

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Osimertinib (TAGRISSO®)

AstraZeneca GmbH

Modul 4 A – Anhang 4-G

Behandlung von erwachsenen Patienten mit lokal fortgeschrittenem, inoperablem NSCLC, deren Tumoren EGFR-Mutationen als Deletion im Exon 19 oder Substitutionsmutation im Exon 21 (L858R) aufweisen und deren Erkrankung während oder nach einer platinhaltigen Radiochemotherapie nicht fortgeschritten ist

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

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Table LT1QFI10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Fatigue - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Fatigue	LAURA	Osimertinib	Deterioration	143	102 (71.3)
			No deterioration at time of analysis	143	23 (16.1)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	0 (0.0)
			>= 2 consecutive missed visits	143	5 (3.5)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	41 (56.2)
			No deterioration at time of analysis	73	22 (30.1)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	0 (0.0)
			>= 2 consecutive missed visits	73	5 (6.8)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

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Table LT1QPI10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Pain - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Pain	LAURA	Osimertinib	Deterioration	143	95 (66.4)
			No deterioration at time of analysis	143	28 (19.6)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	1 (0.7)
			>= 2 consecutive missed visits	143	6 (4.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	45 (61.6)
			No deterioration at time of analysis	73	16 (21.9)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	6 (8.2)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
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Table LT1QVI10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Nausea/Vomiting - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Nausea/Vomiting	LAURA	Osimertinib	Deterioration	143	61 (42.7)
			No deterioration at time of analysis	143	57 (39.9)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	5 (3.5)
			>= 2 consecutive missed visits	143	7 (4.9)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	22 (30.1)
			No deterioration at time of analysis	73	35 (47.9)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	9 (12.3)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
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Table LT1QDI10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Dyspnoea - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Dyspnoea	LAURA	Osimertinib	Deterioration	143	90 (62.9)
			No deterioration at time of analysis	143	31 (21.7)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	3 (2.1)
			>= 2 consecutive missed visits	143	6 (4.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	38 (52.1)
			No deterioration at time of analysis	73	20 (27.4)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	8 (11.0)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
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Table LT1QII10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Insomnia - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Insomnia	LAURA	Osimertinib	Deterioration	143	78 (54.5)
			No deterioration at time of analysis	143	43 (30.1)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	1 (0.7)
			>= 2 consecutive missed visits	143	8 (5.6)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	26 (35.6)
			No deterioration at time of analysis	73	33 (45.2)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	8 (11.0)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
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Table LT1QAI10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Appetite loss - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Appetite loss	LAURA	Osimertinib	Deterioration	143	82 (57.3)
			No deterioration at time of analysis	143	39 (27.3)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	3 (2.1)
			>= 2 consecutive missed visits	143	6 (4.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	33 (45.2)
			No deterioration at time of analysis	73	27 (37.0)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	6 (8.2)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
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Table LT1QCI10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Constipation - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Constipation	LAURA	Osimertinib	Deterioration	143	72 (50.3)
			No deterioration at time of analysis	143	44 (30.8)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	5 (3.5)
			>= 2 consecutive missed visits	143	9 (6.3)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	24 (32.9)
			No deterioration at time of analysis	73	36 (49.3)
			Baseline score too low/high	73	1 (1.4)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	6 (8.2)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire - Core 30 items.
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Table LT1QHI10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Diarrhoea - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Diarrhoea	LAURA	Osimertinib	Deterioration	143	95 (66.4)
			No deterioration at time of analysis	143	26 (18.2)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	3 (2.1)
			>= 2 consecutive missed visits	143	6 (4.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	33 (45.2)
			No deterioration at time of analysis	73	25 (34.2)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	8 (11.0)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1QMI10T_MFA0: Time to increase by at least 10 points in QLQ-C30 Financial difficulties - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-C30 Financial difficulties	LAURA	Osimertinib	Deterioration	143	50 (35.0)
			No deterioration at time of analysis	143	61 (42.7)
			Baseline score too low/high	143	4 (2.8)
			Death without event	143	8 (5.6)
			>= 2 consecutive missed visits	143	7 (4.9)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	22 (30.1)
			No deterioration at time of analysis	73	34 (46.6)
			Baseline score too low/high	73	1 (1.4)
			Death without event	73	3 (4.1)
			>= 2 consecutive missed visits	73	8 (11.0)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

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Table LT1QF_MFH0: Course of QLQ-C30 Fatigue
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Fatigue	Baseline	Osimertinib	143	131 (91.6)	18.83 (17.80)	0.0	11.11	100.0
		Placebo	73	68 (93.2)	22.39 (15.30)	0.0	22.22	55.6
	Week 4	Osimertinib	143	130 (90.9)	23.59 (20.71)	0.0	22.22	100.0
		Placebo	73	66 (90.4)	24.58 (21.57)	0.0	22.22	88.9
	Week 8	Osimertinib	143	129 (90.2)	26.53 (22.41)	0.0	22.22	100.0
		Placebo	73	59 (80.8)	21.09 (19.97)	0.0	22.22	66.7
	Week 16	Osimertinib	143	119 (83.2)	23.72 (21.26)	0.0	22.22	100.0
		Placebo	73	48 (65.8)	20.37 (21.17)	0.0	11.11	100.0
	Week 24	Osimertinib	143	111 (77.6)	21.42 (18.70)	0.0	22.22	88.9
		Placebo	73	43 (58.9)	22.22 (18.31)	0.0	22.22	77.8
	Week 32	Osimertinib	143	105 (73.4)	21.16 (19.22)	0.0	22.22	88.9
		Placebo	73	30 (41.1)	24.07 (22.81)	0.0	22.22	100.0
	Week 40	Osimertinib	143	108 (75.5)	22.02 (18.67)	0.0	22.22	77.8
		Placebo	73	23 (31.5)	27.05 (24.35)	0.0	22.22	77.8
	Week 48	Osimertinib	143	100 (69.9)	19.44 (19.11)	0.0	16.67	77.8
		Placebo	73	25 (34.2)	20.44 (18.34)	0.0	22.22	66.7
	Week 56	Osimertinib	143	88 (61.5)	22.47 (19.57)	0.0	22.22	100.0
		Placebo	73	13 (17.8)	18.80 (17.20)	0.0	22.22	55.6
	Week 64	Osimertinib	143	93 (65.0)	19.00 (19.49)	0.0	11.11	66.7
		Placebo	73	15 (20.5)	24.44 (25.96)	0.0	22.22	88.9
	Week 72	Osimertinib	143	90 (62.9)	18.89 (19.88)	0.0	11.11	66.7
		Placebo	73	13 (17.8)	22.22 (26.84)	0.0	22.22	100.0
	Week 80	Osimertinib	143	88 (61.5)	19.57 (20.97)	0.0	22.22	88.9
		Placebo	73	9 (12.3)	25.93 (21.52)	0.0	22.22	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Table LT1QF_MFH0: Course of QLQ-C30 Fatigue
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Fatigue	Week 88	Osimertinib	143	79 (55.2)	20.39 (19.77)	0.0	22.22	88.9
		Placebo	73	8 (11.0)	27.78 (27.22)	0.0	22.22	88.9
	Week 96	Osimertinib	143	79 (55.2)	16.17 (19.72)	0.0	11.11	88.9
		Placebo	73	6 (8.2)	29.63 (36.96)	0.0	22.22	100.0
	Week 104	Osimertinib	143	71 (49.7)	16.74 (18.77)	0.0	11.11	88.9
		Placebo	73	8 (11.0)	18.06 (14.47)	0.0	16.67	33.3
	Week 112	Osimertinib	143	63 (44.1)	18.52 (19.96)	0.0	11.11	88.9
		Placebo	73	4 (5.5)	16.67 (14.34)	0.0	16.67	33.3
	Week 120	Osimertinib	143	61 (42.7)	20.77 (20.44)	0.0	22.22	66.7
		Placebo	73	3 (4.1)	14.81 (16.97)	0.0	11.11	33.3
	Week 128	Osimertinib	143	52 (36.4)	20.51 (18.59)	0.0	22.22	66.7
		Placebo	73	2 (2.7)	22.22 (31.43)	0.0	22.22	44.4
	Week 136	Osimertinib	143	44 (30.8)	21.46 (21.49)	0.0	22.22	88.9
		Placebo	73	3 (4.1)	7.41 (12.83)	0.0	0.00	22.2
	Week 144	Osimertinib	143	39 (27.3)	21.37 (19.14)	0.0	22.22	66.7
		Placebo	73	3 (4.1)	7.41 (12.83)	0.0	0.00	22.2
	Week 152	Osimertinib	143	35 (24.5)	22.86 (21.72)	0.0	22.22	100.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	20.74 (22.55)	0.0	22.22	100.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	20.20 (24.40)	0.0	11.11	100.0
		Placebo	73	3 (4.1)	14.81 (25.66)	0.0	0.00	44.4

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Table LT1QP_MFH0: Course of QLQ-C30 Pain
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Pain	Baseline	Osimertinib	143	131 (91.6)	11.07 (15.96)	0.0	0.00	66.7
		Placebo	73	68 (93.2)	12.75 (15.00)	0.0	16.67	66.7
	Week 4	Osimertinib	143	130 (90.9)	17.18 (19.79)	0.0	16.67	83.3
		Placebo	73	66 (90.4)	15.91 (18.12)	0.0	16.67	66.7
	Week 8	Osimertinib	143	129 (90.2)	19.77 (23.46)	0.0	16.67	100.0
		Placebo	73	59 (80.8)	16.10 (19.07)	0.0	16.67	83.3
	Week 16	Osimertinib	143	119 (83.2)	15.97 (21.85)	0.0	16.67	100.0
		Placebo	73	48 (65.8)	14.58 (15.99)	0.0	16.67	66.7
	Week 24	Osimertinib	143	111 (77.6)	13.96 (19.53)	0.0	0.00	100.0
		Placebo	73	43 (58.9)	14.34 (16.90)	0.0	16.67	66.7
	Week 32	Osimertinib	143	105 (73.4)	15.71 (20.91)	0.0	16.67	100.0
		Placebo	73	30 (41.1)	20.00 (22.91)	0.0	16.67	100.0
	Week 40	Osimertinib	143	108 (75.5)	15.12 (18.45)	0.0	16.67	83.3
		Placebo	73	23 (31.5)	22.46 (21.68)	0.0	16.67	83.3
	Week 48	Osimertinib	143	100 (69.9)	13.17 (18.70)	0.0	0.00	83.3
		Placebo	73	25 (34.2)	22.67 (19.17)	0.0	33.33	66.7
	Week 56	Osimertinib	143	88 (61.5)	15.34 (20.56)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	15.38 (14.37)	0.0	16.67	33.3
	Week 64	Osimertinib	143	93 (65.0)	13.44 (18.59)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	24.44 (20.77)	0.0	16.67	66.7
	Week 72	Osimertinib	143	90 (62.9)	15.19 (18.97)	0.0	16.67	66.7
		Placebo	73	13 (17.8)	26.92 (25.04)	0.0	33.33	83.3
	Week 80	Osimertinib	143	88 (61.5)	15.53 (19.86)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	22.22 (22.05)	0.0	16.67	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1QP_MFH0: Course of QLQ-C30 Pain
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Pain	Week 88	Osimertinib	143	79 (55.2)	14.77 (19.24)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	27.08 (23.46)	0.0	25.00	66.7
	Week 96	Osimertinib	143	79 (55.2)	14.35 (23.23)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	16.67 (14.91)	0.0	16.67	33.3
	Week 104	Osimertinib	143	71 (49.7)	12.91 (19.76)	0.0	0.00	83.3
		Placebo	73	8 (11.0)	12.50 (14.77)	0.0	8.33	33.3
	Week 112	Osimertinib	143	63 (44.1)	12.70 (21.11)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	16.67 (13.61)	0.0	16.67	33.3
	Week 120	Osimertinib	143	61 (42.7)	13.11 (20.89)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (9.62)	16.7	16.67	33.3
	Week 128	Osimertinib	143	52 (36.4)	13.46 (21.40)	0.0	0.00	83.3
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 136	Osimertinib	143	44 (30.8)	15.15 (23.52)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (9.62)	0.0	16.67	16.7
	Week 144	Osimertinib	143	39 (27.3)	13.68 (21.59)	0.0	0.00	83.3
		Placebo	73	3 (4.1)	5.56 (9.62)	0.0	0.00	16.7
	Week 152	Osimertinib	143	35 (24.5)	12.38 (22.99)	0.0	0.00	83.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	16.67 (25.14)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	12.12 (23.11)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	27.78 (19.25)	16.7	16.67	50.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QV_MFH0: Course of QLQ-C30 Nausea/vomiting
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Nausea/vomiting	Baseline	Osimertinib	143	131 (91.6)	3.94 (10.30)	0.0	0.00	66.7
		Placebo	73	68 (93.2)	5.88 (12.47)	0.0	0.00	66.7
	Week 4	Osimertinib	143	130 (90.9)	3.21 (9.07)	0.0	0.00	66.7
		Placebo	73	66 (90.4)	2.02 (6.21)	0.0	0.00	33.3
	Week 8	Osimertinib	143	129 (90.2)	4.13 (12.51)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	0.56 (3.04)	0.0	0.00	16.7
	Week 16	Osimertinib	143	119 (83.2)	2.38 (8.48)	0.0	0.00	66.7
		Placebo	73	48 (65.8)	1.39 (5.79)	0.0	0.00	33.3
	Week 24	Osimertinib	143	111 (77.6)	4.50 (12.70)	0.0	0.00	66.7
		Placebo	73	43 (58.9)	3.10 (6.56)	0.0	0.00	16.7
	Week 32	Osimertinib	143	105 (73.4)	3.65 (10.07)	0.0	0.00	66.7
		Placebo	73	30 (41.1)	2.22 (5.76)	0.0	0.00	16.7
	Week 40	Osimertinib	143	108 (75.5)	4.32 (10.53)	0.0	0.00	50.0
		Placebo	73	23 (31.5)	4.35 (10.32)	0.0	0.00	33.3
	Week 48	Osimertinib	143	100 (69.9)	2.83 (9.49)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	2.67 (7.88)	0.0	0.00	33.3
	Week 56	Osimertinib	143	88 (61.5)	3.03 (8.21)	0.0	0.00	33.3
		Placebo	73	13 (17.8)	6.41 (10.84)	0.0	0.00	33.3
	Week 64	Osimertinib	143	93 (65.0)	2.69 (8.96)	0.0	0.00	50.0
		Placebo	73	15 (20.5)	6.67 (18.69)	0.0	0.00	66.7
	Week 72	Osimertinib	143	90 (62.9)	3.33 (8.73)	0.0	0.00	33.3
		Placebo	73	13 (17.8)	2.56 (6.26)	0.0	0.00	16.7
	Week 80	Osimertinib	143	88 (61.5)	3.79 (10.02)	0.0	0.00	50.0
		Placebo	73	9 (12.3)	3.70 (7.35)	0.0	0.00	16.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
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Program Name: LT1_APR0_H0.sas
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Table LT1QV_MFH0: Course of QLQ-C30 Nausea/vomiting
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Nausea/vomiting	Week 88	Osimertinib	143	79 (55.2)	3.38 (8.17)	0.0	0.00	33.3
		Placebo	73	8 (11.0)	0.00 (0.00)	0.0	0.00	0.0
	Week 96	Osimertinib	143	79 (55.2)	4.43 (14.55)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	8.33 (20.41)	0.0	0.00	50.0
	Week 104	Osimertinib	143	71 (49.7)	2.35 (7.07)	0.0	0.00	33.3
		Placebo	73	8 (11.0)	4.17 (7.72)	0.0	0.00	16.7
	Week 112	Osimertinib	143	63 (44.1)	3.17 (7.84)	0.0	0.00	33.3
		Placebo	73	4 (5.5)	8.33 (9.62)	0.0	8.33	16.7
	Week 120	Osimertinib	143	61 (42.7)	4.64 (9.69)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	5.56 (9.62)	0.0	0.00	16.7
	Week 128	Osimertinib	143	52 (36.4)	3.21 (8.76)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	8.33 (11.79)	0.0	8.33	16.7
	Week 136	Osimertinib	143	44 (30.8)	3.03 (8.25)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 144	Osimertinib	143	39 (27.3)	2.14 (6.82)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 152	Osimertinib	143	35 (24.5)	6.19 (11.49)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	2.22 (7.24)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	8.33 (19.75)	0.0	0.00	83.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QD_MFH0: Course of QLQ-C30 Dyspnoea
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Dyspnoea	Baseline	Osimertinib	143	131 (91.6)	10.43 (16.58)	0.0	0.00	66.7
		Placebo	73	68 (93.2)	12.75 (16.32)	0.0	0.00	33.3
	Week 4	Osimertinib	143	130 (90.9)	15.90 (20.00)	0.0	0.00	100.0
		Placebo	73	66 (90.4)	15.66 (20.44)	0.0	0.00	66.7
	Week 8	Osimertinib	143	129 (90.2)	24.55 (23.39)	0.0	33.33	100.0
		Placebo	73	59 (80.8)	16.38 (19.94)	0.0	0.00	66.7
	Week 16	Osimertinib	143	119 (83.2)	21.29 (23.26)	0.0	33.33	100.0
		Placebo	73	48 (65.8)	16.67 (20.63)	0.0	0.00	66.7
	Week 24	Osimertinib	143	111 (77.6)	17.72 (21.47)	0.0	0.00	100.0
		Placebo	73	43 (58.9)	20.93 (19.28)	0.0	33.33	66.7
	Week 32	Osimertinib	143	105 (73.4)	18.73 (21.14)	0.0	0.00	100.0
		Placebo	73	30 (41.1)	16.67 (22.74)	0.0	0.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	19.14 (20.48)	0.0	33.33	66.7
		Placebo	73	23 (31.5)	18.84 (24.26)	0.0	0.00	66.7
	Week 48	Osimertinib	143	100 (69.9)	13.67 (20.15)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	21.33 (18.95)	0.0	33.33	66.7
	Week 56	Osimertinib	143	88 (61.5)	15.15 (20.16)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	12.82 (16.88)	0.0	0.00	33.3
	Week 64	Osimertinib	143	93 (65.0)	15.77 (20.61)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	22.22 (20.57)	0.0	33.33	66.7
	Week 72	Osimertinib	143	90 (62.9)	16.30 (21.92)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	23.08 (25.04)	0.0	33.33	66.7
	Week 80	Osimertinib	143	88 (61.5)	14.02 (21.28)	0.0	0.00	100.0
		Placebo	73	9 (12.3)	22.22 (16.67)	0.0	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Table LT1QD_MFH0: Course of QLQ-C30 Dyspnoea
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Dyspnoea	Week 88	Osimertinib	143	79 (55.2)	10.55 (18.14)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 96	Osimertinib	143	79 (55.2)	13.08 (20.27)	0.0	0.00	66.7
		Placebo	73	6 (8.2)	22.22 (27.22)	0.0	16.67	66.7
	Week 104	Osimertinib	143	71 (49.7)	12.21 (19.71)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	12.50 (17.25)	0.0	0.00	33.3
	Week 112	Osimertinib	143	63 (44.1)	16.40 (23.09)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	16.67 (19.25)	0.0	16.67	33.3
	Week 120	Osimertinib	143	61 (42.7)	12.57 (18.42)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 128	Osimertinib	143	52 (36.4)	9.62 (16.62)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 136	Osimertinib	143	44 (30.8)	12.12 (20.45)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 144	Osimertinib	143	39 (27.3)	12.82 (19.67)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 152	Osimertinib	143	35 (24.5)	13.33 (23.15)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	16.67 (22.74)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	15.15 (24.62)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QI_MFH0: Course of QLQ-C30 Insomnia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Insomnia	Baseline	Osimertinib	143	131 (91.6)	18.83 (23.42)	0.0	0.00	100.0
		Placebo	73	68 (93.2)	17.65 (22.65)	0.0	0.00	66.7
	Week 4	Osimertinib	143	130 (90.9)	16.41 (23.57)	0.0	0.00	100.0
		Placebo	73	66 (90.4)	15.15 (22.02)	0.0	0.00	100.0
	Week 8	Osimertinib	143	129 (90.2)	18.35 (23.56)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	12.43 (19.47)	0.0	0.00	66.7
	Week 16	Osimertinib	143	119 (83.2)	18.77 (24.41)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	15.97 (24.78)	0.0	0.00	100.0
	Week 24	Osimertinib	143	111 (77.6)	15.32 (23.26)	0.0	0.00	100.0
		Placebo	73	43 (58.9)	14.73 (19.66)	0.0	0.00	66.7
	Week 32	Osimertinib	143	105 (73.4)	16.51 (24.07)	0.0	0.00	100.0
		Placebo	73	30 (41.1)	17.78 (25.87)	0.0	0.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	19.14 (24.63)	0.0	0.00	100.0
		Placebo	73	23 (31.5)	18.84 (19.66)	0.0	33.33	66.7
	Week 48	Osimertinib	143	100 (69.9)	19.00 (24.28)	0.0	0.00	100.0
		Placebo	73	25 (34.2)	18.67 (19.44)	0.0	33.33	66.7
	Week 56	Osimertinib	143	88 (61.5)	19.32 (25.63)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	15.38 (22.01)	0.0	0.00	66.7
	Week 64	Osimertinib	143	93 (65.0)	19.00 (22.73)	0.0	0.00	100.0
		Placebo	73	15 (20.5)	20.00 (27.60)	0.0	0.00	100.0
	Week 72	Osimertinib	143	90 (62.9)	18.15 (24.05)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	15.38 (17.30)	0.0	0.00	33.3
	Week 80	Osimertinib	143	88 (61.5)	18.94 (23.05)	0.0	0.00	100.0
		Placebo	73	9 (12.3)	14.81 (24.22)	0.0	0.00	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1QI_MFH0: Course of QLQ-C30 Insomnia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Insomnia	Week 88	Osimertinib	143	79 (55.2)	16.88 (21.93)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	12.50 (17.25)	0.0	0.00	33.3
	Week 96	Osimertinib	143	79 (55.2)	17.72 (23.17)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	16.67 (27.89)	0.0	0.00	66.7
	Week 104	Osimertinib	143	71 (49.7)	17.37 (23.13)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	16.67 (25.20)	0.0	0.00	66.7
	Week 112	Osimertinib	143	63 (44.1)	21.16 (24.90)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	16.67 (19.25)	0.0	16.67	33.3
	Week 120	Osimertinib	143	61 (42.7)	17.49 (20.73)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 128	Osimertinib	143	52 (36.4)	19.23 (25.00)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 136	Osimertinib	143	44 (30.8)	14.39 (18.18)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 144	Osimertinib	143	39 (27.3)	14.53 (18.41)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 152	Osimertinib	143	35 (24.5)	20.00 (21.69)	0.0	33.33	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	18.89 (18.94)	0.0	33.33	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	19.70 (19.68)	0.0	33.33	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QA_MFH0: Course of QLQ-C30 Appetite loss
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Appetite loss	Baseline	Osimertinib	143	131 (91.6)	14.76 (19.46)	0.0	0.00	100.0
		Placebo	73	68 (93.2)	16.67 (21.93)	0.0	0.00	66.7
	Week 4	Osimertinib	143	130 (90.9)	21.03 (24.60)	0.0	16.67	100.0
		Placebo	73	66 (90.4)	17.17 (24.97)	0.0	0.00	100.0
	Week 8	Osimertinib	143	129 (90.2)	24.81 (26.11)	0.0	33.33	100.0
		Placebo	73	59 (80.8)	7.91 (17.87)	0.0	0.00	66.7
	Week 16	Osimertinib	143	119 (83.2)	17.09 (22.49)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	9.72 (19.40)	0.0	0.00	66.7
	Week 24	Osimertinib	143	111 (77.6)	14.11 (22.72)	0.0	0.00	100.0
		Placebo	73	43 (58.9)	10.85 (18.86)	0.0	0.00	66.7
	Week 32	Osimertinib	143	105 (73.4)	13.33 (20.98)	0.0	0.00	66.7
		Placebo	73	30 (41.1)	8.89 (14.99)	0.0	0.00	33.3
	Week 40	Osimertinib	143	108 (75.5)	14.51 (21.51)	0.0	0.00	66.7
		Placebo	73	23 (31.5)	7.25 (19.99)	0.0	0.00	66.7
	Week 48	Osimertinib	143	100 (69.9)	12.00 (19.26)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	9.33 (18.05)	0.0	0.00	66.7
	Week 56	Osimertinib	143	88 (61.5)	15.53 (21.41)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	7.69 (14.62)	0.0	0.00	33.3
	Week 64	Osimertinib	143	93 (65.0)	13.26 (19.12)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	22.22 (27.22)	0.0	0.00	66.7
	Week 72	Osimertinib	143	90 (62.9)	11.48 (18.80)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	10.26 (16.01)	0.0	0.00	33.3
	Week 80	Osimertinib	143	88 (61.5)	12.88 (18.52)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	14.81 (24.22)	0.0	0.00	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Table LT1QA_MFH0: Course of QLQ-C30 Appetite loss
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Appetite loss	Week 88	Osimertinib	143	79 (55.2)	13.92 (23.64)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	16.67 (25.20)	0.0	0.00	66.7
	Week 96	Osimertinib	143	79 (55.2)	11.39 (19.16)	0.0	0.00	66.7
		Placebo	73	6 (8.2)	16.67 (27.89)	0.0	0.00	66.7
	Week 104	Osimertinib	143	71 (49.7)	11.74 (17.91)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 112	Osimertinib	143	63 (44.1)	14.81 (19.65)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 120	Osimertinib	143	61 (42.7)	12.02 (19.28)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 128	Osimertinib	143	52 (36.4)	11.54 (17.32)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 136	Osimertinib	143	44 (30.8)	9.09 (15.02)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 144	Osimertinib	143	39 (27.3)	11.11 (15.92)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 152	Osimertinib	143	35 (24.5)	11.43 (17.97)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	13.33 (16.61)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	10.61 (15.89)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QC_MFH0: Course of QLQ-C30 Constipation
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Constipation	Baseline	Osimertinib	143	131 (91.6)	7.12 (15.47)	0.0	0.00	100.0
		Placebo	73	68 (93.2)	9.31 (20.64)	0.0	0.00	100.0
	Week 4	Osimertinib	143	130 (90.9)	8.72 (17.88)	0.0	0.00	100.0
		Placebo	73	66 (90.4)	7.58 (17.34)	0.0	0.00	66.7
	Week 8	Osimertinib	143	129 (90.2)	7.24 (16.12)	0.0	0.00	66.7
		Placebo	73	59 (80.8)	4.52 (13.07)	0.0	0.00	66.7
	Week 16	Osimertinib	143	119 (83.2)	11.76 (21.08)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	8.33 (17.53)	0.0	0.00	66.7
	Week 24	Osimertinib	143	111 (77.6)	7.81 (15.54)	0.0	0.00	66.7
		Placebo	73	43 (58.9)	8.53 (17.96)	0.0	0.00	66.7
	Week 32	Osimertinib	143	105 (73.4)	9.21 (18.20)	0.0	0.00	66.7
		Placebo	73	30 (41.1)	14.44 (22.63)	0.0	0.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	8.02 (18.15)	0.0	0.00	100.0
		Placebo	73	23 (31.5)	13.04 (26.09)	0.0	0.00	100.0
	Week 48	Osimertinib	143	100 (69.9)	9.00 (16.99)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	14.67 (25.60)	0.0	0.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	13.26 (19.92)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	17.95 (25.88)	0.0	0.00	66.7
	Week 64	Osimertinib	143	93 (65.0)	8.96 (15.65)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	13.33 (21.08)	0.0	0.00	66.7
	Week 72	Osimertinib	143	90 (62.9)	10.37 (18.46)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	17.95 (22.01)	0.0	0.00	66.7
	Week 80	Osimertinib	143	88 (61.5)	9.09 (16.55)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	25.93 (22.22)	0.0	33.33	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QC_MFH0: Course of QLQ-C30 Constipation
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Constipation	Week 88	Osimertinib	143	79 (55.2)	8.02 (17.88)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	16.67 (25.20)	0.0	0.00	66.7
	Week 96	Osimertinib	143	79 (55.2)	8.44 (18.85)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	33.33 (29.81)	0.0	33.33	66.7
	Week 104	Osimertinib	143	71 (49.7)	12.21 (21.26)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	25.00 (38.83)	0.0	0.00	100.0
	Week 112	Osimertinib	143	63 (44.1)	12.17 (18.26)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	33.33 (27.22)	0.0	33.33	66.7
	Week 120	Osimertinib	143	61 (42.7)	8.74 (20.09)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	33.33 (33.33)	0.0	33.33	66.7
	Week 128	Osimertinib	143	52 (36.4)	12.18 (16.21)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	83.33 (23.57)	66.7	83.33	100.0
	Week 136	Osimertinib	143	44 (30.8)	7.58 (14.13)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	22.22 (38.49)	0.0	0.00	66.7
	Week 144	Osimertinib	143	39 (27.3)	9.40 (17.01)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	33.33 (33.33)	0.0	33.33	66.7
	Week 152	Osimertinib	143	35 (24.5)	11.43 (22.78)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	33.33 (47.14)	0.0	33.33	66.7
	Week 160	Osimertinib	143	30 (21.0)	12.22 (18.54)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	33.33 (47.14)	0.0	33.33	66.7
	Week 168	Osimertinib	143	22 (15.4)	10.61 (18.93)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	33.33 (33.33)	0.0	33.33	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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AstraZeneca
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Program Name: LT1_APR0_H0.sas
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Table LT1QH_MFH0: Course of QLQ-C30 Diarrhea
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Diarrhoea	Baseline	Osimertinib	143	131 (91.6)	2.54 (8.89)	0.0	0.00	33.3
		Placebo	73	68 (93.2)	1.96 (7.90)	0.0	0.00	33.3
	Week 4	Osimertinib	143	130 (90.9)	13.85 (21.08)	0.0	0.00	66.7
		Placebo	73	66 (90.4)	4.04 (10.96)	0.0	0.00	33.3
	Week 8	Osimertinib	143	129 (90.2)	14.21 (21.15)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	3.39 (10.16)	0.0	0.00	33.3
	Week 16	Osimertinib	143	119 (83.2)	15.69 (22.89)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	4.17 (11.14)	0.0	0.00	33.3
	Week 24	Osimertinib	143	111 (77.6)	15.02 (19.97)	0.0	0.00	66.7
		Placebo	73	43 (58.9)	5.43 (16.15)	0.0	0.00	66.7
	Week 32	Osimertinib	143	105 (73.4)	16.19 (19.12)	0.0	0.00	66.7
		Placebo	73	30 (41.1)	10.00 (17.83)	0.0	0.00	66.7
	Week 40	Osimertinib	143	108 (75.5)	12.35 (16.17)	0.0	0.00	33.3
		Placebo	73	23 (31.5)	8.70 (18.03)	0.0	0.00	66.7
	Week 48	Osimertinib	143	100 (69.9)	14.00 (18.46)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	10.67 (24.94)	0.0	0.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	12.88 (17.09)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	12.82 (21.68)	0.0	0.00	66.7
	Week 64	Osimertinib	143	93 (65.0)	13.98 (17.94)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	6.67 (18.69)	0.0	0.00	66.7
	Week 72	Osimertinib	143	90 (62.9)	14.07 (18.68)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	7.69 (14.62)	0.0	0.00	33.3
	Week 80	Osimertinib	143	88 (61.5)	16.29 (20.21)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	11.11 (16.67)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1QH_MFH0: Course of QLQ-C30 Diarrhea
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Diarrhoea	Week 88	Osimertinib	143	79 (55.2)	15.61 (18.36)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 96	Osimertinib	143	79 (55.2)	11.39 (16.78)	0.0	0.00	66.7
		Placebo	73	6 (8.2)	5.56 (13.61)	0.0	0.00	33.3
	Week 104	Osimertinib	143	71 (49.7)	13.15 (18.24)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 112	Osimertinib	143	63 (44.1)	13.76 (19.52)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 120	Osimertinib	143	61 (42.7)	17.49 (18.86)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 128	Osimertinib	143	52 (36.4)	16.67 (16.83)	0.0	16.67	33.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 136	Osimertinib	143	44 (30.8)	17.42 (19.67)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 144	Osimertinib	143	39 (27.3)	18.80 (18.41)	0.0	33.33	66.7
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 152	Osimertinib	143	35 (24.5)	16.19 (21.95)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 160	Osimertinib	143	30 (21.0)	12.22 (16.34)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	13.64 (19.68)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

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Program Name: LT1_APR0_H0.sas
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Table LT1QM_MFH0: Course of QLQ-C30 Financial difficulties
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Financial difficulties	Baseline	Osimertinib	143	131 (91.6)	18.07 (26.23)	0.0	0.00	100.0
		Placebo	73	68 (93.2)	15.69 (24.07)	0.0	0.00	100.0
	Week 4	Osimertinib	143	130 (90.9)	16.41 (24.64)	0.0	0.00	100.0
		Placebo	73	66 (90.4)	12.63 (23.94)	0.0	0.00	100.0
	Week 8	Osimertinib	143	129 (90.2)	17.31 (25.03)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	11.30 (21.09)	0.0	0.00	100.0
	Week 16	Osimertinib	143	119 (83.2)	16.81 (25.26)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	13.19 (24.54)	0.0	0.00	100.0
	Week 24	Osimertinib	143	111 (77.6)	15.02 (23.67)	0.0	0.00	100.0
		Placebo	73	43 (58.9)	17.05 (25.59)	0.0	0.00	100.0
	Week 32	Osimertinib	143	105 (73.4)	15.87 (24.93)	0.0	0.00	100.0
		Placebo	73	30 (41.1)	14.44 (25.80)	0.0	0.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	16.05 (24.32)	0.0	0.00	100.0
		Placebo	73	23 (31.5)	13.04 (24.08)	0.0	0.00	100.0
	Week 48	Osimertinib	143	100 (69.9)	17.67 (25.71)	0.0	0.00	100.0
		Placebo	73	25 (34.2)	16.00 (19.53)	0.0	0.00	66.7
	Week 56	Osimertinib	143	88 (61.5)	17.80 (24.21)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	10.26 (16.01)	0.0	0.00	33.3
	Week 64	Osimertinib	143	93 (65.0)	19.00 (27.10)	0.0	0.00	100.0
		Placebo	73	15 (20.5)	11.11 (20.57)	0.0	0.00	66.7
	Week 72	Osimertinib	143	90 (62.9)	17.41 (25.10)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	12.82 (16.88)	0.0	0.00	33.3
	Week 80	Osimertinib	143	88 (61.5)	16.29 (23.70)	0.0	0.00	100.0
		Placebo	73	9 (12.3)	18.52 (24.22)	0.0	0.00	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1QM_MFH0: Course of QLQ-C30 Financial difficulties
 Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Financial difficulties	Week 88	Osimertinib	143	79 (55.2)	14.77 (24.89)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	16.67 (17.82)	0.0	16.67	33.3
	Week 96	Osimertinib	143	79 (55.2)	15.61 (24.36)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	22.22 (27.22)	0.0	16.67	66.7
	Week 104	Osimertinib	143	71 (49.7)	15.96 (23.13)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	12.50 (17.25)	0.0	0.00	33.3
	Week 112	Osimertinib	143	63 (44.1)	15.34 (24.56)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 120	Osimertinib	143	61 (42.7)	14.21 (21.48)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 128	Osimertinib	143	52 (36.4)	17.31 (25.13)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 136	Osimertinib	143	44 (30.8)	14.39 (22.04)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 144	Osimertinib	143	39 (27.3)	13.68 (21.24)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 152	Osimertinib	143	35 (24.5)	15.24 (23.35)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	11.11 (18.22)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	10.61 (15.89)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca

Value Dossier Analysis: D5160C00048

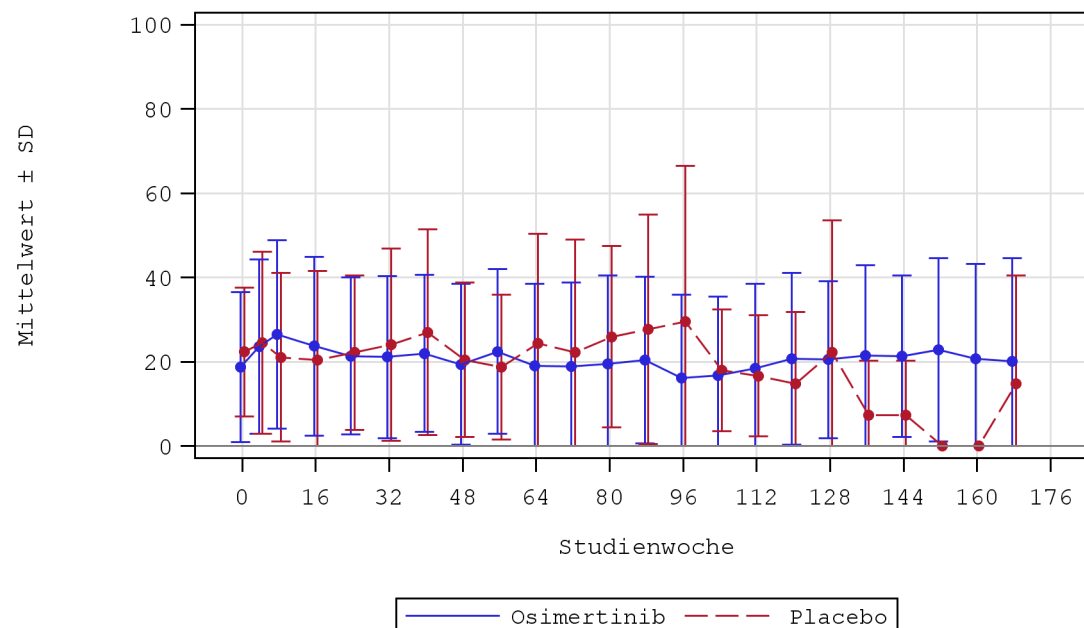
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QF_MFG0: Course of QLQ-C30 Fatigue
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QF_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

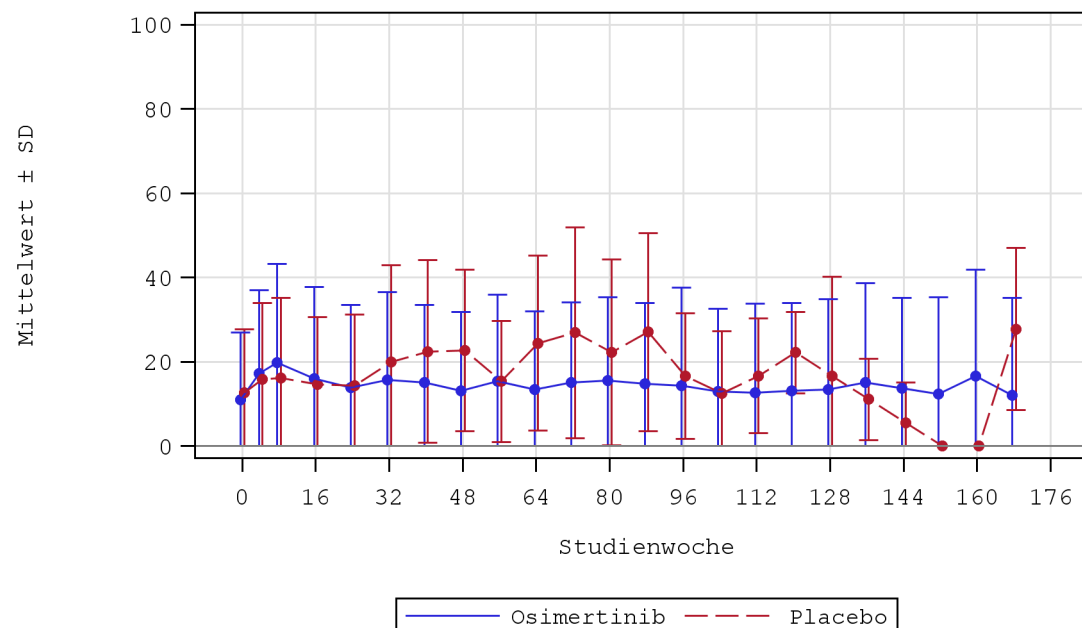
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QP_MFG0: Course of QLQ-C30 Pain
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QP_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

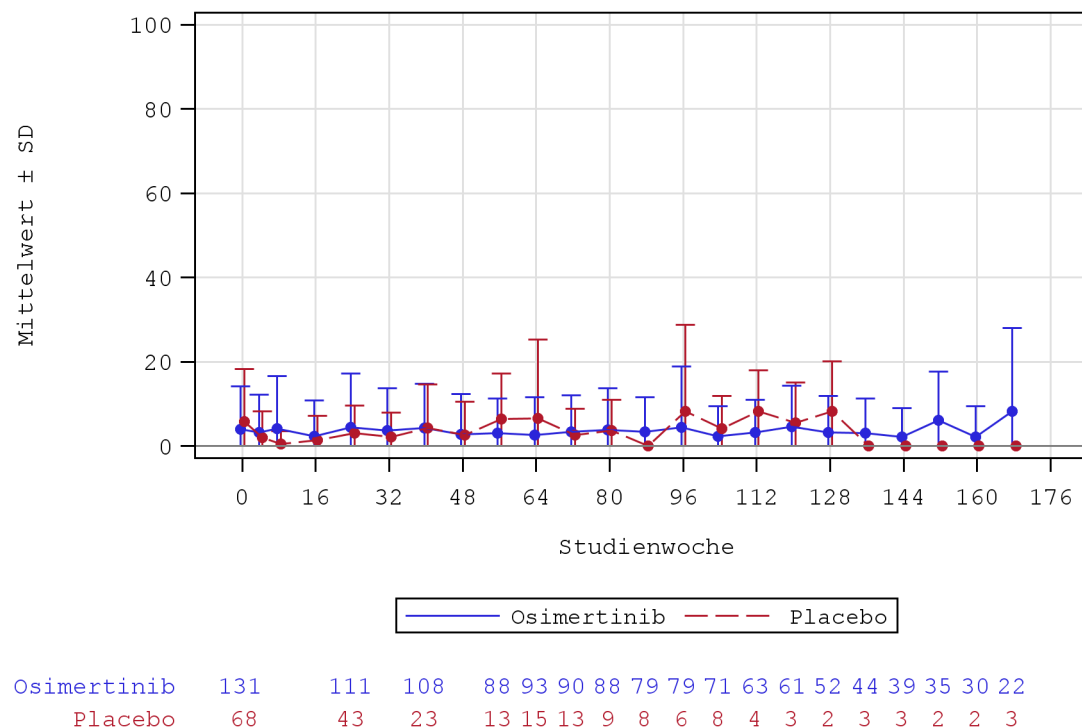
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QV_MFG0: Course of QLQ-C30 Nausea/vomiting
Full Analysis Set
Study: LAURA



Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QV_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

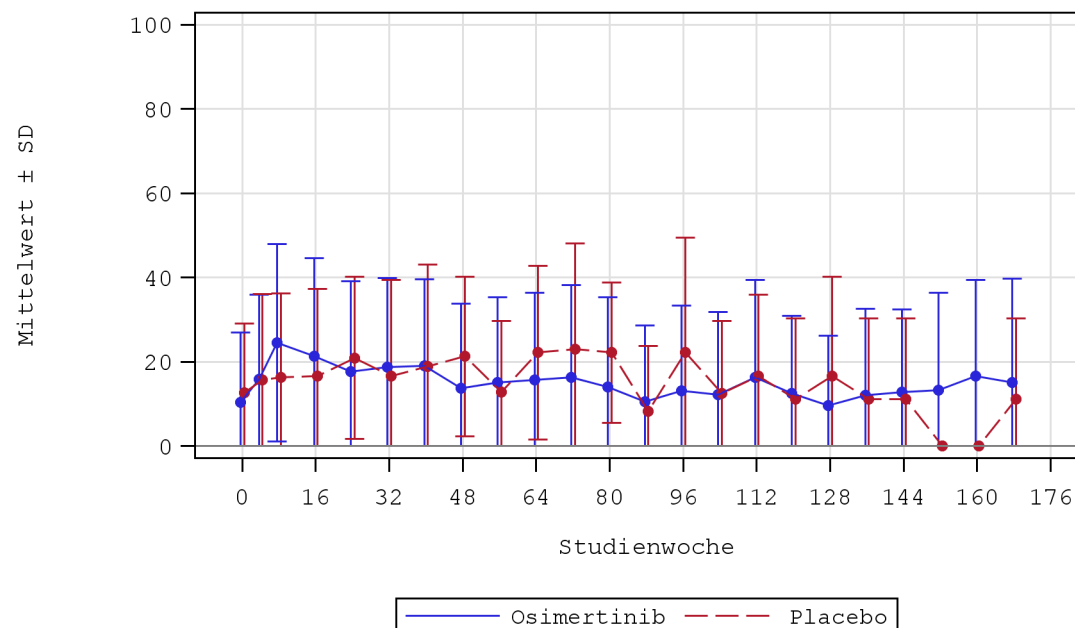
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QD_MFG0: Course of QLQ-C30 Dyspnoea
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QD_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

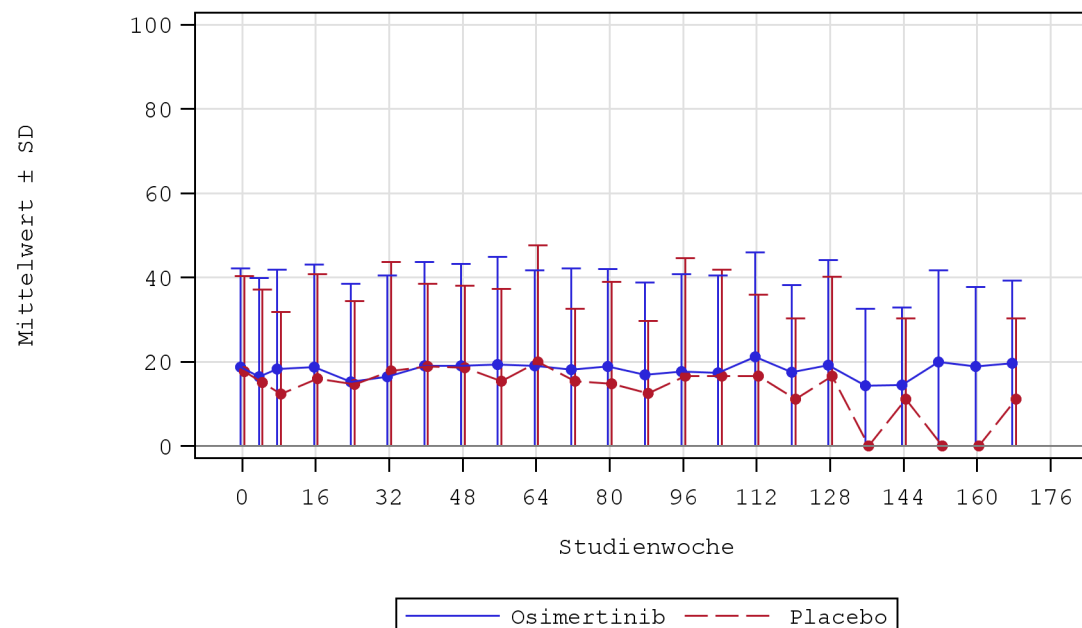
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QI_MFG0: Course of QLQ-C30 Insomnia
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QI_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

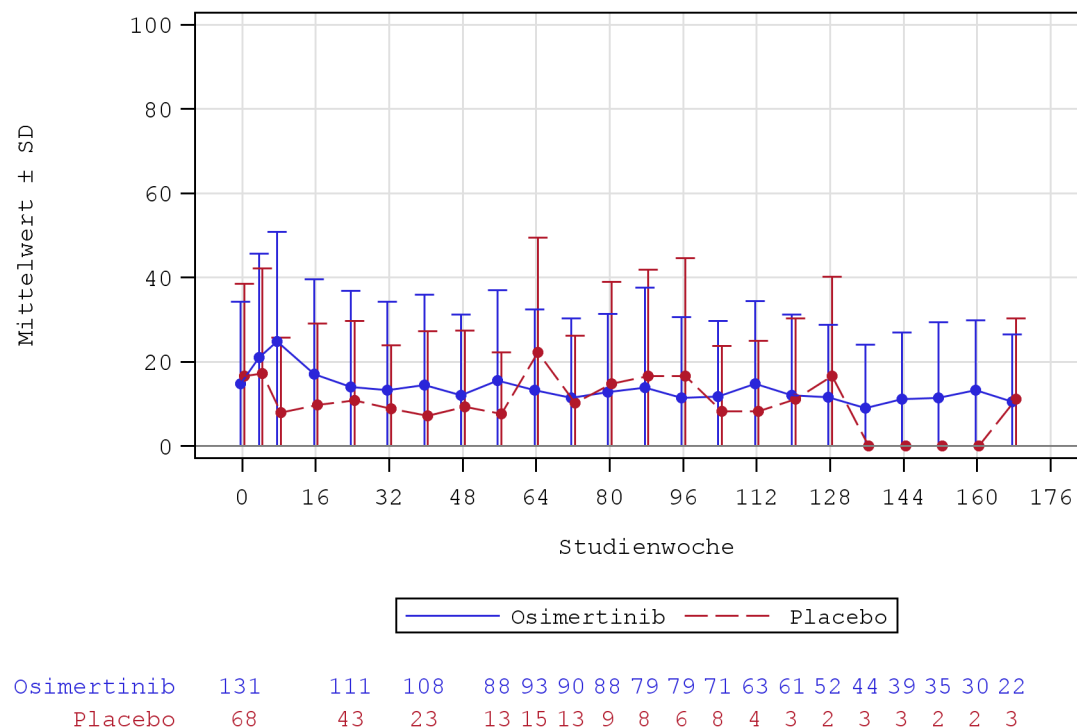
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QA_MFG0: Course of QLQ-C30 Appetite loss
Full Analysis Set
Study: LAURA



Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QA_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

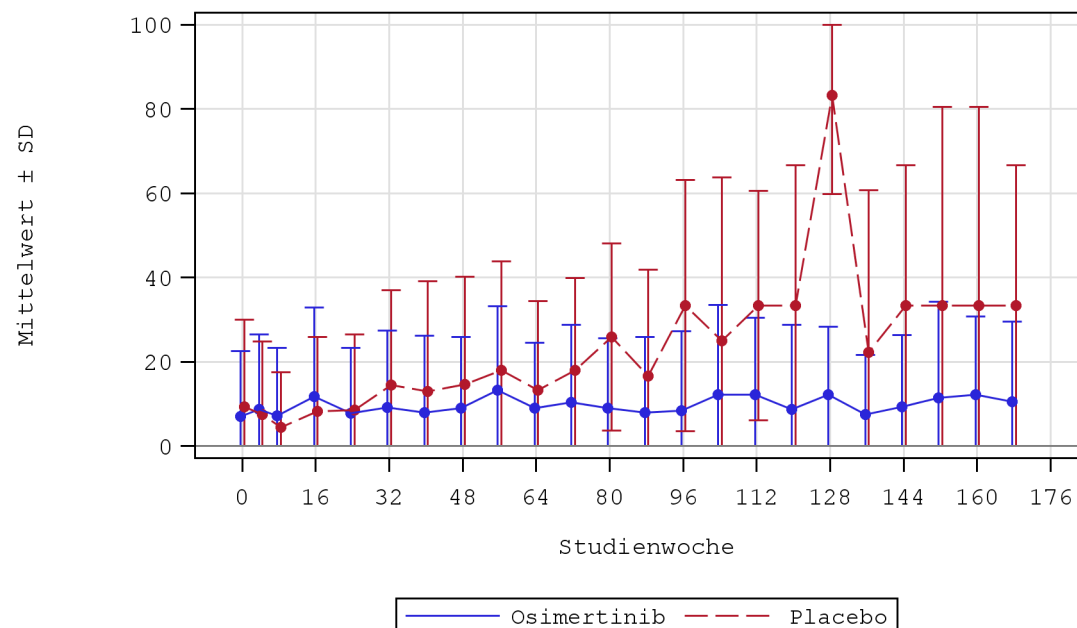
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QC_MFG0: Course of QLQ-C30 Constipation
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QC_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

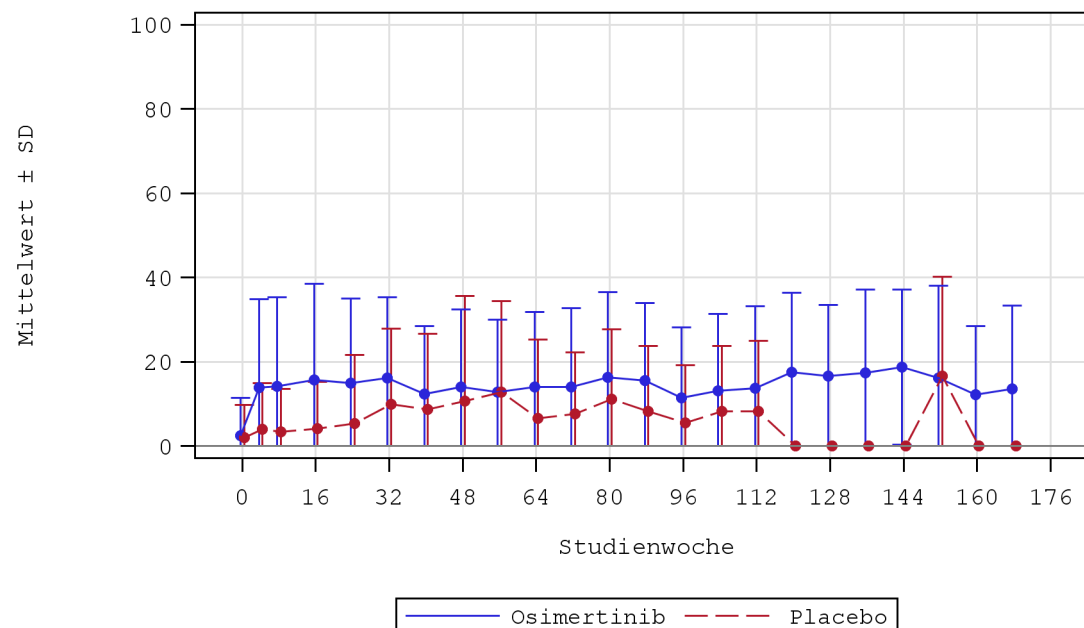
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QH_MFG0: Course of QLQ-C30 Diarrhea
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QH_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

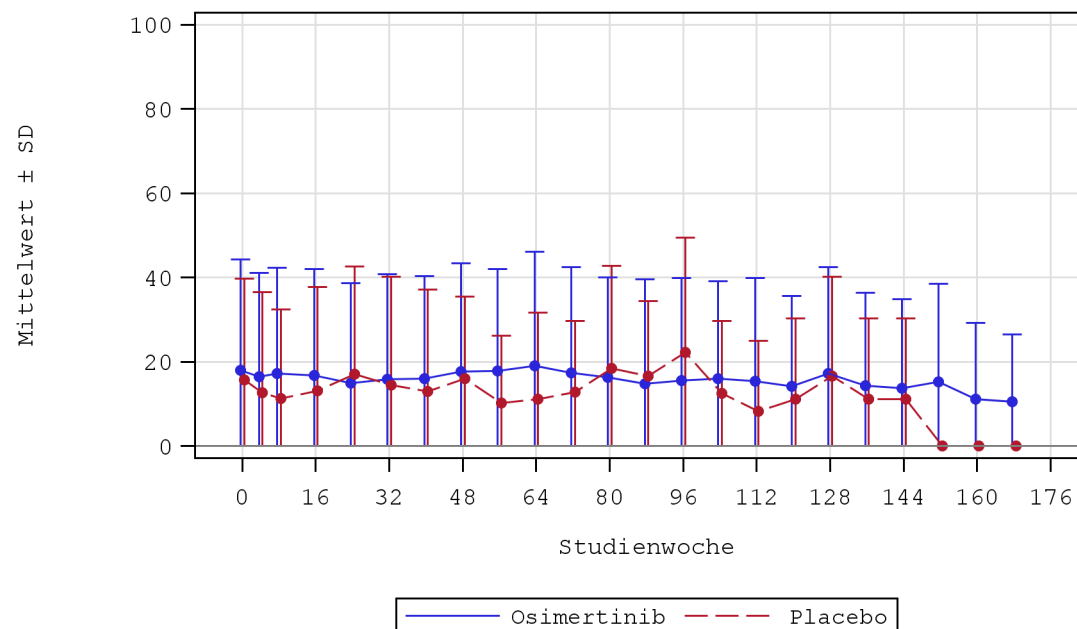
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QM_MFG0: Course of QLQ-C30 Financial difficulties
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QM_MFH0

