 for Adjuvante Chemotherapie = Ja
Full Analysis Set, DCO 11Apr2022

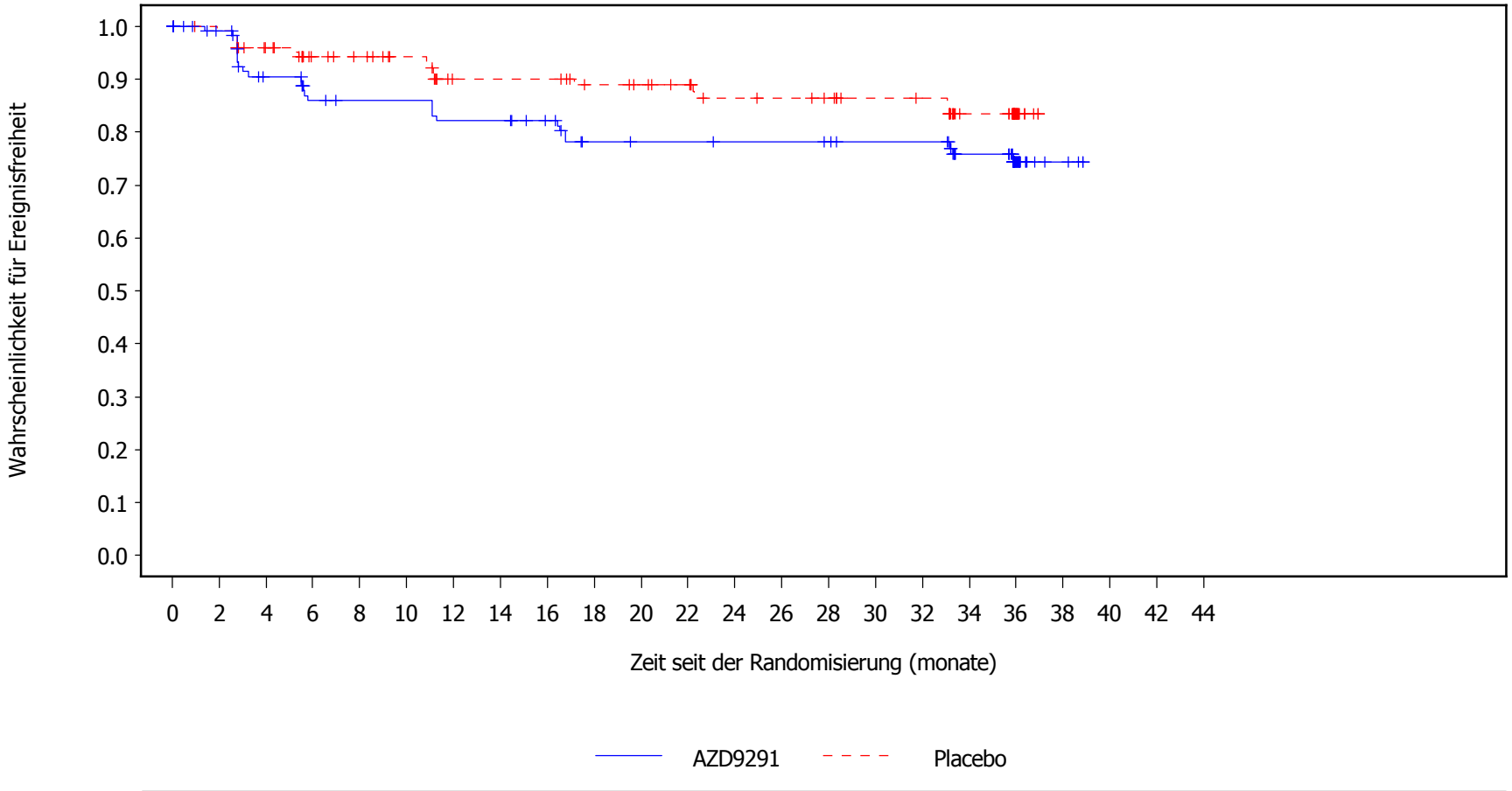


Anzahl an Patienten unter Risiko:

203	183	161	151	149	147	141	139	138	133	130	128	120	119	117	116	115	94	22	1	0	0	0	AZD9291
207	187	169	143	131	122	108	104	103	92	89	83	81	80	69	65	63	52	10	1	1	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in unstratified Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesubpr2.sas gttesubpr2bac 13JUL2023:08:56 kvbv306

Figure 4.2.2.4 ADAURA: Kaplan-Meier plot of SF-36 Zeit bis zur ersten Verschlechterung - Koerperliche Gesundheit PCS: 9.423 for Adjuvante Chemotherapie = Nein
Full Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

136	118	102	93	91	91	87	87	83	75	74	74	73	73	72	70	70	59	24	3	0	0	0	AZD9291
136	122	112	101	98	93	82	82	82	77	75	72	66	65	63	59	58	45	16	0	0	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in unstratified Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesubpr2.sas gttesubpr2bad 13JUL2023:08:56 kvbv306

Table 4.3.1.1 ADAURA: Summary of subgroup analysis of time to first UE
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	108 (99,1)	0,4 [0,3; 0,5]	95	85 (89,5)	1,0 [0,8; 1,3]	2,03	[1,52; 2,71]	<0,0001*
Weiblich	228	222 (97,4)	0,4 [0,3; 0,5]	248	224 (90,3)	0,9 [0,6; 1,1]	1,74	[1,45; 2,10]	<0,0001*
Interaktion p-Wert									0,3858
Alter									
<65 Jahre	184	182 (98,9)	0,4 [0,3; 0,5]	195	180 (92,3)	0,7 [0,6; 1,0]	1,74	[1,41; 2,14]	<0,0001*
>=65 Jahre	153	148 (96,7)	0,5 [0,4; 0,5]	148	129 (87,2)	1,1 [1,0; 2,0]	1,96	[1,54; 2,49]	<0,0001*
Interaktion p-Wert									0,4527
Abstammung									
Asiatisch	215	214 (99,5)	0,3 [0,3; 0,4]	218	208 (95,4)	0,7 [0,6; 1,0]	1,90	[1,56; 2,31]	<0,0001*
Nicht-asiatisch	122	116 (95,1)	0,5 [0,5; 0,8]	125	101 (80,8)	1,8 [1,0; 2,8]	1,88	[1,44; 2,46]	<0,0001*
Interaktion p-Wert									0,9452
EGFR-Mutation									
Exon 19 Deletion	187	182 (97,3)	0,5 [0,4; 0,5]	191	166 (86,9)	1,0 [0,9; 1,9]	1,91	[1,54; 2,36]	<0,0001*
L858R	150	148 (98,7)	0,4 [0,3; 0,5]	152	143 (94,1)	0,7 [0,5; 1,0]	1,73	[1,37; 2,19]	<0,0001*
Interaktion p-Wert									0,5429
Krankheitsstadium Version 7									
Stadium IB	105	103 (98,1)	0,5 [0,3; 0,7]	106	94 (88,7)	0,9 [0,5; 2,1]	1,91	[1,44; 2,54]	<0,0001*
Stadium II	118	115 (97,5)	0,4 [0,3; 0,5]	118	110 (93,2)	1,0 [0,6; 1,4]	1,72	[1,33; 2,24]	<0,0001*
Stadium IIIA	114	112 (98,2)	0,4 [0,3; 0,5]	119	105 (88,2)	1,0 [0,7; 1,1]	1,86	[1,42; 2,43]	<0,0001*
Interaktion p-Wert									0,8616
Krankheitsstadium Version 8									
Stadium IB	100	98 (98,0)	0,5 [0,3; 0,9]	98	88 (89,8)	0,7 [0,5; 1,2]	1,76	[1,31; 2,36]	0,0002*
Stadium II	113	110 (97,3)	0,4 [0,3; 0,5]	119	108 (90,8)	1,1 [0,8; 1,8]	1,93	[1,48; 2,52]	<0,0001*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2aaa 12JUL2023:07:07 kfrh585

Table 4.3.1.1 ADAURA: Summary of subgroup analysis of time to first UE
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	107 (98,2)	0,4 [0,3; 0,5]	115	102 (88,7)	0,9 [0,6; 1,0]	1,80	[1,37; 2,37]	<0,0001*
Interaktion p-Wert									0,8906
Adjuvante Chemotherapie									
Ja	203	200 (98,5)	0,4 [0,3; 0,5]	207	192 (92,8)	0,9 [0,7; 1,0]	1,80	[1,47; 2,20]	<0,0001*
Nein	134	130 (97,0)	0,5 [0,4; 0,7]	136	117 (86,0)	1,0 [0,7; 2,0]	1,88	[1,46; 2,43]	<0,0001*
Interaktion p-Wert									0,7796
Raucherstatus									
Ja	108	104 (96,3)	0,4 [0,3; 0,5]	86	84 (97,7)	1,0 [0,8; 1,3]	1,64	[1,23; 2,20]	0,0007*
Nein	229	226 (98,7)	0,4 [0,3; 0,5]	257	225 (87,5)	0,9 [0,6; 1,0]	1,90	[1,57; 2,29]	<0,0001*
Interaktion p-Wert									0,4163
Region									
Asien	204	203 (99,5)	0,3 [0,3; 0,4]	209	199 (95,2)	0,8 [0,6; 1,0]	1,94	[1,59; 2,36]	<0,0001*
Europa	61	60 (98,4)	0,5 [0,3; 0,5]	69	59 (85,5)	1,1 [0,6; 2,7]	2,49	[1,73; 3,59]	<0,0001*
Nordamerika	14	14 (100)	0,3 [0,0; 0,5]	11	11 (100)	0,5 [0,0; 1,0]	1,27	[0,58; 2,88]	0,5455
Rest der Welt	58	53 (91,4)	1,0 [0,6; 2,4]	54	40 (74,1)	2,7 [1,0; 7,8]	1,64	[1,09; 2,49]	0,0174*
Interaktion p-Wert									0,3220

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2aaa 12JUL2023:07:07 kfrh585

Table 4.3.1.2 ADAURA: Summary of subgroup analysis of time to first SOC: Allgemeine Erkrankungen und Beschwerden am Verabreichungsort
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	33 (30,3)	NE [NE; NE]	95	22 (23,2)	NE [NE; NE]	1,22	[0,72; 2,13]	0,4590
Weiblich	228	76 (33,3)	NE [NE; NE]	248	57 (23,0)	NE [NE; NE]	1,41	[1,004; 2,00]	0,0474*
Interaktion p-Wert									0,6615
Alter									
<65 Jahre	184	62 (33,7)	NE [NE; NE]	195	52 (26,7)	NE [NE; NE]	1,16	[0,80; 1,68]	0,4362
>=65 Jahre	153	47 (30,7)	NE [NE; NE]	148	27 (18,2)	NE [NE; NE]	1,72	[1,08; 2,80]	0,0220*
Interaktion p-Wert									0,1930
Abstammung									
Asiatisch	215	66 (30,7)	NE [NE; NE]	218	48 (22,0)	NE [NE; NE]	1,34	[0,92; 1,95]	0,1261
Nicht-asiatisch	122	43 (35,2)	NE [NE; NE]	125	31 (24,8)	NE [NE; NE]	1,38	[0,87; 2,21]	0,1701
Interaktion p-Wert									0,9147
EGFR-Mutation									
Exon 19 Deletion	187	64 (34,2)	NE [NE; NE]	191	41 (21,5)	NE [NE; NE]	1,49	[1,01; 2,23]	0,0431*
L858R	150	45 (30,0)	NE [NE; NE]	152	38 (25,0)	NE [NE; NE]	1,19	[0,78; 1,85]	0,4198
Interaktion p-Wert									0,4525
Krankheitsstadium Version 7									
Stadium IB	105	32 (30,5)	NE [NE; NE]	106	29 (27,4)	NE [NE; NE]	1,16	[0,70; 1,92]	0,5684
Stadium II	118	37 (31,4)	NE [NE; NE]	118	23 (19,5)	NE [NE; NE]	1,64	[0,98; 2,79]	0,0597
Stadium IIIA	114	40 (35,1)	NE [NE; NE]	119	27 (22,7)	NE [NE; NE]	1,30	[0,80; 2,15]	0,2860
Interaktion p-Wert									0,6329
Krankheitsstadium Version 8									
Stadium IB	100	30 (30,0)	NE [NE; NE]	98	26 (26,5)	NE [NE; NE]	1,20	[0,71; 2,03]	0,5039

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2aab 12JUL2023:07:07 kfrh585

Table 4.3.1.2 ADAURA: Summary of subgroup analysis of time to first SOC: Allgemeine Erkrankungen und Beschwerden am Verabreichungsort
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium II	113	37 (32,7)	NE [NE; NE]	119	24 (20,2)	NE [NE; NE]	1,70	[1,02; 2,88]	0,0402*
Stadium IIIA	109	37 (33,9)	NE [NE; NE]	115	26 (22,6)	NE [NE; NE]	1,23	[0,75; 2,05]	0,4211
Interaktion p-Wert									0,5704
Adjuvante Chemotherapie									
Ja	203	69 (34,0)	NE [NE; NE]	207	45 (21,7)	NE [NE; NE]	1,49	[1,03; 2,19]	0,0354*
Nein	134	40 (29,9)	NE [NE; NE]	136	34 (25,0)	NE [NE; NE]	1,16	[0,74; 1,85]	0,5129
Interaktion p-Wert									0,4129
Raucherstatus									
Ja	108	38 (35,2)	NE [NE; NE]	86	24 (27,9)	NE [NE; NE]	1,17	[0,71; 1,98]	0,5439
Nein	229	71 (31,0)	NE [NE; NE]	257	55 (21,4)	NE [NE; NE]	1,41	[0,99; 2,02]	0,0544
Interaktion p-Wert									0,5560
Region									
Asien	204	61 (29,9)	NE [NE; NE]	209	45 (21,5)	NE [NE; NE]	1,32	[0,90; 1,95]	0,1550
Europa	61	30 (49,2)	35,9 [5,7; NE]	69	18 (26,1)	NE [NE; NE]	2,02	[1,13; 3,68]	0,0166*
Nordamerika	14	5 (35,7)	NE [NE; NE]	11	4 (36,4)	NE [NE; NE]	1,00	[0,26; 4,02]	0,9942
Rest der Welt	58	13 (22,4)	NE [NE; NE]	54	12 (22,2)	NE [NE; NE]	0,91	[0,41; 2,02]	0,8080
Interaktion p-Wert									0,3883

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2aab 12JUL2023:07:07 kfrh585

Table 4.3.1.3 ADAURA: Summary of subgroup analysis of time to first PT: Ermuedung
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	11 (10,1)	NE [NE; NE]	95	5 (5,3)	NE [NE; NE]	1,78	[0,65; 5,66]	0,2692
Weiblich	228	21 (9,2)	NE [NE; NE]	248	12 (4,8)	NE [NE; NE]	1,82	[0,91; 3,82]	0,0915
Interaktion p-Wert									0,9746
Alter									
<65 Jahre	184	16 (8,7)	NE [NE; NE]	195	9 (4,6)	NE [NE; NE]	1,75	[0,79; 4,15]	0,1698
>=65 Jahre	153	16 (10,5)	NE [NE; NE]	148	8 (5,4)	NE [NE; NE]	1,88	[0,83; 4,64]	0,1334
Interaktion p-Wert									0,9064
Abstammung									
Asiatisch	215	14 (6,5)	NE [NE; NE]	218	11 (5,0)	NE [NE; NE]	1,20	[0,54; 2,70]	0,6523
Nicht-asiatisch	122	18 (14,8)	NE [NE; NE]	125	6 (4,8)	NE [NE; NE]	3,03	[1,27; 8,35]	0,0115*
Interaktion p-Wert									0,1287
EGFR-Mutation									
Exon 19 Deletion	187	21 (11,2)	NE [NE; NE]	191	7 (3,7)	NE [NE; NE]	2,86	[1,27; 7,27]	0,0100*
L858R	150	11 (7,3)	NE [NE; NE]	152	10 (6,6)	NE [NE; NE]	1,08	[0,46; 2,60]	0,8529
Interaktion p-Wert									0,1122
Krankheitsstadium Version 7									
Stadium IB	105	10 (9,5)	NE [NE; NE]	106	8 (7,5)	NE [NE; NE]	1,29	[0,51; 3,37]	0,5928
Stadium II	118	13 (11,0)	NE [NE; NE]	118	5 (4,2)	NE [NE; NE]	2,52	[0,95; 7,84]	0,0644
Stadium IIIA	114	9 (7,9)	NE [NE; NE]	119	4 (3,4)	NE [NE; NE]	2,05	[0,67; 7,59]	0,2155
Interaktion p-Wert									0,6196
Krankheitsstadium Version 8									
Stadium IB	100	10 (10,0)	NE [NE; NE]	98	8 (8,2)	NE [NE; NE]	1,25	[0,49; 3,29]	0,6322
Stadium II	113	12 (10,6)	NE [NE; NE]	119	5 (4,2)	NE [NE; NE]	2,48	[0,92; 7,79]	0,0740

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.3 ADAURA: Summary of subgroup analysis of time to first PT: Ermuedung
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	9 (8,3)	NE [NE; NE]	115	4 (3,5)	NE [NE; NE]	2,06	[0,67; 7,62]	0,2128
Interaktion p-Wert									0,6080
Adjuvante Chemotherapie									
Ja	203	21 (10,3)	NE [NE; NE]	207	7 (3,4)	NE [NE; NE]	2,88	[1,28; 7,32]	0,0094*
Nein	134	11 (8,2)	NE [NE; NE]	136	10 (7,4)	NE [NE; NE]	1,08	[0,45; 2,58]	0,8674
Interaktion p-Wert									0,1063
Raucherstatus									
Ja	108	14 (13,0)	NE [NE; NE]	86	6 (7,0)	NE [NE; NE]	1,75	[0,70; 4,94]	0,2382
Nein	229	18 (7,9)	NE [NE; NE]	257	11 (4,3)	NE [NE; NE]	1,75	[0,84; 3,82]	0,1389
Interaktion p-Wert									0,9998
Region									
Asien	204	11 (5,4)	NE [NE; NE]	209	9 (4,3)	NE [NE; NE]	1,16	[0,48; 2,87]	0,7467
Europa	61	14 (23,0)	NE [NE; NE]	69	5 (7,2)	NE [NE; NE]	3,24	[1,24; 10,03]	0,0156*
Nordamerika	14	3 (21,4)	NE [NE; NE]	11	2 (18,2)	NE [NE; NE]	1,17	[0,19; 8,91]	0,8611
Rest der Welt	58	4 (6,9)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	3,55	[0,53; 69,41]	0,2078
Interaktion p-Wert									0,4007

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.4 ADAURA: Summary of subgroup analysis of time to first PT: Schleimhautentzuendung
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	1 (0,9)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	9 (3,9)	NE [NE; NE]	248	1 (0,4)	NE [NE; NE]	9,25	[1,73;170,57]	0,0060*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	10 (5,4)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	0	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	8 (3,7)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	2 (1,6)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	8 (4,3)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	2 (1,3)	NE [NE; NE]	152	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	4 (3,8)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	3 (2,5)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	3 (2,6)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	4 (4,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	3 (2,7)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.4 ADAURA: Summary of subgroup analysis of time to first PT: Schleimhautentzuendung
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	3 (2,8)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	4 (2,0)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	6 (4,5)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	3 (2,8)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	NC	[NC]	NC
Nein	229	7 (3,1)	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	7 (3,4)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	1 (1,6)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	1 (1,7)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.5 ADAURA: Summary of subgroup analysis of time to first SOC: Augenerkrankungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	16 (14,7)	NE [NE; NE]	95	5 (5,3)	NE [NE; NE]	2,74	[1,07; 8,37]	0,0346*
Weiblich	228	50 (21,9)	NE [NE; NE]	248	37 (14,9)	NE [NE; NE]	1,44	[0,94; 2,22]	0,0899
Interaktion p-Wert									0,2324
Alter									
<65 Jahre	184	38 (20,7)	NE [NE; NE]	195	26 (13,3)	NE [NE; NE]	1,47	[0,89; 2,44]	0,1301
>=65 Jahre	153	28 (18,3)	NE [NE; NE]	148	16 (10,8)	NE [NE; NE]	1,73	[0,95; 3,27]	0,0739
Interaktion p-Wert									0,6787
Abstammung									
Asiatisch	215	48 (22,3)	NE [NE; NE]	218	34 (15,6)	NE [NE; NE]	1,39	[0,90; 2,18]	0,1355
Nicht-asiatisch	122	18 (14,8)	NE [NE; NE]	125	8 (6,4)	NE [NE; NE]	2,28	[1,03; 5,56]	0,0432*
Interaktion p-Wert									0,2973
EGFR-Mutation									
Exon 19 Deletion	187	42 (22,5)	NE [NE; NE]	191	20 (10,5)	NE [NE; NE]	2,04	[1,21; 3,55]	0,0068*
L858R	150	24 (16,0)	NE [NE; NE]	152	22 (14,5)	NE [NE; NE]	1,13	[0,63; 2,02]	0,6898
Interaktion p-Wert									0,1363
Krankheitsstadium Version 7									
Stadium IB	105	19 (18,1)	NE [NE; NE]	106	13 (12,3)	NE [NE; NE]	1,61	[0,80; 3,33]	0,1826
Stadium II	118	22 (18,6)	NE [NE; NE]	118	16 (13,6)	NE [NE; NE]	1,36	[0,72; 2,63]	0,3515
Stadium IIIA	114	25 (21,9)	NE [NE; NE]	119	13 (10,9)	NE [NE; NE]	1,77	[0,92; 3,57]	0,0890
Interaktion p-Wert									0,8510
Krankheitsstadium Version 8									
Stadium IB	100	17 (17,0)	NE [NE; NE]	98	14 (14,3)	NE [NE; NE]	1,28	[0,63; 2,64]	0,4915
Stadium II	113	23 (20,4)	NE [NE; NE]	119	15 (12,6)	NE [NE; NE]	1,65	[0,87; 3,23]	0,1253

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.5 ADAURA: Summary of subgroup analysis of time to first SOC: Augenerkrankungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	24 (22,0)	NE [NE; NE]	115	13 (11,3)	NE [NE; NE]	1,69	[0,87; 3,42]	0,1212
Interaktion p-Wert									0,8285
Adjuvante Chemotherapie									
Ja	203	45 (22,2)	NE [NE; NE]	207	28 (13,5)	NE [NE; NE]	1,58	[0,99; 2,57]	0,0538
Nein	134	21 (15,7)	NE [NE; NE]	136	14 (10,3)	NE [NE; NE]	1,53	[0,78; 3,07]	0,2163
Interaktion p-Wert									0,9309
Raucherstatus									
Ja	108	21 (19,4)	NE [NE; NE]	86	8 (9,3)	NE [NE; NE]	2,11	[0,97; 5,07]	0,0602
Nein	229	45 (19,7)	NE [NE; NE]	257	34 (13,2)	NE [NE; NE]	1,44	[0,92; 2,26]	0,1079
Interaktion p-Wert									0,4129
Region									
Asien	204	43 (21,1)	NE [NE; NE]	209	33 (15,8)	NE [NE; NE]	1,29	[0,82; 2,04]	0,2707
Europa	61	11 (18,0)	NE [NE; NE]	69	5 (7,2)	NE [NE; NE]	2,51	[0,91; 7,98]	0,0749
Nordamerika	14	6 (42,9)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	5,28	[0,90; 99,58]	0,0674
Rest der Welt	58	6 (10,3)	NE [NE; NE]	54	3 (5,6)	NE [NE; NE]	1,80	[0,48; 8,54]	0,3929
Interaktion p-Wert									0,3623

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.6 ADAURA: Summary of subgroup analysis of time to first PT: Sehen verschwommen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	3 (2,8)	NE [NE; NE]	95	2 (2,1)	NE [NE; NE]	1,20	[0,20; 9,15]	0,8382
Weiblich	228	9 (3,9)	NE [NE; NE]	248	1 (0,4)	NE [NE; NE]	9,18	[1,72;169,27]	0,0061*
Interaktion p-Wert									0,1303
Alter									
<65 Jahre	184	8 (4,3)	NE [NE; NE]	195	3 (1,5)	NE [NE; NE]	2,64	[0,76; 12,06]	0,1305
>=65 Jahre	153	4 (2,6)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	9 (4,2)	NE [NE; NE]	218	3 (1,4)	NE [NE; NE]	2,91	[0,87; 13,13]	0,0857
Nicht-asiatisch	122	3 (2,5)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	9 (4,8)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	3 (2,0)	NE [NE; NE]	152	3 (2,0)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	3 (2,9)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	5 (4,2)	NE [NE; NE]	118	2 (1,7)	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	4 (3,5)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	2 (2,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	6 (5,3)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.6 ADAURA: Summary of subgroup analysis of time to first PT: Sehen verschwommen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	4 (3,7)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	8 (3,9)	NE [NE; NE]	207	2 (1,0)	NE [NE; NE]	3,72	[0,93; 24,68]	0,0644
Nein	134	4 (3,0)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	3,94	[0,58; 77,10]	0,1698
Interaktion p-Wert									0,9661
Raucherstatus									
Ja	108	3 (2,8)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	2,25	[0,29; 45,56]	0,4561
Nein	229	9 (3,9)	NE [NE; NE]	257	2 (0,8)	NE [NE; NE]	4,70	[1,21; 30,87]	0,0236*
Interaktion p-Wert									0,6074
Region									
Asien	204	7 (3,4)	NE [NE; NE]	209	3 (1,4)	NE [NE; NE]	2,26	[0,63; 10,49]	0,2189
Europa	61	2 (3,3)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	2 (14,3)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	1 (1,7)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2aaf 12JUL2023:07:07 kfrh585

Table 4.3.1.7 ADAURA: Summary of subgroup analysis of time to first PT: Epistaxis
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	5 (4,6)	NE [NE; NE]	95	2 (2,1)	NE [NE; NE]	1,87	[0,40; 13,06]	0,4381
Weiblich	228	16 (7,0)	NE [NE; NE]	248	3 (1,2)	NE [NE; NE]	5,01	[1,67; 21,57]	0,0028*
Interaktion p-Wert									0,3573
Alter									
<65 Jahre	184	12 (6,5)	NE [NE; NE]	195	1 (0,5)	NE [NE; NE]	10,42	[2,05;189,93]	0,0021*
>=65 Jahre	153	9 (5,9)	NE [NE; NE]	148	4 (2,7)	NE [NE; NE]	2,02	[0,66; 7,46]	0,2255
Interaktion p-Wert									0,1328
Abstammung									
Asiatisch	215	13 (6,0)	NE [NE; NE]	218	4 (1,8)	NE [NE; NE]	2,83	[1,001; 10,08]	0,0498*
Nicht-asiatisch	122	8 (6,6)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	7,17	[1,31;133,13]	0,0195*
Interaktion p-Wert									0,4133
EGFR-Mutation									
Exon 19 Deletion	187	11 (5,9)	NE [NE; NE]	191	4 (2,1)	NE [NE; NE]	2,22	[0,76; 8,02]	0,1525
L858R	150	10 (6,7)	NE [NE; NE]	152	1 (0,7)	NE [NE; NE]	9,78	[1,87;179,52]	0,0039*
Interaktion p-Wert									0,1768
Krankheitsstadium Version 7									
Stadium IB	105	6 (5,7)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	9 (7,6)	NE [NE; NE]	118	3 (2,5)	NE [NE; NE]	2,68	[0,80; 12,09]	0,1143
Stadium IIIA	114	6 (5,3)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	2,05	[0,47; 14,08]	0,3579
Interaktion p-Wert									0,8008
Krankheitsstadium Version 8									
Stadium IB	100	6 (6,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.7 ADAURA: Summary of subgroup analysis of time to first PT: Epistaxis
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium II	113	8 (7,1)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	2,59	[0,75; 11,82]	0,1374
Stadium IIIA	109	6 (5,5)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	2,14	[0,49; 14,72]	0,3270
Interaktion p-Wert									0,8601
Adjuvante Chemotherapie									
Ja	203	13 (6,4)	NE [NE; NE]	207	3 (1,4)	NE [NE; NE]	3,58	[1,15; 15,64]	0,0263*
Nein	134	8 (6,0)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	3,88	[0,97; 25,73]	0,0551
Interaktion p-Wert									0,9358
Raucherstatus									
Ja	108	8 (7,4)	NE [NE; NE]	86	4 (4,7)	NE [NE; NE]	1,38	[0,43; 5,18]	0,5928
Nein	229	13 (5,7)	NE [NE; NE]	257	1 (0,4)	NE [NE; NE]	12,53	[2,49;227,61]	0,0006*
Interaktion p-Wert									0,0401*
Region									
Asien	204	12 (5,9)	NE [NE; NE]	209	4 (1,9)	NE [NE; NE]	2,62	[0,91; 9,38]	0,0755
Europa	61	5 (8,2)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	5,06	[0,82; 97,00]	0,0855
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	3 (5,2)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,5803

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.8 ADAURA: Summary of subgroup analysis of time to first PT: Nasenschleimhaut trocken
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	2 (1,8)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	9 (3,9)	NE [NE; NE]	248	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	9 (4,9)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	2 (1,3)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	4 (1,9)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	7 (5,7)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	10 (5,3)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	1 (0,7)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	3 (2,5)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	3 (2,6)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	5 (5,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	3 (2,7)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.8 ADAURA: Summary of subgroup analysis of time to first PT: Nasenschleimhaut trocken
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	2 (1,8)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	6 (3,0)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	5 (3,7)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	6 (2,6)	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	4 (2,0)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	1 (1,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	6 (10,3)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2aah 12JUL2023:07:07 kfrh585

Table 4.3.1.9 ADAURA: Summary of subgroup analysis of time to first SOC: Erkrankungen der Haut und des Unterhautgewebes
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	79 (72,5)	1,8 [1,0; 4,8]	95	37 (38,9)	NE [NE; NE]	2,61	[1,78; 3,90]	<0,0001*
Weiblich	228	170 (74,6)	2,8 [1,9; 5,4]	248	93 (37,5)	NE [NE; NE]	2,76	[2,15; 3,57]	<0,0001*
Interaktion p-Wert									0,8160
Alter									
<65 Jahre	184	139 (75,5)	2,3 [1,0; 3,7]	195	73 (37,4)	NE [NE; NE]	2,86	[2,16; 3,82]	<0,0001*
>=65 Jahre	153	110 (71,9)	3,9 [1,8; 6,4]	148	57 (38,5)	NE [NE; NE]	2,56	[1,87; 3,55]	<0,0001*
Interaktion p-Wert									0,6138
Abstammung									
Asiatisch	215	172 (80,0)	1,9 [1,1; 3,1]	218	92 (42,2)	NE [NE; NE]	2,79	[2,17; 3,61]	<0,0001*
Nicht-asiatisch	122	77 (63,1)	5,5 [2,3;10,8]	125	38 (30,4)	NE [NE; NE]	2,67	[1,82; 3,98]	<0,0001*
Interaktion p-Wert									0,8546
EGFR-Mutation									
Exon 19 Deletion	187	145 (77,5)	2,4 [1,2; 5,0]	191	68 (35,6)	NE [NE; NE]	2,98	[2,24; 4,00]	<0,0001*
L858R	150	104 (69,3)	2,8 [1,4; 5,6]	152	62 (40,8)	NE [NE; NE]	2,42	[1,77; 3,33]	<0,0001*
Interaktion p-Wert									0,3379
Krankheitsstadium Version 7									
Stadium IB	105	70 (66,7)	4,6 [1,9; 7,6]	106	40 (37,7)	NE [NE; NE]	2,51	[1,71; 3,73]	<0,0001*
Stadium II	118	88 (74,6)	2,8 [1,4; 5,6]	118	46 (39,0)	NE [NE; NE]	2,61	[1,83; 3,76]	<0,0001*
Stadium IIIA	114	91 (79,8)	1,3 [0,8; 4,2]	119	44 (37,0)	NE [NE; NE]	3,03	[2,13; 4,39]	<0,0001*
Interaktion p-Wert									0,7494
Krankheitsstadium Version 8									
Stadium IB	100	64 (64,0)	5,1 [2,3;13,8]	98	39 (39,8)	NE [NE; NE]	2,21	[1,49; 3,31]	<0,0001*
Stadium II	113	87 (77,0)	2,6 [1,0; 5,3]	119	44 (37,0)	NE [NE; NE]	3,01	[2,11; 4,37]	<0,0001*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.9 ADAURA: Summary of subgroup analysis of time to first SOC: Erkrankungen der Haut und des Unterhautgewebes
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	86 (78,9)	1,4 [0,9; 4,6]	115	44 (38,3)	NE [NE; NE]	2,81	[1,96; 4,07]	<0,0001*
Interaktion p-Wert									0,5051
Adjuvante Chemotherapie									
Ja	203	153 (75,4)	2,6 [1,1; 5,3]	207	81 (39,1)	NE [NE; NE]	2,69	[2,06; 3,54]	<0,0001*
Nein	134	96 (71,6)	3,1 [1,8; 5,6]	136	49 (36,0)	NE [NE; NE]	2,76	[1,96; 3,92]	<0,0001*
Interaktion p-Wert									0,9161
Raucherstatus									
Ja	108	86 (79,6)	1,5 [0,9; 3,7]	86	33 (38,4)	NE [NE; NE]	3,33	[2,25; 5,05]	<0,0001*
Nein	229	163 (71,2)	3,4 [2,2; 5,8]	257	97 (37,7)	NE [NE; NE]	2,48	[1,93; 3,20]	<0,0001*
Interaktion p-Wert									0,2194
Region									
Asien	204	162 (79,4)	2,3 [1,1; 3,4]	209	85 (40,7)	NE [NE; NE]	2,88	[2,22; 3,76]	<0,0001*
Europa	61	41 (67,2)	5,4 [0,7;10,8]	69	20 (29,0)	NE [NE; NE]	3,24	[1,92; 5,64]	<0,0001*
Nordamerika	14	13 (92,9)	0,9 [0,5; 5,6]	11	8 (72,7)	1,0 [0,3;30,9]	1,51	[0,64; 3,83]	0,3498
Rest der Welt	58	33 (56,9)	8,2 [2,8; NE]	54	17 (31,5)	NE [NE; NE]	2,19	[1,24; 4,02]	0,0069*
Interaktion p-Wert									0,4371

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.10 ADAURA: Summary of subgroup analysis of time to first PT: Alopezie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	3 (2,8)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	18 (7,9)	NE [NE; NE]	248	8 (3,2)	NE [NE; NE]	2,33	[1,05; 5,69]	0,0380*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	14 (7,6)	NE [NE; NE]	195	4 (2,1)	NE [NE; NE]	3,47	[1,24; 12,24]	0,0163*
>=65 Jahre	153	7 (4,6)	NE [NE; NE]	148	4 (2,7)	NE [NE; NE]	1,66	[0,50; 6,36]	0,4077
Interaktion p-Wert									0,3857
Abstammung									
Asiatisch	215	14 (6,5)	NE [NE; NE]	218	3 (1,4)	NE [NE; NE]	4,53	[1,48; 19,65]	0,0066*
Nicht-asiatisch	122	7 (5,7)	NE [NE; NE]	125	5 (4,0)	NE [NE; NE]	1,37	[0,44; 4,62]	0,5906
Interaktion p-Wert									0,1578
EGFR-Mutation									
Exon 19 Deletion	187	13 (7,0)	NE [NE; NE]	191	3 (1,6)	NE [NE; NE]	4,07	[1,31; 17,78]	0,0134*
L858R	150	8 (5,3)	NE [NE; NE]	152	5 (3,3)	NE [NE; NE]	1,63	[0,54; 5,39]	0,3857
Interaktion p-Wert									0,2775
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	2,68	[0,58; 18,70]	0,2139
Stadium II	118	6 (5,1)	NE [NE; NE]	118	3 (2,5)	NE [NE; NE]	1,91	[0,50; 9,03]	0,3487
Stadium IIIA	114	10 (8,8)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	3,02	[0,92; 13,50]	0,0697
Interaktion p-Wert									0,8894
Krankheitsstadium Version 8									
Stadium IB	100	6 (6,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	3,15	[0,73; 21,48]	0,1303
Stadium II	113	5 (4,4)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	1,69	[0,41; 8,23]	0,4660

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.10 ADAURA: Summary of subgroup analysis of time to first PT: Alopezie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	9 (8,3)	NE [NE; NE]	115	3 (2,6)	NE [NE; NE]	2,71	[0,81; 12,26]	0,1107
Interaktion p-Wert									0,8302
Adjuvante Chemotherapie									
Ja	203	12 (5,9)	NE [NE; NE]	207	4 (1,9)	NE [NE; NE]	2,86	[0,99; 10,23]	0,0517
Nein	134	9 (6,7)	NE [NE; NE]	136	4 (2,9)	NE [NE; NE]	2,26	[0,74; 8,36]	0,1569
Interaktion p-Wert									0,7808
Raucherstatus									
Ja	108	8 (7,4)	NE [NE; NE]	86	2 (2,3)	NE [NE; NE]	3,05	[0,76; 20,23]	0,1206
Nein	229	13 (5,7)	NE [NE; NE]	257	6 (2,3)	NE [NE; NE]	2,32	[0,92; 6,60]	0,0768
Interaktion p-Wert									0,7654
Region									
Asien	204	13 (6,4)	NE [NE; NE]	209	2 (1,0)	NE [NE; NE]	6,40	[1,77; 40,94]	0,0030*
Europa	61	2 (3,3)	NE [NE; NE]	69	3 (4,3)	NE [NE; NE]	0,72	[0,10; 4,36]	0,7197
Nordamerika	14	4 (28,6)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	3,04	[0,45; 59,46]	0,2738
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	2 (3,7)	NE [NE; NE]	0,86	[0,10; 7,19]	0,8831
Interaktion p-Wert									0,1787