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 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LCI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Coughing - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Coughing	LAURA	Osimertinib	Deterioration	143	99 (69.2)
			No deterioration at time of analysis	143	21 (14.7)
			Baseline score too low/high	143	1 (0.7)
			Death without event	143	2 (1.4)
			>= 2 consecutive missed visits	143	8 (5.6)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	46 (63.0)
			No deterioration at time of analysis	73	16 (21.9)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	4 (5.5)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LHI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Haemoptysis - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Haemoptysis	LAURA	Osimertinib	Deterioration	143	49 (34.3)
			No deterioration at time of analysis	143	57 (39.9)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	7 (4.9)
			>= 2 consecutive missed visits	143	18 (12.6)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	17 (23.3)
			No deterioration at time of analysis	73	43 (58.9)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	6 (8.2)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LPI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Dysphagia - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Dysphagia	LAURA	Osimertinib	Deterioration	143	62 (43.4)
			No deterioration at time of analysis	143	49 (34.3)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	3 (2.1)
			>= 2 consecutive missed visits	143	17 (11.9)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	28 (38.4)
			No deterioration at time of analysis	73	32 (43.8)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	6 (8.2)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LEI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder	LAURA	Osimertinib	Deterioration	143	93 (65.0)
			No deterioration at time of analysis	143	21 (14.7)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	3 (2.1)
			>= 2 consecutive missed visits	143	14 (9.8)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	34 (46.6)
			No deterioration at time of analysis	73	29 (39.7)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	0 (0.0)
			>= 2 consecutive missed visits	73	5 (6.8)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LOI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Pain in other parts - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Pain in other parts	LAURA	Osimertinib	Deterioration	143	84 (58.7)
			No deterioration at time of analysis	143	27 (18.9)
			Baseline score too low/high	143	1 (0.7)
			Death without event	143	3 (2.1)
			>= 2 consecutive missed visits	143	16 (11.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	46 (63.0)
			No deterioration at time of analysis	73	15 (20.5)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	6 (8.2)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LBI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Pain in chest - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Pain in chest	LAURA	Osimertinib	Deterioration	143	86 (60.1)
			No deterioration at time of analysis	143	29 (20.3)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	3 (2.1)
			>= 2 consecutive missed visits	143	13 (9.1)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	36 (49.3)
			No deterioration at time of analysis	73	27 (37.0)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	0 (0.0)
			>= 2 consecutive missed visits	73	5 (6.8)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LSI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Sore mouth - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Sore mouth	LAURA	Osimertinib	Deterioration	143	90 (62.9)
			No deterioration at time of analysis	143	25 (17.5)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	3 (2.1)
			>= 2 consecutive missed visits	143	13 (9.1)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	40 (54.8)
			No deterioration at time of analysis	73	21 (28.8)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	6 (8.2)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LDI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Dyspnoea - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Dyspnoea	LAURA	Osimertinib	Deterioration	143	110 (76.9)
			No deterioration at time of analysis	143	15 (10.5)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	0 (0.0)
			>= 2 consecutive missed visits	143	6 (4.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	48 (65.8)
			No deterioration at time of analysis	73	18 (24.7)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	1 (1.4)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LNI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy	LAURA	Osimertinib	Deterioration	143	87 (60.8)
			No deterioration at time of analysis	143	22 (15.4)
			Baseline score too low/high	143	3 (2.1)
			Death without event	143	4 (2.8)
			>= 2 consecutive missed visits	143	15 (10.5)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	35 (47.9)
			No deterioration at time of analysis	73	26 (35.6)
			Baseline score too low/high	73	1 (1.4)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	5 (6.8)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LAI10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Alopecia - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Alopecia	LAURA	Osimertinib	Deterioration	143	44 (30.8)
			No deterioration at time of analysis	143	61 (42.7)
			Baseline score too low/high	143	1 (0.7)
			Death without event	143	9 (6.3)
			>= 2 consecutive missed visits	143	16 (11.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	0 (0.0)
		Placebo	Deterioration	73	20 (27.4)
			No deterioration at time of analysis	73	37 (50.7)
			Baseline score too low/high	73	2 (2.7)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	8 (11.0)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1LTII10T_MFA0: Time to increase by at least 10 points in QLQ-LC13 Take any medicine - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain	LAURA	Osimertinib	Deterioration	143	7 (4.9)
			No deterioration at time of analysis	143	4 (2.8)
			Baseline score too low/high	143	2 (1.4)
			Death without event	143	0 (0.0)
			>= 2 consecutive missed visits	143	12 (8.4)
			No baseline data recorded at time of analysis	143	116 (81.1)
			No post-baseline data recorded at time of analysis	143	2 (1.4)
		Placebo	Deterioration	73	1 (1.4)
			No deterioration at time of analysis	73	6 (8.2)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	0 (0.0)
			>= 2 consecutive missed visits	73	12 (16.4)
			No baseline data recorded at time of analysis	73	52 (71.2)
			No post-baseline data recorded at time of analysis	73	2 (2.7)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-LC13: EORTC Cancer Quality of Life Questionnaire - Lung Cancer 13 items.
 Source Data: APRO_TTE, created on: 03SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1LC_MFH0: Course of QLQ-LC13 Coughing
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Coughing	Baseline	Osimertinib	143	131 (91.6)	20.61 (20.02)	0.0	33.33	100.0
		Placebo	73	68 (93.2)	24.51 (20.46)	0.0	33.33	100.0
	Week 2	Osimertinib	143	139 (97.2)	24.46 (22.55)	0.0	33.33	100.0
		Placebo	73	71 (97.3)	26.29 (23.85)	0.0	33.33	66.7
	Week 3	Osimertinib	143	129 (90.2)	23.51 (22.21)	0.0	33.33	100.0
		Placebo	73	64 (87.7)	33.85 (21.82)	0.0	33.33	100.0
	Week 4	Osimertinib	143	132 (92.3)	29.04 (23.45)	0.0	33.33	100.0
		Placebo	73	70 (95.9)	29.05 (24.02)	0.0	33.33	100.0
	Week 5	Osimertinib	143	125 (87.4)	27.73 (23.85)	0.0	33.33	100.0
		Placebo	73	66 (90.4)	28.28 (22.83)	0.0	33.33	100.0
	Week 6	Osimertinib	143	125 (87.4)	30.13 (24.84)	0.0	33.33	100.0
		Placebo	73	67 (91.8)	29.85 (24.71)	0.0	33.33	100.0
	Week 7	Osimertinib	143	125 (87.4)	34.13 (26.25)	0.0	33.33	100.0
		Placebo	73	64 (87.7)	30.21 (21.18)	0.0	33.33	66.7
	Week 8	Osimertinib	143	129 (90.2)	34.37 (25.32)	0.0	33.33	100.0
		Placebo	73	59 (80.8)	32.20 (23.13)	0.0	33.33	100.0
	Week 12	Osimertinib	143	125 (87.4)	36.27 (27.44)	0.0	33.33	100.0
		Placebo	73	63 (86.3)	32.28 (23.16)	0.0	33.33	66.7
	Week 16	Osimertinib	143	120 (83.9)	31.94 (24.60)	0.0	33.33	100.0
		Placebo	73	48 (65.8)	27.08 (21.37)	0.0	33.33	66.7
	Week 20	Osimertinib	143	118 (82.5)	31.07 (24.16)	0.0	33.33	100.0
		Placebo	73	56 (76.7)	27.38 (20.21)	0.0	33.33	66.7
	Week 24	Osimertinib	143	112 (78.3)	27.38 (22.47)	0.0	33.33	100.0
		Placebo	73	43 (58.9)	34.11 (24.65)	0.0	33.33	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1LC_MFH0: Course of QLQ-LC13 Coughing
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Coughing	Week 28	Osimertinib	143	106 (74.1)	28.93 (23.04)	0.0	33.33	100.0
		Placebo	73	35 (47.9)	28.57 (24.45)	0.0	33.33	100.0
	Week 32	Osimertinib	143	107 (74.8)	24.61 (20.65)	0.0	33.33	66.7
		Placebo	73	30 (41.1)	28.89 (28.68)	0.0	33.33	100.0
	Week 36	Osimertinib	143	105 (73.4)	26.98 (22.69)	0.0	33.33	100.0
		Placebo	73	26 (35.6)	23.08 (26.28)	0.0	33.33	100.0
	Week 40	Osimertinib	143	108 (75.5)	28.09 (21.93)	0.0	33.33	100.0
		Placebo	73	24 (32.9)	25.00 (20.26)	0.0	33.33	66.7
	Week 44	Osimertinib	143	96 (67.1)	26.39 (22.12)	0.0	33.33	100.0
		Placebo	73	23 (31.5)	21.74 (21.58)	0.0	33.33	66.7
	Week 48	Osimertinib	143	100 (69.9)	26.67 (22.22)	0.0	33.33	66.7
		Placebo	73	25 (34.2)	26.67 (21.52)	0.0	33.33	66.7
	Week 52	Osimertinib	143	94 (65.7)	21.63 (22.24)	0.0	33.33	100.0
		Placebo	73	19 (26.0)	28.07 (25.49)	0.0	33.33	100.0
	Week 56	Osimertinib	143	88 (61.5)	25.38 (22.60)	0.0	33.33	100.0
		Placebo	73	13 (17.8)	20.51 (16.88)	0.0	33.33	33.3
	Week 60	Osimertinib	143	97 (67.8)	26.46 (25.88)	0.0	33.33	100.0
		Placebo	73	18 (24.7)	25.93 (24.40)	0.0	33.33	100.0
	Week 64	Osimertinib	143	94 (65.7)	25.89 (24.02)	0.0	33.33	100.0
		Placebo	73	15 (20.5)	17.78 (17.21)	0.0	33.33	33.3
	Week 68	Osimertinib	143	89 (62.2)	24.34 (19.95)	0.0	33.33	66.7
		Placebo	73	11 (15.1)	27.27 (29.13)	0.0	33.33	100.0
	Week 72	Osimertinib	143	90 (62.9)	25.93 (24.37)	0.0	33.33	100.0
		Placebo	73	13 (17.8)	23.08 (16.01)	0.0	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Program Name: LT1_APR0_H0.sas
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Table LT1LC_MFH0: Course of QLQ-LC13 Coughing
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Coughing	Week 76	Osimertinib	143	89 (62.2)	23.97 (19.46)	0.0	33.33	66.7
		Placebo	73	8 (11.0)	33.33 (17.82)	0.0	33.33	66.7
	Week 80	Osimertinib	143	89 (62.2)	24.72 (22.77)	0.0	33.33	100.0
		Placebo	73	9 (12.3)	29.63 (30.93)	0.0	33.33	100.0
	Week 84	Osimertinib	143	83 (58.0)	25.70 (19.70)	0.0	33.33	66.7
		Placebo	73	10 (13.7)	23.33 (31.62)	0.0	16.67	100.0
	Week 88	Osimertinib	143	79 (55.2)	22.36 (21.16)	0.0	33.33	66.7
		Placebo	73	8 (11.0)	16.67 (17.82)	0.0	16.67	33.3
	Week 92	Osimertinib	143	77 (53.8)	27.71 (26.16)	0.0	33.33	100.0
		Placebo	73	8 (11.0)	29.17 (11.79)	0.0	33.33	33.3
	Week 96	Osimertinib	143	79 (55.2)	22.36 (23.09)	0.0	33.33	100.0
		Placebo	73	6 (8.2)	27.78 (13.61)	0.0	33.33	33.3
	Week 100	Osimertinib	143	67 (46.9)	23.88 (21.56)	0.0	33.33	100.0
		Placebo	73	7 (9.6)	19.05 (17.82)	0.0	33.33	33.3
	Week 104	Osimertinib	143	70 (49.0)	24.76 (23.18)	0.0	33.33	100.0
		Placebo	73	8 (11.0)	29.17 (11.79)	0.0	33.33	33.3
	Week 108	Osimertinib	143	69 (48.3)	23.19 (23.08)	0.0	33.33	66.7
		Placebo	73	5 (6.8)	33.33 (0.00)	33.3	33.33	33.3
	Week 112	Osimertinib	143	62 (43.4)	23.12 (26.02)	0.0	33.33	100.0
		Placebo	73	4 (5.5)	16.67 (19.25)	0.0	16.67	33.3
	Week 116	Osimertinib	143	64 (44.8)	23.44 (24.97)	0.0	33.33	100.0
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 120	Osimertinib	143	61 (42.7)	23.50 (21.38)	0.0	33.33	100.0
		Placebo	73	3 (4.1)	33.33 (0.00)	33.3	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LC_MFH0: Course of QLQ-LC13 Coughing
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Coughing	Week 124	Osimertinib	143	47 (32.9)	19.15 (22.78)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 128	Osimertinib	143	51 (35.7)	22.22 (19.63)	0.0	33.33	66.7
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 132	Osimertinib	143	49 (34.3)	22.45 (25.81)	0.0	33.33	100.0
		Placebo	73	4 (5.5)	33.33 (0.00)	33.3	33.33	33.3
	Week 136	Osimertinib	143	44 (30.8)	21.97 (26.84)	0.0	16.67	100.0
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 140	Osimertinib	143	43 (30.1)	20.93 (25.22)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 144	Osimertinib	143	39 (27.3)	22.22 (23.36)	0.0	33.33	100.0
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 148	Osimertinib	143	37 (25.9)	24.32 (29.03)	0.0	33.33	100.0
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 152	Osimertinib	143	35 (24.5)	25.71 (28.11)	0.0	33.33	100.0
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 156	Osimertinib	143	32 (22.4)	32.29 (26.07)	0.0	33.33	100.0
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 160	Osimertinib	143	30 (21.0)	30.00 (28.16)	0.0	33.33	100.0
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 164	Osimertinib	143	28 (19.6)	28.57 (28.28)	0.0	33.33	100.0
		Placebo	73	3 (4.1)	33.33 (0.00)	33.3	33.33	33.3
	Week 168	Osimertinib	143	22 (15.4)	27.27 (28.43)	0.0	33.33	100.0
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1LH_MFH0: Course of QLQ-LC13 Haemoptysis
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Haemoptysis	Baseline	Osimertinib	143	131 (91.6)	0.76 (5.01)	0.0	0.00	33.3
		Placebo	73	68 (93.2)	1.47 (6.90)	0.0	0.00	33.3
	Week 2	Osimertinib	143	139 (97.2)	1.44 (6.80)	0.0	0.00	33.3
		Placebo	73	71 (97.3)	0.94 (5.55)	0.0	0.00	33.3
	Week 3	Osimertinib	143	129 (90.2)	1.29 (6.46)	0.0	0.00	33.3
		Placebo	73	64 (87.7)	3.65 (12.05)	0.0	0.00	66.7
	Week 4	Osimertinib	143	132 (92.3)	1.01 (5.74)	0.0	0.00	33.3
		Placebo	73	70 (95.9)	1.43 (6.80)	0.0	0.00	33.3
	Week 5	Osimertinib	143	125 (87.4)	2.93 (10.38)	0.0	0.00	66.7
		Placebo	73	66 (90.4)	2.02 (8.01)	0.0	0.00	33.3
	Week 6	Osimertinib	143	125 (87.4)	0.53 (4.20)	0.0	0.00	33.3
		Placebo	73	67 (91.8)	2.49 (8.83)	0.0	0.00	33.3
	Week 7	Osimertinib	143	125 (87.4)	1.33 (6.56)	0.0	0.00	33.3
		Placebo	73	64 (87.7)	2.08 (8.13)	0.0	0.00	33.3
	Week 8	Osimertinib	143	129 (90.2)	1.29 (6.46)	0.0	0.00	33.3
		Placebo	73	59 (80.8)	0.56 (4.34)	0.0	0.00	33.3
	Week 12	Osimertinib	143	125 (87.4)	1.33 (7.81)	0.0	0.00	66.7
		Placebo	73	63 (86.3)	2.12 (8.19)	0.0	0.00	33.3
	Week 16	Osimertinib	143	120 (83.9)	1.94 (10.84)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	4.17 (13.09)	0.0	0.00	66.7
	Week 20	Osimertinib	143	118 (82.5)	1.98 (9.03)	0.0	0.00	66.7
		Placebo	73	56 (76.7)	1.79 (9.89)	0.0	0.00	66.7
	Week 24	Osimertinib	143	112 (78.3)	1.79 (7.54)	0.0	0.00	33.3
		Placebo	73	43 (58.9)	3.10 (9.80)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LH_MFH0: Course of QLQ-LC13 Haemoptysis
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Haemoptysis	Week 28	Osimertinib	143	106 (74.1)	0.31 (3.24)	0.0	0.00	33.3
		Placebo	73	35 (47.9)	1.90 (7.85)	0.0	0.00	33.3
	Week 32	Osimertinib	143	107 (74.8)	0.93 (5.53)	0.0	0.00	33.3
		Placebo	73	30 (41.1)	2.22 (8.46)	0.0	0.00	33.3
	Week 36	Osimertinib	143	105 (73.4)	1.90 (7.77)	0.0	0.00	33.3
		Placebo	73	26 (35.6)	1.28 (6.54)	0.0	0.00	33.3
	Week 40	Osimertinib	143	108 (75.5)	0.93 (5.50)	0.0	0.00	33.3
		Placebo	73	24 (32.9)	1.39 (6.80)	0.0	0.00	33.3
	Week 44	Osimertinib	143	96 (67.1)	2.08 (8.11)	0.0	0.00	33.3
		Placebo	73	23 (31.5)	0.00 (0.00)	0.0	0.00	0.0
	Week 48	Osimertinib	143	100 (69.9)	0.33 (3.33)	0.0	0.00	33.3
		Placebo	73	25 (34.2)	0.00 (0.00)	0.0	0.00	0.0
	Week 52	Osimertinib	143	94 (65.7)	1.42 (6.76)	0.0	0.00	33.3
		Placebo	73	19 (26.0)	1.75 (7.65)	0.0	0.00	33.3
	Week 56	Osimertinib	143	88 (61.5)	0.76 (5.00)	0.0	0.00	33.3
		Placebo	73	13 (17.8)	0.00 (0.00)	0.0	0.00	0.0
	Week 60	Osimertinib	143	97 (67.8)	2.41 (12.03)	0.0	0.00	100.0
		Placebo	73	18 (24.7)	1.85 (7.86)	0.0	0.00	33.3
	Week 64	Osimertinib	143	94 (65.7)	2.13 (8.19)	0.0	0.00	33.3
		Placebo	73	15 (20.5)	4.44 (11.73)	0.0	0.00	33.3
	Week 68	Osimertinib	143	89 (62.2)	1.87 (7.72)	0.0	0.00	33.3
		Placebo	73	11 (15.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 72	Osimertinib	143	90 (62.9)	1.11 (6.02)	0.0	0.00	33.3
		Placebo	73	13 (17.8)	0.00 (0.00)	0.0	0.00	0.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
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Table LT1LH_MFH0: Course of QLQ-LC13 Haemoptysis
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Haemoptysis	Week 76	Osimertinib	143	89 (62.2)	0.75 (4.97)	0.0	0.00	33.3
		Placebo	73	8 (11.0)	0.00 (0.00)	0.0	0.00	0.0
	Week 80	Osimertinib	143	89 (62.2)	0.37 (3.53)	0.0	0.00	33.3
		Placebo	73	9 (12.3)	0.00 (0.00)	0.0	0.00	0.0
	Week 84	Osimertinib	143	83 (58.0)	0.80 (5.14)	0.0	0.00	33.3
		Placebo	73	10 (13.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 88	Osimertinib	143	79 (55.2)	0.84 (5.27)	0.0	0.00	33.3
		Placebo	73	8 (11.0)	0.00 (0.00)	0.0	0.00	0.0
	Week 92	Osimertinib	143	77 (53.8)	0.00 (0.00)	0.0	0.00	0.0
		Placebo	73	8 (11.0)	0.00 (0.00)	0.0	0.00	0.0
	Week 96	Osimertinib	143	79 (55.2)	0.42 (3.75)	0.0	0.00	33.3
		Placebo	73	6 (8.2)	0.00 (0.00)	0.0	0.00	0.0
	Week 100	Osimertinib	143	67 (46.9)	0.50 (4.07)	0.0	0.00	33.3
		Placebo	73	7 (9.6)	0.00 (0.00)	0.0	0.00	0.0
	Week 104	Osimertinib	143	70 (49.0)	0.00 (0.00)	0.0	0.00	0.0
		Placebo	73	8 (11.0)	0.00 (0.00)	0.0	0.00	0.0
	Week 108	Osimertinib	143	69 (48.3)	0.97 (5.63)	0.0	0.00	33.3
		Placebo	73	5 (6.8)	0.00 (0.00)	0.0	0.00	0.0
	Week 112	Osimertinib	143	62 (43.4)	0.54 (4.23)	0.0	0.00	33.3
		Placebo	73	4 (5.5)	0.00 (0.00)	0.0	0.00	0.0
	Week 116	Osimertinib	143	64 (44.8)	1.04 (8.33)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	0.00 (0.00)	0.0	0.00	0.0
	Week 120	Osimertinib	143	61 (42.7)	0.55 (4.27)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
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Table LT1LH_MFH0: Course of QLQ-LC13 Haemoptysis
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Haemoptysis	Week 124	Osimertinib	143	47 (32.9)	2.13 (8.24)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 128	Osimertinib	143	51 (35.7)	3.27 (12.03)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 132	Osimertinib	143	49 (34.3)	2.04 (10.56)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	0.00 (0.00)	0.0	0.00	0.0
	Week 136	Osimertinib	143	44 (30.8)	0.00 (0.00)	0.0	0.00	0.0
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 140	Osimertinib	143	43 (30.1)	0.78 (5.08)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 144	Osimertinib	143	39 (27.3)	0.85 (5.34)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 148	Osimertinib	143	37 (25.9)	0.90 (5.48)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 152	Osimertinib	143	35 (24.5)	0.00 (0.00)	0.0	0.00	0.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 156	Osimertinib	143	32 (22.4)	2.08 (11.79)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	4.44 (16.91)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 164	Osimertinib	143	28 (19.6)	5.95 (18.27)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	4.55 (15.59)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1LP_MFH0: Course of QLQ-LC13 Dysphagia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Dysphagia	Baseline	Osimertinib	143	131 (91.6)	10.18 (17.49)	0.0	0.00	66.7
		Placebo	73	68 (93.2)	10.29 (17.52)	0.0	0.00	66.7
	Week 2	Osimertinib	143	139 (97.2)	7.67 (16.21)	0.0	0.00	66.7
		Placebo	73	71 (97.3)	8.45 (17.56)	0.0	0.00	100.0
	Week 3	Osimertinib	143	129 (90.2)	8.01 (15.46)	0.0	0.00	66.7
		Placebo	73	64 (87.7)	9.38 (19.22)	0.0	0.00	100.0
	Week 4	Osimertinib	143	132 (92.3)	8.84 (16.91)	0.0	0.00	66.7
		Placebo	73	70 (95.9)	10.00 (19.12)	0.0	0.00	100.0
	Week 5	Osimertinib	143	125 (87.4)	10.13 (15.97)	0.0	0.00	66.7
		Placebo	73	66 (90.4)	6.57 (15.71)	0.0	0.00	66.7
	Week 6	Osimertinib	143	125 (87.4)	9.87 (17.47)	0.0	0.00	100.0
		Placebo	73	67 (91.8)	7.96 (18.43)	0.0	0.00	100.0
	Week 7	Osimertinib	143	125 (87.4)	9.60 (16.84)	0.0	0.00	66.7
		Placebo	73	64 (87.7)	6.25 (14.40)	0.0	0.00	66.7
	Week 8	Osimertinib	143	129 (90.2)	9.82 (18.82)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	6.78 (14.88)	0.0	0.00	66.7
	Week 12	Osimertinib	143	125 (87.4)	8.27 (17.28)	0.0	0.00	100.0
		Placebo	73	63 (86.3)	7.94 (18.66)	0.0	0.00	100.0
	Week 16	Osimertinib	143	120 (83.9)	7.50 (16.99)	0.0	0.00	66.7
		Placebo	73	48 (65.8)	6.25 (13.15)	0.0	0.00	33.3
	Week 20	Osimertinib	143	118 (82.5)	7.91 (17.80)	0.0	0.00	100.0
		Placebo	73	56 (76.7)	5.95 (18.10)	0.0	0.00	100.0
	Week 24	Osimertinib	143	112 (78.3)	6.85 (14.93)	0.0	0.00	66.7
		Placebo	73	43 (58.9)	6.98 (21.28)	0.0	0.00	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Table LT1LP_MFH0: Course of QLQ-LC13 Dysphagia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Dysphagia	Week 28	Osimertinib	143	106 (74.1)	5.03 (11.99)	0.0	0.00	33.3
		Placebo	73	35 (47.9)	4.76 (14.33)	0.0	0.00	66.7
	Week 32	Osimertinib	143	107 (74.8)	8.41 (15.25)	0.0	0.00	66.7
		Placebo	73	30 (41.1)	8.89 (23.05)	0.0	0.00	100.0
	Week 36	Osimertinib	143	105 (73.4)	5.71 (12.62)	0.0	0.00	33.3
		Placebo	73	26 (35.6)	10.26 (22.65)	0.0	0.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	7.10 (13.71)	0.0	0.00	33.3
		Placebo	73	24 (32.9)	8.33 (22.52)	0.0	0.00	100.0
	Week 44	Osimertinib	143	96 (67.1)	6.94 (15.23)	0.0	0.00	66.7
		Placebo	73	23 (31.5)	13.04 (24.08)	0.0	0.00	100.0
	Week 48	Osimertinib	143	100 (69.9)	7.33 (15.41)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	10.67 (23.01)	0.0	0.00	100.0
	Week 52	Osimertinib	143	94 (65.7)	7.09 (14.56)	0.0	0.00	66.7
		Placebo	73	19 (26.0)	8.77 (24.45)	0.0	0.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	7.95 (14.29)	0.0	0.00	33.3
		Placebo	73	13 (17.8)	12.82 (28.99)	0.0	0.00	100.0
	Week 60	Osimertinib	143	97 (67.8)	6.87 (15.91)	0.0	0.00	66.7
		Placebo	73	18 (24.7)	9.26 (25.06)	0.0	0.00	100.0
	Week 64	Osimertinib	143	94 (65.7)	7.45 (15.58)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	6.67 (13.80)	0.0	0.00	33.3
	Week 68	Osimertinib	143	89 (62.2)	6.74 (13.47)	0.0	0.00	33.3
		Placebo	73	11 (15.1)	3.03 (10.05)	0.0	0.00	33.3
	Week 72	Osimertinib	143	90 (62.9)	7.04 (15.40)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	10.26 (16.01)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Program Name: LT1_APR0_H0.sas
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Table LT1LP_MFH0: Course of QLQ-LC13 Dysphagia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Dysphagia	Week 76	Osimertinib	143	89 (62.2)	8.61 (15.51)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 80	Osimertinib	143	89 (62.2)	7.49 (14.87)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	7.41 (14.70)	0.0	0.00	33.3
	Week 84	Osimertinib	143	83 (58.0)	6.83 (14.50)	0.0	0.00	66.7
		Placebo	73	10 (13.7)	6.67 (14.05)	0.0	0.00	33.3
	Week 88	Osimertinib	143	79 (55.2)	6.75 (14.50)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 92	Osimertinib	143	77 (53.8)	4.76 (11.74)	0.0	0.00	33.3
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 96	Osimertinib	143	79 (55.2)	5.91 (12.81)	0.0	0.00	33.3
		Placebo	73	6 (8.2)	5.56 (13.61)	0.0	0.00	33.3
	Week 100	Osimertinib	143	67 (46.9)	5.97 (12.88)	0.0	0.00	33.3
		Placebo	73	7 (9.6)	9.52 (16.27)	0.0	0.00	33.3
	Week 104	Osimertinib	143	70 (49.0)	8.10 (16.48)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	4.17 (11.79)	0.0	0.00	33.3
	Week 108	Osimertinib	143	69 (48.3)	7.25 (16.04)	0.0	0.00	66.7
		Placebo	73	5 (6.8)	6.67 (14.91)	0.0	0.00	33.3
	Week 112	Osimertinib	143	62 (43.4)	6.45 (13.28)	0.0	0.00	33.3
		Placebo	73	4 (5.5)	16.67 (19.25)	0.0	16.67	33.3
	Week 116	Osimertinib	143	64 (44.8)	6.77 (14.76)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 120	Osimertinib	143	61 (42.7)	7.10 (15.05)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LP_MFH0: Course of QLQ-LC13 Dysphagia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Dysphagia	Week 124	Osimertinib	143	47 (32.9)	8.51 (17.68)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 128	Osimertinib	143	51 (35.7)	6.54 (13.37)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 132	Osimertinib	143	49 (34.3)	8.16 (14.48)	0.0	0.00	33.3
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 136	Osimertinib	143	44 (30.8)	5.30 (12.33)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 140	Osimertinib	143	43 (30.1)	6.20 (13.12)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 144	Osimertinib	143	39 (27.3)	5.98 (12.96)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 148	Osimertinib	143	37 (25.9)	9.91 (15.45)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 152	Osimertinib	143	35 (24.5)	7.62 (14.20)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 156	Osimertinib	143	32 (22.4)	10.42 (17.84)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	6.67 (13.56)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 164	Osimertinib	143	28 (19.6)	8.33 (14.70)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	7.58 (14.30)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1LE_MFH0: Course of QLQ-LC13 Pain in arm/shoulder
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in arm/shoulder	Baseline	Osimertinib	143	131 (91.6)	10.69 (17.18)	0.0	0.00	66.7
		Placebo	73	68 (93.2)	14.71 (19.43)	0.0	0.00	66.7
	Week 2	Osimertinib	143	139 (97.2)	13.19 (21.47)	0.0	0.00	100.0
		Placebo	73	71 (97.3)	18.78 (21.63)	0.0	0.00	66.7
	Week 3	Osimertinib	143	129 (90.2)	10.59 (17.67)	0.0	0.00	66.7
		Placebo	73	64 (87.7)	17.71 (21.39)	0.0	0.00	66.7
	Week 4	Osimertinib	143	132 (92.3)	12.12 (21.11)	0.0	0.00	100.0
		Placebo	73	70 (95.9)	19.52 (22.34)	0.0	0.00	66.7
	Week 5	Osimertinib	143	125 (87.4)	13.33 (20.30)	0.0	0.00	66.7
		Placebo	73	66 (90.4)	16.67 (20.46)	0.0	0.00	66.7
	Week 6	Osimertinib	143	125 (87.4)	14.93 (20.50)	0.0	0.00	66.7
		Placebo	73	67 (91.8)	14.93 (18.61)	0.0	0.00	66.7
	Week 7	Osimertinib	143	125 (87.4)	15.20 (20.52)	0.0	0.00	66.7
		Placebo	73	64 (87.7)	17.19 (20.57)	0.0	0.00	66.7
	Week 8	Osimertinib	143	129 (90.2)	14.99 (22.03)	0.0	0.00	66.7
		Placebo	73	59 (80.8)	18.64 (19.84)	0.0	33.33	66.7
	Week 12	Osimertinib	143	125 (87.4)	11.47 (20.78)	0.0	0.00	100.0
		Placebo	73	63 (86.3)	16.40 (19.74)	0.0	0.00	66.7
	Week 16	Osimertinib	143	120 (83.9)	13.89 (20.08)	0.0	0.00	66.7
		Placebo	73	48 (65.8)	12.50 (16.31)	0.0	0.00	33.3
	Week 20	Osimertinib	143	118 (82.5)	13.28 (19.56)	0.0	0.00	66.7
		Placebo	73	56 (76.7)	16.67 (22.02)	0.0	0.00	66.7
	Week 24	Osimertinib	143	112 (78.3)	15.48 (23.65)	0.0	0.00	100.0
		Placebo	73	43 (58.9)	13.95 (19.56)	0.0	0.00	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LE_MFH0: Course of QLQ-LC13 Pain in arm/shoulder
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in arm/shoulder	Week 28	Osimertinib	143	106 (74.1)	17.30 (22.17)	0.0	0.00	100.0
		Placebo	73	35 (47.9)	13.33 (18.44)	0.0	0.00	66.7
	Week 32	Osimertinib	143	107 (74.8)	14.95 (23.45)	0.0	0.00	100.0
		Placebo	73	30 (41.1)	18.89 (20.87)	0.0	16.67	66.7
	Week 36	Osimertinib	143	105 (73.4)	13.02 (19.88)	0.0	0.00	66.7
		Placebo	73	26 (35.6)	21.79 (24.84)	0.0	33.33	100.0
	Week 40	Osimertinib	143	108 (75.5)	15.43 (23.87)	0.0	0.00	100.0
		Placebo	73	24 (32.9)	20.83 (21.56)	0.0	33.33	66.7
	Week 44	Osimertinib	143	96 (67.1)	13.89 (23.53)	0.0	0.00	100.0
		Placebo	73	23 (31.5)	23.19 (23.43)	0.0	33.33	66.7
	Week 48	Osimertinib	143	100 (69.9)	14.67 (23.36)	0.0	0.00	100.0
		Placebo	73	25 (34.2)	21.33 (25.24)	0.0	0.00	66.7
	Week 52	Osimertinib	143	94 (65.7)	15.96 (21.15)	0.0	0.00	100.0
		Placebo	73	19 (26.0)	17.54 (28.04)	0.0	0.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	15.53 (21.41)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	12.82 (16.88)	0.0	0.00	33.3
	Week 60	Osimertinib	143	97 (67.8)	14.43 (20.92)	0.0	0.00	66.7
		Placebo	73	18 (24.7)	25.93 (29.27)	0.0	33.33	100.0
	Week 64	Osimertinib	143	94 (65.7)	15.25 (22.22)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	22.22 (24.12)	0.0	33.33	66.7
	Week 68	Osimertinib	143	89 (62.2)	13.86 (19.98)	0.0	0.00	66.7
		Placebo	73	11 (15.1)	12.12 (16.82)	0.0	0.00	33.3
	Week 72	Osimertinib	143	90 (62.9)	15.56 (21.90)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	20.51 (21.68)	0.0	33.33	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
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Table LT1LE_MFH0: Course of QLQ-LC13 Pain in arm/shoulder
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in arm/shoulder	Week 76	Osimertinib	143	89 (62.2)	14.61 (23.00)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	20.83 (17.25)	0.0	33.33	33.3
	Week 80	Osimertinib	143	89 (62.2)	18.73 (23.55)	0.0	0.00	100.0
		Placebo	73	9 (12.3)	18.52 (24.22)	0.0	0.00	66.7
	Week 84	Osimertinib	143	83 (58.0)	15.66 (19.71)	0.0	0.00	66.7
		Placebo	73	10 (13.7)	20.00 (23.31)	0.0	16.67	66.7
	Week 88	Osimertinib	143	79 (55.2)	14.35 (21.14)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	20.83 (24.80)	0.0	16.67	66.7
	Week 92	Osimertinib	143	77 (53.8)	16.88 (23.34)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	20.83 (24.80)	0.0	16.67	66.7
	Week 96	Osimertinib	143	79 (55.2)	17.30 (25.52)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	16.67 (18.26)	0.0	16.67	33.3
	Week 100	Osimertinib	143	67 (46.9)	12.94 (22.44)	0.0	0.00	100.0
		Placebo	73	7 (9.6)	14.29 (17.82)	0.0	0.00	33.3
	Week 104	Osimertinib	143	70 (49.0)	12.38 (22.10)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	20.83 (24.80)	0.0	16.67	66.7
	Week 108	Osimertinib	143	69 (48.3)	12.08 (20.59)	0.0	0.00	66.7
		Placebo	73	5 (6.8)	13.33 (18.26)	0.0	0.00	33.3
	Week 112	Osimertinib	143	62 (43.4)	13.44 (23.73)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	16.67 (19.25)	0.0	16.67	33.3
	Week 116	Osimertinib	143	64 (44.8)	11.98 (20.89)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	25.00 (31.91)	0.0	16.67	66.7
	Week 120	Osimertinib	143	61 (42.7)	10.38 (17.79)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
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Program Name: LT1_APR0_H0.sas
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Table LT1LE_MFH0: Course of QLQ-LC13 Pain in arm/shoulder
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in arm/shoulder	Week 124	Osimertinib	143	47 (32.9)	16.31 (23.95)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 128	Osimertinib	143	51 (35.7)	16.34 (22.48)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 132	Osimertinib	143	49 (34.3)	14.29 (20.41)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	25.00 (31.91)	0.0	16.67	66.7
	Week 136	Osimertinib	143	44 (30.8)	13.64 (23.09)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 140	Osimertinib	143	43 (30.1)	8.53 (20.69)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 144	Osimertinib	143	39 (27.3)	8.55 (16.61)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 148	Osimertinib	143	37 (25.9)	9.01 (18.67)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 152	Osimertinib	143	35 (24.5)	10.48 (19.42)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 156	Osimertinib	143	32 (22.4)	17.71 (29.31)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	15.56 (24.34)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 164	Osimertinib	143	28 (19.6)	11.90 (18.62)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 168	Osimertinib	143	22 (15.4)	12.12 (24.22)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	22.22 (38.49)	0.0	0.00	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1L0_MFH0: Course of QLQ-LC13 Pain in other parts
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in other parts	Baseline	Osimertinib	143	131 (91.6)	12.47 (21.22)	0.0	0.00	100.0
		Placebo	73	68 (93.2)	15.20 (18.60)	0.0	0.00	66.7
	Week 2	Osimertinib	143	139 (97.2)	15.35 (22.79)	0.0	0.00	100.0
		Placebo	73	71 (97.3)	16.90 (18.58)	0.0	0.00	66.7
	Week 3	Osimertinib	143	129 (90.2)	11.63 (18.47)	0.0	0.00	66.7
		Placebo	73	64 (87.7)	21.35 (20.02)	0.0	33.33	66.7
	Week 4	Osimertinib	143	132 (92.3)	14.90 (20.72)	0.0	0.00	66.7
		Placebo	73	70 (95.9)	17.62 (21.02)	0.0	0.00	66.7
	Week 5	Osimertinib	143	125 (87.4)	19.20 (24.05)	0.0	0.00	100.0
		Placebo	73	66 (90.4)	17.17 (21.28)	0.0	0.00	66.7
	Week 6	Osimertinib	143	125 (87.4)	17.07 (21.00)	0.0	0.00	66.7
		Placebo	73	67 (91.8)	14.43 (19.44)	0.0	0.00	66.7
	Week 7	Osimertinib	143	125 (87.4)	16.00 (22.64)	0.0	0.00	100.0
		Placebo	73	64 (87.7)	18.75 (21.31)	0.0	0.00	66.7
	Week 8	Osimertinib	143	129 (90.2)	17.31 (22.48)	0.0	0.00	66.7
		Placebo	73	59 (80.8)	14.69 (18.85)	0.0	0.00	66.7
	Week 12	Osimertinib	143	125 (87.4)	14.93 (21.36)	0.0	0.00	100.0
		Placebo	73	63 (86.3)	15.87 (19.73)	0.0	0.00	66.7
	Week 16	Osimertinib	143	120 (83.9)	15.56 (22.43)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	18.06 (20.58)	0.0	0.00	66.7
	Week 20	Osimertinib	143	118 (82.5)	16.10 (22.53)	0.0	0.00	100.0
		Placebo	73	56 (76.7)	19.64 (21.81)	0.0	16.67	66.7
	Week 24	Osimertinib	143	112 (78.3)	13.69 (23.06)	0.0	0.00	100.0
		Placebo	73	43 (58.9)	16.28 (19.75)	0.0	0.00	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1L0_MFH0: Course of QLQ-LC13 Pain in other parts
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in other parts	Week 28	Osimertinib	143	106 (74.1)	17.92 (22.15)	0.0	0.00	100.0
		Placebo	73	35 (47.9)	18.10 (18.69)	0.0	33.33	66.7
	Week 32	Osimertinib	143	107 (74.8)	15.89 (23.05)	0.0	0.00	100.0
		Placebo	73	30 (41.1)	23.33 (23.41)	0.0	33.33	66.7
	Week 36	Osimertinib	143	105 (73.4)	16.51 (23.17)	0.0	0.00	100.0
		Placebo	73	26 (35.6)	25.64 (21.72)	0.0	33.33	66.7
	Week 40	Osimertinib	143	108 (75.5)	18.21 (24.28)	0.0	0.00	100.0
		Placebo	73	24 (32.9)	22.22 (21.23)	0.0	33.33	66.7
	Week 44	Osimertinib	143	96 (67.1)	12.50 (18.26)	0.0	0.00	66.7
		Placebo	73	23 (31.5)	28.99 (23.15)	0.0	33.33	66.7
	Week 48	Osimertinib	143	100 (69.9)	15.67 (21.95)	0.0	0.00	100.0
		Placebo	73	25 (34.2)	24.00 (24.57)	0.0	33.33	66.7
	Week 52	Osimertinib	143	94 (65.7)	14.89 (22.20)	0.0	0.00	100.0
		Placebo	73	19 (26.0)	31.58 (26.00)	0.0	33.33	100.0
	Week 56	Osimertinib	143	88 (61.5)	16.29 (24.24)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	15.38 (17.30)	0.0	0.00	33.3
	Week 60	Osimertinib	143	97 (67.8)	13.75 (21.92)	0.0	0.00	100.0
		Placebo	73	18 (24.7)	29.63 (22.55)	0.0	33.33	66.7
	Week 64	Osimertinib	143	94 (65.7)	17.38 (23.81)	0.0	0.00	100.0
		Placebo	73	15 (20.5)	28.89 (21.33)	0.0	33.33	66.7
	Week 68	Osimertinib	143	89 (62.2)	13.11 (19.86)	0.0	0.00	66.7
		Placebo	73	11 (15.1)	15.15 (17.41)	0.0	0.00	33.3
	Week 72	Osimertinib	143	90 (62.9)	17.04 (22.48)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	28.21 (22.96)	0.0	33.33	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
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Table LT1L0_MFH0: Course of QLQ-LC13 Pain in other parts
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in other parts	Week 76	Osimertinib	143	89 (62.2)	15.73 (21.37)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	20.83 (17.25)	0.0	33.33	33.3
	Week 80	Osimertinib	143	89 (62.2)	16.48 (21.98)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	22.22 (23.57)	0.0	33.33	66.7
	Week 84	Osimertinib	143	83 (58.0)	17.67 (22.89)	0.0	0.00	66.7
		Placebo	73	10 (13.7)	33.33 (22.22)	0.0	33.33	66.7
	Week 88	Osimertinib	143	79 (55.2)	19.41 (23.64)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	29.17 (21.36)	0.0	33.33	66.7
	Week 92	Osimertinib	143	77 (53.8)	16.88 (24.56)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	25.00 (23.57)	0.0	33.33	66.7
	Week 96	Osimertinib	143	79 (55.2)	13.92 (23.64)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	27.78 (13.61)	0.0	33.33	33.3
	Week 100	Osimertinib	143	67 (46.9)	13.43 (21.76)	0.0	0.00	66.7
		Placebo	73	7 (9.6)	28.57 (23.00)	0.0	33.33	66.7
	Week 104	Osimertinib	143	70 (49.0)	13.33 (21.54)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	20.83 (17.25)	0.0	33.33	33.3
	Week 108	Osimertinib	143	69 (48.3)	17.39 (24.66)	0.0	0.00	100.0
		Placebo	73	5 (6.8)	13.33 (18.26)	0.0	0.00	33.3
	Week 112	Osimertinib	143	62 (43.4)	12.90 (22.06)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 116	Osimertinib	143	64 (44.8)	16.15 (23.75)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 120	Osimertinib	143	61 (42.7)	12.57 (21.23)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	33.33 (0.00)	33.3	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Table LT1L0_MFH0: Course of QLQ-LC13 Pain in other parts
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in other parts	Week 124	Osimertinib	143	47 (32.9)	14.18 (21.70)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 128	Osimertinib	143	51 (35.7)	14.38 (24.27)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 132	Osimertinib	143	49 (34.3)	18.37 (27.27)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	41.67 (41.94)	0.0	33.33	100.0
	Week 136	Osimertinib	143	44 (30.8)	12.88 (22.98)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 140	Osimertinib	143	43 (30.1)	17.05 (26.60)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 144	Osimertinib	143	39 (27.3)	14.53 (25.13)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 148	Osimertinib	143	37 (25.9)	9.91 (17.33)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 152	Osimertinib	143	35 (24.5)	8.57 (18.69)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 156	Osimertinib	143	32 (22.4)	12.50 (22.00)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 160	Osimertinib	143	30 (21.0)	11.11 (18.22)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 164	Osimertinib	143	28 (19.6)	13.10 (20.96)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 168	Osimertinib	143	22 (15.4)	12.12 (24.22)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	44.44 (19.25)	33.3	33.33	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1LB_MFH0: Course of QLQ-LC13 Pain in chest
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in chest	Baseline	Osimertinib	143	131 (91.6)	9.92 (17.39)	0.0	0.00	66.7
		Placebo	73	68 (93.2)	13.73 (16.53)	0.0	0.00	33.3
	Week 2	Osimertinib	143	139 (97.2)	12.95 (19.46)	0.0	0.00	100.0
		Placebo	73	71 (97.3)	15.02 (20.15)	0.0	0.00	66.7
	Week 3	Osimertinib	143	129 (90.2)	13.70 (18.92)	0.0	0.00	100.0
		Placebo	73	64 (87.7)	13.02 (20.24)	0.0	0.00	100.0
	Week 4	Osimertinib	143	132 (92.3)	15.66 (21.96)	0.0	0.00	100.0
		Placebo	73	70 (95.9)	18.57 (20.96)	0.0	0.00	66.7
	Week 5	Osimertinib	143	125 (87.4)	15.47 (21.81)	0.0	0.00	100.0
		Placebo	73	66 (90.4)	18.18 (21.23)	0.0	0.00	66.7
	Week 6	Osimertinib	143	125 (87.4)	18.67 (22.95)	0.0	0.00	100.0
		Placebo	73	67 (91.8)	15.42 (19.53)	0.0	0.00	66.7
	Week 7	Osimertinib	143	125 (87.4)	17.07 (21.43)	0.0	0.00	66.7
		Placebo	73	64 (87.7)	13.02 (20.24)	0.0	0.00	66.7
	Week 8	Osimertinib	143	129 (90.2)	17.31 (22.48)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	15.25 (20.83)	0.0	0.00	66.7
	Week 12	Osimertinib	143	125 (87.4)	15.73 (20.56)	0.0	0.00	100.0
		Placebo	73	63 (86.3)	12.17 (17.25)	0.0	0.00	66.7
	Week 16	Osimertinib	143	120 (83.9)	14.17 (18.67)	0.0	0.00	66.7
		Placebo	73	48 (65.8)	18.06 (21.70)	0.0	0.00	100.0
	Week 20	Osimertinib	143	118 (82.5)	14.12 (19.20)	0.0	0.00	66.7
		Placebo	73	56 (76.7)	14.88 (20.02)	0.0	0.00	66.7
	Week 24	Osimertinib	143	112 (78.3)	12.80 (19.63)	0.0	0.00	66.7
		Placebo	73	43 (58.9)	12.40 (17.85)	0.0	0.00	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1LB_MFH0: Course of QLQ-LC13 Pain in chest
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in chest	Week 28	Osimertinib	143	106 (74.1)	13.21 (19.88)	0.0	0.00	66.7
		Placebo	73	35 (47.9)	8.57 (14.78)	0.0	0.00	33.3
	Week 32	Osimertinib	143	107 (74.8)	13.71 (19.93)	0.0	0.00	66.7
		Placebo	73	30 (41.1)	13.33 (18.77)	0.0	0.00	66.7
	Week 36	Osimertinib	143	105 (73.4)	11.43 (18.39)	0.0	0.00	66.7
		Placebo	73	26 (35.6)	17.95 (25.35)	0.0	0.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	12.04 (17.92)	0.0	0.00	66.7
		Placebo	73	24 (32.9)	12.50 (21.56)	0.0	0.00	66.7
	Week 44	Osimertinib	143	96 (67.1)	11.11 (18.52)	0.0	0.00	66.7
		Placebo	73	23 (31.5)	15.94 (19.77)	0.0	0.00	66.7
	Week 48	Osimertinib	143	100 (69.9)	11.00 (18.98)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	14.67 (19.44)	0.0	0.00	66.7
	Week 52	Osimertinib	143	94 (65.7)	10.99 (17.21)	0.0	0.00	66.7
		Placebo	73	19 (26.0)	15.79 (25.74)	0.0	0.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	12.88 (20.49)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	7.69 (14.62)	0.0	0.00	33.3
	Week 60	Osimertinib	143	97 (67.8)	9.97 (16.78)	0.0	0.00	66.7
		Placebo	73	18 (24.7)	9.26 (15.36)	0.0	0.00	33.3
	Week 64	Osimertinib	143	94 (65.7)	10.99 (19.79)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	6.67 (13.80)	0.0	0.00	33.3
	Week 68	Osimertinib	143	89 (62.2)	11.61 (18.87)	0.0	0.00	66.7
		Placebo	73	11 (15.1)	6.06 (13.48)	0.0	0.00	33.3
	Week 72	Osimertinib	143	90 (62.9)	13.33 (20.48)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	10.26 (16.01)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LB_MFH0: Course of QLQ-LC13 Pain in chest
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in chest	Week 76	Osimertinib	143	89 (62.2)	11.61 (18.87)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	20.83 (24.80)	0.0	16.67	66.7
	Week 80	Osimertinib	143	89 (62.2)	11.61 (18.87)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	11.11 (16.67)	0.0	0.00	33.3
	Week 84	Osimertinib	143	83 (58.0)	10.84 (18.11)	0.0	0.00	66.7
		Placebo	73	10 (13.7)	10.00 (16.10)	0.0	0.00	33.3
	Week 88	Osimertinib	143	79 (55.2)	10.97 (17.48)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	16.67 (17.82)	0.0	16.67	33.3
	Week 92	Osimertinib	143	77 (53.8)	10.82 (20.55)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	12.50 (17.25)	0.0	0.00	33.3
	Week 96	Osimertinib	143	79 (55.2)	9.70 (20.08)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	5.56 (13.61)	0.0	0.00	33.3
	Week 100	Osimertinib	143	67 (46.9)	8.96 (17.00)	0.0	0.00	66.7
		Placebo	73	7 (9.6)	9.52 (16.27)	0.0	0.00	33.3
	Week 104	Osimertinib	143	70 (49.0)	9.52 (17.16)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 108	Osimertinib	143	69 (48.3)	12.08 (22.12)	0.0	0.00	100.0
		Placebo	73	5 (6.8)	13.33 (18.26)	0.0	0.00	33.3
	Week 112	Osimertinib	143	62 (43.4)	11.29 (21.71)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 116	Osimertinib	143	64 (44.8)	11.46 (18.99)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 120	Osimertinib	143	61 (42.7)	11.48 (19.13)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Run Date: 29AUG2024:16:11:00

Table LT1LB_MFH0: Course of QLQ-LC13 Pain in chest
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Pain in chest	Week 124	Osimertinib	143	47 (32.9)	12.06 (18.94)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 128	Osimertinib	143	51 (35.7)	9.80 (18.01)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 132	Osimertinib	143	49 (34.3)	11.56 (21.03)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 136	Osimertinib	143	44 (30.8)	11.36 (21.50)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 140	Osimertinib	143	43 (30.1)	10.08 (19.97)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 144	Osimertinib	143	39 (27.3)	10.26 (17.36)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 148	Osimertinib	143	37 (25.9)	10.81 (19.33)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 152	Osimertinib	143	35 (24.5)	13.33 (23.15)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 156	Osimertinib	143	32 (22.4)	13.54 (22.17)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	11.11 (18.22)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 164	Osimertinib	143	28 (19.6)	13.10 (24.58)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 168	Osimertinib	143	22 (15.4)	10.61 (23.87)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Program Name: LT1_APR0_H0.sas
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Table LT1LS_MFH0: Course of QLQ-LC13 Sore mouth
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Sore mouth	Baseline	Osimertinib	143	131 (91.6)	3.05 (9.65)	0.0	0.00	33.3
		Placebo	73	68 (93.2)	4.90 (11.89)	0.0	0.00	33.3
	Week 2	Osimertinib	143	139 (97.2)	13.91 (21.20)	0.0	0.00	100.0
		Placebo	73	71 (97.3)	6.57 (17.48)	0.0	0.00	100.0
	Week 3	Osimertinib	143	129 (90.2)	9.82 (16.35)	0.0	0.00	66.7
		Placebo	73	64 (87.7)	6.25 (16.67)	0.0	0.00	66.7
	Week 4	Osimertinib	143	132 (92.3)	11.62 (17.47)	0.0	0.00	66.7
		Placebo	73	70 (95.9)	4.29 (11.24)	0.0	0.00	33.3
	Week 5	Osimertinib	143	125 (87.4)	12.00 (17.66)	0.0	0.00	66.7
		Placebo	73	66 (90.4)	3.03 (9.66)	0.0	0.00	33.3
	Week 6	Osimertinib	143	125 (87.4)	9.87 (17.97)	0.0	0.00	100.0
		Placebo	73	67 (91.8)	4.98 (13.30)	0.0	0.00	66.7
	Week 7	Osimertinib	143	125 (87.4)	11.47 (19.45)	0.0	0.00	100.0
		Placebo	73	64 (87.7)	6.77 (16.99)	0.0	0.00	100.0
	Week 8	Osimertinib	143	129 (90.2)	9.30 (17.67)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	2.82 (9.36)	0.0	0.00	33.3
	Week 12	Osimertinib	143	125 (87.4)	10.67 (20.13)	0.0	0.00	100.0
		Placebo	73	63 (86.3)	4.23 (11.19)	0.0	0.00	33.3
	Week 16	Osimertinib	143	120 (83.9)	8.61 (17.01)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	3.47 (10.29)	0.0	0.00	33.3
	Week 20	Osimertinib	143	118 (82.5)	10.17 (20.68)	0.0	0.00	100.0
		Placebo	73	56 (76.7)	5.36 (12.35)	0.0	0.00	33.3
	Week 24	Osimertinib	143	112 (78.3)	7.14 (14.45)	0.0	0.00	66.7
		Placebo	73	43 (58.9)	3.10 (9.80)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LS_MFH0: Course of QLQ-LC13 Sore mouth
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Sore mouth	Week 28	Osimertinib	143	106 (74.1)	9.43 (16.43)	0.0	0.00	66.7
		Placebo	73	35 (47.9)	4.76 (11.83)	0.0	0.00	33.3
	Week 32	Osimertinib	143	107 (74.8)	9.66 (17.14)	0.0	0.00	66.7
		Placebo	73	30 (41.1)	5.56 (12.63)	0.0	0.00	33.3
	Week 36	Osimertinib	143	105 (73.4)	9.52 (18.90)	0.0	0.00	100.0
		Placebo	73	26 (35.6)	6.41 (16.38)	0.0	0.00	66.7
	Week 40	Osimertinib	143	108 (75.5)	12.35 (23.05)	0.0	0.00	100.0
		Placebo	73	24 (32.9)	6.94 (13.83)	0.0	0.00	33.3
	Week 44	Osimertinib	143	96 (67.1)	9.03 (16.39)	0.0	0.00	66.7
		Placebo	73	23 (31.5)	4.35 (11.48)	0.0	0.00	33.3
	Week 48	Osimertinib	143	100 (69.9)	10.67 (18.28)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	5.33 (12.47)	0.0	0.00	33.3
	Week 52	Osimertinib	143	94 (65.7)	11.70 (19.37)	0.0	0.00	66.7
		Placebo	73	19 (26.0)	7.02 (17.84)	0.0	0.00	66.7
	Week 56	Osimertinib	143	88 (61.5)	12.50 (23.87)	0.0	0.00	100.0
		Placebo	73	13 (17.8)	10.26 (16.01)	0.0	0.00	33.3
	Week 60	Osimertinib	143	97 (67.8)	9.97 (19.34)	0.0	0.00	100.0
		Placebo	73	18 (24.7)	7.41 (18.28)	0.0	0.00	66.7
	Week 64	Osimertinib	143	94 (65.7)	10.64 (19.68)	0.0	0.00	66.7
		Placebo	73	15 (20.5)	11.11 (20.57)	0.0	0.00	66.7
	Week 68	Osimertinib	143	89 (62.2)	13.48 (20.55)	0.0	0.00	66.7
		Placebo	73	11 (15.1)	9.09 (15.57)	0.0	0.00	33.3
	Week 72	Osimertinib	143	90 (62.9)	11.85 (20.18)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	12.82 (16.88)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Program Name: LT1_APR0_H0.sas
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Table LT1LS_MFH0: Course of QLQ-LC13 Sore mouth
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Sore mouth	Week 76	Osimertinib	143	89 (62.2)	10.49 (19.20)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 80	Osimertinib	143	89 (62.2)	10.11 (17.70)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	7.41 (14.70)	0.0	0.00	33.3
	Week 84	Osimertinib	143	83 (58.0)	10.84 (17.35)	0.0	0.00	66.7
		Placebo	73	10 (13.7)	6.67 (14.05)	0.0	0.00	33.3
	Week 88	Osimertinib	143	79 (55.2)	11.81 (20.00)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	12.50 (17.25)	0.0	0.00	33.3
	Week 92	Osimertinib	143	77 (53.8)	10.39 (18.14)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 96	Osimertinib	143	79 (55.2)	10.13 (17.99)	0.0	0.00	66.7
		Placebo	73	6 (8.2)	11.11 (17.21)	0.0	0.00	33.3
	Week 100	Osimertinib	143	67 (46.9)	9.45 (17.22)	0.0	0.00	66.7
		Placebo	73	7 (9.6)	9.52 (16.27)	0.0	0.00	33.3
	Week 104	Osimertinib	143	70 (49.0)	9.52 (17.16)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 108	Osimertinib	143	69 (48.3)	13.04 (20.78)	0.0	0.00	66.7
		Placebo	73	5 (6.8)	13.33 (18.26)	0.0	0.00	33.3
	Week 112	Osimertinib	143	62 (43.4)	12.90 (19.42)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 116	Osimertinib	143	64 (44.8)	9.90 (15.35)	0.0	0.00	33.3
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 120	Osimertinib	143	61 (42.7)	11.48 (19.13)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LS_MFH0: Course of QLQ-LC13 Sore mouth
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Sore mouth	Week 124	Osimertinib	143	47 (32.9)	10.64 (17.18)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 128	Osimertinib	143	51 (35.7)	11.76 (19.80)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 132	Osimertinib	143	49 (34.3)	14.29 (20.41)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 136	Osimertinib	143	44 (30.8)	12.12 (21.68)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 140	Osimertinib	143	43 (30.1)	11.63 (17.64)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 144	Osimertinib	143	39 (27.3)	11.11 (19.25)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 148	Osimertinib	143	37 (25.9)	9.91 (19.03)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 152	Osimertinib	143	35 (24.5)	9.52 (17.29)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 156	Osimertinib	143	32 (22.4)	12.50 (18.45)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 160	Osimertinib	143	30 (21.0)	8.89 (17.36)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 164	Osimertinib	143	28 (19.6)	10.71 (24.09)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 168	Osimertinib	143	22 (15.4)	9.09 (23.42)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Table LT1LD_MFH0: Course of QLQ-LC13 Dyspnea
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Dyspnoea	Baseline	Osimertinib	143	131 (91.6)	12.64 (13.27)	0.0	11.11	44.4
		Placebo	73	68 (93.2)	18.14 (15.47)	0.0	22.22	66.7
	Week 2	Osimertinib	143	139 (97.2)	14.47 (14.13)	0.0	11.11	44.4
		Placebo	73	71 (97.3)	16.59 (16.03)	0.0	11.11	66.7
	Week 3	Osimertinib	143	129 (90.2)	14.73 (16.79)	0.0	11.11	100.0
		Placebo	73	64 (87.7)	19.97 (19.52)	0.0	22.22	66.7
	Week 4	Osimertinib	143	132 (92.3)	17.26 (18.38)	0.0	11.11	100.0
		Placebo	73	70 (95.9)	18.41 (18.81)	0.0	22.22	55.6
	Week 5	Osimertinib	143	125 (87.4)	17.96 (18.11)	0.0	11.11	100.0
		Placebo	73	66 (90.4)	18.52 (17.58)	0.0	11.11	55.6
	Week 6	Osimertinib	143	125 (87.4)	19.02 (17.39)	0.0	22.22	77.8
		Placebo	73	67 (91.8)	19.57 (18.86)	0.0	22.22	66.7
	Week 7	Osimertinib	143	125 (87.4)	22.58 (18.45)	0.0	22.22	77.8
		Placebo	73	64 (87.7)	19.27 (19.92)	0.0	16.67	77.8
	Week 8	Osimertinib	143	129 (90.2)	24.89 (20.02)	0.0	22.22	77.8
		Placebo	73	59 (80.8)	20.15 (19.30)	0.0	22.22	77.8
	Week 12	Osimertinib	143	125 (87.4)	24.18 (20.84)	0.0	22.22	100.0
		Placebo	73	63 (86.3)	18.52 (18.61)	0.0	11.11	66.7
	Week 16	Osimertinib	143	120 (83.9)	22.13 (19.51)	0.0	22.22	100.0
		Placebo	73	48 (65.8)	18.75 (19.60)	0.0	22.22	77.8
	Week 20	Osimertinib	143	118 (82.5)	19.68 (18.05)	0.0	22.22	100.0
		Placebo	73	56 (76.7)	20.63 (18.64)	0.0	22.22	66.7
	Week 24	Osimertinib	143	112 (78.3)	19.64 (17.20)	0.0	22.22	77.8
		Placebo	73	43 (58.9)	21.19 (19.06)	0.0	22.22	88.9

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1LD_MFH0: Course of QLQ-LC13 Dyspnea
 Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Dyspnoea	Week 28	Osimertinib	143	106 (74.1)	19.29 (16.54)	0.0	22.22	66.7
		Placebo	73	35 (47.9)	20.00 (18.83)	0.0	22.22	77.8
	Week 32	Osimertinib	143	107 (74.8)	20.25 (17.92)	0.0	22.22	88.9
		Placebo	73	30 (41.1)	22.59 (24.32)	0.0	16.67	100.0
	Week 36	Osimertinib	143	105 (73.4)	20.00 (18.83)	0.0	22.22	88.9
		Placebo	73	26 (35.6)	24.36 (24.55)	0.0	22.22	77.8
	Week 40	Osimertinib	143	108 (75.5)	19.86 (18.17)	0.0	22.22	77.8
		Placebo	73	24 (32.9)	24.54 (20.97)	0.0	22.22	77.8
	Week 44	Osimertinib	143	96 (67.1)	18.98 (18.52)	0.0	11.11	88.9
		Placebo	73	23 (31.5)	17.39 (15.29)	0.0	22.22	44.4
	Week 48	Osimertinib	143	100 (69.9)	19.22 (18.20)	0.0	16.67	77.8
		Placebo	73	25 (34.2)	24.00 (19.16)	0.0	33.33	66.7
	Week 52	Osimertinib	143	94 (65.7)	19.03 (18.62)	0.0	11.11	88.9
		Placebo	73	19 (26.0)	21.64 (24.42)	0.0	22.22	100.0
	Week 56	Osimertinib	143	88 (61.5)	20.08 (21.37)	0.0	16.67	100.0
		Placebo	73	13 (17.8)	16.24 (19.04)	0.0	11.11	55.6
	Week 60	Osimertinib	143	97 (67.8)	18.56 (18.75)	0.0	11.11	88.9
		Placebo	73	18 (24.7)	20.37 (24.48)	0.0	16.67	88.9
	Week 64	Osimertinib	143	94 (65.7)	18.44 (18.47)	0.0	11.11	77.8
		Placebo	73	15 (20.5)	18.52 (16.62)	0.0	33.33	33.3
	Week 68	Osimertinib	143	89 (62.2)	16.85 (17.42)	0.0	11.11	66.7
		Placebo	73	11 (15.1)	19.19 (27.71)	0.0	0.00	88.9
	Week 72	Osimertinib	143	90 (62.9)	19.01 (19.37)	0.0	11.11	77.8
		Placebo	73	13 (17.8)	19.66 (19.33)	0.0	33.33	44.4