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.11 ADAURA: Summary of subgroup analysis of time to first PT: Ausschlag
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	11 (10,1)	NE [NE; NE]	95	5 (5,3)	NE [NE; NE]	1,75	[0,63; 5,54]	0,2882
Weiblich	228	22 (9,6)	NE [NE; NE]	248	7 (2,8)	NE [NE; NE]	3,13	[1,40; 7,92]	0,0046*
Interaktion p-Wert									0,4035
Alter									
<65 Jahre	184	25 (13,6)	NE [NE; NE]	195	4 (2,1)	NE [NE; NE]	6,00	[2,33; 20,41]	<0,0001*
>=65 Jahre	153	8 (5,2)	NE [NE; NE]	148	8 (5,4)	NE [NE; NE]	0,90	[0,33; 2,45]	0,8343
Interaktion p-Wert									0,0072*
Abstammung									
Asiatisch	215	22 (10,2)	NE [NE; NE]	218	9 (4,1)	NE [NE; NE]	2,26	[1,08; 5,19]	0,0309*
Nicht-asiatisch	122	11 (9,0)	NE [NE; NE]	125	3 (2,4)	NE [NE; NE]	3,46	[1,08; 15,33]	0,0356*
Interaktion p-Wert									0,5697
EGFR-Mutation									
Exon 19 Deletion	187	20 (10,7)	NE [NE; NE]	191	5 (2,6)	NE [NE; NE]	3,55	[1,43; 10,69]	0,0050*
L858R	150	13 (8,7)	NE [NE; NE]	152	7 (4,6)	NE [NE; NE]	1,84	[0,76; 4,91]	0,1812
Interaktion p-Wert									0,3359
Krankheitsstadium Version 7									
Stadium IB	105	14 (13,3)	NE [NE; NE]	106	5 (4,7)	NE [NE; NE]	3,13	[1,20; 9,69]	0,0190*
Stadium II	118	7 (5,9)	NE [NE; NE]	118	5 (4,2)	NE [NE; NE]	1,25	[0,40; 4,23]	0,6990
Stadium IIIA	114	12 (10,5)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	4,89	[1,33; 31,53]	0,0144*
Interaktion p-Wert									0,3029
Krankheitsstadium Version 8									
Stadium IB	100	13 (13,0)	NE [NE; NE]	98	5 (5,1)	NE [NE; NE]	2,84	[1,07; 8,84]	0,0358*
Stadium II	113	6 (5,3)	NE [NE; NE]	119	5 (4,2)	NE [NE; NE]	1,15	[0,35; 4,00]	0,8143

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.11 ADAURA: Summary of subgroup analysis of time to first PT: Ausschlag
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	13 (11,9)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	5,37	[1,48; 34,45]	0,0081*
Interaktion p-Wert									0,2431
Adjuvante Chemotherapie									
Ja	203	19 (9,4)	NE [NE; NE]	207	6 (2,9)	NE [NE; NE]	2,85	[1,20; 7,83]	0,0164*
Nein	134	14 (10,4)	NE [NE; NE]	136	6 (4,4)	NE [NE; NE]	2,30	[0,92; 6,50]	0,0744
Interaktion p-Wert									0,7539
Raucherstatus									
Ja	108	15 (13,9)	NE [NE; NE]	86	5 (5,8)	NE [NE; NE]	2,19	[0,85; 6,72]	0,1099
Nein	229	18 (7,9)	NE [NE; NE]	257	7 (2,7)	NE [NE; NE]	2,63	[1,15; 6,78]	0,0218*
Interaktion p-Wert									0,7850
Region									
Asien	204	20 (9,8)	NE [NE; NE]	209	9 (4,3)	NE [NE; NE]	2,10	[0,98; 4,85]	0,0562
Europa	61	6 (9,8)	NE [NE; NE]	69	3 (4,3)	NE [NE; NE]	2,10	[0,55; 9,98]	0,2779
Nordamerika	14	2 (14,3)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	5 (8,6)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,9958

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.12 ADAURA: Summary of subgroup analysis of time to first PT: Ausschlag papuloes
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	6 (5,5)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	11 (4,8)	NE [NE; NE]	248	3 (1,2)	NE [NE; NE]	3,71	[1,15; 16,41]	0,0264*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	14 (7,6)	NE [NE; NE]	195	2 (1,0)	NE [NE; NE]	6,89	[1,92; 43,92]	0,0017*
>=65 Jahre	153	3 (2,0)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	2,81	[0,36; 56,84]	0,3371
Interaktion p-Wert									0,5307
Abstammung									
Asiatisch	215	12 (5,6)	NE [NE; NE]	218	3 (1,4)	NE [NE; NE]	3,93	[1,25; 17,25]	0,0179*
Nicht-asiatisch	122	5 (4,1)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	10 (5,3)	NE [NE; NE]	191	1 (0,5)	NE [NE; NE]	9,24	[1,77;169,58]	0,0052*
L858R	150	7 (4,7)	NE [NE; NE]	152	2 (1,3)	NE [NE; NE]	3,55	[0,86; 23,80]	0,0829
Interaktion p-Wert									0,4557
Krankheitsstadium Version 7									
Stadium IB	105	6 (5,7)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	9 (7,6)	NE [NE; NE]	118	2 (1,7)	NE [NE; NE]	4,27	[1,10; 28,07]	0,0347*
Stadium IIIA	114	2 (1,8)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	1,62	[0,15; 34,92]	0,6885
Interaktion p-Wert									0,5157
Krankheitsstadium Version 8									
Stadium IB	100	5 (5,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	7 (6,2)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.12 ADAURA: Summary of subgroup analysis of time to first PT: Ausschlag papuloes
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	4 (3,7)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	11 (5,4)	NE [NE; NE]	207	1 (0,5)	NE [NE; NE]	10,36	[2,01;189,50]	0,0025*
Nein	134	6 (4,5)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	2,98	[0,69; 20,35]	0,1504
Interaktion p-Wert									0,3315
Raucherstatus									
Ja	108	6 (5,6)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	11 (4,8)	NE [NE; NE]	257	3 (1,2)	NE [NE; NE]	3,86	[1,20; 17,07]	0,0219*
Interaktion p-Wert									NC
Region									
Asien	204	10 (4,9)	NE [NE; NE]	209	3 (1,4)	NE [NE; NE]	3,26	[0,996; 14,57]	0,0507
Europa	61	1 (1,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	5 (8,6)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.13 ADAURA: Summary of subgroup analysis of time to first PT: Dermatitis akneiform
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	17 (15,6)	NE [NE; NE]	95	5 (5,3)	NE [NE; NE]	3,04	[1,20; 9,26]	0,0175*
Weiblich	228	24 (10,5)	NE [NE; NE]	248	11 (4,4)	NE [NE; NE]	2,34	[1,18; 4,98]	0,0150*
Interaktion p-Wert									0,6744
Alter									
<65 Jahre	184	26 (14,1)	NE [NE; NE]	195	12 (6,2)	NE [NE; NE]	2,25	[1,16; 4,63]	0,0157*
>=65 Jahre	153	15 (9,8)	NE [NE; NE]	148	4 (2,7)	NE [NE; NE]	3,73	[1,35; 13,07]	0,0096*
Interaktion p-Wert									0,4382
Abstammung									
Asiatisch	215	29 (13,5)	NE [NE; NE]	218	13 (6,0)	NE [NE; NE]	2,27	[1,20; 4,51]	0,0109*
Nicht-asiatisch	122	12 (9,8)	NE [NE; NE]	125	3 (2,4)	NE [NE; NE]	4,10	[1,30; 18,01]	0,0142*
Interaktion p-Wert									0,3988
EGFR-Mutation									
Exon 19 Deletion	187	26 (13,9)	NE [NE; NE]	191	9 (4,7)	NE [NE; NE]	2,87	[1,40; 6,49]	0,0036*
L858R	150	15 (10,0)	NE [NE; NE]	152	7 (4,6)	NE [NE; NE]	2,25	[0,95; 5,90]	0,0654
Interaktion p-Wert									0,6874
Krankheitsstadium Version 7									
Stadium IB	105	10 (9,5)	NE [NE; NE]	106	5 (4,7)	NE [NE; NE]	2,12	[0,75; 6,79]	0,1582
Stadium II	118	11 (9,3)	NE [NE; NE]	118	5 (4,2)	NE [NE; NE]	2,21	[0,80; 7,01]	0,1270
Stadium IIIA	114	20 (17,5)	NE [NE; NE]	119	6 (5,0)	NE [NE; NE]	3,33	[1,42; 9,12]	0,0049*
Interaktion p-Wert									0,7701
Krankheitsstadium Version 8									
Stadium IB	100	10 (10,0)	NE [NE; NE]	98	5 (5,1)	NE [NE; NE]	2,06	[0,73; 6,60]	0,1751
Stadium II	113	10 (8,8)	NE [NE; NE]	119	5 (4,2)	NE [NE; NE]	2,14	[0,76; 6,86]	0,1528

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.13 ADAURA: Summary of subgroup analysis of time to first PT: Dermatitis akneiform
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	18 (16,5)	NE [NE; NE]	115	6 (5,2)	NE [NE; NE]	2,98	[1,25; 8,22]	0,0131*
Interaktion p-Wert									0,8452
Adjuvante Chemotherapie									
Ja	203	31 (15,3)	NE [NE; NE]	207	10 (4,8)	NE [NE; NE]	3,16	[1,61; 6,80]	0,0006*
Nein	134	10 (7,5)	NE [NE; NE]	136	6 (4,4)	NE [NE; NE]	1,70	[0,63; 4,99]	0,2981
Interaktion p-Wert									0,3286
Raucherstatus									
Ja	108	14 (13,0)	NE [NE; NE]	86	3 (3,5)	NE [NE; NE]	3,76	[1,23; 16,32]	0,0185*
Nein	229	27 (11,8)	NE [NE; NE]	257	13 (5,1)	NE [NE; NE]	2,32	[1,22; 4,65]	0,0097*
Interaktion p-Wert									0,4907
Region									
Asien	204	27 (13,2)	NE [NE; NE]	209	12 (5,7)	NE [NE; NE]	2,32	[1,20; 4,74]	0,0118*
Europa	61	3 (4,9)	NE [NE; NE]	69	2 (2,9)	NE [NE; NE]	1,69	[0,28; 12,86]	0,5593
Nordamerika	14	5 (35,7)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	3,92	[0,63; 75,05]	0,1547
Rest der Welt	58	6 (10,3)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	5,53	[0,94;104,43]	0,0590
Interaktion p-Wert									0,7884

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.14 ADAURA: Summary of subgroup analysis of time to first PT: Hautfissuren
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	7 (6,4)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	12 (5,3)	NE [NE; NE]	248	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	15 (8,2)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	4 (2,6)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	14 (6,5)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	5 (4,1)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	11 (5,9)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	8 (5,3)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	7 (6,7)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	7 (5,9)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	5 (4,4)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	6 (6,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	8 (7,1)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.14 ADAURA: Summary of subgroup analysis of time to first PT: Hautfissuren
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	4 (3,7)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	11 (5,4)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	8 (6,0)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	9 (8,3)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	10 (4,4)	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	13 (6,4)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	1 (1,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	4 (6,9)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.15 ADAURA: Summary of subgroup analysis of time to first PT: Nagelerkrankung
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	5 (4,6)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	17 (7,5)	NE [NE; NE]	248	3 (1,2)	NE [NE; NE]	5,65	[1,90; 24,22]	0,0010*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	11 (6,0)	NE [NE; NE]	195	2 (1,0)	NE [NE; NE]	5,08	[1,36; 32,87]	0,0131*
>=65 Jahre	153	11 (7,2)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	10,53	[2,05;192,39]	0,0023*
Interaktion p-Wert									0,5650
Abstammung									
Asiatisch	215	15 (7,0)	NE [NE; NE]	218	2 (0,9)	NE [NE; NE]	7,00	[1,97; 44,44]	0,0013*
Nicht-asiatisch	122	7 (5,7)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	6,63	[1,18;124,03]	0,0294*
Interaktion p-Wert									0,9671
EGFR-Mutation									
Exon 19 Deletion	187	13 (7,0)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	9 (6,0)	NE [NE; NE]	152	3 (2,0)	NE [NE; NE]	3,03	[0,90; 13,65]	0,0739
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	5,52	[0,89;105,71]	0,0684
Stadium II	118	10 (8,5)	NE [NE; NE]	118	1 (0,8)	NE [NE; NE]	9,38	[1,80;172,14]	0,0047*
Stadium IIIA	114	7 (6,1)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	5,59	[0,99;104,58]	0,0513
Interaktion p-Wert									0,9188
Krankheitsstadium Version 8									
Stadium IB	100	5 (5,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	5,45	[0,88;104,33]	0,0708
Stadium II	113	9 (8,0)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	9,17	[1,72;169,19]	0,0061*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.15 ADAURA: Summary of subgroup analysis of time to first PT: Nagelerkrankung
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	7 (6,4)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	5,57	[0,99;104,21]	0,0519
Interaktion p-Wert									0,9234
Adjuvante Chemotherapie									
Ja	203	16 (7,9)	NE [NE; NE]	207	2 (1,0)	NE [NE; NE]	7,23	[2,06; 45,76]	0,0009*
Nein	134	6 (4,5)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	5,96	[1,02;112,54]	0,0475*
Interaktion p-Wert									0,8840
Raucherstatus									
Ja	108	9 (8,3)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	13 (5,7)	NE [NE; NE]	257	3 (1,2)	NE [NE; NE]	4,38	[1,41; 19,11]	0,0090*
Interaktion p-Wert									NC
Region									
Asien	204	14 (6,9)	NE [NE; NE]	209	2 (1,0)	NE [NE; NE]	6,63	[1,85; 42,22]	0,0021*
Europa	61	3 (4,9)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	5 (8,6)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	4,40	[0,71; 84,35]	0,1193
Interaktion p-Wert									0,7627

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.16 ADAURA: Summary of subgroup analysis of time to first PT: Onychoklasie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	1 (0,9)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	14 (6,1)	NE [NE; NE]	248	2 (0,8)	NE [NE; NE]	7,03	[1,96; 44,77]	0,0014*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	12 (6,5)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	3 (2,0)	NE [NE; NE]	148	2 (1,4)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	7 (3,3)	NE [NE; NE]	218	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	8 (6,6)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	9 (4,8)	NE [NE; NE]	191	2 (1,0)	NE [NE; NE]	4,05	[1,04; 26,58]	0,0428*
L858R	150	6 (4,0)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	7 (5,9)	NE [NE; NE]	118	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	3 (2,6)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	5 (5,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	6 (5,3)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.16 ADAURA: Summary of subgroup analysis of time to first PT: Onychoklasie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	3 (2,8)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	8 (3,9)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	7 (5,2)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	10 (4,4)	NE [NE; NE]	257	2 (0,8)	NE [NE; NE]	4,99	[1,31; 32,47]	0,0161*
Interaktion p-Wert									NC
Region									
Asien	204	6 (2,9)	NE [NE; NE]	209	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Europa	61	2 (3,3)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	3 (21,4)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	4 (6,9)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.17 ADAURA: Summary of subgroup analysis of time to first PT: Pruritus
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	21 (19,3)	NE [NE; NE]	95	8 (8,4)	NE [NE; NE]	2,32	[1,07; 5,57]	0,0331*
Weiblich	228	49 (21,5)	NE [NE; NE]	248	22 (8,9)	NE [NE; NE]	2,40	[1,47; 4,05]	0,0004*
Interaktion p-Wert									0,9446
Alter									
<65 Jahre	184	42 (22,8)	NE [NE; NE]	195	16 (8,2)	NE [NE; NE]	2,74	[1,57; 5,02]	0,0003*
>=65 Jahre	153	28 (18,3)	NE [NE; NE]	148	14 (9,5)	NE [NE; NE]	1,97	[1,05; 3,85]	0,0332*
Interaktion p-Wert									0,4534
Abstammung									
Asiatisch	215	54 (25,1)	NE [NE; NE]	218	23 (10,6)	NE [NE; NE]	2,42	[1,50; 4,01]	0,0002*
Nicht-asiatisch	122	16 (13,1)	NE [NE; NE]	125	7 (5,6)	NE [NE; NE]	2,28	[0,97; 5,93]	0,0583
Interaktion p-Wert									0,9098
EGFR-Mutation									
Exon 19 Deletion	187	46 (24,6)	NE [NE; NE]	191	17 (8,9)	NE [NE; NE]	2,71	[1,58; 4,86]	0,0002*
L858R	150	24 (16,0)	NE [NE; NE]	152	13 (8,6)	NE [NE; NE]	1,91	[0,99; 3,87]	0,0536
Interaktion p-Wert									0,4380
Krankheitsstadium Version 7									
Stadium IB	105	19 (18,1)	NE [NE; NE]	106	9 (8,5)	NE [NE; NE]	2,35	[1,09; 5,46]	0,0283*
Stadium II	118	26 (22,0)	NE [NE; NE]	118	11 (9,3)	NE [NE; NE]	2,36	[1,20; 4,99]	0,0124*
Stadium IIIA	114	25 (21,9)	NE [NE; NE]	119	10 (8,4)	NE [NE; NE]	2,36	[1,17; 5,16]	0,0162*
Interaktion p-Wert									1,0000
Krankheitsstadium Version 8									
Stadium IB	100	15 (15,0)	NE [NE; NE]	98	8 (8,2)	NE [NE; NE]	2,00	[0,87; 4,97]	0,1037
Stadium II	113	29 (25,7)	NE [NE; NE]	119	10 (8,4)	NE [NE; NE]	3,20	[1,61; 6,91]	0,0006*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.17 ADAURA: Summary of subgroup analysis of time to first PT: Pruritus
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	25 (22,9)	NE [NE; NE]	115	11 (9,6)	NE [NE; NE]	2,16	[1,09; 4,58]	0,0274*
Interaktion p-Wert									0,6428
Adjuvante Chemotherapie									
Ja	203	48 (23,6)	NE [NE; NE]	207	18 (8,7)	NE [NE; NE]	2,68	[1,59; 4,72]	0,0002*
Nein	134	22 (16,4)	NE [NE; NE]	136	12 (8,8)	NE [NE; NE]	1,90	[0,96; 3,97]	0,0671
Interaktion p-Wert									0,4515
Raucherstatus									
Ja	108	25 (23,1)	NE [NE; NE]	86	6 (7,0)	NE [NE; NE]	3,47	[1,52; 9,34]	0,0023*
Nein	229	45 (19,7)	NE [NE; NE]	257	24 (9,3)	NE [NE; NE]	2,06	[1,27; 3,43]	0,0034*
Interaktion p-Wert									0,3027
Region									
Asien	204	54 (26,5)	NE [NE; NE]	209	23 (11,0)	NE [NE; NE]	2,46	[1,53; 4,09]	0,0002*
Europa	61	8 (13,1)	NE [NE; NE]	69	6 (8,7)	NE [NE; NE]	1,46	[0,51; 4,42]	0,4846
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	0,70	[0,03; 17,59]	0,7985
Rest der Welt	58	7 (12,1)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,4957

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.18 ADAURA: Summary of subgroup analysis of time to first PT: Trockene Haut
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	20 (18,3)	NE [NE; NE]	95	3 (3,2)	NE [NE; NE]	6,06	[2,08; 25,72]	0,0004*
Weiblich	228	64 (28,1)	NE [NE; NE]	248	20 (8,1)	NE [NE; NE]	3,68	[2,27; 6,24]	<0,0001*
Interaktion p-Wert									0,4380
Alter									
<65 Jahre	184	51 (27,7)	NE [NE; NE]	195	14 (7,2)	NE [NE; NE]	3,92	[2,23; 7,37]	<0,0001*
>=65 Jahre	153	33 (21,6)	NE [NE; NE]	148	9 (6,1)	NE [NE; NE]	3,91	[1,96; 8,70]	<0,0001*
Interaktion p-Wert									0,9954
Abstammung									
Asiatisch	215	59 (27,4)	NE [NE; NE]	218	12 (5,5)	NE [NE; NE]	5,31	[2,96; 10,38]	<0,0001*
Nicht-asiatisch	122	25 (20,5)	NE [NE; NE]	125	11 (8,8)	NE [NE; NE]	2,41	[1,22; 5,10]	0,0112*
Interaktion p-Wert									0,1021
EGFR-Mutation									
Exon 19 Deletion	187	48 (25,7)	NE [NE; NE]	191	14 (7,3)	NE [NE; NE]	3,47	[1,97; 6,54]	<0,0001*
L858R	150	36 (24,0)	NE [NE; NE]	152	9 (5,9)	NE [NE; NE]	4,61	[2,32; 10,20]	<0,0001*
Interaktion p-Wert									0,5534
Krankheitsstadium Version 7									
Stadium IB	105	16 (15,2)	NE [NE; NE]	106	7 (6,6)	NE [NE; NE]	2,52	[1,07; 6,55]	0,0332*
Stadium II	118	35 (29,7)	NE [NE; NE]	118	6 (5,1)	NE [NE; NE]	6,51	[2,95; 17,20]	<0,0001*
Stadium IIIA	114	33 (28,9)	NE [NE; NE]	119	10 (8,4)	NE [NE; NE]	3,31	[1,69; 7,10]	0,0003*
Interaktion p-Wert									0,2742
Krankheitsstadium Version 8									
Stadium IB	100	13 (13,0)	NE [NE; NE]	98	6 (6,1)	NE [NE; NE]	2,32	[0,92; 6,60]	0,0765
Stadium II	113	35 (31,0)	NE [NE; NE]	119	6 (5,0)	NE [NE; NE]	6,99	[3,16; 18,47]	<0,0001*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.18 ADAURA: Summary of subgroup analysis of time to first PT: Trockene Haut
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	32 (29,4)	NE [NE; NE]	115	9 (7,8)	NE [NE; NE]	3,60	[1,79; 8,03]	0,0002*
Interaktion p-Wert									0,2247
Adjuvante Chemotherapie									
Ja	203	56 (27,6)	NE [NE; NE]	207	14 (6,8)	NE [NE; NE]	4,22	[2,42; 7,89]	<0,0001*
Nein	134	28 (20,9)	NE [NE; NE]	136	9 (6,6)	NE [NE; NE]	3,42	[1,68; 7,69]	0,0005*
Interaktion p-Wert									0,6668
Raucherstatus									
Ja	108	27 (25,0)	NE [NE; NE]	86	5 (5,8)	NE [NE; NE]	4,62	[1,94; 13,65]	0,0003*
Nein	229	57 (24,9)	NE [NE; NE]	257	18 (7,0)	NE [NE; NE]	3,71	[2,23; 6,48]	<0,0001*
Interaktion p-Wert									0,6880
Region									
Asien	204	51 (25,0)	NE [NE; NE]	209	10 (4,8)	NE [NE; NE]	5,50	[2,92; 11,50]	<0,0001*
Europa	61	10 (16,4)	NE [NE; NE]	69	4 (5,8)	NE [NE; NE]	2,92	[0,98; 10,66]	0,0551
Nordamerika	14	9 (64,3)	13,8 [0,7; NE]	11	3 (27,3)	NE [NE; NE]	2,88	[0,86; 13,00]	0,0884
Rest der Welt	58	14 (24,1)	NE [NE; NE]	54	6 (11,1)	NE [NE; NE]	2,25	[0,90; 6,34]	0,0838
Interaktion p-Wert									0,4461

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.19 ADAURA: Summary of subgroup analysis of time to first PT: Haematurie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	4 (3,7)	NE [NE; NE]	95	3 (3,2)	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	0	NE [NE; NE]	248	11 (4,4)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	1 (0,5)	NE [NE; NE]	195	10 (5,1)	NE [NE; NE]	0,09	[0,00; 0,45]	0,0016*
>=65 Jahre	153	3 (2,0)	NE [NE; NE]	148	4 (2,7)	NE [NE; NE]	0,65	[0,13; 2,97]	0,5754
Interaktion p-Wert									0,0906
Abstammung									
Asiatisch	215	0	NE [NE; NE]	218	9 (4,1)	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	4 (3,3)	NE [NE; NE]	125	5 (4,0)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	3 (1,6)	NE [NE; NE]	191	3 (1,6)	NE [NE; NE]	0,83	[0,15; 4,49]	0,8178
L858R	150	1 (0,7)	NE [NE; NE]	152	11 (7,2)	NE [NE; NE]	0,08	[0,00; 0,43]	0,0011*
Interaktion p-Wert									0,0601
Krankheitsstadium Version 7									
Stadium IB	105	1 (1,0)	NE [NE; NE]	106	8 (7,5)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	1 (0,8)	NE [NE; NE]	118	3 (2,5)	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	2 (1,8)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	1 (1,0)	NE [NE; NE]	98	7 (7,1)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	0	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2aas 12JUL2023:07:07 kfrh585

Table 4.3.1.19 ADAURA: Summary of subgroup analysis of time to first PT: Haematurie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	3 (2,8)	NE [NE; NE]	115	3 (2,6)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	1 (0,5)	NE [NE; NE]	207	6 (2,9)	NE [NE; NE]	0,14	[0,01; 0,82]	0,0268*
Nein	134	3 (2,2)	NE [NE; NE]	136	8 (5,9)	NE [NE; NE]	0,34	[0,07; 1,18]	0,0910
Interaktion p-Wert									0,4641
Raucherstatus									
Ja	108	3 (2,8)	NE [NE; NE]	86	2 (2,3)	NE [NE; NE]	1,03	[0,17; 7,80]	0,9772
Nein	229	1 (0,4)	NE [NE; NE]	257	12 (4,7)	NE [NE; NE]	0,08	[0,00; 0,40]	0,0007*
Interaktion p-Wert									0,0420*
Region									
Asien	204	0	NE [NE; NE]	209	9 (4,3)	NE [NE; NE]	NC	[NC]	NC
Europa	61	2 (3,3)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	4 (7,4)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.20 ADAURA: Summary of subgroup analysis of time to first PT: Proteinurie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	8 (7,3)	NE [NE; NE]	95	3 (3,2)	NE [NE; NE]	2,11	[0,61; 9,64]	0,2483
Weiblich	228	6 (2,6)	NE [NE; NE]	248	1 (0,4)	NE [NE; NE]	5,91	[1,01;111,64]	0,0488*
Interaktion p-Wert									0,3973
Alter									
<65 Jahre	184	8 (4,3)	NE [NE; NE]	195	3 (1,5)	NE [NE; NE]	2,46	[0,71; 11,24]	0,1608
>=65 Jahre	153	6 (3,9)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	5,60	[0,96;105,79]	0,0569
Interaktion p-Wert									0,5022
Abstammung									
Asiatisch	215	11 (5,1)	NE [NE; NE]	218	4 (1,8)	NE [NE; NE]	2,50	[0,85; 9,04]	0,0968
Nicht-asiatisch	122	3 (2,5)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	8 (4,3)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	6 (4,0)	NE [NE; NE]	152	4 (2,6)	NE [NE; NE]	1,53	[0,44; 5,97]	0,5077
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	7 (6,7)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	3 (2,5)	NE [NE; NE]	118	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	4 (3,5)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	5 (5,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	3 (2,7)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.20 ADAURA: Summary of subgroup analysis of time to first PT: Proteinurie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	6 (5,5)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	7 (3,4)	NE [NE; NE]	207	3 (1,4)	NE [NE; NE]	2,08	[0,58; 9,66]	0,2705
Nein	134	7 (5,2)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	6,88	[1,22;128,60]	0,0260*
Interaktion p-Wert									0,3214
Raucherstatus									
Ja	108	6 (5,6)	NE [NE; NE]	86	3 (3,5)	NE [NE; NE]	NC	[NC]	NC
Nein	229	8 (3,5)	NE [NE; NE]	257	1 (0,4)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	11 (5,4)	NE [NE; NE]	209	4 (1,9)	NE [NE; NE]	2,53	[0,86; 9,15]	0,0923
Europa	61	1 (1,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.21 ADAURA: Summary of subgroup analysis of time to first SOC: Erkrankungen des Blutes und des Lymphsystems
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	22 (20,2)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	19,54	[4,11;349,80]	<0,0001*
Weiblich	228	55 (24,1)	NE [NE; NE]	248	11 (4,4)	NE [NE; NE]	5,63	[3,07; 11,34]	<0,0001*
Interaktion p-Wert									0,1789
Alter									
<65 Jahre	184	45 (24,5)	NE [NE; NE]	195	10 (5,1)	NE [NE; NE]	4,79	[2,52; 10,07]	<0,0001*
>=65 Jahre	153	32 (20,9)	NE [NE; NE]	148	2 (1,4)	NE [NE; NE]	16,49	[5,00;101,75]	<0,0001*
Interaktion p-Wert									0,0907
Abstammung									
Asiatisch	215	47 (21,9)	NE [NE; NE]	218	9 (4,1)	NE [NE; NE]	5,37	[2,76; 11,72]	<0,0001*
Nicht-asiatisch	122	30 (24,6)	NE [NE; NE]	125	3 (2,4)	NE [NE; NE]	10,88	[3,88; 45,37]	<0,0001*
Interaktion p-Wert									0,2981
EGFR-Mutation									
Exon 19 Deletion	187	39 (20,9)	NE [NE; NE]	191	5 (2,6)	NE [NE; NE]	7,77	[3,36; 22,54]	<0,0001*
L858R	150	38 (25,3)	NE [NE; NE]	152	7 (4,6)	NE [NE; NE]	6,08	[2,89; 14,88]	<0,0001*
Interaktion p-Wert									0,6966
Krankheitsstadium Version 7									
Stadium IB	105	28 (26,7)	NE [NE; NE]	106	4 (3,8)	NE [NE; NE]	8,68	[3,41; 29,33]	<0,0001*
Stadium II	118	25 (21,2)	NE [NE; NE]	118	7 (5,9)	NE [NE; NE]	3,66	[1,67; 9,17]	0,0008*
Stadium IIIA	114	24 (21,1)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	22,05	[4,66;394,16]	<0,0001*
Interaktion p-Wert									0,1337
Krankheitsstadium Version 8									
Stadium IB	100	28 (28,0)	NE [NE; NE]	98	3 (3,1)	NE [NE; NE]	11,49	[4,07; 48,05]	<0,0001*
Stadium II	113	21 (18,6)	NE [NE; NE]	119	6 (5,0)	NE [NE; NE]	3,79	[1,62; 10,33]	0,0015*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.21 ADAURA: Summary of subgroup analysis of time to first SOC: Erkrankungen des Blutes und des Lymphsystems
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	25 (22,9)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	11,67	[3,47; 72,54]	<0,0001*
Interaktion p-Wert									0,2393
Adjuvante Chemotherapie									
Ja	203	39 (19,2)	NE [NE; NE]	207	7 (3,4)	NE [NE; NE]	5,55	[2,64; 13,56]	<0,0001*
Nein	134	38 (28,4)	NE [NE; NE]	136	5 (3,7)	NE [NE; NE]	8,64	[3,73; 25,09]	<0,0001*
Interaktion p-Wert									0,4776
Raucherstatus									
Ja	108	21 (19,4)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	17,21	[3,60;308,43]	<0,0001*
Nein	229	56 (24,5)	NE [NE; NE]	257	11 (4,3)	NE [NE; NE]	5,90	[3,22; 11,88]	<0,0001*
Interaktion p-Wert									0,2575
Region									
Asien	204	45 (22,1)	NE [NE; NE]	209	9 (4,3)	NE [NE; NE]	5,20	[2,67; 11,37]	<0,0001*
Europa	61	11 (18,0)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	12,57	[2,45;229,75]	0,0008*
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	20 (34,5)	NE [NE; NE]	54	2 (3,7)	NE [NE; NE]	10,77	[3,14; 67,42]	<0,0001*
Interaktion p-Wert									0,5080

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.22 ADAURA: Summary of subgroup analysis of time to first PT: Anaemie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	4 (3,7)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	3,03	[0,45; 59,31]	0,2750
Weiblich	228	24 (10,5)	NE [NE; NE]	248	6 (2,4)	NE [NE; NE]	4,02	[1,75; 10,86]	0,0006*
Interaktion p-Wert									0,8189
Alter									
<65 Jahre	184	10 (5,4)	NE [NE; NE]	195	6 (3,1)	NE [NE; NE]	1,48	[0,55; 4,37]	0,4396
>=65 Jahre	153	18 (11,8)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	17,49	[3,61;314,67]	<0,0001*
Interaktion p-Wert									0,0106*
Abstammung									
Asiatisch	215	16 (7,4)	NE [NE; NE]	218	5 (2,3)	NE [NE; NE]	2,91	[1,14; 8,91]	0,0245*
Nicht-asiatisch	122	12 (9,8)	NE [NE; NE]	125	2 (1,6)	NE [NE; NE]	5,72	[1,56; 36,76]	0,0064*
Interaktion p-Wert									0,4508
EGFR-Mutation									
Exon 19 Deletion	187	12 (6,4)	NE [NE; NE]	191	3 (1,6)	NE [NE; NE]	3,43	[1,09; 15,07]	0,0344*
L858R	150	16 (10,7)	NE [NE; NE]	152	4 (2,6)	NE [NE; NE]	4,07	[1,49; 14,21]	0,0049*
Interaktion p-Wert									0,8420
Krankheitsstadium Version 7									
Stadium IB	105	7 (6,7)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	7,83	[1,39;146,47]	0,0164*
Stadium II	118	11 (9,3)	NE [NE; NE]	118	5 (4,2)	NE [NE; NE]	2,00	[0,73; 6,34]	0,1848
Stadium IIIA	114	10 (8,8)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	7,80	[1,49;143,27]	0,0111*
Interaktion p-Wert									0,2998
Krankheitsstadium Version 8									
Stadium IB	100	7 (7,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	7,74	[1,38;144,79]	0,0171*
Stadium II	113	10 (8,8)	NE [NE; NE]	119	4 (3,4)	NE [NE; NE]	2,44	[0,81; 8,89]	0,1136

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.22 ADAURA: Summary of subgroup analysis of time to first PT: Anaemie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	10 (9,2)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	3,87	[1,02; 25,23]	0,0470*
Interaktion p-Wert									0,5952
Adjuvante Chemotherapie									
Ja	203	15 (7,4)	NE [NE; NE]	207	5 (2,4)	NE [NE; NE]	2,63	[1,02; 8,09]	0,0459*
Nein	134	13 (9,7)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	6,53	[1,80; 41,74]	0,0026*
Interaktion p-Wert									0,3050
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	3,60	[0,58; 68,97]	0,1850
Nein	229	23 (10,0)	NE [NE; NE]	257	6 (2,3)	NE [NE; NE]	3,92	[1,70; 10,62]	0,0009*
Interaktion p-Wert									0,9430
Region									
Asien	204	15 (7,4)	NE [NE; NE]	209	5 (2,4)	NE [NE; NE]	2,76	[1,07; 8,48]	0,0357*
Europa	61	6 (9,8)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	6,31	[1,08;119,21]	0,0400*
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	6 (10,3)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	5,24	[0,89; 98,96]	0,0687
Interaktion p-Wert									0,7066

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.23 ADAURA: Summary of subgroup analysis of time to first PT: Leukopenie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	5 (4,6)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	15 (6,6)	NE [NE; NE]	248	6 (2,4)	NE [NE; NE]	2,54	[1,03; 7,12]	0,0427*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	16 (8,7)	NE [NE; NE]	195	4 (2,1)	NE [NE; NE]	3,78	[1,38; 13,20]	0,0081*
>=65 Jahre	153	4 (2,6)	NE [NE; NE]	148	2 (1,4)	NE [NE; NE]	1,87	[0,36; 13,49]	0,4577
Interaktion p-Wert									0,5031
Abstammung									
Asiatisch	215	13 (6,0)	NE [NE; NE]	218	5 (2,3)	NE [NE; NE]	2,41	[0,91; 7,53]	0,0784
Nicht-asiatisch	122	7 (5,7)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	6,72	[1,20;125,66]	0,0282*
Interaktion p-Wert									0,3562
EGFR-Mutation									
Exon 19 Deletion	187	12 (6,4)	NE [NE; NE]	191	2 (1,0)	NE [NE; NE]	5,35	[1,46; 34,39]	0,0092*
L858R	150	8 (5,3)	NE [NE; NE]	152	4 (2,6)	NE [NE; NE]	2,01	[0,63; 7,52]	0,2411
Interaktion p-Wert									0,3047
Krankheitsstadium Version 7									
Stadium IB	105	8 (7,6)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	4,47	[1,12; 29,60]	0,0330*
Stadium II	118	6 (5,1)	NE [NE; NE]	118	3 (2,5)	NE [NE; NE]	1,83	[0,48; 8,66]	0,3820
Stadium IIIA	114	6 (5,3)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	4,90	[0,83; 92,73]	0,0828
Interaktion p-Wert									0,6224
Krankheitsstadium Version 8									
Stadium IB	100	8 (8,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	4,37	[1,10; 28,97]	0,0358*
Stadium II	113	3 (2,7)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	0,97	[0,18; 5,23]	0,9684

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.23 ADAURA: Summary of subgroup analysis of time to first PT: Leukopenie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	8 (7,3)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	6,73	[1,23;125,08]	0,0250*
Interaktion p-Wert									0,2491
Adjuvante Chemotherapie									
Ja	203	12 (5,9)	NE [NE; NE]	207	4 (1,9)	NE [NE; NE]	2,70	[0,94; 9,68]	0,0662
Nein	134	8 (6,0)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	4,00	[1,002; 26,50]	0,0497*
Interaktion p-Wert									0,6852
Raucherstatus									
Ja	108	6 (5,6)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	14 (6,1)	NE [NE; NE]	257	6 (2,3)	NE [NE; NE]	2,44	[0,98; 6,90]	0,0559
Interaktion p-Wert									NC
Region									
Asien	204	13 (6,4)	NE [NE; NE]	209	5 (2,4)	NE [NE; NE]	2,43	[0,92; 7,60]	0,0753
Europa	61	4 (6,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	3 (5,2)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	2,59	[0,33; 52,26]	0,3800
Interaktion p-Wert									0,9621