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
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Table LT1LD_MFH0: Course of QLQ-LC13 Dyspnea
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Dyspnoea	Week 76	Osimertinib	143	89 (62.2)	19.23 (18.78)	0.0	11.11	77.8
		Placebo	73	8 (11.0)	16.67 (18.78)	0.0	11.11	44.4
	Week 80	Osimertinib	143	89 (62.2)	18.85 (17.84)	0.0	11.11	88.9
		Placebo	73	9 (12.3)	28.40 (21.60)	0.0	33.33	66.7
	Week 84	Osimertinib	143	83 (58.0)	16.60 (16.77)	0.0	11.11	66.7
		Placebo	73	10 (13.7)	24.44 (21.47)	0.0	22.22	66.7
	Week 88	Osimertinib	143	79 (55.2)	16.88 (16.20)	0.0	11.11	66.7
		Placebo	73	8 (11.0)	16.67 (13.28)	0.0	16.67	33.3
	Week 92	Osimertinib	143	77 (53.8)	18.76 (20.09)	0.0	11.11	88.9
		Placebo	73	8 (11.0)	13.89 (15.43)	0.0	11.11	33.3
	Week 96	Osimertinib	143	79 (55.2)	15.61 (17.93)	0.0	11.11	88.9
		Placebo	73	6 (8.2)	20.37 (23.74)	0.0	16.67	55.6
	Week 100	Osimertinib	143	67 (46.9)	16.75 (17.12)	0.0	11.11	88.9
		Placebo	73	7 (9.6)	15.87 (16.80)	0.0	11.11	33.3
	Week 104	Osimertinib	143	70 (49.0)	15.71 (15.88)	0.0	11.11	66.7
		Placebo	73	8 (11.0)	19.44 (15.43)	0.0	22.22	33.3
	Week 108	Osimertinib	143	69 (48.3)	16.91 (17.21)	0.0	11.11	88.9
		Placebo	73	5 (6.8)	24.44 (24.09)	0.0	33.33	55.6
	Week 112	Osimertinib	143	62 (43.4)	18.28 (16.72)	0.0	11.11	88.9
		Placebo	73	4 (5.5)	16.67 (19.25)	0.0	16.67	33.3
	Week 116	Osimertinib	143	64 (44.8)	16.67 (17.03)	0.0	11.11	77.8
		Placebo	73	4 (5.5)	16.67 (19.25)	0.0	16.67	33.3
	Week 120	Osimertinib	143	61 (42.7)	15.30 (15.47)	0.0	11.11	77.8
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LD_MFH0: Course of QLQ-LC13 Dyspnea
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Dyspnoea	Week 124	Osimertinib	143	47 (32.9)	16.31 (18.66)	0.0	11.11	77.8
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 128	Osimertinib	143	51 (35.7)	14.81 (14.00)	0.0	11.11	55.6
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 132	Osimertinib	143	49 (34.3)	17.01 (15.73)	0.0	11.11	77.8
		Placebo	73	4 (5.5)	13.89 (16.67)	0.0	11.11	33.3
	Week 136	Osimertinib	143	44 (30.8)	15.15 (18.11)	0.0	11.11	100.0
		Placebo	73	3 (4.1)	7.41 (12.83)	0.0	0.00	22.2
	Week 140	Osimertinib	143	43 (30.1)	17.31 (18.19)	0.0	11.11	88.9
		Placebo	73	3 (4.1)	7.41 (12.83)	0.0	0.00	22.2
	Week 144	Osimertinib	143	39 (27.3)	18.23 (21.10)	0.0	11.11	100.0
		Placebo	73	3 (4.1)	7.41 (12.83)	0.0	0.00	22.2
	Week 148	Osimertinib	143	37 (25.9)	18.02 (18.95)	0.0	11.11	100.0
		Placebo	73	3 (4.1)	7.41 (12.83)	0.0	0.00	22.2
	Week 152	Osimertinib	143	35 (24.5)	16.19 (17.74)	0.0	11.11	88.9
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 156	Osimertinib	143	32 (22.4)	16.32 (16.45)	0.0	11.11	77.8
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	17.78 (15.60)	0.0	16.67	77.8
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 164	Osimertinib	143	28 (19.6)	20.63 (19.06)	0.0	16.67	88.9
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 168	Osimertinib	143	22 (15.4)	18.69 (21.52)	0.0	11.11	100.0
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LN_MFH0: Course of QLQ-LC13 Peripheral neuropathy
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Peripheral neuropathy	Baseline	Osimertinib	143	131 (91.6)	9.92 (21.36)	0.0	0.00	100.0
		Placebo	73	68 (93.2)	14.22 (21.02)	0.0	0.00	100.0
	Week 2	Osimertinib	143	139 (97.2)	11.75 (20.41)	0.0	0.00	100.0
		Placebo	73	71 (97.3)	12.68 (19.81)	0.0	0.00	66.7
	Week 3	Osimertinib	143	129 (90.2)	11.37 (21.04)	0.0	0.00	100.0
		Placebo	73	64 (87.7)	12.50 (20.14)	0.0	0.00	66.7
	Week 4	Osimertinib	143	132 (92.3)	13.38 (22.13)	0.0	0.00	66.7
		Placebo	73	70 (95.9)	13.33 (20.77)	0.0	0.00	100.0
	Week 5	Osimertinib	143	125 (87.4)	14.67 (21.34)	0.0	0.00	100.0
		Placebo	73	66 (90.4)	13.64 (19.37)	0.0	0.00	66.7
	Week 6	Osimertinib	143	125 (87.4)	15.73 (21.82)	0.0	0.00	100.0
		Placebo	73	67 (91.8)	13.93 (20.23)	0.0	0.00	66.7
	Week 7	Osimertinib	143	125 (87.4)	15.47 (21.40)	0.0	0.00	100.0
		Placebo	73	64 (87.7)	13.02 (21.10)	0.0	0.00	100.0
	Week 8	Osimertinib	143	129 (90.2)	13.95 (21.53)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	15.25 (23.43)	0.0	0.00	100.0
	Week 12	Osimertinib	143	125 (87.4)	16.27 (21.00)	0.0	0.00	66.7
		Placebo	73	63 (86.3)	15.34 (23.05)	0.0	0.00	100.0
	Week 16	Osimertinib	143	120 (83.9)	14.17 (21.89)	0.0	0.00	100.0
		Placebo	73	48 (65.8)	14.58 (18.07)	0.0	0.00	66.7
	Week 20	Osimertinib	143	118 (82.5)	16.10 (22.95)	0.0	0.00	100.0
		Placebo	73	56 (76.7)	12.50 (20.66)	0.0	0.00	100.0
	Week 24	Osimertinib	143	112 (78.3)	16.67 (23.25)	0.0	0.00	100.0
		Placebo	73	43 (58.9)	8.53 (14.72)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LN_MFH0: Course of QLQ-LC13 Peripheral neuropathy
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Peripheral neuropathy	Week 28	Osimertinib	143	106 (74.1)	13.52 (19.40)	0.0	0.00	66.7
		Placebo	73	35 (47.9)	13.33 (16.57)	0.0	0.00	33.3
	Week 32	Osimertinib	143	107 (74.8)	14.64 (21.07)	0.0	0.00	100.0
		Placebo	73	30 (41.1)	10.00 (15.54)	0.0	0.00	33.3
	Week 36	Osimertinib	143	105 (73.4)	14.60 (22.61)	0.0	0.00	100.0
		Placebo	73	26 (35.6)	7.69 (17.15)	0.0	0.00	66.7
	Week 40	Osimertinib	143	108 (75.5)	18.83 (25.49)	0.0	0.00	100.0
		Placebo	73	24 (32.9)	12.50 (21.56)	0.0	0.00	66.7
	Week 44	Osimertinib	143	96 (67.1)	16.67 (23.69)	0.0	0.00	100.0
		Placebo	73	23 (31.5)	11.59 (16.23)	0.0	0.00	33.3
	Week 48	Osimertinib	143	100 (69.9)	17.00 (21.45)	0.0	0.00	66.7
		Placebo	73	25 (34.2)	13.33 (16.67)	0.0	0.00	33.3
	Week 52	Osimertinib	143	94 (65.7)	15.96 (21.15)	0.0	0.00	66.7
		Placebo	73	19 (26.0)	12.28 (16.52)	0.0	0.00	33.3
	Week 56	Osimertinib	143	88 (61.5)	17.80 (23.68)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	12.82 (16.88)	0.0	0.00	33.3
	Week 60	Osimertinib	143	97 (67.8)	16.49 (21.04)	0.0	0.00	66.7
		Placebo	73	18 (24.7)	12.96 (16.72)	0.0	0.00	33.3
	Week 64	Osimertinib	143	94 (65.7)	15.60 (22.77)	0.0	0.00	100.0
		Placebo	73	15 (20.5)	15.56 (21.33)	0.0	0.00	66.7
	Week 68	Osimertinib	143	89 (62.2)	13.11 (18.54)	0.0	0.00	66.7
		Placebo	73	11 (15.1)	15.15 (17.41)	0.0	0.00	33.3
	Week 72	Osimertinib	143	90 (62.9)	15.56 (21.90)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	17.95 (17.30)	0.0	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Table LT1LN_MFH0: Course of QLQ-LC13 Peripheral neuropathy
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Peripheral neuropathy	Week 76	Osimertinib	143	89 (62.2)	13.48 (21.15)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	20.83 (17.25)	0.0	33.33	33.3
	Week 80	Osimertinib	143	89 (62.2)	16.10 (21.39)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	14.81 (17.57)	0.0	0.00	33.3
	Week 84	Osimertinib	143	83 (58.0)	16.47 (22.91)	0.0	0.00	66.7
		Placebo	73	10 (13.7)	13.33 (17.21)	0.0	0.00	33.3
	Week 88	Osimertinib	143	79 (55.2)	16.46 (22.57)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	12.50 (17.25)	0.0	0.00	33.3
	Week 92	Osimertinib	143	77 (53.8)	17.75 (24.53)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	12.50 (17.25)	0.0	0.00	33.3
	Week 96	Osimertinib	143	79 (55.2)	14.35 (22.45)	0.0	0.00	100.0
		Placebo	73	6 (8.2)	16.67 (18.26)	0.0	16.67	33.3
	Week 100	Osimertinib	143	67 (46.9)	13.43 (21.76)	0.0	0.00	100.0
		Placebo	73	7 (9.6)	19.05 (17.82)	0.0	33.33	33.3
	Week 104	Osimertinib	143	70 (49.0)	15.71 (23.21)	0.0	0.00	100.0
		Placebo	73	8 (11.0)	12.50 (17.25)	0.0	0.00	33.3
	Week 108	Osimertinib	143	69 (48.3)	15.94 (23.30)	0.0	0.00	100.0
		Placebo	73	5 (6.8)	13.33 (18.26)	0.0	0.00	33.3
	Week 112	Osimertinib	143	62 (43.4)	15.05 (23.12)	0.0	0.00	100.0
		Placebo	73	4 (5.5)	25.00 (16.67)	0.0	33.33	33.3
	Week 116	Osimertinib	143	64 (44.8)	14.58 (22.12)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	16.67 (19.25)	0.0	16.67	33.3
	Week 120	Osimertinib	143	61 (42.7)	14.21 (22.33)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Table LT1LN_MFH0: Course of QLQ-LC13 Peripheral neuropathy
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Peripheral neuropathy	Week 124	Osimertinib	143	47 (32.9)	12.77 (22.58)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 128	Osimertinib	143	51 (35.7)	12.42 (18.81)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 132	Osimertinib	143	49 (34.3)	14.97 (21.58)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 136	Osimertinib	143	44 (30.8)	14.39 (22.04)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 140	Osimertinib	143	43 (30.1)	13.18 (23.16)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 144	Osimertinib	143	39 (27.3)	14.53 (21.35)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 148	Osimertinib	143	37 (25.9)	15.32 (20.18)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 152	Osimertinib	143	35 (24.5)	13.33 (20.13)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 156	Osimertinib	143	32 (22.4)	19.79 (25.20)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	17.78 (25.87)	0.0	0.00	100.0
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 164	Osimertinib	143	28 (19.6)	16.67 (23.13)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3
	Week 168	Osimertinib	143	22 (15.4)	16.67 (26.73)	0.0	0.00	100.0
		Placebo	73	3 (4.1)	22.22 (19.25)	0.0	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LA_MFH0: Course of QLQ-LC13 Alopecia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Alopecia	Baseline	Osimertinib	143	131 (91.6)	17.56 (22.77)	0.0	0.00	100.0
		Placebo	73	68 (93.2)	20.10 (27.10)	0.0	0.00	100.0
	Week 2	Osimertinib	143	139 (97.2)	11.03 (17.67)	0.0	0.00	66.7
		Placebo	73	71 (97.3)	9.86 (17.27)	0.0	0.00	66.7
	Week 3	Osimertinib	143	129 (90.2)	10.59 (17.67)	0.0	0.00	66.7
		Placebo	73	64 (87.7)	11.46 (20.76)	0.0	0.00	100.0
	Week 4	Osimertinib	143	132 (92.3)	10.61 (17.63)	0.0	0.00	66.7
		Placebo	73	70 (95.9)	9.52 (18.07)	0.0	0.00	66.7
	Week 5	Osimertinib	143	125 (87.4)	12.00 (19.58)	0.0	0.00	66.7
		Placebo	73	66 (90.4)	12.12 (22.37)	0.0	0.00	100.0
	Week 6	Osimertinib	143	125 (87.4)	10.40 (19.13)	0.0	0.00	100.0
		Placebo	73	67 (91.8)	11.44 (22.14)	0.0	0.00	100.0
	Week 7	Osimertinib	143	125 (87.4)	11.20 (20.28)	0.0	0.00	100.0
		Placebo	73	64 (87.7)	11.46 (18.99)	0.0	0.00	66.7
	Week 8	Osimertinib	143	129 (90.2)	11.37 (19.32)	0.0	0.00	100.0
		Placebo	73	59 (80.8)	11.30 (20.16)	0.0	0.00	66.7
	Week 12	Osimertinib	143	125 (87.4)	10.13 (20.40)	0.0	0.00	100.0
		Placebo	73	63 (86.3)	10.58 (18.77)	0.0	0.00	66.7
	Week 16	Osimertinib	143	120 (83.9)	9.44 (16.84)	0.0	0.00	66.7
		Placebo	73	48 (65.8)	5.56 (14.31)	0.0	0.00	66.7
	Week 20	Osimertinib	143	118 (82.5)	7.91 (16.12)	0.0	0.00	66.7
		Placebo	73	56 (76.7)	5.95 (14.36)	0.0	0.00	66.7
	Week 24	Osimertinib	143	112 (78.3)	6.85 (14.93)	0.0	0.00	66.7
		Placebo	73	43 (58.9)	6.20 (15.01)	0.0	0.00	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LA_MFH0: Course of QLQ-LC13 Alopecia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Alopecia	Week 28	Osimertinib	143	106 (74.1)	5.97 (13.64)	0.0	0.00	66.7
		Placebo	73	35 (47.9)	7.62 (19.94)	0.0	0.00	100.0
	Week 32	Osimertinib	143	107 (74.8)	7.48 (14.70)	0.0	0.00	66.7
		Placebo	73	30 (41.1)	7.78 (16.80)	0.0	0.00	66.7
	Week 36	Osimertinib	143	105 (73.4)	6.67 (16.28)	0.0	0.00	100.0
		Placebo	73	26 (35.6)	6.41 (13.40)	0.0	0.00	33.3
	Week 40	Osimertinib	143	108 (75.5)	6.17 (15.22)	0.0	0.00	100.0
		Placebo	73	24 (32.9)	6.94 (13.83)	0.0	0.00	33.3
	Week 44	Osimertinib	143	96 (67.1)	6.25 (13.94)	0.0	0.00	66.7
		Placebo	73	23 (31.5)	4.35 (11.48)	0.0	0.00	33.3
	Week 48	Osimertinib	143	100 (69.9)	5.67 (12.58)	0.0	0.00	33.3
		Placebo	73	25 (34.2)	8.00 (17.43)	0.0	0.00	66.7
	Week 52	Osimertinib	143	94 (65.7)	7.09 (13.72)	0.0	0.00	33.3
		Placebo	73	19 (26.0)	7.02 (13.96)	0.0	0.00	33.3
	Week 56	Osimertinib	143	88 (61.5)	6.82 (13.52)	0.0	0.00	33.3
		Placebo	73	13 (17.8)	7.69 (14.62)	0.0	0.00	33.3
	Week 60	Osimertinib	143	97 (67.8)	8.25 (14.46)	0.0	0.00	33.3
		Placebo	73	18 (24.7)	5.56 (12.78)	0.0	0.00	33.3
	Week 64	Osimertinib	143	94 (65.7)	8.51 (14.61)	0.0	0.00	33.3
		Placebo	73	15 (20.5)	6.67 (13.80)	0.0	0.00	33.3
	Week 68	Osimertinib	143	89 (62.2)	6.74 (13.47)	0.0	0.00	33.3
		Placebo	73	11 (15.1)	9.09 (15.57)	0.0	0.00	33.3
	Week 72	Osimertinib	143	90 (62.9)	8.15 (16.05)	0.0	0.00	66.7
		Placebo	73	13 (17.8)	7.69 (14.62)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

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Table LT1LA_MFH0: Course of QLQ-LC13 Alopecia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Alopecia	Week 76	Osimertinib	143	89 (62.2)	8.24 (14.46)	0.0	0.00	33.3
		Placebo	73	8 (11.0)	4.17 (11.79)	0.0	0.00	33.3
	Week 80	Osimertinib	143	89 (62.2)	5.99 (13.82)	0.0	0.00	66.7
		Placebo	73	9 (12.3)	7.41 (14.70)	0.0	0.00	33.3
	Week 84	Osimertinib	143	83 (58.0)	6.02 (12.90)	0.0	0.00	33.3
		Placebo	73	10 (13.7)	6.67 (14.05)	0.0	0.00	33.3
	Week 88	Osimertinib	143	79 (55.2)	6.75 (13.48)	0.0	0.00	33.3
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 92	Osimertinib	143	77 (53.8)	8.23 (15.44)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	8.33 (15.43)	0.0	0.00	33.3
	Week 96	Osimertinib	143	79 (55.2)	5.49 (12.44)	0.0	0.00	33.3
		Placebo	73	6 (8.2)	5.56 (13.61)	0.0	0.00	33.3
	Week 100	Osimertinib	143	67 (46.9)	5.97 (12.88)	0.0	0.00	33.3
		Placebo	73	7 (9.6)	4.76 (12.60)	0.0	0.00	33.3
	Week 104	Osimertinib	143	70 (49.0)	6.19 (14.24)	0.0	0.00	66.7
		Placebo	73	8 (11.0)	4.17 (11.79)	0.0	0.00	33.3
	Week 108	Osimertinib	143	69 (48.3)	5.80 (15.08)	0.0	0.00	66.7
		Placebo	73	5 (6.8)	6.67 (14.91)	0.0	0.00	33.3
	Week 112	Osimertinib	143	62 (43.4)	6.45 (14.58)	0.0	0.00	66.7
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 116	Osimertinib	143	64 (44.8)	8.33 (14.55)	0.0	0.00	33.3
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 120	Osimertinib	143	61 (42.7)	7.10 (15.05)	0.0	0.00	66.7
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Table LT1LA_MFH0: Course of QLQ-LC13 Alopecia
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Alopecia	Week 124	Osimertinib	143	47 (32.9)	4.96 (12.00)	0.0	0.00	33.3
		Placebo	73	2 (2.7)	16.67 (23.57)	0.0	16.67	33.3
	Week 128	Osimertinib	143	51 (35.7)	6.54 (14.94)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	33.33 (47.14)	0.0	33.33	66.7
	Week 132	Osimertinib	143	49 (34.3)	4.08 (11.04)	0.0	0.00	33.3
		Placebo	73	4 (5.5)	8.33 (16.67)	0.0	0.00	33.3
	Week 136	Osimertinib	143	44 (30.8)	3.03 (9.69)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 140	Osimertinib	143	43 (30.1)	4.65 (11.69)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 144	Osimertinib	143	39 (27.3)	4.27 (11.29)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 148	Osimertinib	143	37 (25.9)	5.41 (12.46)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0
	Week 152	Osimertinib	143	35 (24.5)	6.67 (17.71)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 156	Osimertinib	143	32 (22.4)	5.21 (14.93)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	6.67 (18.36)	0.0	0.00	66.7
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 164	Osimertinib	143	28 (19.6)	5.95 (13.00)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	11.11 (19.25)	0.0	0.00	33.3
	Week 168	Osimertinib	143	22 (15.4)	4.55 (11.71)	0.0	0.00	33.3
		Placebo	73	3 (4.1)	0.00 (0.00)	0.0	0.00	0.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1LT_MFH0: Course of QLQ-LC13 Take any medicine for pain
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Take any medicine for pain	Baseline	Osimertinib	143	27 (18.9)	65.43 (21.64)	33.3	66.67	100.0
		Placebo	73	21 (28.8)	55.56 (24.34)	0.0	66.67	100.0
	Week 2	Osimertinib	143	25 (17.5)	54.67 (30.25)	0.0	66.67	100.0
		Placebo	73	22 (30.1)	53.03 (22.20)	33.3	50.00	100.0
	Week 3	Osimertinib	143	13 (9.1)	51.28 (29.24)	0.0	33.33	100.0
		Placebo	73	9 (12.3)	37.04 (11.11)	33.3	33.33	66.7
	Week 4	Osimertinib	143	20 (14.0)	56.67 (24.42)	33.3	66.67	100.0
		Placebo	73	12 (16.4)	44.44 (16.41)	33.3	33.33	66.7
	Week 5	Osimertinib	143	24 (16.8)	51.39 (25.97)	0.0	66.67	100.0
		Placebo	73	13 (17.8)	46.15 (16.88)	33.3	33.33	66.7
	Week 6	Osimertinib	143	20 (14.0)	48.33 (20.16)	0.0	50.00	66.7
		Placebo	73	13 (17.8)	46.15 (16.88)	33.3	33.33	66.7
	Week 7	Osimertinib	143	17 (11.9)	52.94 (23.74)	0.0	66.67	100.0
		Placebo	73	11 (15.1)	45.45 (16.82)	33.3	33.33	66.7
	Week 8	Osimertinib	143	18 (12.6)	53.70 (20.26)	33.3	66.67	100.0
		Placebo	73	9 (12.3)	40.74 (14.70)	33.3	33.33	66.7
	Week 12	Osimertinib	143	17 (11.9)	58.82 (25.08)	33.3	66.67	100.0
		Placebo	73	11 (15.1)	48.48 (17.41)	33.3	33.33	66.7
	Week 16	Osimertinib	143	16 (11.2)	58.33 (22.77)	33.3	66.67	100.0
		Placebo	73	9 (12.3)	48.15 (17.57)	33.3	33.33	66.7
	Week 20	Osimertinib	143	16 (11.2)	47.92 (20.97)	33.3	33.33	100.0
		Placebo	73	11 (15.1)	42.42 (26.21)	0.0	33.33	100.0
	Week 24	Osimertinib	143	14 (9.8)	42.86 (20.37)	0.0	33.33	66.7
		Placebo	73	7 (9.6)	47.62 (17.82)	33.3	33.33	66.7

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1LT_MFH0: Course of QLQ-LC13 Take any medicine for pain
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Take any medicine for pain	Week 28	Osimertinib	143	11 (7.7)	42.42 (15.57)	33.3	33.33	66.7
		Placebo	73	4 (5.5)	41.67 (16.67)	33.3	33.33	66.7
	Week 32	Osimertinib	143	12 (8.4)	55.56 (21.71)	33.3	66.67	100.0
		Placebo	73	7 (9.6)	42.86 (16.27)	33.3	33.33	66.7
	Week 36	Osimertinib	143	11 (7.7)	54.55 (22.47)	33.3	66.67	100.0
		Placebo	73	5 (6.8)	40.00 (14.91)	33.3	33.33	66.7
	Week 40	Osimertinib	143	18 (12.6)	51.85 (20.52)	33.3	50.00	100.0
		Placebo	73	6 (8.2)	38.89 (13.61)	33.3	33.33	66.7
	Week 44	Osimertinib	143	8 (5.6)	41.67 (15.43)	33.3	33.33	66.7
		Placebo	73	5 (6.8)	60.00 (27.89)	33.3	66.67	100.0
	Week 48	Osimertinib	143	11 (7.7)	45.45 (16.82)	33.3	33.33	66.7
		Placebo	73	7 (9.6)	42.86 (16.27)	33.3	33.33	66.7
	Week 52	Osimertinib	143	14 (9.8)	38.10 (17.82)	0.0	33.33	66.7
		Placebo	73	4 (5.5)	33.33 (0.00)	33.3	33.33	33.3
	Week 56	Osimertinib	143	12 (8.4)	44.44 (16.41)	33.3	33.33	66.7
		Placebo	73	1 (1.4)	33.33 (NC)	33.3	33.33	33.3
	Week 60	Osimertinib	143	10 (7.0)	46.67 (23.31)	33.3	33.33	100.0
		Placebo	73	4 (5.5)	50.00 (33.33)	33.3	33.33	100.0
	Week 64	Osimertinib	143	9 (6.3)	33.33 (0.00)	33.3	33.33	33.3
		Placebo	73	4 (5.5)	33.33 (0.00)	33.3	33.33	33.3
	Week 68	Osimertinib	143	9 (6.3)	44.44 (23.57)	33.3	33.33	100.0
		Placebo	73	0 (0.0)				
	Week 72	Osimertinib	143	13 (9.1)	53.85 (28.99)	33.3	33.33	100.0
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1LT_MFH0: Course of QLQ-LC13 Take any medicine for pain
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Take any medicine for pain	Week 76	Osimertinib	143	6 (4.2)	33.33 (0.00)	33.3	33.33	33.3
		Placebo	73	2 (2.7)	66.67 (47.14)	33.3	66.67	100.0
	Week 80	Osimertinib	143	10 (7.0)	46.67 (23.31)	33.3	33.33	100.0
		Placebo	73	3 (4.1)	33.33 (0.00)	33.3	33.33	33.3
	Week 84	Osimertinib	143	13 (9.1)	41.03 (24.17)	0.0	33.33	100.0
		Placebo	73	2 (2.7)	33.33 (0.00)	33.3	33.33	33.3
	Week 88	Osimertinib	143	14 (9.8)	50.00 (21.68)	33.3	33.33	100.0
		Placebo	73	1 (1.4)	33.33 (NC)	33.3	33.33	33.3
	Week 92	Osimertinib	143	10 (7.0)	46.67 (17.21)	33.3	33.33	66.7
		Placebo	73	2 (2.7)	66.67 (0.00)	66.7	66.67	66.7
	Week 96	Osimertinib	143	10 (7.0)	36.67 (10.54)	33.3	33.33	66.7
		Placebo	73	1 (1.4)	66.67 (NC)	66.7	66.67	66.7
	Week 100	Osimertinib	143	5 (3.5)	40.00 (14.91)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				
	Week 104	Osimertinib	143	6 (4.2)	55.56 (27.22)	33.3	50.00	100.0
		Placebo	73	0 (0.0)				
	Week 108	Osimertinib	143	9 (6.3)	44.44 (16.67)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				
	Week 112	Osimertinib	143	4 (2.8)	25.00 (16.67)	0.0	33.33	33.3
		Placebo	73	0 (0.0)				
	Week 116	Osimertinib	143	8 (5.6)	41.67 (15.43)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				
	Week 120	Osimertinib	143	7 (4.9)	47.62 (17.82)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1LT_MFH0: Course of QLQ-LC13 Take any medicine for pain
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-LC13 Take any medicine for pain	Week 124	Osimertinib	143	7 (4.9)	52.38 (17.82)	33.3	66.67	66.7
		Placebo	73	0 (0.0)				
	Week 128	Osimertinib	143	8 (5.6)	50.00 (17.82)	33.3	50.00	66.7
		Placebo	73	0 (0.0)				
	Week 132	Osimertinib	143	8 (5.6)	58.33 (23.57)	33.3	66.67	100.0
		Placebo	73	0 (0.0)				
	Week 136	Osimertinib	143	6 (4.2)	38.89 (32.77)	0.0	33.33	100.0
		Placebo	73	0 (0.0)				
	Week 140	Osimertinib	143	7 (4.9)	52.38 (32.53)	33.3	33.33	100.0
		Placebo	73	0 (0.0)				
	Week 144	Osimertinib	143	3 (2.1)	44.44 (19.25)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				
	Week 148	Osimertinib	143	2 (1.4)	50.00 (23.57)	33.3	50.00	66.7
		Placebo	73	0 (0.0)				
	Week 152	Osimertinib	143	3 (2.1)	44.44 (19.25)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				
	Week 156	Osimertinib	143	6 (4.2)	38.89 (13.61)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				
	Week 160	Osimertinib	143	3 (2.1)	44.44 (19.25)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				
	Week 164	Osimertinib	143	3 (2.1)	44.44 (19.25)	33.3	33.33	66.7
		Placebo	73	0 (0.0)				
	Week 168	Osimertinib	143	2 (1.4)	50.00 (23.57)	33.3	50.00	66.7
		Placebo	73	0 (0.0)				

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca

Value Dossier Analysis: D5160C00048

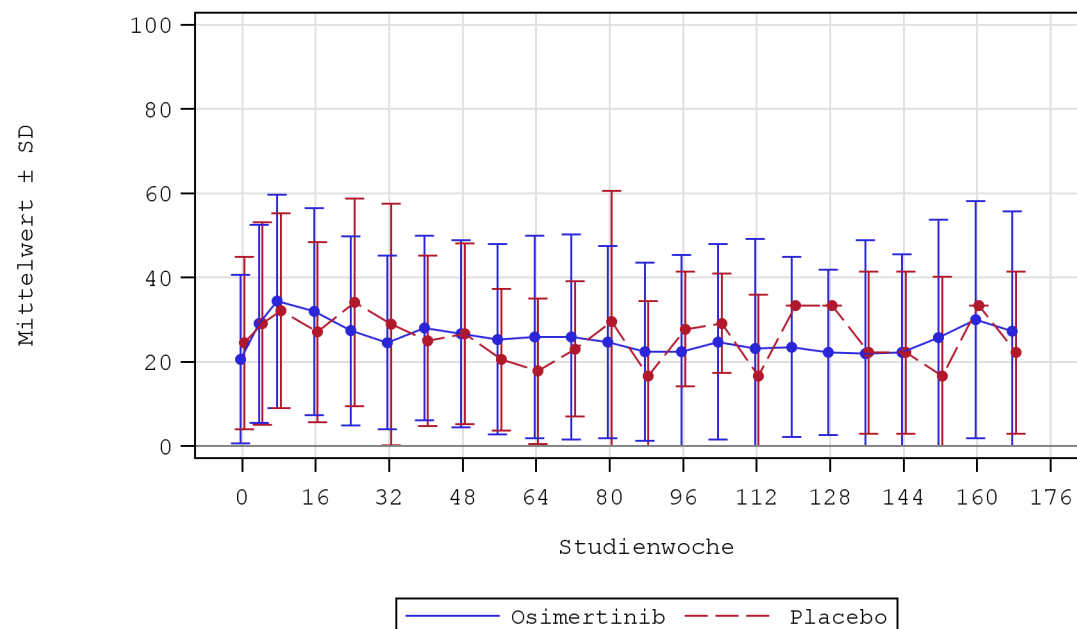
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LC_MFG0: Course of QLQ-LC13 Coughing
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LC_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

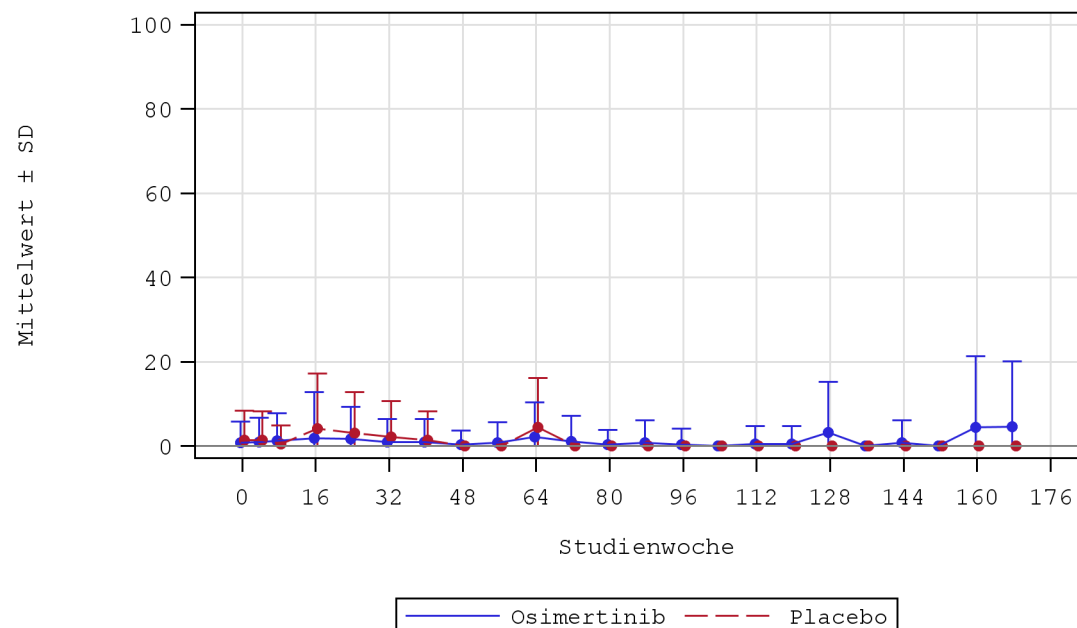
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LH_MFG0: Course of QLQ-LC13 Haemoptysis
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LH_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

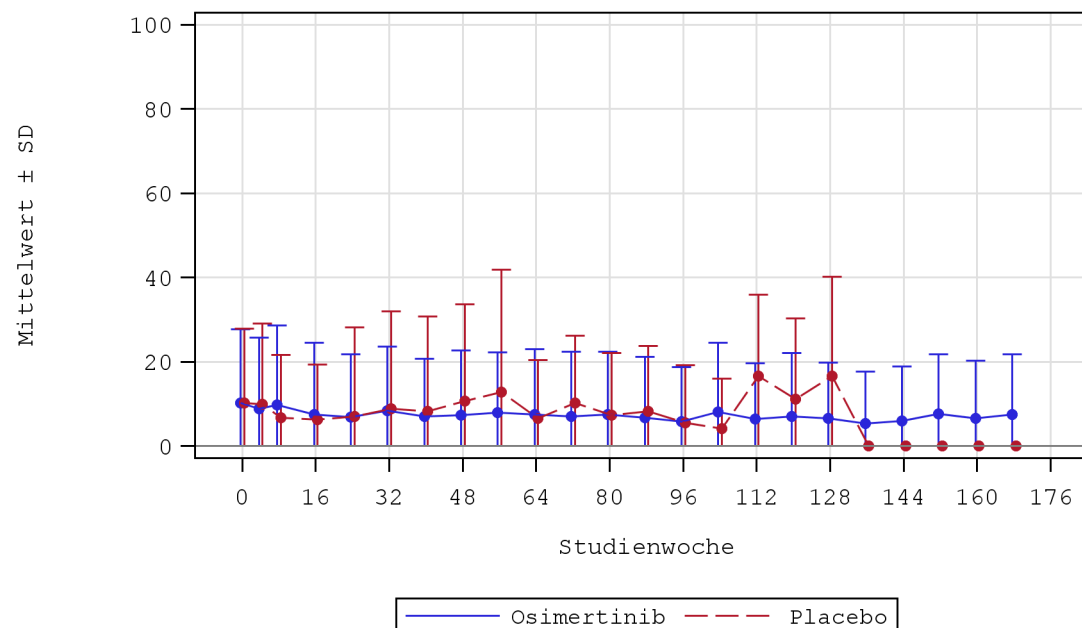
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LP_MFG0: Course of QLQ-LC13 Dysphagia
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LP_MFH0

AstraZeneca

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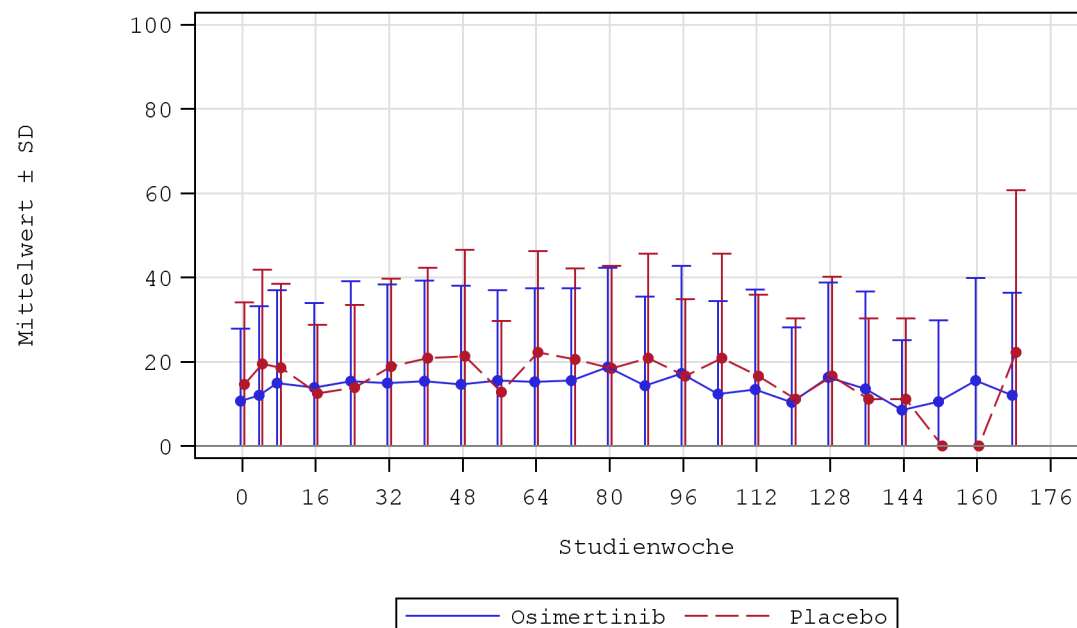
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LE_MFG0: Course of QLQ-LC13 Pain in arm/shoulder
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LE_MFH0

AstraZeneca

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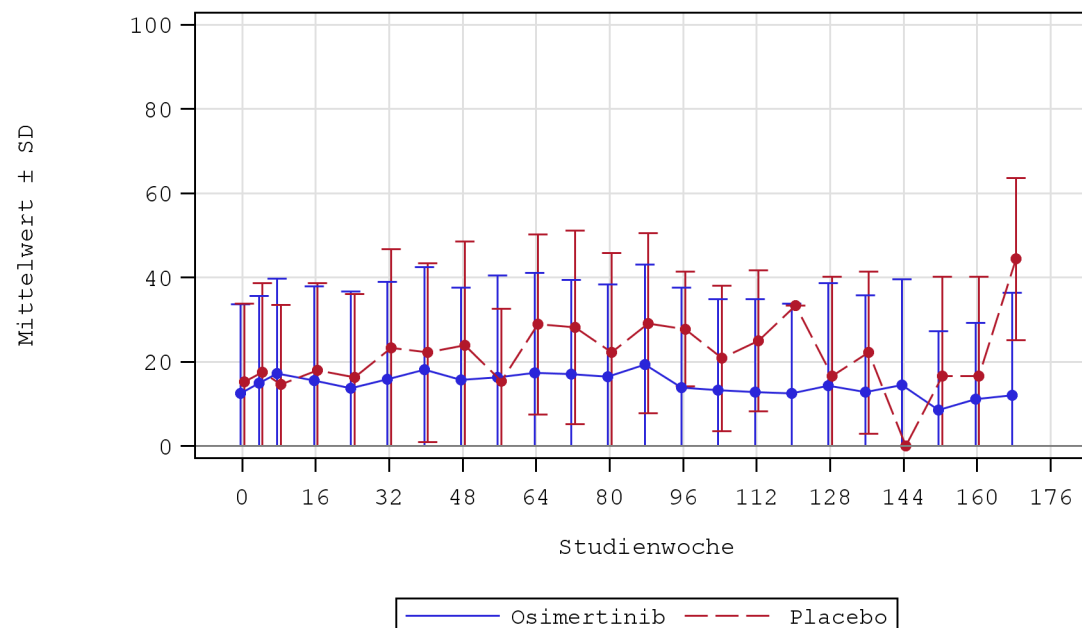
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1L0_MFG0: Course of QLQ-LC13 Pain in other parts
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1L0_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

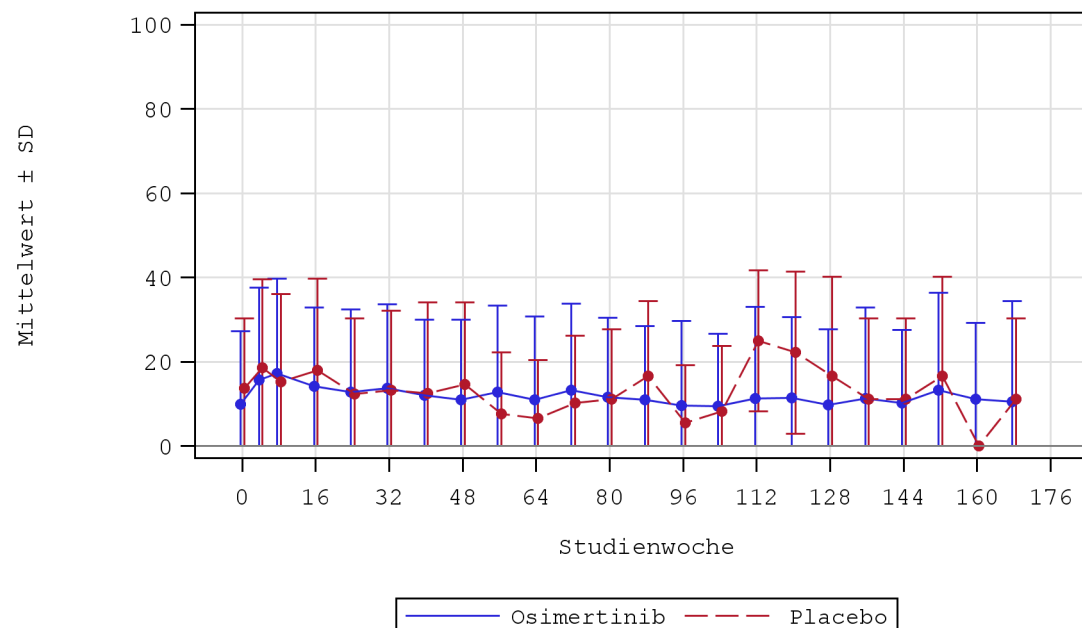
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LB_MFG0: Course of QLQ-LC13 Pain in chest
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LB_MFH0

AstraZeneca

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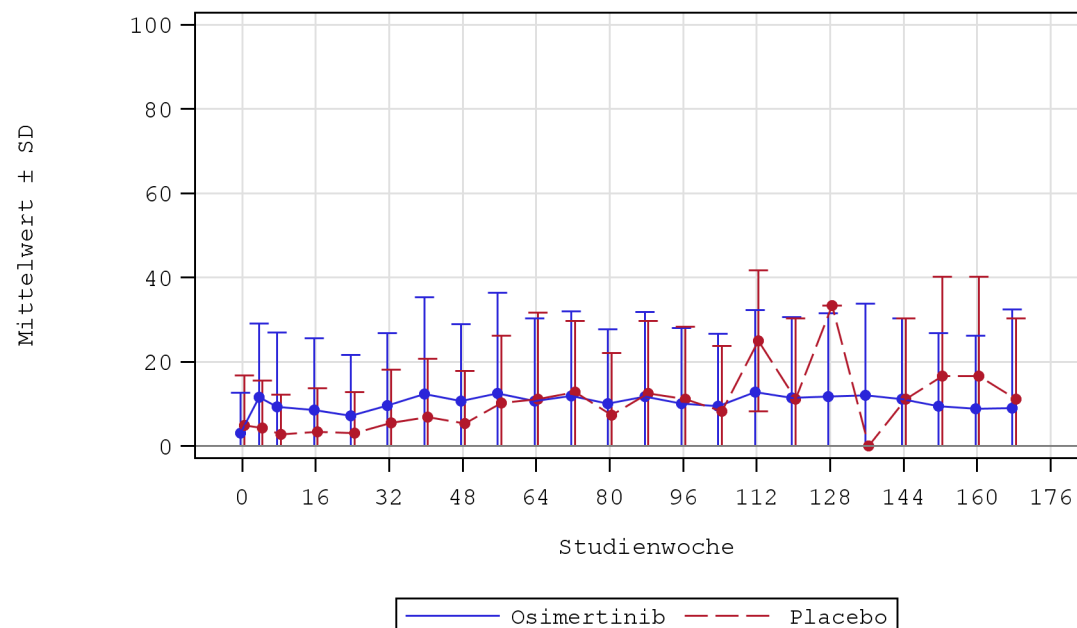
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LS_MFG0: Course of QLQ-LC13 Sore mouth
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LS_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

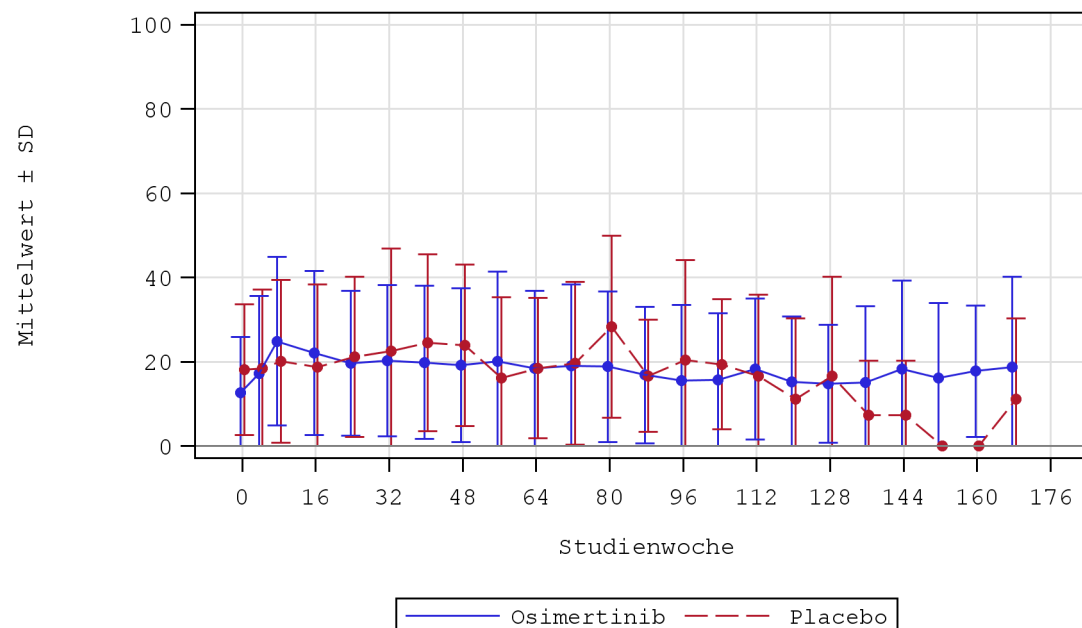
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LD_MFG0: Course of QLQ-LC13 Dyspnea
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LD_MFH0

AstraZeneca

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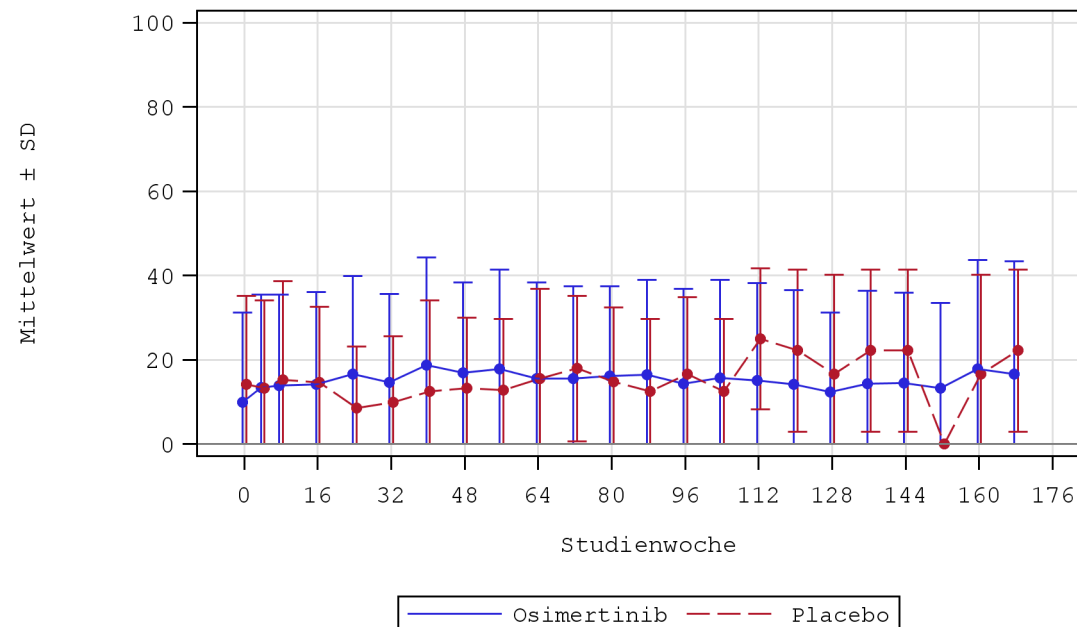
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LN_MFG0: Course of QLQ-LC13 Peripheral neuropathy
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LN_MFH0

AstraZeneca

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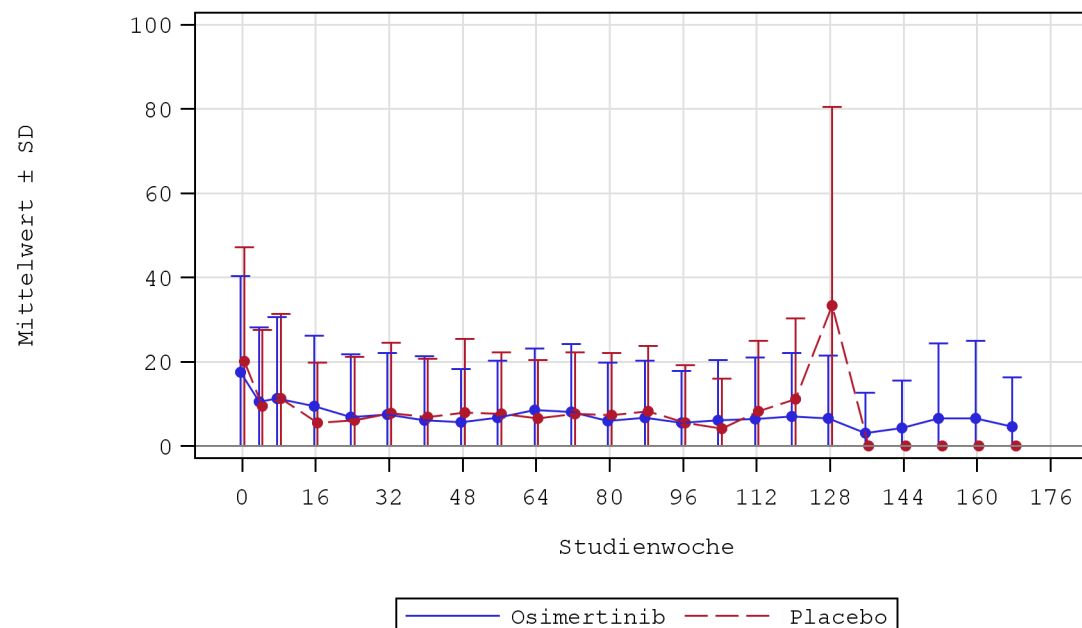
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LA_MFG0: Course of QLQ-LC13 Alopecia
Full Analysis Set
Study: LAURA



Osimertinib	131	112	108	88	94	90	89	79	79	70	62	61	51	44	39	35	30	22
Placebo	68	43	24	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LA_MFH0

AstraZeneca

Value Dossier Analysis: D5160C00048

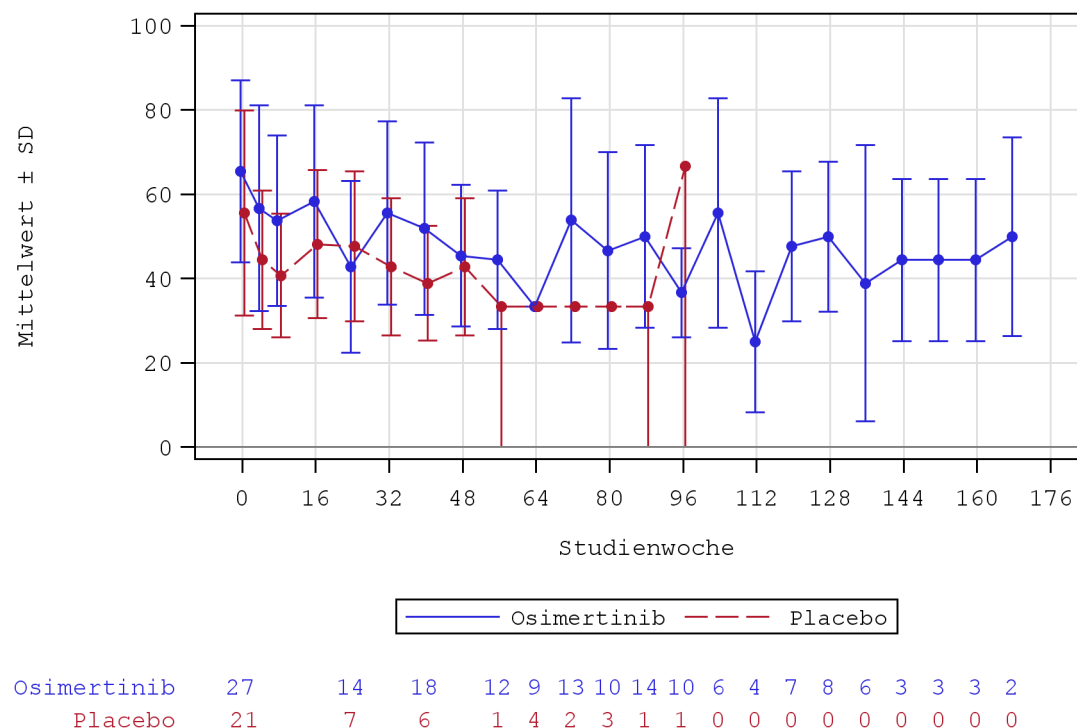
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1LT_MFG0: Course of QLQ-LC13 Take any medicine for pain
Full Analysis Set
Study: LAURA



Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1LT_MFH0

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1EVD15T_MFA0: Time to decrease by at least 15 points in EQ-5D VAS - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to decrease by at least 15 points in EQ-5D LAURA VAS		Osimertinib	Deterioration	143	72 (50.3)
			No deterioration at time of analysis	143	45 (31.5)
			Baseline score too low/high	143	1 (0.7)
			Death without event	143	4 (2.8)
			>= 2 consecutive missed visits	143	7 (4.9)
			No baseline data recorded at time of analysis	143	13 (9.1)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	27 (37.0)
			No deterioration at time of analysis	73	29 (39.7)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	10 (13.7)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	1 (1.4)

N = total number of patients in analysis set. n = number of patients in category.
 EQ-5D VAS: EuroQoL 5-Dimension visual analogue scale.
 Source Data: APRO_TTE, created on: 03SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1EV_MFH0: Course of EQ-5D VAS
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
EQ-5D VAS	Baseline	Osimertinib	143	130 (90.9)	76.80 (15.66)	9.0	80.00	100.0
		Placebo	73	68 (93.2)	79.81 (14.26)	38.0	80.50	100.0
	Week 4	Osimertinib	143	129 (90.2)	73.69 (16.00)	16.0	78.00	100.0
		Placebo	73	65 (89.0)	77.28 (16.68)	30.0	80.00	100.0
	Week 8	Osimertinib	143	127 (88.8)	71.02 (15.60)	38.0	70.00	100.0
		Placebo	73	58 (79.5)	76.43 (16.45)	28.0	80.00	100.0
	Week 16	Osimertinib	143	116 (81.1)	74.59 (15.90)	23.0	78.50	100.0
		Placebo	73	46 (63.0)	76.63 (14.19)	49.0	80.00	100.0
	Week 24	Osimertinib	143	110 (76.9)	74.40 (15.66)	11.0	75.00	100.0
		Placebo	73	43 (58.9)	74.65 (15.69)	22.0	80.00	100.0
	Week 32	Osimertinib	143	104 (72.7)	74.63 (14.45)	30.0	77.00	100.0
		Placebo	73	30 (41.1)	73.53 (19.46)	30.0	78.00	100.0
	Week 40	Osimertinib	143	107 (74.8)	74.86 (15.14)	30.0	79.00	100.0
		Placebo	73	22 (30.1)	71.73 (21.48)	29.0	79.50	100.0
	Week 48	Osimertinib	143	100 (69.9)	77.51 (13.58)	41.0	80.00	100.0
		Placebo	73	25 (34.2)	74.84 (15.60)	49.0	80.00	100.0
	Week 56	Osimertinib	143	87 (60.8)	76.70 (13.40)	36.0	80.00	100.0
		Placebo	73	13 (17.8)	80.85 (13.33)	59.0	85.00	100.0
	Week 64	Osimertinib	143	92 (64.3)	78.01 (13.66)	46.0	80.00	100.0
		Placebo	73	15 (20.5)	74.20 (21.68)	30.0	81.00	100.0
	Week 72	Osimertinib	143	89 (62.2)	76.91 (14.53)	40.0	80.00	100.0
		Placebo	73	13 (17.8)	71.15 (24.46)	33.0	85.00	100.0
	Week 80	Osimertinib	143	88 (61.5)	76.99 (13.50)	40.0	80.00	100.0
		Placebo	73	9 (12.3)	72.00 (21.52)	40.0	76.00	97.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

EQ-5D VAS: EuroQoL 5-Dimension visual analogue scale.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APR0_H0.sas
 Run Date: 29AUG2024:16:11:00

Table LT1EV_MFH0: Course of EQ-5D VAS
 Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
EQ-5D VAS	Week 88	Osimertinib	143	79 (55.2)	77.72 (13.59)	41.0	80.00	100.0
		Placebo	73	8 (11.0)	69.75 (18.20)	48.0	74.00	95.0
	Week 96	Osimertinib	143	79 (55.2)	77.39 (15.05)	28.0	80.00	100.0
		Placebo	73	6 (8.2)	66.83 (25.20)	36.0	67.00	93.0
	Week 104	Osimertinib	143	71 (49.7)	77.20 (13.07)	46.0	80.00	100.0
		Placebo	73	8 (11.0)	79.50 (13.15)	57.0	84.00	93.0
	Week 112	Osimertinib	143	62 (43.4)	77.47 (12.75)	46.0	80.00	100.0
		Placebo	73	4 (5.5)	71.25 (21.78)	48.0	71.50	94.0
	Week 120	Osimertinib	143	61 (42.7)	77.07 (13.47)	40.0	80.00	100.0
		Placebo	73	3 (4.1)	76.00 (17.35)	57.0	80.00	91.0
	Week 128	Osimertinib	143	52 (36.4)	76.85 (13.26)	31.0	79.50	100.0
		Placebo	73	2 (2.7)	71.00 (26.87)	52.0	71.00	90.0
	Week 136	Osimertinib	143	44 (30.8)	75.43 (14.88)	35.0	80.00	100.0
		Placebo	73	3 (4.1)	80.00 (10.00)	70.0	80.00	90.0
	Week 144	Osimertinib	143	39 (27.3)	73.33 (16.63)	20.0	77.00	100.0
		Placebo	73	3 (4.1)	73.33 (29.30)	40.0	85.00	95.0
	Week 152	Osimertinib	143	35 (24.5)	75.94 (16.36)	20.0	80.00	100.0
		Placebo	73	2 (2.7)	90.50 (7.78)	85.0	90.50	96.0
	Week 160	Osimertinib	143	30 (21.0)	75.23 (12.26)	49.0	78.00	100.0
		Placebo	73	2 (2.7)	87.50 (10.61)	80.0	87.50	95.0
	Week 168	Osimertinib	143	22 (15.4)	78.23 (16.91)	23.0	81.00	100.0
		Placebo	73	3 (4.1)	81.33 (10.97)	69.0	85.00	90.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

EQ-5D VAS: EuroQoL 5-Dimension visual analogue scale.

Source Data: APR0, created on: 28AUG2024

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Value Dossier Analysis: D5160C00048

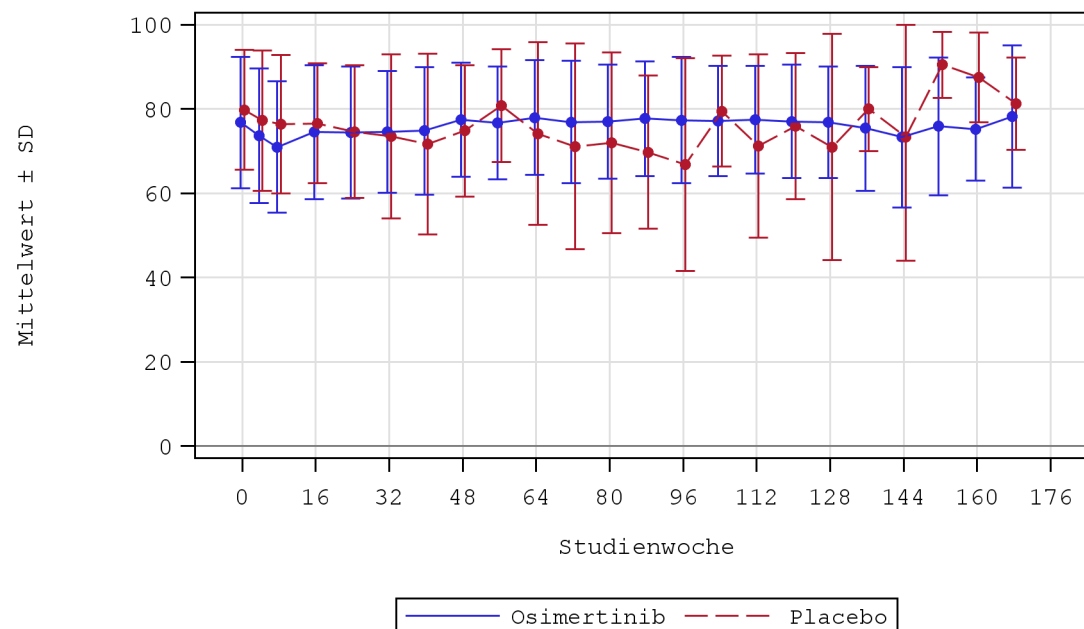
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1EV_MFG0: Course of EQ-5D VAS
Full Analysis Set
Study: LAURA



Osimertinib	130	110	107	87	92	89	88	79	79	71	62	61	52	44	39	35	30	22
Placebo	68	43	22	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. EQ-5D VAS: EuroQoL 5-Dimension visual analogue scale.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1EV_MFH0

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
 Run Date: 04SEP2024:14:40:07

Table LT1IIII1T_MFA0: Time to increase by at least 1 points in PGIS - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to increase by at least 1 point in PGIS	LAURA	Osimertinib	Deterioration	143	73 (51.0)
			No deterioration at time of analysis	143	40 (28.0)
			Baseline score too low/high	143	1 (0.7)
			Death without event	143	7 (4.9)
			>= 2 consecutive missed visits	143	7 (4.9)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	3 (2.1)
		Placebo	Deterioration	73	51 (69.9)
			No deterioration at time of analysis	73	12 (16.4)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	3 (4.1)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	1 (1.4)

N = total number of patients in analysis set. n = number of patients in category.
 PGIS: Patients Global Impression of Severity.
 Source Data: APRO_TTE, created on: 03SEP2024

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Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1III_MFH0: Course of PGIS
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
PGIS	Baseline	Osimertinib	143	131 (91.6)	1.43 (1.32)	0.0	1.00	5.0
		Placebo	73	68 (93.2)	1.32 (1.15)	0.0	1.00	4.0
	Week 8	Osimertinib	143	128 (89.5)	1.66 (1.21)	0.0	2.00	5.0
		Placebo	73	59 (80.8)	1.44 (1.33)	0.0	1.00	4.0
	Week 16	Osimertinib	143	118 (82.5)	1.36 (1.14)	0.0	1.00	4.0
		Placebo	73	47 (64.4)	1.49 (1.28)	0.0	1.00	4.0
	Week 24	Osimertinib	143	110 (76.9)	1.34 (1.17)	0.0	1.00	4.0
		Placebo	73	42 (57.5)	1.50 (1.31)	0.0	1.00	4.0
	Week 32	Osimertinib	143	104 (72.7)	1.44 (1.16)	0.0	1.00	4.0
		Placebo	73	30 (41.1)	1.43 (1.59)	0.0	1.00	5.0
	Week 40	Osimertinib	143	107 (74.8)	1.33 (1.21)	0.0	1.00	4.0
		Placebo	73	22 (30.1)	1.59 (1.44)	0.0	2.00	4.0
	Week 48	Osimertinib	143	100 (69.9)	1.25 (1.17)	0.0	1.00	4.0
		Placebo	73	25 (34.2)	1.76 (1.23)	0.0	2.00	3.0
	Week 56	Osimertinib	143	88 (61.5)	1.32 (1.18)	0.0	1.00	5.0
		Placebo	73	13 (17.8)	1.15 (1.28)	0.0	1.00	3.0
	Week 64	Osimertinib	143	93 (65.0)	1.30 (1.20)	0.0	1.00	4.0
		Placebo	73	15 (20.5)	1.27 (1.33)	0.0	1.00	3.0
	Week 72	Osimertinib	143	90 (62.9)	1.26 (1.16)	0.0	1.00	5.0
		Placebo	73	13 (17.8)	0.92 (1.19)	0.0	0.00	3.0
	Week 80	Osimertinib	143	88 (61.5)	1.17 (1.13)	0.0	1.00	4.0
		Placebo	73	9 (12.3)	0.89 (1.05)	0.0	1.00	3.0
	Week 88	Osimertinib	143	79 (55.2)	1.11 (1.09)	0.0	1.00	4.0
		Placebo	73	8 (11.0)	0.88 (1.36)	0.0	0.00	3.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

PGIS: Patients Global Impression of Severity.

Source Data: APR0, created on: 28AUG2024

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 Program Name: LT1_APR0_H0.sas
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Table LT1III_MFH0: Course of PGIS
 Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
PGIS	Week 96	Osimertinib	143	79 (55.2)	1.28 (1.20)	0.0	1.00	4.0
		Placebo	73	6 (8.2)	1.17 (1.83)	0.0	0.00	4.0
	Week 104	Osimertinib	143	71 (49.7)	1.14 (1.12)	0.0	1.00	4.0
		Placebo	73	8 (11.0)	0.75 (1.16)	0.0	0.00	3.0
	Week 112	Osimertinib	143	62 (43.4)	1.11 (1.15)	0.0	1.00	4.0
		Placebo	73	4 (5.5)	1.50 (1.73)	0.0	1.50	3.0
	Week 120	Osimertinib	143	61 (42.7)	1.07 (1.26)	0.0	1.00	5.0
		Placebo	73	3 (4.1)	1.00 (1.73)	0.0	0.00	3.0
	Week 128	Osimertinib	143	52 (36.4)	1.13 (1.07)	0.0	1.00	4.0
		Placebo	73	2 (2.7)	1.50 (2.12)	0.0	1.50	3.0
	Week 136	Osimertinib	143	44 (30.8)	1.09 (1.12)	0.0	1.00	4.0
		Placebo	73	3 (4.1)	1.00 (1.73)	0.0	0.00	3.0
	Week 144	Osimertinib	143	39 (27.3)	1.13 (1.08)	0.0	1.00	3.0
		Placebo	73	3 (4.1)	0.67 (1.15)	0.0	0.00	2.0
	Week 152	Osimertinib	143	35 (24.5)	1.20 (1.18)	0.0	1.00	4.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 160	Osimertinib	143	30 (21.0)	1.23 (1.01)	0.0	1.00	3.0
		Placebo	73	2 (2.7)	0.00 (0.00)	0.0	0.00	0.0
	Week 168	Osimertinib	143	22 (15.4)	1.05 (1.09)	0.0	1.00	3.0
		Placebo	73	3 (4.1)	0.67 (1.15)	0.0	0.00	2.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

PGIS: Patients Global Impression of Severity.

Source Data: APR0, created on: 28AUG2024

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Value Dossier Analysis: D5160C00048

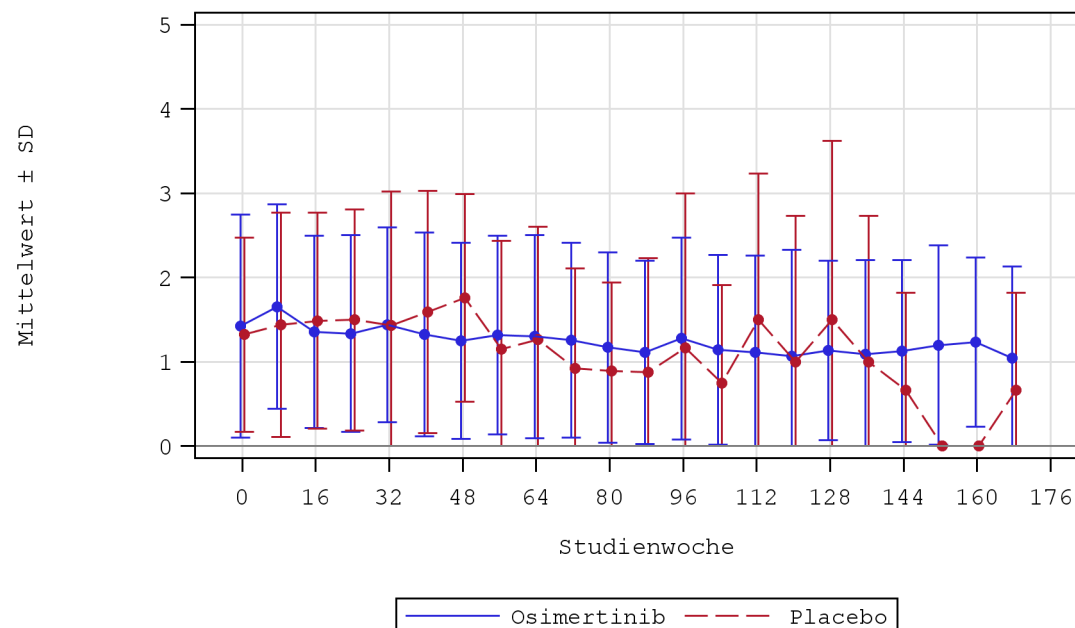
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1III_MFG0: Course of PGIS
Full Analysis Set
Study: LAURA



Osimertinib	131	110	107	88	93	90	88	79	79	71	62	61	52	44	39	35	30	22
Placebo	68	42	22	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. PGIS: Patients Global Impression of Severity.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1III_MFH0

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 Program Name: LT1_APRO_TTE_A0.sas
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Table LT1QGD10T_MFA0: Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL	LAURA	Osimertinib	Deterioration	143	84 (58.7)
			No deterioration at time of analysis	143	38 (26.6)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	2 (1.4)
			>= 2 consecutive missed visits	143	6 (4.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	37 (50.7)
			No deterioration at time of analysis	73	23 (31.5)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	7 (9.6)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

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Table LT1QYD10T_MFA0: Time to decrease by at least 10 points in QLQ-C30 Physical Functioning - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to decrease by at least 10 points in QLQ-C30 Physical Functioning	LAURA	Osimertinib	Deterioration	143	75 (52.4)
			No deterioration at time of analysis	143	44 (30.8)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	2 (1.4)
			>= 2 consecutive missed visits	143	9 (6.3)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	31 (42.5)
			No deterioration at time of analysis	73	30 (41.1)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	5 (6.8)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1QRD10T_MFA0: Time to decrease by at least 10 points in QLQ-C30 Role Functioning - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to decrease by at least 10 points in QLQ-C30 Role Functioning	LAURA	Osimertinib	Deterioration	143	86 (60.1)
			No deterioration at time of analysis	143	38 (26.6)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	1 (0.7)
			>= 2 consecutive missed visits	143	5 (3.5)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	41 (56.2)
			No deterioration at time of analysis	73	19 (26.0)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	7 (9.6)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

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 Program Name: LT1_APRO_TTE_A0.sas
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Table LT1QTD10T_MFA0: Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning	LAURA	Osimertinib	Deterioration	143	82 (57.3)
			No deterioration at time of analysis	143	36 (25.2)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	4 (2.8)
			>= 2 consecutive missed visits	143	8 (5.6)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	37 (50.7)
			No deterioration at time of analysis	73	23 (31.5)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	7 (9.6)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_A0.sas
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Table LT1QED10T_MFA0: Time to decrease by at least 10 points in QLQ-C30 Emotional Functioning - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to decrease by at least 10 points in QLQ-C30 Emotional Functioning	LAURA	Osimertinib	Deterioration	143	77 (53.8)
			No deterioration at time of analysis	143	42 (29.4)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	4 (2.8)
			>= 2 consecutive missed visits	143	7 (4.9)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	31 (42.5)
			No deterioration at time of analysis	73	28 (38.4)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	2 (2.7)
			>= 2 consecutive missed visits	73	7 (9.6)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

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 Value Dossier Analysis: D5160C00048
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 Program Name: LT1_APRO_TTE_A0.sas
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Table LT1QSD10T_MFA0: Time to decrease by at least 10 points in QLQ-C30 Social Functioning - censoring status
 Full Analysis Set

Parameter	Study	Treatment	Category	N	n (%)
Time to decrease by at least 10 points in QLQ-C30 Social Functioning	LAURA	Osimertinib	Deterioration	143	88 (61.5)
			No deterioration at time of analysis	143	34 (23.8)
			Baseline score too low/high	143	0 (0.0)
			Death without event	143	2 (1.4)
			>= 2 consecutive missed visits	143	6 (4.2)
			No baseline data recorded at time of analysis	143	12 (8.4)
			No post-baseline data recorded at time of analysis	143	1 (0.7)
		Placebo	Deterioration	73	33 (45.2)
			No deterioration at time of analysis	73	27 (37.0)
			Baseline score too low/high	73	0 (0.0)
			Death without event	73	1 (1.4)
			>= 2 consecutive missed visits	73	7 (9.6)
			No baseline data recorded at time of analysis	73	5 (6.8)
			No post-baseline data recorded at time of analysis	73	0 (0.0)

N = total number of patients in analysis set. n = number of patients in category.
 QLQ-C30: EORTC Quality of Life Questionnaire - Core 30 items.
 Source Data: APRO_TTE, created on: 03SEP2024

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Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QG_MFH0: Course of QLQ-C30 Global Health status/QoL
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Global Health status/QoL	Baseline	Osimertinib	143	131 (91.6)	72.07 (14.43)	33.3	75.00	100.0
		Placebo	73	68 (93.2)	71.69 (16.98)	33.3	70.83	100.0
	Week 4	Osimertinib	143	130 (90.9)	65.83 (16.27)	16.7	66.67	100.0
		Placebo	73	66 (90.4)	74.75 (17.60)	33.3	83.33	100.0
	Week 8	Osimertinib	143	129 (90.2)	65.12 (17.73)	0.0	66.67	100.0
		Placebo	73	59 (80.8)	72.88 (19.85)	16.7	83.33	100.0
	Week 16	Osimertinib	143	119 (83.2)	70.59 (16.38)	33.3	66.67	100.0
		Placebo	73	48 (65.8)	72.05 (14.23)	33.3	66.67	100.0
	Week 24	Osimertinib	143	111 (77.6)	69.52 (15.05)	33.3	66.67	100.0
		Placebo	73	43 (58.9)	69.38 (16.54)	33.3	66.67	100.0
	Week 32	Osimertinib	143	105 (73.4)	70.24 (15.58)	25.0	66.67	100.0
		Placebo	73	30 (41.1)	68.89 (19.69)	16.7	66.67	100.0
	Week 40	Osimertinib	143	108 (75.5)	70.68 (14.96)	33.3	66.67	100.0
		Placebo	73	23 (31.5)	68.48 (21.31)	25.0	75.00	100.0
	Week 48	Osimertinib	143	100 (69.9)	72.58 (13.83)	41.7	70.83	100.0
		Placebo	73	25 (34.2)	71.33 (16.33)	41.7	75.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	71.88 (14.37)	41.7	66.67	100.0
		Placebo	73	13 (17.8)	73.72 (20.37)	33.3	83.33	100.0
	Week 64	Osimertinib	143	93 (65.0)	72.85 (14.43)	33.3	66.67	100.0
		Placebo	73	15 (20.5)	67.22 (22.15)	25.0	66.67	100.0
	Week 72	Osimertinib	143	90 (62.9)	72.13 (15.51)	33.3	66.67	100.0
		Placebo	73	13 (17.8)	68.59 (21.56)	33.3	66.67	100.0
	Week 80	Osimertinib	143	88 (61.5)	72.06 (15.58)	33.3	70.83	100.0
		Placebo	73	9 (12.3)	69.44 (21.65)	41.7	66.67	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1QG_MFH0: Course of QLQ-C30 Global Health status/QoL
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Global Health status/QoL	Week 88	Osimertinib	143	79 (55.2)	74.26 (13.29)	50.0	75.00	100.0
		Placebo	73	8 (11.0)	63.54 (16.63)	33.3	66.67	83.3
	Week 96	Osimertinib	143	79 (55.2)	71.31 (15.77)	33.3	66.67	100.0
		Placebo	73	6 (8.2)	63.89 (22.15)	33.3	66.67	83.3
	Week 104	Osimertinib	143	71 (49.7)	74.06 (15.01)	33.3	75.00	100.0
		Placebo	73	8 (11.0)	71.88 (14.04)	50.0	70.83	91.7
	Week 112	Osimertinib	143	63 (44.1)	72.35 (14.95)	33.3	75.00	100.0
		Placebo	73	4 (5.5)	66.67 (19.25)	50.0	66.67	83.3
	Week 120	Osimertinib	143	61 (42.7)	70.90 (13.66)	41.7	66.67	100.0
		Placebo	73	3 (4.1)	75.00 (14.43)	58.3	83.33	83.3
	Week 128	Osimertinib	143	52 (36.4)	71.96 (14.10)	33.3	70.83	100.0
		Placebo	73	2 (2.7)	66.67 (23.57)	50.0	66.67	83.3
	Week 136	Osimertinib	143	44 (30.8)	73.86 (14.22)	33.3	75.00	100.0
		Placebo	73	3 (4.1)	69.44 (17.35)	50.0	75.00	83.3
	Week 144	Osimertinib	143	39 (27.3)	71.58 (18.01)	16.7	66.67	100.0
		Placebo	73	3 (4.1)	63.89 (20.97)	41.7	66.67	83.3
	Week 152	Osimertinib	143	35 (24.5)	71.90 (18.42)	16.7	66.67	100.0
		Placebo	73	2 (2.7)	79.17 (5.89)	75.0	79.17	83.3
	Week 160	Osimertinib	143	30 (21.0)	71.11 (15.59)	33.3	66.67	100.0
		Placebo	73	2 (2.7)	79.17 (5.89)	75.0	79.17	83.3
	Week 168	Osimertinib	143	22 (15.4)	71.21 (18.50)	16.7	70.83	100.0
		Placebo	73	3 (4.1)	75.00 (14.43)	58.3	83.33	83.3

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1QY_MFH0: Course of QLQ-C30 Physical Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Physical Functioning	Baseline	Osimertinib	143	131 (91.6)	88.24 (14.53)	0.0	93.33	100.0
		Placebo	73	68 (93.2)	86.76 (11.08)	60.0	86.67	100.0
	Week 4	Osimertinib	143	130 (90.9)	86.15 (15.45)	20.0	86.67	100.0
		Placebo	73	66 (90.4)	85.15 (15.42)	33.3	86.67	100.0
	Week 8	Osimertinib	143	129 (90.2)	83.67 (16.60)	26.7	86.67	100.0
		Placebo	73	59 (80.8)	88.14 (16.66)	20.0	93.33	100.0
	Week 16	Osimertinib	143	119 (83.2)	86.16 (14.63)	26.7	86.67	100.0
		Placebo	73	48 (65.8)	87.08 (15.09)	33.3	86.67	100.0
	Week 24	Osimertinib	143	111 (77.6)	87.63 (13.51)	40.0	93.33	100.0
		Placebo	73	43 (58.9)	85.27 (15.43)	26.7	86.67	100.0
	Week 32	Osimertinib	143	105 (73.4)	87.11 (15.64)	13.3	86.67	100.0
		Placebo	73	30 (41.1)	83.11 (17.40)	20.0	86.67	100.0
	Week 40	Osimertinib	143	108 (75.5)	86.36 (15.72)	26.7	93.33	100.0
		Placebo	73	23 (31.5)	79.71 (19.12)	20.0	80.00	100.0
	Week 48	Osimertinib	143	100 (69.9)	88.40 (12.27)	40.0	90.00	100.0
		Placebo	73	25 (34.2)	84.27 (12.60)	60.0	86.67	100.0
	Week 56	Osimertinib	143	88 (61.5)	88.03 (14.44)	26.7	93.33	100.0
		Placebo	73	13 (17.8)	87.69 (10.83)	73.3	86.67	100.0
	Week 64	Osimertinib	143	93 (65.0)	87.10 (14.57)	40.0	93.33	100.0
		Placebo	73	15 (20.5)	84.00 (17.42)	40.0	86.67	100.0
	Week 72	Osimertinib	143	90 (62.9)	87.56 (14.83)	33.3	93.33	100.0
		Placebo	73	13 (17.8)	83.08 (21.19)	26.7	93.33	100.0
	Week 80	Osimertinib	143	88 (61.5)	87.73 (14.43)	33.3	93.33	100.0
		Placebo	73	9 (12.3)	80.74 (17.46)	46.7	80.00	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
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Program Name: LT1_APR0_H0.sas
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Table LT1QY_MFH0: Course of QLQ-C30 Physical Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Physical Functioning	Week 88	Osimertinib	143	79 (55.2)	88.27 (13.55)	40.0	93.33	100.0
		Placebo	73	8 (11.0)	82.50 (18.15)	46.7	80.00	100.0
	Week 96	Osimertinib	143	79 (55.2)	89.37 (15.27)	20.0	93.33	100.0
		Placebo	73	6 (8.2)	78.89 (31.10)	20.0	90.00	100.0
	Week 104	Osimertinib	143	71 (49.7)	88.64 (14.67)	20.0	93.33	100.0
		Placebo	73	8 (11.0)	88.33 (12.72)	73.3	90.00	100.0
	Week 112	Osimertinib	143	63 (44.1)	87.83 (14.40)	26.7	93.33	100.0
		Placebo	73	4 (5.5)	88.33 (13.74)	73.3	90.00	100.0
	Week 120	Osimertinib	143	61 (42.7)	87.65 (16.86)	20.0	93.33	100.0
		Placebo	73	3 (4.1)	93.33 (11.55)	80.0	100.00	100.0
	Week 128	Osimertinib	143	52 (36.4)	88.46 (12.53)	53.3	93.33	100.0
		Placebo	73	2 (2.7)	86.67 (18.86)	73.3	86.67	100.0
	Week 136	Osimertinib	143	44 (30.8)	86.52 (19.42)	20.0	93.33	100.0
		Placebo	73	3 (4.1)	95.56 (7.70)	86.7	100.00	100.0
	Week 144	Osimertinib	143	39 (27.3)	87.35 (14.00)	40.0	86.67	100.0
		Placebo	73	3 (4.1)	95.56 (7.70)	86.7	100.00	100.0
	Week 152	Osimertinib	143	35 (24.5)	87.05 (17.41)	13.3	86.67	100.0
		Placebo	73	2 (2.7)	100.00 (0.00)	100.0	100.00	100.0
	Week 160	Osimertinib	143	30 (21.0)	87.33 (17.10)	13.3	93.33	100.0
		Placebo	73	2 (2.7)	100.00 (0.00)	100.0	100.00	100.0
	Week 168	Osimertinib	143	22 (15.4)	88.18 (18.39)	13.3	90.00	100.0
		Placebo	73	3 (4.1)	93.33 (11.55)	80.0	100.00	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QR_MFH0: Course of QLQ-C30 Role Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Role Functioning	Baseline	Osimertinib	143	131 (91.6)	90.84 (16.04)	33.3	100.00	100.0
		Placebo	73	68 (93.2)	90.44 (16.11)	33.3	100.00	100.0
	Week 4	Osimertinib	143	130 (90.9)	86.79 (20.30)	0.0	100.00	100.0
		Placebo	73	66 (90.4)	88.13 (18.67)	16.7	100.00	100.0
	Week 8	Osimertinib	143	129 (90.2)	83.85 (21.64)	0.0	100.00	100.0
		Placebo	73	59 (80.8)	90.11 (20.56)	0.0	100.00	100.0
	Week 16	Osimertinib	143	119 (83.2)	87.11 (20.17)	16.7	100.00	100.0
		Placebo	73	48 (65.8)	91.32 (15.75)	33.3	100.00	100.0
	Week 24	Osimertinib	143	111 (77.6)	87.54 (20.65)	0.0	100.00	100.0
		Placebo	73	43 (58.9)	86.82 (19.44)	33.3	100.00	100.0
	Week 32	Osimertinib	143	105 (73.4)	86.67 (21.48)	0.0	100.00	100.0
		Placebo	73	30 (41.1)	87.78 (18.54)	33.3	100.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	87.04 (20.80)	16.7	100.00	100.0
		Placebo	73	23 (31.5)	86.23 (21.11)	33.3	100.00	100.0
	Week 48	Osimertinib	143	100 (69.9)	88.67 (18.02)	16.7	100.00	100.0
		Placebo	73	25 (34.2)	90.00 (16.67)	33.3	100.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	87.50 (20.72)	16.7	100.00	100.0
		Placebo	73	13 (17.8)	89.74 (14.50)	66.7	100.00	100.0
	Week 64	Osimertinib	143	93 (65.0)	87.28 (20.32)	0.0	100.00	100.0
		Placebo	73	15 (20.5)	82.22 (20.38)	33.3	83.33	100.0
	Week 72	Osimertinib	143	90 (62.9)	87.59 (21.43)	0.0	100.00	100.0
		Placebo	73	13 (17.8)	80.77 (27.93)	0.0	83.33	100.0
	Week 80	Osimertinib	143	88 (61.5)	87.50 (20.72)	0.0	100.00	100.0
		Placebo	73	9 (12.3)	79.63 (24.69)	33.3	83.33	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QR_MFH0: Course of QLQ-C30 Role Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Role Functioning	Week 88	Osimertinib	143	79 (55.2)	86.71 (21.41)	0.0	100.00	100.0
		Placebo	73	8 (11.0)	85.42 (22.60)	33.3	91.67	100.0
	Week 96	Osimertinib	143	79 (55.2)	88.82 (21.30)	16.7	100.00	100.0
		Placebo	73	6 (8.2)	83.33 (27.89)	33.3	100.00	100.0
	Week 104	Osimertinib	143	71 (49.7)	86.38 (22.77)	0.0	100.00	100.0
		Placebo	73	8 (11.0)	87.50 (14.77)	66.7	91.67	100.0
	Week 112	Osimertinib	143	63 (44.1)	85.45 (22.89)	0.0	100.00	100.0
		Placebo	73	4 (5.5)	91.67 (16.67)	66.7	100.00	100.0
	Week 120	Osimertinib	143	61 (42.7)	87.16 (21.81)	33.3	100.00	100.0
		Placebo	73	3 (4.1)	88.89 (19.25)	66.7	100.00	100.0
	Week 128	Osimertinib	143	52 (36.4)	85.58 (22.87)	0.0	100.00	100.0
		Placebo	73	2 (2.7)	91.67 (11.79)	83.3	91.67	100.0
	Week 136	Osimertinib	143	44 (30.8)	85.23 (23.08)	33.3	100.00	100.0
		Placebo	73	3 (4.1)	100.00 (0.00)	100.0	100.00	100.0
	Week 144	Osimertinib	143	39 (27.3)	88.03 (16.64)	50.0	100.00	100.0
		Placebo	73	3 (4.1)	100.00 (0.00)	100.0	100.00	100.0
	Week 152	Osimertinib	143	35 (24.5)	82.38 (24.90)	16.7	100.00	100.0
		Placebo	73	2 (2.7)	100.00 (0.00)	100.0	100.00	100.0
	Week 160	Osimertinib	143	30 (21.0)	87.22 (20.85)	16.7	100.00	100.0
		Placebo	73	2 (2.7)	100.00 (0.00)	100.0	100.00	100.0
	Week 168	Osimertinib	143	22 (15.4)	87.88 (23.11)	0.0	100.00	100.0
		Placebo	73	3 (4.1)	94.44 (9.62)	83.3	100.00	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1QT_MFH0: Course of QLQ-C30 Cognitive Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Cognitive Functioning	Baseline	Osimertinib	143	131 (91.6)	90.46 (13.87)	16.7	100.00	100.0
		Placebo	73	68 (93.2)	90.44 (12.32)	50.0	100.00	100.0
	Week 4	Osimertinib	143	130 (90.9)	88.46 (15.37)	16.7	100.00	100.0
		Placebo	73	66 (90.4)	89.14 (14.17)	50.0	100.00	100.0
	Week 8	Osimertinib	143	129 (90.2)	89.15 (15.54)	16.7	100.00	100.0
		Placebo	73	59 (80.8)	89.27 (13.76)	33.3	100.00	100.0
	Week 16	Osimertinib	143	119 (83.2)	88.52 (14.68)	33.3	100.00	100.0
		Placebo	73	48 (65.8)	90.28 (14.11)	33.3	100.00	100.0
	Week 24	Osimertinib	143	111 (77.6)	89.19 (16.31)	16.7	100.00	100.0
		Placebo	73	43 (58.9)	88.76 (17.71)	16.7	100.00	100.0
	Week 32	Osimertinib	143	105 (73.4)	84.60 (18.45)	33.3	83.33	100.0
		Placebo	73	30 (41.1)	89.44 (17.77)	16.7	100.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	86.11 (16.51)	16.7	83.33	100.0
		Placebo	73	23 (31.5)	89.86 (19.94)	16.7	100.00	100.0
	Week 48	Osimertinib	143	100 (69.9)	85.17 (16.90)	33.3	83.33	100.0
		Placebo	73	25 (34.2)	89.33 (16.58)	50.0	100.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	85.42 (16.92)	33.3	83.33	100.0
		Placebo	73	13 (17.8)	91.03 (12.94)	66.7	100.00	100.0
	Week 64	Osimertinib	143	93 (65.0)	84.95 (17.04)	33.3	83.33	100.0
		Placebo	73	15 (20.5)	83.33 (23.57)	33.3	100.00	100.0
	Week 72	Osimertinib	143	90 (62.9)	86.11 (16.99)	33.3	83.33	100.0
		Placebo	73	13 (17.8)	85.90 (20.24)	33.3	100.00	100.0
	Week 80	Osimertinib	143	88 (61.5)	85.80 (17.24)	33.3	91.67	100.0
		Placebo	73	9 (12.3)	77.78 (18.63)	50.0	83.33	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1QT_MFH0: Course of QLQ-C30 Cognitive Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Cognitive Functioning	Week 88	Osimertinib	143	79 (55.2)	83.76 (17.90)	33.3	83.33	100.0
		Placebo	73	8 (11.0)	85.42 (13.91)	66.7	83.33	100.0
	Week 96	Osimertinib	143	79 (55.2)	86.92 (17.64)	33.3	100.00	100.0
		Placebo	73	6 (8.2)	88.89 (13.61)	66.7	91.67	100.0
	Week 104	Osimertinib	143	71 (49.7)	86.85 (18.88)	33.3	100.00	100.0
		Placebo	73	8 (11.0)	89.58 (8.63)	83.3	83.33	100.0
	Week 112	Osimertinib	143	63 (44.1)	84.66 (22.66)	0.0	100.00	100.0
		Placebo	73	4 (5.5)	87.50 (15.96)	66.7	91.67	100.0
	Week 120	Osimertinib	143	61 (42.7)	85.79 (17.96)	33.3	100.00	100.0
		Placebo	73	3 (4.1)	94.44 (9.62)	83.3	100.00	100.0
	Week 128	Osimertinib	143	52 (36.4)	83.65 (18.81)	33.3	83.33	100.0
		Placebo	73	2 (2.7)	91.67 (11.79)	83.3	91.67	100.0
	Week 136	Osimertinib	143	44 (30.8)	84.47 (20.77)	16.7	91.67	100.0
		Placebo	73	3 (4.1)	94.44 (9.62)	83.3	100.00	100.0
	Week 144	Osimertinib	143	39 (27.3)	84.62 (15.94)	50.0	83.33	100.0
		Placebo	73	3 (4.1)	88.89 (9.62)	83.3	83.33	100.0
	Week 152	Osimertinib	143	35 (24.5)	81.90 (18.24)	33.3	83.33	100.0
		Placebo	73	2 (2.7)	91.67 (11.79)	83.3	91.67	100.0
	Week 160	Osimertinib	143	30 (21.0)	81.67 (22.89)	0.0	83.33	100.0
		Placebo	73	2 (2.7)	91.67 (11.79)	83.3	91.67	100.0
	Week 168	Osimertinib	143	22 (15.4)	83.33 (15.43)	50.0	83.33	100.0
		Placebo	73	3 (4.1)	94.44 (9.62)	83.3	100.00	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APR0_H0.sas
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Table LT1QE_MFH0: Course of QLQ-C30 Emotional Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Emotional Functioning	Baseline	Osimertinib	143	131 (91.6)	89.44 (12.99)	25.0	91.67	100.0
		Placebo	73	68 (93.2)	86.40 (14.17)	41.7	91.67	100.0
	Week 4	Osimertinib	143	130 (90.9)	87.18 (16.51)	16.7	91.67	100.0
		Placebo	73	66 (90.4)	87.63 (15.00)	33.3	91.67	100.0
	Week 8	Osimertinib	143	129 (90.2)	84.88 (19.70)	0.0	91.67	100.0
		Placebo	73	59 (80.8)	86.72 (17.99)	33.3	100.00	100.0
	Week 16	Osimertinib	143	119 (83.2)	88.17 (15.70)	33.3	91.67	100.0
		Placebo	73	48 (65.8)	88.02 (16.66)	25.0	100.00	100.0
	Week 24	Osimertinib	143	111 (77.6)	87.39 (15.96)	33.3	91.67	100.0
		Placebo	73	43 (58.9)	88.37 (16.88)	25.0	100.00	100.0
	Week 32	Osimertinib	143	105 (73.4)	87.86 (16.43)	16.7	91.67	100.0
		Placebo	73	30 (41.1)	85.28 (18.53)	25.0	95.83	100.0
	Week 40	Osimertinib	143	108 (75.5)	86.73 (16.94)	0.0	91.67	100.0
		Placebo	73	23 (31.5)	85.87 (18.88)	33.3	91.67	100.0
	Week 48	Osimertinib	143	100 (69.9)	87.42 (16.00)	33.3	91.67	100.0
		Placebo	73	25 (34.2)	89.33 (15.31)	50.0	100.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	86.65 (16.69)	25.0	91.67	100.0
		Placebo	73	13 (17.8)	90.38 (15.16)	66.7	100.00	100.0
	Week 64	Osimertinib	143	93 (65.0)	86.38 (15.19)	33.3	91.67	100.0
		Placebo	73	15 (20.5)	82.22 (26.33)	8.3	100.00	100.0
	Week 72	Osimertinib	143	90 (62.9)	87.41 (13.87)	50.0	91.67	100.0
		Placebo	73	13 (17.8)	89.10 (14.18)	66.7	100.00	100.0
	Week 80	Osimertinib	143	88 (61.5)	87.97 (14.94)	33.3	91.67	100.0
		Placebo	73	9 (12.3)	82.41 (17.40)	50.0	83.33	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

Page 2 of 2
Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1QE_MFH0: Course of QLQ-C30 Emotional Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Emotional Functioning	Week 88	Osimertinib	143	79 (55.2)	87.97 (16.22)	33.3	100.00	100.0
		Placebo	73	8 (11.0)	90.63 (15.06)	66.7	100.00	100.0
	Week 96	Osimertinib	143	79 (55.2)	88.82 (16.06)	16.7	100.00	100.0
		Placebo	73	6 (8.2)	75.00 (32.91)	16.7	83.33	100.0
	Week 104	Osimertinib	143	71 (49.7)	88.97 (15.92)	41.7	100.00	100.0
		Placebo	73	8 (11.0)	92.71 (12.15)	66.7	100.00	100.0
	Week 112	Osimertinib	143	63 (44.1)	88.76 (15.85)	33.3	100.00	100.0
		Placebo	73	4 (5.5)	83.33 (19.25)	66.7	83.33	100.0
	Week 120	Osimertinib	143	61 (42.7)	88.25 (15.32)	41.7	100.00	100.0
		Placebo	73	3 (4.1)	88.89 (19.25)	66.7	100.00	100.0
	Week 128	Osimertinib	143	52 (36.4)	87.34 (16.79)	33.3	95.83	100.0
		Placebo	73	2 (2.7)	83.33 (23.57)	66.7	83.33	100.0
	Week 136	Osimertinib	143	44 (30.8)	87.12 (15.92)	41.7	91.67	100.0
		Placebo	73	3 (4.1)	88.89 (19.25)	66.7	100.00	100.0
	Week 144	Osimertinib	143	39 (27.3)	88.25 (14.90)	41.7	91.67	100.0
		Placebo	73	3 (4.1)	86.11 (17.35)	66.7	91.67	100.0
	Week 152	Osimertinib	143	35 (24.5)	88.81 (14.98)	50.0	100.00	100.0
		Placebo	73	2 (2.7)	100.00 (0.00)	100.0	100.00	100.0
	Week 160	Osimertinib	143	30 (21.0)	87.22 (15.43)	41.7	91.67	100.0
		Placebo	73	2 (2.7)	95.83 (5.89)	91.7	95.83	100.0
	Week 168	Osimertinib	143	22 (15.4)	88.26 (14.92)	50.0	91.67	100.0
		Placebo	73	3 (4.1)	97.22 (4.81)	91.7	100.00	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

Page 1 of 2
Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1QS_MFH0: Course of QLQ-C30 Social Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Social Functioning	Baseline	Osimertinib	143	131 (91.6)	89.31 (16.55)	33.3	100.00	100.0
		Placebo	73	68 (93.2)	87.01 (16.50)	33.3	100.00	100.0
	Week 4	Osimertinib	143	130 (90.9)	87.69 (18.39)	0.0	100.00	100.0
		Placebo	73	66 (90.4)	90.15 (16.53)	33.3	100.00	100.0
	Week 8	Osimertinib	143	129 (90.2)	85.53 (20.66)	0.0	100.00	100.0
		Placebo	73	59 (80.8)	88.98 (20.67)	0.0	100.00	100.0
	Week 16	Osimertinib	143	119 (83.2)	88.10 (20.83)	0.0	100.00	100.0
		Placebo	73	48 (65.8)	89.24 (19.60)	0.0	100.00	100.0
	Week 24	Osimertinib	143	111 (77.6)	89.49 (18.25)	33.3	100.00	100.0
		Placebo	73	43 (58.9)	84.50 (23.12)	16.7	100.00	100.0
	Week 32	Osimertinib	143	105 (73.4)	87.30 (21.25)	0.0	100.00	100.0
		Placebo	73	30 (41.1)	88.89 (18.74)	33.3	100.00	100.0
	Week 40	Osimertinib	143	108 (75.5)	86.57 (21.06)	33.3	100.00	100.0
		Placebo	73	23 (31.5)	87.68 (22.60)	16.7	100.00	100.0
	Week 48	Osimertinib	143	100 (69.9)	86.67 (19.82)	16.7	100.00	100.0
		Placebo	73	25 (34.2)	89.33 (17.92)	33.3	100.00	100.0
	Week 56	Osimertinib	143	88 (61.5)	87.12 (19.69)	16.7	100.00	100.0
		Placebo	73	13 (17.8)	91.03 (16.12)	50.0	100.00	100.0
	Week 64	Osimertinib	143	93 (65.0)	85.84 (22.78)	0.0	100.00	100.0
		Placebo	73	15 (20.5)	84.44 (21.33)	33.3	100.00	100.0
	Week 72	Osimertinib	143	90 (62.9)	86.67 (20.93)	0.0	100.00	100.0
		Placebo	73	13 (17.8)	83.33 (23.57)	33.3	100.00	100.0
	Week 80	Osimertinib	143	88 (61.5)	88.07 (20.05)	33.3	100.00	100.0
		Placebo	73	9 (12.3)	83.33 (20.41)	50.0	100.00	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

Page 2 of 2
Program Name: LT1_APR0_H0.sas
Run Date: 29AUG2024:16:11:00

Table LT1QS_MFH0: Course of QLQ-C30 Social Functioning
Full Analysis Set

Parameter	Time	Treatment	N	n (%)	Mean (SD)	Min	Q50	Max
QLQ-C30 Social Functioning	Week 88	Osimertinib	143	79 (55.2)	87.76 (21.13)	33.3	100.00	100.0
		Placebo	73	8 (11.0)	81.25 (20.77)	50.0	83.33	100.0
	Week 96	Osimertinib	143	79 (55.2)	86.08 (22.56)	16.7	100.00	100.0
		Placebo	73	6 (8.2)	80.56 (22.15)	50.0	83.33	100.0
	Week 104	Osimertinib	143	71 (49.7)	85.92 (22.30)	33.3	100.00	100.0
		Placebo	73	8 (11.0)	89.58 (15.27)	66.7	100.00	100.0
	Week 112	Osimertinib	143	63 (44.1)	87.83 (20.35)	33.3	100.00	100.0
		Placebo	73	4 (5.5)	91.67 (16.67)	66.7	100.00	100.0
	Week 120	Osimertinib	143	61 (42.7)	86.89 (20.89)	33.3	100.00	100.0
		Placebo	73	3 (4.1)	88.89 (19.25)	66.7	100.00	100.0
	Week 128	Osimertinib	143	52 (36.4)	85.58 (24.03)	16.7	100.00	100.0
		Placebo	73	2 (2.7)	91.67 (11.79)	83.3	91.67	100.0
	Week 136	Osimertinib	143	44 (30.8)	84.47 (23.68)	33.3	100.00	100.0
		Placebo	73	3 (4.1)	100.00 (0.00)	100.0	100.00	100.0
	Week 144	Osimertinib	143	39 (27.3)	87.18 (18.52)	33.3	100.00	100.0
		Placebo	73	3 (4.1)	88.89 (19.25)	66.7	100.00	100.0
	Week 152	Osimertinib	143	35 (24.5)	84.29 (23.55)	16.7	100.00	100.0
		Placebo	73	2 (2.7)	100.00 (0.00)	100.0	100.00	100.0
	Week 160	Osimertinib	143	30 (21.0)	86.11 (22.35)	0.0	100.00	100.0
		Placebo	73	2 (2.7)	100.00 (0.00)	100.0	100.00	100.0
	Week 168	Osimertinib	143	22 (15.4)	87.88 (18.67)	33.3	100.00	100.0
		Placebo	73	3 (4.1)	88.89 (19.25)	66.7	100.00	100.0

N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile. NC = not calculated.

Only visits up to Week 168 are displayed.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APR0, created on: 28AUG2024

AstraZeneca

Value Dossier Analysis: D5160C00048

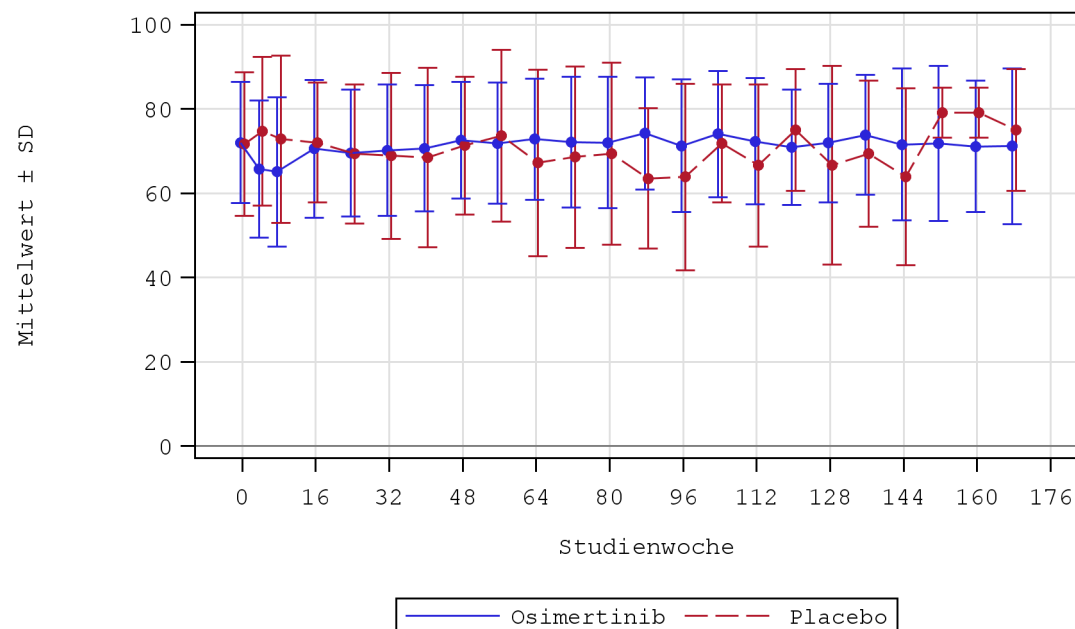
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QG_MFG0: Course of QLQ-C30 Global Health status/QoL
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QG_MFH0

AstraZeneca

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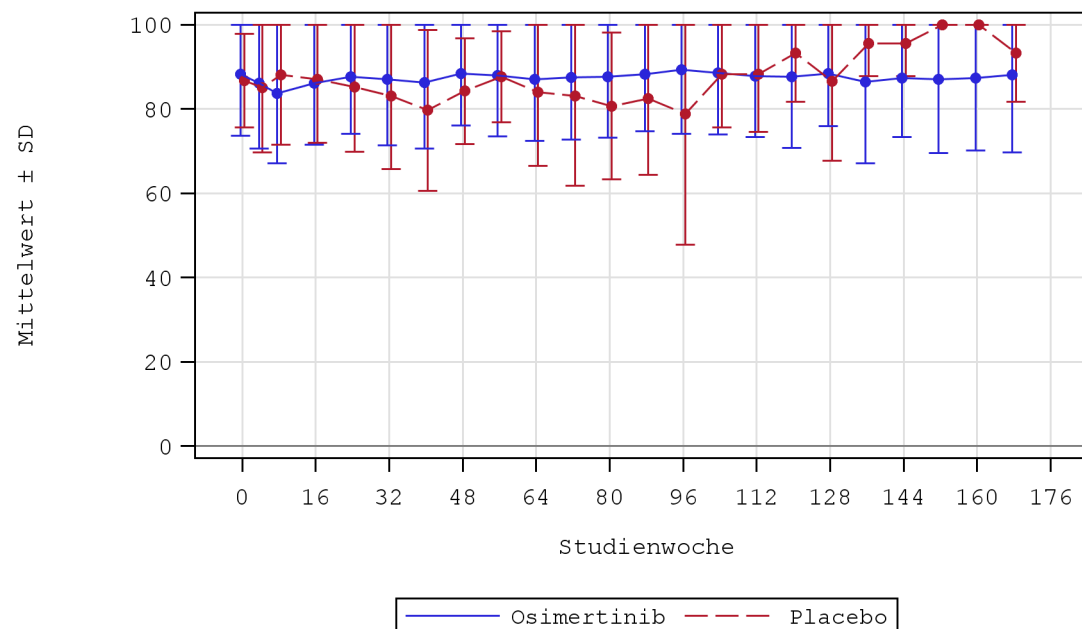
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QY_MFG0: Course of QLQ-C30 Physical Functioning
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QY_MFH0

AstraZeneca

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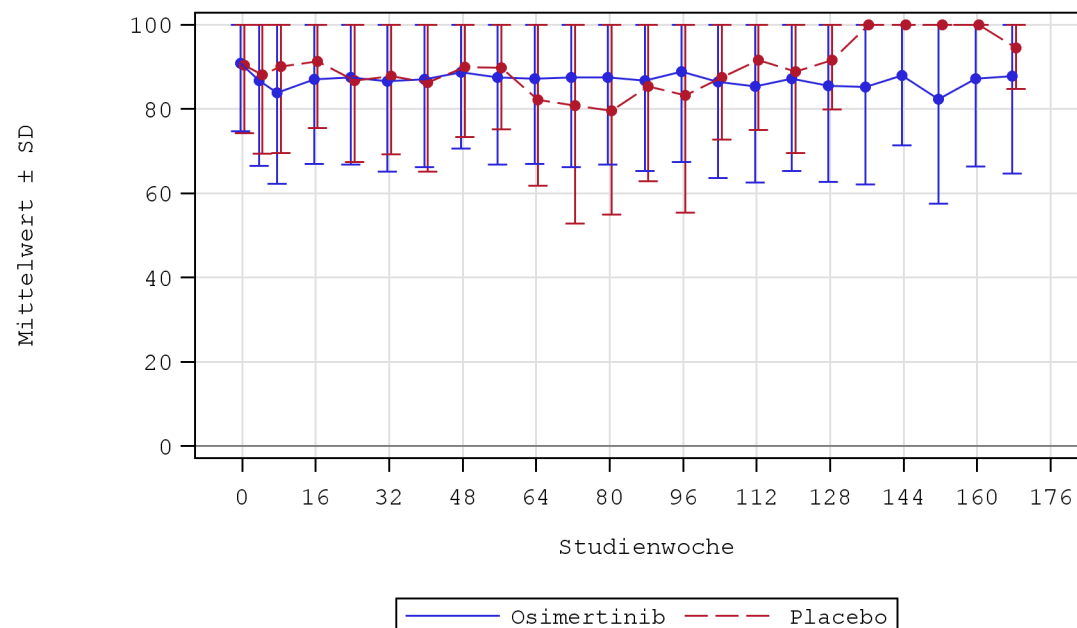
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QR_MFG0: Course of QLQ-C30 Role Functioning
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QR_MFH0

AstraZeneca

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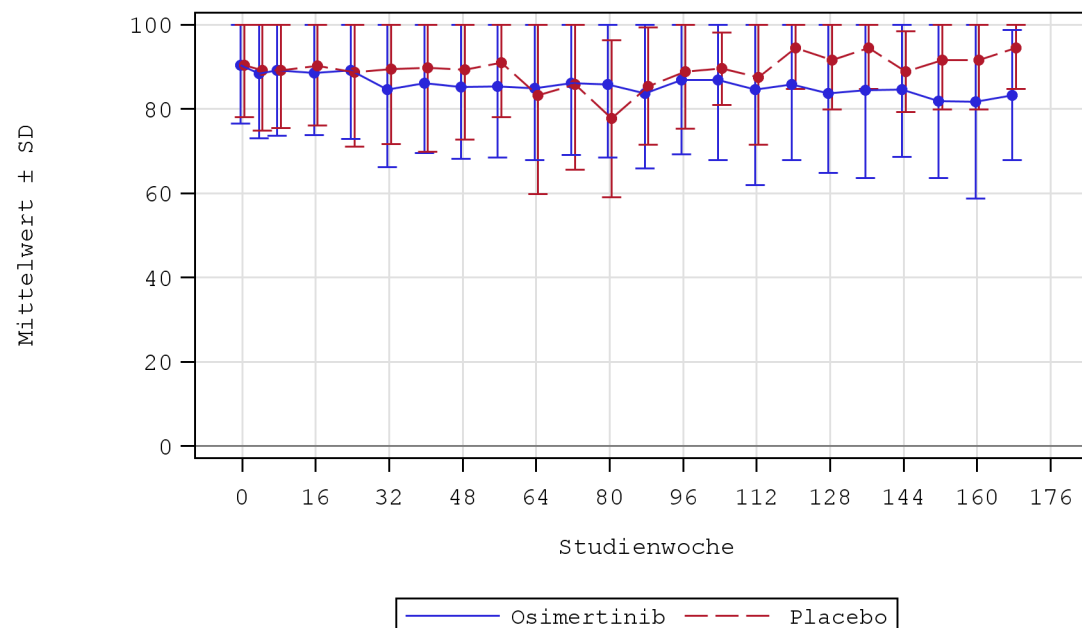
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QT_MFG0: Course of QLQ-C30 Cognitive Functioning
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire - Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QT_MFH0

AstraZeneca

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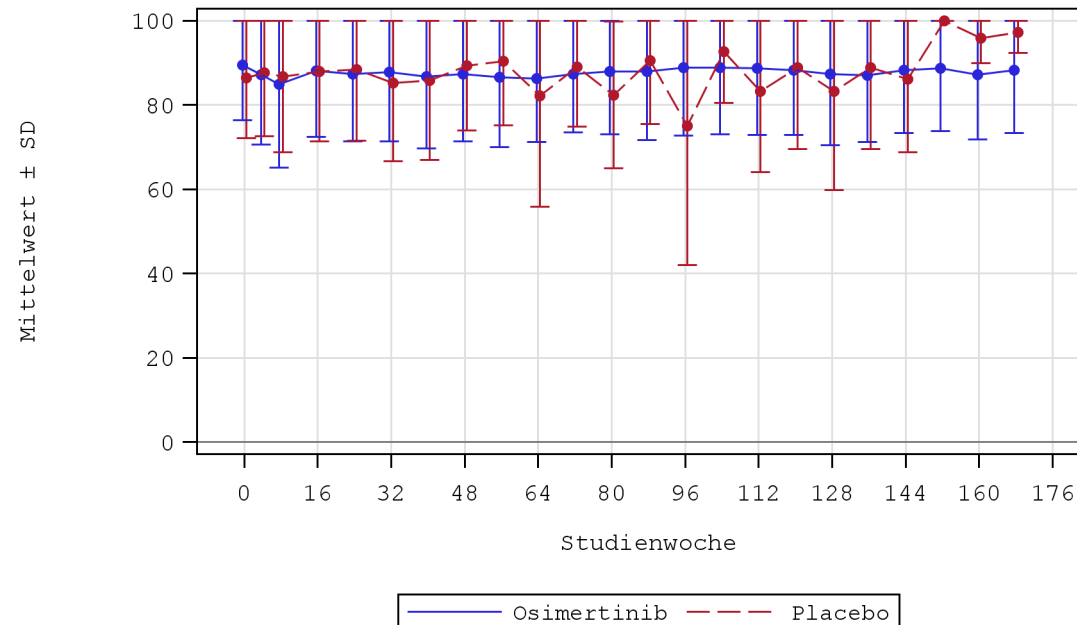
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QE_MFG0: Course of QLQ-C30 Emotional Functioning
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire - Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QE_MFH0

AstraZeneca

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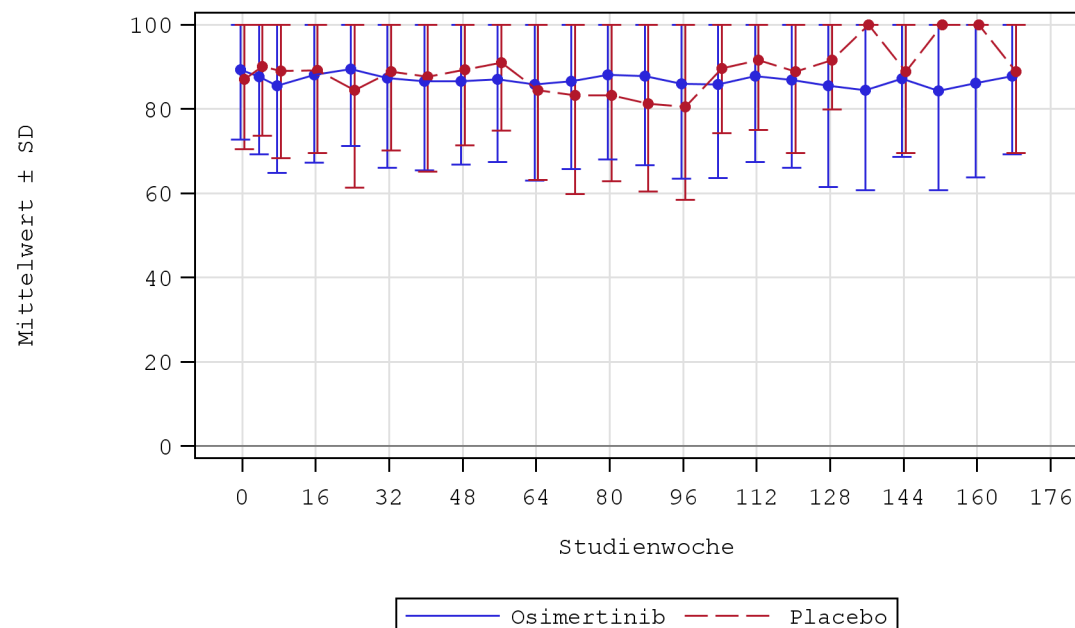
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APR0_G0.sas

Run Date: 29AUG2024:17:32:09

Figure LF1QS_MFG0: Course of QLQ-C30 Social Functioning
Full Analysis Set
Study: LAURA



Osimertinib	131	111	108	88	93	90	88	79	79	71	63	61	52	44	39	35	30	22
Placebo	68	43	23	13	15	13	9	8	6	8	4	3	2	3	3	2	2	3

Error bars are truncated at the maximum/minimum scale that is possible for the endpoint. SD = standard deviation.

Only visits up to Week 168 are displayed. QLQ-C30: EORTC Quality of Life Questionnaire - Core 30 items.

Datapoints are reduced to baseline and the following Weeks: 4, 8, 16, 24, 32, 40, 48, 56, 64, 72, 80, 88, 96, 104, 112, 120, 128, 136, 144, 152, 160 and 168.

Reference table: LT1QS_MFH0

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

Page 1 of 4
Program Name: LT1_AAE_TTE_U0.sas
Run Date: 08OCT2024:11:21:24

Table LT1A_MSU0: Time to any AE by SOC/PT
Safety Set

Time to any AE				Kaplan-Meier analysis		Log-Rank Test		
SOC/PT	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Blood and lymphatic system disorders	Osimertinib	143	26 (18.2)	NC		1.91	(0.87, 4.23)	0.1083
	Placebo	73	5 (6.8)	NC				
PT: Anaemia	Osimertinib	143	14 (9.8)	NC		1.60	(0.52, 4.87)	0.4124
	Placebo	73	3 (4.1)	NC				
SOC: Cardiac disorders	Osimertinib	143	21 (14.7)	NC		2.33	(0.96, 5.66)	0.0610
	Placebo	73	3 (4.1)	NC				
SOC: Gastrointestinal disorders	Osimertinib	143	84 (58.7)	13.2	(3.4, 24.4)	1.66	(1.10, 2.51)	0.0152 *
	Placebo	73	24 (32.9)	NC				
PT: Diarrhoea	Osimertinib	143	51 (35.7)	NC		2.25	(1.32, 3.82)	0.0029 *
	Placebo	73	10 (13.7)	NC				
PT: Stomatitis	Osimertinib	143	17 (11.9)	NC		2.52	(0.91, 6.96)	0.0752
	Placebo	73	2 (2.7)	NC				
SOC: General disorders and administration site conditions	Osimertinib	143	27 (18.9)	NC		0.84	(0.41, 1.72)	0.6268
	Placebo	73	12 (16.4)	NC				
SOC: Infections and infestations	Osimertinib	143	93 (65.0)	7.3	(5.2, 12.7)	1.73	(1.17, 2.56)	0.0065 *
	Placebo	73	24 (32.9)	15.8	(13.6, NC)			
PT: COVID-19	Osimertinib	143	29 (20.3)	NC		1.03	(0.42, 2.52)	0.9409
	Placebo	73	6 (8.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

The p-value was derived using an unstratified log-rank test, the hazard ratio and CI were calculated from U and V statistics.

The CI for median time was calculated based on Brookmeyer/Crowley.

Only events are reported with at least 10 patients and 1% affected in Osimertinib arm or 10% affected patients in Placebo arm.

CI = Confidence Interval. NC = Not calculated. * = significant treatment effect.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Source Data: AAES_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

Page 2 of 4
Program Name: LT1_AAE_TTE_U0.sas
Run Date: 08OCT2024:11:21:24

Table LT1A_MSU0: Time to any AE by SOC/PT
Safety Set

Time to any AE				Kaplan-Meier analysis		Log-Rank Test		
SOC/PT	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Herpes zoster	Osimertinib	143	13 (9.1)	NC		1.68	(0.47, 5.97)	0.4200
	Placebo	73	2 (2.7)	NC				
PT: Paronychia	Osimertinib	143	24 (16.8)	NC		3.62	(1.52, 8.59)	0.0036 *
	Placebo	73	1 (1.4)	NC				
PT: Pneumonia	Osimertinib	143	16 (11.2)	NC		1.10	(0.43, 2.81)	0.8345
	Placebo	73	6 (8.2)	NC				
PT: Upper respiratory tract infection	Osimertinib	143	10 (7.0)	NC		2.48	(0.62, 9.87)	0.1964
	Placebo	73	1 (1.4)	NC				
PT: Urinary tract infection	Osimertinib	143	11 (7.7)	NC		1.77	(0.49, 6.35)	0.3837
	Placebo	73	2 (2.7)	NC				
SOC: Injury, poisoning and procedural complications	Osimertinib	143	77 (53.8)	3.8	(1.9, NC)	1.18	(0.80, 1.75)	0.4110
	Placebo	73	34 (46.6)	12.4	(1.9, NC)			
PT: Radiation pneumonitis	Osimertinib	143	68 (47.6)	NC		1.31	(0.86, 1.99)	0.2070
	Placebo	73	28 (38.4)	NC				
SOC: Investigations	Osimertinib	143	45 (31.5)	NC		2.17	(1.18, 4.00)	0.0126 *
	Placebo	73	7 (9.6)	NC				
PT: Alanine aminotransferase increased	Osimertinib	143	10 (7.0)	NC		1.79	(0.49, 6.50)	0.3744
	Placebo	73	2 (2.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

The p-value was derived using an unstratified log-rank test, the hazard ratio and CI were calculated from U and V statistics.

The CI for median time was calculated based on Brookmeyer/Crowley.

Only events are reported with at least 10 patients and 1% affected in Osimertinib arm or 10% affected patients in Placebo arm.

CI = Confidence Interval. NC = Not calculated. * = significant treatment effect.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Source Data: AAES_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AAE_TTE_U0.sas
Run Date: 08OCT2024:11:21:24

Table LT1A_MSU0: Time to any AE by SOC/PT
Safety Set

Time to any AE				Kaplan-Meier analysis		Log-Rank Test		
SOC/PT	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: White blood cell count decreased	Osimertinib	143	17 (11.9)	NC		2.44	(0.88, 6.80)	0.0878
	Placebo	73	2 (2.7)	NC				
SOC: Metabolism and nutrition disorders	Osimertinib	143	33 (23.1)	NC		1.43	(0.74, 2.75)	0.2865
	Placebo	73	10 (13.7)	NC				
PT: Decreased appetite	Osimertinib	143	21 (14.7)	NC		2.12	(0.91, 4.91)	0.0809
	Placebo	73	4 (5.5)	NC				
SOC: Musculoskeletal and connective tissue disorders	Osimertinib	143	34 (23.8)	NC		0.56	(0.30, 1.02)	0.0587
	Placebo	73	21 (28.8)	NC				
PT: Arthralgia	Osimertinib	143	10 (7.0)	NC		0.58	(0.19, 1.79)	0.3467
	Placebo	73	6 (8.2)	NC				
PT: Musculoskeletal chest pain	Osimertinib	143	5 (3.5)	NC		0.19	(0.06, 0.61)	0.0051 *
	Placebo	73	9 (12.3)	NC				
SOC: Nervous system disorders	Osimertinib	143	18 (12.6)	NC		1.02	(0.44, 2.36)	0.9641
	Placebo	73	8 (11.0)	NC				
SOC: Renal and urinary disorders	Osimertinib	143	13 (9.1)	NC		2.39	(0.62, 9.25)	0.2066
	Placebo	73	1 (1.4)	NC				
SOC: Respiratory, thoracic and mediastinal disorders	Osimertinib	143	56 (39.2)	49.3	(25.0, NC)	0.96	(0.59, 1.59)	0.8841
	Placebo	73	23 (31.5)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

The p-value was derived using an unstratified log-rank test, the hazard ratio and CI were calculated from U and V statistics.

The CI for median time was calculated based on Brookmeyer/Crowley.

Only events are reported with at least 10 patients and 1% affected in Osimertinib arm or 10% affected patients in Placebo arm.