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.24 ADAURA: Summary of subgroup analysis of time to first PT: Neutropenie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	1 (0,9)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	20 (8,8)	NE [NE; NE]	248	1 (0,4)	NE [NE; NE]	20,92	[4,36;375,29]	<0,0001*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	16 (8,7)	NE [NE; NE]	195	1 (0,5)	NE [NE; NE]	15,98	[3,26;288,70]	<0,0001*
>=65 Jahre	153	5 (3,3)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	10 (4,7)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	11 (9,0)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	10,94	[2,12;199,94]	0,0019*
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	14 (7,5)	NE [NE; NE]	191	1 (0,5)	NE [NE; NE]	13,82	[2,78;250,54]	0,0003*
L858R	150	7 (4,7)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	7 (6,7)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	10 (8,5)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	4 (3,5)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	7 (7,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	9 (8,0)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.24 ADAURA: Summary of subgroup analysis of time to first PT: Neutropenie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	4 (3,7)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	10 (4,9)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	11 (8,2)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	11,21	[2,18;204,89]	0,0016*
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	16 (7,0)	NE [NE; NE]	257	1 (0,4)	NE [NE; NE]	17,10	[3,49;308,77]	<0,0001*
Interaktion p-Wert									NC
Region									
Asien	204	9 (4,4)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	4 (6,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	8 (13,8)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.25 ADAURA: Summary of subgroup analysis of time to first PT: Thrombozytopenie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	10 (9,2)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	17 (7,5)	NE [NE; NE]	248	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	17 (9,2)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	10 (6,5)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	15 (7,0)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	12 (9,8)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	14 (7,5)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	13 (8,7)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	12 (11,4)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	6 (5,1)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	9 (7,9)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	12 (12,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	5 (4,4)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.25 ADAURA: Summary of subgroup analysis of time to first PT: Thrombozytopenie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	9 (8,3)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	13 (6,4)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	14 (10,4)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	6 (5,6)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	21 (9,2)	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	15 (7,4)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	0	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	12 (20,7)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.26 ADAURA: Summary of subgroup analysis of time to first SOC: Erkrankungen des Gastrointestinaltrakts
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	75 (68,8)	2,8 [1,1; 4,8]	95	42 (44,2)	26,9 [11,2; NE]	2,00	[1,37; 2,94]	0,0002*
Weiblich	228	168 (73,7)	1,4 [0,9; 2,2]	248	115 (46,4)	25,0 [19,2; NE]	2,32	[1,83; 2,95]	<0,0001*
Interaktion p-Wert									0,5060
Alter									
<65 Jahre	184	143 (77,7)	1,5 [1,0; 2,2]	195	95 (48,7)	20,7 [11,0; NE]	2,27	[1,75; 2,95]	<0,0001*
>=65 Jahre	153	100 (65,4)	2,5 [1,0; 6,7]	148	62 (41,9)	35,4 [21,0; NE]	2,17	[1,58; 2,99]	<0,0001*
Interaktion p-Wert									0,8237
Abstammung									
Asiatisch	215	171 (79,5)	1,1 [0,8; 2,0]	218	115 (52,8)	19,2 [11,6;24,0]	2,30	[1,82; 2,93]	<0,0001*
Nicht-asiatisch	122	72 (59,0)	5,3 [1,8;34,0]	125	42 (33,6)	NE [NE; NE]	2,18	[1,50; 3,21]	<0,0001*
Interaktion p-Wert									0,8103
EGFR-Mutation									
Exon 19 Deletion	187	138 (73,8)	1,7 [0,9; 2,6]	191	86 (45,0)	24,0 [18,1; NE]	2,27	[1,74; 2,98]	<0,0001*
L858R	150	105 (70,0)	1,9 [1,0; 4,3]	152	71 (46,7)	26,9 [13,2; NE]	2,13	[1,58; 2,89]	<0,0001*
Interaktion p-Wert									0,7625
Krankheitsstadium Version 7									
Stadium IB	105	77 (73,3)	1,9 [1,0; 2,6]	106	53 (50,0)	25,0 [12,4; NE]	2,13	[1,51; 3,05]	<0,0001*
Stadium II	118	84 (71,2)	1,5 [0,7; 2,6]	118	56 (47,5)	22,3 [13,9; NE]	2,13	[1,52; 3,00]	<0,0001*
Stadium IIIA	114	82 (71,9)	2,3 [0,9; 5,5]	119	48 (40,3)	26,9 [12,4; NE]	2,38	[1,67; 3,42]	<0,0001*
Interaktion p-Wert									0,8848
Krankheitsstadium Version 8									
Stadium IB	100	73 (73,0)	1,9 [1,0; 2,8]	98	51 (52,0)	24,0 [11,0; NE]	2,01	[1,41; 2,89]	0,0001*
Stadium II	113	80 (70,8)	1,5 [0,9; 2,3]	119	53 (44,5)	35,4 [19,2; NE]	2,31	[1,64; 3,29]	<0,0001*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.26 ADAURA: Summary of subgroup analysis of time to first SOC: Erkrankungen des Gastrointestinaltrakts
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	80 (73,4)	2,8 [0,8; 4,2]	115	47 (40,9)	26,9 [12,4; NE]	2,43	[1,70; 3,51]	<0,0001*
Interaktion p-Wert									0,7425
Adjuvante Chemotherapie									
Ja	203	153 (75,4)	1,5 [0,9; 2,4]	207	94 (45,4)	23,3 [13,2; NE]	2,37	[1,84; 3,08]	<0,0001*
Nein	134	90 (67,2)	1,9 [1,1; 3,1]	136	63 (46,3)	25,0 [16,1; NE]	1,98	[1,44; 2,74]	<0,0001*
Interaktion p-Wert									0,3922
Raucherstatus									
Ja	108	79 (73,1)	2,0 [1,1; 3,0]	86	38 (44,2)	26,9 [11,2; NE]	2,29	[1,56; 3,40]	<0,0001*
Nein	229	164 (71,6)	1,8 [0,9; 2,4]	257	119 (46,3)	24,7 [18,1; NE]	2,18	[1,73; 2,77]	<0,0001*
Interaktion p-Wert									0,8413
Region									
Asien	204	162 (79,4)	1,2 [0,9; 2,1]	209	108 (51,7)	19,6 [12,3;24,7]	2,36	[1,85; 3,02]	<0,0001*
Europa	61	44 (72,1)	1,6 [0,8; 2,8]	69	29 (42,0)	NE [NE; NE]	2,39	[1,51; 3,87]	0,0002*
Nordamerika	14	12 (85,7)	0,5 [0,1; 1,9]	11	8 (72,7)	5,6 [0,2;30,9]	2,08	[0,86; 5,31]	0,1045
Rest der Welt	58	25 (43,1)	NE [NE; NE]	54	12 (22,2)	NE [NE; NE]	2,11	[1,08; 4,35]	0,0279*
Interaktion p-Wert									0,9832

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.27 ADAURA: Summary of subgroup analysis of time to first PT: Abdominalschmerz
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	4 (3,7)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	3,31	[0,49; 64,72]	0,2364
Weiblich	228	16 (7,0)	NE [NE; NE]	248	4 (1,6)	NE [NE; NE]	4,13	[1,51; 14,44]	0,0045*
Interaktion p-Wert									0,8605
Alter									
<65 Jahre	184	11 (6,0)	NE [NE; NE]	195	4 (2,1)	NE [NE; NE]	2,67	[0,91; 9,65]	0,0744
>=65 Jahre	153	9 (5,9)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	8,67	[1,63;159,80]	0,0079*
Interaktion p-Wert									0,2935
Abstammung									
Asiatisch	215	9 (4,2)	NE [NE; NE]	218	4 (1,8)	NE [NE; NE]	2,15	[0,70; 7,95]	0,1852
Nicht-asiatisch	122	11 (9,0)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	10,84	[2,11;198,21]	0,0019*
Interaktion p-Wert									0,1405
EGFR-Mutation									
Exon 19 Deletion	187	15 (8,0)	NE [NE; NE]	191	1 (0,5)	NE [NE; NE]	13,99	[2,83;253,12]	0,0002*
L858R	150	5 (3,3)	NE [NE; NE]	152	4 (2,6)	NE [NE; NE]	1,27	[0,34; 5,13]	0,7204
Interaktion p-Wert									0,0284*
Krankheitsstadium Version 7									
Stadium IB	105	10 (9,5)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	7 (5,9)	NE [NE; NE]	118	4 (3,4)	NE [NE; NE]	1,60	[0,48; 6,11]	0,4477
Stadium IIIA	114	3 (2,6)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	2,39	[0,30; 48,50]	0,4240
Interaktion p-Wert									0,7552
Krankheitsstadium Version 8									
Stadium IB	100	11 (11,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	5 (4,4)	NE [NE; NE]	119	4 (3,4)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.27 ADAURA: Summary of subgroup analysis of time to first PT: Abdominalschmerz
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	4 (3,7)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	11 (5,4)	NE [NE; NE]	207	3 (1,4)	NE [NE; NE]	3,44	[1,07; 15,22]	0,0372*
Nein	134	9 (6,7)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	4,57	[1,18; 29,98]	0,0265*
Interaktion p-Wert									0,7786
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	3,79	[0,61; 72,72]	0,1659
Nein	229	15 (6,6)	NE [NE; NE]	257	4 (1,6)	NE [NE; NE]	4,00	[1,45; 14,03]	0,0062*
Interaktion p-Wert									0,9669
Region									
Asien	204	8 (3,9)	NE [NE; NE]	209	4 (1,9)	NE [NE; NE]	1,92	[0,60; 7,20]	0,2744
Europa	61	9 (14,8)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	9,96	[1,87;183,68]	0,0042*
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,1391

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.28 ADAURA: Summary of subgroup analysis of time to first PT: Aphthoeses Ulkus
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	3 (2,8)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	9 (3,9)	NE [NE; NE]	248	1 (0,4)	NE [NE; NE]	9,14	[1,71;168,58]	0,0063*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	11 (6,0)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	1 (0,7)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	11 (5,1)	NE [NE; NE]	218	1 (0,5)	NE [NE; NE]	10,39	[2,02;190,03]	0,0025*
Nicht-asiatisch	122	1 (0,8)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	9 (4,8)	NE [NE; NE]	191	1 (0,5)	NE [NE; NE]	8,02	[1,50;148,01]	0,0112*
L858R	150	3 (2,0)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	2 (1,9)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	1 (0,8)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	9 (7,9)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	1 (1,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	2 (1,8)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.28 ADAURA: Summary of subgroup analysis of time to first PT: Aphthoeses Ulkus
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	9 (8,3)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	10 (4,9)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	2 (1,5)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	3 (2,8)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	9 (3,9)	NE [NE; NE]	257	1 (0,4)	NE [NE; NE]	9,43	[1,77;173,99]	0,0055*
Interaktion p-Wert									NC
Region									
Asien	204	10 (4,9)	NE [NE; NE]	209	1 (0,5)	NE [NE; NE]	9,69	[1,85;177,89]	0,0041*
Europa	61	1 (1,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	0	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.29 ADAURA: Summary of subgroup analysis of time to first PT: Diarrhoe
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	41 (37,6)	NE [NE; NE]	95	15 (15,8)	NE [NE; NE]	2,58	[1,46; 4,81]	0,0009*
Weiblich	228	118 (51,8)	20,7 [2,8; NE]	248	55 (22,2)	NE [NE; NE]	2,91	[2,13; 4,04]	<0,0001*
Interaktion p-Wert									0,7209
Alter									
<65 Jahre	184	95 (51,6)	18,0 [7,4; NE]	195	46 (23,6)	NE [NE; NE]	2,55	[1,80; 3,65]	<0,0001*
>=65 Jahre	153	64 (41,8)	NE [NE; NE]	148	24 (16,2)	NE [NE; NE]	3,14	[1,99; 5,12]	<0,0001*
Interaktion p-Wert									0,4803
Abstammung									
Asiatisch	215	106 (49,3)	24,6 [5,6; NE]	218	51 (23,4)	NE [NE; NE]	2,54	[1,83; 3,57]	<0,0001*
Nicht-asiatisch	122	53 (43,4)	NE [NE; NE]	125	19 (15,2)	NE [NE; NE]	3,32	[2,00; 5,75]	<0,0001*
Interaktion p-Wert									0,3913
EGFR-Mutation									
Exon 19 Deletion	187	89 (47,6)	NE [NE; NE]	191	41 (21,5)	NE [NE; NE]	2,53	[1,76; 3,69]	<0,0001*
L858R	150	70 (46,7)	NE [NE; NE]	152	29 (19,1)	NE [NE; NE]	3,06	[2,01; 4,79]	<0,0001*
Interaktion p-Wert									0,5103
Krankheitsstadium Version 7									
Stadium IB	105	54 (51,4)	16,6 [2,8; NE]	106	20 (18,9)	NE [NE; NE]	3,52	[2,14; 6,01]	<0,0001*
Stadium II	118	53 (44,9)	NE [NE; NE]	118	25 (21,2)	NE [NE; NE]	2,53	[1,59; 4,14]	<0,0001*
Stadium IIIA	114	52 (45,6)	NE [NE; NE]	119	25 (21,0)	NE [NE; NE]	2,38	[1,49; 3,90]	0,0002*
Interaktion p-Wert									0,5048
Krankheitsstadium Version 8									
Stadium IB	100	52 (52,0)	16,6 [2,6; NE]	98	20 (20,4)	NE [NE; NE]	3,26	[1,98; 5,60]	<0,0001*
Stadium II	113	50 (44,2)	NE [NE; NE]	119	23 (19,3)	NE [NE; NE]	2,81	[1,74; 4,69]	<0,0001*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.29 ADAURA: Summary of subgroup analysis of time to first PT: Diarrhoe
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	51 (46,8)	NE [NE; NE]	115	24 (20,9)	NE [NE; NE]	2,46	[1,53; 4,06]	0,0002*
Interaktion p-Wert									0,7345
Adjuvante Chemotherapie									
Ja	203	94 (46,3)	NE [NE; NE]	207	46 (22,2)	NE [NE; NE]	2,43	[1,72; 3,49]	<0,0001*
Nein	134	65 (48,5)	33,5 [4,3; NE]	136	24 (17,6)	NE [NE; NE]	3,35	[2,13; 5,46]	<0,0001*
Interaktion p-Wert									0,2796
Raucherstatus									
Ja	108	48 (44,4)	NE [NE; NE]	86	15 (17,4)	NE [NE; NE]	2,95	[1,69; 5,44]	<0,0001*
Nein	229	111 (48,5)	36,1 [7,4; NE]	257	55 (21,4)	NE [NE; NE]	2,73	[1,99; 3,80]	<0,0001*
Interaktion p-Wert									0,8258
Region									
Asien	204	100 (49,0)	24,6 [7,5; NE]	209	48 (23,0)	NE [NE; NE]	2,57	[1,83; 3,65]	<0,0001*
Europa	61	34 (55,7)	16,6 [1,9; NE]	69	10 (14,5)	NE [NE; NE]	4,88	[2,51; 10,43]	<0,0001*
Nordamerika	14	10 (71,4)	0,8 [0,1; NE]	11	4 (36,4)	NE [NE; NE]	3,47	[1,16; 12,65]	0,0255*
Rest der Welt	58	15 (25,9)	NE [NE; NE]	54	8 (14,8)	NE [NE; NE]	1,72	[0,75; 4,28]	0,2034
Interaktion p-Wert									0,2450

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.30 ADAURA: Summary of subgroup analysis of time to first PT: Dyspepsie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	2 (1,8)	NE [NE; NE]	95	3 (3,2)	NE [NE; NE]	0,49	[0,06; 2,99]	0,4344
Weiblich	228	13 (5,7)	NE [NE; NE]	248	2 (0,8)	NE [NE; NE]	6,19	[1,71; 39,67]	0,0036*
Interaktion p-Wert									0,0267*
Alter									
<65 Jahre	184	9 (4,9)	NE [NE; NE]	195	3 (1,5)	NE [NE; NE]	2,61	[0,77; 11,77]	0,1261
>=65 Jahre	153	6 (3,9)	NE [NE; NE]	148	2 (1,4)	NE [NE; NE]	2,74	[0,63; 18,69]	0,1867
Interaktion p-Wert									0,9624
Abstammung									
Asiatisch	215	11 (5,1)	NE [NE; NE]	218	3 (1,4)	NE [NE; NE]	3,21	[1,0004; 14,22]	0,0499*
Nicht-asiatisch	122	4 (3,3)	NE [NE; NE]	125	2 (1,6)	NE [NE; NE]	1,82	[0,35; 13,13]	0,4783
Interaktion p-Wert									0,6032
EGFR-Mutation									
Exon 19 Deletion	187	11 (5,9)	NE [NE; NE]	191	2 (1,0)	NE [NE; NE]	4,56	[1,22; 29,52]	0,0220*
L858R	150	4 (2,7)	NE [NE; NE]	152	3 (2,0)	NE [NE; NE]	1,29	[0,28; 6,55]	0,7370
Interaktion p-Wert									0,2365
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	3 (2,8)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	6 (5,1)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	4 (3,5)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	4 (4,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.30 ADAURA: Summary of subgroup analysis of time to first PT: Dyspepsie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium II	113	7 (6,2)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	109	4 (3,7)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	10 (4,9)	NE [NE; NE]	207	2 (1,0)	NE [NE; NE]	4,22	[1,11; 27,52]	0,0333*
Nein	134	5 (3,7)	NE [NE; NE]	136	3 (2,2)	NE [NE; NE]	1,60	[0,39; 7,78]	0,5163
Interaktion p-Wert									0,3543
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	3,44	[0,55; 65,95]	0,2031
Nein	229	10 (4,4)	NE [NE; NE]	257	4 (1,6)	NE [NE; NE]	2,45	[0,82; 8,93]	0,1125
Interaktion p-Wert									0,7799
Region									
Asien	204	11 (5,4)	NE [NE; NE]	209	3 (1,4)	NE [NE; NE]	3,26	[1,01; 14,41]	0,0471*
Europa	61	3 (4,9)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	3,10	[0,40; 62,77]	0,2909
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	1 (1,7)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	0,80	[0,03; 20,29]	0,8764
Interaktion p-Wert									0,6719

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.31 ADAURA: Summary of subgroup analysis of time to first PT: Mundtrockenheit
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	3 (2,8)	NE [NE; NE]	95	2 (2,1)	NE [NE; NE]	1,23	[0,20; 9,36]	0,8180
Weiblich	228	13 (5,7)	NE [NE; NE]	248	3 (1,2)	NE [NE; NE]	4,58	[1,47; 20,00]	0,0069*
Interaktion p-Wert									0,2485
Alter									
<65 Jahre	184	10 (5,4)	NE [NE; NE]	195	3 (1,5)	NE [NE; NE]	3,34	[1,02; 14,92]	0,0462*
>=65 Jahre	153	6 (3,9)	NE [NE; NE]	148	2 (1,4)	NE [NE; NE]	2,87	[0,66; 19,57]	0,1664
Interaktion p-Wert									0,8846
Abstammung									
Asiatisch	215	8 (3,7)	NE [NE; NE]	218	3 (1,4)	NE [NE; NE]	2,58	[0,74; 11,77]	0,1396
Nicht-asiatisch	122	8 (6,6)	NE [NE; NE]	125	2 (1,6)	NE [NE; NE]	4,02	[1,01; 26,66]	0,0487*
Interaktion p-Wert									0,6664
EGFR-Mutation									
Exon 19 Deletion	187	11 (5,9)	NE [NE; NE]	191	3 (1,6)	NE [NE; NE]	3,50	[1,09; 15,50]	0,0344*
L858R	150	5 (3,3)	NE [NE; NE]	152	2 (1,3)	NE [NE; NE]	2,54	[0,55; 17,73]	0,2409
Interaktion p-Wert									0,7633
Krankheitsstadium Version 7									
Stadium IB	105	3 (2,9)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	5 (4,2)	NE [NE; NE]	118	3 (2,5)	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	8 (7,0)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	1 (1,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	6 (5,3)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.31 ADAURA: Summary of subgroup analysis of time to first PT: Mundtrockenheit
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	7 (6,4)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	12 (5,9)	NE [NE; NE]	207	4 (1,9)	NE [NE; NE]	2,91	[1,01; 10,41]	0,0479*
Nein	134	4 (3,0)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	4,00	[0,59; 78,22]	0,1650
Interaktion p-Wert									0,7959
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	3,86	[0,62; 73,95]	0,1602
Nein	229	11 (4,8)	NE [NE; NE]	257	4 (1,6)	NE [NE; NE]	2,97	[1,01; 10,71]	0,0472*
Interaktion p-Wert									0,8295
Region									
Asien	204	7 (3,4)	NE [NE; NE]	209	2 (1,0)	NE [NE; NE]	NC	[NC]	NC
Europa	61	1 (1,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	3 (21,4)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	5 (8,6)	NE [NE; NE]	54	2 (3,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.32 ADAURA: Summary of subgroup analysis of time to first PT: Mundulzeration
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	18 (16,5)	NE [NE; NE]	95	3 (3,2)	NE [NE; NE]	5,45	[1,84; 23,27]	0,0012*
Weiblich	228	21 (9,2)	NE [NE; NE]	248	7 (2,8)	NE [NE; NE]	3,23	[1,44; 8,21]	0,0037*
Interaktion p-Wert									0,4838
Alter									
<65 Jahre	184	31 (16,8)	NE [NE; NE]	195	9 (4,6)	NE [NE; NE]	3,68	[1,82; 8,21]	0,0002*
>=65 Jahre	153	8 (5,2)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	7,83	[1,44;145,24]	0,0139*
Interaktion p-Wert									0,4703
Abstammung									
Asiatisch	215	38 (17,7)	NE [NE; NE]	218	9 (4,1)	NE [NE; NE]	4,45	[2,25; 9,81]	<0,0001*
Nicht-asiatisch	122	1 (0,8)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	0,98	[0,04; 24,81]	0,9897
Interaktion p-Wert									0,3188
EGFR-Mutation									
Exon 19 Deletion	187	23 (12,3)	NE [NE; NE]	191	6 (3,1)	NE [NE; NE]	3,82	[1,66; 10,35]	0,0012*
L858R	150	16 (10,7)	NE [NE; NE]	152	4 (2,6)	NE [NE; NE]	4,26	[1,56; 14,86]	0,0036*
Interaktion p-Wert									0,8809
Krankheitsstadium Version 7									
Stadium IB	105	16 (15,2)	NE [NE; NE]	106	3 (2,8)	NE [NE; NE]	6,19	[2,06; 26,62]	0,0006*
Stadium II	118	12 (10,2)	NE [NE; NE]	118	5 (4,2)	NE [NE; NE]	2,40	[0,89; 7,56]	0,0841
Stadium IIIA	114	11 (9,6)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	5,15	[1,38; 33,36]	0,0122*
Interaktion p-Wert									0,4744
Krankheitsstadium Version 8									
Stadium IB	100	15 (15,0)	NE [NE; NE]	98	3 (3,1)	NE [NE; NE]	5,67	[1,87; 24,49]	0,0013*
Stadium II	113	11 (9,7)	NE [NE; NE]	119	5 (4,2)	NE [NE; NE]	2,36	[0,86; 7,50]	0,0971

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.32 ADAURA: Summary of subgroup analysis of time to first PT: Mundulzeration
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	10 (9,2)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	4,67	[1,23; 30,39]	0,0216*
Interaktion p-Wert									0,5385
Adjuvante Chemotherapie									
Ja	203	21 (10,3)	NE [NE; NE]	207	8 (3,9)	NE [NE; NE]	2,61	[1,20; 6,28]	0,0146*
Nein	134	18 (13,4)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	9,67	[2,79; 60,85]	<0,0001*
Interaktion p-Wert									0,0969
Raucherstatus									
Ja	108	13 (12,0)	NE [NE; NE]	86	3 (3,5)	NE [NE; NE]	3,57	[1,15; 15,55]	0,0263*
Nein	229	26 (11,4)	NE [NE; NE]	257	7 (2,7)	NE [NE; NE]	4,16	[1,91; 10,40]	0,0002*
Interaktion p-Wert									0,8418
Region									
Asien	204	38 (18,6)	NE [NE; NE]	209	9 (4,3)	NE [NE; NE]	4,53	[2,29; 9,99]	<0,0001*
Europa	61	0	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	1 (1,7)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.33 ADAURA: Summary of subgroup analysis of time to first PT: Stomatitis
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	19 (17,4)	NE [NE; NE]	95	2 (2,1)	NE [NE; NE]	9,00	[2,61; 56,48]	0,0001*
Weiblich	228	40 (17,5)	NE [NE; NE]	248	13 (5,2)	NE [NE; NE]	3,51	[1,93; 6,83]	<0,0001*
Interaktion p-Wert									0,2072
Alter									
<65 Jahre	184	31 (16,8)	NE [NE; NE]	195	8 (4,1)	NE [NE; NE]	4,29	[2,07; 10,03]	<0,0001*
>=65 Jahre	153	28 (18,3)	NE [NE; NE]	148	7 (4,7)	NE [NE; NE]	4,19	[1,93; 10,41]	0,0001*
Interaktion p-Wert									0,9653
Abstammung									
Asiatisch	215	45 (20,9)	NE [NE; NE]	218	13 (6,0)	NE [NE; NE]	3,82	[2,12; 7,38]	<0,0001*
Nicht-asiatisch	122	14 (11,5)	NE [NE; NE]	125	2 (1,6)	NE [NE; NE]	7,29	[2,04; 46,42]	0,0011*
Interaktion p-Wert									0,4057
EGFR-Mutation									
Exon 19 Deletion	187	40 (21,4)	NE [NE; NE]	191	8 (4,2)	NE [NE; NE]	5,43	[2,68; 12,52]	<0,0001*
L858R	150	19 (12,7)	NE [NE; NE]	152	7 (4,6)	NE [NE; NE]	2,92	[1,28; 7,46]	0,0100*
Interaktion p-Wert									0,2925
Krankheitsstadium Version 7									
Stadium IB	105	14 (13,3)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	7,93	[2,21; 50,48]	0,0006*
Stadium II	118	22 (18,6)	NE [NE; NE]	118	6 (5,1)	NE [NE; NE]	3,94	[1,70; 10,70]	0,0010*
Stadium IIIA	114	23 (20,2)	NE [NE; NE]	119	7 (5,9)	NE [NE; NE]	3,41	[1,54; 8,61]	0,0020*
Interaktion p-Wert									0,5866
Krankheitsstadium Version 8									
Stadium IB	100	14 (14,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	15,57	[3,13;282,09]	0,0001*
Stadium II	113	21 (18,6)	NE [NE; NE]	119	6 (5,0)	NE [NE; NE]	3,99	[1,71; 10,86]	0,0010*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.33 ADAURA: Summary of subgroup analysis of time to first PT: Stomatitis
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	22 (20,2)	NE [NE; NE]	115	6 (5,2)	NE [NE; NE]	3,82	[1,65; 10,39]	0,0013*
Interaktion p-Wert									0,3301
Adjuvante Chemotherapie									
Ja	203	41 (20,2)	NE [NE; NE]	207	11 (5,3)	NE [NE; NE]	4,00	[2,13; 8,18]	<0,0001*
Nein	134	18 (13,4)	NE [NE; NE]	136	4 (2,9)	NE [NE; NE]	4,92	[1,84; 17,03]	0,0009*
Interaktion p-Wert									0,7466
Raucherstatus									
Ja	108	19 (17,6)	NE [NE; NE]	86	4 (4,7)	NE [NE; NE]	3,98	[1,49; 13,72]	0,0043*
Nein	229	40 (17,5)	NE [NE; NE]	257	11 (4,3)	NE [NE; NE]	4,35	[2,31; 8,90]	<0,0001*
Interaktion p-Wert									0,8914
Region									
Asien	204	41 (20,1)	NE [NE; NE]	209	13 (6,2)	NE [NE; NE]	3,49	[1,92; 6,77]	<0,0001*
Europa	61	7 (11,5)	NE [NE; NE]	69	2 (2,9)	NE [NE; NE]	3,98	[0,96; 26,68]	0,0573
Nordamerika	14	5 (35,7)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	6 (10,3)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,8785

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.34 ADAURA: Summary of subgroup analysis of time to first PT: Zahnschmerzen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	4 (3,7)	NE [NE; NE]	95	9 (9,5)	NE [NE; NE]	0,33	[0,09; 1,02]	0,0540
Weiblich	228	4 (1,8)	NE [NE; NE]	248	9 (3,6)	NE [NE; NE]	0,42	[0,11; 1,29]	0,1317
Interaktion p-Wert									0,7814
Alter									
<65 Jahre	184	6 (3,3)	NE [NE; NE]	195	12 (6,2)	NE [NE; NE]	0,44	[0,15; 1,13]	0,0875
>=65 Jahre	153	2 (1,3)	NE [NE; NE]	148	6 (4,1)	NE [NE; NE]	0,30	[0,04; 1,30]	0,1115
Interaktion p-Wert									0,6921
Abstammung									
Asiatisch	215	7 (3,3)	NE [NE; NE]	218	16 (7,3)	NE [NE; NE]	0,38	[0,15; 0,89]	0,0260*
Nicht-asiatisch	122	1 (0,8)	NE [NE; NE]	125	2 (1,6)	NE [NE; NE]	0,46	[0,02; 4,77]	0,5085
Interaktion p-Wert									0,8900
EGFR-Mutation									
Exon 19 Deletion	187	6 (3,2)	NE [NE; NE]	191	9 (4,7)	NE [NE; NE]	0,56	[0,19; 1,56]	0,2665
L858R	150	2 (1,3)	NE [NE; NE]	152	9 (5,9)	NE [NE; NE]	0,21	[0,03; 0,82]	0,0224*
Interaktion p-Wert									0,2806
Krankheitsstadium Version 7									
Stadium IB	105	4 (3,8)	NE [NE; NE]	106	11 (10,4)	NE [NE; NE]	0,38	[0,10; 1,10]	0,0749
Stadium II	118	1 (0,8)	NE [NE; NE]	118	4 (3,4)	NE [NE; NE]	0,22	[0,01; 1,49]	0,1270
Stadium IIIA	114	3 (2,6)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	0,78	[0,14; 4,21]	0,7567
Interaktion p-Wert									0,6166
Krankheitsstadium Version 8									
Stadium IB	100	4 (4,0)	NE [NE; NE]	98	11 (11,2)	NE [NE; NE]	0,37	[0,10; 1,07]	0,0680
Stadium II	113	2 (1,8)	NE [NE; NE]	119	4 (3,4)	NE [NE; NE]	0,48	[0,07; 2,45]	0,3790

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.34 ADAURA: Summary of subgroup analysis of time to first PT: Zahnschmerzen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	2 (1,8)	NE [NE; NE]	115	3 (2,6)	NE [NE; NE]	0,52	[0,07; 3,14]	0,4663
Interaktion p-Wert									0,9383
Adjuvante Chemotherapie									
Ja	203	5 (2,5)	NE [NE; NE]	207	10 (4,8)	NE [NE; NE]	0,43	[0,13; 1,20]	0,1087
Nein	134	3 (2,2)	NE [NE; NE]	136	8 (5,9)	NE [NE; NE]	0,35	[0,08; 1,21]	0,1000
Interaktion p-Wert									0,8214
Raucherstatus									
Ja	108	4 (3,7)	NE [NE; NE]	86	5 (5,8)	NE [NE; NE]	0,56	[0,14; 2,13]	0,3918
Nein	229	4 (1,7)	NE [NE; NE]	257	13 (5,1)	NE [NE; NE]	0,30	[0,08; 0,84]	0,0211*
Interaktion p-Wert									0,4654
Region									
Asien	204	7 (3,4)	NE [NE; NE]	209	16 (7,7)	NE [NE; NE]	0,38	[0,15; 0,90]	0,0279*
Europa	61	1 (1,6)	NE [NE; NE]	69	2 (2,9)	NE [NE; NE]	0,51	[0,02; 5,27]	0,5656
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	0	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,8372

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.35 ADAURA: Summary of subgroup analysis of time to first PT: Dysgeusie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	2 (1,8)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	9 (3,9)	NE [NE; NE]	248	1 (0,4)	NE [NE; NE]	9,95	[1,87;183,49]	0,0042*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	1 (0,5)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	10 (6,5)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	10,05	[1,92;184,30]	0,0034*
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	8 (3,7)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	3 (2,5)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	5 (2,7)	NE [NE; NE]	191	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
L858R	150	6 (4,0)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	1 (1,0)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	6 (5,1)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	4 (3,5)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	6 (5,3)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.35 ADAURA: Summary of subgroup analysis of time to first PT: Dysgeusie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	5 (4,6)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	6 (3,0)	NE [NE; NE]	207	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Nein	134	5 (3,7)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	2 (1,9)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	NC	[NC]	NC
Nein	229	9 (3,9)	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	8 (3,9)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	2 (3,3)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	0	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.36 ADAURA: Summary of subgroup analysis of time to first SOC: Infektionen und parasitaere Erkrankungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	67 (61,5)	8,0 [3,7;13,9]	95	33 (34,7)	NE [NE; NE]	2,21	[1,47; 3,40]	0,0001*
Weiblich	228	160 (70,2)	8,0 [5,7;11,0]	248	119 (48,0)	21,9 [17,3;30,5]	1,79	[1,42; 2,28]	<0,0001*
Interaktion p-Wert									0,3876
Alter									
<65 Jahre	184	131 (71,2)	5,8 [5,0; 8,0]	195	87 (44,6)	24,0 [16,5; NE]	1,98	[1,51; 2,60]	<0,0001*
>=65 Jahre	153	96 (62,7)	10,9 [8,1;18,4]	148	65 (43,9)	24,9 [18,3; NE]	1,76	[1,29; 2,42]	0,0004*
Interaktion p-Wert									0,5856
Abstammung									
Asiatisch	215	166 (77,2)	5,5 [3,3; 7,6]	218	111 (50,9)	18,3 [13,2;24,6]	2,12	[1,67; 2,70]	<0,0001*
Nicht-asiatisch	122	61 (50,0)	23,2 [16,4; NE]	125	41 (32,8)	NE [NE; NE]	1,59	[1,07; 2,38]	0,0202*
Interaktion p-Wert									0,2285
EGFR-Mutation									
Exon 19 Deletion	187	123 (65,8)	8,3 [5,6;13,4]	191	74 (38,7)	30,6 [19,5; NE]	2,05	[1,54; 2,74]	<0,0001*
L858R	150	104 (69,3)	7,9 [5,4;11,0]	152	78 (51,3)	18,4 [13,0;30,1]	1,72	[1,28; 2,31]	0,0003*
Interaktion p-Wert									0,4094
Krankheitsstadium Version 7									
Stadium IB	105	60 (57,1)	11,0 [5,6;22,1]	106	43 (40,6)	NE [NE; NE]	1,86	[1,26; 2,77]	0,0018*
Stadium II	118	81 (68,6)	7,9 [5,3;10,9]	118	56 (47,5)	27,4 [13,5;33,3]	1,90	[1,36; 2,69]	0,0002*
Stadium IIIA	114	86 (75,4)	6,0 [2,8;10,8]	119	53 (44,5)	18,4 [10,6;21,9]	1,80	[1,28; 2,55]	0,0006*
Interaktion p-Wert									0,9756
Krankheitsstadium Version 8									
Stadium IB	100	57 (57,0)	12,9 [5,7;21,4]	98	45 (45,9)	27,6 [17,3; NE]	1,59	[1,08; 2,36]	0,0196*
Stadium II	113	77 (68,1)	7,9 [5,2;11,0]	119	52 (43,7)	30,1 [16,5; NE]	2,10	[1,48; 3,01]	<0,0001*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.36 ADAURA: Summary of subgroup analysis of time to first SOC: Infektionen und parasitaere Erkrankungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	83 (76,1)	6,0 [2,5;10,8]	115	54 (47,0)	18,4 [10,4;21,9]	1,72	[1,23; 2,44]	0,0017*
Interaktion p-Wert									0,5460
Adjuvante Chemotherapie									
Ja	203	150 (73,9)	6,0 [5,1; 9,2]	207	100 (48,3)	18,2 [13,0;30,1]	1,92	[1,49; 2,47]	<0,0001*
Nein	134	77 (57,5)	10,9 [6,5;22,1]	136	52 (38,2)	35,8 [24,0; NE]	1,82	[1,28; 2,60]	0,0007*
Interaktion p-Wert									0,8169
Raucherstatus									
Ja	108	75 (69,4)	5,4 [2,7;10,3]	86	38 (44,2)	27,4 [13,2; NE]	2,13	[1,45; 3,18]	<0,0001*
Nein	229	152 (66,4)	9,3 [6,1;13,4]	257	114 (44,4)	24,6 [18,6;33,3]	1,77	[1,39; 2,26]	<0,0001*
Interaktion p-Wert									0,4206
Region									
Asien	204	158 (77,5)	5,5 [3,1; 7,6]	209	108 (51,7)	18,2 [13,2;21,9]	2,10	[1,64; 2,69]	<0,0001*
Europa	61	38 (62,3)	16,4 [5,3;21,4]	69	27 (39,1)	35,8 [17,3; NE]	1,83	[1,12; 3,03]	0,0152*
Nordamerika	14	11 (78,6)	8,0 [1,2;24,9]	11	2 (18,2)	NE [NE; NE]	5,42	[1,45; 34,99]	0,0095*
Rest der Welt	58	20 (34,5)	NE [NE; NE]	54	15 (27,8)	NE [NE; NE]	1,21	[0,62; 2,40]	0,5821
Interaktion p-Wert									0,2156