CI = Confidence Interval. NC = Not calculated. * = significant treatment effect.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Source Data: AAES_TTE, created on: 08OCT2024

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_AAE_TTE_U0.sas
 Run Date: 08OCT2024:11:21:24

Table LT1A_MSU0: Time to any AE by SOC/PT
 Safety Set

Time to any AE				Kaplan-Meier analysis		Log-Rank Test		
SOC/PT	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Cough	Osimertinib	143	23 (16.1)	NC		1.32	(0.59, 2.93)	0.5017
	Placebo	73	7 (9.6)	NC				
SOC: Skin and subcutaneous tissue disorders	Osimertinib	143	79 (55.2)	7.6	(3.2, 22.2)	2.03	(1.34, 3.09)	0.0009 *
	Placebo	73	19 (26.0)	NC				
PT: Dry skin	Osimertinib	143	18 (12.6)	NC		1.81	(0.72, 4.53)	0.2042
	Placebo	73	4 (5.5)	NC				
PT: Pruritus	Osimertinib	143	18 (12.6)	NC		1.42	(0.57, 3.55)	0.4485
	Placebo	73	5 (6.8)	NC				
PT: Rash	Osimertinib	143	34 (23.8)	NC		1.62	(0.86, 3.04)	0.1319
	Placebo	73	10 (13.7)	NC				
SOC: Vascular disorders	Osimertinib	143	12 (8.4)	58.1	(49.4, 58.1)	1.66	(0.45, 6.18)	0.4468
	Placebo	73	2 (2.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

The p-value was derived using an unstratified log-rank test, the hazard ratio and CI were calculated from U and V statistics.

The CI for median time was calculated based on Brookmeyer/Crowley.

Only events are reported with at least 10 patients and 1% affected in Osimertinib arm or 10% affected patients in Placebo arm.

CI = Confidence Interval. NC = Not calculated. * = significant treatment effect.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Source Data: AAES_TTE, created on: 08OCT2024

AstraZeneca

Value Dossier Analysis: D5160C00048

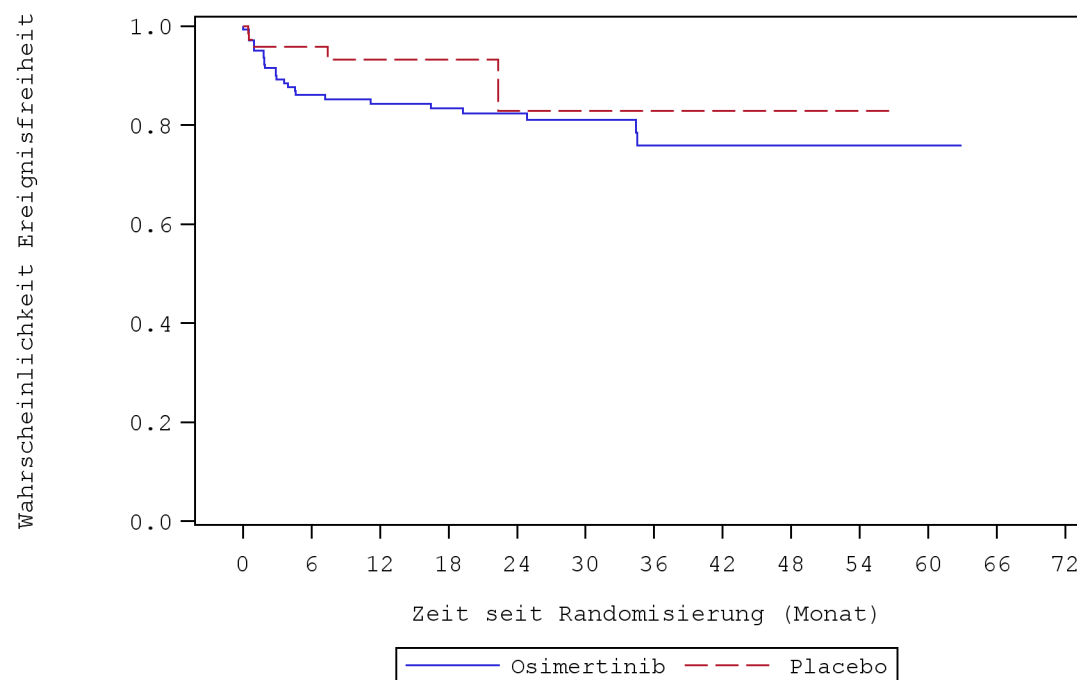
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Blood and lymphatic system disorders
PT: All PTs

Osimertinib	143	104	94	87	66	45	26	13	5	2	1	0
Placebo	73	47	21	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

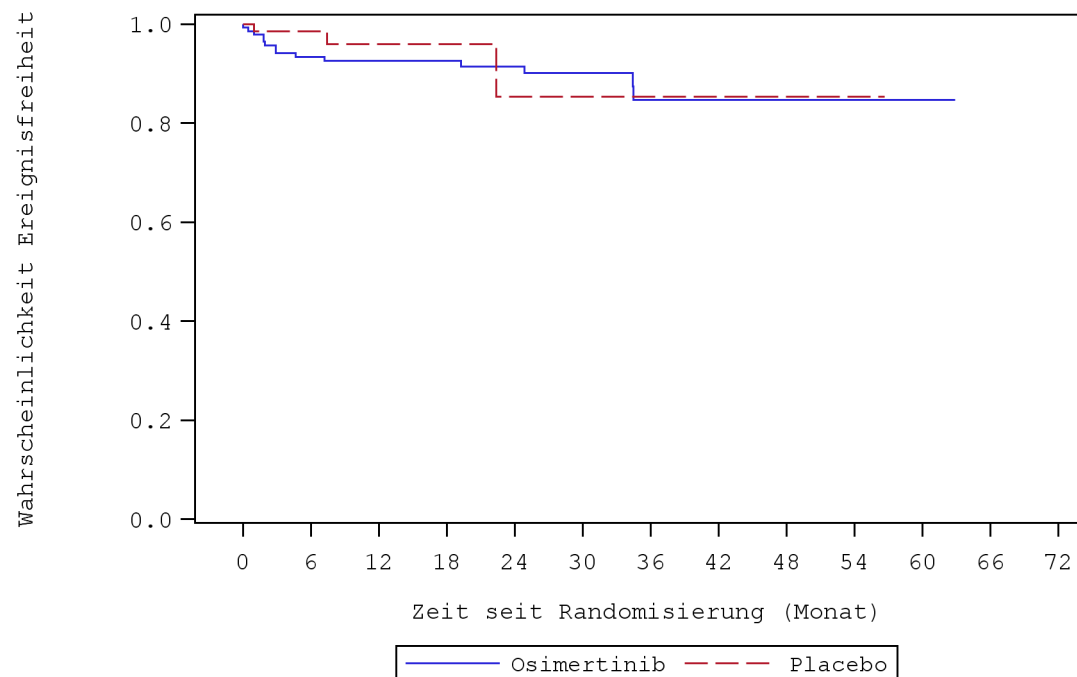
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Blood and lymphatic system disorders
PT: Anaemia

Osimertinib	143	111	101	93	69	47	28	14	5	2	1	0
Placebo	73	48	22	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

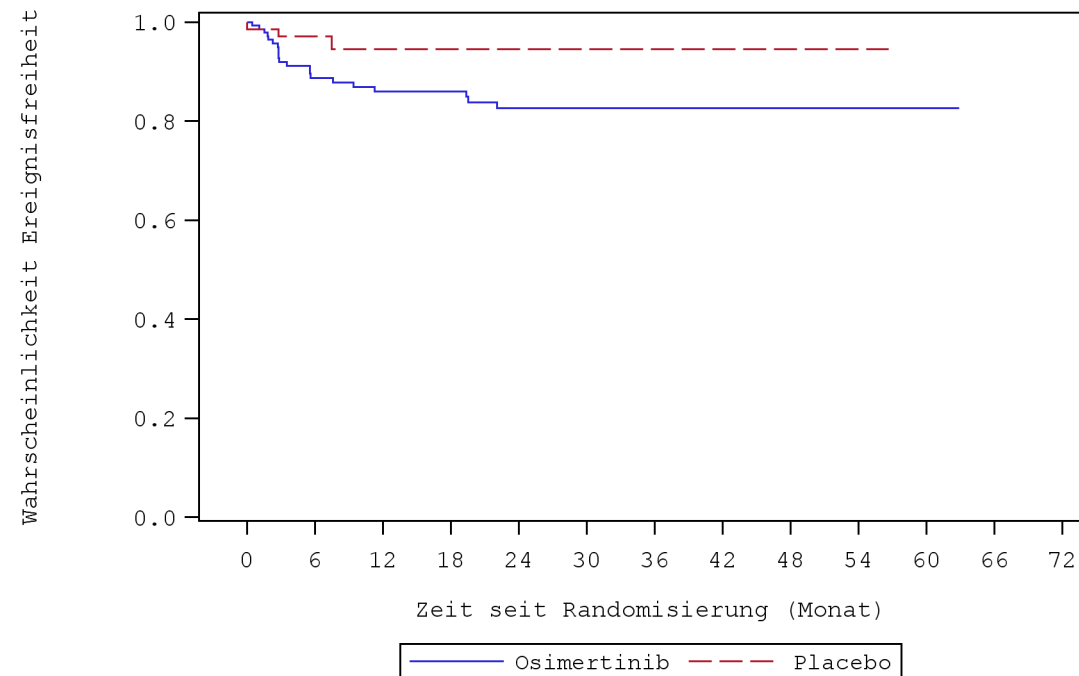
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Cardiac disorders
PT: All PTs

Osimertinib	143	106	91	84	58	39	26	14	5	2	1	0
Placebo	73	47	22	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

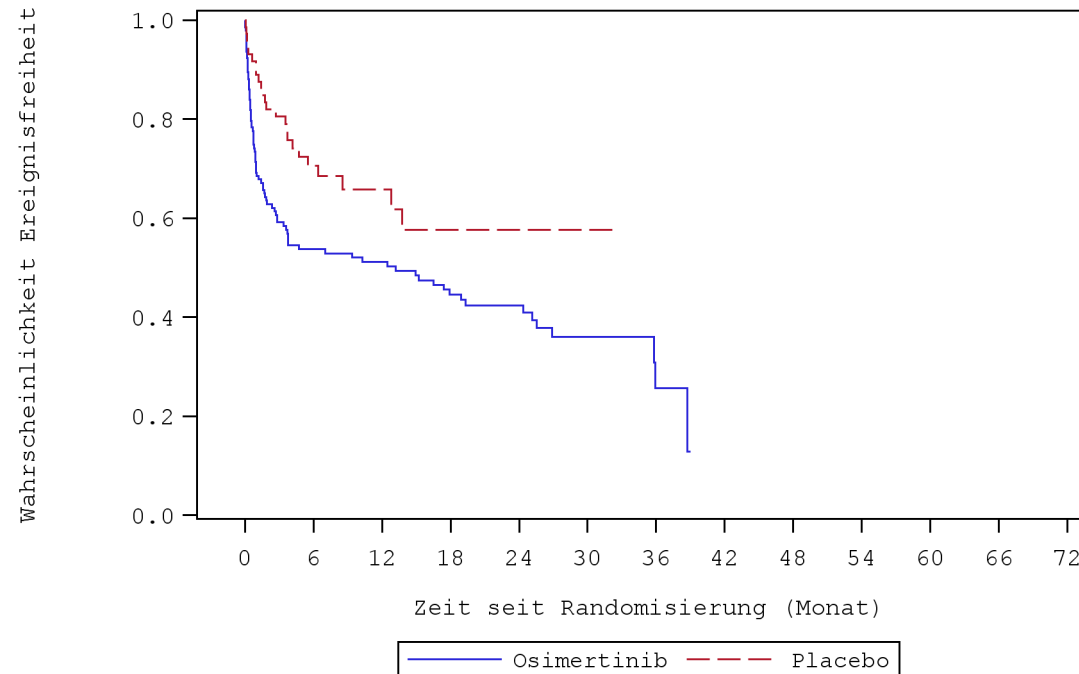
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Gastrointestinal disorders
PT: All PTs

Osimertinib	143	64	57	46	29	14	5	0
Placebo	73	35	17	6	3	2	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

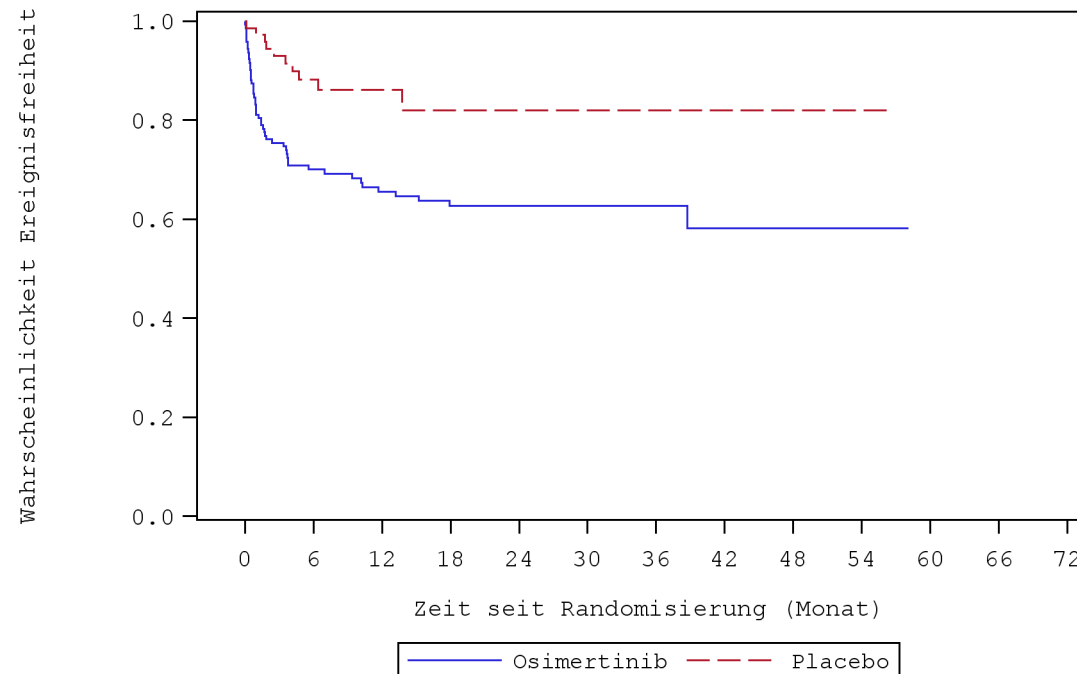
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSU0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Gastrointestinal disorders
PT: Diarrhoea

Osimertinib	143	83	72	63	46	29	18	5	3	1	0
Placebo	73	44	22	10	6	4	2	2	2	1	0

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

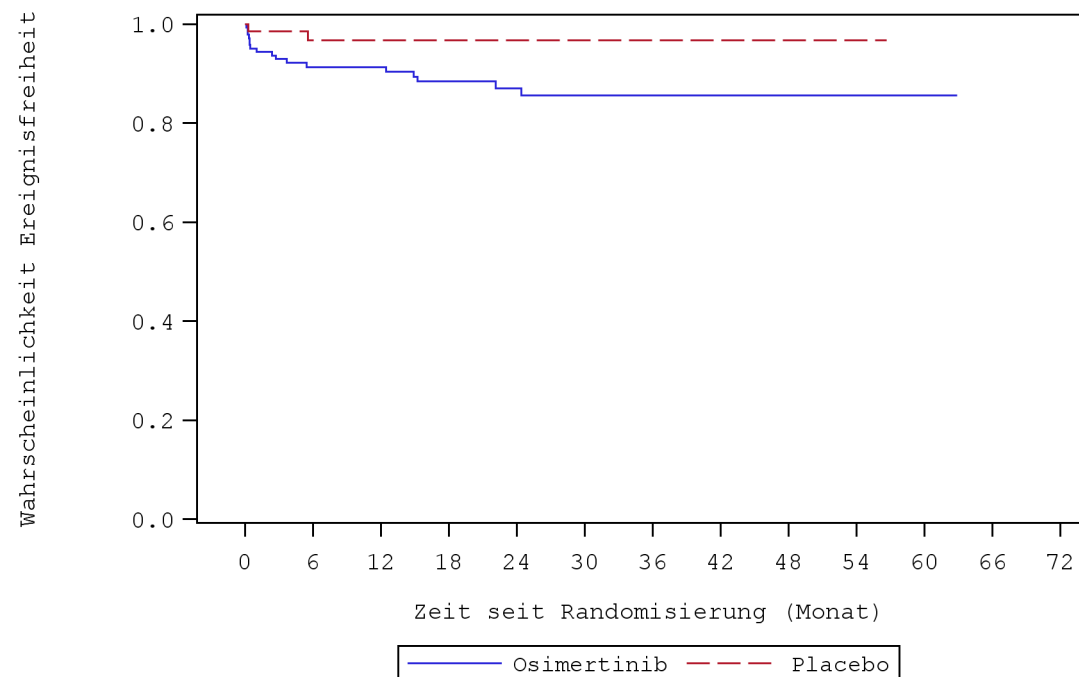
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Gastrointestinal disorders

PT: Stomatitis



Osimertinib	143	109	97	85	58	39	26	13	5	2	1	0
Placebo	73	47	22	10	5	4	2	2	1	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

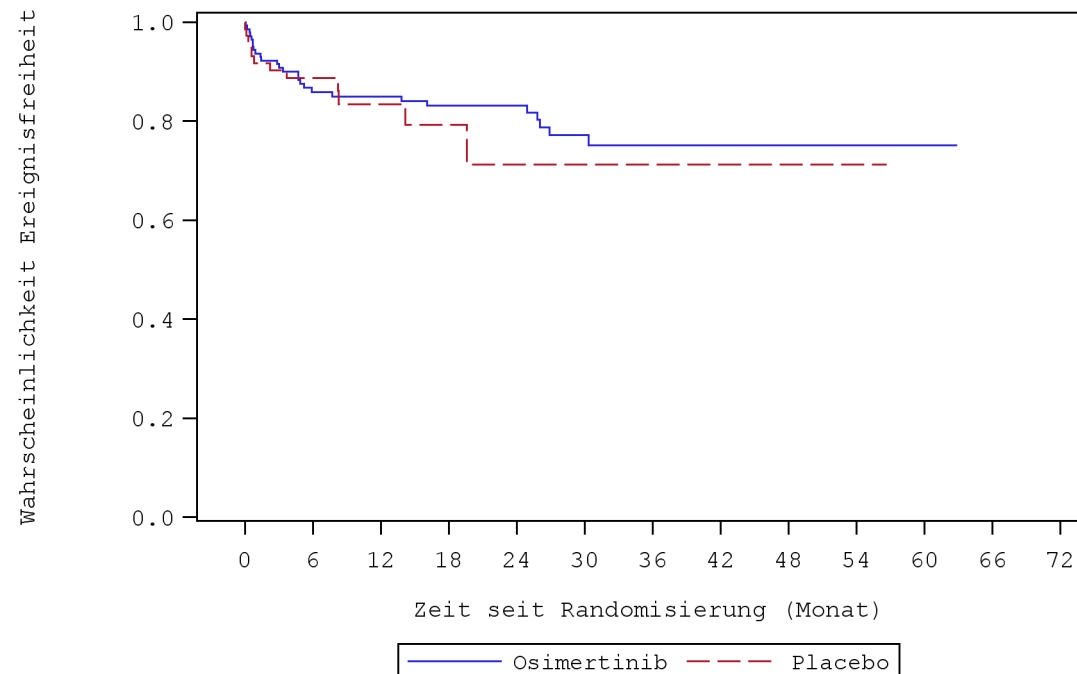
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: General disorders and administration site conditions
PT: All PTs

Osimertinib	143	102	93	84	60	39	24	12	3	1	1	0
Placebo	73	43	21	10	6	4	2	2	1	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

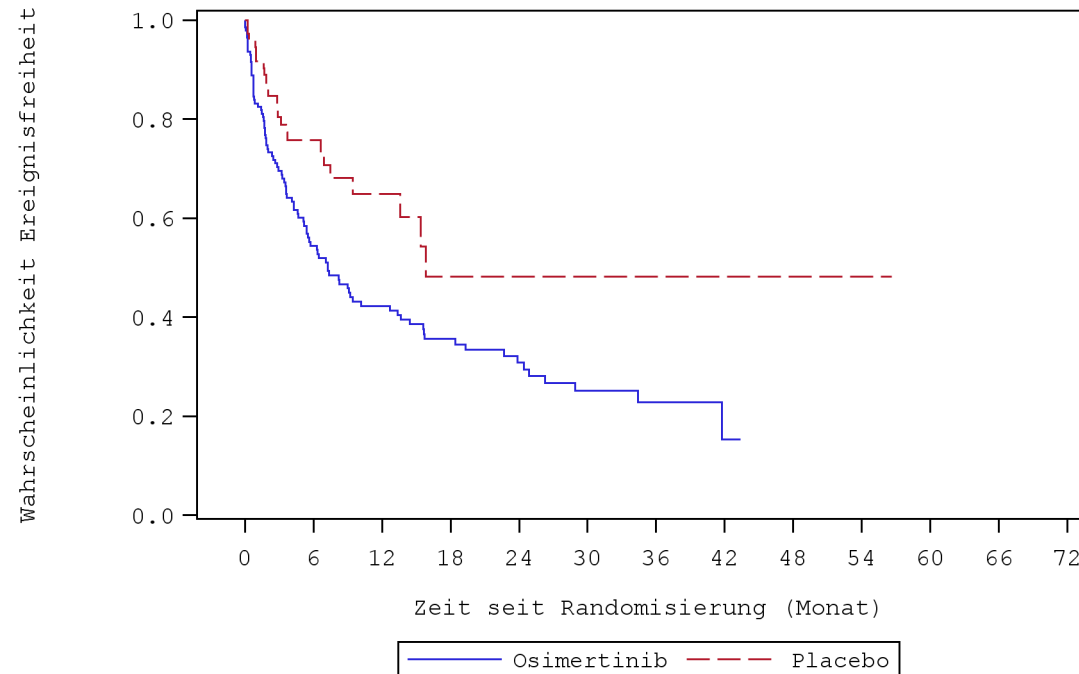
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSU0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Infections and infestations
PT: All PTs

Osimertinib	143	66	46	33	23	15	8	2	0		
Placebo	73	37	14	4	3	2	1	1	1	1	0

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

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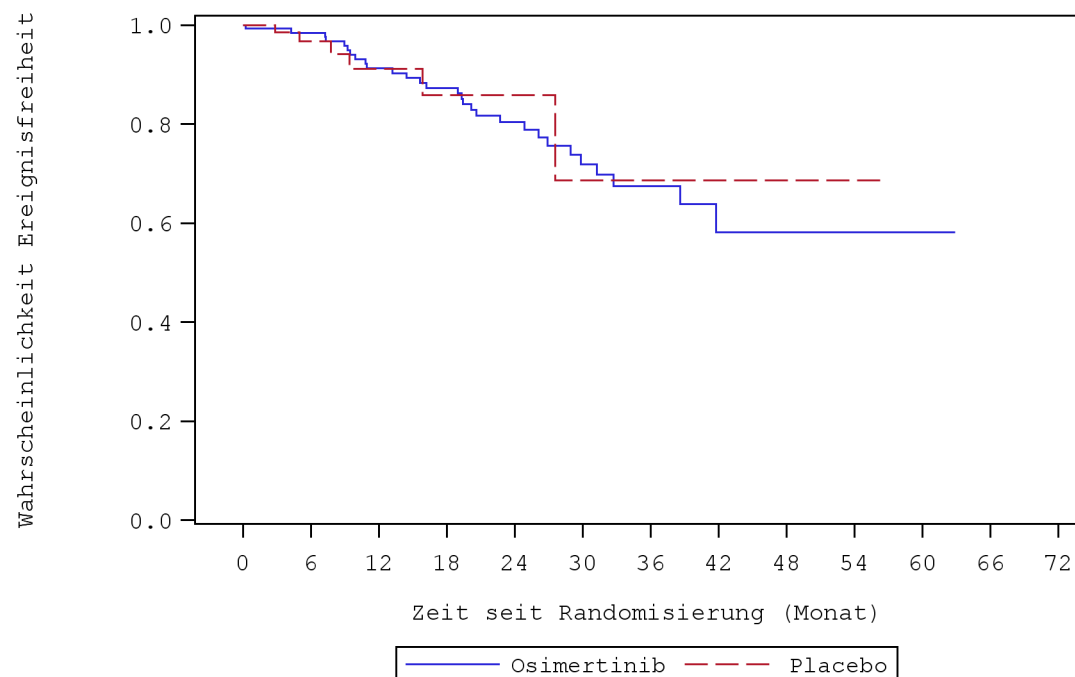
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Infections and infestations

PT: COVID-19



Osimertinib	143	117	97	85	55	37	23	10	3	2	1	0
Placebo	73	49	23	10	7	4	2	2	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

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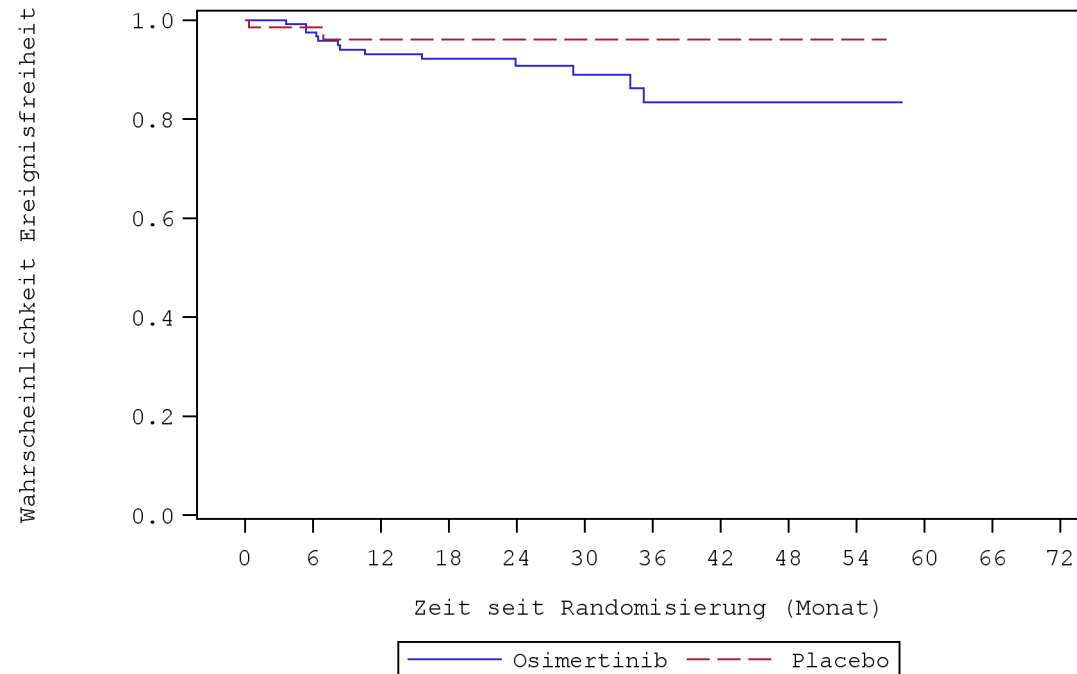
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Infections and infestations

PT: Herpes zoster



Osimertinib	143	116	99	89	66	45	26	13	4	1	0
Placebo	73	48	23	11	6	4	2	2	2	1	0

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

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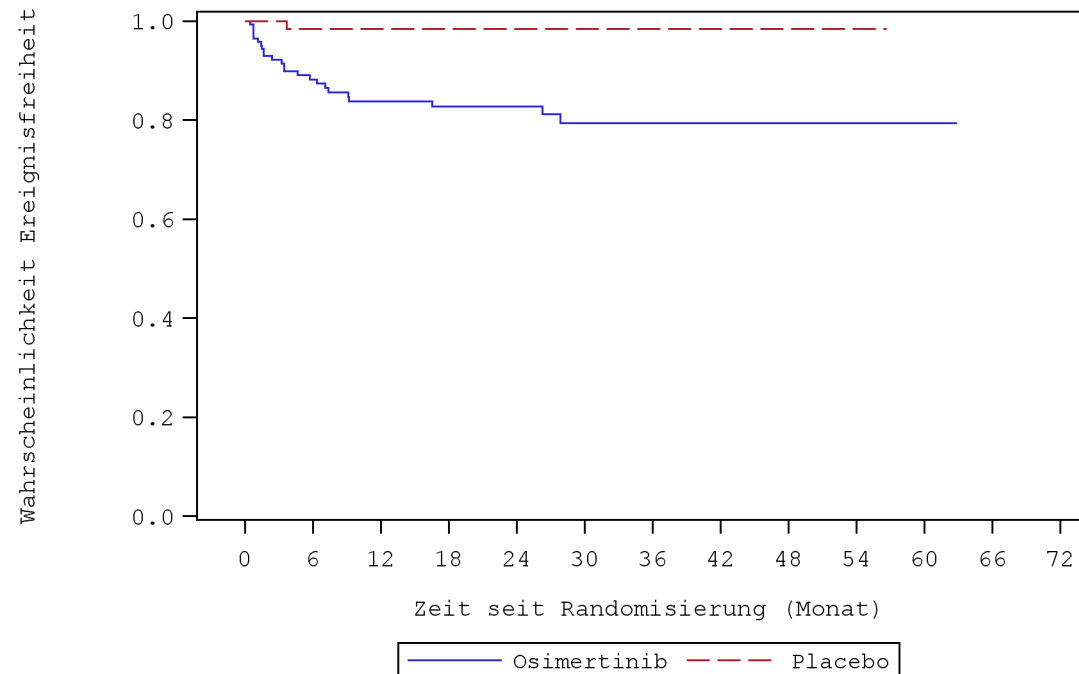
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Infections and infestations

PT: Paronychia



Osimertinib	143	104	88	79	58	37	24	11	2	2	1	0
Placebo	73	48	23	11	6	4	2	2	1	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

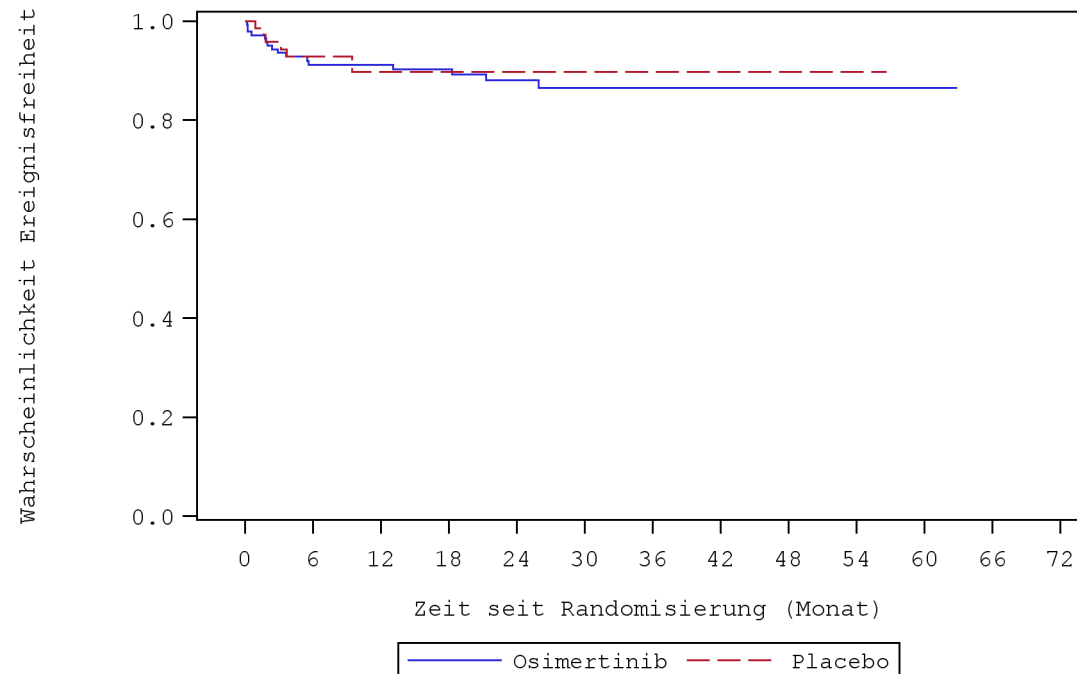
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Infections and infestations

PT: Pneumonia



Osimertinib	143	110	99	89	66	45	29	15	5	2	1	0
Placebo	73	47	23	11	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

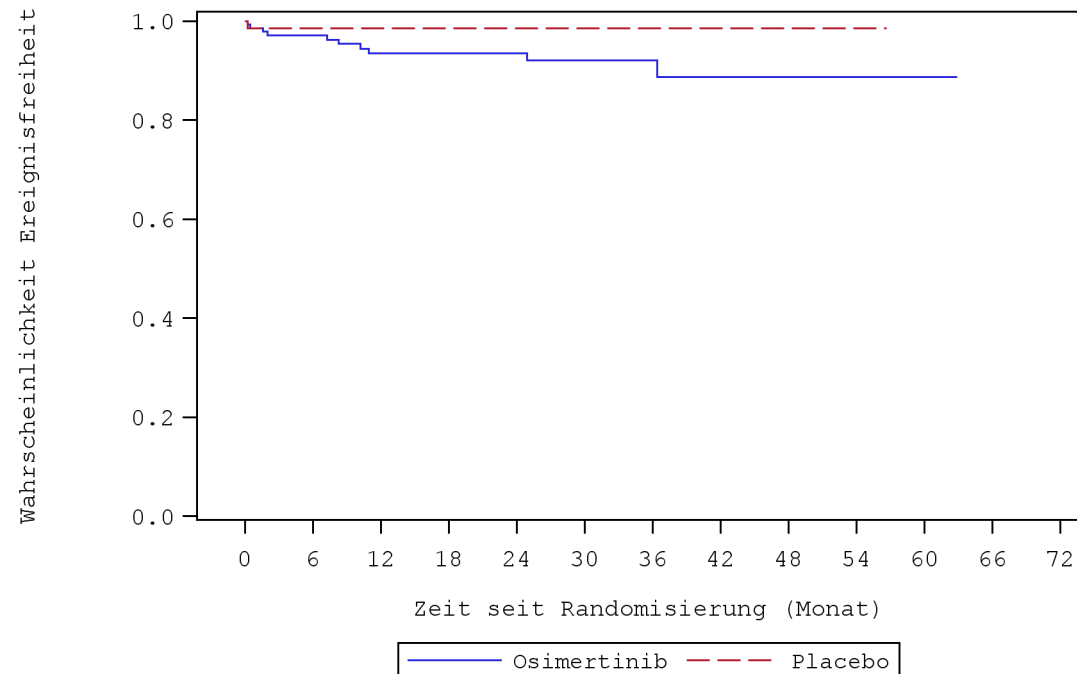
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Infections and infestations
PT: Upper respiratory tract infection

Osimertinib	143	116	100	91	66	45	28	12	4	1	1	0
Placebo	73	48	23	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

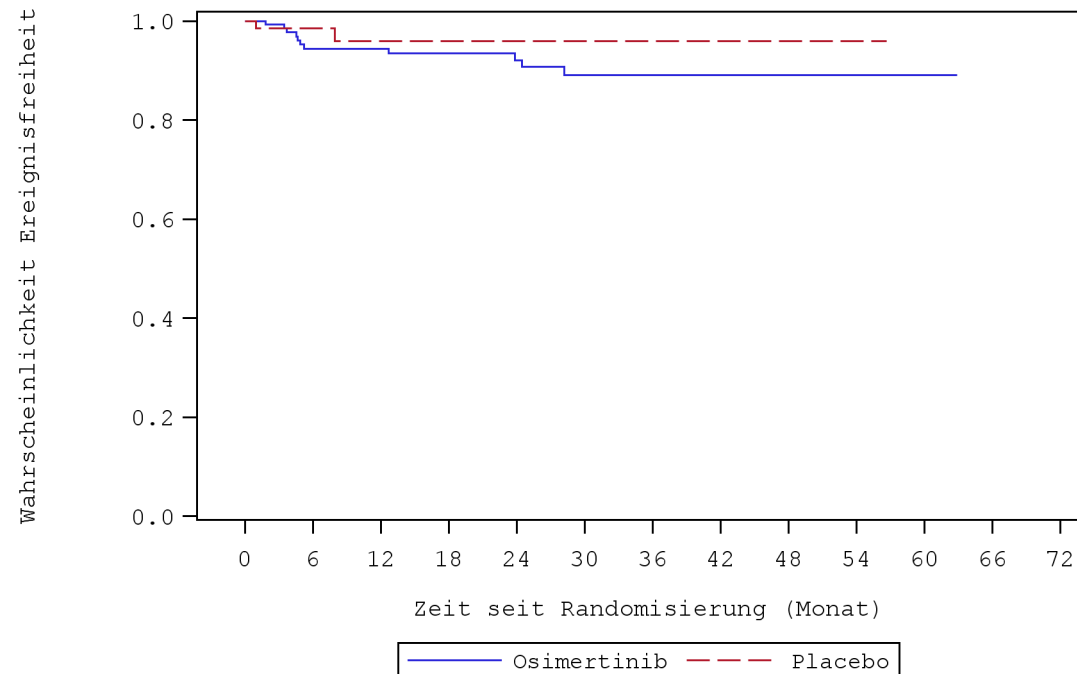
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Infections and infestations
PT: Urinary tract infection

Osimertinib	143	112	101	91	68	47	29	14	5	2	1	0
Placebo	73	48	22	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

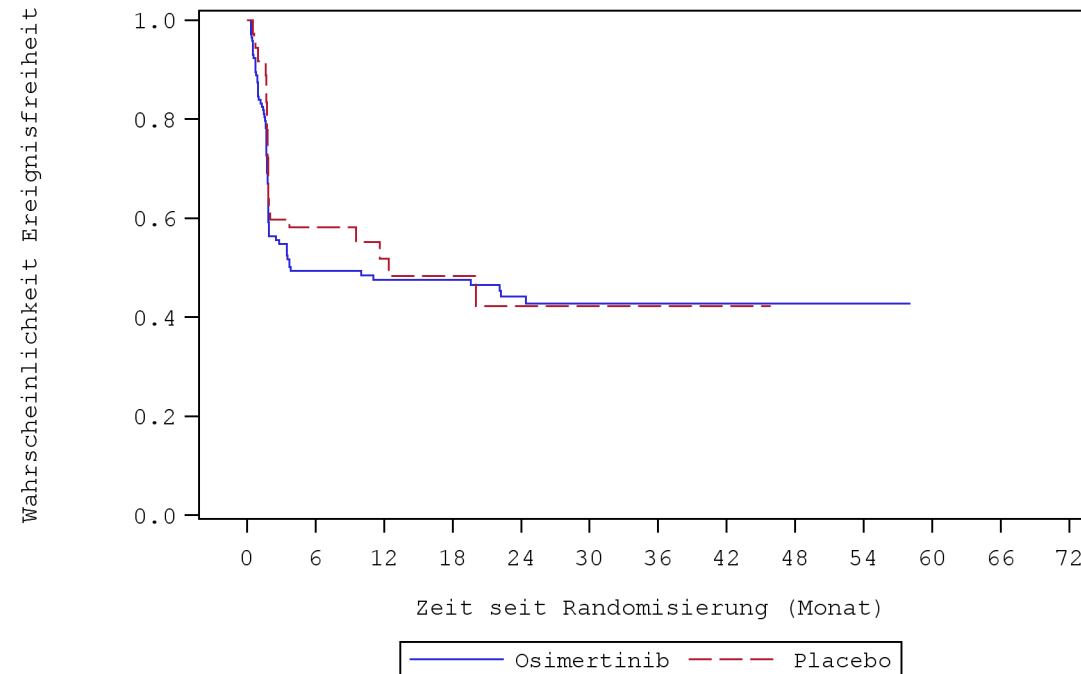
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Injury, poisoning and procedural complications

PT: All PTs



Osimertinib	143	60	53	47	31	23	16	7	1	1	0
Placebo	73	30	15	9	5	3	1	1	0		

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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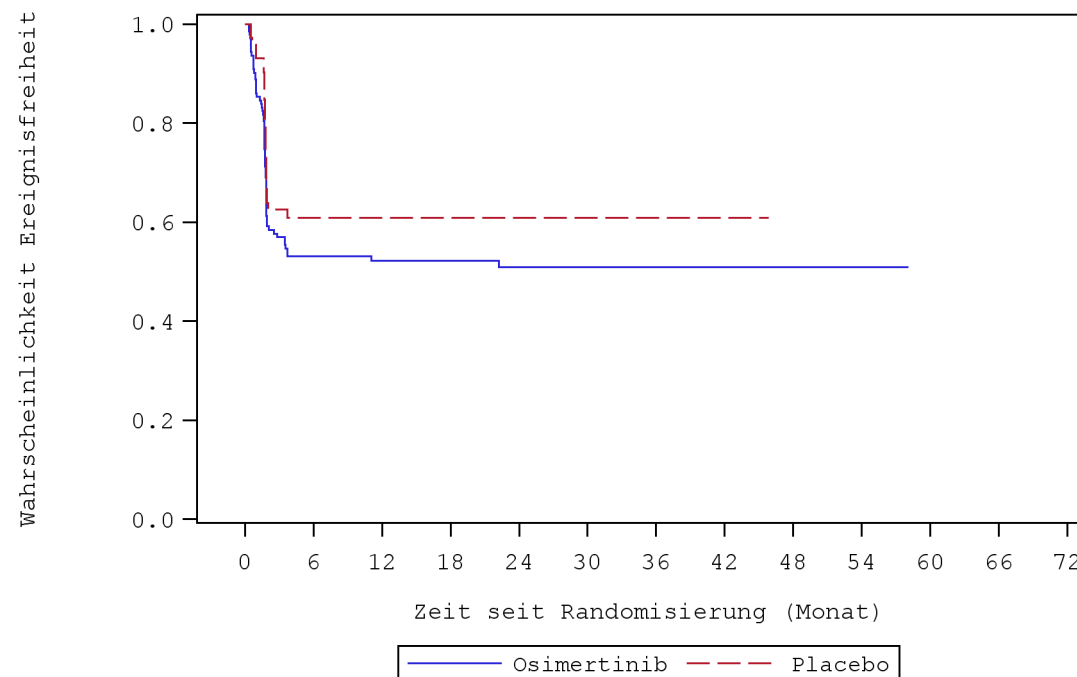
Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSU0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Injury, poisoning and procedural complications
PT: Radiation pneumonitis

Osimertinib	143	65	57	50	34	25	17	8	2	1	0
Placebo	73	31	17	9	5	3	1	1	0		

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

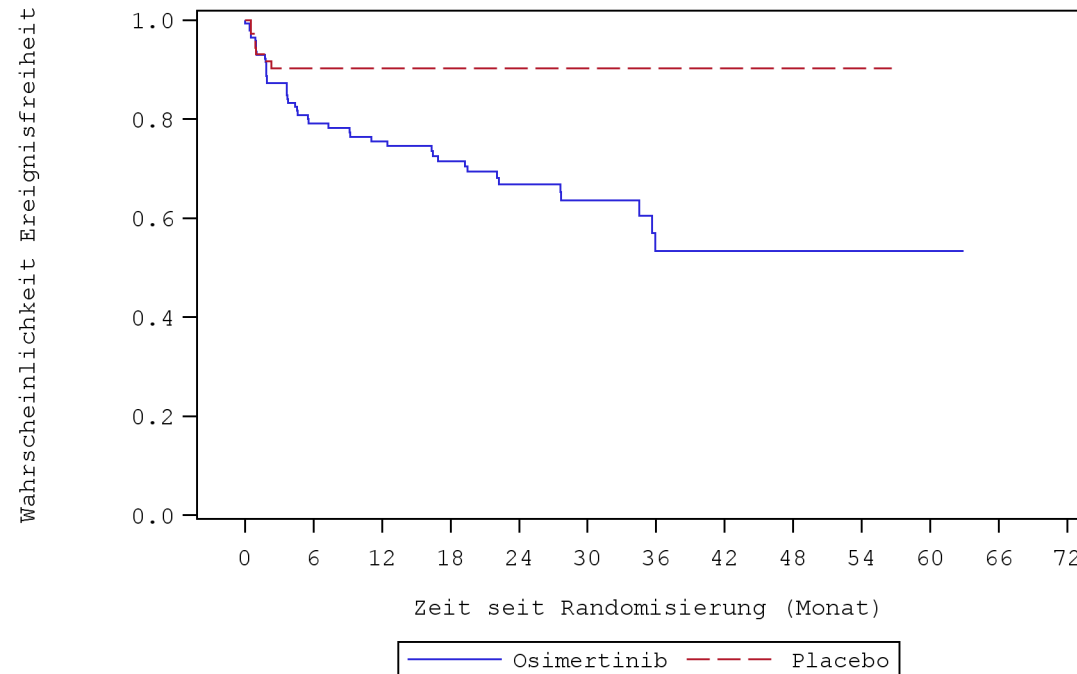
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Investigations
PT: All PTs

Osimertinib	143	93	80	70	49	32	15	8	2	2	1	0
Placebo	73	44	21	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

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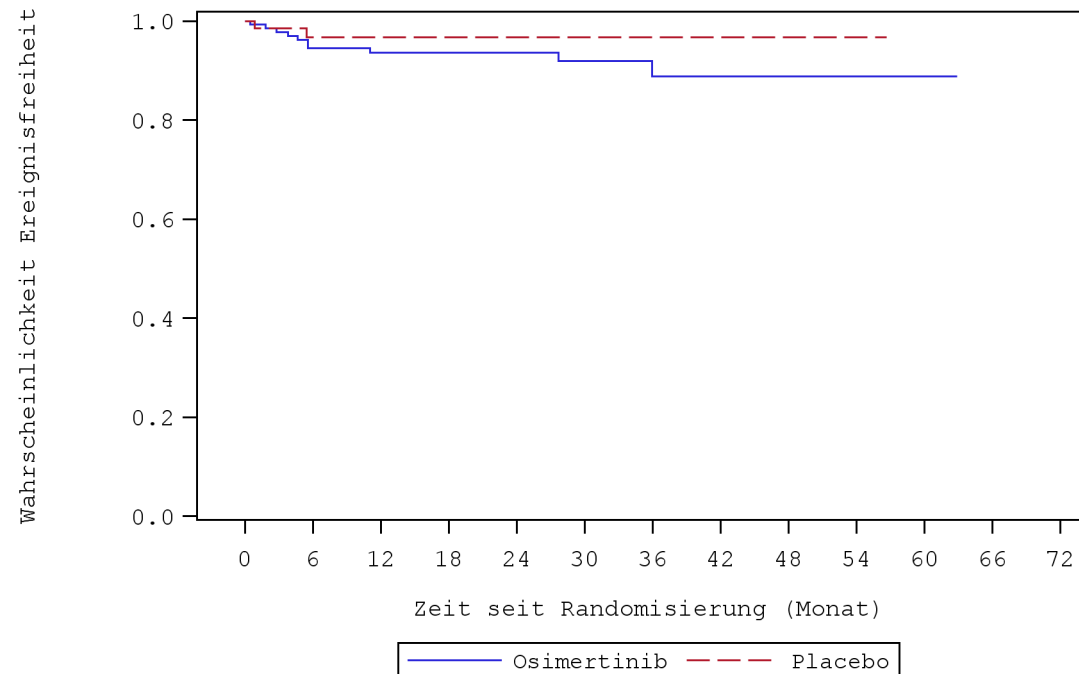
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Investigations

PT: Alanine aminotransferase increased



Osimertinib	143	113	100	91	69	47	28	14	4	2	1	0
Placebo	73	48	24	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

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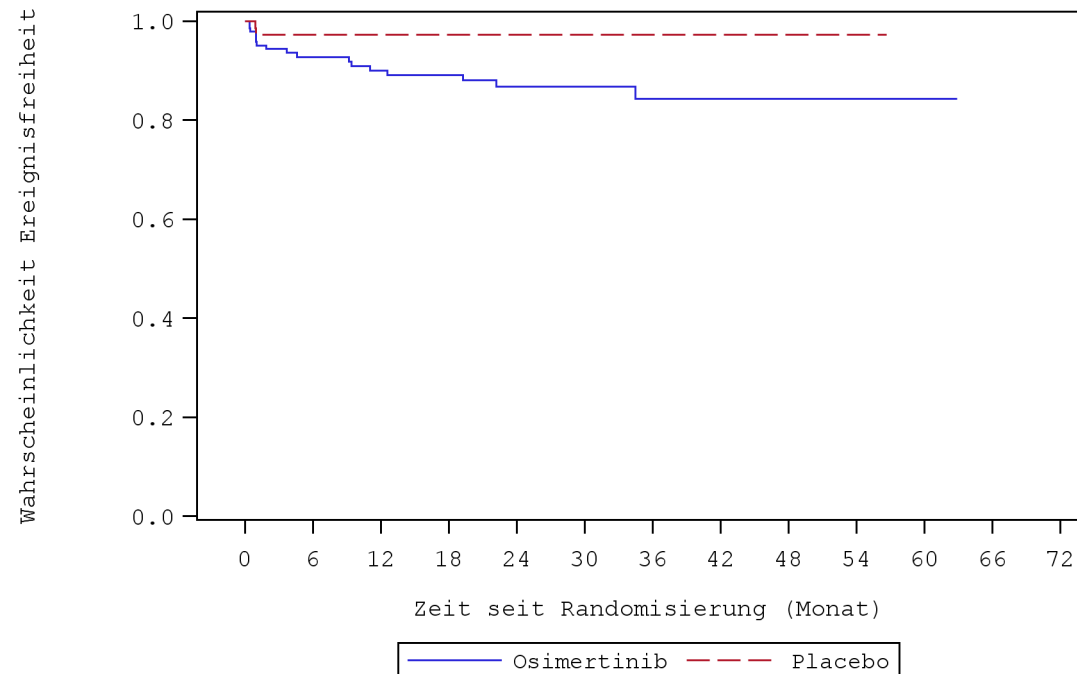
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Investigations

PT: White blood cell count decreased



Osimertinib	143	111	96	87	65	47	30	15	5	2	1	0
Placebo	73	48	23	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

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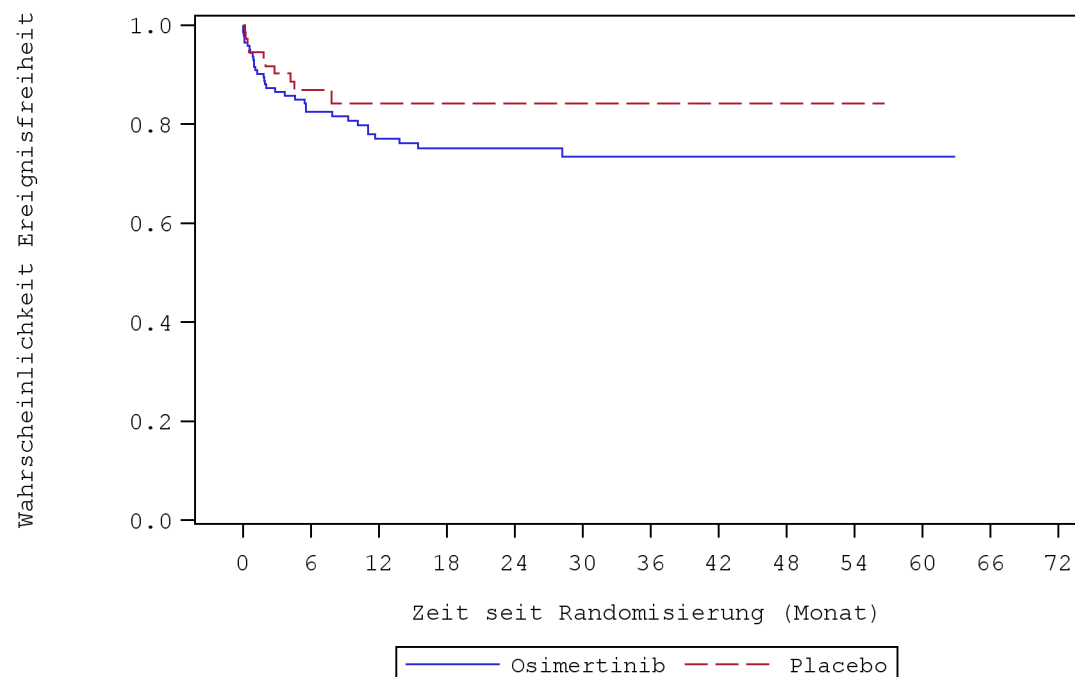
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Metabolism and nutrition disorders
PT: All PTs

Osimertinib	143	98	84	75	57	40	25	13	5	2	1	0
Placebo	73	43	19	10	6	4	2	2	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

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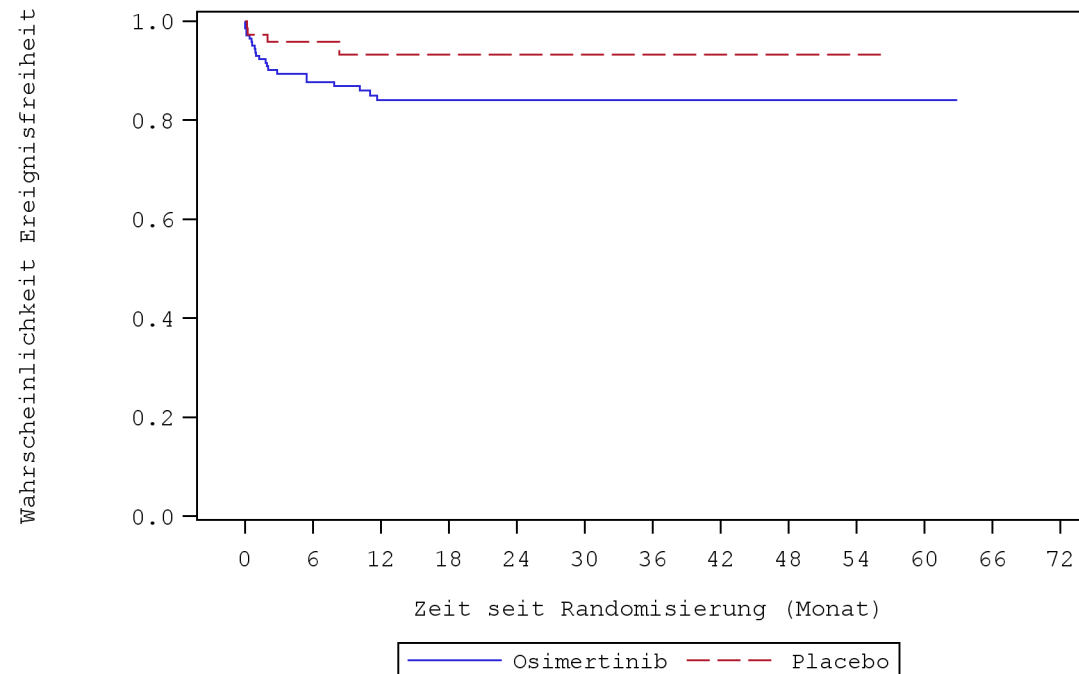
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Metabolism and nutrition disorders
PT: Decreased appetite

Osimertinib	143	105	91	84	61	43	28	13	5	2	1	0
Placebo	73	47	23	11	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

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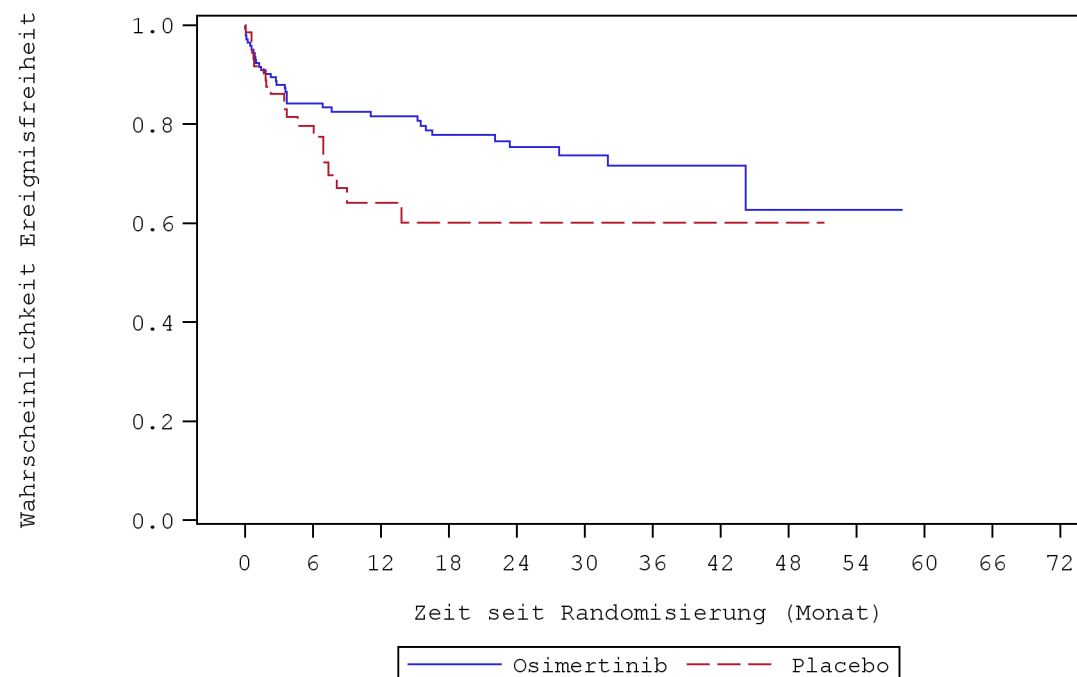
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Musculoskeletal and connective tissue disorders

PT: All PTs



Osimertinib	143	102	90	81	57	38	25	12	3	1	0
Placebo	73	38	17	7	4	2	1	1	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

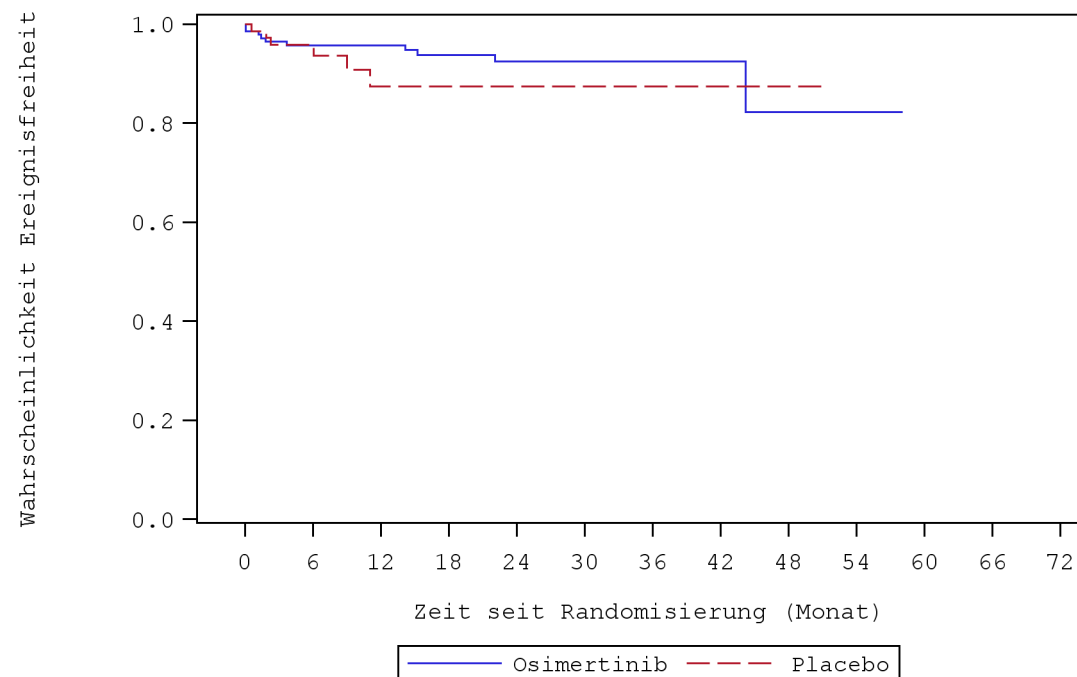
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Musculoskeletal and connective tissue disorders

PT: Arthralgia



Osimertinib	143	116	104	93	67	47	30	14	4	1	0
Placebo	73	47	21	10	6	4	2	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

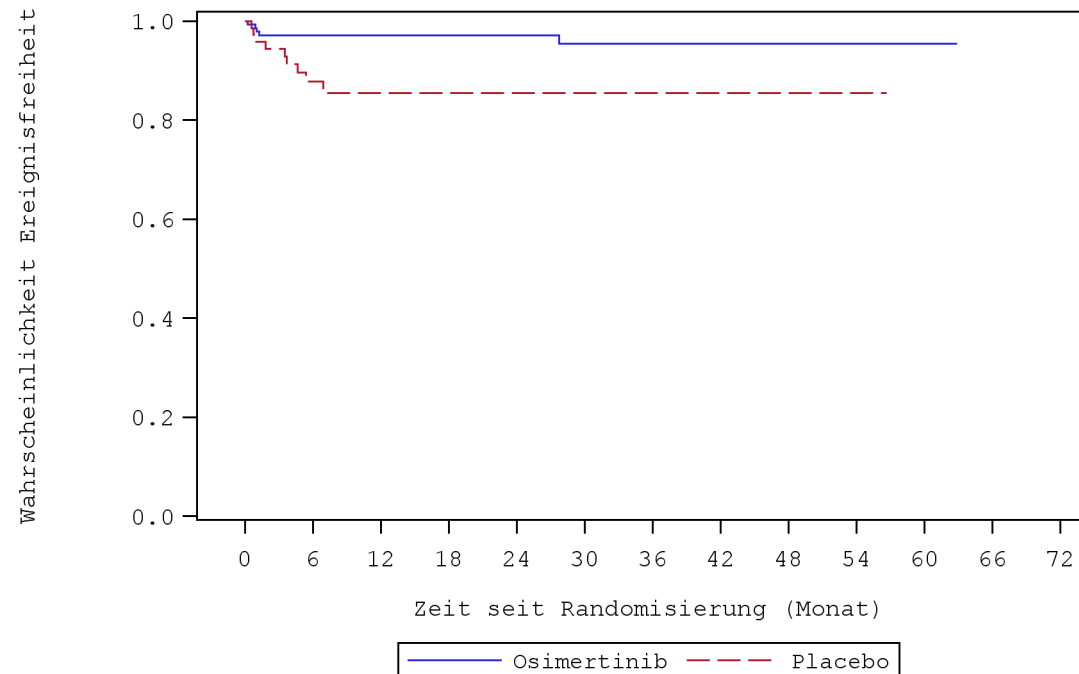
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Musculoskeletal and connective tissue disorders
PT: Musculoskeletal chest pain

Osimertinib	143	116	105	96	71	48	30	14	5	2	1	0
Placebo	73	44	22	11	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

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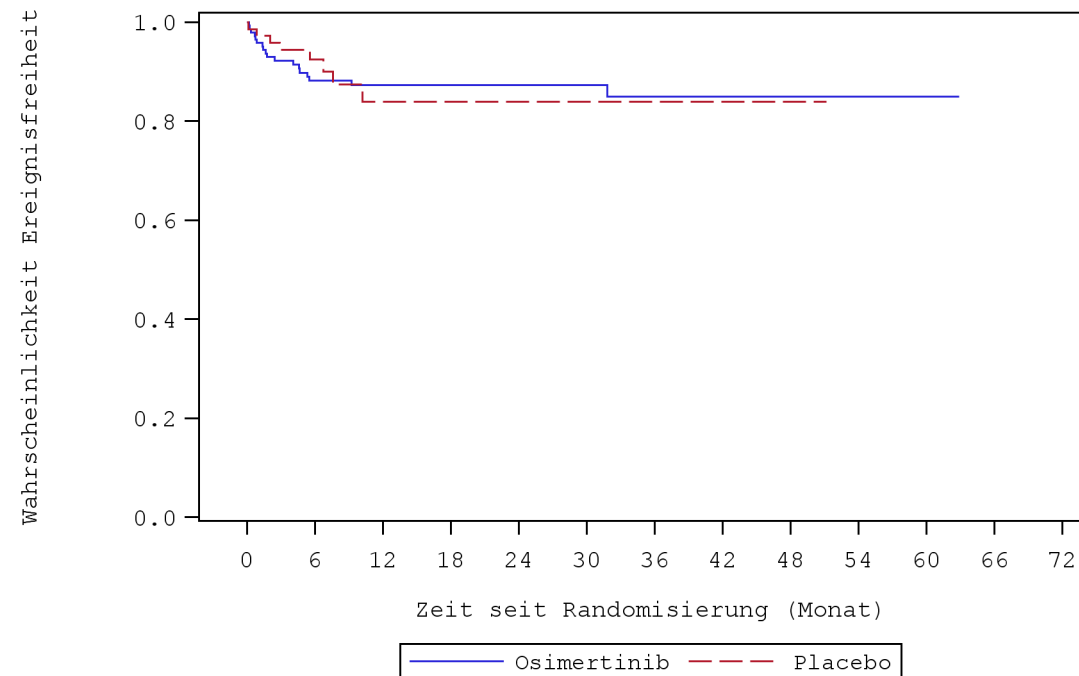
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Nervous system disorders
PT: All PTs

Osimertinib	143	105	93	85	62	42	26	13	5	2	1	0
Placebo	73	45	19	8	5	3	2	2	1	0		

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

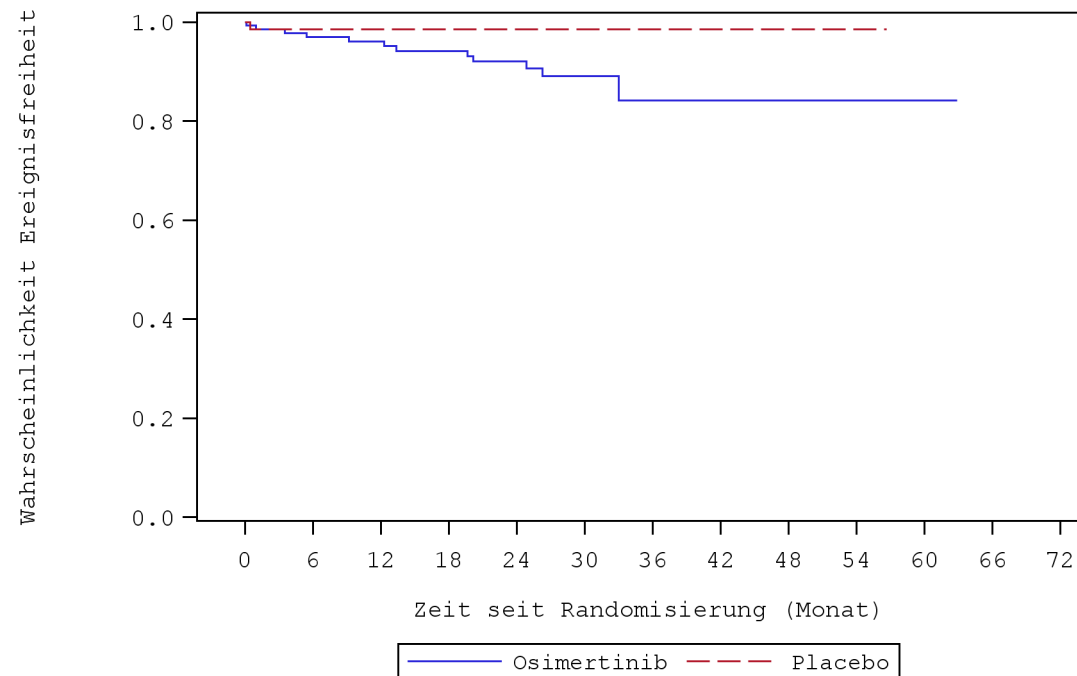
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Renal and urinary disorders
PT: All PTs

Osimertinib	143	116	103	94	68	45	26	13	4	2	1	0
Placebo	73	48	24	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

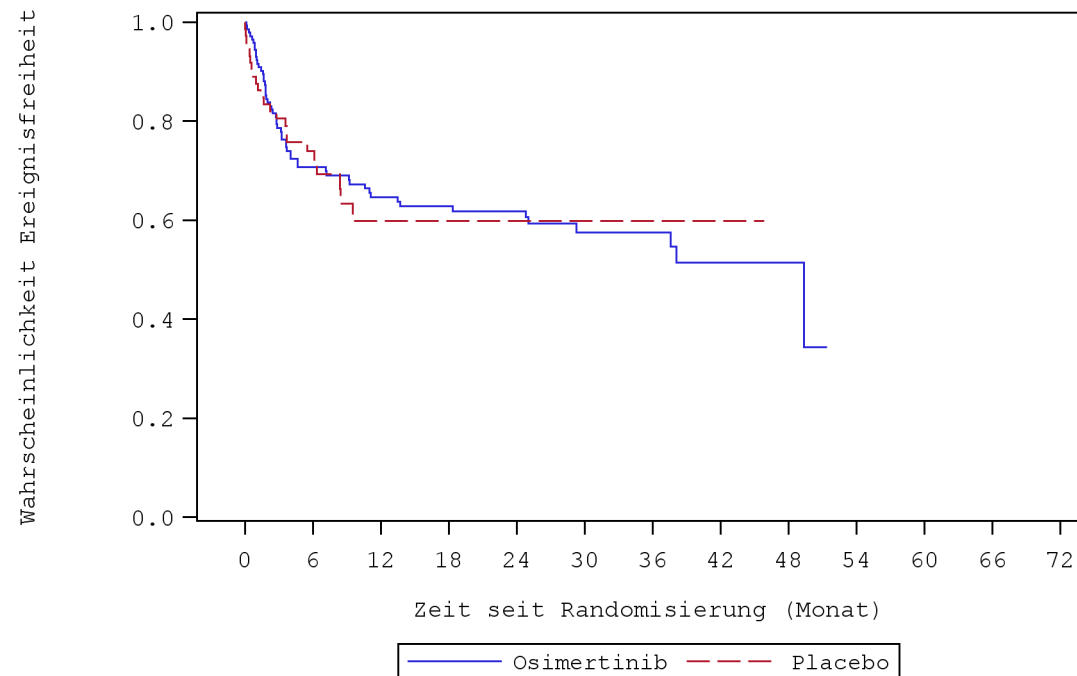
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Respiratory, thoracic and mediastinal disorders
PT: All PTs

Osimertinib	143	86	72	67	50	34	22	11	3	0
Placebo	73	35	13	5	4	2	1	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

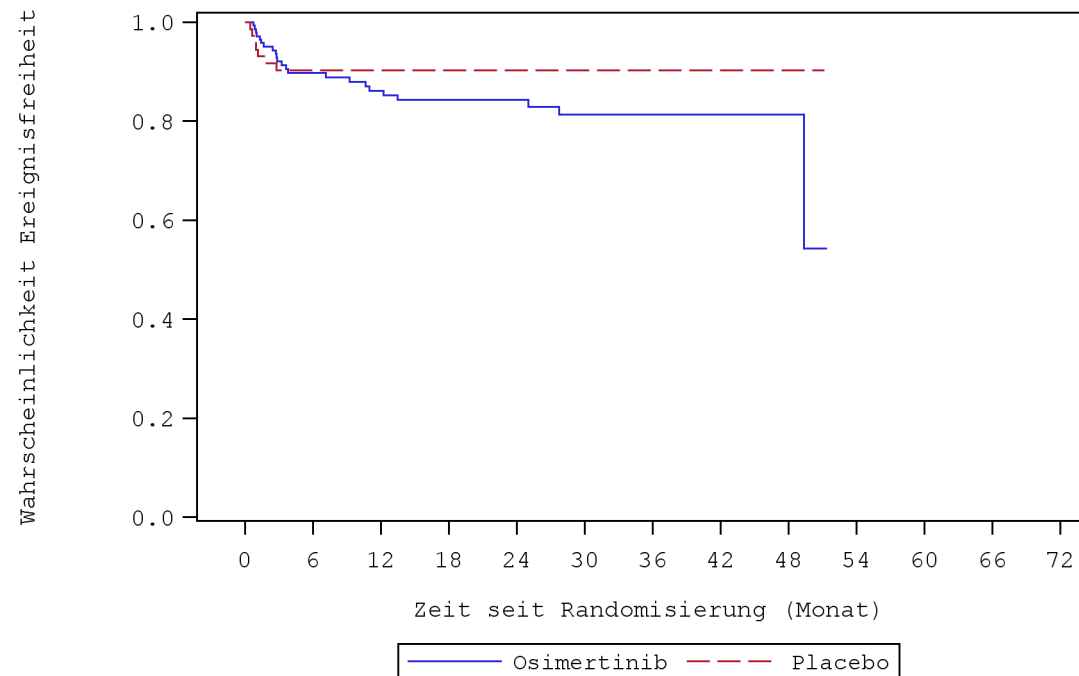
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSU0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Respiratory, thoracic and mediastinal disorders
PT: Cough

Osimertinib	143	107	94	87	64	44	29	13	4	0
Placebo	73	44	22	10	6	4	2	2	1	0

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

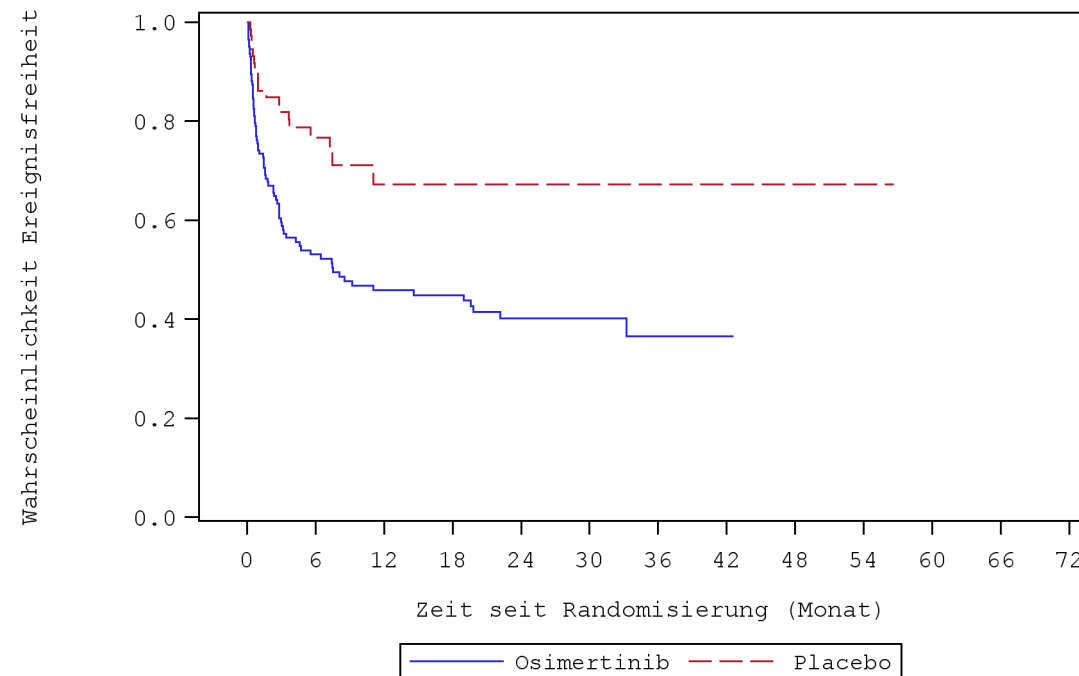
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Skin and subcutaneous tissue disorders
PT: All PTs

Osimertinib	143	60	50	42	29	14	7	1	0		
Placebo	73	36	14	7	3	3	1	1	1	1	0

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

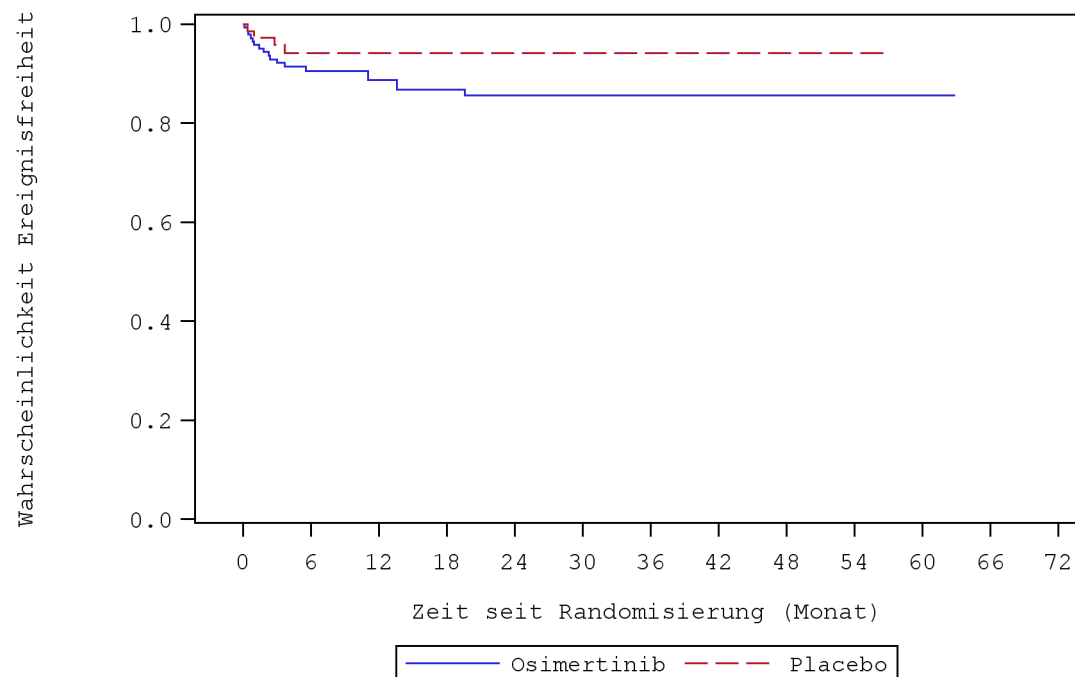
Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Skin and subcutaneous tissue disorders

PT: Dry skin



Osimertinib	143	107	94	84	61	40	26	12	5	2	1	0
Placebo	73	45	22	11	6	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

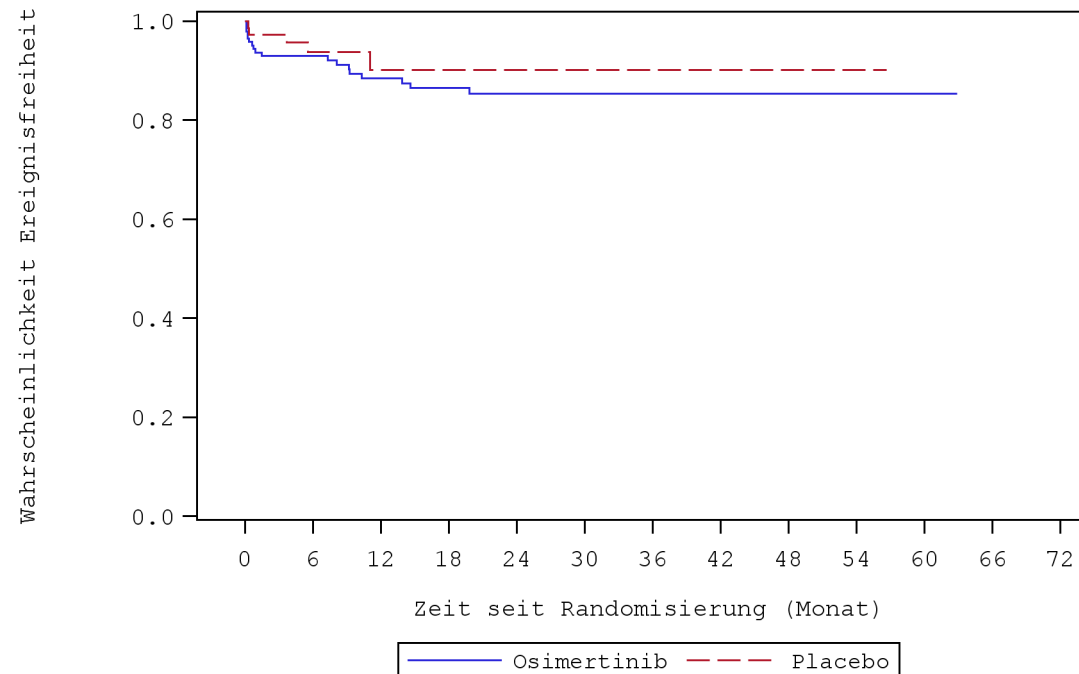
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Skin and subcutaneous tissue disorders
PT: Pruritus

Osimertinib	143	110	93	83	62	42	27	13	5	2	1	0
Placebo	73	45	21	11	6	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

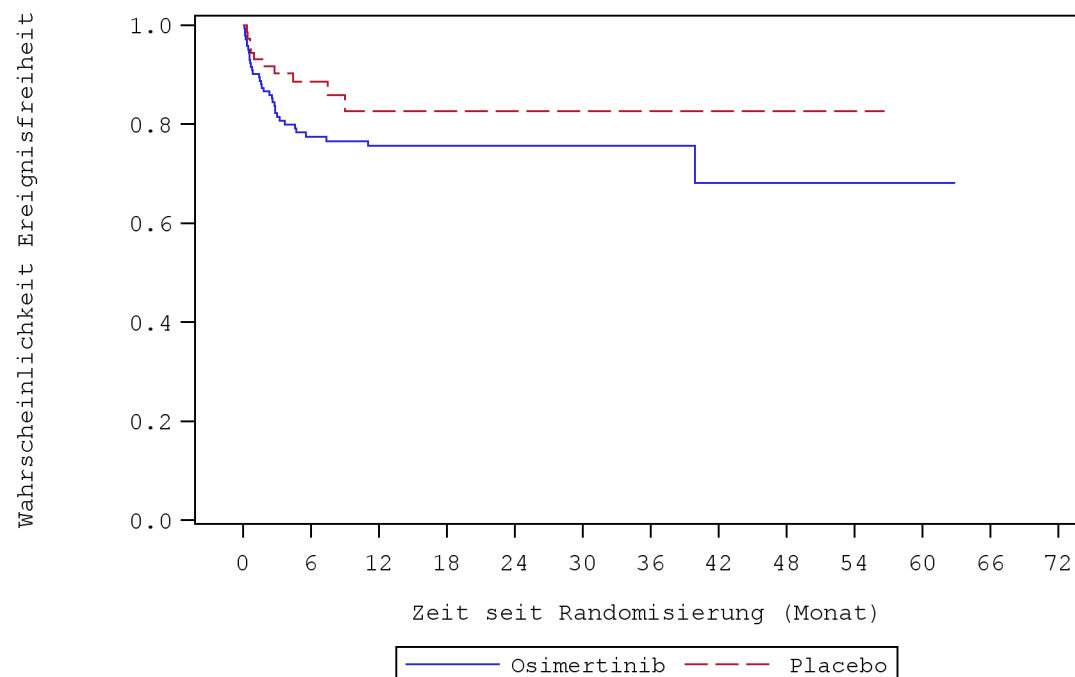
Figure LF1A_MSU0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set

Study: LAURA

SOC: Skin and subcutaneous tissue disorders

PT: Rash



Osimertinib	143	91	81	72	54	36	21	7	2	1	1	0
Placebo	73	43	18	9	5	4	2	2	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

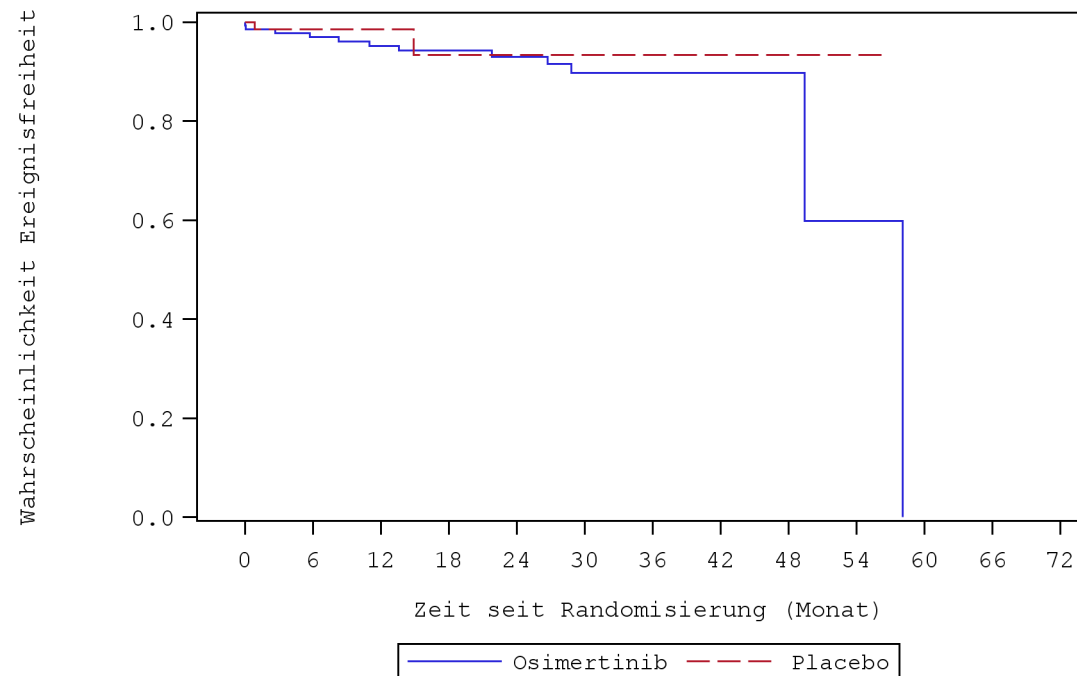
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1A_MSV0: Kaplan-Meier plot for time to any AE by SOC/PT

Safety Set
Study: LAURASOC: Vascular disorders
PT: All PTs

Osimertinib	143	116	103	94	69	46	29	14	4	1	0
Placebo	73	48	23	12	7	5	3	3	2	1	0

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_MSU0

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

Page 1 of 1
 Program Name: LT1_AAE_TTE_U0.sas
 Run Date: 08OCT2024:11:21:24

Table LT1AC_MSU0: Time to any severe AE by SOC/PT
 Safety Set

Time to any severe AE				Kaplan-Meier analysis		Log-Rank Test		
SOC/PT	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Osimertinib	143	14 (9.8)	NC		1.47	(0.53, 4.06)	0.4605
	Placebo	73	4 (5.5)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

The p-value was derived using an unstratified log-rank test, the hazard ratio and CI were calculated from U and V statistics.

The CI for median time was calculated based on Brookmeyer/Crowley.

Only events are reported with at least 5% affected patients in at least 1 treatment arm.

CI = Confidence Interval. NC = Not calculated. * = significant treatment effect.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Severe = maximum CTCAE grade $\geq$ 3. CTCAE = Common terminology criteria for adverse events.

Source Data: AAES_TTE, created on: 08OCT2024

AstraZeneca

Value Dossier Analysis: D5160C00048

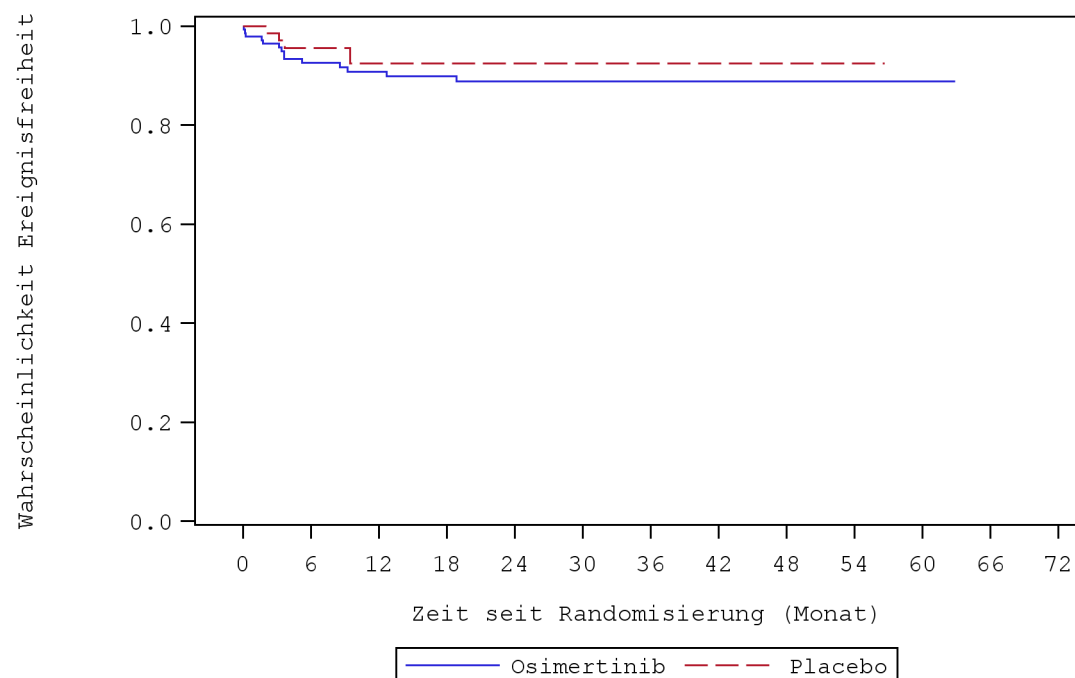
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1AC_MSU0: Kaplan-Meier plot for time to any severe AE by SOC/PT

Safety Set
Study: LAURASOC: Infections and infestations
PT: All PTs

Osimertinib	143	112	100	90	67	48	30	13	5	2	1	0
Placebo	73	47	23	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term. Severe = maximum CTCAE grade ≥ 3 .
Reference table: LT1AC_MSU0

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

Page 1 of 1
 Program Name: LT1_AAE_TTE_U0.sas
 Run Date: 08OCT2024:11:21:24

Table LT1AS_MSU0: Time to any serious AE by SOC/PT
 Safety Set

Time to any serious AE				Kaplan-Meier analysis		Log-Rank Test		
SOC/PT	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Osimertinib	143	17 (11.9)	NC		1.62	(0.62, 4.25)	0.3297
	Placebo	73	4 (5.5)	NC				
SOC: Injury, poisoning and procedural complications	Osimertinib	143	19 (13.3)	NC		2.82	(1.10, 7.27)	0.0314 *
	Placebo	73	2 (2.7)	NC				
PT: Radiation pneumonitis	Osimertinib	143	15 (10.5)	NC		2.73	(1.004, 7.43)	0.0490 *
	Placebo	73	2 (2.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

The p-value was derived using an unstratified log-rank test, the hazard ratio and CI were calculated from U and V statistics.

The CI for median time was calculated based on Brookmeyer/Crowley.

Only events are reported with at least 5% affected patients in at least 1 treatment arm.

CI = Confidence Interval. NC = Not calculated. * = significant treatment effect.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Source Data: AAES_TTE, created on: 08OCT2024

AstraZeneca

Value Dossier Analysis: D5160C00048

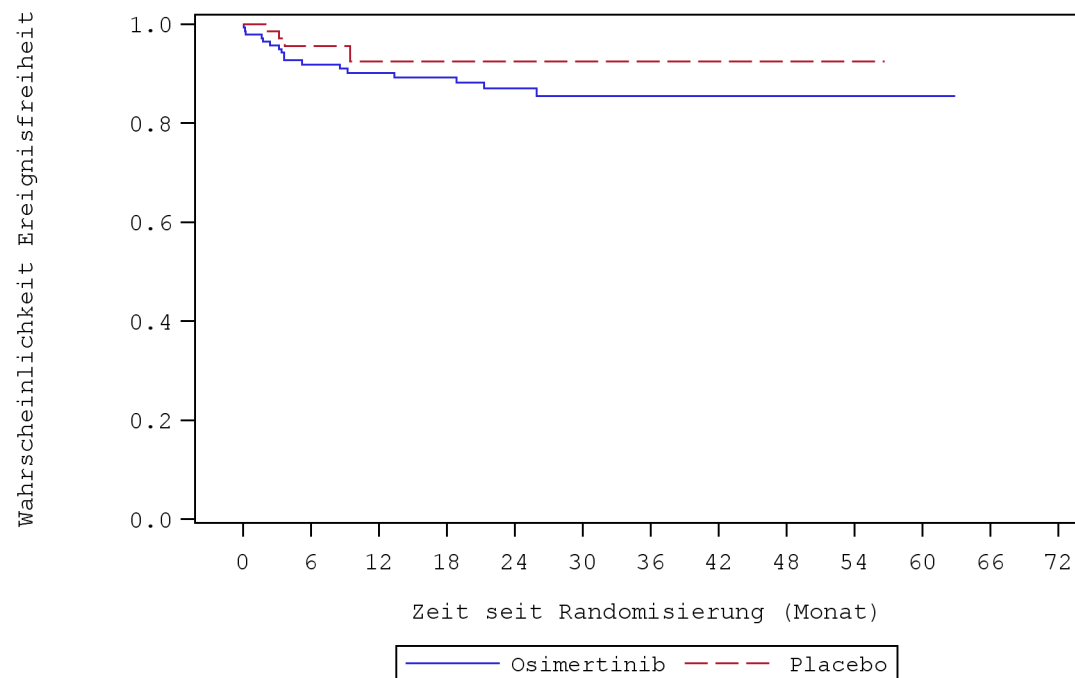
Cutoff Date (Interim): 05/Jan/2024

Page 1 of 3

Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1AS_MSV0: Kaplan-Meier plot for time to any serious AE by SOC/PT

Safety Set
Study: LAURASOC: Infections and infestations
PT: All PTs

Osimertinib	143	111	99	90	65	46	28	13	5	2	1	0
Placebo	73	47	23	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1AS_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_V0.sas

Run Date: 08OCT2024:11:34:46

Figure LF1AS_MSV0: Kaplan-Meier plot for time to any serious AE by SOC/PT

Safety Set

Study: LAURA

SOC: Injury, poisoning and procedural complications

PT: All PTs



Osimertinib	143	110	99	90	67	47	30	14	4	2	1	0
Placebo	73	48	24	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1AS_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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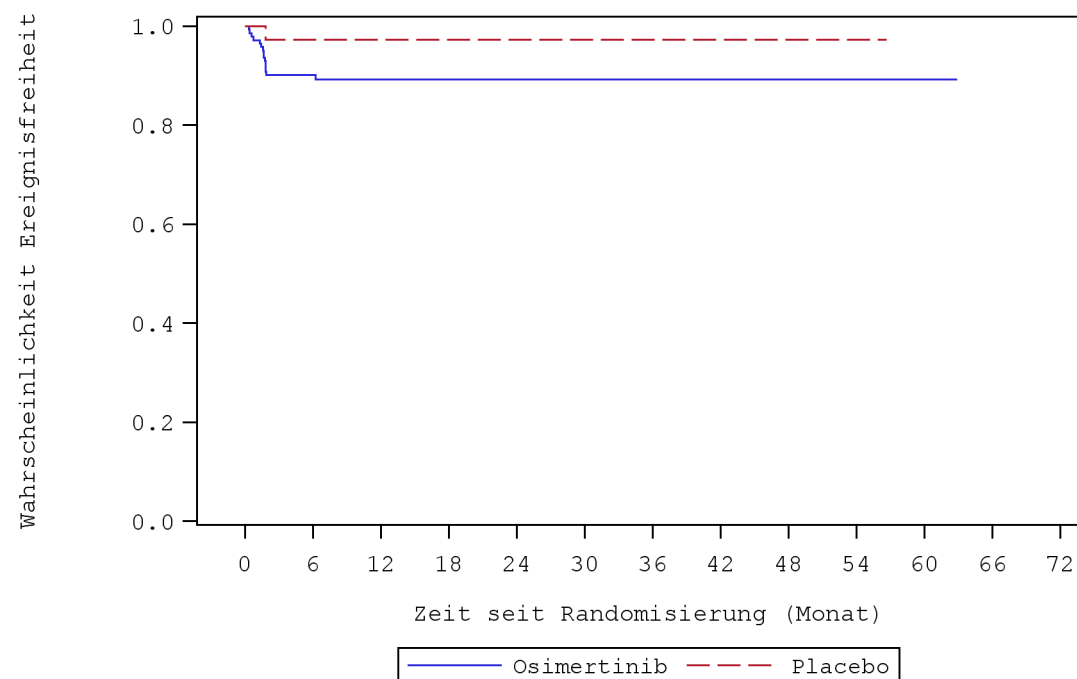
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Figure LF1AS_MSV0: Kaplan-Meier plot for time to any serious AE by SOC/PT

Safety Set

Study: LAURA

SOC: Injury, poisoning and procedural complications
PT: Radiation pneumonitis

Osimertinib	143	111	100	91	68	48	32	15	5	2	1	0
Placebo	73	48	24	12	7	5	3	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1AS_MSU0

AstraZeneca

Value Dossier Analysis: D5160C00048

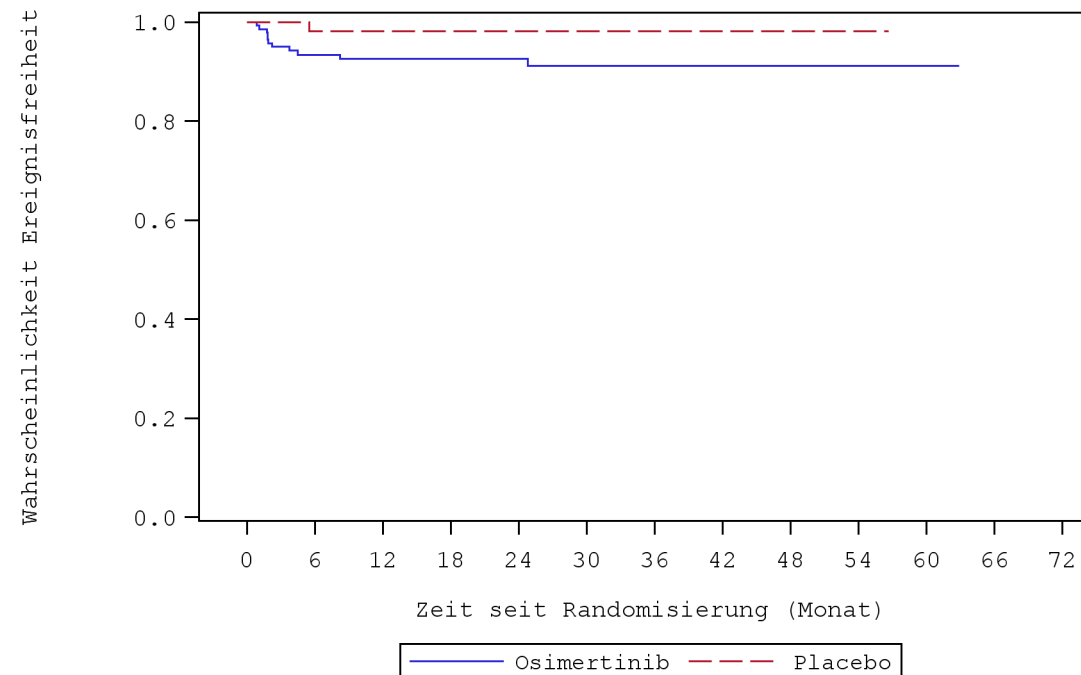
Cutoff Date (Interim): 05/Jan/2024

Page 1 of 1

Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AEI_MSK0: Kaplan-Meier plot for time to any AESI ILD and pneumonitis
Safety Set
Study: LAURA



Osimertinib	143	113	101	93	69	47	31	15	5	2	1	0
Placebo	73	48	23	12	7	5	3	3	2	1	0	

AESI = Adverse Event of special interest. ILD = Interstitial lung disease.
Reference table: LT1AEI_MST0

AstraZeneca

Value Dossier Analysis: D5160C00048

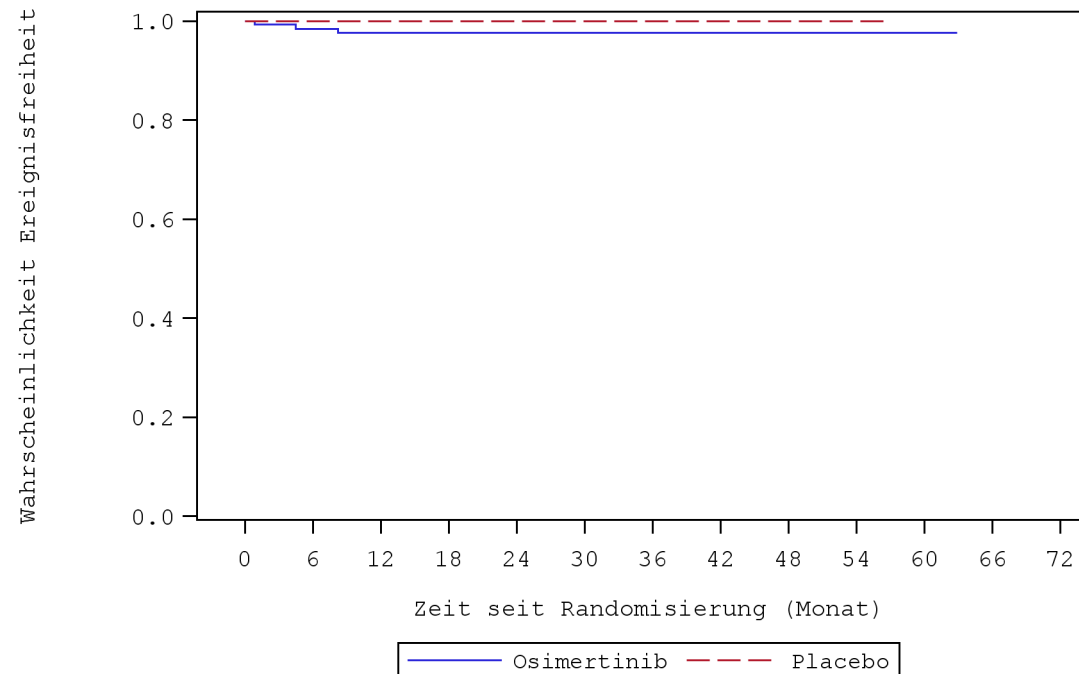
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AEIC_MSK0: Kaplan-Meier plot for time to any severe AESI ILD and pneumonitis
 Safety Set
 Study: LAURA



Osimertinib	143	119	107	98	72	50	32	15	5	2	1	0
Placebo	73	49	24	12	7	5	3	3	2	1	0	

AESI = Adverse Event of special interest. Severe = maximum CTCAE grade ≥ 3 . CTCAE = Common terminology criteria for adverse events.

Reference table: LT1AEIC_MST0

AstraZeneca

Value Dossier Analysis: D5160C00048

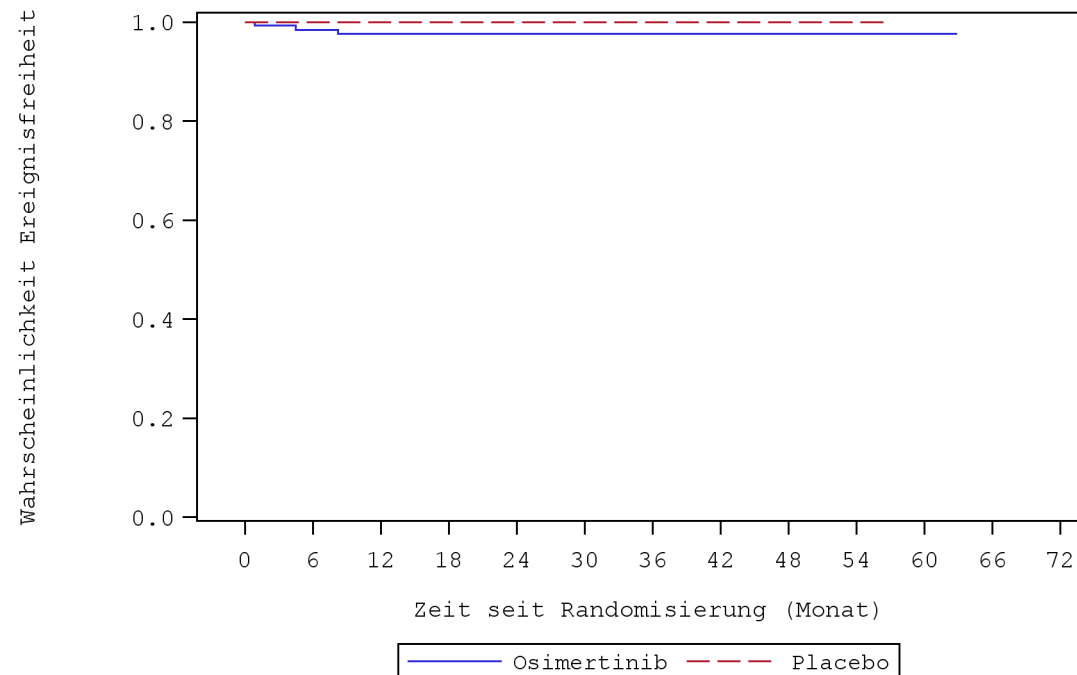
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AEIS_MSK0: Kaplan-Meier plot for time to any serious AESI ILD and pneumonitis
Safety Set
Study: LAURA



Osimertinib	143	119	107	98	72	50	32	15	5	2	1	0
Placebo	73	49	24	12	7	5	3	3	2	1	0	

AESI = Adverse Event of special interest. ILD = Interstitial lung disease.

Reference table: LT1AEIS_MST0

AstraZeneca

Value Dossier Analysis: D5160C00048

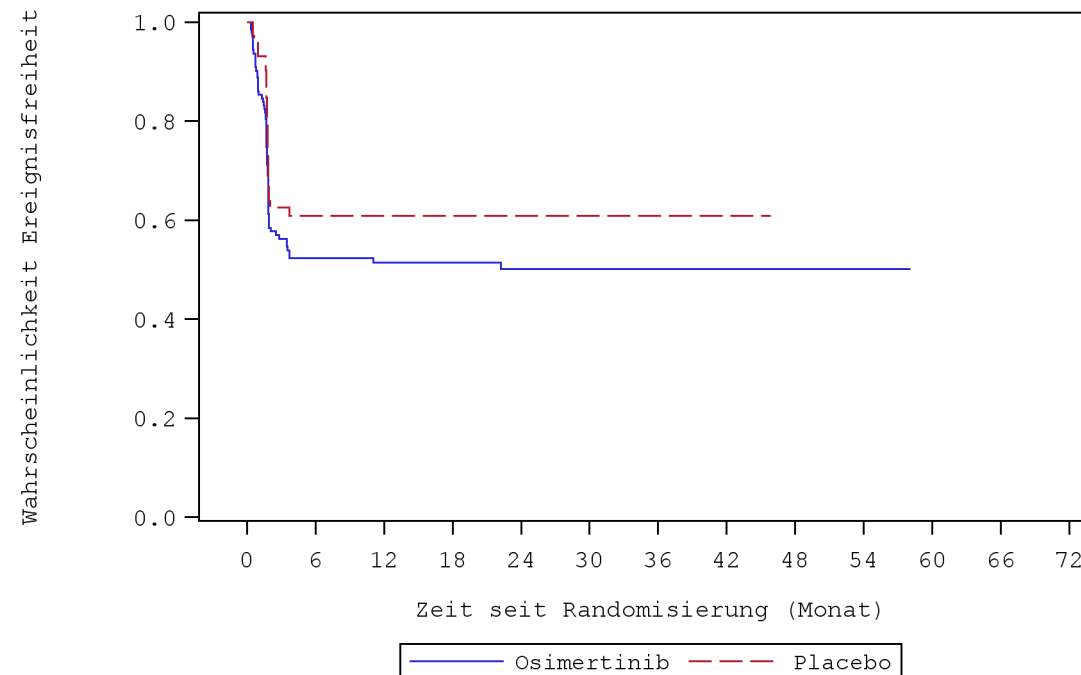
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AER_MSK0: Kaplan-Meier plot for time to any AESI Radiation pneumonitis
 Safety Set
 Study: LAURA



Osimertinib	143	64	56	49	33	25	17	8	2	1	0
Placebo	73	31	17	9	5	3	1	1	0		

AESI = Adverse Event of special interest.
 Reference table: LT1AER_MST0

AstraZeneca

Value Dossier Analysis: D5160C00048

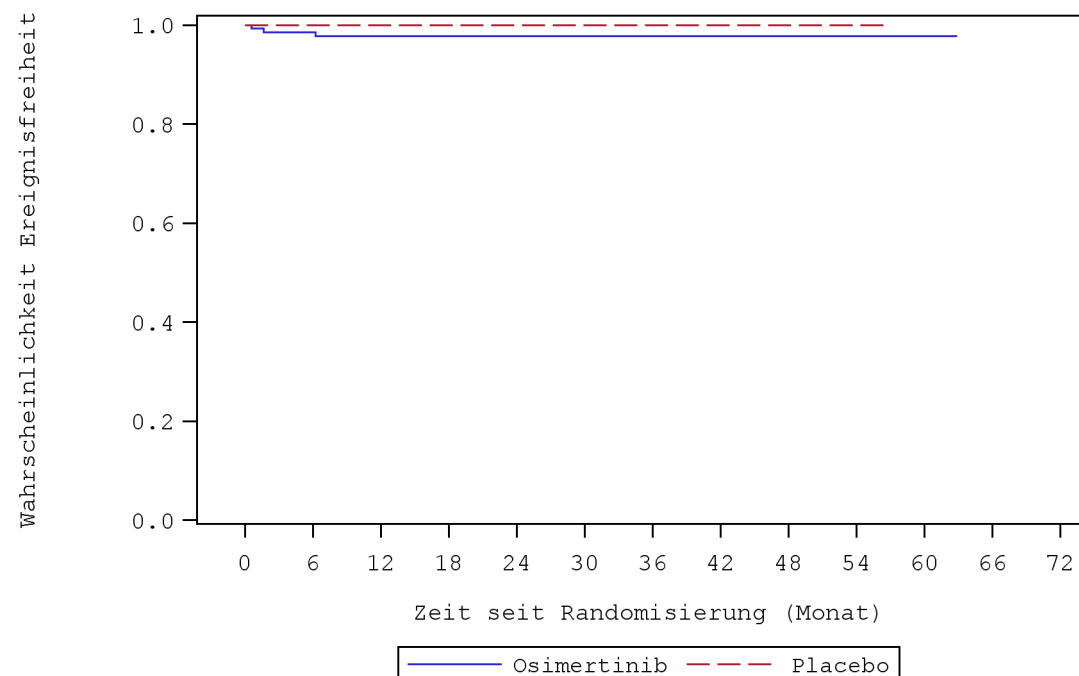
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AERC_MSK0: Kaplan-Meier plot for time to any severe AESI Radiation pneumonitis
Safety Set
Study: LAURA



Osimertinib	143	119	107	98	72	50	32	15	5	2	1	0
Placebo	73	49	24	12	7	5	3	3	2	1	0	

AESI = Adverse Event of special interest. Severe = maximum CTCAE grade ≥ 3 . CTCAE = Common terminology criteria for adverse events.

Reference table: LT1AERC_MST0

AstraZeneca

Value Dossier Analysis: D5160C00048

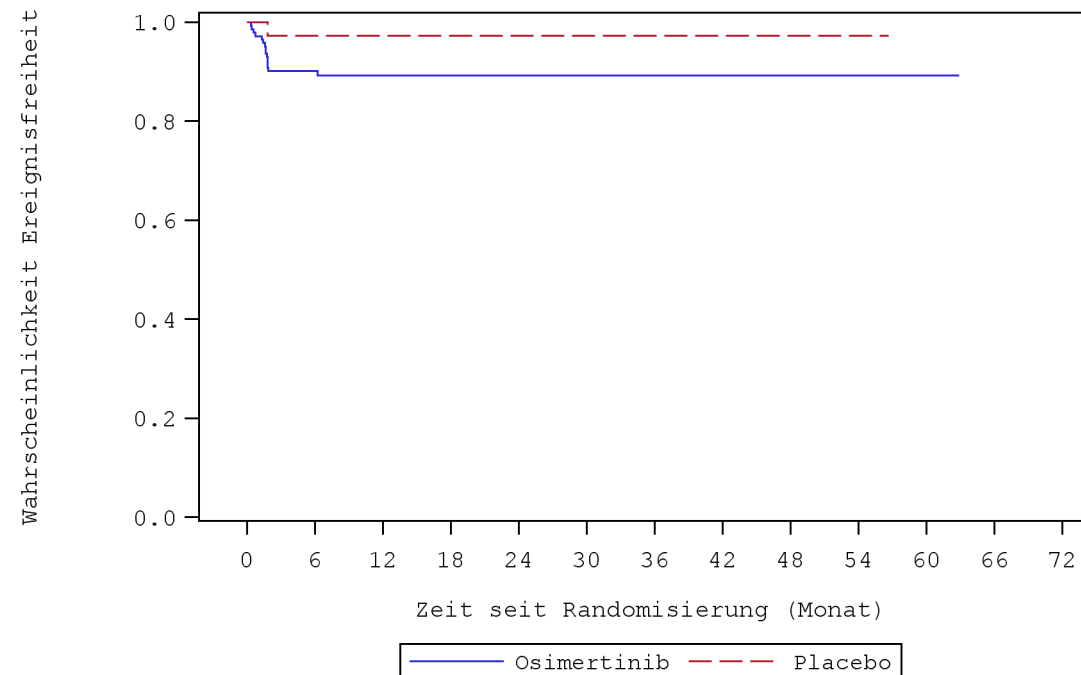
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AERS_MSK0: Kaplan-Meier plot for time to any serious AESI Radiation pneumonitis
Safety Set
Study: LAURA



Osimertinib	143	111	100	91	68	48	32	15	5	2	1	0
Placebo	73	48	24	12	7	5	3	3	2	1	0	

AESI = Adverse Event of special interest.
Reference table: LT1AERS_MST0

AstraZeneca

Value Dossier Analysis: D5160C00048

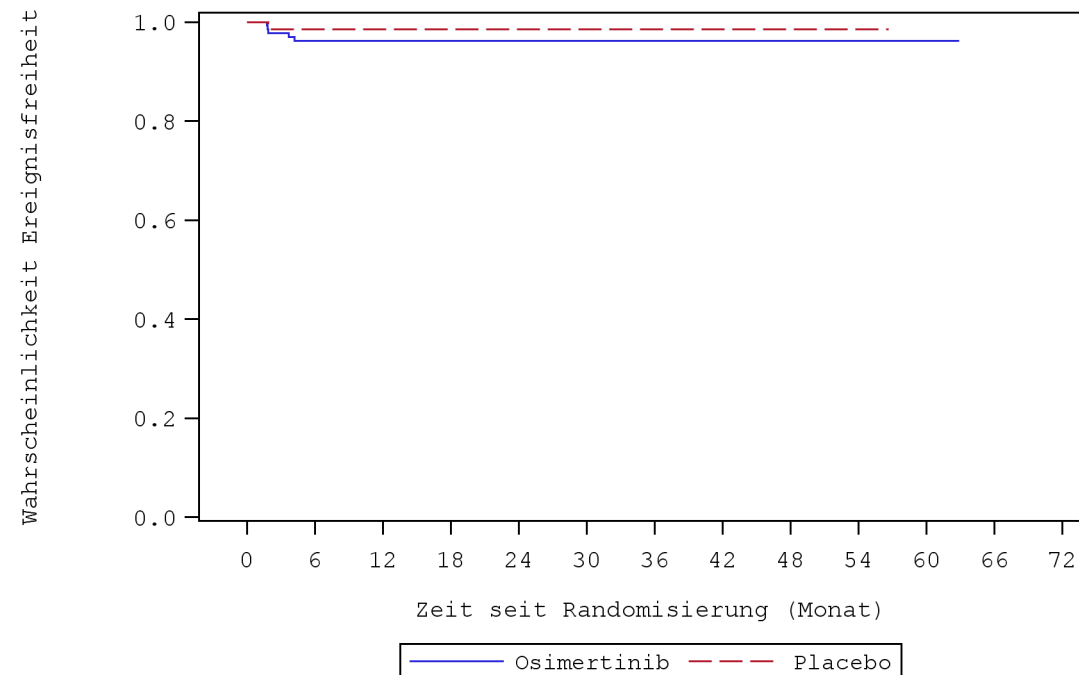
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AEQ_MSK0: Kaplan-Meier plot for time to any AESI cardiac effects (QT)
 Safety Set
 Study: LAURA



Osimertinib	143	114	102	94	68	47	31	14	5	2	1	0
Placebo	73	48	23	12	7	5	3	3	2	1	0	

AESI = Adverse Event of special interest.
 Reference table: LT1AEQ_MST0

AstraZeneca

Value Dossier Analysis: D5160C00048

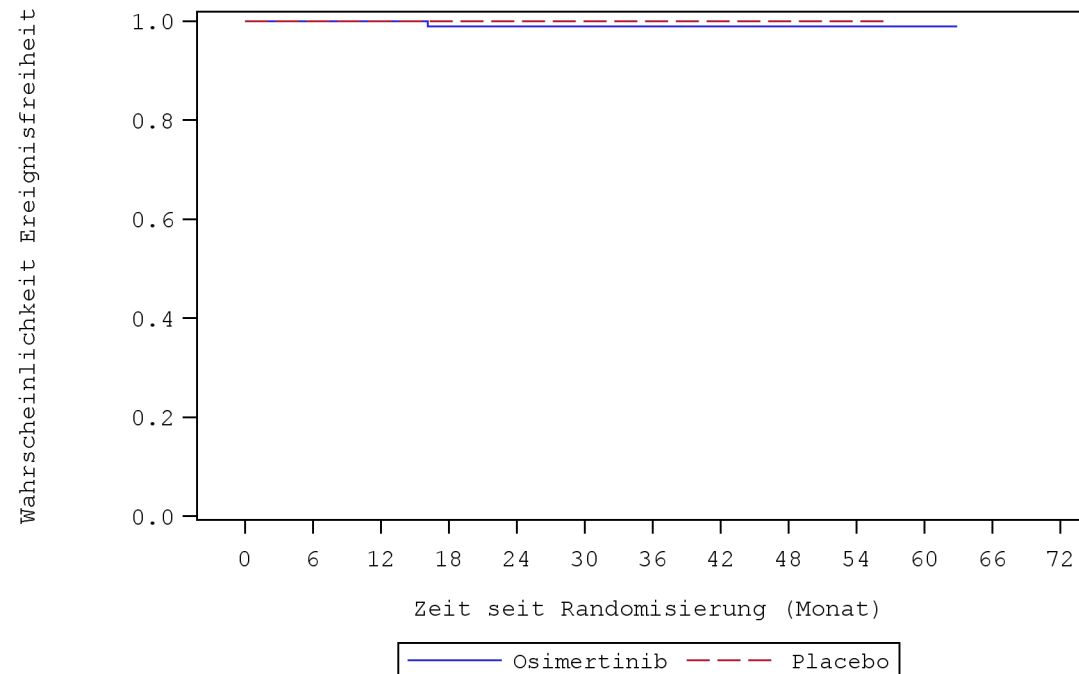
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AEQC_MSK0: Kaplan-Meier plot for time to any severe AESI cardiac effects (QT)

Safety Set
Study: LAURA

Osimertinib	143	119	107	98	72	50	32	15	5	2	1	0
Placebo	73	49	24	12	7	5	3	3	2	1	0	

AESI = Adverse Event of special interest. Severe = maximum CTCAE grade ≥ 3 . CTCAE = Common terminology criteria for adverse events.