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.37 ADAURA: Summary of subgroup analysis of time to first PT: Gastroenteritis
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	3 (2,8)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	7 (3,1)	NE [NE; NE]	248	2 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	4 (2,2)	NE [NE; NE]	195	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	6 (3,9)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	8 (3,7)	NE [NE; NE]	218	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	2 (1,6)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	5 (2,7)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	5 (3,3)	NE [NE; NE]	152	2 (1,3)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	3 (2,9)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	4 (3,4)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	3 (2,6)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	3 (3,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	3 (2,7)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.37 ADAURA: Summary of subgroup analysis of time to first PT: Gastroenteritis
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	3 (2,8)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	5 (2,5)	NE [NE; NE]	207	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Nein	134	5 (3,7)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	3 (2,8)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	7 (3,1)	NE [NE; NE]	257	2 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	8 (3,9)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	2 (3,3)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	0	NE [NE; NE]	54	2 (3,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.38 ADAURA: Summary of subgroup analysis of time to first PT: Paronychie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	27 (24,8)	NE [NE; NE]	95	2 (2,1)	NE [NE; NE]	13,00	[3,90; 80,58]	<0,0001*
Weiblich	228	65 (28,5)	NE [NE; NE]	248	3 (1,2)	NE [NE; NE]	26,16	[9,72;107,00]	<0,0001*
Interaktion p-Wert									0,4700
Alter									
<65 Jahre	184	56 (30,4)	NE [NE; NE]	195	2 (1,0)	NE [NE; NE]	32,62	[10,18;199,13]	<0,0001*
>=65 Jahre	153	36 (23,5)	NE [NE; NE]	148	3 (2,0)	NE [NE; NE]	13,05	[4,71; 54,12]	<0,0001*
Interaktion p-Wert									0,3223
Abstammung									
Asiatisch	215	73 (34,0)	NE [NE; NE]	218	5 (2,3)	NE [NE; NE]	17,09	[7,65; 48,70]	<0,0001*
Nicht-asiatisch	122	19 (15,6)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	54 (28,9)	NE [NE; NE]	191	2 (1,0)	NE [NE; NE]	29,69	[9,25;181,31]	<0,0001*
L858R	150	38 (25,3)	NE [NE; NE]	152	3 (2,0)	NE [NE; NE]	14,82	[5,37; 61,35]	<0,0001*
Interaktion p-Wert									0,4528
Krankheitsstadium Version 7									
Stadium IB	105	16 (15,2)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	18,87	[3,85;340,37]	<0,0001*
Stadium II	118	38 (32,2)	NE [NE; NE]	118	2 (1,7)	NE [NE; NE]	22,14	[6,79;136,09]	<0,0001*
Stadium IIIA	114	38 (33,3)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	19,92	[6,10;122,48]	<0,0001*
Interaktion p-Wert									0,9904
Krankheitsstadium Version 8									
Stadium IB	100	17 (17,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	19,85	[4,08;357,46]	<0,0001*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.38 ADAURA: Summary of subgroup analysis of time to first PT: Paronychie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium II	113	33 (29,2)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	20,08	[6,11;123,79]	<0,0001*
Stadium IIIA	109	38 (34,9)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	20,35	[6,24;125,12]	<0,0001*
Interaktion p-Wert									0,9998
Adjuvante Chemotherapie									
Ja	203	65 (32,0)	NE [NE; NE]	207	3 (1,4)	NE [NE; NE]	24,57	[9,14;100,55]	<0,0001*
Nein	134	27 (20,1)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	15,18	[4,55; 94,15]	<0,0001*
Interaktion p-Wert									0,6153
Raucherstatus									
Ja	108	33 (30,6)	NE [NE; NE]	86	2 (2,3)	NE [NE; NE]	15,07	[4,58; 92,93]	<0,0001*
Nein	229	59 (25,8)	NE [NE; NE]	257	3 (1,2)	NE [NE; NE]	24,12	[8,93; 98,83]	<0,0001*
Interaktion p-Wert									0,6226
Region									
Asien	204	69 (33,8)	NE [NE; NE]	209	5 (2,4)	NE [NE; NE]	16,31	[7,28; 46,55]	<0,0001*
Europa	61	11 (18,0)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	3 (21,4)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	9 (15,5)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.39 ADAURA: Summary of subgroup analysis of time to first SOC: Leber- und Gallenerkrankungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	4 (3,7)	NE [NE; NE]	95	4 (4,2)	NE [NE; NE]	0,72	[0,17; 3,07]	0,6504
Weiblich	228	5 (2,2)	NE [NE; NE]	248	13 (5,2)	NE [NE; NE]	0,35	[0,11; 0,92]	0,0329*
Interaktion p-Wert									0,4003
Alter									
<65 Jahre	184	4 (2,2)	NE [NE; NE]	195	11 (5,6)	NE [NE; NE]	0,30	[0,08; 0,88]	0,0273*
>=65 Jahre	153	5 (3,3)	NE [NE; NE]	148	6 (4,1)	NE [NE; NE]	0,73	[0,21; 2,43]	0,6055
Interaktion p-Wert									0,2840
Abstammung									
Asiatisch	215	7 (3,3)	NE [NE; NE]	218	12 (5,5)	NE [NE; NE]	0,49	[0,18; 1,22]	0,1253
Nicht-asiatisch	122	2 (1,6)	NE [NE; NE]	125	5 (4,0)	NE [NE; NE]	0,35	[0,05; 1,61]	0,1801
Interaktion p-Wert									0,7165
EGFR-Mutation									
Exon 19 Deletion	187	5 (2,7)	NE [NE; NE]	191	8 (4,2)	NE [NE; NE]	0,49	[0,15; 1,48]	0,2051
L858R	150	4 (2,7)	NE [NE; NE]	152	9 (5,9)	NE [NE; NE]	0,41	[0,11; 1,27]	0,1268
Interaktion p-Wert									0,8399
Krankheitsstadium Version 7									
Stadium IB	105	2 (1,9)	NE [NE; NE]	106	5 (4,7)	NE [NE; NE]	0,42	[0,06; 1,94]	0,2726
Stadium II	118	4 (3,4)	NE [NE; NE]	118	6 (5,1)	NE [NE; NE]	0,57	[0,14; 1,99]	0,3733
Stadium IIIA	114	3 (2,6)	NE [NE; NE]	119	6 (5,0)	NE [NE; NE]	0,34	[0,07; 1,29]	0,1120
Interaktion p-Wert									0,8604
Krankheitsstadium Version 8									
Stadium IB	100	2 (2,0)	NE [NE; NE]	98	4 (4,1)	NE [NE; NE]	0,52	[0,07; 2,65]	0,4332
Stadium II	113	4 (3,5)	NE [NE; NE]	119	5 (4,2)	NE [NE; NE]	0,74	[0,18; 2,82]	0,6589

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.39 ADAURA: Summary of subgroup analysis of time to first SOC: Leber- und Gallenerkrankungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	3 (2,8)	NE [NE; NE]	115	7 (6,1)	NE [NE; NE]	0,29	[0,06; 1,06]	0,0621
Interaktion p-Wert									0,6179
Adjuvante Chemotherapie									
Ja	203	4 (2,0)	NE [NE; NE]	207	10 (4,8)	NE [NE; NE]	0,32	[0,09; 0,96]	0,0416*
Nein	134	5 (3,7)	NE [NE; NE]	136	7 (5,1)	NE [NE; NE]	0,66	[0,19; 2,06]	0,4725
Interaktion p-Wert									0,3828
Raucherstatus									
Ja	108	2 (1,9)	NE [NE; NE]	86	5 (5,8)	NE [NE; NE]	0,26	[0,04; 1,21]	0,0874
Nein	229	7 (3,1)	NE [NE; NE]	257	12 (4,7)	NE [NE; NE]	0,55	[0,20; 1,36]	0,1961
Interaktion p-Wert									0,4315
Region									
Asien	204	7 (3,4)	NE [NE; NE]	209	11 (5,3)	NE [NE; NE]	0,55	[0,20; 1,41]	0,2136
Europa	61	0	NE [NE; NE]	69	2 (2,9)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	3 (5,6)	NE [NE; NE]	0,53	[0,07; 3,20]	0,4802
Interaktion p-Wert									0,9675

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.40 ADAURA: Summary of subgroup analysis of time to first PT: Arthralgie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	6 (5,5)	NE [NE; NE]	95	9 (9,5)	NE [NE; NE]	0,48	[0,16; 1,33]	0,1592
Weiblich	228	17 (7,5)	NE [NE; NE]	248	28 (11,3)	NE [NE; NE]	0,53	[0,29; 0,97]	0,0382*
Interaktion p-Wert									0,8637
Alter									
<65 Jahre	184	15 (8,2)	NE [NE; NE]	195	18 (9,2)	NE [NE; NE]	0,68	[0,34; 1,36]	0,2742
>=65 Jahre	153	8 (5,2)	NE [NE; NE]	148	19 (12,8)	NE [NE; NE]	0,36	[0,15; 0,79]	0,0100*
Interaktion p-Wert									0,2300
Abstammung									
Asiatisch	215	16 (7,4)	NE [NE; NE]	218	25 (11,5)	NE [NE; NE]	0,53	[0,27; 0,98]	0,0424*
Nicht-asiatisch	122	7 (5,7)	NE [NE; NE]	125	12 (9,6)	NE [NE; NE]	0,49	[0,18; 1,23]	0,1286
Interaktion p-Wert									0,9078
EGFR-Mutation									
Exon 19 Deletion	187	13 (7,0)	NE [NE; NE]	191	19 (9,9)	NE [NE; NE]	0,52	[0,25; 1,06]	0,0708
L858R	150	10 (6,7)	NE [NE; NE]	152	18 (11,8)	NE [NE; NE]	0,51	[0,23; 1,08]	0,0800
Interaktion p-Wert									0,9564
Krankheitsstadium Version 7									
Stadium IB	105	9 (8,6)	NE [NE; NE]	106	10 (9,4)	NE [NE; NE]	0,95	[0,38; 2,36]	0,9145
Stadium II	118	6 (5,1)	NE [NE; NE]	118	18 (15,3)	NE [NE; NE]	0,27	[0,10; 0,64]	0,0026*
Stadium IIIA	114	8 (7,0)	NE [NE; NE]	119	9 (7,6)	NE [NE; NE]	0,59	[0,22; 1,55]	0,2779
Interaktion p-Wert									0,1433
Krankheitsstadium Version 8									
Stadium IB	100	9 (9,0)	NE [NE; NE]	98	10 (10,2)	NE [NE; NE]	0,94	[0,37; 2,32]	0,8868
Stadium II	113	7 (6,2)	NE [NE; NE]	119	18 (15,1)	NE [NE; NE]	0,34	[0,13; 0,78]	0,0105*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.40 ADAURA: Summary of subgroup analysis of time to first PT: Arthralgie
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	7 (6,4)	NE [NE; NE]	115	9 (7,8)	NE [NE; NE]	0,52	[0,19; 1,41]	0,1972
Interaktion p-Wert									0,2806
Adjuvante Chemotherapie									
Ja	203	17 (8,4)	NE [NE; NE]	207	24 (11,6)	NE [NE; NE]	0,55	[0,29; 1,02]	0,0569
Nein	134	6 (4,5)	NE [NE; NE]	136	13 (9,6)	NE [NE; NE]	0,42	[0,15; 1,07]	0,0693
Interaktion p-Wert									0,6541
Raucherstatus									
Ja	108	9 (8,3)	NE [NE; NE]	86	10 (11,6)	NE [NE; NE]	0,59	[0,23; 1,47]	0,2555
Nein	229	14 (6,1)	NE [NE; NE]	257	27 (10,5)	NE [NE; NE]	0,47	[0,24; 0,88]	0,0185*
Interaktion p-Wert									0,6821
Region									
Asien	204	15 (7,4)	NE [NE; NE]	209	23 (11,0)	NE [NE; NE]	0,54	[0,28; 1,03]	0,0614
Europa	61	7 (11,5)	NE [NE; NE]	69	7 (10,1)	NE [NE; NE]	0,96	[0,33; 2,82]	0,9468
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	2 (18,2)	NE [NE; NE]	0,30	[0,01; 3,10]	0,3023
Rest der Welt	58	0	NE [NE; NE]	54	5 (9,3)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,5407

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.41 ADAURA: Summary of subgroup analysis of time to first PT: Muskelspasmen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	3 (2,8)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	23 (10,1)	NE [NE; NE]	248	5 (2,0)	NE [NE; NE]	4,54	[1,87; 13,54]	0,0005*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	13 (7,1)	NE [NE; NE]	195	2 (1,0)	NE [NE; NE]	5,83	[1,61; 37,32]	0,0051*
>=65 Jahre	153	13 (8,5)	NE [NE; NE]	148	3 (2,0)	NE [NE; NE]	4,07	[1,31; 17,76]	0,0133*
Interaktion p-Wert									0,7155
Abstammung									
Asiatisch	215	15 (7,0)	NE [NE; NE]	218	3 (1,4)	NE [NE; NE]	4,50	[1,48; 19,44]	0,0062*
Nicht-asiatisch	122	11 (9,0)	NE [NE; NE]	125	2 (1,6)	NE [NE; NE]	5,19	[1,39; 33,56]	0,0118*
Interaktion p-Wert									0,8855
EGFR-Mutation									
Exon 19 Deletion	187	17 (9,1)	NE [NE; NE]	191	3 (1,6)	NE [NE; NE]	4,87	[1,63; 20,87]	0,0031*
L858R	150	9 (6,0)	NE [NE; NE]	152	2 (1,3)	NE [NE; NE]	4,46	[1,15; 29,25]	0,0293*
Interaktion p-Wert									0,9306
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	2,75	[0,59; 19,21]	0,2013
Stadium II	118	11 (9,3)	NE [NE; NE]	118	2 (1,7)	NE [NE; NE]	5,07	[1,36; 32,74]	0,0133*
Stadium IIIA	114	10 (8,8)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	7,54	[1,44;138,61]	0,0129*
Interaktion p-Wert									0,7349
Krankheitsstadium Version 8									
Stadium IB	100	3 (3,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	1,62	[0,27; 12,30]	0,5929
Stadium II	113	12 (10,6)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	5,95	[1,62; 38,27]	0,0051*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.41 ADAURA: Summary of subgroup analysis of time to first PT: Muskelspasmen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	8 (7,3)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	5,89	[1,07;109,47]	0,0397*
Interaktion p-Wert									0,5150
Adjuvante Chemotherapie									
Ja	203	18 (8,9)	NE [NE; NE]	207	3 (1,4)	NE [NE; NE]	5,25	[1,77; 22,43]	0,0016*
Nein	134	8 (6,0)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	3,92	[0,98; 26,00]	0,0531
Interaktion p-Wert									0,7744
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	3 (3,5)	NE [NE; NE]	1,17	[0,29; 5,73]	0,8250
Nein	229	21 (9,2)	NE [NE; NE]	257	2 (0,8)	NE [NE; NE]	10,63	[3,12; 66,48]	<0,0001*
Interaktion p-Wert									0,0328*
Region									
Asien	204	14 (6,9)	NE [NE; NE]	209	2 (1,0)	NE [NE; NE]	6,30	[1,76; 40,15]	0,0029*
Europa	61	6 (9,8)	NE [NE; NE]	69	2 (2,9)	NE [NE; NE]	3,07	[0,71; 20,99]	0,1389
Nordamerika	14	4 (28,6)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	3,29	[0,49; 64,31]	0,2389
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,7821

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.42 ADAURA: Summary of subgroup analysis of time to first SOC: Stoffwechsel- und Ernaehrungsstoerungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	28 (25,7)	NE [NE; NE]	95	14 (14,7)	NE [NE; NE]	1,65	[0,88; 3,22]	0,1191
Weiblich	228	67 (29,4)	NE [NE; NE]	248	31 (12,5)	NE [NE; NE]	2,31	[1,53; 3,59]	<0,0001*
Interaktion p-Wert									0,3908
Alter									
<65 Jahre	184	42 (22,8)	NE [NE; NE]	195	27 (13,8)	NE [NE; NE]	1,46	[0,91; 2,40]	0,1198
>=65 Jahre	153	53 (34,6)	NE [NE; NE]	148	18 (12,2)	NE [NE; NE]	3,13	[1,87; 5,50]	<0,0001*
Interaktion p-Wert									0,0366*
Abstammung									
Asiatisch	215	65 (30,2)	NE [NE; NE]	218	34 (15,6)	NE [NE; NE]	1,89	[1,26; 2,90]	0,0020*
Nicht-asiatisch	122	30 (24,6)	NE [NE; NE]	125	11 (8,8)	NE [NE; NE]	2,72	[1,40; 5,68]	0,0026*
Interaktion p-Wert									0,3715
EGFR-Mutation									
Exon 19 Deletion	187	52 (27,8)	NE [NE; NE]	191	19 (9,9)	NE [NE; NE]	2,59	[1,56; 4,50]	0,0002*
L858R	150	43 (28,7)	NE [NE; NE]	152	26 (17,1)	NE [NE; NE]	1,74	[1,08; 2,87]	0,0232*
Interaktion p-Wert									0,2749
Krankheitsstadium Version 7									
Stadium IB	105	28 (26,7)	NE [NE; NE]	106	15 (14,2)	NE [NE; NE]	2,03	[1,10; 3,90]	0,0232*
Stadium II	118	34 (28,8)	NE [NE; NE]	118	16 (13,6)	NE [NE; NE]	2,16	[1,21; 4,03]	0,0083*
Stadium IIIA	114	33 (28,9)	NE [NE; NE]	119	14 (11,8)	NE [NE; NE]	2,07	[1,13; 4,01]	0,0177*
Interaktion p-Wert									0,9888
Krankheitsstadium Version 8									
Stadium IB	100	28 (28,0)	NE [NE; NE]	98	15 (15,3)	NE [NE; NE]	2,01	[1,09; 3,86]	0,0250*
Stadium II	113	29 (25,7)	NE [NE; NE]	119	14 (11,8)	NE [NE; NE]	2,23	[1,20; 4,34]	0,0108*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.42 ADAURA: Summary of subgroup analysis of time to first SOC: Stoffwechsel- und Ernaehrungsstoerungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	31 (28,4)	NE [NE; NE]	115	16 (13,9)	NE [NE; NE]	1,66	[0,92; 3,12]	0,0934
Interaktion p-Wert									0,8003
Adjuvante Chemotherapie									
Ja	203	53 (26,1)	NE [NE; NE]	207	26 (12,6)	NE [NE; NE]	1,96	[1,24; 3,19]	0,0038*
Nein	134	42 (31,3)	NE [NE; NE]	136	19 (14,0)	NE [NE; NE]	2,29	[1,35; 4,03]	0,0018*
Interaktion p-Wert									0,6698
Raucherstatus									
Ja	108	29 (26,9)	NE [NE; NE]	86	10 (11,6)	NE [NE; NE]	2,20	[1,11; 4,75]	0,0232*
Nein	229	66 (28,8)	NE [NE; NE]	257	35 (13,6)	NE [NE; NE]	2,08	[1,39; 3,17]	0,0003*
Interaktion p-Wert									0,8965
Region									
Asien	204	64 (31,4)	NE [NE; NE]	209	33 (15,8)	NE [NE; NE]	1,95	[1,29; 3,01]	0,0013*
Europa	61	19 (31,1)	NE [NE; NE]	69	6 (8,7)	NE [NE; NE]	3,74	[1,58; 10,27]	0,0021*
Nordamerika	14	3 (21,4)	NE [NE; NE]	11	3 (27,3)	NE [NE; NE]	0,71	[0,13; 3,81]	0,6702
Rest der Welt	58	9 (15,5)	NE [NE; NE]	54	3 (5,6)	NE [NE; NE]	2,52	[0,75; 11,34]	0,1401
Interaktion p-Wert									0,3142

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.43 ADAURA: Summary of subgroup analysis of time to first PT: Appetit vermindert
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	12 (11,0)	NE [NE; NE]	95	5 (5,3)	NE [NE; NE]	2,10	[0,78; 6,61]	0,1456
Weiblich	228	36 (15,8)	NE [NE; NE]	248	8 (3,2)	NE [NE; NE]	5,00	[2,45; 11,58]	<0,0001*
Interaktion p-Wert									0,1992
Alter									
<65 Jahre	184	17 (9,2)	NE [NE; NE]	195	7 (3,6)	NE [NE; NE]	2,48	[1,07; 6,41]	0,0342*
>=65 Jahre	153	31 (20,3)	NE [NE; NE]	148	6 (4,1)	NE [NE; NE]	5,45	[2,44; 14,49]	<0,0001*
Interaktion p-Wert									0,2117
Abstammung									
Asiatisch	215	29 (13,5)	NE [NE; NE]	218	9 (4,1)	NE [NE; NE]	3,35	[1,65; 7,51]	0,0006*
Nicht-asiatisch	122	19 (15,6)	NE [NE; NE]	125	4 (3,2)	NE [NE; NE]	4,89	[1,84; 16,86]	0,0009*
Interaktion p-Wert									0,5666
EGFR-Mutation									
Exon 19 Deletion	187	26 (13,9)	NE [NE; NE]	191	8 (4,2)	NE [NE; NE]	3,26	[1,54; 7,72]	0,0015*
L858R	150	22 (14,7)	NE [NE; NE]	152	5 (3,3)	NE [NE; NE]	4,73	[1,94; 14,13]	0,0003*
Interaktion p-Wert									0,5582
Krankheitsstadium Version 7									
Stadium IB	105	12 (11,4)	NE [NE; NE]	106	3 (2,8)	NE [NE; NE]	4,28	[1,36; 18,80]	0,0113*
Stadium II	118	18 (15,3)	NE [NE; NE]	118	3 (2,5)	NE [NE; NE]	6,31	[2,13; 26,91]	0,0004*
Stadium IIIA	114	18 (15,8)	NE [NE; NE]	119	7 (5,9)	NE [NE; NE]	2,53	[1,10; 6,53]	0,0279*
Interaktion p-Wert									0,4604
Krankheitsstadium Version 8									
Stadium IB	100	12 (12,0)	NE [NE; NE]	98	3 (3,1)	NE [NE; NE]	4,21	[1,34; 18,48]	0,0124*
Stadium II	113	16 (14,2)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	8,85	[2,52; 55,96]	0,0002*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.43 ADAURA: Summary of subgroup analysis of time to first PT: Appetit vermindert
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	15 (13,8)	NE [NE; NE]	115	8 (7,0)	NE [NE; NE]	1,86	[0,81; 4,62]	0,1485
Interaktion p-Wert									0,1383
Adjuvante Chemotherapie									
Ja	203	25 (12,3)	NE [NE; NE]	207	6 (2,9)	NE [NE; NE]	4,25	[1,86; 11,44]	0,0003*
Nein	134	23 (17,2)	NE [NE; NE]	136	7 (5,1)	NE [NE; NE]	3,48	[1,57; 8,78]	0,0016*
Interaktion p-Wert									0,7517
Raucherstatus									
Ja	108	11 (10,2)	NE [NE; NE]	86	4 (4,7)	NE [NE; NE]	2,18	[0,75; 7,88]	0,1596
Nein	229	37 (16,2)	NE [NE; NE]	257	9 (3,5)	NE [NE; NE]	4,74	[2,39; 10,47]	<0,0001*
Interaktion p-Wert									0,2770
Region									
Asien	204	28 (13,7)	NE [NE; NE]	209	8 (3,8)	NE [NE; NE]	3,69	[1,76; 8,68]	0,0003*
Europa	61	13 (21,3)	NE [NE; NE]	69	3 (4,3)	NE [NE; NE]	5,06	[1,63; 22,07]	0,0038*
Nordamerika	14	3 (21,4)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	2,44	[0,31; 49,36]	0,4104
Rest der Welt	58	4 (6,9)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	3,57	[0,53; 69,80]	0,2056
Interaktion p-Wert									0,9504

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.44 ADAURA: Summary of subgroup analysis of time to first SOC: Untersuchungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	48 (44,0)	NE [NE; NE]	95	35 (36,8)	NE [NE; NE]	1,25	[0,81; 1,94]	0,3219
Weiblich	228	100 (43,9)	NE [NE; NE]	248	50 (20,2)	NE [NE; NE]	2,39	[1,71; 3,38]	<0,0001*
Interaktion p-Wert									0,0212*
Alter									
<65 Jahre	184	80 (43,5)	NE [NE; NE]	195	53 (27,2)	NE [NE; NE]	1,60	[1,14; 2,28]	0,0070*
>=65 Jahre	153	68 (44,4)	33,0 [13,8; NE]	148	32 (21,6)	NE [NE; NE]	2,48	[1,64; 3,82]	<0,0001*
Interaktion p-Wert									0,1167
Abstammung									
Asiatisch	215	109 (50,7)	16,6 [13,8; NE]	218	69 (31,7)	NE [NE; NE]	1,75	[1,30; 2,38]	0,0002*
Nicht-asiatisch	122	39 (32,0)	NE [NE; NE]	125	16 (12,8)	NE [NE; NE]	2,69	[1,53; 4,96]	0,0004*
Interaktion p-Wert									0,1903
EGFR-Mutation									
Exon 19 Deletion	187	84 (44,9)	NE [NE; NE]	191	40 (20,9)	NE [NE; NE]	2,22	[1,53; 3,26]	<0,0001*
L858R	150	64 (42,7)	NE [NE; NE]	152	45 (29,6)	NE [NE; NE]	1,67	[1,15; 2,46]	0,0077*
Interaktion p-Wert									0,2999
Krankheitsstadium Version 7									
Stadium IB	105	45 (42,9)	30,3 [16,6; NE]	106	31 (29,2)	NE [NE; NE]	1,80	[1,14; 2,86]	0,0111*
Stadium II	118	50 (42,4)	NE [NE; NE]	118	27 (22,9)	NE [NE; NE]	2,05	[1,29; 3,31]	0,0021*
Stadium IIIA	114	53 (46,5)	NE [NE; NE]	119	27 (22,7)	NE [NE; NE]	1,94	[1,23; 3,14]	0,0039*
Interaktion p-Wert									0,9250
Krankheitsstadium Version 8									
Stadium IB	100	41 (41,0)	NE [NE; NE]	98	28 (28,6)	NE [NE; NE]	1,77	[1,10; 2,89]	0,0186*
Stadium II	113	47 (41,6)	NE [NE; NE]	119	28 (23,5)	NE [NE; NE]	1,90	[1,20; 3,08]	0,0060*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.44 ADAURA: Summary of subgroup analysis of time to first SOC: Untersuchungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	50 (45,9)	NE [NE; NE]	115	27 (23,5)	NE [NE; NE]	1,87	[1,18; 3,02]	0,0076*
Interaktion p-Wert									0,9760
Adjuvante Chemotherapie									
Ja	203	95 (46,8)	27,7 [16,4; NE]	207	59 (28,5)	NE [NE; NE]	1,74	[1,26; 2,42]	0,0007*
Nein	134	53 (39,6)	NE [NE; NE]	136	26 (19,1)	NE [NE; NE]	2,34	[1,48; 3,79]	0,0002*
Interaktion p-Wert									0,3050
Raucherstatus									
Ja	108	43 (39,8)	NE [NE; NE]	86	22 (25,6)	NE [NE; NE]	1,63	[0,98; 2,76]	0,0582
Nein	229	105 (45,9)	33,4 [16,6; NE]	257	63 (24,5)	NE [NE; NE]	2,08	[1,52; 2,85]	<0,0001*
Interaktion p-Wert									0,4288
Region									
Asien	204	106 (52,0)	16,6 [13,0; NE]	209	66 (31,6)	NE [NE; NE]	1,83	[1,35; 2,50]	<0,0001*
Europa	61	19 (31,1)	NE [NE; NE]	69	9 (13,0)	NE [NE; NE]	2,61	[1,21; 6,06]	0,0136*
Nordamerika	14	5 (35,7)	NE [NE; NE]	11	6 (54,5)	13,8 [2,8; NE]	0,48	[0,14; 1,61]	0,2310
Rest der Welt	58	18 (31,0)	NE [NE; NE]	54	4 (7,4)	NE [NE; NE]	4,55	[1,70; 15,75]	0,0018*
Interaktion p-Wert									0,0356*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.45 ADAURA: Summary of subgroup analysis of time to first PT: Blutharnstoff erhoeht
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	1 (0,9)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	9 (3,9)	NE [NE; NE]	248	1 (0,4)	NE [NE; NE]	8,85	[1,66;163,12]	0,0072*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	5 (2,7)	NE [NE; NE]	195	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	5 (3,3)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	8 (3,7)	NE [NE; NE]	218	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	2 (1,6)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	5 (2,7)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	5 (3,3)	NE [NE; NE]	152	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	2 (1,7)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	3 (2,6)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	4 (4,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	2 (1,8)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.45 ADAURA: Summary of subgroup analysis of time to first PT: Blutharnstoff erhoeht
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	3 (2,8)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	7 (3,4)	NE [NE; NE]	207	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Nein	134	3 (2,2)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	0	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	10 (4,4)	NE [NE; NE]	257	1 (0,4)	NE [NE; NE]	9,86	[1,89;180,95]	0,0038*
Interaktion p-Wert									NC
Region									
Asien	204	8 (3,9)	NE [NE; NE]	209	1 (0,5)	NE [NE; NE]	NC	[NC]	NC
Europa	61	0	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.46 ADAURA: Summary of subgroup analysis of time to first PT: Elektrokardiogramm QT verlaengert
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	7 (6,4)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	23 (10,1)	NE [NE; NE]	248	8 (3,2)	NE [NE; NE]	2,77	[1,29; 6,63]	0,0081*
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	17 (9,2)	NE [NE; NE]	195	4 (2,1)	NE [NE; NE]	3,77	[1,39; 13,14]	0,0075*
>=65 Jahre	153	13 (8,5)	NE [NE; NE]	148	4 (2,7)	NE [NE; NE]	2,97	[1,05; 10,55]	0,0395*
Interaktion p-Wert									0,7643
Abstammung									
Asiatisch	215	18 (8,4)	NE [NE; NE]	218	7 (3,2)	NE [NE; NE]	2,26	[0,98; 5,83]	0,0547
Nicht-asiatisch	122	12 (9,8)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	11,20	[2,21;204,14]	0,0014*
Interaktion p-Wert									0,1052
EGFR-Mutation									
Exon 19 Deletion	187	13 (7,0)	NE [NE; NE]	191	3 (1,6)	NE [NE; NE]	3,56	[1,14; 15,54]	0,0269*
L858R	150	17 (11,3)	NE [NE; NE]	152	5 (3,3)	NE [NE; NE]	3,42	[1,35; 10,41]	0,0082*
Interaktion p-Wert									0,9615
Krankheitsstadium Version 7									
Stadium IB	105	11 (10,5)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	12,34	[2,40;225,55]	0,0009*
Stadium II	118	7 (5,9)	NE [NE; NE]	118	5 (4,2)	NE [NE; NE]	1,22	[0,39; 4,11]	0,7375
Stadium IIIA	114	12 (10,5)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	4,44	[1,20; 28,63]	0,0230*
Interaktion p-Wert									0,0776
Krankheitsstadium Version 8									
Stadium IB	100	9 (9,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	9,90	[1,86;182,52]	0,0043*
Stadium II	113	6 (5,3)	NE [NE; NE]	119	6 (5,0)	NE [NE; NE]	0,92	[0,29; 2,94]	0,8832

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.46 ADAURA: Summary of subgroup analysis of time to first PT: Elektrokardiogramm QT verlaengert
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	10 (9,2)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	7,20	[1,37;132,28]	0,0158*
Interaktion p-Wert									0,0371*
Adjuvante Chemotherapie									
Ja	203	17 (8,4)	NE [NE; NE]	207	7 (3,4)	NE [NE; NE]	2,04	[0,88; 5,29]	0,0995
Nein	134	13 (9,7)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	12,89	[2,57;234,44]	0,0005*
Interaktion p-Wert									0,0569
Raucherstatus									
Ja	108	11 (10,2)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	19 (8,3)	NE [NE; NE]	257	8 (3,1)	NE [NE; NE]	2,33	[1,05; 5,67]	0,0361*
Interaktion p-Wert									NC
Region									
Asien	204	18 (8,8)	NE [NE; NE]	209	6 (2,9)	NE [NE; NE]	2,67	[1,11; 7,37]	0,0267*
Europa	61	7 (11,5)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	2 (18,2)	NE [NE; NE]	0,28	[0,01; 2,91]	0,2776
Rest der Welt	58	4 (6,9)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,0755

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.47 ADAURA: Summary of subgroup analysis of time to first PT: Gewicht erniedrigt
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	7 (6,4)	NE [NE; NE]	95	3 (3,2)	NE [NE; NE]	1,86	[0,52; 8,64]	0,3516
Weiblich	228	28 (12,3)	NE [NE; NE]	248	6 (2,4)	NE [NE; NE]	4,85	[2,15; 12,96]	<0,0001*
Interaktion p-Wert									0,2603
Alter									
<65 Jahre	184	14 (7,6)	NE [NE; NE]	195	6 (3,1)	NE [NE; NE]	2,17	[0,87; 6,13]	0,0988
>=65 Jahre	153	21 (13,7)	NE [NE; NE]	148	3 (2,0)	NE [NE; NE]	7,02	[2,42; 29,72]	<0,0001*
Interaktion p-Wert									0,1243
Abstammung									
Asiatisch	215	29 (13,5)	NE [NE; NE]	218	8 (3,7)	NE [NE; NE]	3,53	[1,69; 8,28]	0,0005*
Nicht-asiatisch	122	6 (4,9)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	5,64	[0,96;106,63]	0,0556
Interaktion p-Wert									0,6708
EGFR-Mutation									
Exon 19 Deletion	187	16 (8,6)	NE [NE; NE]	191	6 (3,1)	NE [NE; NE]	2,36	[0,97; 6,59]	0,0586
L858R	150	19 (12,7)	NE [NE; NE]	152	3 (2,0)	NE [NE; NE]	6,72	[2,29; 28,61]	0,0002*
Interaktion p-Wert									0,1710
Krankheitsstadium Version 7									
Stadium IB	105	10 (9,5)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	5,73	[1,51; 37,29]	0,0083*
Stadium II	118	11 (9,3)	NE [NE; NE]	118	2 (1,7)	NE [NE; NE]	5,06	[1,36; 32,70]	0,0133*
Stadium IIIA	114	14 (12,3)	NE [NE; NE]	119	5 (4,2)	NE [NE; NE]	2,36	[0,90; 7,32]	0,0828
Interaktion p-Wert									0,5437
Krankheitsstadium Version 8									
Stadium IB	100	11 (11,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	6,29	[1,69; 40,64]	0,0044*
Stadium II	113	8 (7,1)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	3,89	[0,98; 25,81]	0,0546

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.47 ADAURA: Summary of subgroup analysis of time to first PT: Gewicht erniedrigt
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	12 (11,0)	NE [NE; NE]	115	5 (4,3)	NE [NE; NE]	1,97	[0,73; 6,21]	0,1871
Interaktion p-Wert									0,4232
Adjuvante Chemotherapie									
Ja	203	19 (9,4)	NE [NE; NE]	207	5 (2,4)	NE [NE; NE]	3,46	[1,39; 10,46]	0,0064*
Nein	134	16 (11,9)	NE [NE; NE]	136	4 (2,9)	NE [NE; NE]	4,17	[1,53; 14,56]	0,0041*
Interaktion p-Wert									0,8042
Raucherstatus									
Ja	108	7 (6,5)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	5,20	[0,92; 97,20]	0,0632
Nein	229	28 (12,2)	NE [NE; NE]	257	8 (3,1)	NE [NE; NE]	3,73	[1,78; 8,77]	0,0003*
Interaktion p-Wert									0,7643
Region									
Asien	204	28 (13,7)	NE [NE; NE]	209	8 (3,8)	NE [NE; NE]	3,46	[1,65; 8,14]	0,0007*
Europa	61	3 (4,9)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	3 (21,4)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	2,12	[0,27; 42,89]	0,4916
Rest der Welt	58	1 (1,7)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,6990

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.48 ADAURA: Summary of subgroup analysis of time to first PT: Kreatinin im Blut erhoeht
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	12 (11,0)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	10,11	[1,99;184,17]	0,0025*
Weiblich	228	19 (8,3)	NE [NE; NE]	248	6 (2,4)	NE [NE; NE]	3,25	[1,37; 8,94]	0,0064*
Interaktion p-Wert									0,2737
Alter									
<65 Jahre	184	10 (5,4)	NE [NE; NE]	195	3 (1,5)	NE [NE; NE]	3,17	[0,97; 14,13]	0,0573
>=65 Jahre	153	21 (13,7)	NE [NE; NE]	148	4 (2,7)	NE [NE; NE]	5,21	[1,98; 17,86]	0,0004*
Interaktion p-Wert									0,5636
Abstammung									
Asiatisch	215	24 (11,2)	NE [NE; NE]	218	4 (1,8)	NE [NE; NE]	5,85	[2,26; 19,91]	<0,0001*
Nicht-asiatisch	122	7 (5,7)	NE [NE; NE]	125	3 (2,4)	NE [NE; NE]	2,25	[0,63; 10,45]	0,2200
Interaktion p-Wert									0,2844
EGFR-Mutation									
Exon 19 Deletion	187	15 (8,0)	NE [NE; NE]	191	1 (0,5)	NE [NE; NE]	13,74	[2,78;248,50]	0,0002*
L858R	150	16 (10,7)	NE [NE; NE]	152	6 (3,9)	NE [NE; NE]	2,79	[1,15; 7,76]	0,0231*
Interaktion p-Wert									0,1099
Krankheitsstadium Version 7									
Stadium IB	105	6 (5,7)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	3,22	[0,74; 21,97]	0,1225
Stadium II	118	14 (11,9)	NE [NE; NE]	118	5 (4,2)	NE [NE; NE]	2,67	[1,02; 8,25]	0,0456*
Stadium IIIA	114	11 (9,6)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,8445
Krankheitsstadium Version 8									
Stadium IB	100	3 (3,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	1,56	[0,26; 11,82]	0,6240
Stadium II	113	15 (13,3)	NE [NE; NE]	119	4 (3,4)	NE [NE; NE]	3,89	[1,41; 13,66]	0,0073*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.48 ADAURA: Summary of subgroup analysis of time to first PT: Kreatinin im Blut erhoeht
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	11 (10,1)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	9,67	[1,87;176,85]	0,0036*
Interaktion p-Wert									0,3899
Adjuvante Chemotherapie									
Ja	203	22 (10,8)	NE [NE; NE]	207	5 (2,4)	NE [NE; NE]	4,20	[1,72; 12,56]	0,0011*
Nein	134	9 (6,7)	NE [NE; NE]	136	2 (1,5)	NE [NE; NE]	4,47	[1,15; 29,33]	0,0289*
Interaktion p-Wert									0,9462
Raucherstatus									
Ja	108	9 (8,3)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	22 (9,6)	NE [NE; NE]	257	7 (2,7)	NE [NE; NE]	3,34	[1,50; 8,47]	0,0026*
Interaktion p-Wert									NC
Region									
Asien	204	23 (11,3)	NE [NE; NE]	209	4 (1,9)	NE [NE; NE]	5,78	[2,22; 19,73]	0,0001*
Europa	61	5 (8,2)	NE [NE; NE]	69	3 (4,3)	NE [NE; NE]	1,84	[0,45; 8,98]	0,3946
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,2152

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.49 ADAURA: Summary of subgroup analysis of time to first PT: Leukozytenzahl erniedrigt
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	6 (5,5)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	19 (8,3)	NE [NE; NE]	248	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	15 (8,2)	NE [NE; NE]	195	1 (0,5)	NE [NE; NE]	14,17	[2,87;256,45]	0,0002*
>=65 Jahre	153	10 (6,5)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	25 (11,6)	NE [NE; NE]	218	1 (0,5)	NE [NE; NE]	24,47	[5,19;437,00]	<0,0001*
Nicht-asiatisch	122	0	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	13 (7,0)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	12 (8,0)	NE [NE; NE]	152	1 (0,7)	NE [NE; NE]	12,26	[2,41;223,28]	0,0008*
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	8 (7,6)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	10 (8,5)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	7 (6,1)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	7 (7,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	9 (8,0)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.49 ADAURA: Summary of subgroup analysis of time to first PT: Leukozytenzahl erniedrigt
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	8 (7,3)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	15 (7,4)	NE [NE; NE]	207	1 (0,5)	NE [NE; NE]	14,26	[2,89;257,95]	0,0002*
Nein	134	10 (7,5)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	5 (4,6)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	20 (8,7)	NE [NE; NE]	257	1 (0,4)	NE [NE; NE]	21,33	[4,44;382,65]	<0,0001*
Interaktion p-Wert									NC
Region									
Asien	204	24 (11,8)	NE [NE; NE]	209	1 (0,5)	NE [NE; NE]	23,67	[5,00;423,12]	<0,0001*
Europa	61	0	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	1 (1,7)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.50 ADAURA: Summary of subgroup analysis of time to first PT: Neutrophilenzahl erniedrigt
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	7 (6,4)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	5,53	[0,98;103,44]	0,0527
Weiblich	228	19 (8,3)	NE [NE; NE]	248	2 (0,8)	NE [NE; NE]	9,66	[2,80; 60,65]	<0,0001*
Interaktion p-Wert									0,6770
Alter									
<65 Jahre	184	16 (8,7)	NE [NE; NE]	195	2 (1,0)	NE [NE; NE]	7,47	[2,12; 47,27]	0,0007*
>=65 Jahre	153	10 (6,5)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	9,59	[1,84;176,05]	0,0042*
Interaktion p-Wert									0,8443
Abstammung									
Asiatisch	215	26 (12,1)	NE [NE; NE]	218	3 (1,4)	NE [NE; NE]	8,29	[2,92; 34,78]	<0,0001*
Nicht-asiatisch	122	0	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	13 (7,0)	NE [NE; NE]	191	1 (0,5)	NE [NE; NE]	11,49	[2,28;208,79]	0,0011*
L858R	150	13 (8,7)	NE [NE; NE]	152	2 (1,3)	NE [NE; NE]	6,67	[1,84; 42,62]	0,0023*
Interaktion p-Wert									0,6655
Krankheitsstadium Version 7									
Stadium IB	105	10 (9,5)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	11,25	[2,15;206,39]	0,0019*
Stadium II	118	8 (6,8)	NE [NE; NE]	118	1 (0,8)	NE [NE; NE]	7,52	[1,38;139,54]	0,0163*
Stadium IIIA	114	8 (7,0)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	6,38	[1,16;118,52]	0,0303*
Interaktion p-Wert									0,9245
Krankheitsstadium Version 8									
Stadium IB	100	9 (9,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	9,88	[1,86;182,20]	0,0044*
Stadium II	113	9 (8,0)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	9,15	[1,72;168,68]	0,0062*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.50 ADAURA: Summary of subgroup analysis of time to first PT: Neutrophilenzahl erniedrigt
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	7 (6,4)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	5,52	[0,98;103,37]	0,0537
Interaktion p-Wert									0,9195
Adjuvante Chemotherapie									
Ja	203	16 (7,9)	NE [NE; NE]	207	2 (1,0)	NE [NE; NE]	7,22	[2,05; 45,72]	0,0009*
Nein	134	10 (7,5)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	10,10	[1,93;185,31]	0,0033*
Interaktion p-Wert									0,7921
Raucherstatus									
Ja	108	6 (5,6)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	4,33	[0,74; 81,79]	0,1130
Nein	229	20 (8,7)	NE [NE; NE]	257	2 (0,8)	NE [NE; NE]	10,51	[3,07; 65,84]	<0,0001*
Interaktion p-Wert									0,5178
Region									
Asien	204	26 (12,7)	NE [NE; NE]	209	3 (1,4)	NE [NE; NE]	8,42	[2,96; 35,32]	<0,0001*
Europa	61	0	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	0	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.51 ADAURA: Summary of subgroup analysis of time to first PT: Thrombozytenzahl vermindert
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	8 (7,3)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	7,02	[1,29;130,28]	0,0211*
Weiblich	228	13 (5,7)	NE [NE; NE]	248	1 (0,4)	NE [NE; NE]	14,14	[2,82;256,91]	0,0003*
Interaktion p-Wert									0,6394
Alter									
<65 Jahre	184	12 (6,5)	NE [NE; NE]	195	1 (0,5)	NE [NE; NE]	12,68	[2,50;230,98]	0,0007*
>=65 Jahre	153	9 (5,9)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	8,81	[1,65;162,34]	0,0073*
Interaktion p-Wert									0,8059
Abstammung									
Asiatisch	215	14 (6,5)	NE [NE; NE]	218	2 (0,9)	NE [NE; NE]	7,18	[2,01; 45,72]	0,0012*
Nicht-asiatisch	122	7 (5,7)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	14 (7,5)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	7 (4,7)	NE [NE; NE]	152	2 (1,3)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	6 (5,1)	NE [NE; NE]	118	1 (0,8)	NE [NE; NE]	5,93	[1,01;111,94]	0,0483*
Stadium IIIA	114	10 (8,8)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	9,91	[1,89;181,90]	0,0037*
Interaktion p-Wert									0,7339
Krankheitsstadium Version 8									
Stadium IB	100	5 (5,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	4 (3,5)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	4,16	[0,62; 81,35]	0,1525

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.1.51 ADAURA: Summary of subgroup analysis of time to first PT: Thrombozytenzahl vermindert
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	11 (10,1)	NE [NE; NE]	115	1 (0,9)	NE [NE; NE]	10,99	[2,13;201,03]	0,0018*
Interaktion p-Wert									0,5299
Adjuvante Chemotherapie									
Ja	203	15 (7,4)	NE [NE; NE]	207	2 (1,0)	NE [NE; NE]	7,58	[2,14; 48,14]	0,0007*
Nein	134	6 (4,5)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	7 (6,5)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	14 (6,1)	NE [NE; NE]	257	2 (0,8)	NE [NE; NE]	7,93	[2,21; 50,50]	0,0006*
Interaktion p-Wert									NC
Region									
Asien	204	13 (6,4)	NE [NE; NE]	209	2 (1,0)	NE [NE; NE]	6,73	[1,86; 43,01]	0,0022*
Europa	61	4 (6,6)	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	3 (5,2)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.2.1 ADAURA: Summary of subgroup analysis of time to first SUE
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	24 (22,0)	NE [NE; NE]	95	16 (16,8)	NE [NE; NE]	1,07	[0,57; 2,05]	0,8423
Weiblich	228	44 (19,3)	NE [NE; NE]	248	31 (12,5)	NE [NE; NE]	1,37	[0,87; 2,18]	0,1811
Interaktion p-Wert									0,5363
Alter									
<65 Jahre	184	28 (15,2)	NE [NE; NE]	195	26 (13,3)	NE [NE; NE]	0,91	[0,53; 1,57]	0,7388
>=65 Jahre	153	40 (26,1)	NE [NE; NE]	148	21 (14,2)	NE [NE; NE]	1,78	[1,06; 3,07]	0,0285*
Interaktion p-Wert									0,0799
Abstammung									
Asiatisch	215	47 (21,9)	NE [NE; NE]	218	33 (15,1)	NE [NE; NE]	1,26	[0,81; 1,98]	0,3061
Nicht-asiatisch	122	21 (17,2)	NE [NE; NE]	125	14 (11,2)	NE [NE; NE]	1,33	[0,68; 2,67]	0,4078
Interaktion p-Wert									0,8996
EGFR-Mutation									
Exon 19 Deletion	187	35 (18,7)	NE [NE; NE]	191	25 (13,1)	NE [NE; NE]	1,14	[0,69; 1,93]	0,6063
L858R	150	33 (22,0)	NE [NE; NE]	152	22 (14,5)	NE [NE; NE]	1,46	[0,86; 2,54]	0,1650
Interaktion p-Wert									0,5213
Krankheitsstadium Version 7									
Stadium IB	105	21 (20,0)	NE [NE; NE]	106	16 (15,1)	NE [NE; NE]	1,42	[0,75; 2,77]	0,2847
Stadium II	118	23 (19,5)	NE [NE; NE]	118	21 (17,8)	NE [NE; NE]	0,96	[0,53; 1,75]	0,8910
Stadium IIIA	114	24 (21,1)	NE [NE; NE]	119	10 (8,4)	NE [NE; NE]	1,74	[0,85; 3,81]	0,1318
Interaktion p-Wert									0,4303
Krankheitsstadium Version 8									
Stadium IB	100	20 (20,0)	NE [NE; NE]	98	14 (14,3)	NE [NE; NE]	1,53	[0,78; 3,10]	0,2164
Stadium II	113	22 (19,5)	NE [NE; NE]	119	22 (18,5)	NE [NE; NE]	0,94	[0,52; 1,70]	0,8361

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.2.1 ADAURA: Summary of subgroup analysis of time to first SUE
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	24 (22,0)	NE [NE; NE]	115	10 (8,7)	NE [NE; NE]	1,76	[0,87; 3,87]	0,1206
Interaktion p-Wert									0,3567
Adjuvante Chemotherapie									
Ja	203	38 (18,7)	NE [NE; NE]	207	33 (15,9)	NE [NE; NE]	0,95	[0,60; 1,53]	0,8467
Nein	134	30 (22,4)	NE [NE; NE]	136	14 (10,3)	NE [NE; NE]	2,08	[1,12; 4,04]	0,0194*
Interaktion p-Wert									0,0497*
Raucherstatus									
Ja	108	28 (25,9)	NE [NE; NE]	86	15 (17,4)	NE [NE; NE]	1,25	[0,67; 2,40]	0,4879
Nein	229	40 (17,5)	NE [NE; NE]	257	32 (12,5)	NE [NE; NE]	1,23	[0,77; 1,97]	0,3822
Interaktion p-Wert									0,9730
Region									
Asien	204	45 (22,1)	NE [NE; NE]	209	32 (15,3)	NE [NE; NE]	1,26	[0,80; 1,99]	0,3242
Europa	61	16 (26,2)	NE [NE; NE]	69	8 (11,6)	NE [NE; NE]	2,07	[0,91; 5,10]	0,0843
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	6 (10,3)	NE [NE; NE]	54	7 (13,0)	NE [NE; NE]	0,67	[0,21; 2,01]	0,4653
Interaktion p-Wert									0,2650

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.3.1 ADAURA: Summary of subgroup analysis of time to first Therapieabbruch aufgrund von UE
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	16 (14,7)	NE [NE; NE]	95	3 (3,2)	NE [NE; NE]	4,24	[1,41; 18,26]	0,0080*
Weiblich	228	27 (11,8)	NE [NE; NE]	248	6 (2,4)	NE [NE; NE]	4,44	[1,96; 11,90]	0,0002*
Interaktion p-Wert									0,9541
Alter									
<65 Jahre	184	14 (7,6)	NE [NE; NE]	195	4 (2,1)	NE [NE; NE]	3,21	[1,15; 11,34]	0,0248*
>=65 Jahre	153	29 (19,0)	NE [NE; NE]	148	5 (3,4)	NE [NE; NE]	5,43	[2,29; 15,98]	<0,0001*
Interaktion p-Wert									0,4839
Abstammung									
Asiatisch	215	26 (12,1)	NE [NE; NE]	218	4 (1,8)	NE [NE; NE]	5,95	[2,32; 20,19]	<0,0001*
Nicht-asiatisch	122	17 (13,9)	NE [NE; NE]	125	5 (4,0)	NE [NE; NE]	3,22	[1,27; 9,80]	0,0123*
Interaktion p-Wert									0,4040
EGFR-Mutation									
Exon 19 Deletion	187	17 (9,1)	NE [NE; NE]	191	7 (3,7)	NE [NE; NE]	2,11	[0,91; 5,47]	0,0837
L858R	150	26 (17,3)	NE [NE; NE]	152	2 (1,3)	NE [NE; NE]	13,04	[3,90; 80,94]	<0,0001*
Interaktion p-Wert									0,0203*
Krankheitsstadium Version 7									
Stadium IB	105	17 (16,2)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	9,16	[2,63; 57,76]	0,0001*
Stadium II	118	13 (11,0)	NE [NE; NE]	118	4 (3,4)	NE [NE; NE]	3,00	[1,06; 10,67]	0,0375*
Stadium IIIA	114	13 (11,4)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	3,47	[1,11; 15,17]	0,0307*
Interaktion p-Wert									0,4262
Krankheitsstadium Version 8									
Stadium IB	100	17 (17,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	8,98	[2,58; 56,65]	0,0001*
Stadium II	113	12 (10,6)	NE [NE; NE]	119	4 (3,4)	NE [NE; NE]	2,97	[1,03; 10,63]	0,0429*

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.

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Table 4.3.3.1 ADAURA: Summary of subgroup analysis of time to first Therapieabbruch aufgrund von UE
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	11 (10,1)	NE [NE; NE]	115	3 (2,6)	NE [NE; NE]	2,94	[0,92; 13,05]	0,0715
Interaktion p-Wert									0,3920
Adjuvante Chemotherapie									
Ja	203	25 (12,3)	NE [NE; NE]	207	6 (2,9)	NE [NE; NE]	3,72	[1,63; 10,04]	0,0013*
Nein	134	18 (13,4)	NE [NE; NE]	136	3 (2,2)	NE [NE; NE]	5,87	[1,99; 25,10]	0,0007*
Interaktion p-Wert									0,5482
Raucherstatus									
Ja	108	20 (18,5)	NE [NE; NE]	86	5 (5,8)	NE [NE; NE]	2,93	[1,18; 8,81]	0,0186*
Nein	229	23 (10,0)	NE [NE; NE]	257	4 (1,6)	NE [NE; NE]	5,84	[2,24; 19,94]	0,0001*
Interaktion p-Wert									0,3469
Region									
Asien	204	26 (12,7)	NE [NE; NE]	209	4 (1,9)	NE [NE; NE]	6,04	[2,35; 20,47]	<0,0001*
Europa	61	7 (11,5)	NE [NE; NE]	69	3 (4,3)	NE [NE; NE]	2,46	[0,68; 11,43]	0,1720
Nordamerika	14	2 (14,3)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	1,35	[0,13; 29,02]	0,8040
Rest der Welt	58	8 (13,8)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	6,83	[1,25;126,80]	0,0233*
Interaktion p-Wert									0,5716

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.4.1 ADAURA: Summary of subgroup analysis of time to first UE mit CTCAE Grad >=3
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	29 (26,6)	NE [NE; NE]	95	15 (15,8)	NE [NE; NE]	1,57	[0,85; 3,00]	0,1510
Weiblich	228	50 (21,9)	NE [NE; NE]	248	33 (13,3)	NE [NE; NE]	1,53	[0,99; 2,40]	0,0545
Interaktion p-Wert									0,9572
Alter									
<65 Jahre	184	39 (21,2)	NE [NE; NE]	195	28 (14,4)	NE [NE; NE]	1,28	[0,79; 2,11]	0,3102
>=65 Jahre	153	40 (26,1)	NE [NE; NE]	148	20 (13,5)	NE [NE; NE]	1,97	[1,17; 3,44]	0,0108*
Interaktion p-Wert									0,2449
Abstammung									
Asiatisch	215	53 (24,7)	NE [NE; NE]	218	32 (14,7)	NE [NE; NE]	1,58	[1,03; 2,48]	0,0380*
Nicht-asiatisch	122	26 (21,3)	NE [NE; NE]	125	16 (12,8)	NE [NE; NE]	1,53	[0,83; 2,91]	0,1765
Interaktion p-Wert									0,9292
EGFR-Mutation									
Exon 19 Deletion	187	41 (21,9)	NE [NE; NE]	191	24 (12,6)	NE [NE; NE]	1,51	[0,92; 2,54]	0,1021
L858R	150	38 (25,3)	NE [NE; NE]	152	24 (15,8)	NE [NE; NE]	1,64	[0,99; 2,77]	0,0553
Interaktion p-Wert									0,8314
Krankheitsstadium Version 7									
Stadium IB	105	23 (21,9)	NE [NE; NE]	106	17 (16,0)	NE [NE; NE]	1,49	[0,80; 2,83]	0,2107
Stadium II	118	28 (23,7)	NE [NE; NE]	118	21 (17,8)	NE [NE; NE]	1,26	[0,72; 2,25]	0,4168
Stadium IIIA	114	28 (24,6)	NE [NE; NE]	119	10 (8,4)	NE [NE; NE]	2,30	[1,15; 4,99]	0,0174*
Interaktion p-Wert									0,4233
Krankheitsstadium Version 8									
Stadium IB	100	22 (22,0)	NE [NE; NE]	98	15 (15,3)	NE [NE; NE]	1,59	[0,83; 3,12]	0,1636
Stadium II	113	25 (22,1)	NE [NE; NE]	119	22 (18,5)	NE [NE; NE]	1,14	[0,64; 2,04]	0,6497

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.4.1 ADAURA: Summary of subgroup analysis of time to first UE mit CTCAE Grad >=3
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	28 (25,7)	NE [NE; NE]	115	10 (8,7)	NE [NE; NE]	2,31	[1,16; 5,00]	0,0169*
Interaktion p-Wert									0,3138
Adjuvante Chemotherapie									
Ja	203	44 (21,7)	NE [NE; NE]	207	30 (14,5)	NE [NE; NE]	1,34	[0,84; 2,15]	0,2164
Nein	134	35 (26,1)	NE [NE; NE]	136	18 (13,2)	NE [NE; NE]	1,96	[1,12; 3,53]	0,0174*
Interaktion p-Wert									0,3086
Raucherstatus									
Ja	108	35 (32,4)	NE [NE; NE]	86	14 (16,3)	NE [NE; NE]	1,91	[1,05; 3,67]	0,0339*
Nein	229	44 (19,2)	NE [NE; NE]	257	34 (13,2)	NE [NE; NE]	1,34	[0,86; 2,10]	0,2039
Interaktion p-Wert									0,3558
Region									
Asien	204	51 (25,0)	NE [NE; NE]	209	31 (14,8)	NE [NE; NE]	1,60	[1,03; 2,52]	0,0374*
Europa	61	16 (26,2)	NE [NE; NE]	69	10 (14,5)	NE [NE; NE]	1,67	[0,77; 3,81]	0,1985
Nordamerika	14	2 (14,3)	NE [NE; NE]	11	1 (9,1)	NE [NE; NE]	1,35	[0,13; 28,93]	0,8060
Rest der Welt	58	10 (17,2)	NE [NE; NE]	54	6 (11,1)	NE [NE; NE]	1,43	[0,53; 4,19]	0,4874
Interaktion p-Wert									0,9945

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.4.2 ADAURA: Summary of subgroup analysis of time to first G>=3 SOC: Erkrankungen des Gastrointestinaltrakts
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	5 (4,6)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	4,04	[0,65; 77,41]	0,1451
Weiblich	228	16 (7,0)	NE [NE; NE]	248	2 (0,8)	NE [NE; NE]	8,15	[2,32; 51,60]	0,0004*
Interaktion p-Wert									0,6086
Alter									
<65 Jahre	184	12 (6,5)	NE [NE; NE]	195	2 (1,0)	NE [NE; NE]	5,72	[1,56; 36,78]	0,0065*
>=65 Jahre	153	9 (5,9)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	8,55	[1,61;157,71]	0,0084*
Interaktion p-Wert									0,7535
Abstammung									
Asiatisch	215	15 (7,0)	NE [NE; NE]	218	2 (0,9)	NE [NE; NE]	7,12	[2,00; 45,18]	0,0012*
Nicht-asiatisch	122	6 (4,9)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	5,75	[0,98;108,66]	0,0528
Interaktion p-Wert									0,8728
EGFR-Mutation									
Exon 19 Deletion	187	9 (4,8)	NE [NE; NE]	191	2 (1,0)	NE [NE; NE]	4,06	[1,04; 26,69]	0,0427*
L858R	150	12 (8,0)	NE [NE; NE]	152	1 (0,7)	NE [NE; NE]	12,17	[2,40;221,58]	0,0009*
Interaktion p-Wert									0,3844
Krankheitsstadium Version 7									
Stadium IB	105	6 (5,7)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	6,38	[1,09;120,43]	0,0387*
Stadium II	118	9 (7,6)	NE [NE; NE]	118	2 (1,7)	NE [NE; NE]	4,22	[1,08; 27,67]	0,0368*
Stadium IIIA	114	6 (5,3)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,7530
Krankheitsstadium Version 8									
Stadium IB	100	5 (5,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	5,15	[0,83; 98,65]	0,0817

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.4.2 ADAURA: Summary of subgroup analysis of time to first G>=3 SOC: Erkrankungen des Gastrointestinaltrakts
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium II	113	8 (7,1)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	3,98	[0,996; 26,41]	0,0507
Stadium IIIA	109	6 (5,5)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,8478
Adjuvante Chemotherapie									
Ja	203	12 (5,9)	NE [NE; NE]	207	2 (1,0)	NE [NE; NE]	5,53	[1,50; 35,61]	0,0077*
Nein	134	9 (6,7)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	8,98	[1,69;165,48]	0,0068*
Interaktion p-Wert									0,7054
Raucherstatus									
Ja	108	4 (3,7)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	17 (7,4)	NE [NE; NE]	257	3 (1,2)	NE [NE; NE]	6,09	[2,04; 26,09]	0,0006*
Interaktion p-Wert									NC
Region									
Asien	204	15 (7,4)	NE [NE; NE]	209	2 (1,0)	NE [NE; NE]	7,15	[2,01; 45,42]	0,0011*
Europa	61	4 (6,6)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	4,23	[0,62; 82,63]	0,1479
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	1 (1,7)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,7022

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.4.3 ADAURA: Summary of subgroup analysis of time to first G>=3 SOC: Untersuchungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	6 (5,5)	NE [NE; NE]	95	2 (2,1)	NE [NE; NE]	2,18	[0,50; 14,92]	0,3126
Weiblich	228	8 (3,5)	NE [NE; NE]	248	2 (0,8)	NE [NE; NE]	3,65	[0,91; 24,22]	0,0686
Interaktion p-Wert									0,6517
Alter									
<65 Jahre	184	7 (3,8)	NE [NE; NE]	195	1 (0,5)	NE [NE; NE]	5,90	[1,05;110,34]	0,0436*
>=65 Jahre	153	7 (4,6)	NE [NE; NE]	148	3 (2,0)	NE [NE; NE]	2,04	[0,57; 9,49]	0,2819
Interaktion p-Wert									0,3822
Abstammung									
Asiatisch	215	9 (4,2)	NE [NE; NE]	218	3 (1,4)	NE [NE; NE]	2,54	[0,76; 11,48]	0,1362
Nicht-asiatisch	122	5 (4,1)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	4,37	[0,70; 83,76]	0,1217
Interaktion p-Wert									0,6649
EGFR-Mutation									
Exon 19 Deletion	187	8 (4,3)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	6 (4,0)	NE [NE; NE]	152	4 (2,6)	NE [NE; NE]	1,45	[0,41; 5,68]	0,5601
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	2 (1,9)	NE [NE; NE]	106	2 (1,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	6 (5,1)	NE [NE; NE]	118	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	6 (5,3)	NE [NE; NE]	119	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	2 (2,0)	NE [NE; NE]	98	2 (2,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	5 (4,4)	NE [NE; NE]	119	2 (1,7)	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.4.3 ADAURA: Summary of subgroup analysis of time to first G>=3 SOC: Untersuchungen
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	5 (4,6)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	9 (4,4)	NE [NE; NE]	207	1 (0,5)	NE [NE; NE]	7,29	[1,37;134,66]	0,0164*
Nein	134	5 (3,7)	NE [NE; NE]	136	3 (2,2)	NE [NE; NE]	1,56	[0,38; 7,59]	0,5390
Interaktion p-Wert									0,1988
Raucherstatus									
Ja	108	8 (7,4)	NE [NE; NE]	86	2 (2,3)	NE [NE; NE]	2,72	[0,68; 18,05]	0,1679
Nein	229	6 (2,6)	NE [NE; NE]	257	2 (0,8)	NE [NE; NE]	2,80	[0,64; 19,14]	0,1767
Interaktion p-Wert									0,9790
Region									
Asien	204	9 (4,4)	NE [NE; NE]	209	3 (1,4)	NE [NE; NE]	2,59	[0,77; 11,72]	0,1277
Europa	61	4 (6,6)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	3,96	[0,59; 77,45]	0,1687
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	1 (1,7)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									0,7408

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms. Analysis done for SOC and PT only if main effect for that SOC or PT is statistically significant at 5% level. [a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached. [b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable. HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.5.1 ADAURA: Summary of subgroup analysis of time to first UESI GT: ILD UND PNEUMONITIS
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	4 (3,7)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	7 (3,1)	NE [NE; NE]	248	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	5 (2,7)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	6 (3,9)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	8 (3,7)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	3 (2,5)	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	4 (2,1)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	7 (4,7)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	2 (1,9)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	3 (2,5)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	6 (5,3)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	2 (2,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	3 (2,7)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo. Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.

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Table 4.3.5.1 ADAURA: Summary of subgroup analysis of time to first UESI GT: ILD UND PNEUMONITIS
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	4 (3,7)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	9 (4,4)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	2 (1,5)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	6 (5,6)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	5 (2,2)	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	8 (3,9)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	0	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	1 (7,1)	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	2 (3,4)	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.5.2 ADAURA: Summary of subgroup analysis of time to first UESI GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	7 (6,4)	NE [NE; NE]	95	5 (5,3)	NE [NE; NE]	0,99	[0,31; 3,34]	0,9816
Weiblich	228	12 (5,3)	NE [NE; NE]	248	4 (1,6)	NE [NE; NE]	2,77	[0,96; 9,92]	0,0592
Interaktion p-Wert									0,2066
Alter									
<65 Jahre	184	7 (3,8)	NE [NE; NE]	195	5 (2,6)	NE [NE; NE]	1,16	[0,37; 3,94]	0,7958
>=65 Jahre	153	12 (7,8)	NE [NE; NE]	148	4 (2,7)	NE [NE; NE]	2,67	[0,93; 9,55]	0,0692
Interaktion p-Wert									0,3098
Abstammung									
Asiatisch	215	13 (6,0)	NE [NE; NE]	218	6 (2,8)	NE [NE; NE]	1,81	[0,71; 5,17]	0,2155
Nicht-asiatisch	122	6 (4,9)	NE [NE; NE]	125	3 (2,4)	NE [NE; NE]	1,79	[0,47; 8,51]	0,3965
Interaktion p-Wert									0,9908
EGFR-Mutation									
Exon 19 Deletion	187	12 (6,4)	NE [NE; NE]	191	5 (2,6)	NE [NE; NE]	1,90	[0,70; 5,99]	0,2119
L858R	150	7 (4,7)	NE [NE; NE]	152	4 (2,6)	NE [NE; NE]	1,65	[0,50; 6,31]	0,4144
Interaktion p-Wert									0,8649
Krankheitsstadium Version 7									
Stadium IB	105	5 (4,8)	NE [NE; NE]	106	3 (2,8)	NE [NE; NE]	1,76	[0,43; 8,59]	0,4302
Stadium II	118	3 (2,5)	NE [NE; NE]	118	3 (2,5)	NE [NE; NE]	0,86	[0,16; 4,62]	0,8482
Stadium IIIA	114	11 (9,6)	NE [NE; NE]	119	3 (2,5)	NE [NE; NE]	2,52	[0,78; 11,21]	0,1279
Interaktion p-Wert									0,5805
Krankheitsstadium Version 8									
Stadium IB	100	5 (5,0)	NE [NE; NE]	98	3 (3,1)	NE [NE; NE]	1,73	[0,42; 8,42]	0,4470
Stadium II	113	5 (4,4)	NE [NE; NE]	119	4 (3,4)	NE [NE; NE]	1,17	[0,31; 4,72]	0,8171

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.

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Table 4.3.5.2 ADAURA: Summary of subgroup analysis of time to first UESI GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	8 (7,3)	NE [NE; NE]	115	2 (1,7)	NE [NE; NE]	2,86	[0,71; 19,01]	0,1475
Interaktion p-Wert									0,6777
Adjuvante Chemotherapie									
Ja	203	10 (4,9)	NE [NE; NE]	207	4 (1,9)	NE [NE; NE]	2,03	[0,68; 7,43]	0,2123
Nein	134	9 (6,7)	NE [NE; NE]	136	5 (3,7)	NE [NE; NE]	1,67	[0,58; 5,44]	0,3482
Interaktion p-Wert									0,8094
Raucherstatus									
Ja	108	6 (5,6)	NE [NE; NE]	86	5 (5,8)	NE [NE; NE]	0,78	[0,23; 2,70]	0,6790
Nein	229	13 (5,7)	NE [NE; NE]	257	4 (1,6)	NE [NE; NE]	3,09	[1,09; 10,99]	0,0326*
Interaktion p-Wert									0,0944
Region									
Asien	204	13 (6,4)	NE [NE; NE]	209	6 (2,9)	NE [NE; NE]	1,84	[0,72; 5,24]	0,2051
Europa	61	3 (4,9)	NE [NE; NE]	69	2 (2,9)	NE [NE; NE]	1,49	[0,25; 11,34]	0,6578
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	3 (5,2)	NE [NE; NE]	54	1 (1,9)	NE [NE; NE]	2,44	[0,31; 49,34]	0,4111
Interaktion p-Wert									0,9445

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.
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Table 4.3.6.1 ADAURA: Summary of subgroup analysis of time to first UESI G>=3 GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	3 (2,8)	NE [NE; NE]	95	1 (1,1)	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	1 (0,4)	NE [NE; NE]	248	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	1 (0,5)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	3 (2,0)	NE [NE; NE]	148	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	3 (1,4)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	1 (0,8)	NE [NE; NE]	125	1 (0,8)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	2 (1,1)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	2 (1,3)	NE [NE; NE]	152	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	3 (2,9)	NE [NE; NE]	106	1 (0,9)	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	1 (0,8)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	0	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	3 (3,0)	NE [NE; NE]	98	1 (1,0)	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	1 (0,9)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.

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Table 4.3.6.1 ADAURA: Summary of subgroup analysis of time to first UESI G>=3 GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	0	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	0	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	4 (3,0)	NE [NE; NE]	136	1 (0,7)	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	3 (2,8)	NE [NE; NE]	86	1 (1,2)	NE [NE; NE]	NC	[NC]	NC
Nein	229	1 (0,4)	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	3 (1,5)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	1 (1,6)	NE [NE; NE]	69	1 (1,4)	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	0	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2faa 12JUL2023:07:07 kfrh585

Table 4.3.7.1 ADAURA: Summary of subgroup analysis of time to first SUESI GT: ILD UND PNEUMONITIS
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	1 (0,9)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	1 (0,4)	NE [NE; NE]	248	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	0	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	2 (1,3)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	2 (0,9)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	0	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	0	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	2 (1,3)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	0	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	2 (1,7)	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	0	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	0	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	2 (1,8)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.

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Table 4.3.7.1 ADAURA: Summary of subgroup analysis of time to first SUESI GT: ILD UND PNEUMONITIS
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	0	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	2 (1,0)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	0	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	2 (1,9)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	0	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	2 (1,0)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	0	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	0	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2gaa 12JUL2023:07:07 kfrh585

Table 4.3.7.2 ADAURA: Summary of subgroup analysis of time to first SUESI GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Geschlecht									
Maennlich	109	1 (0,9)	NE [NE; NE]	95	0	NE [NE; NE]	NC	[NC]	NC
Weiblich	228	1 (0,4)	NE [NE; NE]	248	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Alter									
<65 Jahre	184	1 (0,5)	NE [NE; NE]	195	0	NE [NE; NE]	NC	[NC]	NC
>=65 Jahre	153	1 (0,7)	NE [NE; NE]	148	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Abstammung									
Asiatisch	215	2 (0,9)	NE [NE; NE]	218	0	NE [NE; NE]	NC	[NC]	NC
Nicht-asiatisch	122	0	NE [NE; NE]	125	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
EGFR-Mutation									
Exon 19 Deletion	187	1 (0,5)	NE [NE; NE]	191	0	NE [NE; NE]	NC	[NC]	NC
L858R	150	1 (0,7)	NE [NE; NE]	152	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 7									
Stadium IB	105	1 (1,0)	NE [NE; NE]	106	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	118	0	NE [NE; NE]	118	0	NE [NE; NE]	NC	[NC]	NC
Stadium IIIA	114	1 (0,9)	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Krankheitsstadium Version 8									
Stadium IB	100	1 (1,0)	NE [NE; NE]	98	0	NE [NE; NE]	NC	[NC]	NC
Stadium II	113	0	NE [NE; NE]	119	0	NE [NE; NE]	NC	[NC]	NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2gab 12JUL2023:07:07 kfrh585

Table 4.3.7.2 ADAURA: Summary of subgroup analysis of time to first SUESI GT: KARDIALE EFFEKTE (HERZINSUFFIZIENZ)
Safety Analysis Set, DCO 11Apr2022

	AZD9291 (N=337)			Placebo (N=343)					
Subgruppen	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	n	Anzahl (%) der Patienten mit Ereignis	Mediane Zeit [95%-KI] (Monate) [a]	Hazard Ratio [b]	[95%-KI] [b]	2-seitiger p-Wert [b]
Stadium IIIA	109	1 (0,9)	NE [NE; NE]	115	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Adjuvante Chemotherapie									
Ja	203	1 (0,5)	NE [NE; NE]	207	0	NE [NE; NE]	NC	[NC]	NC
Nein	134	1 (0,7)	NE [NE; NE]	136	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Raucherstatus									
Ja	108	1 (0,9)	NE [NE; NE]	86	0	NE [NE; NE]	NC	[NC]	NC
Nein	229	1 (0,4)	NE [NE; NE]	257	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC
Region									
Asien	204	2 (1,0)	NE [NE; NE]	209	0	NE [NE; NE]	NC	[NC]	NC
Europa	61	0	NE [NE; NE]	69	0	NE [NE; NE]	NC	[NC]	NC
Nordamerika	14	0	NE [NE; NE]	11	0	NE [NE; NE]	NC	[NC]	NC
Rest der Welt	58	0	NE [NE; NE]	54	0	NE [NE; NE]	NC	[NC]	NC
Interaktion p-Wert									NC

Time to event of AE is defined as the time from first dose of study treatment to first onset of the respective AE or the time to censoring if the AE has not occurred by 28 days following discontinuation of study treatment, before administration of subsequent cancer therapy or death, whichever comes first. All AEs are coded using MedDRA version 24.1. Includes AEs with onset date on or after the date of first dose and up to and including 28 days following discontinuation of Osimertinib/Placebo.
Analysis done if >=10 patients at each subgroup level and >=10 events in at least one subgroup level combined for both arms.
[a] Median time to event based on the Kaplan Meier estimate. NE = Not estimable as median (or 95% CLs) is not reached.
[b] Estimated from main effects of unstratified Cox proportional hazard model including trt., subgroup and subgroup-by-trt. interaction. Ties handled using Efron method and 95% CI derived from profile likelihood estimation. NC = Not calculable.
HR <1 favours Osimertinib. * p<0.05.
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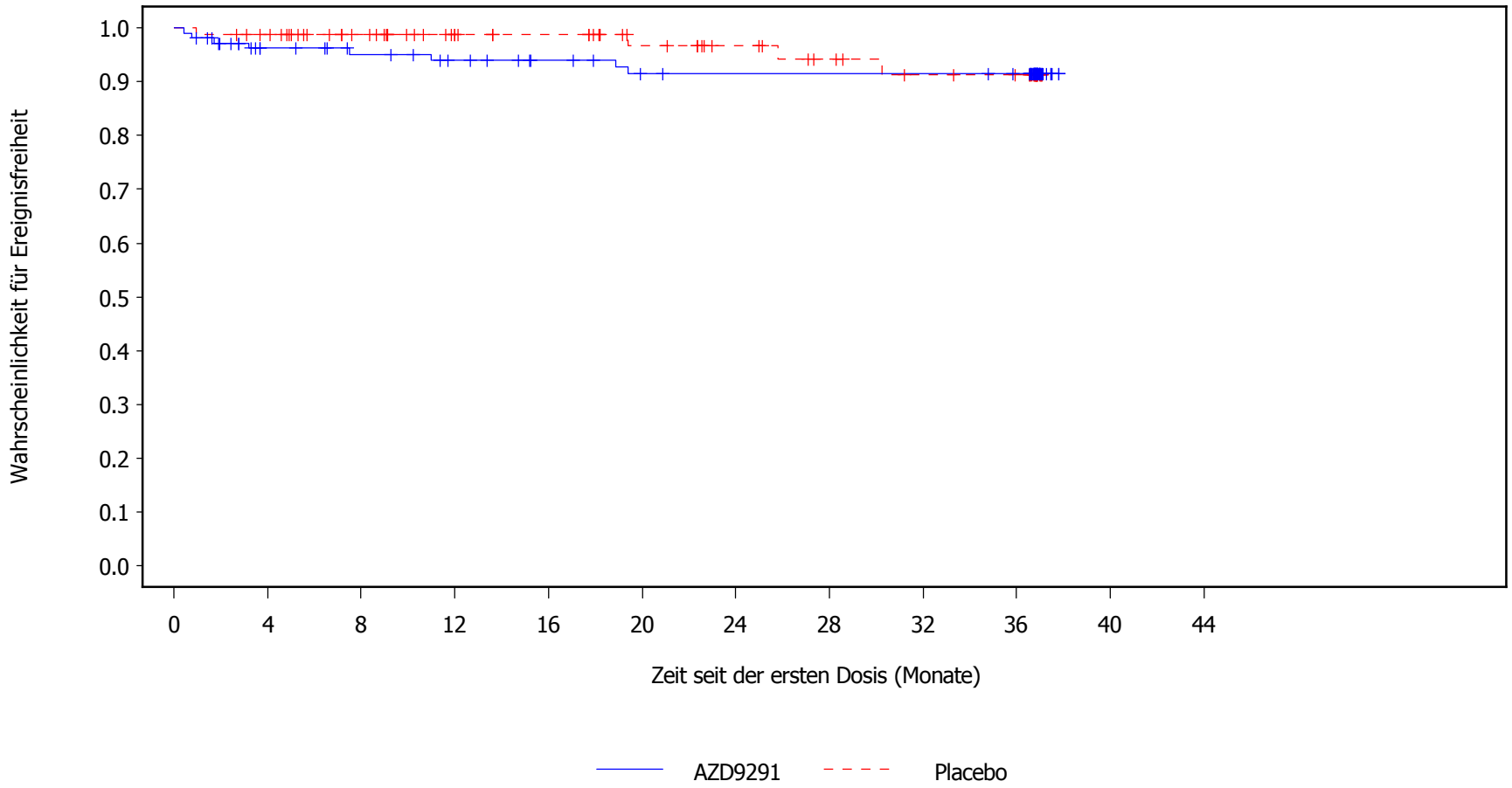
Figure 4.4.1.1 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Epistaxis for Raucherstatus=Ja
Safety Analysis Set, DCO 11Apr2022