Reference table: LT1AEQC_MST0

AstraZeneca

Value Dossier Analysis: D5160C00048

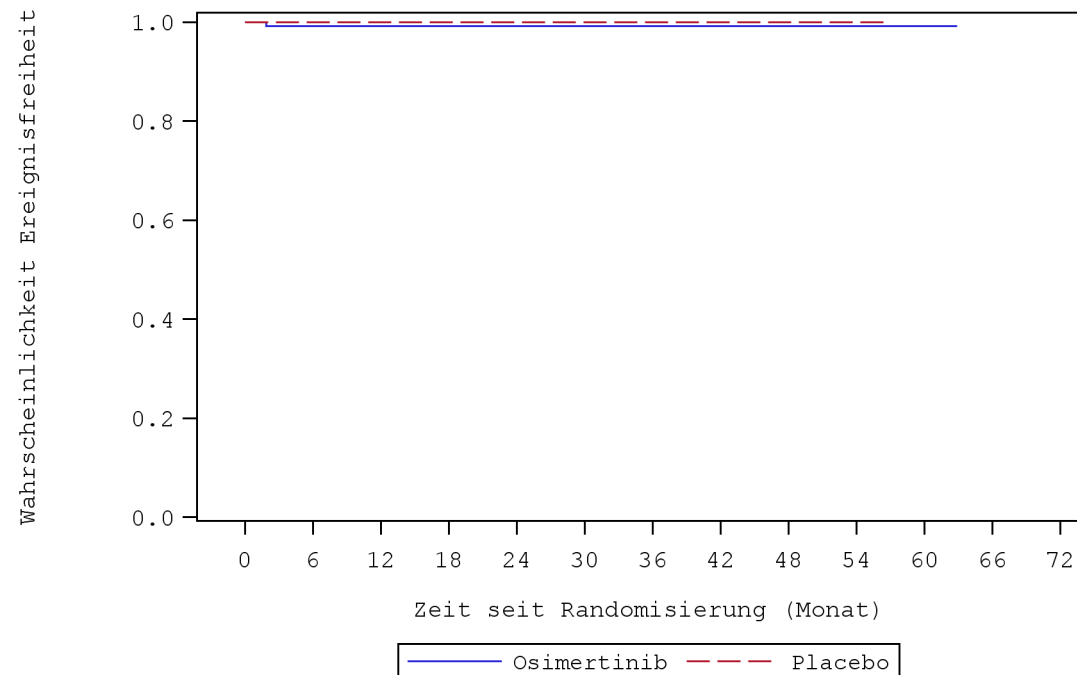
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_K0.sas

Run Date: 05SEP2024:11:53:25

Figure LF1AEF_MSK0: Kaplan-Meier plot for time to any AESI cardiac failure
 Safety Set
 Study: LAURA



Osimertinib	143	118	106	97	71	50	32	15	5	2	1	0
Placebo	73	49	24	12	7	5	3	3	2	1	0	

AESI = Adverse Event of special interest.
 Reference table: LT1AEF_MST0

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AEFF_TTE_TS.sas
Run Date: 24OCT2024:12:13:22

Table LT10ST_SFTM: Time to death by main subgroups
Full Analysis Set

Time to death				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.6323
Male	Osimertinib	53	12 (22.6)	53.9	(43.6, NC)	1.01	(0.38, 2.71)	0.9778
	Placebo	31	6 (19.4)	NC				
Female	Osimertinib	90	16 (17.8)	55.2	(43.5, NC)	0.74	(0.33, 1.68)	0.4757
	Placebo	42	9 (21.4)	47.4	(32.0, NC)			
Age	Osimertinib						Interaction test:	0.4386
< 65 years	Osimertinib	81	14 (17.3)	55.2	(46.5, NC)	1.17	(0.42, 3.26)	0.7604
	Placebo	39	5 (12.8)	NC				
>= 65 years	Osimertinib	62	14 (22.6)	53.9	(43.6, NC)	0.70	(0.31, 1.59)	0.3970
	Placebo	34	10 (29.4)	47.4	(34.5, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT10ST_SFTM: Time to death by main subgroups
Full Analysis Set

Time to death				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.0713
Current/former	Osimertinib	41	10 (24.4)	53.9	(43.6, NC)	2.09	(0.57, 7.63)	0.2655
	Placebo	24	3 (12.5)	NC				
Never	Osimertinib	102	18 (17.6)	55.2	(43.5, NC)	0.56	(0.27, 1.18)	0.1262
	Placebo	49	12 (24.5)	42.1	(34.5, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.3469
CCRT	Osimertinib	131	26 (19.8)	55.2	(46.5, NC)	0.99	(0.49, 2.01)	0.9781
	Placebo	62	11 (17.7)	NC				
SCRT	Osimertinib	12	2 (16.7)	43.5	(28.7, NC)	0.41	(0.07, 2.31)	0.3149
	Placebo	11	4 (36.4)	37.3	(28.0, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT10ST_SFTM: Time to death by main subgroups
Full Analysis Set

Time to death				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.9445
IIIA	Osimertinib	52	12 (23.1)	48.2	(43.5, NC)	0.86	(0.30, 2.44)	0.7750
	Placebo	24	5 (20.8)	47.4	(47.4, NC)			
IIIB/IIIC	Osimertinib	91	16 (17.6)	NC		0.82	(0.37, 1.81)	0.6221
	Placebo	49	10 (20.4)	NC				
Race	Osimertinib						Interaction test:	0.4849
Asian	Osimertinib	116	21 (18.1)	55.2	(48.2, NC)	0.96	(0.45, 2.04)	0.9154
	Placebo	62	10 (16.1)	NC				
Non-Asian	Osimertinib	27	7 (25.9)	46.5	(46.5, NC)	0.59	(0.18, 1.86)	0.3630
	Placebo	11	5 (45.5)	37.3	(13.0, 47.4)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Full Analysis Set

Time to death				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.5203
Yes	Osimertinib	27	2 (7.4)	NC		0.46	(0.06, 3.25)	0.4343
	Placebo	13	2 (15.4)	NC				
No	Osimertinib	116	26 (22.4)	53.9	(46.5, NC)	0.91	(0.47, 1.76)	0.7715
	Placebo	60	13 (21.7)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.7235
CR+PR	Osimertinib	71	16 (22.5)	55.2	(41.8, NC)	1.10	(0.43, 2.81)	0.8430
	Placebo	30	6 (20.0)	NC				
SD	Osimertinib	61	11 (18.0)	53.9	(46.5, NC)	0.66	(0.26, 1.64)	0.3713
	Placebo	37	8 (21.6)	47.4	(37.3, NC)			
NE	Osimertinib	11	1 (9.1)	NC		0.60	(0.04, 9.67)	0.7215
	Placebo	6	1 (16.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Full Analysis Set

Time to death				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.4445
Asia	Osimertinib	120	21 (17.5)	55.2	(48.2, NC)	0.95	(0.45, 2.03)	0.8989
	Placebo	64	10 (15.6)	NC				
Europe	Osimertinib	11	2 (18.2)	NC		0.30	(0.05, 1.64)	0.1629
	Placebo	7	4 (57.1)	37.3	(24.7, 47.4)			
Rest of the World	Osimertinib	12	5 (41.7)	46.5	(8.3, 46.5)	0.65	(0.08, 5.65)	0.6985
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.7770
Positive	Osimertinib	10	1 (10.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	19 (16.8)	53.9	(46.5, NC)	0.80	(0.39, 1.64)	0.5351
	Placebo	58	12 (20.7)	NC				
Unknown	Osimertinib	20	8 (40.0)	55.2	(28.7, 55.2)	0.84	(0.22, 3.21)	0.7934
	Placebo	11	3 (27.3)	37.3	(18.6, 37.3)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT10ST_SFTM: Time to death by main subgroups
Full Analysis Set

Time to death				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.4077				
Ex19Del	Osimertinib	74	13 (17.6)	55.2	(43.6, NC)	0.65	(0.27, 1.59)	0.3470
	Placebo	43	8 (18.6)	NC				
L858R	Osimertinib	68	15 (22.1)	48.2	(43.5, NC)	1.12	(0.45, 2.75)	0.8114
	Placebo	30	7 (23.3)	NC				

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Table LT1PFST_SFTM: Time to progression (BICR) by main subgroups
Full Analysis Set

Time to progression (BICR)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test: 0.5225	
Male	Osimertinib	53	23 (43.4)	38.4	(19.2, NC)	0.26	(0.15, 0.46)	<0.0001
	Placebo	31	27 (87.1)	7.2	(3.7, 9.5)			
Female	Osimertinib	90	34 (37.8)	39.1	(28.7, NC)	0.21	(0.13, 0.33)	<0.0001
	Placebo	42	36 (85.7)	5.5	(3.7, 7.4)			
Age	Osimertinib						Interaction test: 0.0469	
< 65 years	Osimertinib	81	31 (38.3)	38.8	(30.2, NC)	0.16	(0.10, 0.26)	<0.0001
	Placebo	39	36 (92.3)	3.7	(3.5, 5.6)			
>= 65 years	Osimertinib	62	26 (41.9)	39.1	(16.9, NC)	0.33	(0.19, 0.57)	<0.0001
	Placebo	34	27 (79.4)	7.4	(5.6, 11.1)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Full Analysis Set

Time to progression (BICR)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test: 0.6405	
Current/former	Osimertinib	41	20 (48.8)	31.5	(16.5, NC)	0.26	(0.14, 0.48)	<0.0001
	Placebo	24	22 (91.7)	4.7	(3.5, 9.2)			
Never	Osimertinib	102	37 (36.3)	39.1	(38.4, NC)	0.22	(0.14, 0.34)	<0.0001
	Placebo	49	41 (83.7)	5.6	(3.7, 9.0)			
Prior chemoradiation strategy	Osimertinib						Interaction test: 0.4503	
CCRT	Osimertinib	131	53 (40.5)	38.8	(30.4, NC)	0.24	(0.16, 0.36)	<0.0001
	Placebo	62	54 (87.1)	5.6	(3.7, 7.7)			
SCRT	Osimertinib	12	4 (33.3)	39.1	(13.6, NC)	0.15	(0.05, 0.50)	0.0018
	Placebo	11	9 (81.8)	5.2	(1.9, 9.5)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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The CI for median time was calculated based on Brookmeyer/Crowley.

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Full Analysis Set

Time to progression (BICR)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib							Interaction test: 0.4159
IIIA	Osimertinib	52	22 (42.3)	39.3	(19.2, NC)	0.28	(0.15, 0.52)	<0.0001
	Placebo	24	20 (83.3)	5.6	(3.5, 9.5)			
IIIB/IIIC	Osimertinib	91	35 (38.5)	39.1	(30.2, NC)	0.21	(0.13, 0.33)	<0.0001
	Placebo	49	43 (87.8)	5.6	(3.7, 9.0)			
Race	Osimertinib							Interaction test: 0.0637
Asian	Osimertinib	116	43 (37.1)	39.3	(31.5, NC)	0.20	(0.13, 0.30)	<0.0001
	Placebo	62	55 (88.7)	5.5	(3.7, 7.4)			
Non-Asian	Osimertinib	27	14 (51.9)	39.1	(8.3, NC)	0.48	(0.20, 1.14)	0.0943
	Placebo	11	8 (72.7)	7.6	(2.0, 11.1)			

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Full Analysis Set

Time to progression (BICR)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test: 0.1008	
Yes	Osimertinib	27	7 (25.9)	NC		0.11	(0.04, 0.29)	<0.0001
	Placebo	13	11 (84.6)	3.6	(1.8, 7.7)			
No	Osimertinib	116	50 (43.1)	38.8	(30.2, NC)	0.26	(0.18, 0.39)	<0.0001
	Placebo	60	52 (86.7)	5.7	(4.8, 9.0)			
Response to prior CRT	Osimertinib						Interaction test: 0.1492	
CR+PR	Osimertinib	71	29 (40.8)	39.3	(27.9, NC)	0.23	(0.13, 0.39)	<0.0001
	Placebo	30	27 (90.0)	5.6	(3.7, 9.0)			
SD	Osimertinib	61	24 (39.3)	38.4	(30.4, NC)	0.19	(0.11, 0.33)	<0.0001
	Placebo	37	34 (91.9)	5.6	(3.7, 9.0)			
NE	Osimertinib	11	4 (36.4)	NC		1.05	(0.19, 5.74)	0.9540
	Placebo	6	2 (33.3)	NC				

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Full Analysis Set

Time to progression (BICR)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.3067
Asia	Osimertinib	120	44 (36.7)	39.3	(31.5, NC)	0.20	(0.13, 0.30)	<0.0001
	Placebo	64	56 (87.5)	5.5	(3.7, 7.4)			
Europe	Osimertinib	11	6 (54.5)	39.1	(3.7, NC)	0.46	(0.14, 1.51)	0.1985
	Placebo	7	5 (71.4)	8.4	(2.0, NC)			
Rest of the World	Osimertinib	12	7 (58.3)	14.0	(3.4, NC)	0.40	(0.08, 1.95)	0.2581
	Placebo	2	2 (100.0)	7.6	(5.7, 9.5)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.0185
Positive	Osimertinib	10	4 (40.0)	38.8	(10.9, 38.8)	0.04	(0.01, 0.15)	<0.0001
	Placebo	4	4 (100.0)	1.8	(1.8, 3.7)			
Negative	Osimertinib	113	42 (37.2)	NC		0.21	(0.14, 0.33)	<0.0001
	Placebo	58	51 (87.9)	5.6	(3.7, 7.7)			
Unknown	Osimertinib	20	11 (55.0)	28.7	(9.0, NC)	0.44	(0.18, 1.10)	0.0793
	Placebo	11	8 (72.7)	8.4	(1.9, 24.8)			

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Table LT1PFST_SFTM: Time to progression (BICR) by main subgroups
Full Analysis Set

Time to progression (BICR)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.0969				
Ex19Del	Osimertinib	74	26 (35.1)	38.8	(30.4, NC)	0.17	(0.10, 0.29)	<0.0001 *
	Placebo	43	39 (90.7)	5.6	(3.7, 7.7)			
L858R	Osimertinib	68	31 (45.6)	39.1	(16.6, NC)	0.32	(0.19, 0.55)	<0.0001 *
	Placebo	30	24 (80.0)	5.6	(3.6, 9.2)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

Source Data: AEFF_TTE, created on: 24SEP2024

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AEFF_TTE_KS.sas

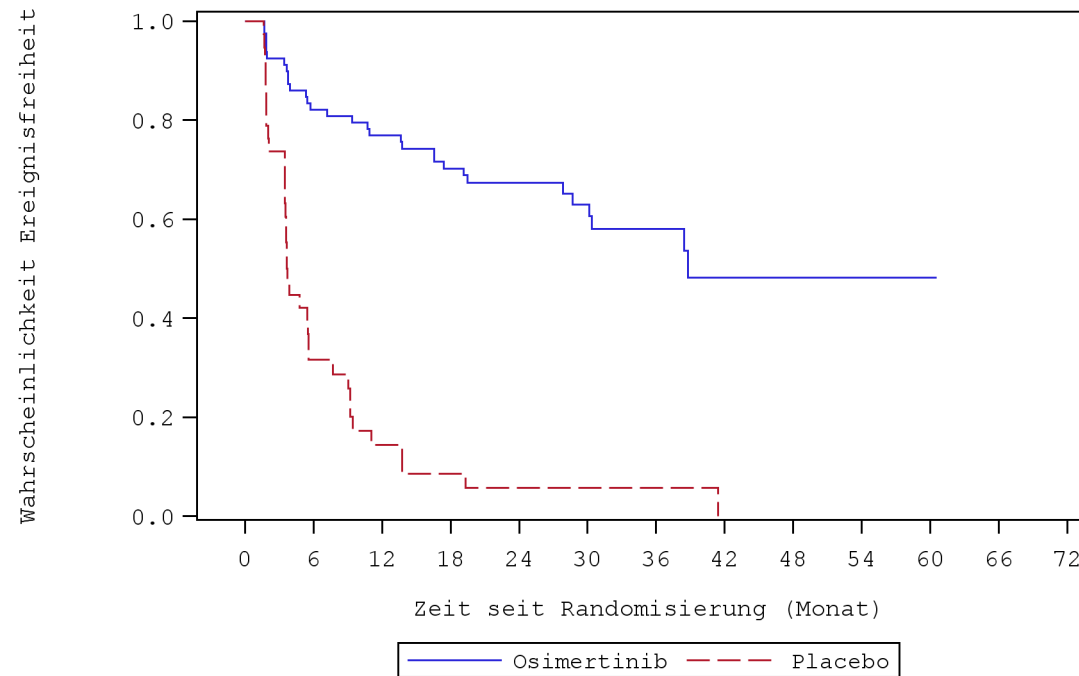
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Figure LF1PFST_SFkm: Kaplan Meier plot for time to progression (BICR) by main subgroups

Full Analysis Set

Study: LAURA

Age: < 65 years



Osimertinib	81	63	59	51	41	28	13	6	3	2	1	0
Placebo	39	11	5	3	2	2	1	0				

Reference table: LT1PFST_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AEFF_TTE_KS.sas

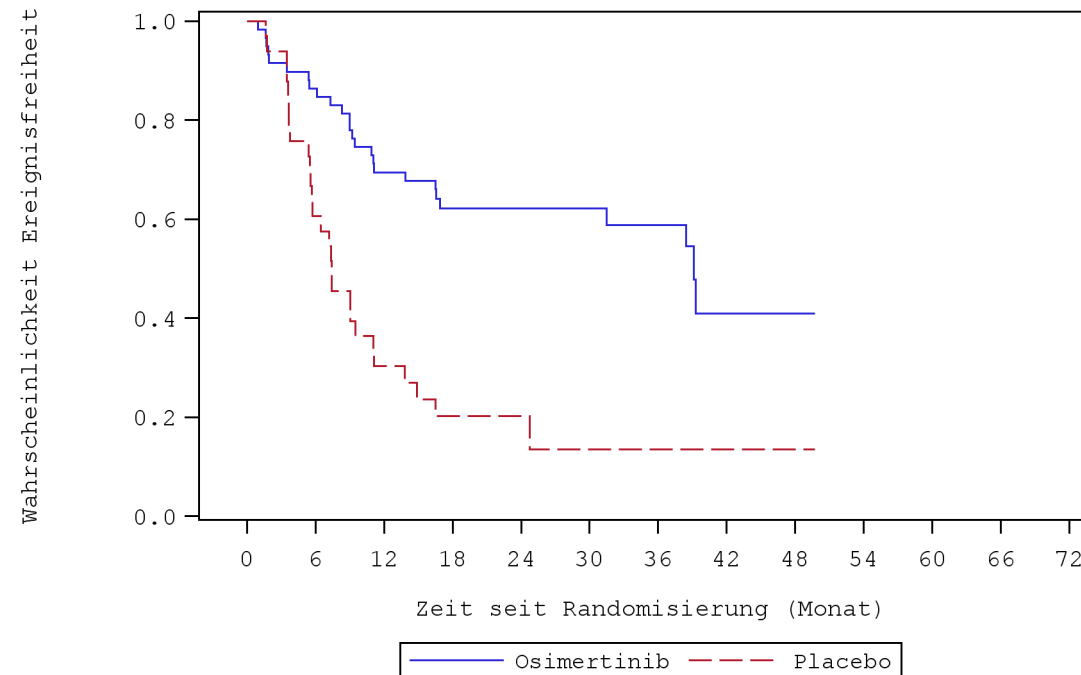
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Figure LF1PFST_SFKM: Kaplan Meier plot for time to progression (BICR) by main subgroups

Full Analysis Set

Study: LAURA

Age: >= 65 years



Osimertinib	62	51	40	32	28	21	15	3	1	0
Placebo	34	20	10	6	4	2	2	2	1	0

Reference table: LT1PFST_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

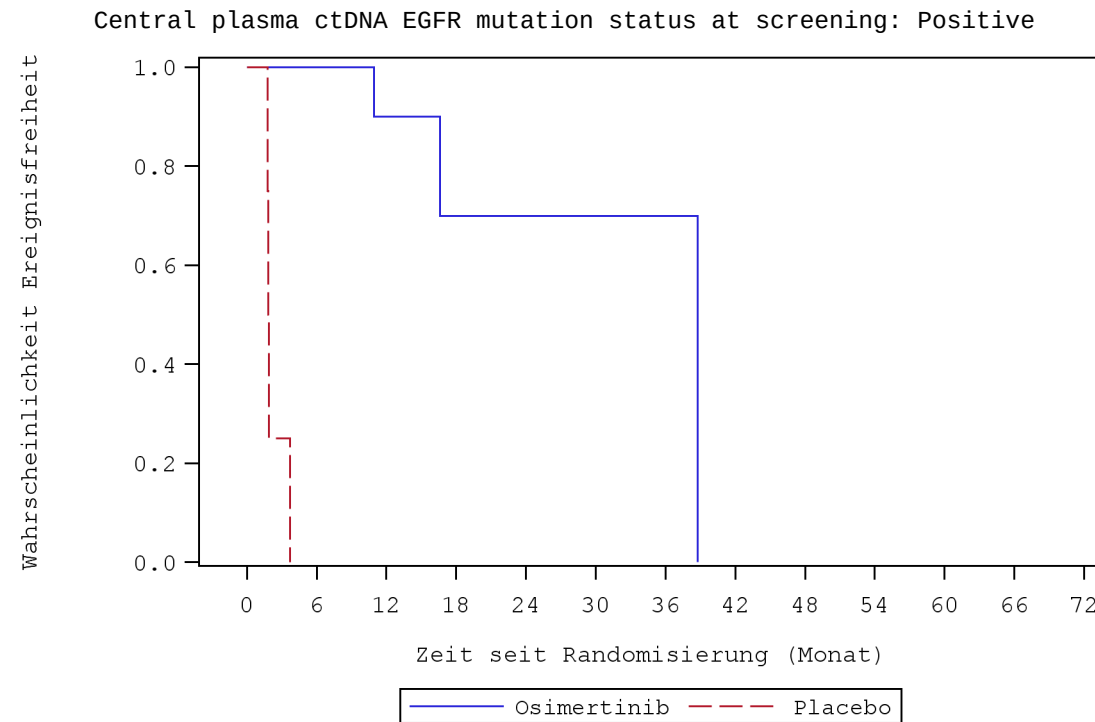
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AEFF_TTE_KS.sas

Run Date: 27SEP2024:11:33:42

Figure LF1PFST_SFKM: Kaplan Meier plot for time to progression (BICR) by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	10	10	9	7	7	4	2	0
Placebo	4	0						

Reference table: LT1PFST_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

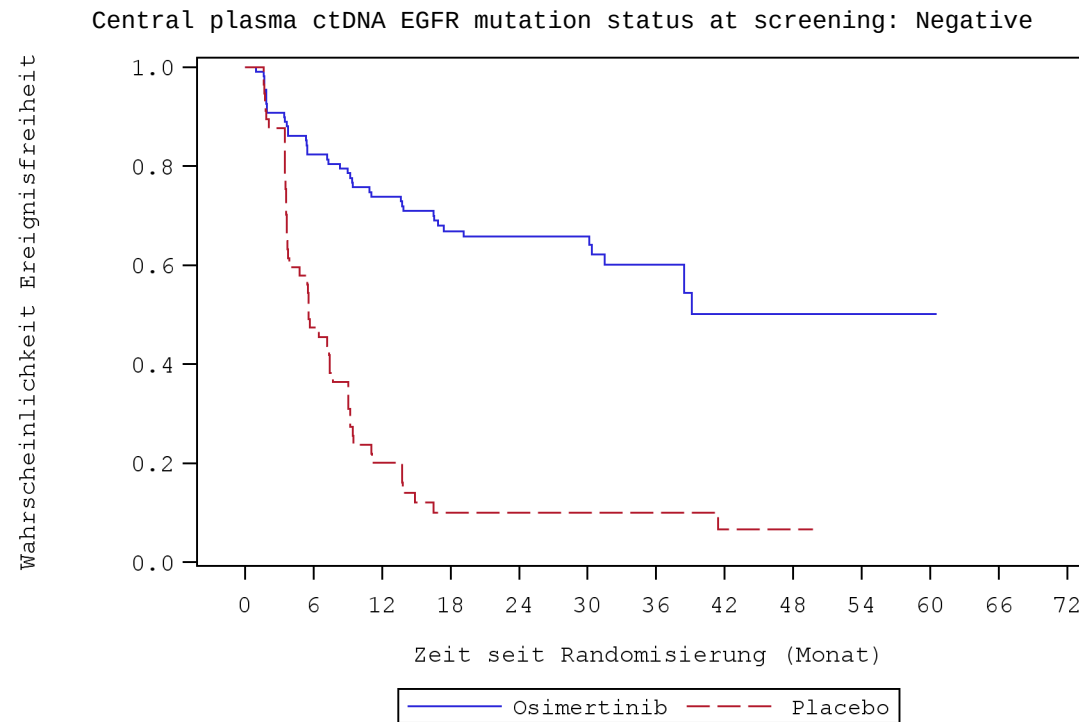
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AEFF_TTE_KS.sas

Run Date: 27SEP2024:11:33:42

Figure LF1PFST_SFkm: Kaplan Meier plot for time to progression (BICR) by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	113	87	77	63	52	38	22	8	4	2	1	0
Placebo	58	26	11	5	4	3	3	2	1	0		

Reference table: LT1PFST_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

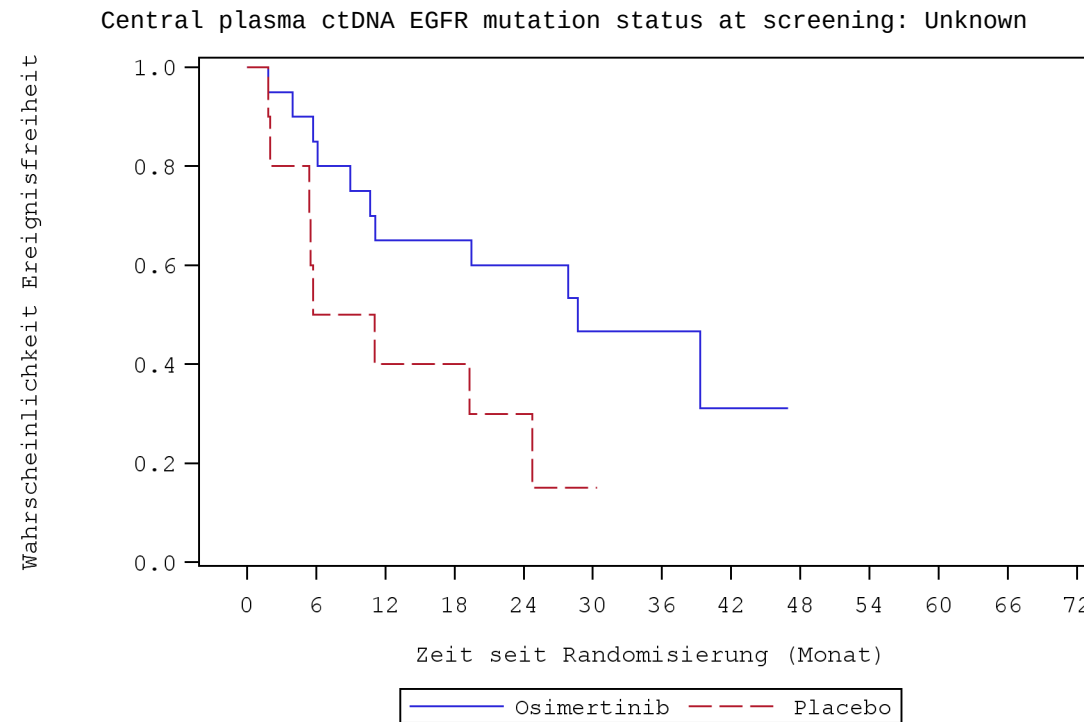
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AEFF_TTE_KS.sas

Run Date: 27SEP2024:11:33:42

Figure LF1PFST_SFKM: Kaplan Meier plot for time to progression (BICR) by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	20	17	13	13	10	7	4	1	0
Placebo	11	5	4	4	2	1	0		

Reference table: LT1PFST_SFTM

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QFI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Fatigue by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Fatigue				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.4653
Male	Osimertinib	53	39 (73.6)	1.8	(1.0, 3.7)	1.72	(0.96, 3.09)	0.0694
	Placebo	31	16 (51.6)	9.6	(1.9, NC)			
Female	Osimertinib	90	63 (70.0)	1.8	(1.0, 3.6)	1.30	(0.82, 2.07)	0.2611
	Placebo	42	25 (59.5)	3.6	(1.0, 20.9)			
Age	Osimertinib						Interaction test:	0.4004
< 65 years	Osimertinib	81	56 (69.1)	1.9	(1.8, 3.8)	1.28	(0.77, 2.12)	0.3379
	Placebo	39	21 (53.8)	5.3	(1.0, 20.9)			
>= 65 years	Osimertinib	62	46 (74.2)	1.8	(1.0, 3.6)	1.75	(1.03, 2.96)	0.0376 *
	Placebo	34	20 (58.8)	5.6	(1.9, 29.4)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QFI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Fatigue by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Fatigue				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.3935
Current/former	Osimertinib	41	29 (70.7)	1.8	(1.0, 3.8)	1.84	(0.93, 3.62)	0.0780
	Placebo	24	12 (50.0)	10.1	(1.9, NC)			
Never	Osimertinib	102	73 (71.6)	1.9	(1.0, 3.6)	1.30	(0.85, 2.00)	0.2319
	Placebo	49	29 (59.2)	2.0	(1.1, 7.3)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.3182
CCRT	Osimertinib	131	95 (72.5)	1.8	(1.0, 2.9)	1.57	(1.06, 2.32)	0.0236 *
	Placebo	62	35 (56.5)	7.3	(1.9, 20.9)			
SCRT	Osimertinib	12	7 (58.3)	3.6	(1.0, NC)	0.86	(0.29, 2.58)	0.7924
	Placebo	11	6 (54.5)	1.9	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QFI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Fatigue by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Fatigue				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.8076
IIIA	Osimertinib	52	37 (71.2)	1.8	(1.0, 3.6)	1.56	(0.84, 2.90)	0.1550
	Placebo	24	14 (58.3)	7.3	(1.9, 11.1)			
IIIB/IIIC	Osimertinib	91	65 (71.4)	1.8	(1.0, 3.6)	1.42	(0.91, 2.24)	0.1251
	Placebo	49	27 (55.1)	4.2	(1.1, 29.4)			
Race	Osimertinib						Interaction test:	0.0324 #
Asian	Osimertinib	116	89 (76.7)	1.8	(1.0, 2.9)	1.68	(1.13, 2.49)	0.0096 *
	Placebo	62	35 (56.5)	5.6	(1.9, 29.4)			
Non-Asian	Osimertinib	27	13 (48.1)	3.6	(1.0, 3.7)	0.49	(0.19, 1.30)	0.1547
	Placebo	11	6 (54.5)	0.9	(0.9, 10.1)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Value Dossier Analysis: D5160C00048
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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QFI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Fatigue by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Fatigue				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.9690
Yes	Osimertinib	27	16 (59.3)	7.4	(1.8, 22.0)	1.58	(0.53, 4.73)	0.4141
	Placebo	13	4 (30.8)	NC				
No	Osimertinib	116	86 (74.1)	1.8	(1.0, 1.9)	1.54	(1.05, 2.28)	0.0280 *
	Placebo	60	37 (61.7)	4.2	(1.9, 10.1)			
Response to prior CRT	Osimertinib						Interaction test:	0.2333
CR+PR	Osimertinib	71	51 (71.8)	1.8	(1.0, 2.1)	1.63	(0.95, 2.79)	0.0777
	Placebo	30	18 (60.0)	4.9	(1.9, 9.6)			
SD	Osimertinib	61	46 (75.4)	1.8	(1.0, 3.7)	1.55	(0.90, 2.64)	0.1111
	Placebo	37	19 (51.4)	10.1	(1.8, 29.4)			
NE	Osimertinib	11	5 (45.5)	3.8	(0.9, NC)	0.46	(0.12, 1.71)	0.2433
	Placebo	6	4 (66.7)	1.0	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire - Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QFI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Fatigue by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Fatigue				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.1373
Asia	Osimertinib	120	91 (75.8)	1.8	(1.0, 3.6)	1.59	(1.08, 2.35)	0.0185 *
	Placebo	64	36 (56.3)	5.6	(1.9, 20.9)			
Europe	Osimertinib	11	4 (36.4)	3.6	(1.9, NC)	0.29	(0.07, 1.33)	0.1112
	Placebo	7	3 (42.9)	1.4	(0.9, 1.9)			
Rest of the World	Osimertinib	12	7 (58.3)	1.0	(0.9, 1.8)	1.81	(0.37, 8.79)	0.4619
	Placebo	2	2 (100.0)	5.5	(0.9, 10.1)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.9854
Positive	Osimertinib	10	9 (90.0)	1.9	(0.9, 5.6)	1.30	(0.28, 6.02)	0.7376
	Placebo	4	2 (50.0)	NC				
Negative	Osimertinib	113	79 (69.9)	1.8	(1.0, 3.6)	1.47	(0.98, 2.20)	0.0634
	Placebo	58	34 (58.6)	5.6	(1.9, 20.9)			
Unknown	Osimertinib	20	14 (70.0)	1.9	(0.9, 3.6)	1.53	(0.55, 4.26)	0.4159
	Placebo	11	5 (45.5)	1.9	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_TS.sas
 Run Date: 24OCT2024:12:15:20

Table LT1QFI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Fatigue by main subgroups
 Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Fatigue				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.9426				
Ex19Del	Osimertinib	74	53 (71.6)	1.9	(1.0, 3.6)	1.44	(0.88, 2.35)	0.1466
	Placebo	43	23 (53.5)	7.3	(1.0, NC)			
L858R	Osimertinib	68	48 (70.6)	1.8	(1.0, 3.6)	1.48	(0.86, 2.54)	0.1578
	Placebo	30	18 (60.0)	4.9	(1.1, 11.1)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QPI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Pain by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.3150
Male	Osimertinib	53	33 (62.3)	3.7	(1.8, 20.2)	0.87	(0.49, 1.52)	0.6140
	Placebo	31	20 (64.5)	5.6	(3.6, 9.2)			
Female	Osimertinib	90	62 (68.9)	2.6	(1.8, 3.8)	1.26	(0.79, 2.00)	0.3323
	Placebo	42	25 (59.5)	5.6	(1.1, 7.4)			
Age	Osimertinib						Interaction test:	0.0810
< 65 years	Osimertinib	81	53 (65.4)	3.6	(1.1, 7.3)	0.81	(0.51, 1.29)	0.3747
	Placebo	39	27 (69.2)	3.4	(1.0, 6.0)			
>= 65 years	Osimertinib	62	42 (67.7)	3.6	(1.8, 7.4)	1.54	(0.88, 2.67)	0.1281
	Placebo	34	18 (52.9)	7.3	(3.6, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QPI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Pain by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.2942
Current/former	Osimertinib	41	31 (75.6)	1.9	(1.0, 11.0)	1.41	(0.76, 2.63)	0.2734
	Placebo	24	15 (62.5)	6.1	(3.8, 12.0)			
Never	Osimertinib	102	64 (62.7)	3.6	(1.9, 5.7)	0.95	(0.61, 1.46)	0.8038
	Placebo	49	30 (61.2)	1.9	(1.1, 7.3)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.4558
CCRT	Osimertinib	131	89 (67.9)	3.6	(1.8, 4.0)	1.14	(0.78, 1.67)	0.4931
	Placebo	62	38 (61.3)	5.6	(1.9, 7.4)			
SCRT	Osimertinib	12	6 (50.0)	7.4	(0.9, NC)	0.74	(0.25, 2.20)	0.5839
	Placebo	11	7 (63.6)	7.3	(0.9, 16.5)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1QPI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Pain by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.1212
IIIA	Osimertinib	52	34 (65.4)	3.6	(1.8, 3.8)	1.64	(0.85, 3.18)	0.1396
	Placebo	24	12 (50.0)	9.1	(3.6, NC)			
IIIB/IIIC	Osimertinib	91	61 (67.0)	3.7	(1.8, 9.1)	0.89	(0.58, 1.37)	0.6054
	Placebo	49	33 (67.3)	3.8	(1.1, 6.0)			
Race	Osimertinib						Interaction test:	0.5840
Asian	Osimertinib	116	79 (68.1)	3.6	(1.8, 7.3)	1.04	(0.71, 1.53)	0.8289
	Placebo	62	40 (64.5)	5.6	(1.9, 7.4)			
Non-Asian	Osimertinib	27	16 (59.3)	3.6	(0.9, 5.5)	1.40	(0.51, 3.83)	0.5108
	Placebo	11	5 (45.5)	6.4	(0.9, 16.5)			

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.9462
Yes	Osimertinib	27	14 (51.9)	10.0	(0.9, NC)	1.15	(0.41, 3.20)	0.7911
	Placebo	13	5 (38.5)	NC				
No	Osimertinib	116	81 (69.8)	3.6	(1.8, 3.8)	1.11	(0.76, 1.62)	0.6030
	Placebo	60	40 (66.7)	5.5	(1.9, 7.3)			
Response to prior CRT	Osimertinib						Interaction test:	0.4456
CR+PR	Osimertinib	71	43 (60.6)	3.6	(1.9, 7.3)	1.00	(0.59, 1.70)	0.9970
	Placebo	30	20 (66.7)	5.6	(1.9, 7.3)			
SD	Osimertinib	61	48 (78.7)	1.9	(1.0, 7.3)	1.29	(0.78, 2.15)	0.3196
	Placebo	37	22 (59.5)	6.0	(1.8, 16.5)			
NE	Osimertinib	11	4 (36.4)	1.8	(0.9, NC)	0.48	(0.11, 2.17)	0.3403
	Placebo	6	3 (50.0)	1.0	(1.0, NC)			

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.1391
Asia	Osimertinib	120	83 (69.2)	3.7	(1.8, 7.3)	1.07	(0.73, 1.55)	0.7369
	Placebo	64	41 (64.1)	5.6	(1.9, 7.4)			
Europe	Osimertinib	11	5 (45.5)	3.6	(0.9, NC)	0.48	(0.11, 2.01)	0.3127
	Placebo	7	3 (42.9)	1.1	(0.9, 7.3)			
Rest of the World	Osimertinib	12	7 (58.3)	1.8	(0.9, 3.6)	4.92	(0.60, 40.12)	0.1371
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.1860
Positive	Osimertinib	10	9 (90.0)	1.9	(0.9, 12.9)	5.05	(0.64, 39.94)	0.1245
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	74 (65.5)	3.7	(1.9, 7.3)	0.99	(0.67, 1.47)	0.9591
	Placebo	58	38 (65.5)	5.5	(1.9, 7.4)			
Unknown	Osimertinib	20	12 (60.0)	1.9	(0.9, 9.3)	1.12	(0.42, 2.97)	0.8276
	Placebo	11	6 (54.5)	3.7	(0.9, NC)			

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib		Interaction test: 0.8535				
Ex19Del	Osimertinib	74	50 (67.6)	3.6	(1.1, 5.5)	1.12	(0.70, 1.78)	0.6301
	Placebo	43	28 (65.1)	6.0	(1.9, 7.4)			
L858R	Osimertinib	68	44 (64.7)	3.6	(1.8, 7.4)	1.05	(0.60, 1.84)	0.8744
	Placebo	30	17 (56.7)	5.6	(1.7, 9.2)			

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Table LT1QVI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Nausea/Vomiting by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Nausea/Vomiting				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.3187
Male	Osimertinib	53	23 (43.4)	33.1	(12.8, NC)	0.82	(0.39, 1.69)	0.5883
	Placebo	31	11 (35.5)	28.8	(9.1, 28.8)			
Female	Osimertinib	90	38 (42.2)	24.0	(11.0, NC)	1.35	(0.69, 2.66)	0.3844
	Placebo	42	11 (26.2)	NC				
Age	Osimertinib						Interaction test:	0.2415
< 65 years	Osimertinib	81	33 (40.7)	33.1	(18.5, NC)	0.82	(0.42, 1.62)	0.5700
	Placebo	39	12 (30.8)	NC				
>= 65 years	Osimertinib	62	28 (45.2)	20.3	(9.2, NC)	1.48	(0.72, 3.05)	0.2890
	Placebo	34	10 (29.4)	28.8	(10.2, NC)			

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Nausea/Vomiting				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.3599
Current/former	Osimertinib	41	17 (41.5)	35.0	(11.1, NC)	0.79	(0.35, 1.79)	0.5713
	Placebo	24	9 (37.5)	28.8	(8.2, 28.8)			
Never	Osimertinib	102	44 (43.1)	24.0	(11.0, NC)	1.28	(0.68, 2.38)	0.4455
	Placebo	49	13 (26.5)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.9565
CCRT	Osimertinib	131	57 (43.5)	24.0	(16.6, 42.8)	1.08	(0.64, 1.81)	0.7812
	Placebo	62	20 (32.3)	28.8	(10.2, NC)			
SCRT	Osimertinib	12	4 (33.3)	27.5	(1.9, NC)	1.13	(0.21, 6.20)	0.8881
	Placebo	11	2 (18.2)	NC				

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Nausea/Vomiting				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.2445
IIIA	Osimertinib	52	17 (32.7)	NC		0.71	(0.31, 1.66)	0.4350
	Placebo	24	8 (33.3)	28.8	(8.2, NC)			
IIIB/IIIC	Osimertinib	91	44 (48.4)	18.5	(9.2, 27.7)	1.33	(0.72, 2.45)	0.3581
	Placebo	49	14 (28.6)	NC				
Race	Osimertinib						Interaction test:	0.5038
Asian	Osimertinib	116	49 (42.2)	33.1	(20.3, 42.8)	1.09	(0.63, 1.88)	0.7686
	Placebo	62	18 (29.0)	28.8	(11.3, NC)			
Non-Asian	Osimertinib	27	12 (44.4)	7.3	(1.8, NC)	0.70	(0.22, 2.19)	0.5386
	Placebo	11	4 (36.4)	5.5	(0.9, 8.2)			

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Nausea/Vomiting				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.0909
Yes	Osimertinib	27	5 (18.5)	NC		0.37	(0.10, 1.37)	0.1358
	Placebo	13	4 (30.8)	NC				
No	Osimertinib	116	56 (48.3)	21.1	(11.0, 35.0)	1.30	(0.76, 2.23)	0.3372
	Placebo	60	18 (30.0)	28.8	(10.2, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.8742
CR+PR	Osimertinib	71	31 (43.7)	21.1	(9.2, NC)	1.07	(0.52, 2.20)	0.8506
	Placebo	30	10 (33.3)	NC				
SD	Osimertinib	61	27 (44.3)	33.1	(18.5, NC)	1.01	(0.50, 2.06)	0.9756
	Placebo	37	11 (29.7)	28.8	(8.7, NC)			
NE	Osimertinib	11	3 (27.3)	18.5	(0.9, NC)	1.85	(0.19, 17.81)	0.5940
	Placebo	6	1 (16.7)	NC				

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Time to increase by at least 10 points in QLQ-C30 Nausea/Vomiting				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.2965
Asia	Osimertinib	120	52 (43.3)	27.7	(20.2, 42.8)	1.08	(0.63, 1.84)	0.7849
	Placebo	64	19 (29.7)	28.8	(11.3, NC)			
Europe	Osimertinib	11	6 (54.5)	2.8	(0.9, NC)	2.09	(0.25, 17.42)	0.4972
	Placebo	7	1 (14.3)	NC				
Rest of the World	Osimertinib	12	3 (25.0)	NC		0.26	(0.04, 1.60)	0.1470
	Placebo	2	2 (100.0)	4.6	(0.9, 8.2)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.7850
Positive	Osimertinib	10	5 (50.0)	27.7	(1.9, NC)	1.19	(0.14, 10.30)	0.8713
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	47 (41.6)	33.1	(18.5, 42.8)	1.01	(0.59, 1.74)	0.9618
	Placebo	58	19 (32.8)	NC				
Unknown	Osimertinib	20	9 (45.0)	16.6	(1.9, NC)	1.75	(0.38, 8.14)	0.4736
	Placebo	11	2 (18.2)	28.8	(5.3, 28.8)			

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.5763				
Ex19Del	Osimertinib	74	34 (45.9)	27.5	(9.2, NC)	1.00	(0.54, 1.85)	0.9963
	Placebo	43	15 (34.9)	NC				
L858R	Osimertinib	68	27 (39.7)	22.0	(18.5, NC)	1.34	(0.58, 3.09)	0.4968
	Placebo	30	7 (23.3)	28.8	(10.2, NC)			

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Table LT1QDI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Dyspnoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.0842
Male	Osimertinib	53	36 (67.9)	1.9	(1.8, 5.6)	1.91	(1.01, 3.62)	0.0453 *
	Placebo	31	13 (41.9)	27.0	(2.0, 27.0)			
Female	Osimertinib	90	54 (60.0)	3.7	(1.9, 6.4)	0.96	(0.60, 1.54)	0.8685
	Placebo	42	25 (59.5)	3.7	(1.8, 8.7)			
Age	Osimertinib						Interaction test:	0.8566
< 65 years	Osimertinib	81	50 (61.7)	3.6	(1.8, 5.6)	1.23	(0.72, 2.09)	0.4412
	Placebo	39	19 (48.7)	6.6	(1.8, NC)			
>= 65 years	Osimertinib	62	40 (64.5)	3.6	(1.8, 6.4)	1.32	(0.76, 2.28)	0.3181
	Placebo	34	19 (55.9)	3.8	(1.9, 27.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.0071 #
Current/former	Osimertinib	41	28 (68.3)	1.9	(1.8, 5.6)	2.85	(1.30, 6.26)	0.0092 *
	Placebo	24	8 (33.3)	27.0	(3.7, 27.0)			
Never	Osimertinib	102	62 (60.8)	3.8	(1.9, 6.4)	0.87	(0.57, 1.35)	0.5482
	Placebo	49	30 (61.2)	2.0	(1.8, 6.6)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.0205 #
CCRT	Osimertinib	131	86 (65.6)	3.6	(1.8, 5.5)	1.47	(0.97, 2.22)	0.0671
	Placebo	62	31 (50.0)	6.6	(2.0, NC)			
SCRT	Osimertinib	12	4 (33.3)	NC		0.33	(0.10, 1.12)	0.0759
	Placebo	11	7 (63.6)	1.9	(0.9, NC)			

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.2857
IIIA	Osimertinib	52	37 (71.2)	1.9	(1.8, 5.6)	1.67	(0.87, 3.20)	0.1243
	Placebo	24	12 (50.0)	6.6	(1.9, 27.0)			
IIIB/IIIC	Osimertinib	91	53 (58.2)	3.7	(1.8, 9.2)	1.08	(0.68, 1.73)	0.7427
	Placebo	49	26 (53.1)	3.7	(1.8, NC)			
Race	Osimertinib						Interaction test:	0.4678
Asian	Osimertinib	116	77 (66.4)	3.6	(1.8, 5.5)	1.24	(0.83, 1.84)	0.2909
	Placebo	62	36 (58.1)	3.8	(1.9, 11.0)			
Non-Asian	Osimertinib	27	13 (48.1)	7.3	(1.8, 27.5)	2.12	(0.48, 9.41)	0.3213
	Placebo	11	2 (18.2)	NC				

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.2084
Yes	Osimertinib	27	12 (44.4)	10.0	(1.8, NC)	0.73	(0.29, 1.85)	0.5018
	Placebo	13	7 (53.8)	5.6	(1.0, NC)			
No	Osimertinib	116	78 (67.2)	3.6	(1.8, 5.5)	1.42	(0.94, 2.16)	0.0980
	Placebo	60	31 (51.7)	4.9	(1.9, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.0476 #
CR+PR	Osimertinib	71	43 (60.6)	1.9	(1.8, 5.6)	1.08	(0.61, 1.89)	0.7958
	Placebo	30	17 (56.7)	3.6	(1.0, NC)			
SD	Osimertinib	61	45 (73.8)	3.6	(1.8, 5.6)	1.72	(0.996, 2.98)	0.0518
	Placebo	37	18 (48.6)	8.7	(3.7, NC)			
NE	Osimertinib	11	2 (18.2)	NC		0.18	(0.03, 1.06)	0.0579
	Placebo	6	3 (50.0)	1.8	(1.0, NC)			

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.1984
Asia	Osimertinib	120	81 (67.5)	3.6	(1.8, 5.5)	1.30	(0.88, 1.93)	0.1930
	Placebo	64	36 (56.3)	4.9	(1.9, 27.0)			
Europe	Osimertinib	11	5 (45.5)	17.4	(1.0, 27.5)	0.52	(0.10, 2.68)	0.4319
	Placebo	7	2 (28.6)	1.1	(0.9, NC)			
Rest of the World	Osimertinib	12	4 (33.3)	7.3	(1.0, NC)	NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.8809
Positive	Osimertinib	10	7 (70.0)	4.6	(0.9, NC)	1.57	(0.33, 7.58)	0.5732
	Placebo	4	2 (50.0)	NC				
Negative	Osimertinib	113	71 (62.8)	1.9	(1.8, 5.5)	1.29	(0.85, 1.97)	0.2346
	Placebo	58	31 (53.4)	4.9	(1.9, NC)			
Unknown	Osimertinib	20	12 (60.0)	5.0	(1.0, 27.5)	1.01	(0.36, 2.88)	0.9801
	Placebo	11	5 (45.5)	14.4	(0.9, 27.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib		Interaction test: 0.9569				
Ex19Del	Osimertinib	74	46 (62.2)	3.7	(1.9, 5.6)	1.27	(0.76, 2.11)	0.3655
	Placebo	43	22 (51.2)	6.6	(1.8, NC)			
L858R	Osimertinib	68	43 (63.2)	2.7	(1.8, 7.4)	1.24	(0.70, 2.20)	0.4649
	Placebo	30	16 (53.3)	3.6	(1.9, NC)			

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Table LT1QII10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Insomnia by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Insomnia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.5557
Male	Osimertinib	53	29 (54.7)	21.5	(3.8, 29.5)	1.21	(0.61, 2.38)	0.5911
	Placebo	31	12 (38.7)	11.0	(7.3, NC)			
Female	Osimertinib	90	49 (54.4)	7.3	(3.6, 14.7)	1.58	(0.87, 2.87)	0.1328
	Placebo	42	14 (33.3)	23.9	(5.6, 23.9)			
Age	Osimertinib						Interaction test:	0.9644
< 65 years	Osimertinib	81	46 (56.8)	9.2	(3.6, 21.5)	1.40	(0.77, 2.58)	0.2719
	Placebo	39	14 (35.9)	11.0	(6.9, NC)			
>= 65 years	Osimertinib	62	32 (51.6)	9.2	(3.7, 27.6)	1.43	(0.74, 2.79)	0.2890
	Placebo	34	12 (35.3)	23.9	(7.3, NC)			

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Time to increase by at least 10 points in QLQ-C30 Insomnia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.8752
Current/former	Osimertinib	41	24 (58.5)	16.6	(3.6, 25.7)	1.35	(0.64, 2.84)	0.4277
	Placebo	24	10 (41.7)	11.0	(6.9, NC)			
Never	Osimertinib	102	54 (52.9)	9.1	(3.7, 14.8)	1.46	(0.83, 2.55)	0.1911
	Placebo	49	16 (32.7)	23.9	(7.4, 23.9)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.3812
CCRT	Osimertinib	131	72 (55.0)	9.2	(5.5, 21.5)	1.32	(0.83, 2.11)	0.2431
	Placebo	62	24 (38.7)	23.9	(9.1, NC)			
SCRT	Osimertinib	12	6 (50.0)	7.4	(1.0, NC)	2.69	(0.54, 13.40)	0.2262
	Placebo	11	2 (18.2)	NC				

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.2223
IIIA	Osimertinib	52	29 (55.8)	11.1	(3.6, 24.0)	2.20	(0.91, 5.32)	0.0786
	Placebo	24	6 (25.0)	NC				
IIIB/IIIC	Osimertinib	91	49 (53.8)	9.1	(3.8, 25.7)	1.19	(0.70, 2.01)	0.5211
	Placebo	49	20 (40.8)	11.0	(6.9, 23.9)			
Race	Osimertinib						Interaction test:	0.5812
Asian	Osimertinib	116	65 (56.0)	9.2	(3.8, 24.0)	1.35	(0.84, 2.18)	0.2123
	Placebo	62	24 (38.7)	23.9	(7.4, NC)			
Non-Asian	Osimertinib	27	13 (48.1)	9.2	(3.6, 27.6)	2.06	(0.47, 9.15)	0.3406
	Placebo	11	2 (18.2)	11.0	(3.6, NC)			

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.5844
Yes	Osimertinib	27	14 (51.9)	7.4	(1.8, NC)	1.09	(0.39, 3.03)	0.8709
	Placebo	13	5 (38.5)	6.9	(1.0, NC)			
No	Osimertinib	116	64 (55.2)	9.2	(5.5, 22.1)	1.50	(0.91, 2.47)	0.1103
	Placebo	60	21 (35.0)	23.9	(9.2, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.1171
CR+PR	Osimertinib	71	35 (49.3)	9.2	(5.5, 29.5)	1.25	(0.65, 2.42)	0.5066
	Placebo	30	12 (40.0)	11.0	(7.3, NC)			
SD	Osimertinib	61	39 (63.9)	9.2	(3.6, 21.5)	1.94	(0.99, 3.80)	0.0544
	Placebo	37	11 (29.7)	23.9	(9.2, NC)			
NE	Osimertinib	11	4 (36.4)	5.5	(1.8, NC)	0.32	(0.07, 1.44)	0.1364
	Placebo	6	3 (50.0)	1.4	(1.0, NC)			

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Table LT1QII10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Insomnia by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Insomnia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.2470
Asia	Osimertinib	120	69 (57.5)	9.2	(5.5, 21.5)	1.43	(0.89, 2.28)	0.1404
	Placebo	64	24 (37.5)	23.9	(9.1, NC)			
Europe	Osimertinib	11	5 (45.5)	11.0	(1.9, NC)	NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	4 (33.3)	27.6	(0.9, 27.6)	0.62	(0.11, 3.37)	0.5753
	Placebo	2	2 (100.0)	7.3	(3.6, 11.0)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.0263 #
Positive	Osimertinib	10	8 (80.0)	9.2	(1.9, 43.8)	1.24	(0.26, 5.88)	0.7848
	Placebo	4	2 (50.0)	6.9	(5.6, NC)			
Negative	Osimertinib	113	59 (52.2)	9.2	(5.5, 22.1)	1.20	(0.74, 1.94)	0.4641
	Placebo	58	24 (41.4)	23.9	(7.4, 23.9)			
Unknown	Osimertinib	20	11 (55.0)	6.4	(1.9, 29.5)	NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Table LT1QII10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Insomnia by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Insomnia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.3320				
Ex19Del	Osimertinib	74	39 (52.7)	9.2	(3.7, 43.8)	1.17	(0.65, 2.08)	0.6018
	Placebo	43	17 (39.5)	11.0	(7.3, NC)			
L858R	Osimertinib	68	38 (55.9)	9.2	(3.6, 22.1)	1.83	(0.89, 3.80)	0.1027
	Placebo	30	9 (30.0)	23.9	(6.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QAI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Appetite loss				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.9152
Male	Osimertinib	53	30 (56.6)	12.9	(3.7, 33.1)	1.35	(0.69, 2.66)	0.3775
	Placebo	31	12 (38.7)	27.0	(8.3, 27.0)			
Female	Osimertinib	90	52 (57.8)	3.7	(1.9, 12.9)	1.29	(0.78, 2.15)	0.3221
	Placebo	42	21 (50.0)	7.3	(4.9, NC)			
Age	Osimertinib						Interaction test:	0.7368
< 65 years	Osimertinib	81	45 (55.6)	9.1	(3.7, 25.7)	1.45	(0.79, 2.67)	0.2259
	Placebo	39	14 (35.9)	11.8	(7.3, NC)			
>= 65 years	Osimertinib	62	37 (59.7)	3.6	(1.9, 12.9)	1.26	(0.73, 2.20)	0.4072
	Placebo	34	19 (55.9)	8.3	(3.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QAI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Appetite loss				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.3727
Current/former	Osimertinib	41	26 (63.4)	3.8	(1.8, 25.7)	1.72	(0.83, 3.58)	0.1473
	Placebo	24	10 (41.7)	27.0	(8.3, 27.0)			
Never	Osimertinib	102	56 (54.9)	6.9	(3.6, 18.3)	1.16	(0.71, 1.89)	0.5572
	Placebo	49	23 (46.9)	7.4	(4.9, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.0011 #
CCRT	Osimertinib	131	80 (61.1)	5.5	(1.9, 12.9)	1.63	(1.05, 2.55)	0.0310 *
	Placebo	62	26 (41.9)	12.7	(7.4, NC)			
SCRT	Osimertinib	12	2 (16.7)	NC		0.14	(0.03, 0.70)	0.0160 *
	Placebo	11	7 (63.6)	3.8	(0.9, 7.3)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QAI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Appetite loss				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.7275
IIIA	Osimertinib	52	29 (55.8)	5.5	(1.9, 22.0)	1.46	(0.72, 2.92)	0.2916
	Placebo	24	11 (45.8)	11.4	(6.6, NC)			
IIIB/IIIC	Osimertinib	91	53 (58.2)	9.2	(2.0, 20.2)	1.25	(0.76, 2.07)	0.3837
	Placebo	49	22 (44.9)	11.8	(3.9, NC)			
Race	Osimertinib						Interaction test:	0.4092
Asian	Osimertinib	116	68 (58.6)	5.6	(2.1, 20.2)	1.38	(0.88, 2.15)	0.1570
	Placebo	62	28 (45.2)	11.8	(7.3, NC)			
Non-Asian	Osimertinib	27	14 (51.9)	6.4	(1.8, 18.3)	0.85	(0.31, 2.37)	0.7578
	Placebo	11	5 (45.5)	3.8	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Table LT1QAI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Appetite loss				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.3205
Yes	Osimertinib	27	10 (37.0)	NC		0.78	(0.24, 2.51)	0.6795
	Placebo	13	4 (30.8)	NC				
No	Osimertinib	116	72 (62.1)	3.7	(1.9, 9.1)	1.50	(0.97, 2.32)	0.0657
	Placebo	60	29 (48.3)	11.4	(5.9, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.2125
CR+PR	Osimertinib	71	46 (64.8)	3.6	(1.9, 6.4)	1.61	(0.89, 2.90)	0.1123
	Placebo	30	15 (50.0)	11.0	(5.6, NC)			
SD	Osimertinib	61	33 (54.1)	18.3	(3.7, NC)	1.22	(0.66, 2.26)	0.5206
	Placebo	37	15 (40.5)	27.0	(6.6, NC)			
NE	Osimertinib	11	3 (27.3)	NC		0.34	(0.07, 1.68)	0.1845
	Placebo	6	3 (50.0)	1.0	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QAI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Appetite loss				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.0099 #
Asia	Osimertinib	120	71 (59.2)	6.9	(3.6, 18.3)	1.35	(0.88, 2.10)	0.1732
	Placebo	64	29 (45.3)	11.4	(7.3, NC)			
Europe	Osimertinib	11	5 (45.5)	6.4	(1.8, NC)	0.26	(0.07, 0.98)	0.0467 *
	Placebo	7	4 (57.1)	1.0	(0.9, 3.8)			
Rest of the World	Osimertinib	12	6 (50.0)	1.8	(0.9, 12.9)	NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.9865
Positive	Osimertinib	10	7 (70.0)	6.2	(1.8, NC)	1.22	(0.25, 5.87)	0.8074
	Placebo	4	2 (50.0)	12.7	(0.9, 12.7)			
Negative	Osimertinib	113	64 (56.6)	9.1	(2.0, 20.2)	1.31	(0.83, 2.07)	0.2403
	Placebo	58	27 (46.6)	11.1	(6.6, NC)			
Unknown	Osimertinib	20	11 (55.0)	3.6	(0.9, NC)	1.42	(0.45, 4.48)	0.5466
	Placebo	11	4 (36.4)	27.0	(0.9, 27.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Table LT1QAI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Appetite loss				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib		Interaction test: 0.8085				
Ex19Del	Osimertinib	74	40 (54.1)	6.9	(3.7, 22.0)	1.34	(0.77, 2.35)	0.3011
	Placebo	43	18 (41.9)	11.8	(7.3, NC)			
L858R	Osimertinib	68	41 (60.3)	5.6	(1.9, 18.3)	1.22	(0.67, 2.20)	0.5204
	Placebo	30	15 (50.0)	8.3	(3.7, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QCI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Constipation by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Constipation				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.1091
Male	Osimertinib	53	27 (50.9)	14.7	(3.8, NC)	0.91	(0.47, 1.75)	0.7756
	Placebo	31	14 (45.2)	11.5	(5.9, NC)			
Female	Osimertinib	90	45 (50.0)	14.7	(7.4, 25.8)	1.95	(0.98, 3.89)	0.0573
	Placebo	42	10 (23.8)	22.0	(22.0, NC)			
Age	Osimertinib						Interaction test:	0.9454
< 65 years	Osimertinib	81	43 (53.1)	14.7	(5.5, 25.8)	1.36	(0.71, 2.61)	0.3555
	Placebo	39	12 (30.8)	NC				
>= 65 years	Osimertinib	62	29 (46.8)	14.7	(6.9, NC)	1.32	(0.67, 2.58)	0.4253
	Placebo	34	12 (35.3)	22.0	(8.2, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QCI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Constipation by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Constipation				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.7169
Current/former	Osimertinib	41	22 (53.7)	11.1	(4.6, NC)	1.21	(0.57, 2.57)	0.6150
	Placebo	24	10 (41.7)	16.9	(8.2, NC)			
Never	Osimertinib	102	50 (49.0)	14.7	(7.3, 25.8)	1.45	(0.79, 2.63)	0.2269
	Placebo	49	14 (28.6)	22.0	(7.3, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.3673
CCRT	Osimertinib	131	67 (51.1)	13.0	(9.1, 25.7)	1.46	(0.88, 2.42)	0.1435
	Placebo	62	20 (32.3)	22.0	(11.5, NC)			
SCRT	Osimertinib	12	5 (41.7)	16.5	(0.9, NC)	0.76	(0.20, 2.83)	0.6778
	Placebo	11	4 (36.4)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QCI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Constipation by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Constipation				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.1560
IIIA	Osimertinib	52	32 (61.5)	11.1	(3.6, 18.9)	2.10	(0.93, 4.77)	0.0756
	Placebo	24	7 (29.2)	NC				
IIIB/IIIC	Osimertinib	91	40 (44.0)	25.7	(9.2, NC)	1.04	(0.58, 1.85)	0.8940
	Placebo	49	17 (34.7)	22.0	(7.3, 22.0)			
Race	Osimertinib						Interaction test:	0.7412
Asian	Osimertinib	116	62 (53.4)	14.7	(9.2, 25.8)	1.37	(0.83, 2.26)	0.2212
	Placebo	62	21 (33.9)	22.0	(11.5, NC)			
Non-Asian	Osimertinib	27	10 (37.0)	7.3	(1.9, NC)	1.08	(0.30, 3.93)	0.9067
	Placebo	11	3 (27.3)	8.2	(1.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1QCI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Constipation by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Constipation				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.0261 #
Yes	Osimertinib	27	13 (48.1)	16.5	(3.6, NC)	0.48	(0.19, 1.22)	0.1238
	Placebo	13	7 (53.8)	5.6	(0.9, NC)			
No	Osimertinib	116	59 (50.9)	13.0	(7.3, 25.8)	1.71	(0.99, 2.96)	0.0532
	Placebo	60	17 (28.3)	22.0	(16.9, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.6916
CR+PR	Osimertinib	71	37 (52.1)	11.0	(3.6, 25.7)	1.67	(0.83, 3.37)	0.1543
	Placebo	30	10 (33.3)	16.9	(5.9, NC)			
SD	Osimertinib	61	33 (54.1)	16.5	(7.4, NC)	1.13	(0.59, 2.15)	0.7184
	Placebo	37	13 (35.1)	22.0	(7.3, NC)			
NE	Osimertinib	11	2 (18.2)	NC		0.96	(0.09, 10.55)	0.9702
	Placebo	6	1 (16.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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QLQ-C30: EORTC Quality of Life Questionnaire - Core 30 items.