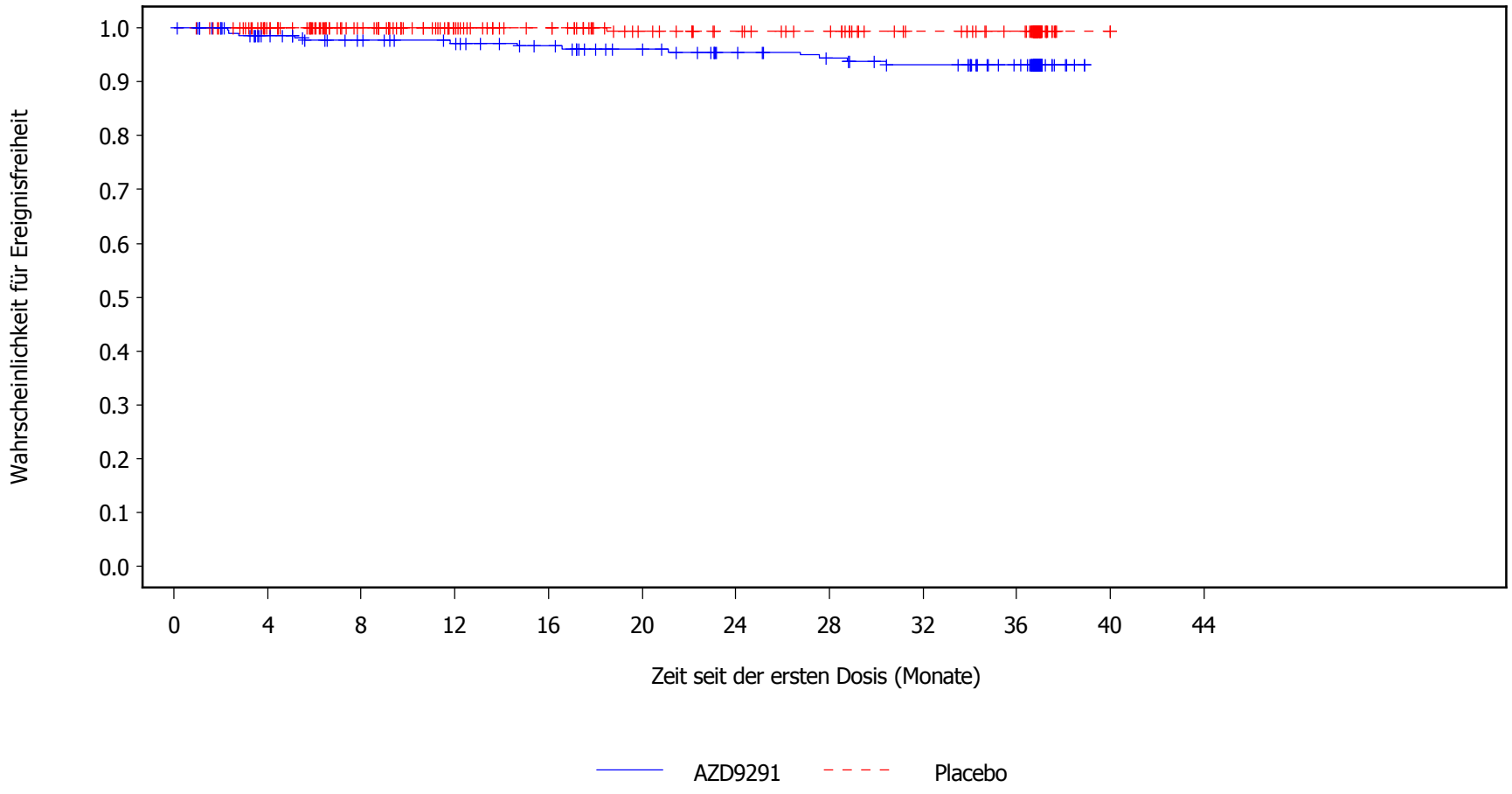
Anzahl an Patienten unter Risiko:

108	92	87	82	77	72	71	71	71	69	0	0	AZD9291
86	82	70	57	54	46	40	35	31	29	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2haa 12JUL2023:07:07 kfrh585

Nutzenbewertung nach AMNOG Seite 1 von 1

Figure 4.4.1.2 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Epistaxis for Raucherstatus=Nein
Safety Analysis Set, DCO 11Apr2022

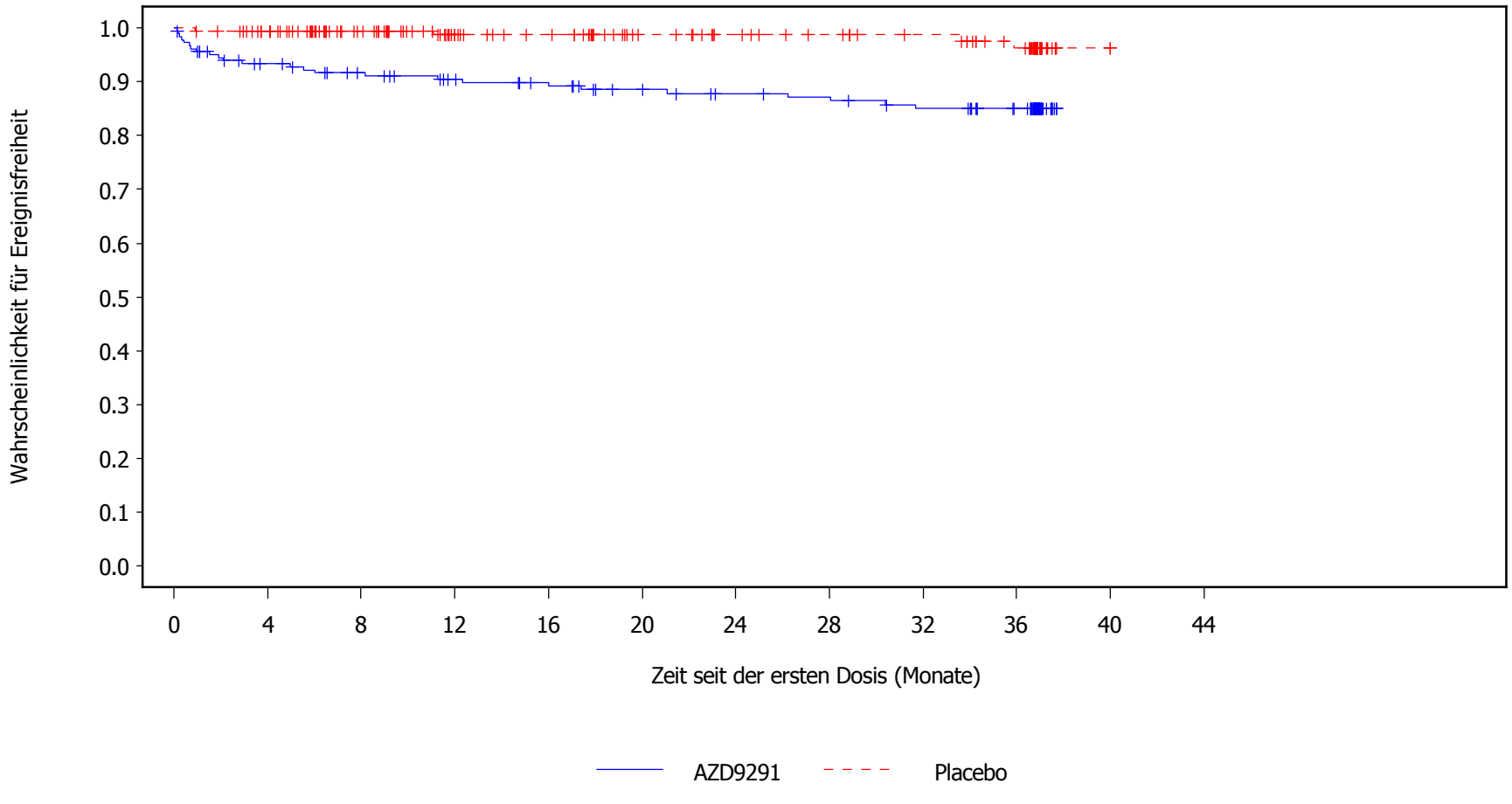


Anzahl an Patienten unter Risiko:

229	209	197	191	183	173	163	157	151	138	0	0	AZD9291
257	238	208	177	164	145	136	130	117	109	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hab 12JUL2023:07:07 kfrh585

Figure 4.4.1.3 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Ausschlag for Alter=<65 Jahre
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

184	163	154	146	141	133	128	126	121	113	0	0	AZD9291
195	185	158	127	120	103	96	91	86	76	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hac 12JUL2023:07:07 kfrh585

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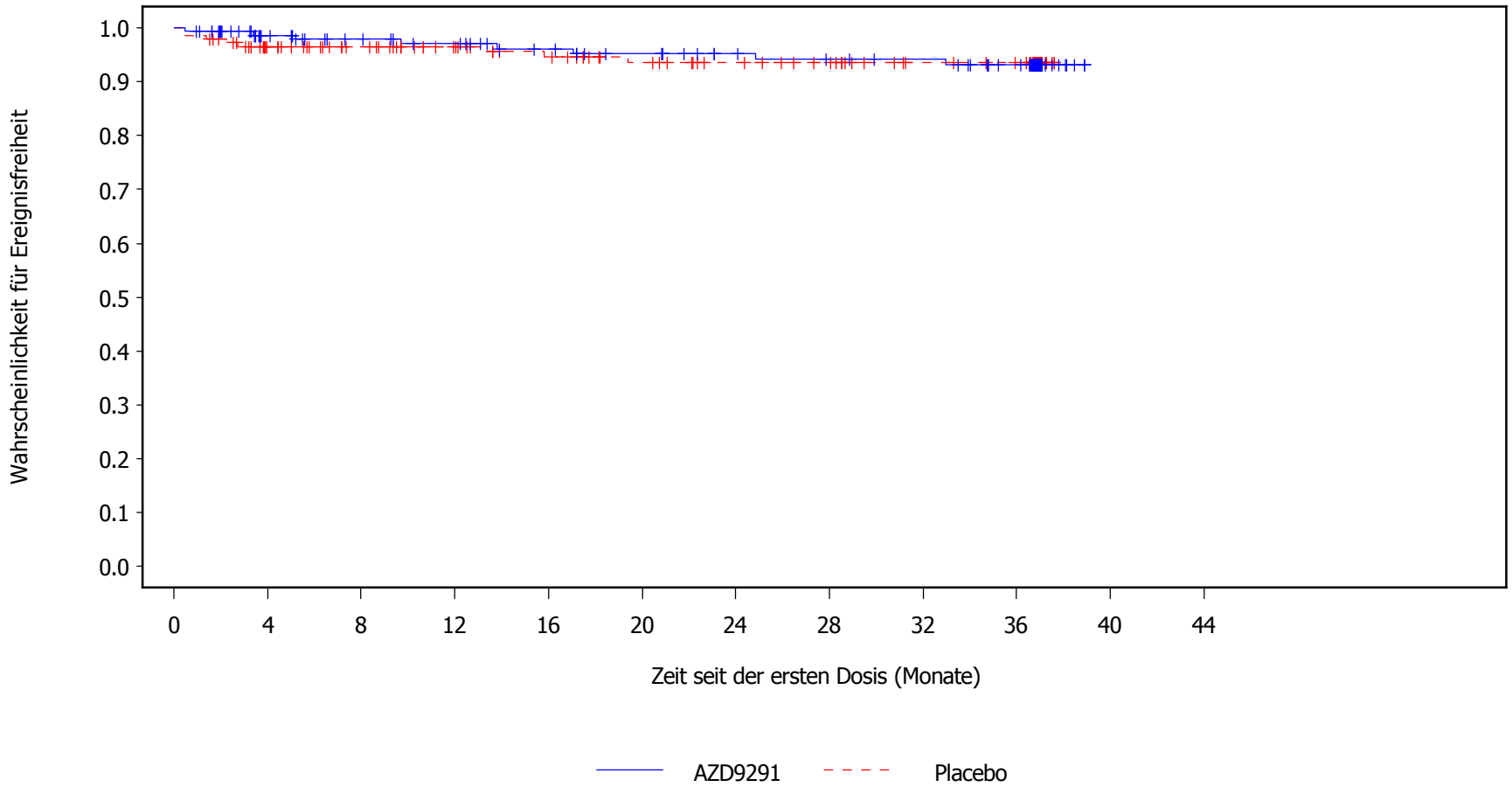
Figure 4.4.1.4 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Ausschlag for Alter=>=65 Jahre
Safety Analysis Set, DCO 11Apr2022

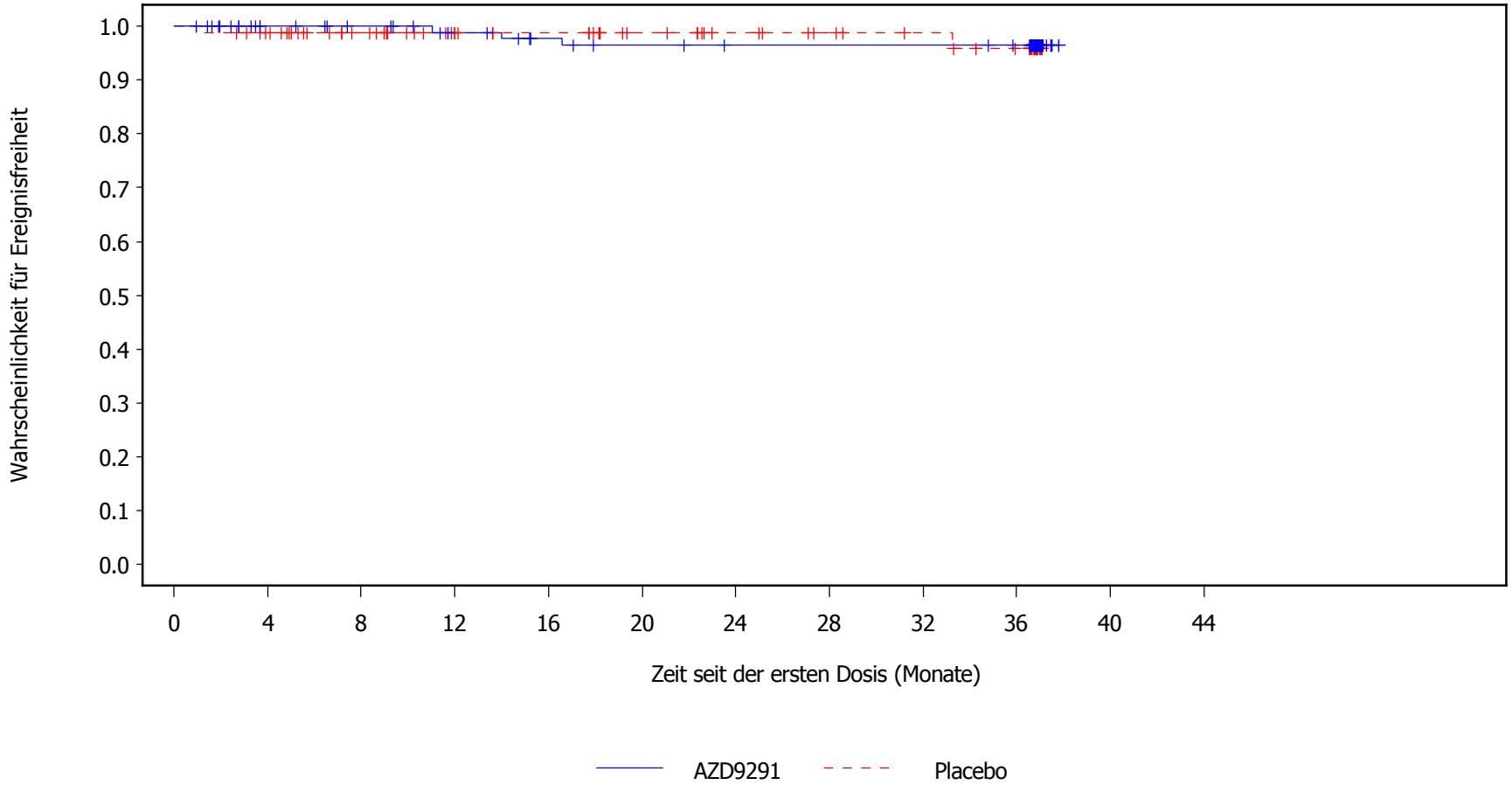


Anzahl an Patienten unter Risiko:

153	132	122	117	109	103	97	94	92	84	0	0	AZD9291
148	129	116	103	94	85	78	73	63	60	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2had 12JUL2023:07:07 kfrh585

Figure 4.4.1.5 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Haematurie for Raucherstatus=Ja
Safety Analysis Set, DCO 11Apr2022

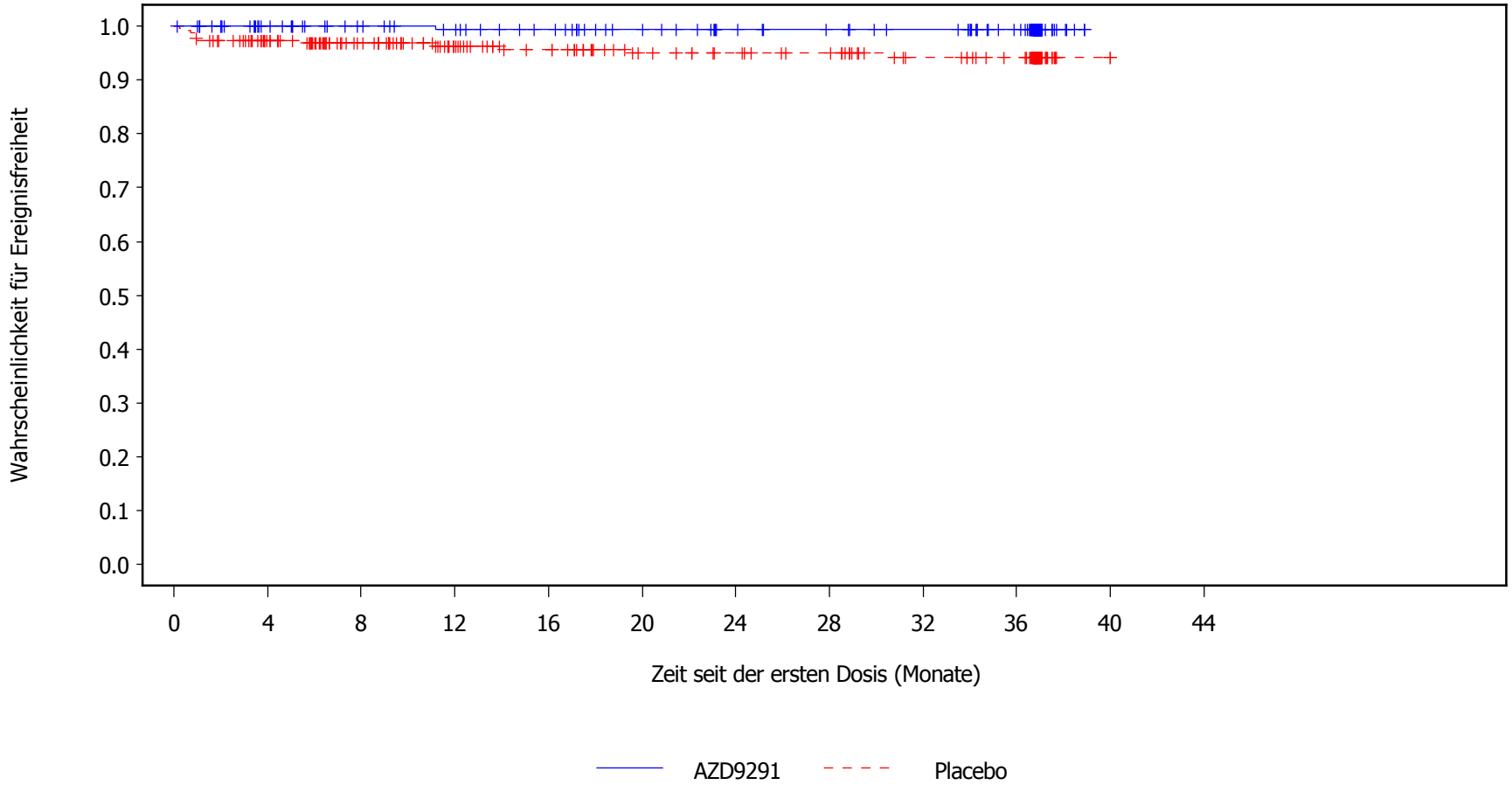


Anzahl an Patienten unter Risiko:

108	96	92	86	81	78	76	76	76	74	0	0	AZD9291
86	81	69	56	53	46	40	36	33	29	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hae 12JUL2023:07:07 kfrh585

Figure 4.4.1.6 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Haematurie for Raucherstatus=Nein
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

229	212	201	195	188	178	169	165	161	148	0	0	AZD9291
257	231	200	169	155	137	131	126	112	105	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2haf 12JUL2023:07:07 kfrh585

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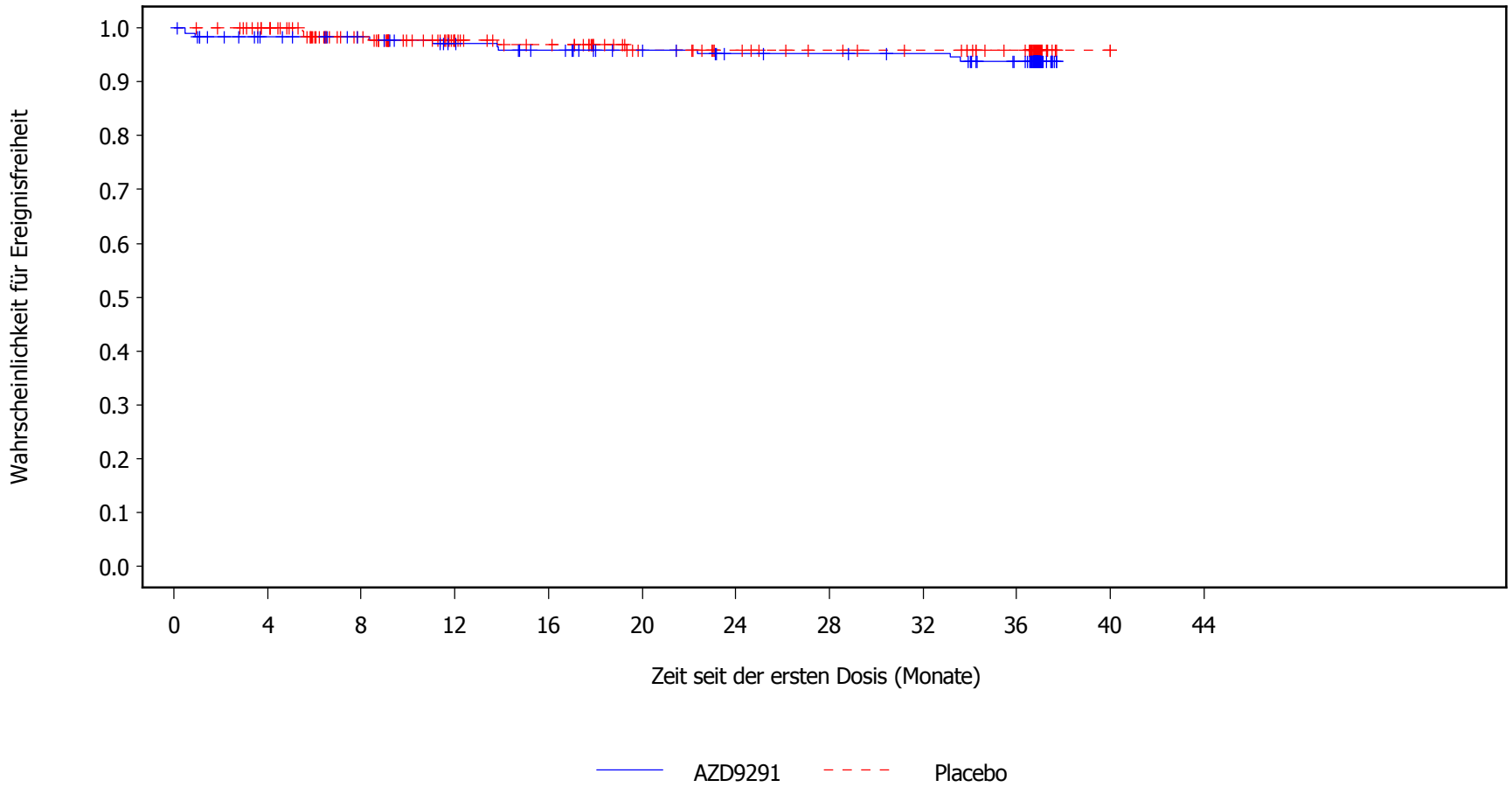
Figure 4.4.1.7 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Anaemie for Alter=<65 Jahre
Safety Analysis Set, DCO 11Apr2022

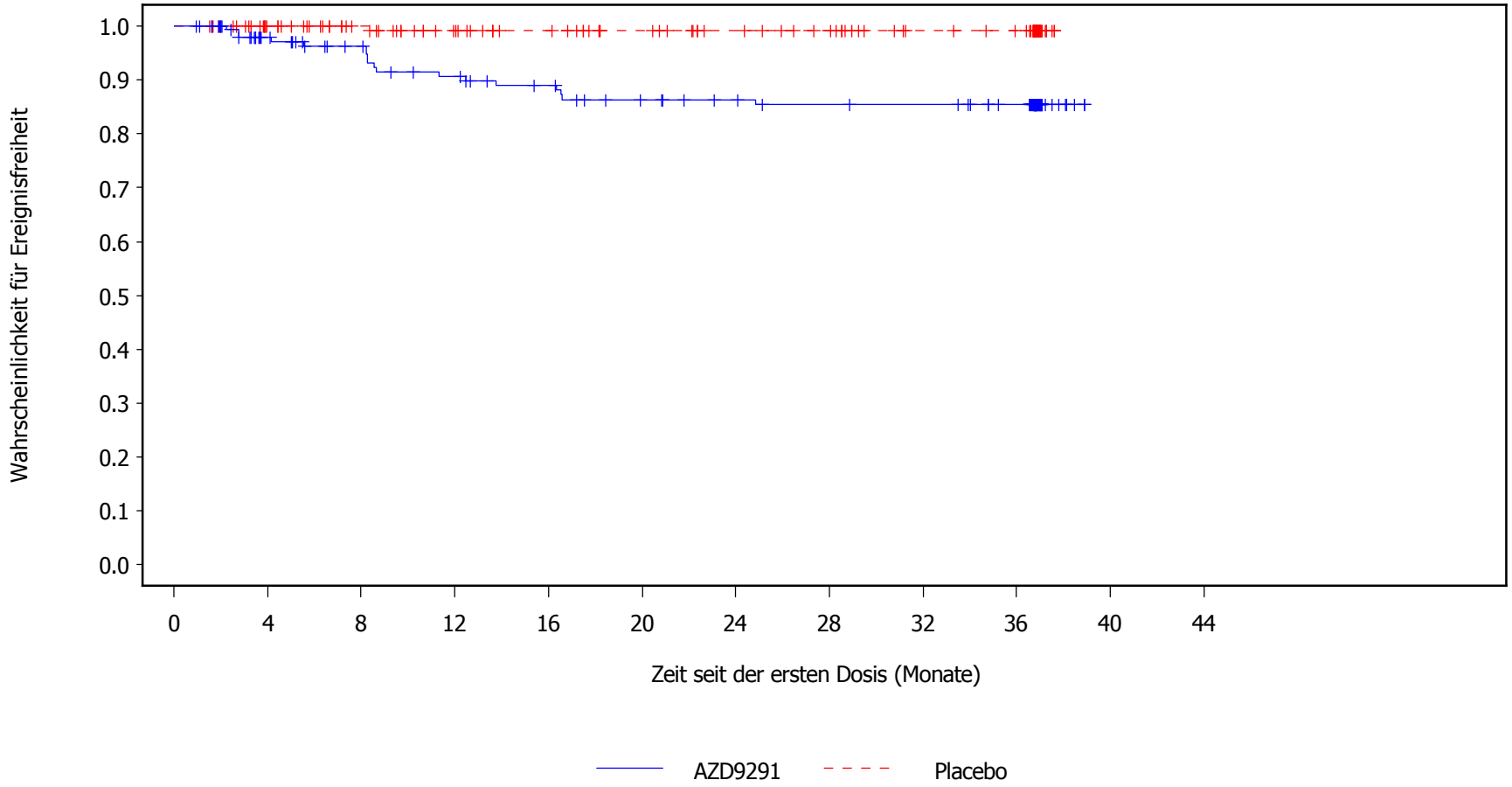


Anzahl an Patienten unter Risiko:

184	171	165	157	151	144	138	137	135	126	0	0 AZD9291
195	186	157	126	118	100	93	88	85	77	0	0 Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hag 12JUL2023:07:07 kfrh585

Figure 4.4.1.8 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Anaemie for Alter=>=65 Jahre
Safety Analysis Set, DCO 11Apr2022

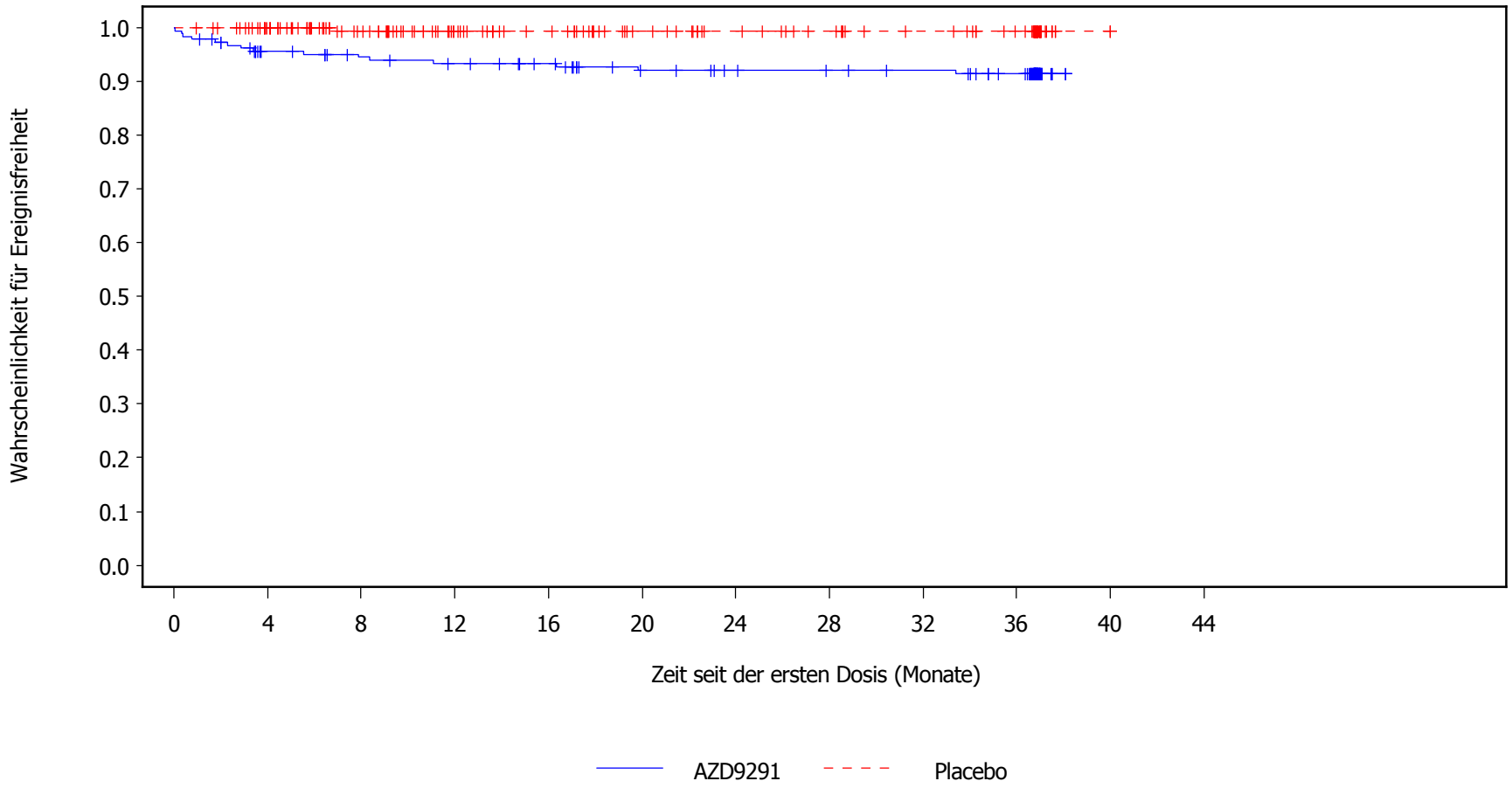


Anzahl an Patienten unter Risiko:

153	131	120	110	103	95	91	88	87	81	0	0	AZD9291
148	134	119	106	97	89	81	76	65	62	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hah 12JUL2023:07:07 kfrh585

Figure 4.4.1.9 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Abdominalschmerz for EGFR-Mutation=Exon 19 Deletion
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

187	168	161	157	152	141	137	135	133	126	0	0	AZD9291
191	177	150	124	112	96	87	81	74	67	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hai 12JUL2023:07:07 kfrh585

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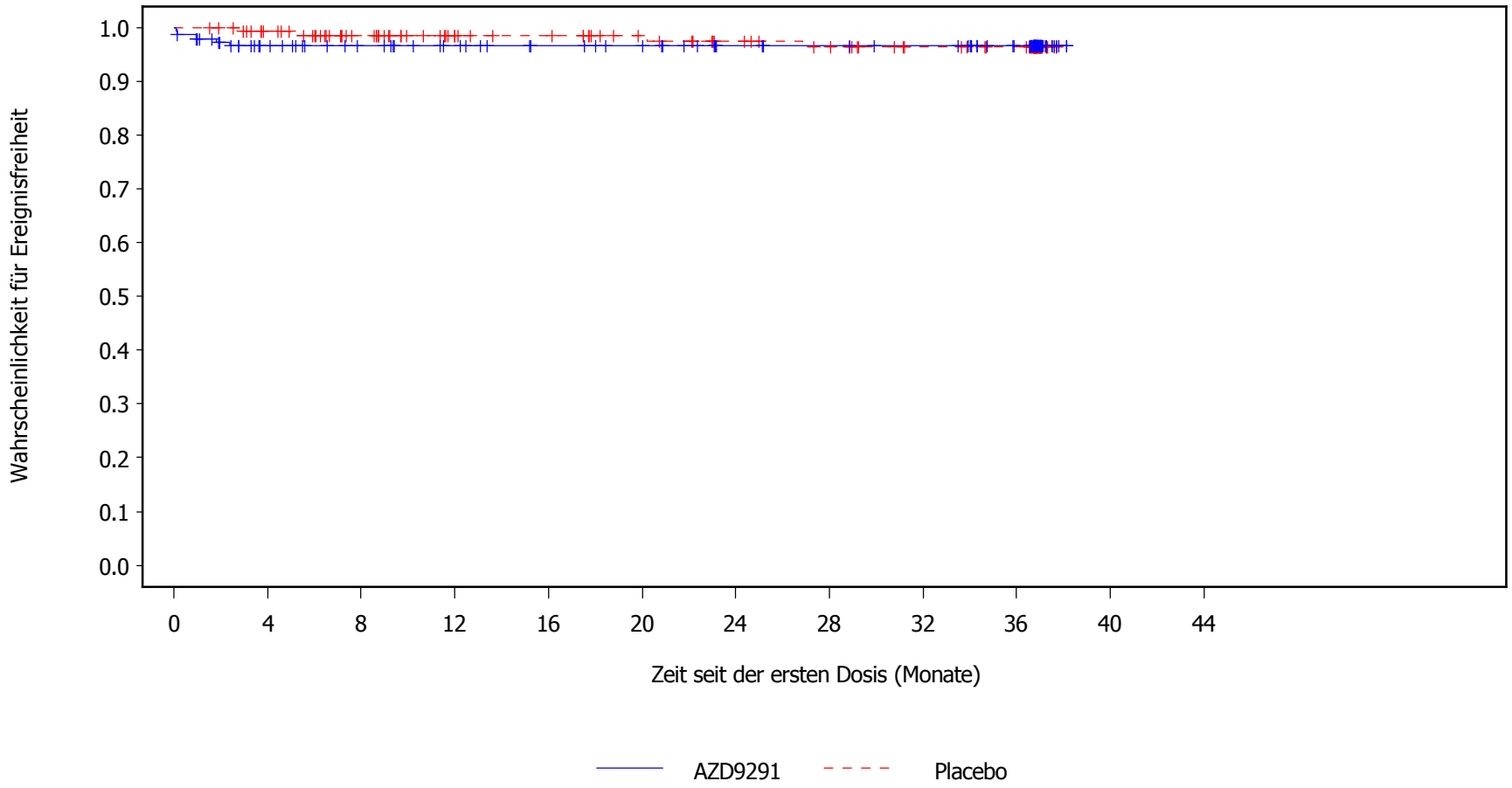
Figure 4.4.1.10 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Abdominalschmerz for EGFR-Mutation=L858R
Safety Analysis Set, DCO 11Apr2022

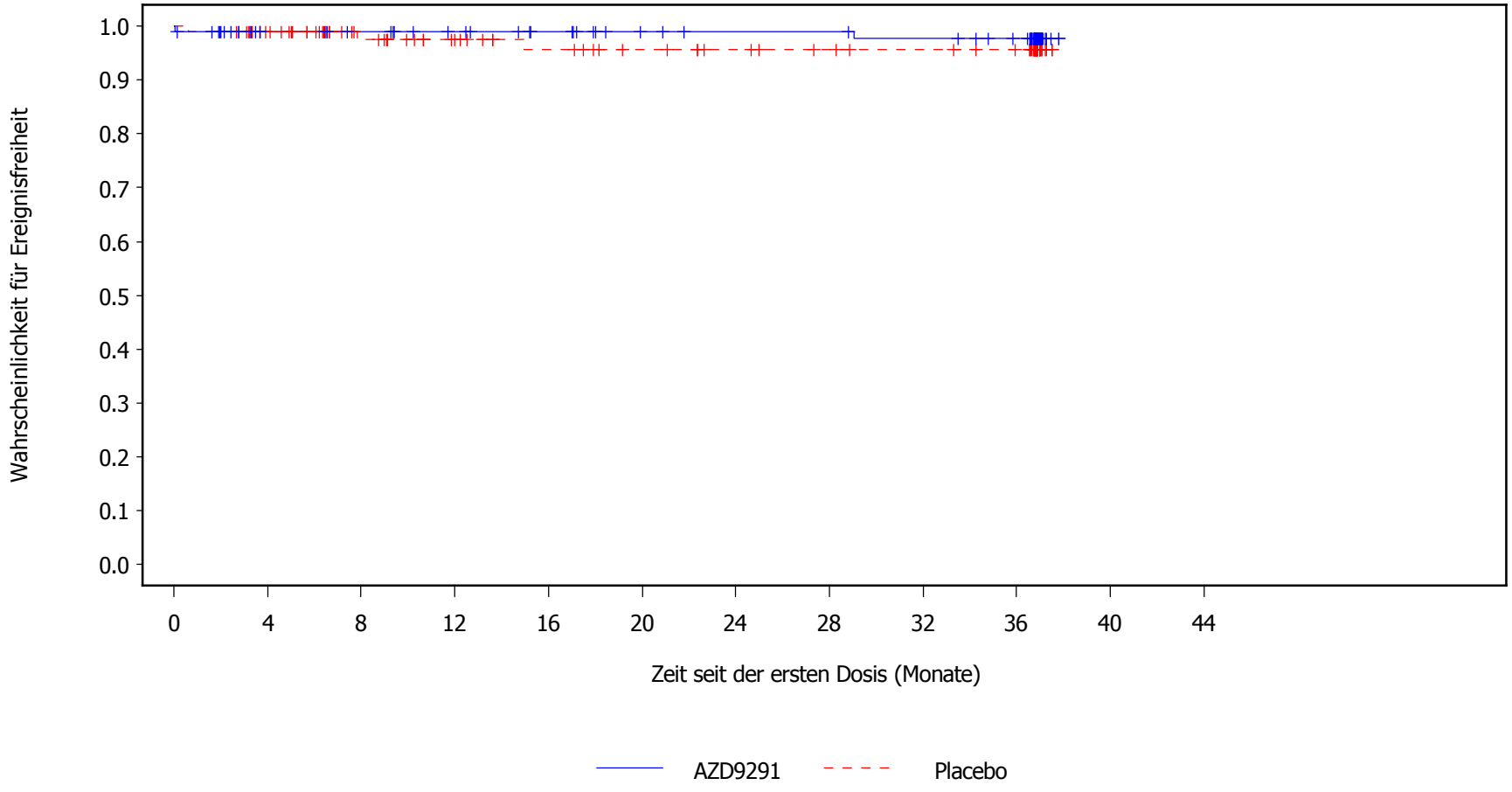


Anzahl an Patienten unter Risiko:

150	131	122	115	109	106	98	96	94	85	0	0	AZD9291
152	142	125	107	104	95	88	83	74	70	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2haj 12JUL2023:07:07 kfrh585

Figure 4.4.1.11 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Dyspepsie for Geschlecht=Maennlich
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

109	94	91	86	81	74	72	72	70	66	0	0	AZD9291
95	88	70	59	53	48	44	41	39	36	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hak 12JUL2023:07:07 kfrh585

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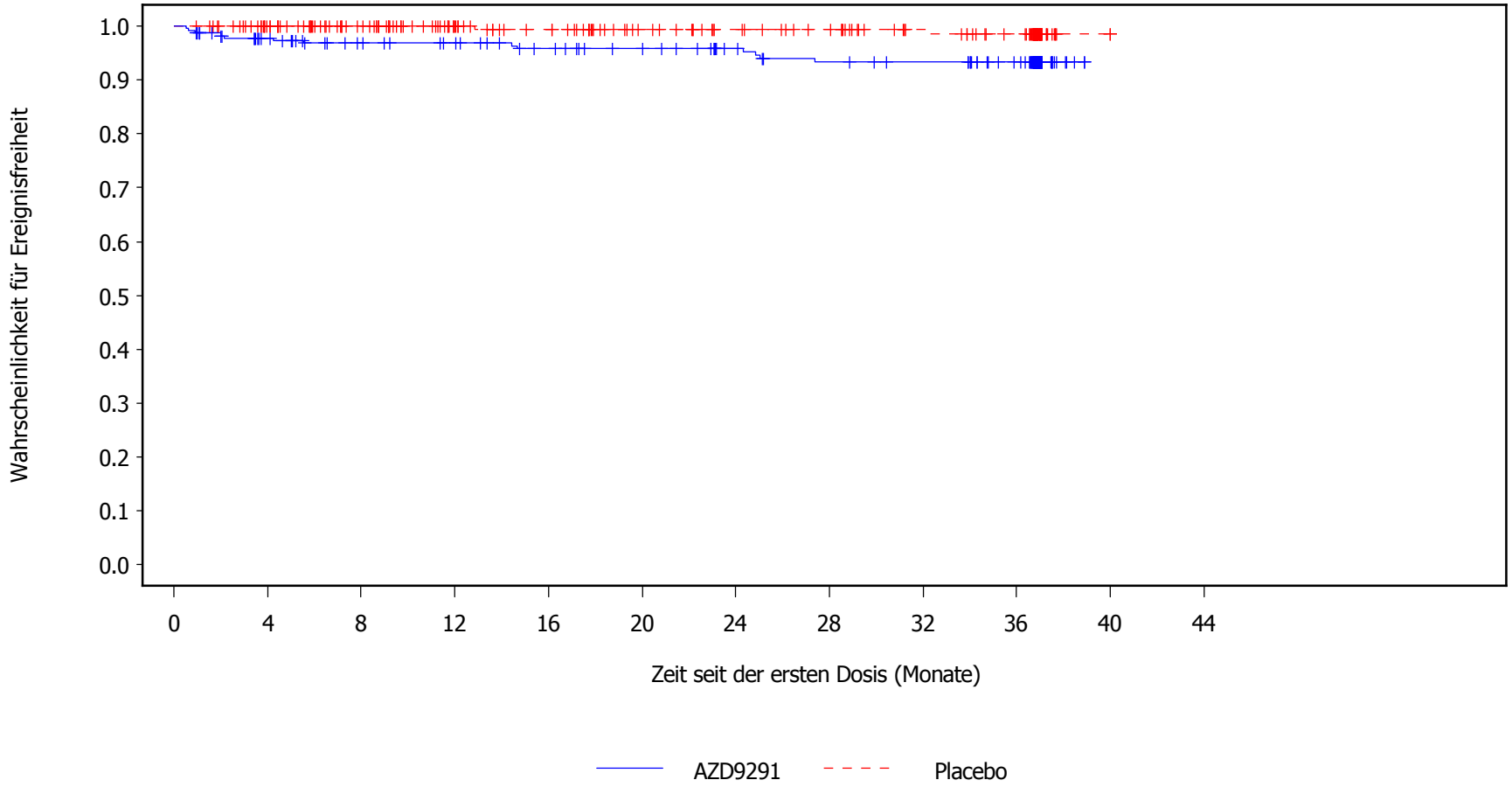
Figure 4.4.1.12 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Dyspepsie for Geschlecht=Weiblich
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

228	209	196	191	182	176	166	159	156	145	0	0	AZD9291
248	231	206	175	163	144	134	127	113	104	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hal 12JUL2023:07:07 kfrh585

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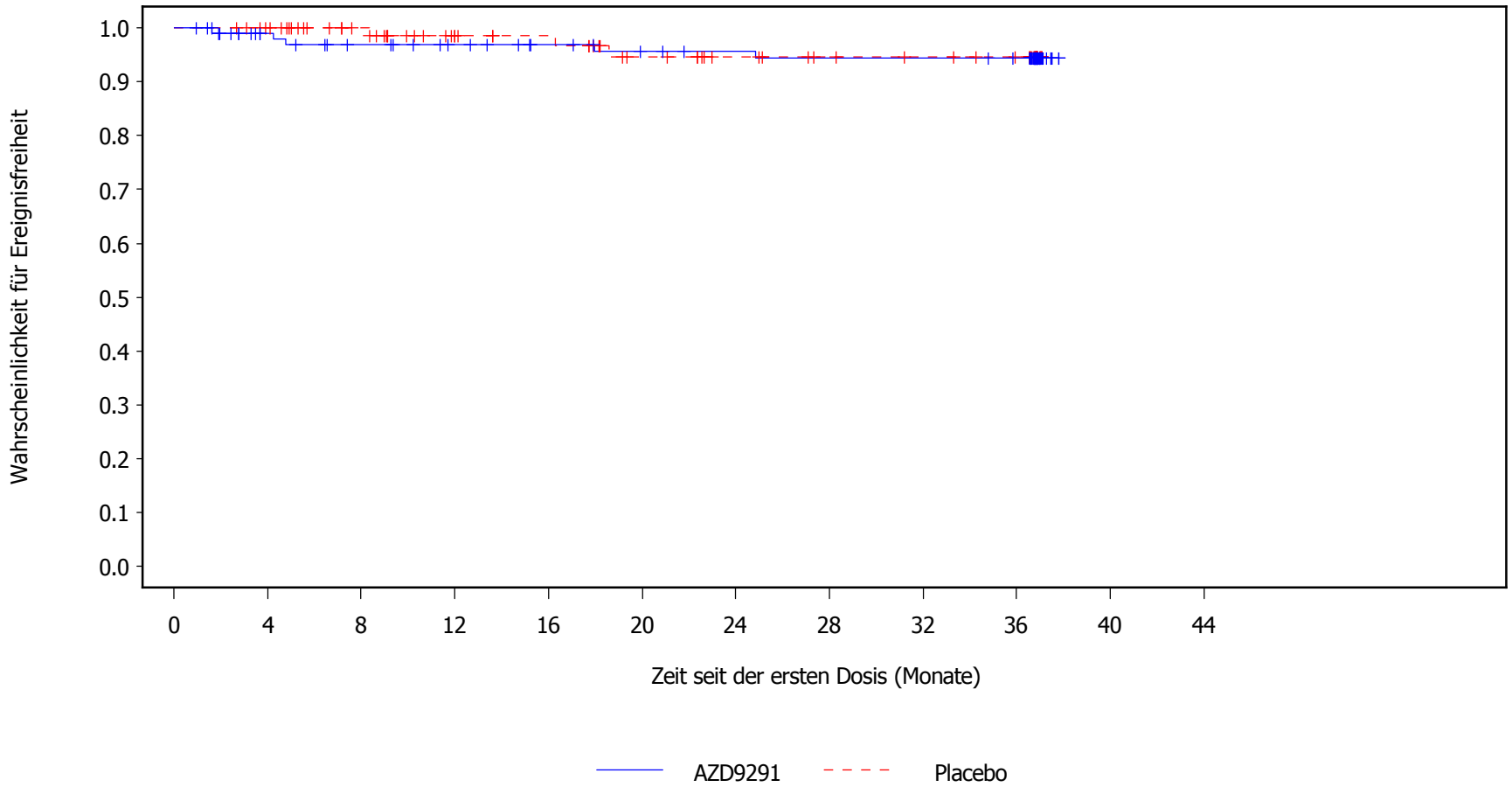
Figure 4.4.1.13 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Muskelspasmen for Raucherstatus=Ja
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

108	95	89	84	79	75	73	72	72	70	0	0	AZD9291
86	82	70	56	53	44	38	34	32	29	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2ham 12JUL2023:07:07 kfrh585

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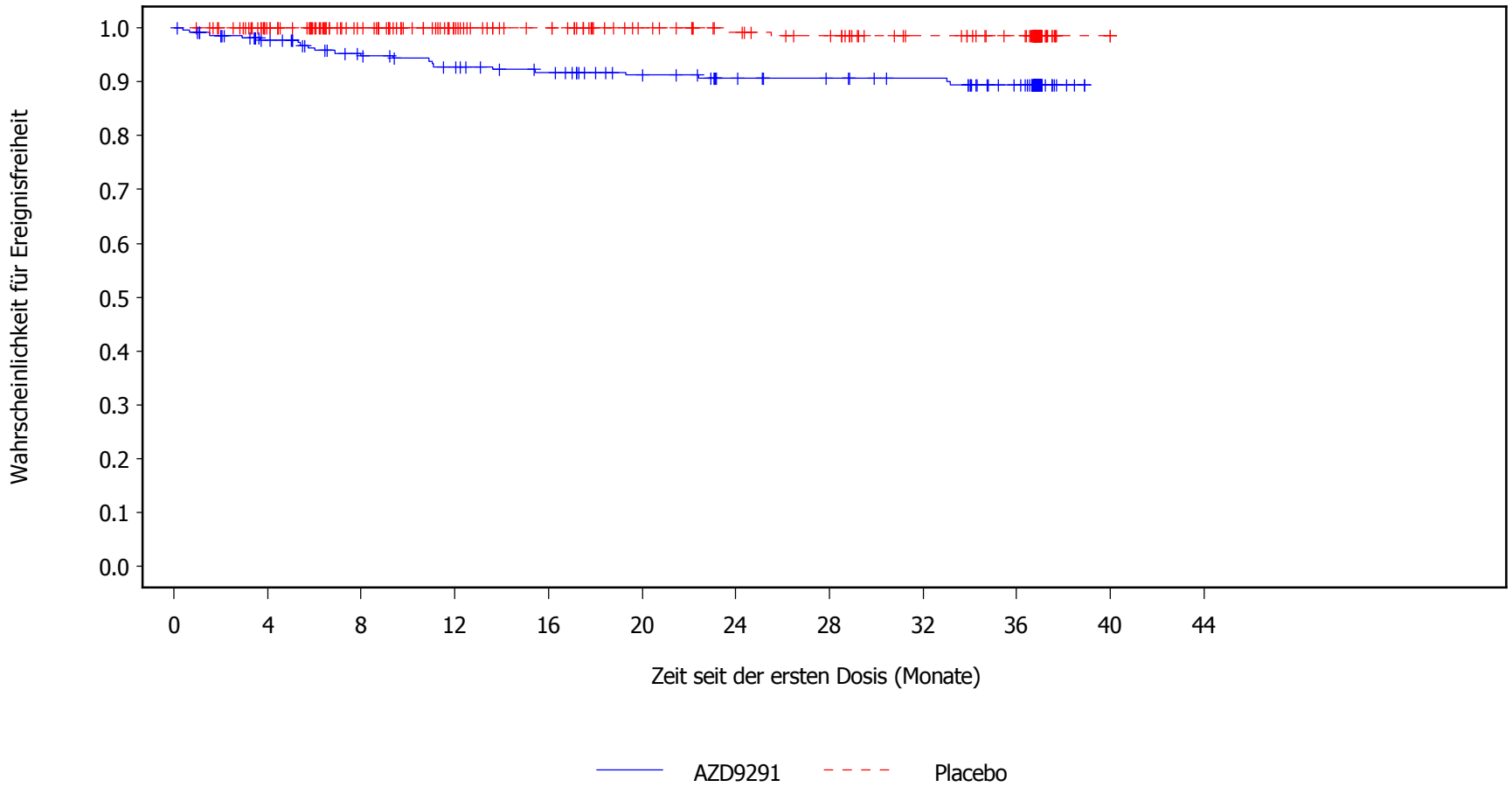
Figure 4.4.1.14 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Muskelspasmen for Raucherstatus=Nein
Safety Analysis Set, DCO 11Apr2022

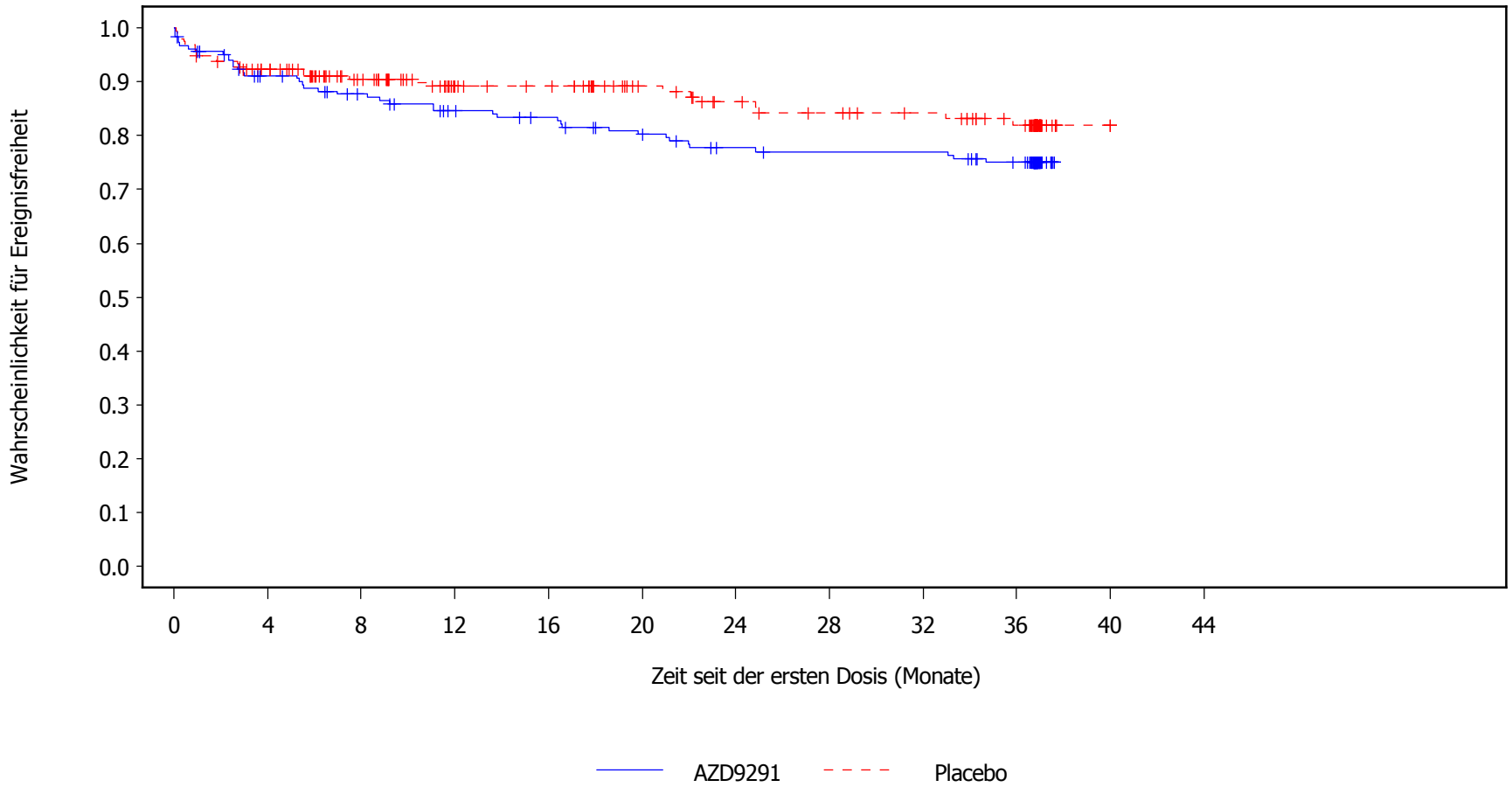


Anzahl an Patienten unter Risiko:

229	209	192	184	176	165	156	152	148	135	0	0	AZD9291
257	238	208	177	164	146	136	130	117	109	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2han 12JUL2023:07:07 kfrh585

Figure 4.4.1.15 ADAURA Subgroup Analysis: Kaplan-Meier plot of SOC: Stoffwechsel- und Ernaehrungsstoerungen for Alter=<65 Jahre
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

184	159	148	138	133	125	117	115	115	107	0	0	AZD9291
195	171	145	116	112	95	86	81	77	67	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hao 12JUL2023:07:07 kfrh585

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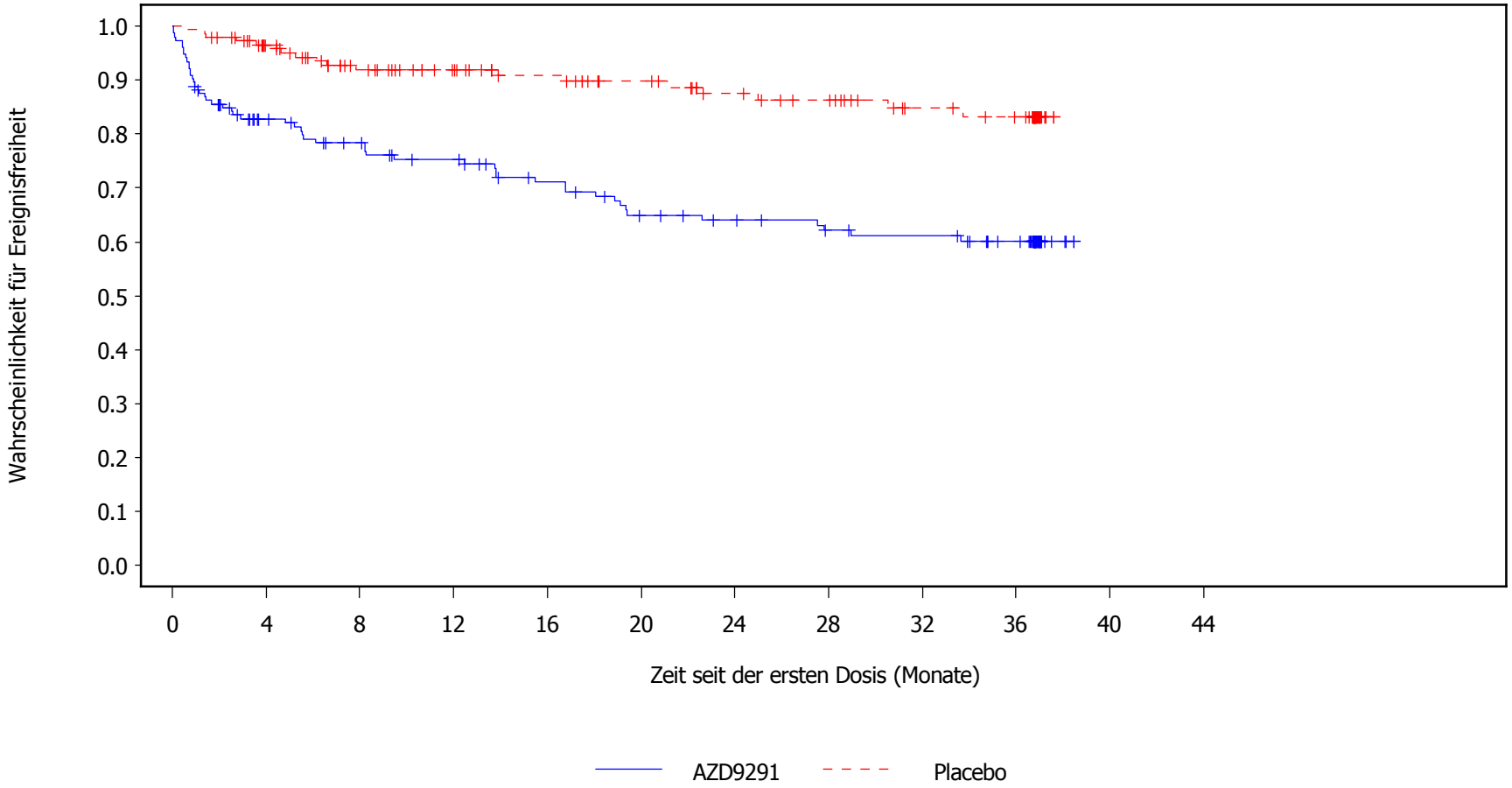
Figure 4.4.1.16 ADAURA Subgroup Analysis: Kaplan-Meier plot of SOC: Stoffwechsel- und Ernaehrungsstoerungen for Alter=>=65 Jahre
Safety Analysis Set, DCO 11Apr2022

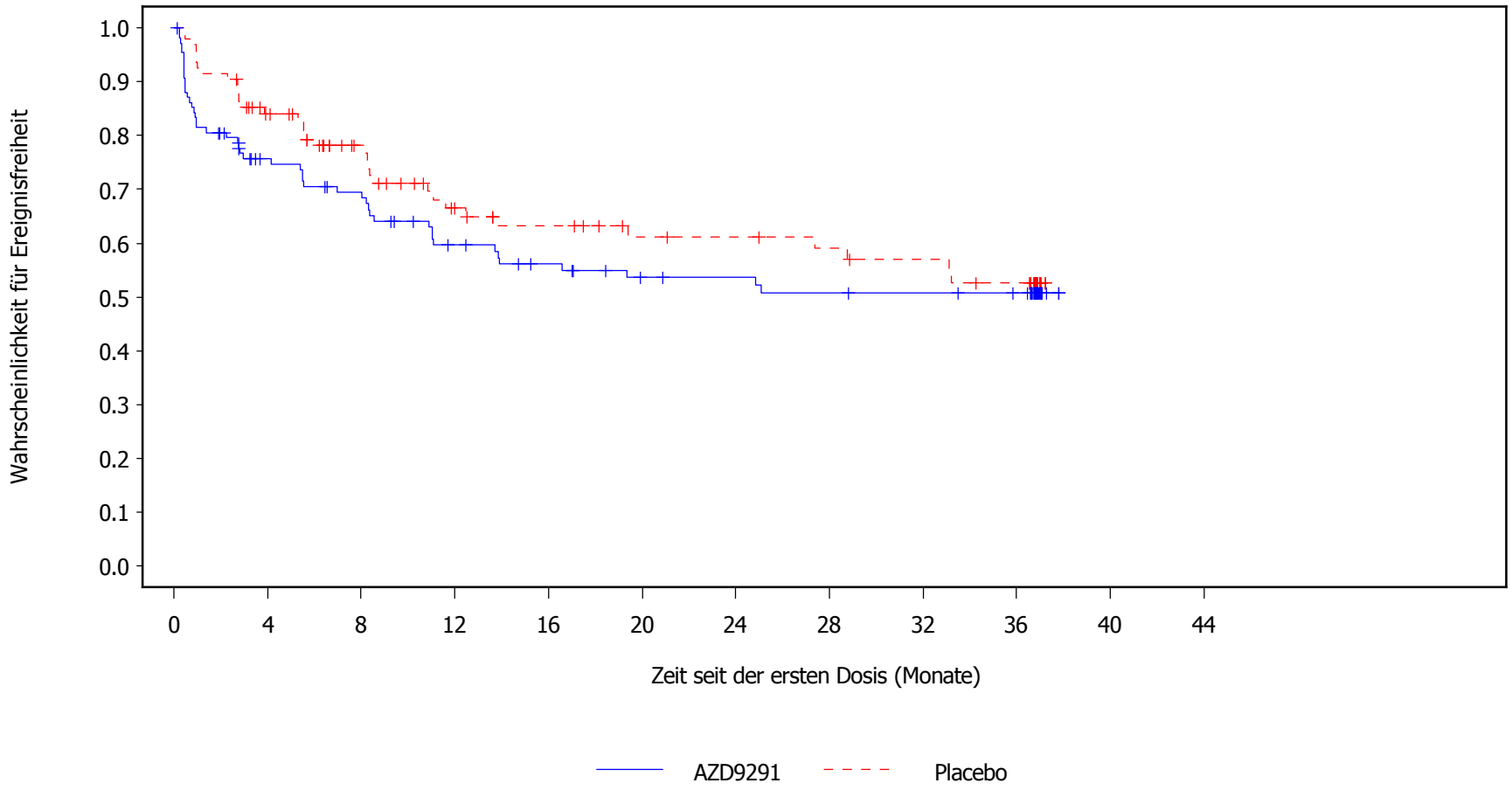


Anzahl an Patienten unter Risiko:

153	113	102	94	83	73	69	64	62	54	0	0	AZD9291
148	130	110	98	88	80	71	66	56	52	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hap 12JUL2023:07:07 kfrh585

Figure 4.4.1.17 ADAURA Subgroup Analysis: Kaplan-Meier plot of SOC: Untersuchungen for Geschlecht=Maennlich
Safety Analysis Set, DCO 11Apr2022

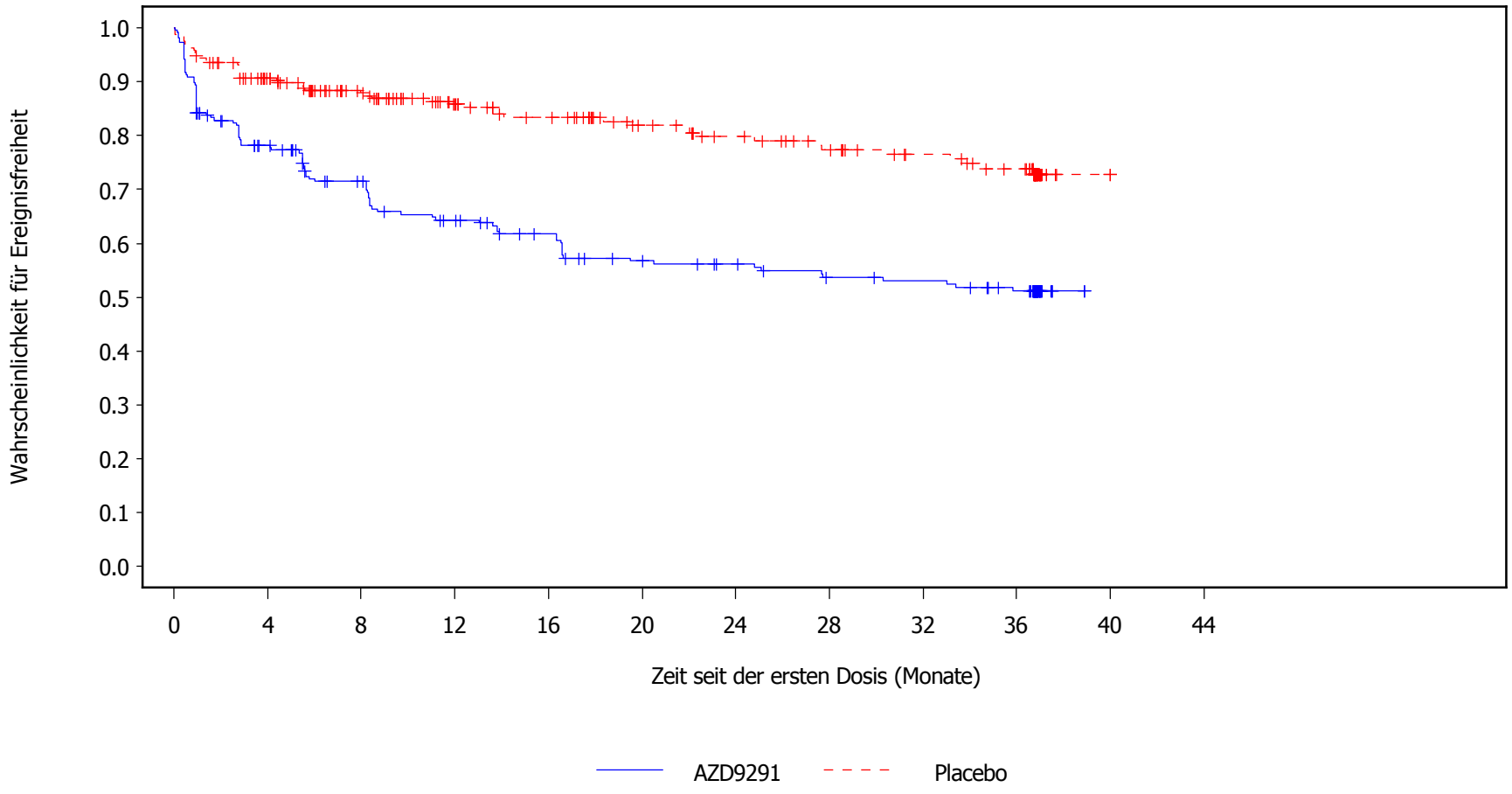


Anzahl an Patienten unter Risiko:

109	73	65	52	46	40	39	37	36	34	0	0	AZD9291
95	74	56	41	36	31	30	28	26	23	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2haq 12JUL2023:07:07 kfrh585

Figure 4.4.1.18 ADAURA Subgroup Analysis: Kaplan-Meier plot of SOC: Untersuchungen for Geschlecht=Weiblich
Safety Analysis Set, DCO 11Apr2022

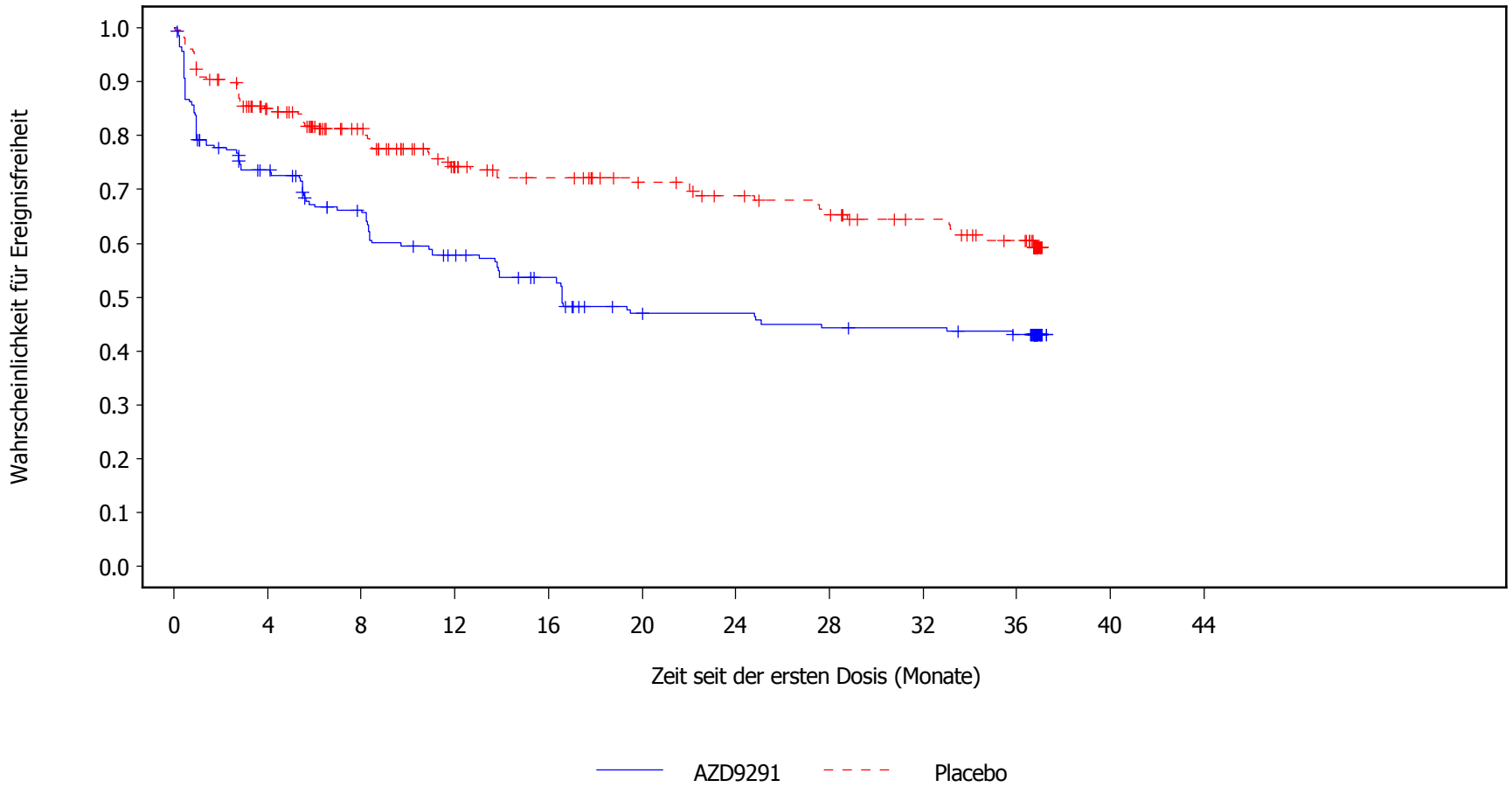


Anzahl an Patienten unter Risiko:

228	167	142	124	112	99	94	87	85	78	0	0	AZD9291
248	209	178	147	134	116	106	97	87	79	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2har 12JUL2023:07:07 kfrh585

Figure 4.4.1.19 ADAURA Subgroup Analysis: Kaplan-Meier plot of SOC: Untersuchungen for Region=Asien
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

204	141	119	101	89	72	71	67	66	62	0	0	AZD9291
209	164	137	106	97	88	81	75	66	57	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2has 12JUL2023:07:07 kfrh585

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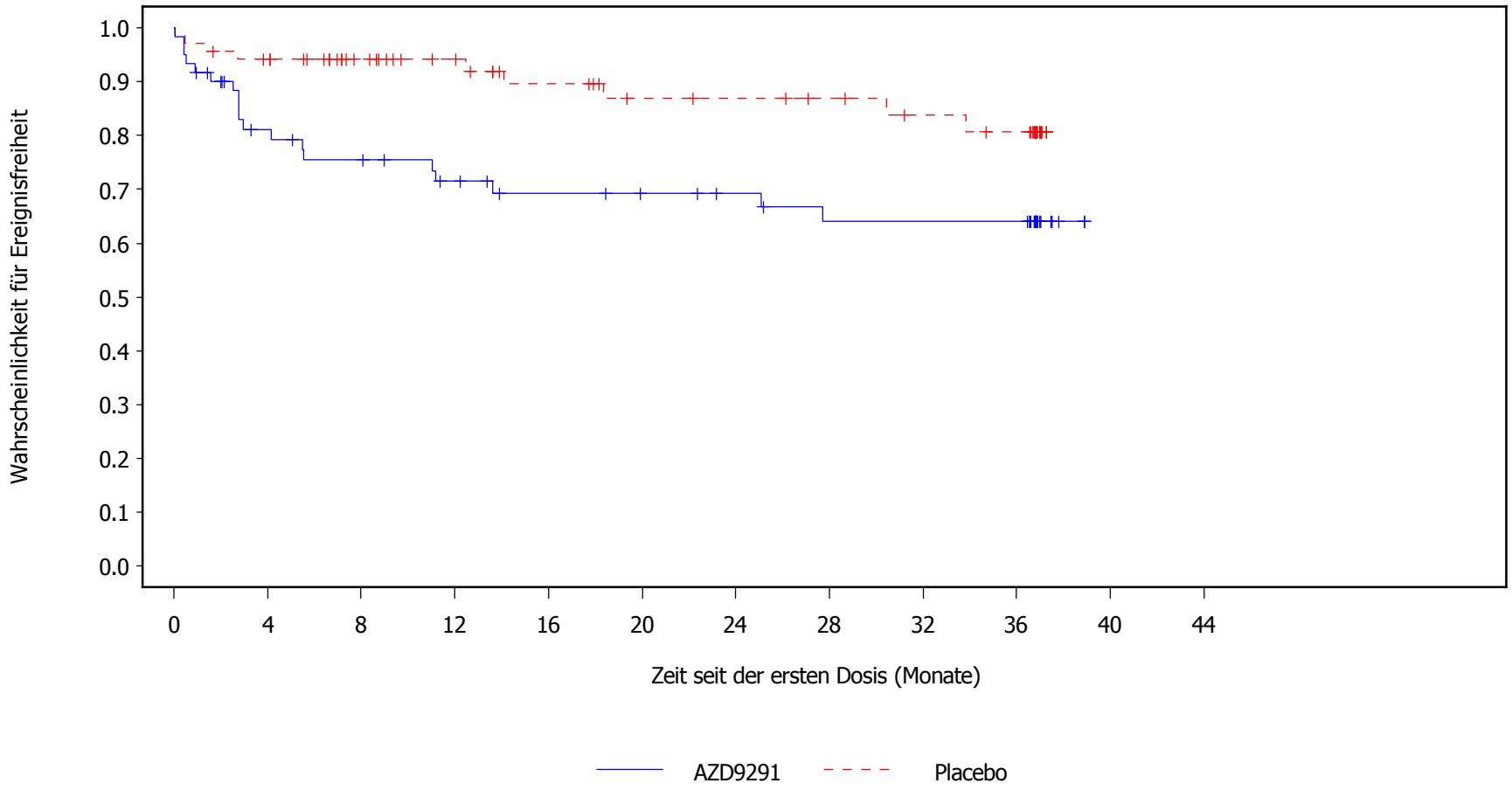
Figure 4.4.1.20 ADAURA Subgroup Analysis: Kaplan-Meier plot of SOC: Untersuchungen for Region=Europa
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

61	44	40	35	31	29	27	24	24	24	0	0	AZD9291
69	63	51	44	37	32	31	29	26	24	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hat 12JUL2023:07:07 kfrh585

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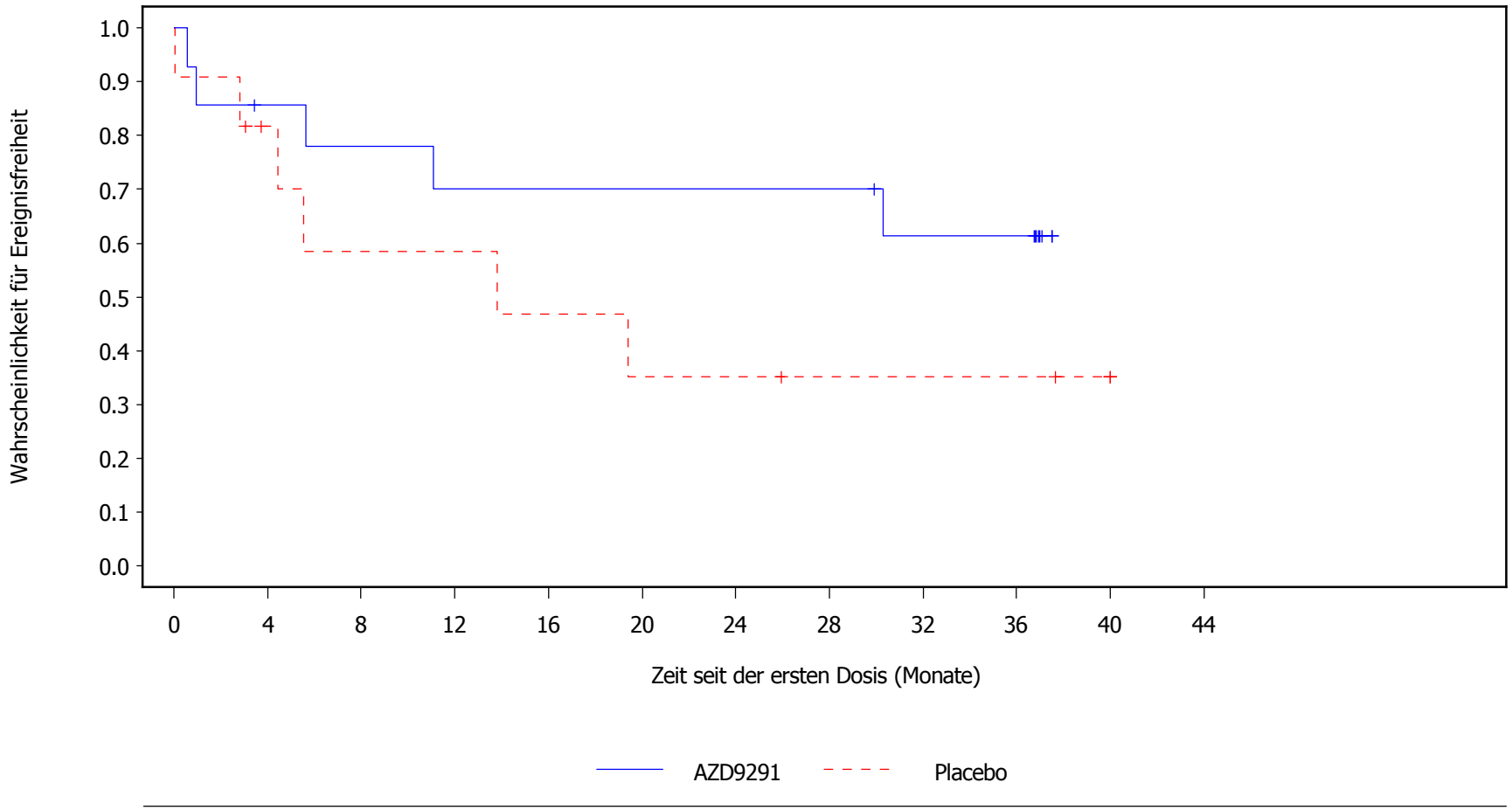
Figure 4.4.1.21 ADAURA Subgroup Analysis: Kaplan-Meier plot of SOC: Untersuchungen for Region=Nordamerika
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

14	11	10	9	9	9	9	9	7	7	0	0	AZD9291
11	7	5	5	4	3	3	2	2	2	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hau 12JUL2023:07:07 kfrh585

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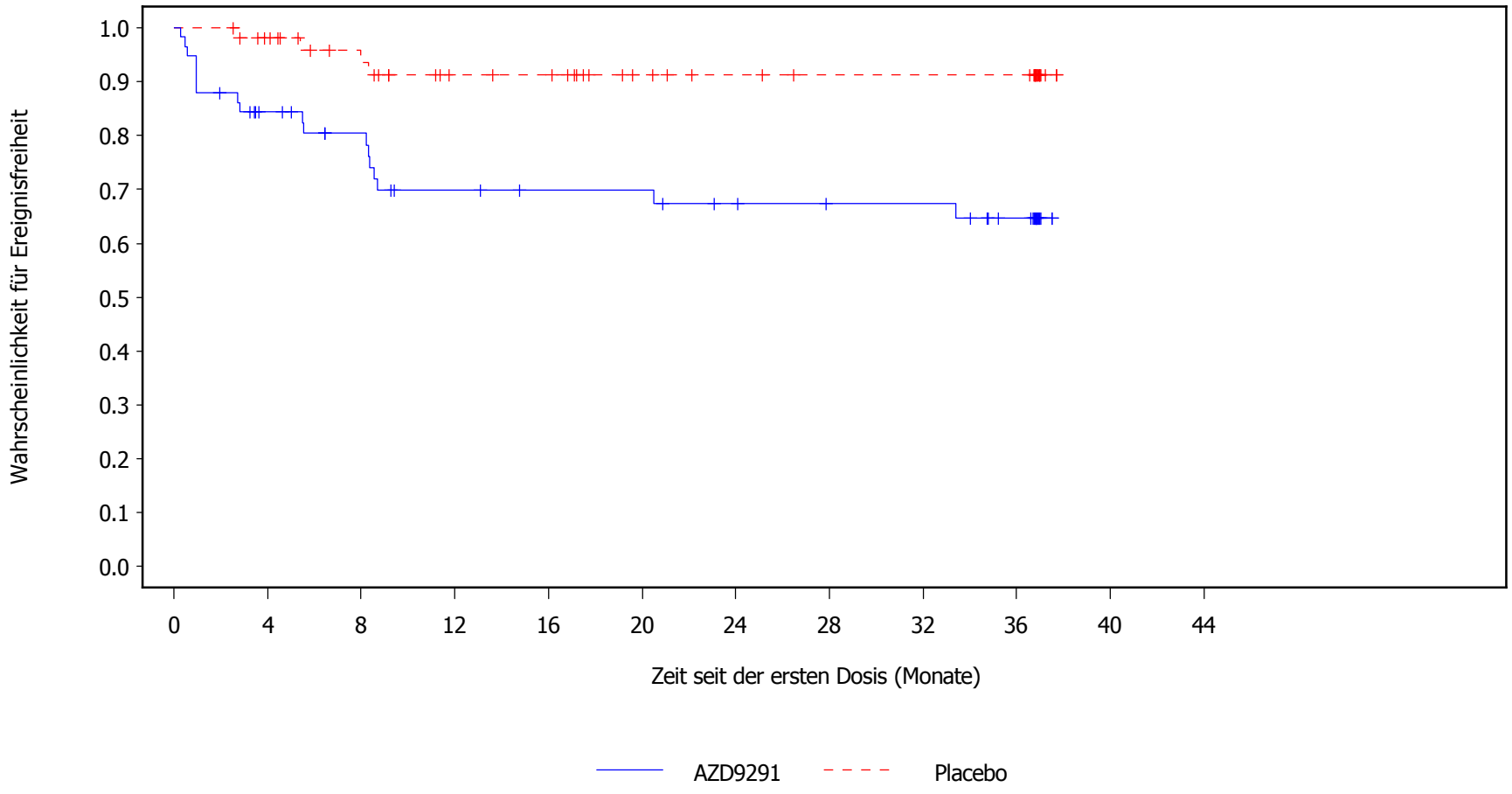
Figure 4.4.1.22 ADAURA Subgroup Analysis: Kaplan-Meier plot of SOC: Untersuchungen for Region=Rest der Welt
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

58	44	38	31	29	29	26	24	24	19	0	0	AZD9291
54	49	41	33	32	24	21	19	19	19	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hav 12JUL2023:07:07 kfrh585

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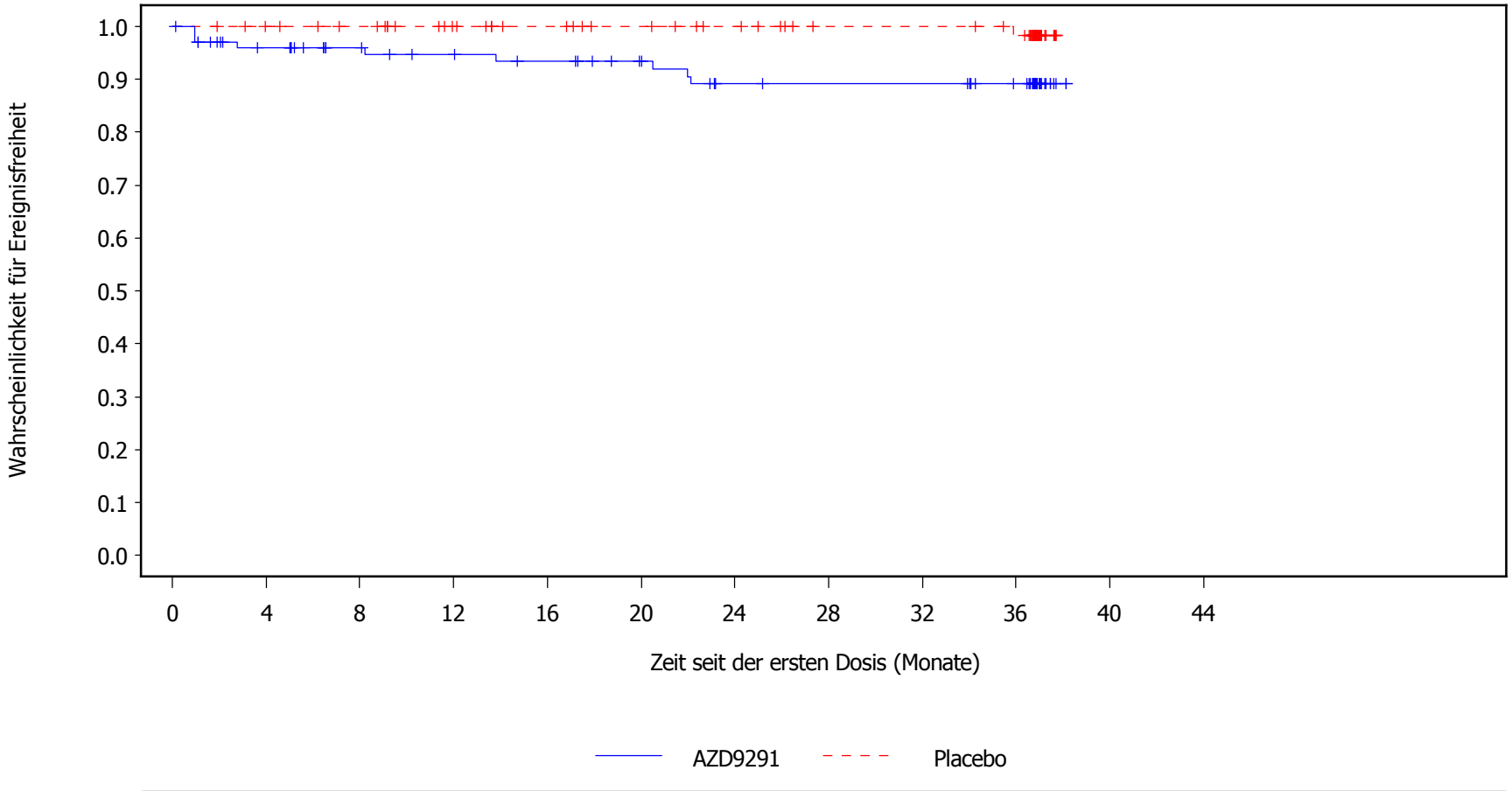
Figure 4.4.1.23 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Elektrokardiogramm QT verlaengert for Krankheitsstadium Version 8=Stadium IB
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

100	88	79	75	72	67	60	59	59	54	0	0	AZD9291
98	95	92	84	79	75	71	65	65	62	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2haw 12JUL2023:07:07 kfrh585

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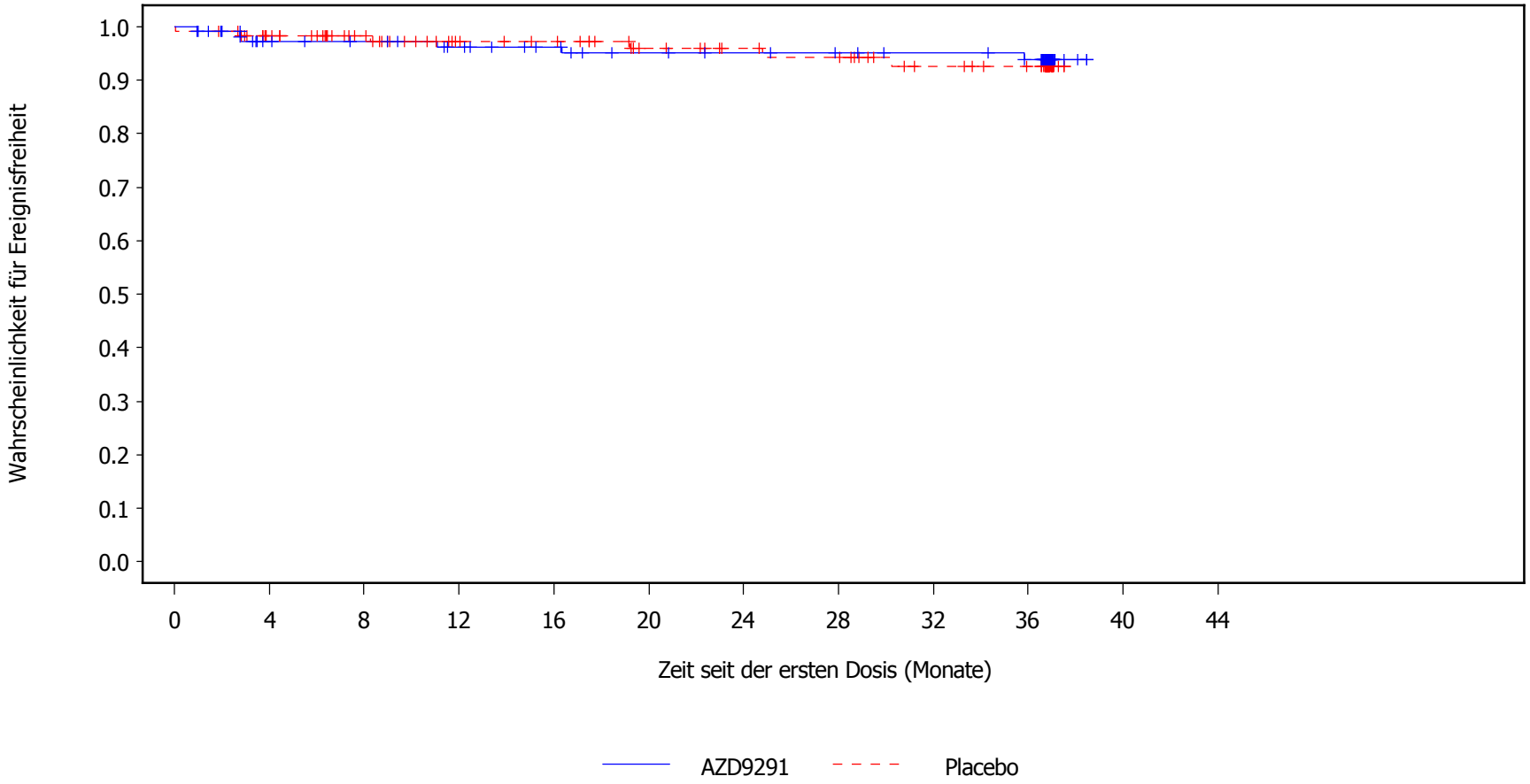
Figure 4.4.1.24 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Elektrokardiogramm QT verlaengert for Krankheitsstadium Version 8=Stadium II
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

113	99	96	91	86	81	79	77	75	72	0	0	AZD9291
119	108	95	81	78	68	63	61	52	48	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hax 12JUL2023:07:07 kfrh585

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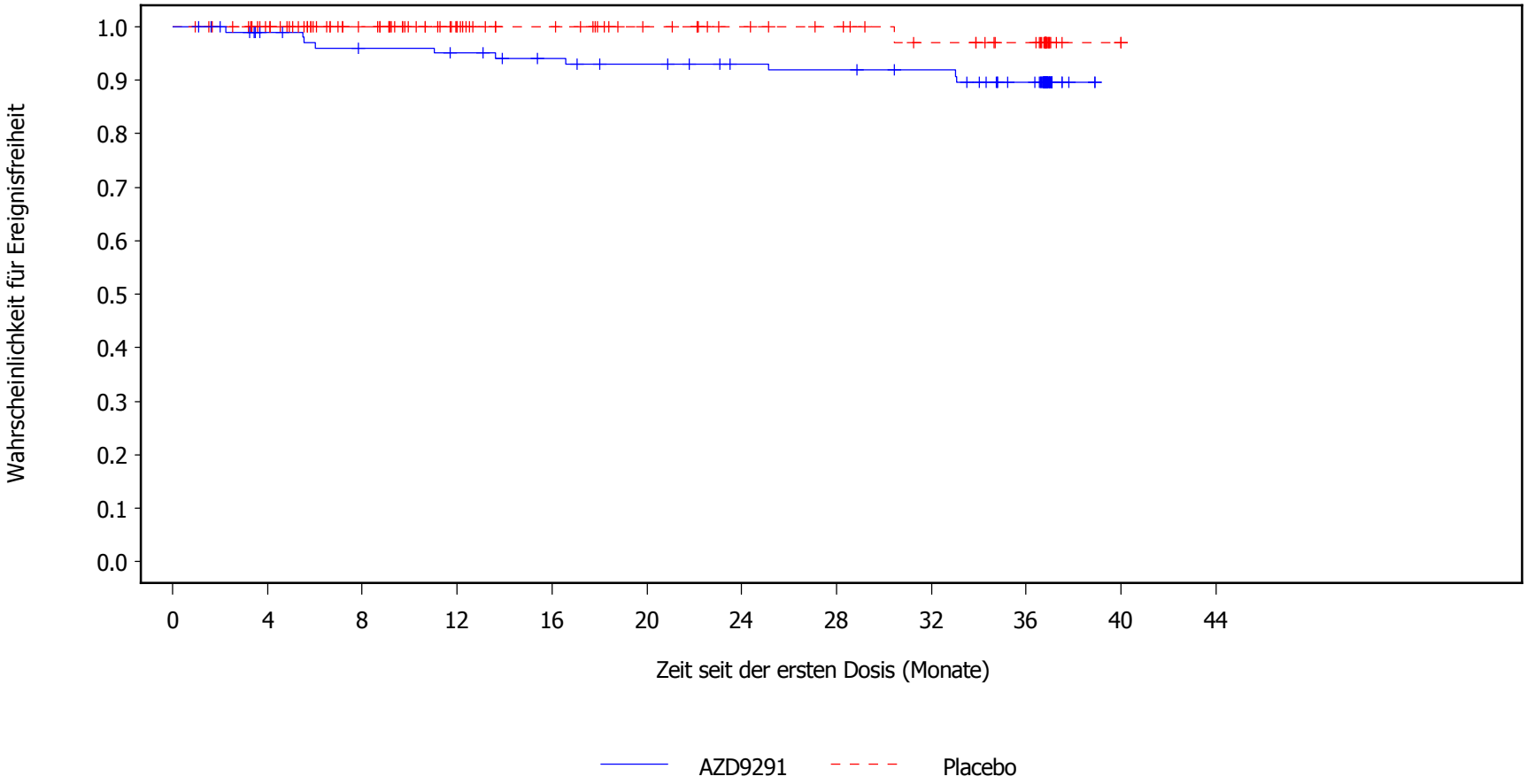
Figure 4.4.1.25 ADAURA Subgroup Analysis: Kaplan-Meier plot of PT: Elektrokardiogramm QT verlaengert for Krankheitsstadium Version 8=Stadium IIIA
Safety Analysis Set, DCO 11Apr2022

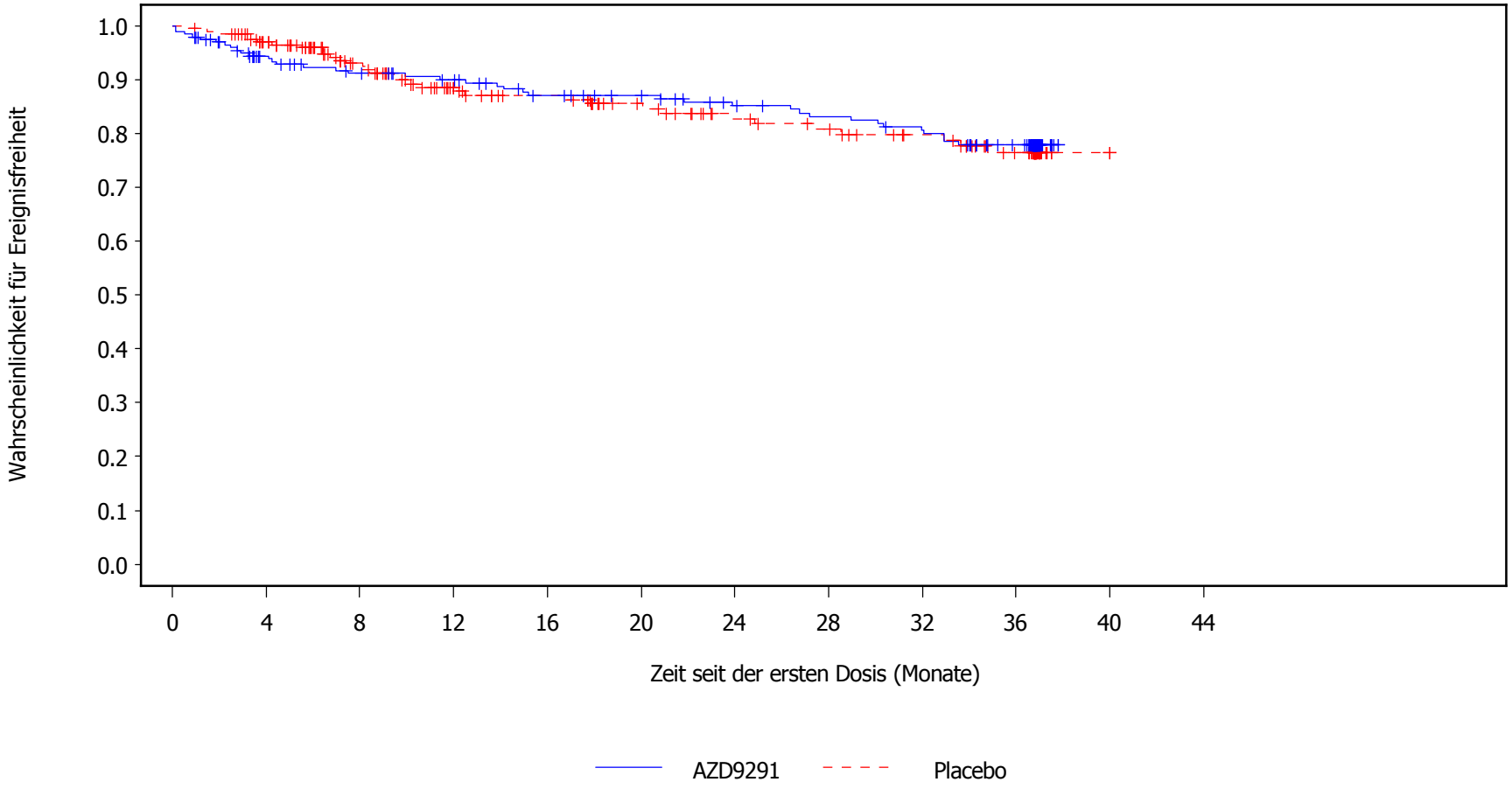


Anzahl an Patienten unter Risiko:

109	101	96	94	90	87	83	82	80	71	0	0	AZD9291
115	105	84	62	54	45	39	36	31	26	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2hay 12JUL2023:07:07 kfrh585

Figure 4.4.2.1 ADAURA Subgroup Analysis: Kaplan-Meier plot of SUE for Adjuvante Chemotherapie=Ja
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

203	175	164	157	146	141	132	127	122	109	0	0	AZD9291
207	188	153	122	112	98	86	81	73	60	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.

root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2iaa 12JUL2023:07:07 kfrh585

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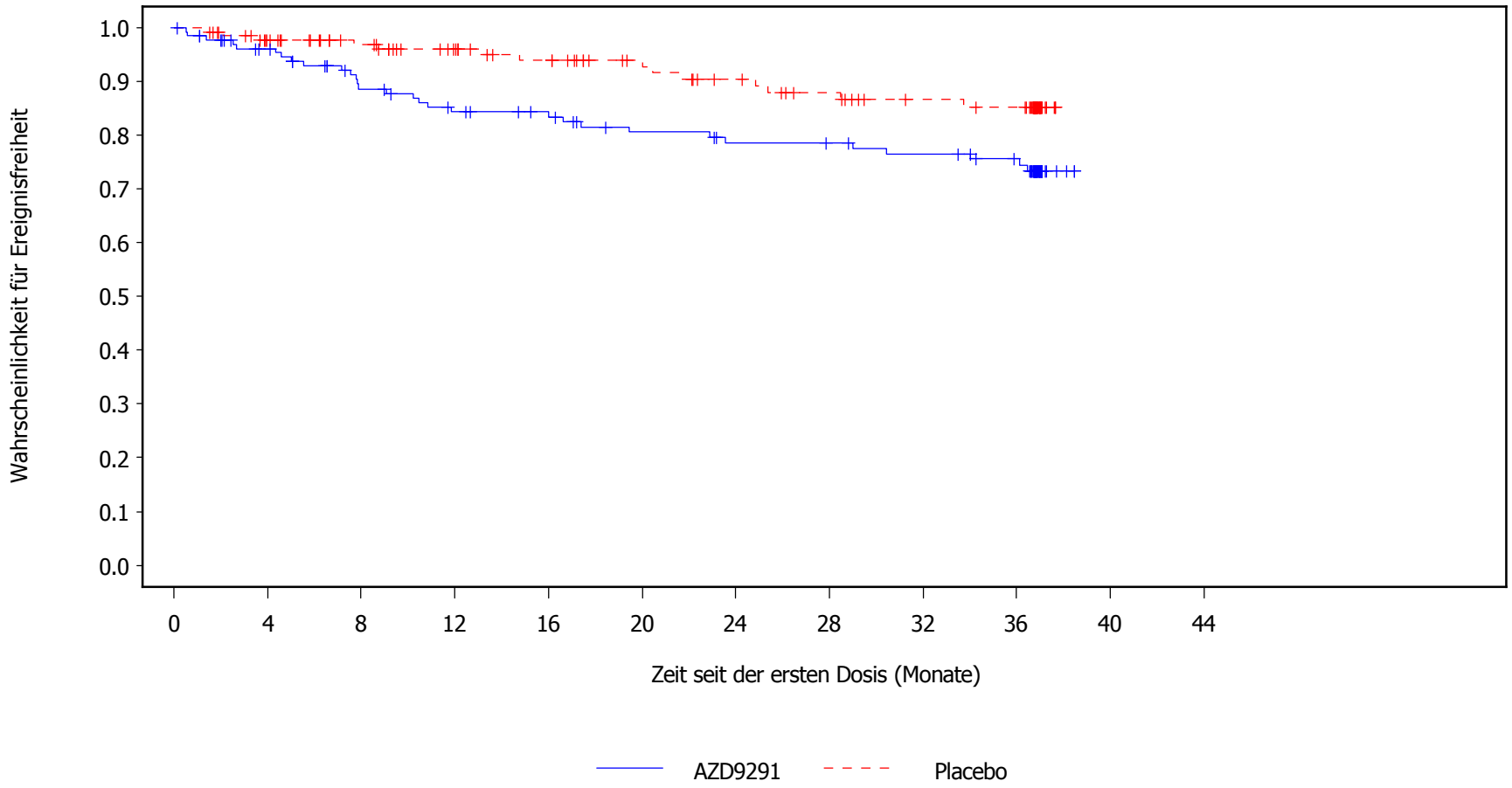
Figure 4.4.2.2 ADAURA Subgroup Analysis: Kaplan-Meier plot of SUE for Adjuvante Chemotherapie=Nein
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

134	120	104	96	92	84	80	79	76	71	0	0	AZD9291
136	123	111	99	91	81	74	68	61	59	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2iab 12JUL2023:07:07 kfrh585

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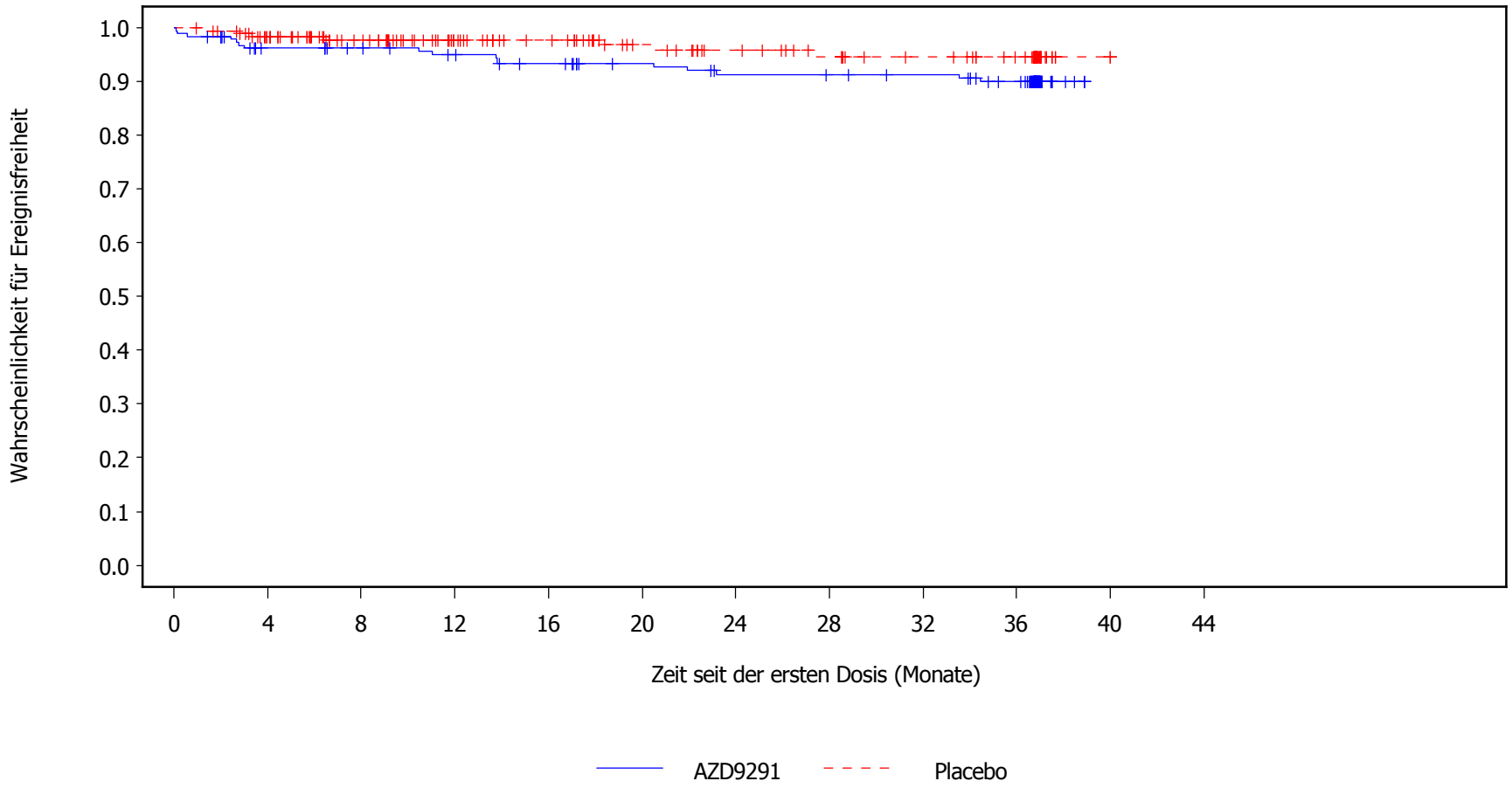
Figure 4.4.3.1 ADAURA Subgroup Analysis: Kaplan-Meier plot of Therapieabbruch aufgrund von UE for EGFR-Mutation=Exon 19 Deletion
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

187	171	167	162	156	149	144	143	141	134	0	0 AZD9291
191	175	150	125	113	97	88	81	75	68	0	0 Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2jaa 12JUL2023:07:07 kfrh585

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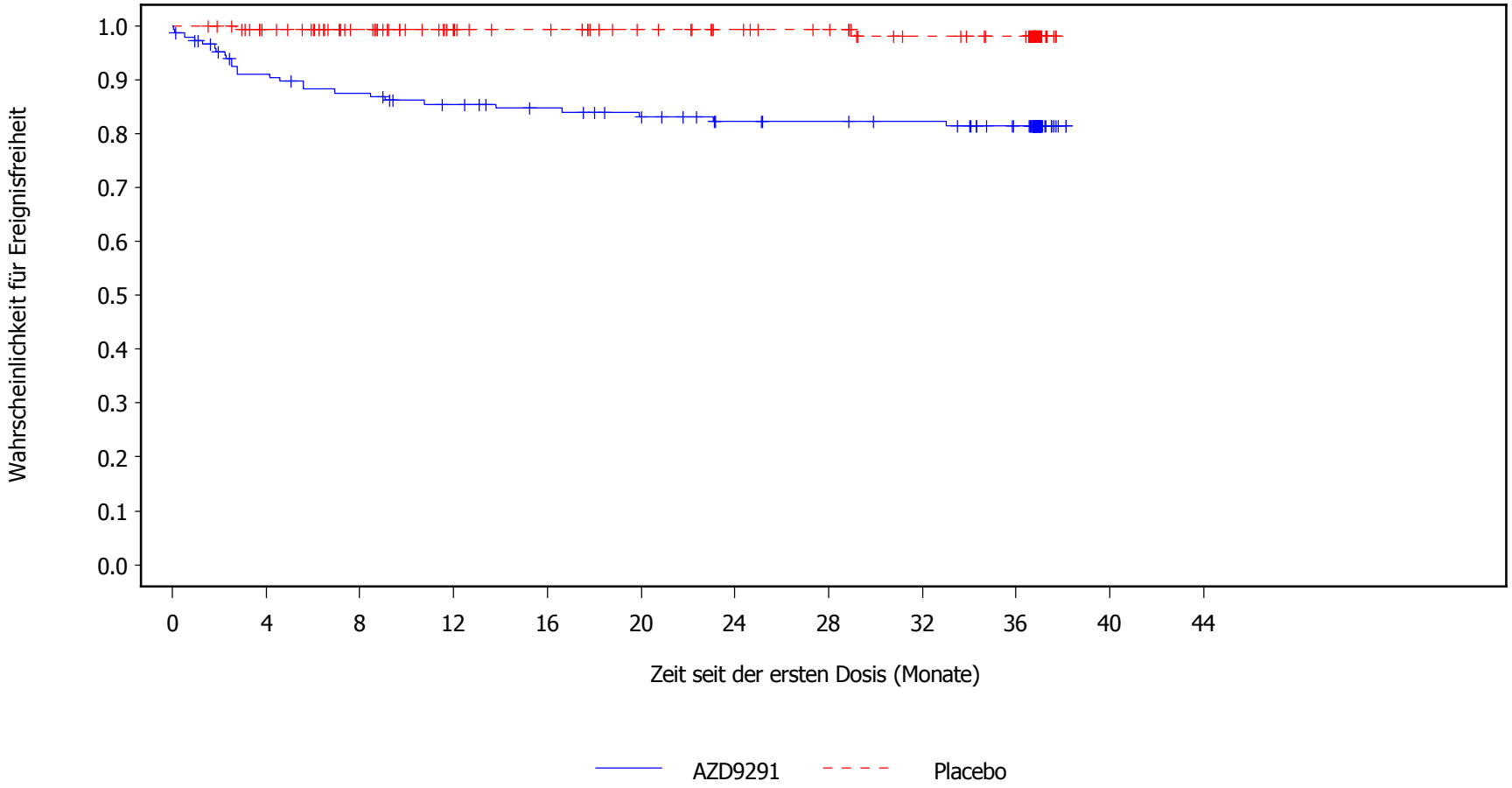
Figure 4.4.3.2 ADAURA Subgroup Analysis: Kaplan-Meier plot of Therapieabbruch aufgrund von UE for EGFR-Mutation=L858R
Safety Analysis Set, DCO 11Apr2022



Anzahl an Patienten unter Risiko:

150	131	125	118	113	108	101	99	97	88	0	0	AZD9291
152	142	127	109	105	96	90	86	77	73	0	0	Placebo

Kaplan-Meier plot is presented only if the interaction term in Cox regression model with treatment, subgroup and treatment-by-subgroup interaction is statistically significant at 5% level.
root/cdar/d516/payer_germany/ar/d5164c00001_payer_germany_s2/tlf/prod/program/ttesae_v2.sas gttesae_v2jab 12JUL2023:07:07 kfrh585