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Table LT1QCI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Constipation by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Constipation				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.2796
Asia	Osimertinib	120	66 (55.0)	14.7	(9.2, 25.7)	1.46	(0.89, 2.40)	0.1386
	Placebo	64	21 (32.8)	22.0	(11.5, NC)			
Europe	Osimertinib	11	3 (27.3)	NC		0.28	(0.05, 1.70)	0.1676
	Placebo	7	2 (28.6)	3.6	(1.9, 5.3)			
Rest of the World	Osimertinib	12	3 (25.0)	3.6	(0.9, NC)	1.47	(0.15, 14.14)	0.7405
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.4195
Positive	Osimertinib	10	8 (80.0)	10.1	(0.9, 25.8)	0.71	(0.19, 2.69)	0.6104
	Placebo	4	3 (75.0)	5.3	(1.9, NC)			
Negative	Osimertinib	113	55 (48.7)	14.7	(9.1, 27.6)	1.56	(0.90, 2.70)	0.1144
	Placebo	58	17 (29.3)	22.0	(16.9, NC)			
Unknown	Osimertinib	20	9 (45.0)	16.5	(1.0, NC)	0.81	(0.25, 2.64)	0.7254
	Placebo	11	4 (36.4)	5.9	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Table LT1QCI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Constipation by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Constipation				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib		Interaction test: 0.5459				
Ex19Del	Osimertinib	74	41 (55.4)	12.8	(5.5, 25.7)	1.54	(0.83, 2.84)	0.1667
	Placebo	43	14 (32.6)	NC				
L858R	Osimertinib	68	30 (44.1)	14.7	(9.2, NC)	1.15	(0.56, 2.37)	0.6990
	Placebo	30	10 (33.3)	16.9	(5.6, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1QHI10T_SFTM: Time to increase by at least 10 points in EORTC QLQ-C30 Diarrhoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Diarrhoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.1276
Male	Osimertinib	53	38 (71.7)	3.8	(3.6, 9.2)	1.37	(0.78, 2.41)	0.2699
	Placebo	31	18 (58.1)	8.3	(5.1, 11.4)			
Female	Osimertinib	90	57 (63.3)	3.7	(1.9, 7.3)	2.55	(1.44, 4.51)	0.0013 *
	Placebo	42	15 (35.7)	13.0	(7.8, NC)			
Age	Osimertinib						Interaction test:	0.4744
< 65 years	Osimertinib	81	56 (69.1)	3.7	(1.8, 5.5)	1.66	(0.99, 2.77)	0.0543
	Placebo	39	20 (51.3)	7.8	(5.9, 11.4)			
>= 65 years	Osimertinib	62	39 (62.9)	5.5	(1.9, 11.0)	2.23	(1.19, 4.17)	0.0126 *
	Placebo	34	13 (38.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QHI10T_SFTM: Time to increase by at least 10 points in EORTC QLQ-C30 Diarrhoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Diarrhoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.0828
Current/former	Osimertinib	41	31 (75.6)	5.5	(1.0, 9.2)	1.27	(0.70, 2.29)	0.4318
	Placebo	24	17 (70.8)	7.8	(5.1, 11.4)			
Never	Osimertinib	102	64 (62.7)	3.7	(1.9, 7.3)	2.59	(1.49, 4.49)	0.0007 *
	Placebo	49	16 (32.7)	13.0	(8.0, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.6744
CCRT	Osimertinib	131	89 (67.9)	3.7	(1.9, 5.6)	1.95	(1.28, 2.97)	0.0019 *
	Placebo	62	29 (46.8)	10.5	(7.3, NC)			
SCRT	Osimertinib	12	6 (50.0)	5.5	(0.9, NC)	1.46	(0.41, 5.18)	0.5597
	Placebo	11	4 (36.4)	13.0	(1.1, 13.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QHI10T_SFTM: Time to increase by at least 10 points in EORTC QLQ-C30 Diarrhoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Diarrhoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.2516
IIIA	Osimertinib	52	37 (71.2)	3.7	(1.9, 7.3)	2.63	(1.30, 5.31)	0.0070 *
	Placebo	24	10 (41.7)	13.0	(7.2, NC)			
IIIB/IIIC	Osimertinib	91	58 (63.7)	5.5	(1.9, 7.3)	1.60	(0.98, 2.61)	0.0584
	Placebo	49	23 (46.9)	8.0	(7.3, NC)			
Race	Osimertinib						Interaction test:	0.2933
Asian	Osimertinib	116	82 (70.7)	3.8	(3.6, 5.6)	2.04	(1.32, 3.13)	0.0012 *
	Placebo	62	28 (45.2)	11.0	(7.4, NC)			
Non-Asian	Osimertinib	27	13 (48.1)	1.9	(1.8, 7.3)	1.09	(0.39, 3.08)	0.8649
	Placebo	11	5 (45.5)	8.1	(1.0, 13.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QHI10T_SFTM: Time to increase by at least 10 points in EORTC QLQ-C30 Diarrhoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Diarrhoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.0833
Yes	Osimertinib	27	14 (51.9)	14.7	(1.8, NC)	0.85	(0.32, 2.22)	0.7386
	Placebo	13	6 (46.2)	7.4	(2.0, NC)			
No	Osimertinib	116	81 (69.8)	3.7	(1.9, 5.5)	2.27	(1.46, 3.52)	0.0003 *
	Placebo	60	27 (45.0)	11.0	(7.8, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.9143
CR+PR	Osimertinib	71	48 (67.6)	3.8	(1.9, 7.3)	1.77	(1.002, 3.12)	0.0494 *
	Placebo	30	16 (53.3)	8.3	(7.2, 11.4)			
SD	Osimertinib	61	42 (68.9)	5.5	(1.9, 11.0)	1.96	(1.09, 3.55)	0.0257 *
	Placebo	37	15 (40.5)	18.8	(7.4, NC)			
NE	Osimertinib	11	5 (45.5)	1.8	(0.9, NC)	2.49	(0.48, 12.83)	0.2769
	Placebo	6	2 (33.3)	NC				

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Table LT1QHI10T_SFTM: Time to increase by at least 10 points in EORTC QLQ-C30 Diarrhoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Diarrhoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.5771
Asia	Osimertinib	120	85 (70.8)	3.8	(3.6, 5.6)	2.03	(1.33, 3.10)	0.0010 *
	Placebo	64	29 (45.3)	11.0	(7.4, NC)			
Europe	Osimertinib	11	5 (45.5)	4.6	(1.8, NC)	0.88	(0.17, 4.57)	0.8837
	Placebo	7	2 (28.6)	8.9	(1.1, 8.9)			
Rest of the World	Osimertinib	12	5 (41.7)	1.9	(0.9, 3.6)	1.21	(0.23, 6.31)	0.8187
	Placebo	2	2 (100.0)	4.1	(1.0, 7.3)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.8177
Positive	Osimertinib	10	9 (90.0)	4.6	(0.9, 16.6)	3.48	(0.44, 27.56)	0.2371
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	74 (65.5)	3.8	(3.6, 7.3)	1.85	(1.20, 2.86)	0.0058 *
	Placebo	58	28 (48.3)	10.5	(7.4, 18.8)			
Unknown	Osimertinib	20	12 (60.0)	1.9	(0.9, 20.2)	1.89	(0.61, 5.88)	0.2702
	Placebo	11	4 (36.4)	8.9	(1.1, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Table LT1QHI10T_SFTM: Time to increase by at least 10 points in EORTC QLQ-C30 Diarrhoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Diarrhoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.8528				
Ex19Del	Osimertinib	74	50 (67.6)	3.7	(1.9, 5.5)	1.95	(1.16, 3.29)	0.0118 *
	Placebo	43	20 (46.5)	11.4	(7.2, NC)			
L858R	Osimertinib	68	44 (64.7)	5.5	(1.9, 9.2)	1.81	(0.97, 3.36)	0.0605
	Placebo	30	13 (43.3)	10.5	(7.4, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1QMI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Financial difficulties by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Financial difficulties				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.4843
Male	Osimertinib	53	18 (34.0)	NC		0.78	(0.36, 1.71)	0.5388
	Placebo	31	10 (32.3)	NC				
Female	Osimertinib	90	32 (35.6)	33.2	(13.2, NC)	1.13	(0.58, 2.20)	0.7254
	Placebo	42	12 (28.6)	18.8	(13.0, NC)			
Age	Osimertinib						Interaction test:	0.9769
< 65 years	Osimertinib	81	35 (43.2)	25.8	(11.0, NC)	0.92	(0.49, 1.73)	0.7976
	Placebo	39	14 (35.9)	NC				
>= 65 years	Osimertinib	62	15 (24.2)	NC		0.94	(0.40, 2.21)	0.8786
	Placebo	34	8 (23.5)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QMI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Financial difficulties by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Financial difficulties				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.2339
Current/former	Osimertinib	41	13 (31.7)	NC		0.63	(0.27, 1.49)	0.2917
	Placebo	24	9 (37.5)	NC				
Never	Osimertinib	102	37 (36.3)	33.2	(13.2, NC)	1.20	(0.64, 2.28)	0.5676
	Placebo	49	13 (26.5)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.2187
CCRT	Osimertinib	131	46 (35.1)	NC		0.88	(0.52, 1.48)	0.6195
	Placebo	62	21 (33.9)	NC				
SCRT	Osimertinib	12	4 (33.3)	23.9	(0.9, NC)	3.17	(0.35, 28.38)	0.3032
	Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QMI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Financial difficulties by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Financial difficulties				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib							Interaction test: 0.7833
IIIA	Osimertinib	52	17 (32.7)	NC		1.09	(0.43, 2.78)	0.8521
	Placebo	24	6 (25.0)	NC				
IIIB/IIIC	Osimertinib	91	33 (36.3)	NC		0.94	(0.51, 1.72)	0.8320
	Placebo	49	16 (32.7)	18.8	(8.7, NC)			
Race	Osimertinib							Interaction test: 0.7731
Asian	Osimertinib	116	41 (35.3)	NC		0.97	(0.56, 1.68)	0.9124
	Placebo	62	19 (30.6)	NC				
Non-Asian	Osimertinib	27	9 (33.3)	NC		0.78	(0.21, 2.91)	0.7169
	Placebo	11	3 (27.3)	13.0	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QMI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Financial difficulties by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Financial difficulties				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.9609
Yes	Osimertinib	27	8 (29.6)	NC		0.95	(0.25, 3.60)	0.9381
	Placebo	13	3 (23.1)	NC				
No	Osimertinib	116	42 (36.2)	NC		0.98	(0.57, 1.70)	0.9520
	Placebo	60	19 (31.7)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.1363
CR+PR	Osimertinib	71	25 (35.2)	NC		0.68	(0.35, 1.34)	0.2651
	Placebo	30	13 (43.3)	9.2	(3.7, NC)			
SD	Osimertinib	61	22 (36.1)	NC		1.16	(0.53, 2.54)	0.7055
	Placebo	37	9 (24.3)	NC				
NE	Osimertinib	11	3 (27.3)	12.9	(1.8, NC)	NC		NC
	Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QMI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Financial difficulties by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Financial difficulties				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.7789
Asia	Osimertinib	120	43 (35.8)	NC		0.96	(0.56, 1.64)	0.8746
	Placebo	64	20 (31.3)	NC				
Europe	Osimertinib	11	5 (45.5)	7.4	(1.0, NC)	1.35	(0.16, 11.61)	0.7861
	Placebo	7	1 (14.3)	NC				
Rest of the World	Osimertinib	12	2 (16.7)	NC		0.42	(0.04, 4.67)	0.4827
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.4977
Positive	Osimertinib	10	5 (50.0)	33.2	(0.9, NC)	1.42	(0.16, 12.26)	0.7502
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	36 (31.9)	NC		0.84	(0.48, 1.47)	0.5316
	Placebo	58	19 (32.8)	18.8	(11.0, NC)			
Unknown	Osimertinib	20	9 (45.0)	9.2	(0.9, NC)	2.01	(0.43, 9.33)	0.3741
	Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QMI10T_SFTM: Time to increase by at least 10 points in QLQ-C30 Financial difficulties by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-C30 Financial difficulties				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib							Interaction test: 0.3012
Ex19Del	Osimertinib	74	25 (33.8)	NC		0.79	(0.41, 1.51)	0.4727
	Placebo	43	15 (34.9)	18.8	(9.2, NC)			
L858R	Osimertinib	68	25 (36.8)	NC		1.36	(0.59, 3.16)	0.4687
	Placebo	30	7 (23.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca

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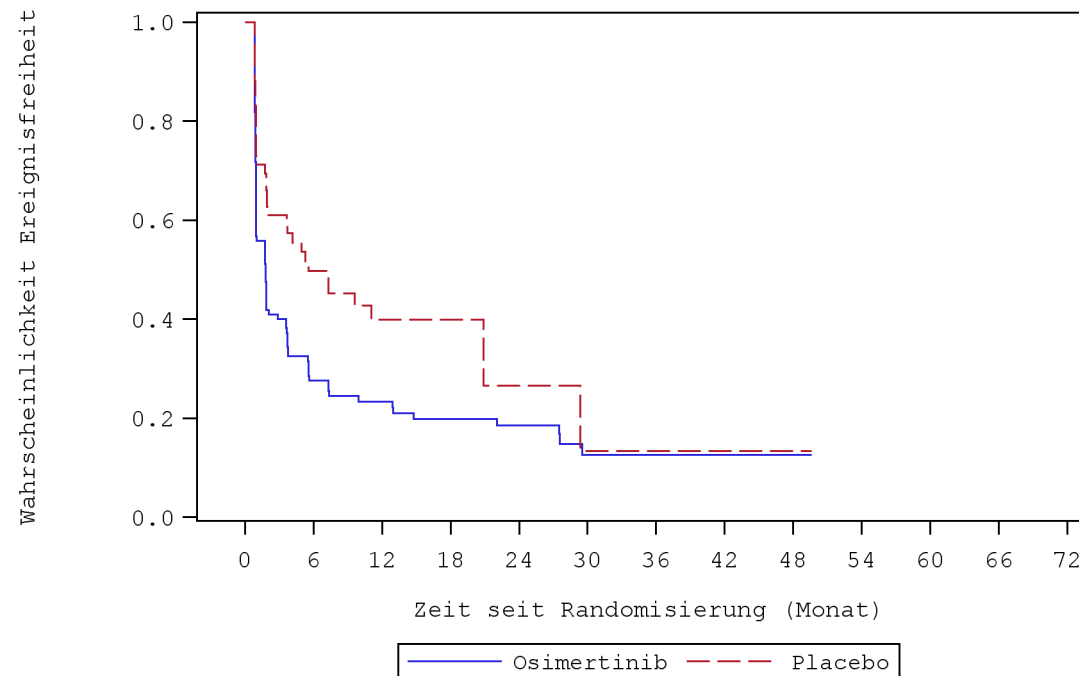
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Figure LF1QFI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Fatigue by main subgroups

Full Analysis Set

Study: LAURA

Race: Asian



Osimertinib	116	27	20	17	11	6	6	3	1	0
Placebo	62	25	10	6	2	1	1	1	1	0

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QFI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

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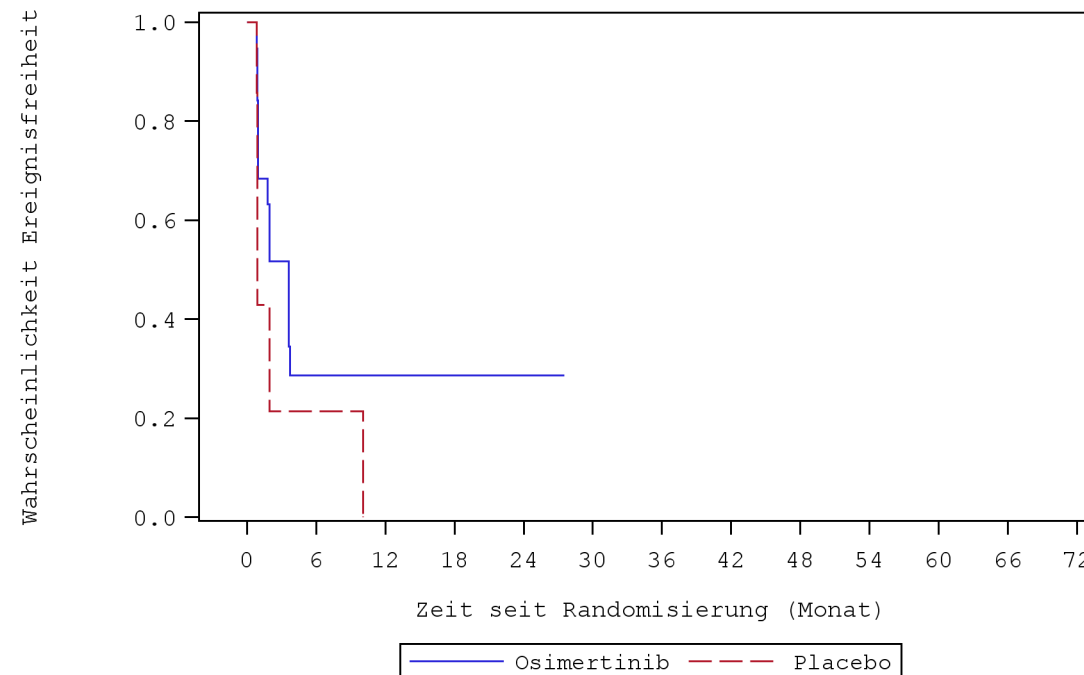
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Figure LF1QFI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Fatigue by main subgroups

Full Analysis Set

Study: LAURA

Race: Non-Asian



Osimertinib	27	5	4	3	3	0
Placebo	11	1	0			

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QFI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

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Program Name: LF1_APRO_TTE_KS.sas

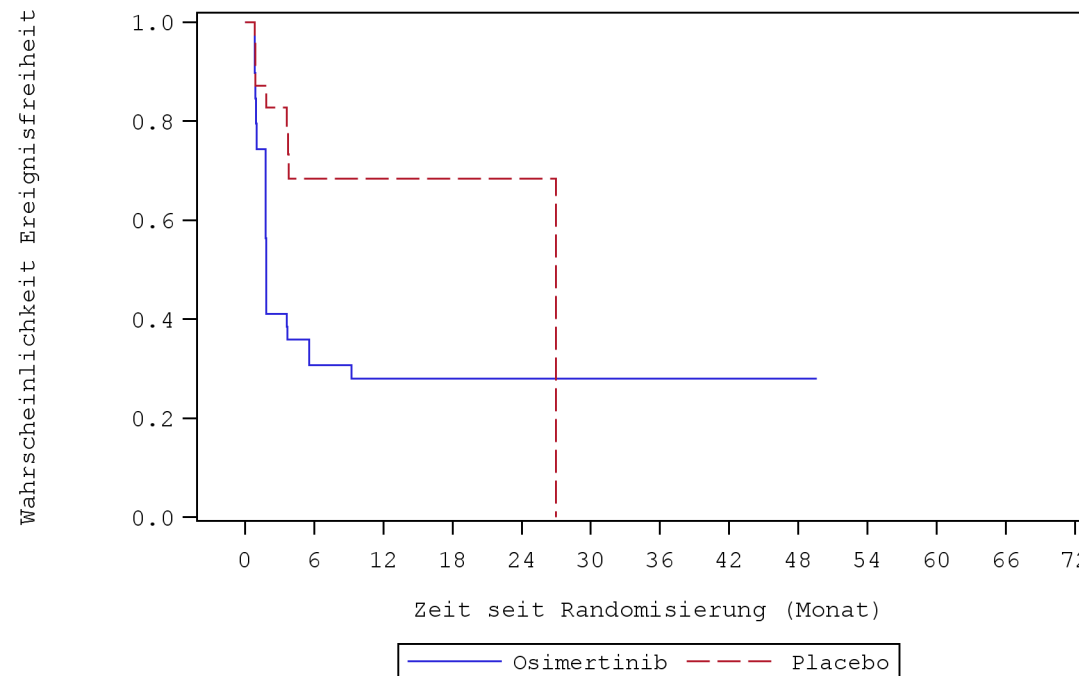
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Figure LF1QDI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Dyspnoea by main subgroups

Full Analysis Set

Study: LAURA

Smoking status: Current/former



Osimertinib	41	11	7	7	5	4	2	1	1	0
Placebo	24	14	5	2	1	0				

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QDI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APRO_TTE_KS.sas

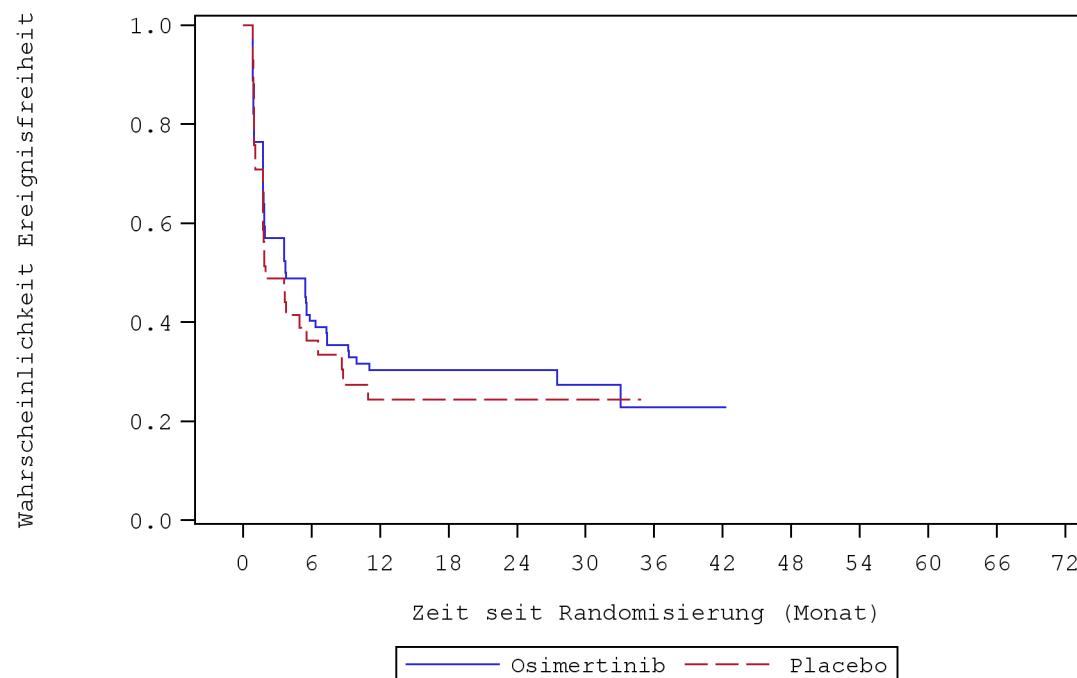
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Figure LF1QDI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Dyspnoea by main subgroups

Full Analysis Set

Study: LAURA

Smoking status: Never



Osimertinib	102	33	23	18	12	8	3	1	0
Placebo	49	14	7	2	1	1	0		

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QDI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

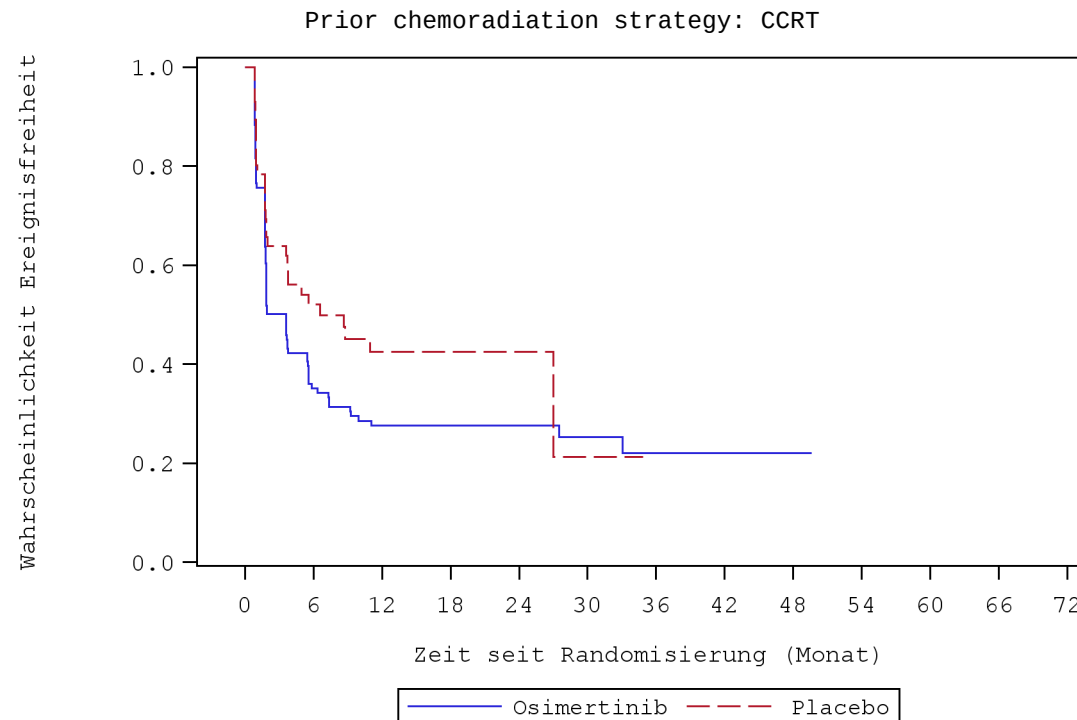
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Figure LF1QDI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Dyspnoea by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	131	38	25	21	14	10	4	1	1	0
Placebo	62	26	11	4	2	1	0			

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
Reference table: LT1QDI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

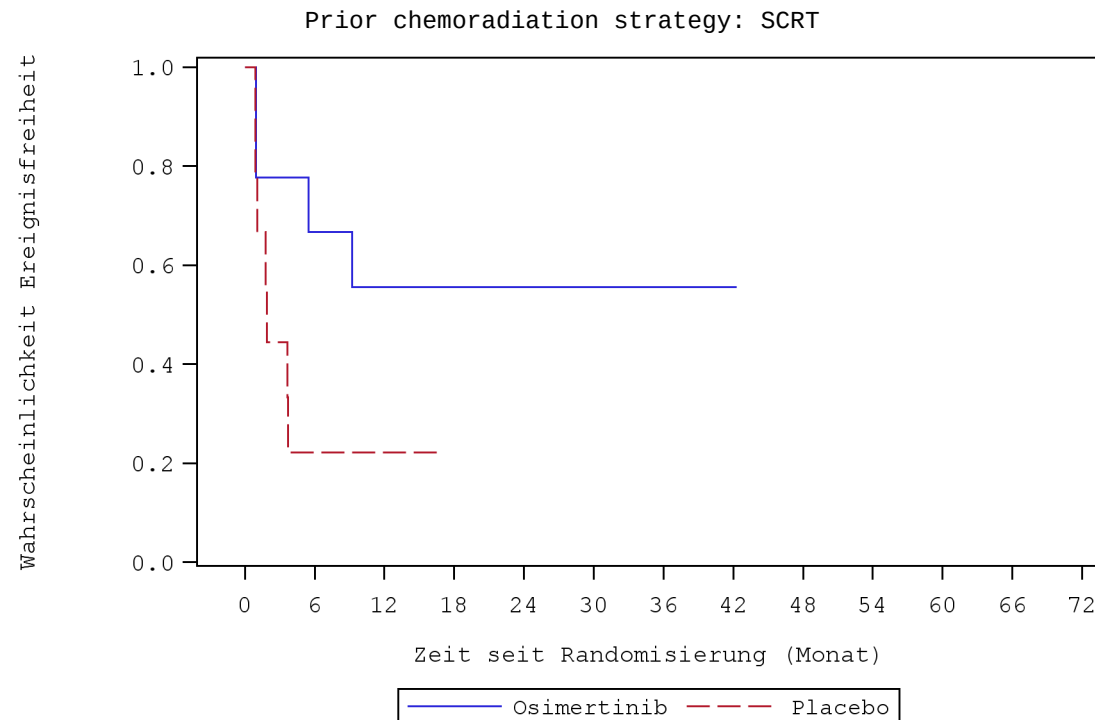
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Figure LF1QDI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Dyspnoea by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	12	6	5	4	3	2	1	1	0
Placebo	11	2	1	0					

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
Reference table: LT1QDI10T_SFTM

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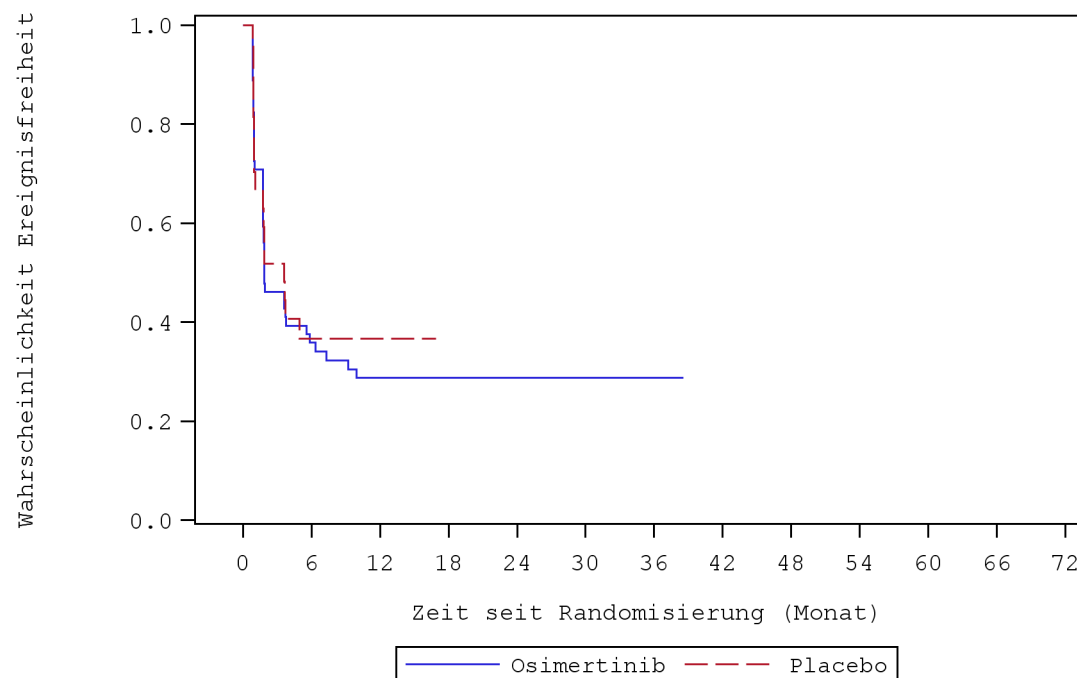
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Figure LF1QDI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Dyspnoea by main subgroups

Full Analysis Set

Study: LAURA

Response to prior CRT: CR+PR



Osimertinib	71	20	15	12	9	7	3	0
Placebo	30	9	3	0				

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QDI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

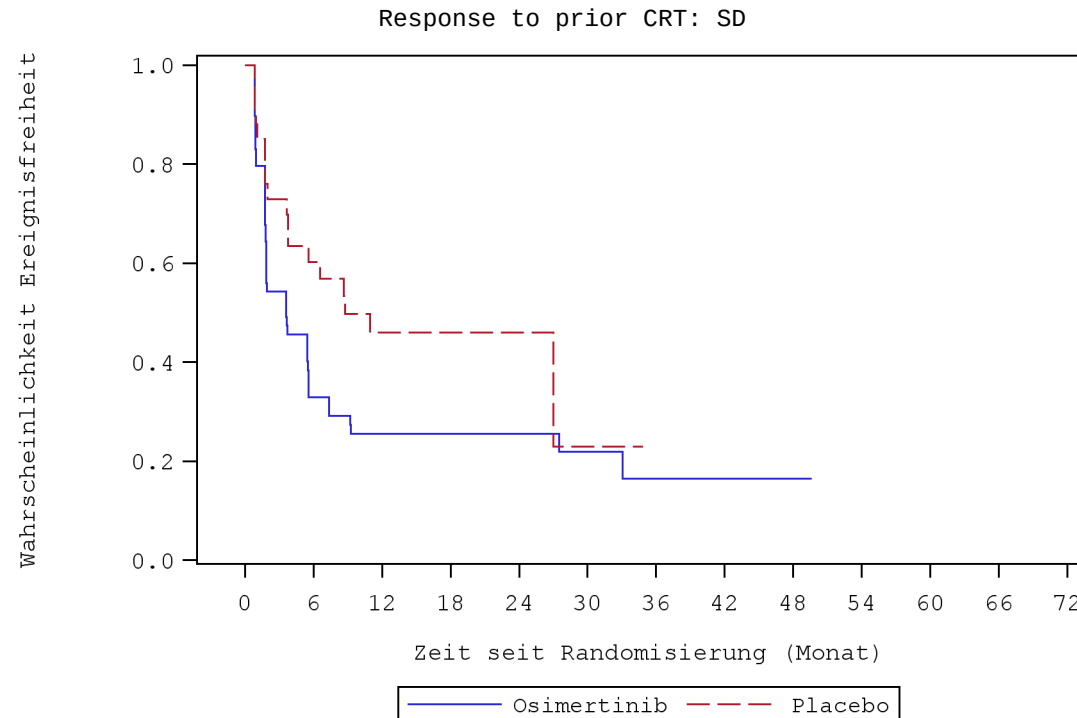
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Figure LF1QDI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Dyspnoea by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	61	18	13	11	7	5	2	2	1	0
Placebo	37	19	9	4	2	1	0			

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
Reference table: LT1QDI10T_SFTM

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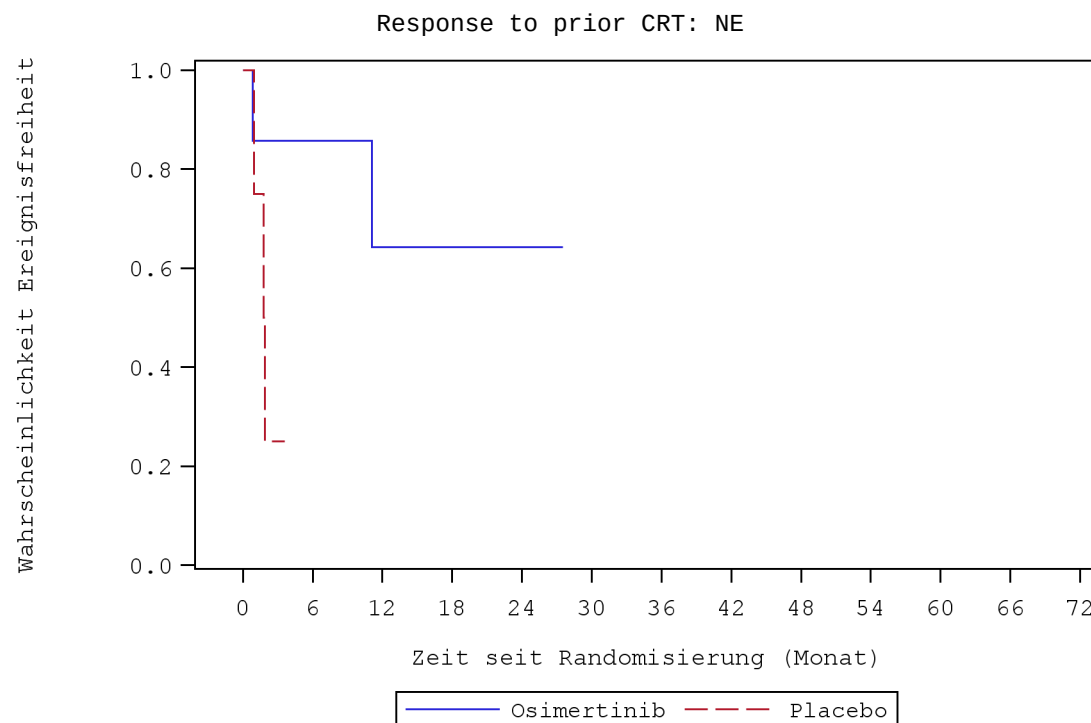
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Figure LF1QDI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Dyspnoea by main subgroups

Full Analysis Set

Study: LAURA



Osimertinib	11	6	2	2	1	0
Placebo	6	0				

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QDI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

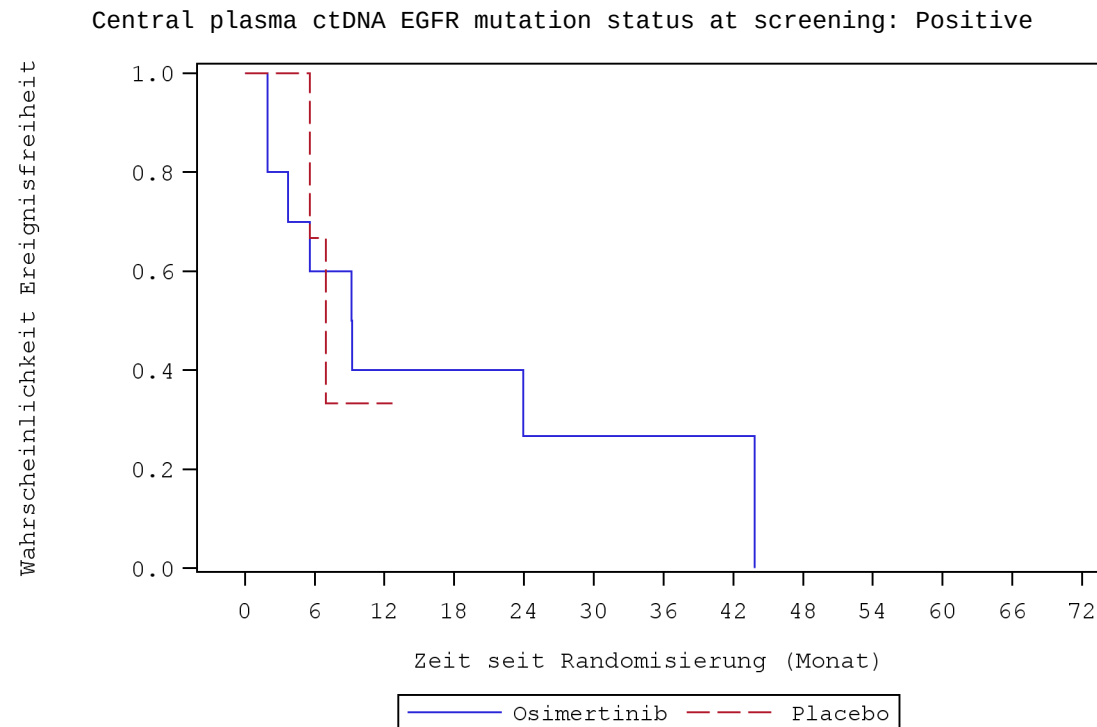
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Figure LF1QII10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Insomnia by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	10	6	4	4	2	2	2	1	0
Placebo	4	2	1	0					

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
Reference table: LT1QII10T_SFTM

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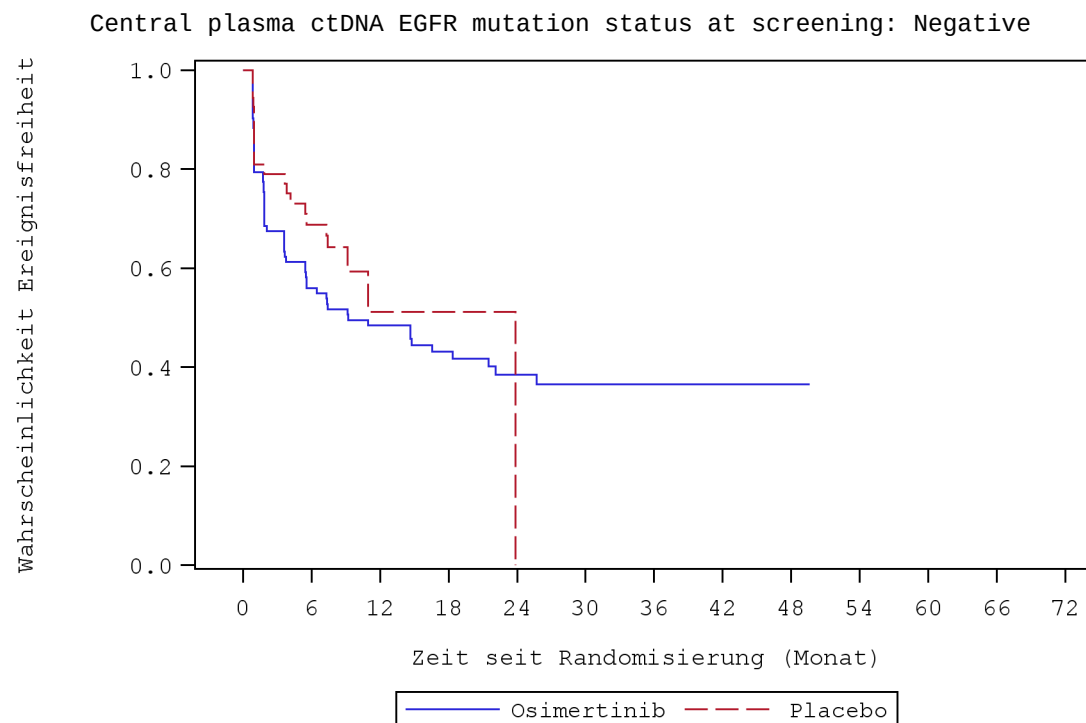
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Figure LF1QII10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Insomnia by main subgroups

Full Analysis Set

Study: LAURA



Osimertinib	113	52	39	31	20	13	10	5	2	0
Placebo	58	32	15	5	0					

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QII10T_SFTM

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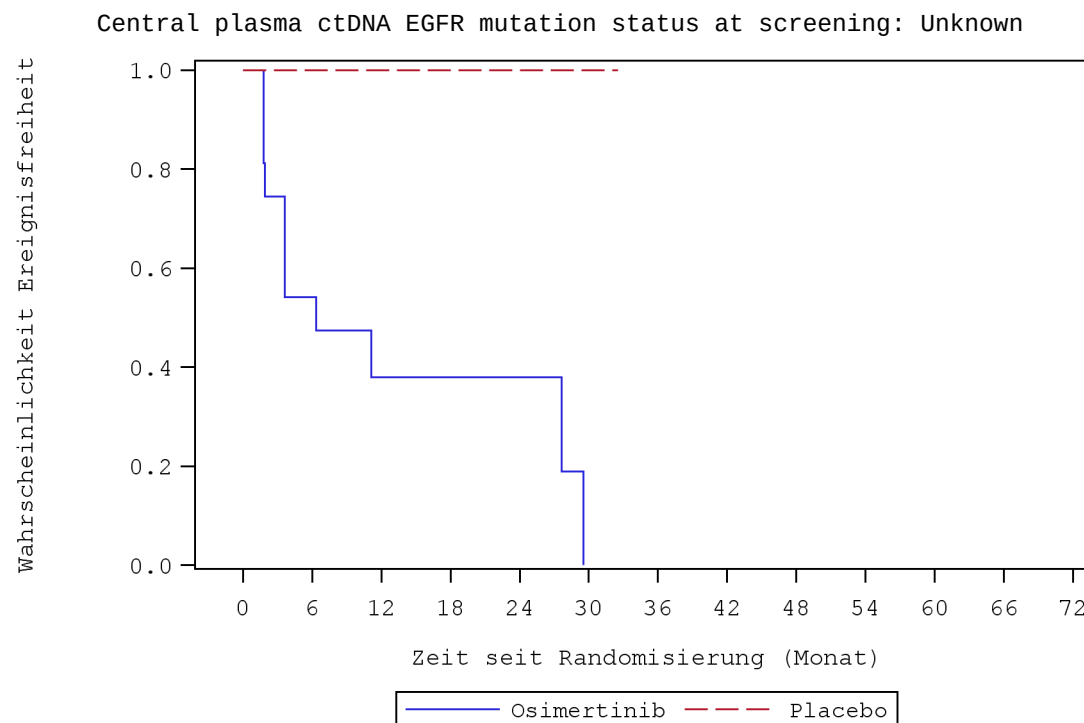
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Figure LF1QII10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Insomnia by main subgroups

Full Analysis Set

Study: LAURA



Osimertinib	20	8	4	3	3	0	
Placebo	11	5	2	1	1	1	0

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QII10T_SFTM

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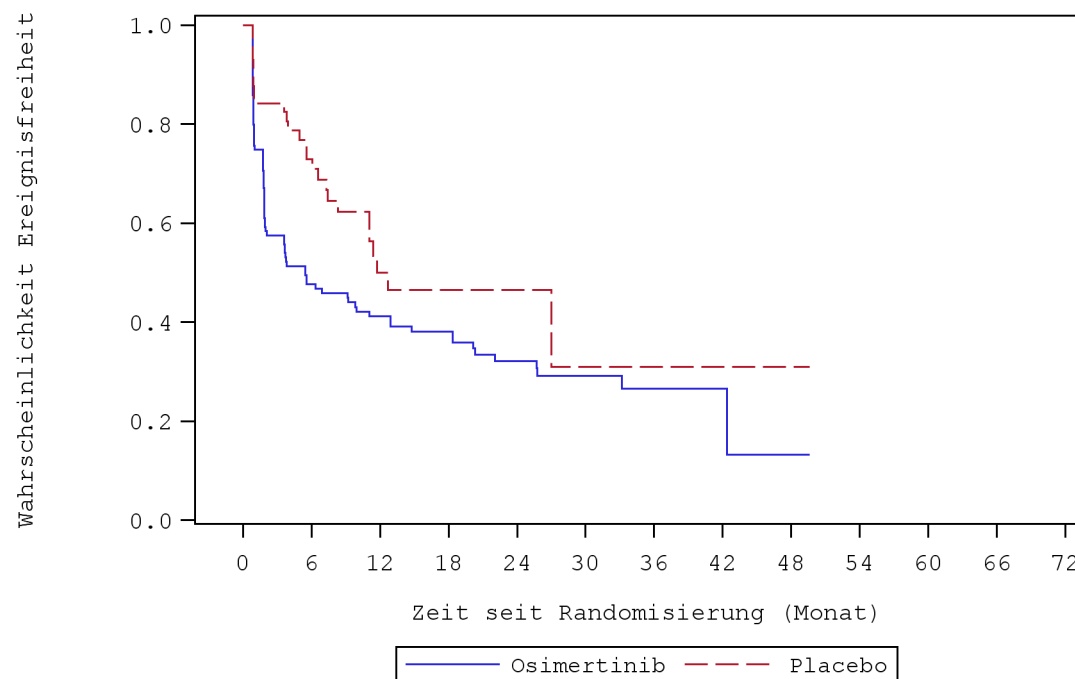
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Figure LF1QAI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups

Full Analysis Set

Study: LAURA

Prior chemoradiation strategy: CCRT



Osimertinib	131	52	40	36	23	15	7	2	1	0
Placebo	62	38	14	6	3	2	1	1	1	0

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QAI10T_SFTM

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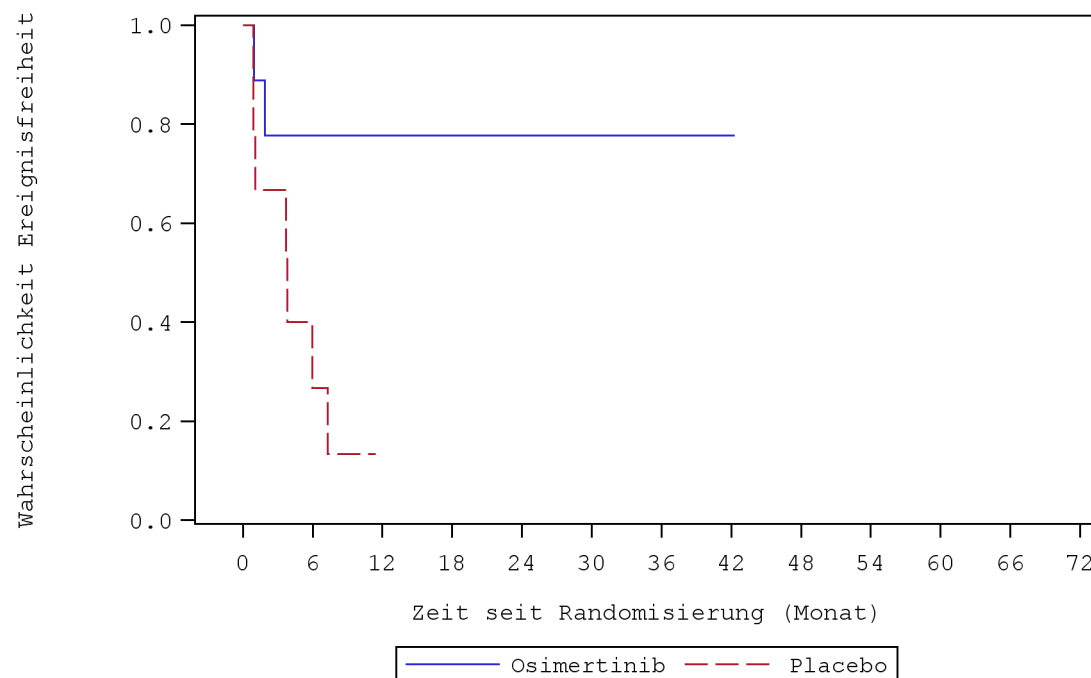
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Figure LF1QAI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups

Full Analysis Set

Study: LAURA

Prior chemoradiation strategy: SCRT



Osimertinib	12	7	7	5	4	3	1	1	0
Placebo	11	2	0						

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QAI10T_SFTM

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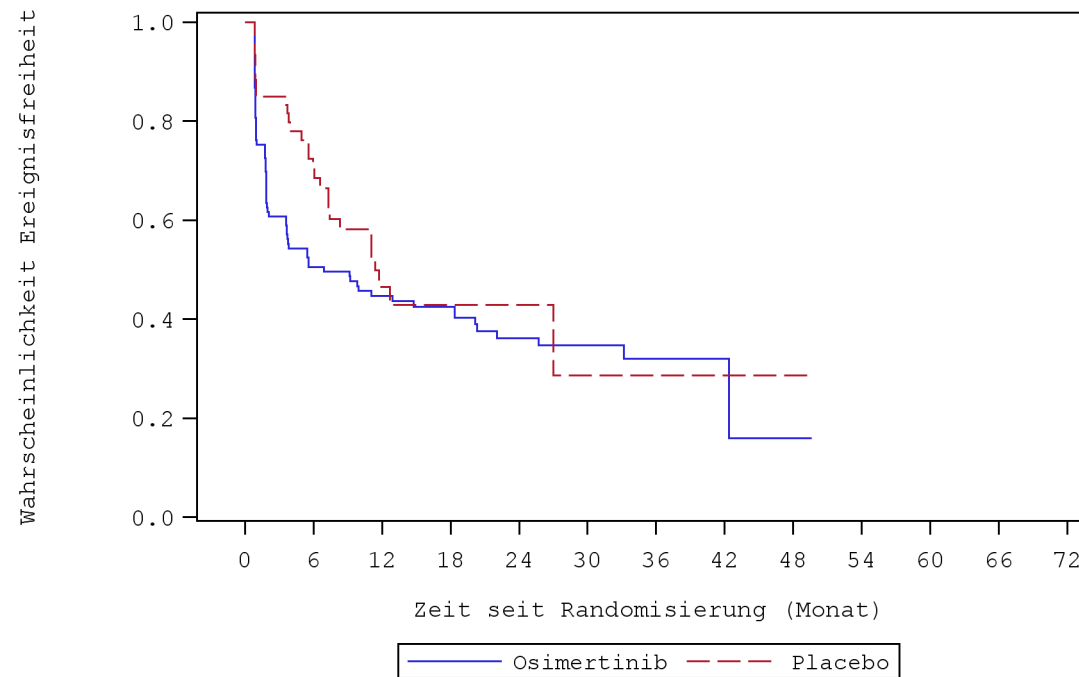
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Figure LF1QAI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups

Full Analysis Set

Study: LAURA

Region: Asia



Osimertinib	120	53	42	38	24	17	8	3	1	0
Placebo	64	38	13	6	3	2	1	1	1	0

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QAI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

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Program Name: LF1_APRO_TTE_KS.sas

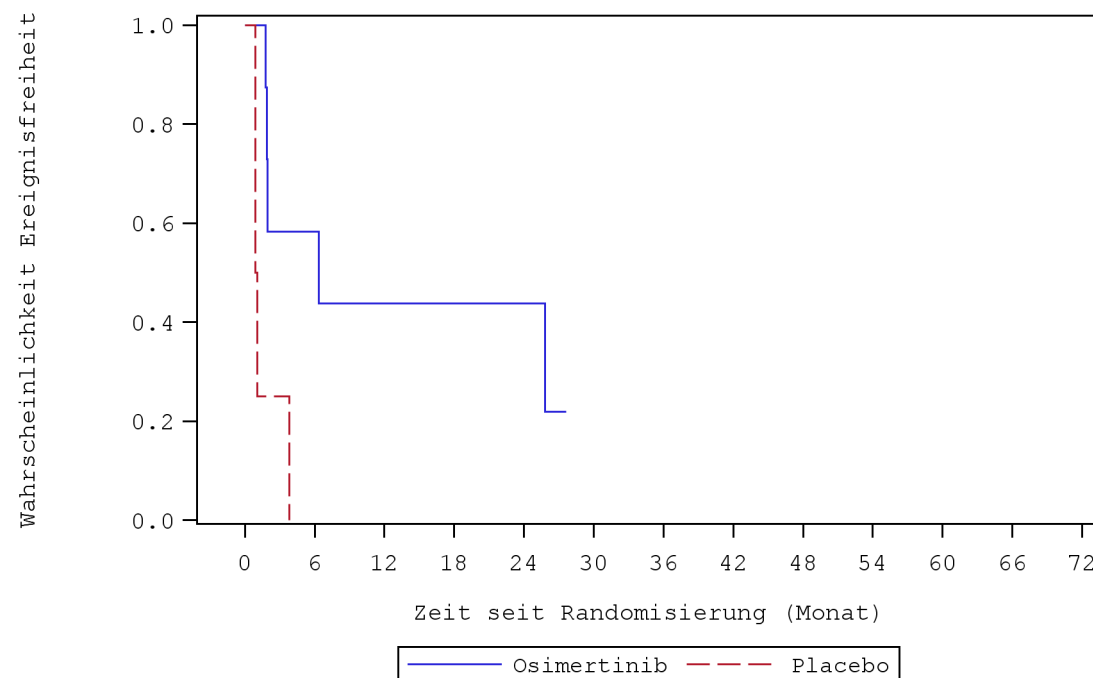
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Figure LF1QAI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups

Full Analysis Set

Study: LAURA

Region: Europe



Osimertinib	11	4	3	2	2	0
Placebo	7	0				

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QAI10T_SFTM

AstraZeneca

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Program Name: LF1_APRO_TTE_KS.sas

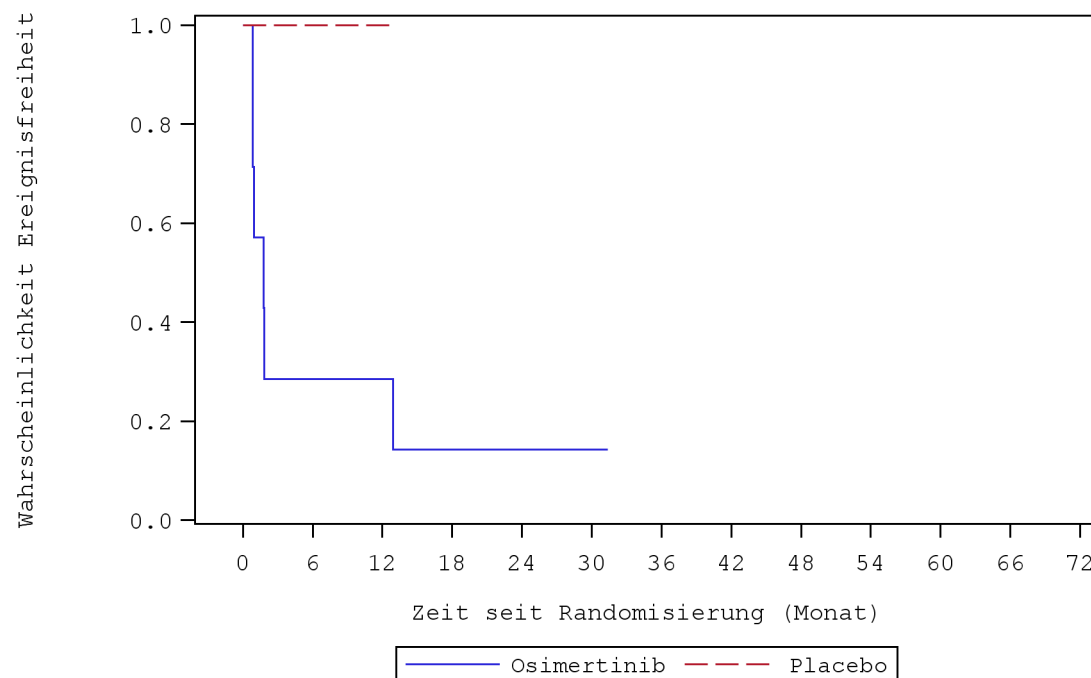
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Figure LF1QAI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Appetite loss by main subgroups

Full Analysis Set

Study: LAURA

Region: Rest of the World



Osimertinib	12	2	2	1	1	1	0
Placebo	2	2	1	0			

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QAI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

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Program Name: LF1_APRO_TTE_KS.sas

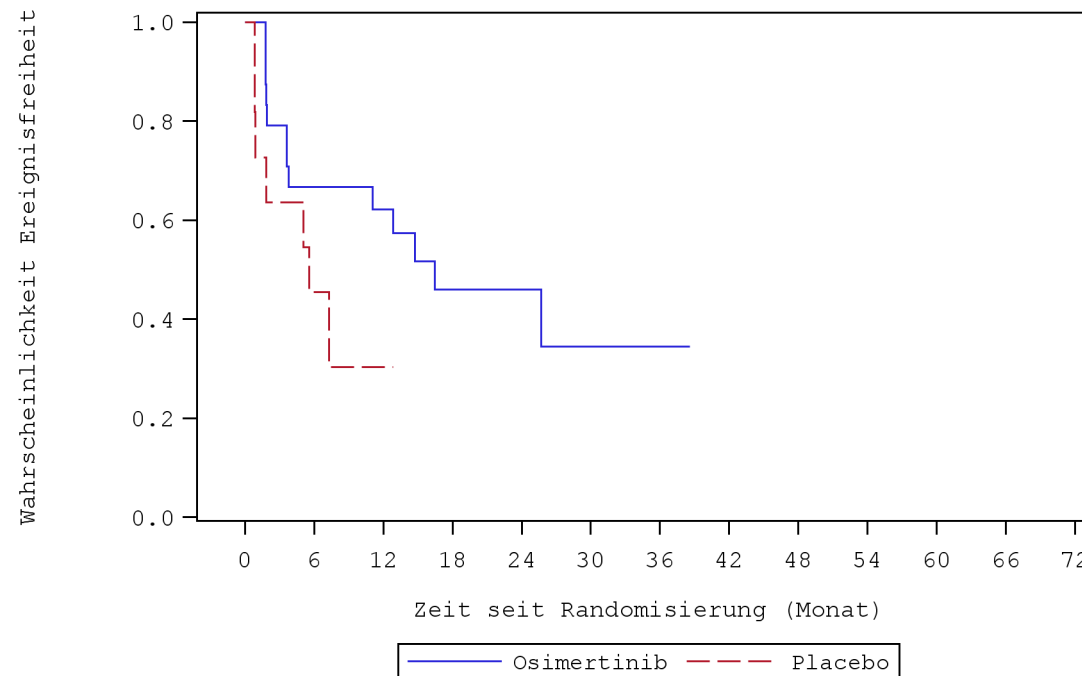
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Figure LF1QCI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Constipation by main subgroups

Full Analysis Set

Study: LAURA

China Cohort: Yes



Osimertinib	27	16	13	8	4	2	2	0
Placebo	13	5	1	0				

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QCI10T_SFTM

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

AstraZeneca

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Program Name: LF1_APRO_TTE_KS.sas

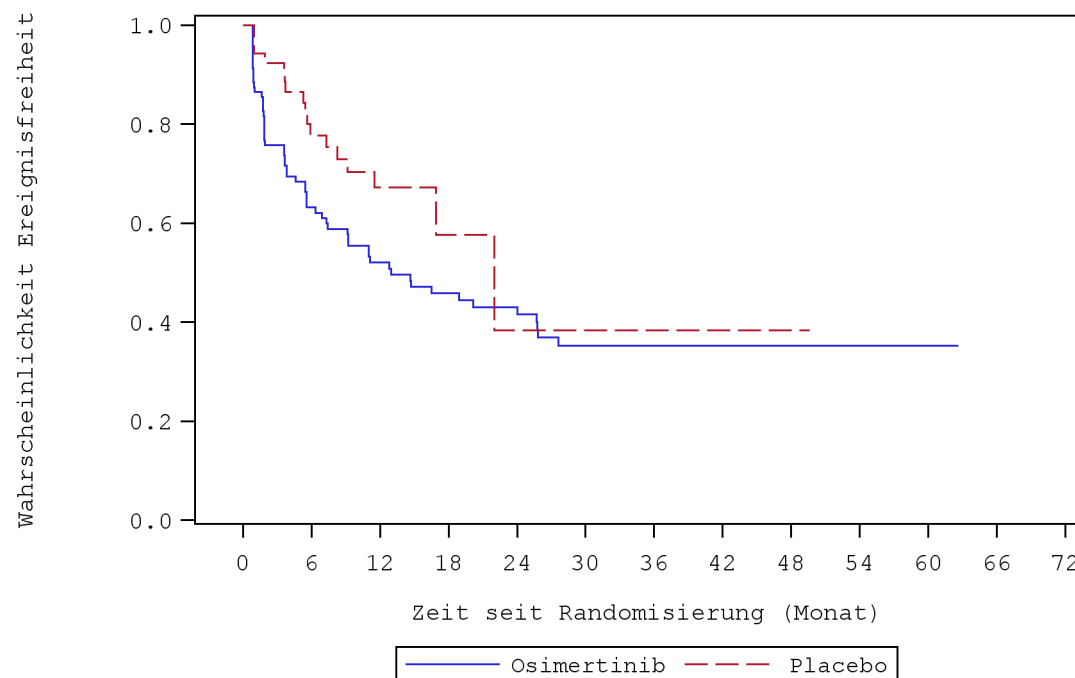
Run Date: 27SEP2024:11:28:15

Figure LF1QCI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-C30 Constipation by main subgroups

Full Analysis Set

Study: LAURA

China Cohort: No



Osimertinib	116	59	43	33	29	17	10	5	2	1	1	0
Placebo	60	35	19	6	2	2	1	1	1	0		

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QCI10T_SFTM

AstraZeneca
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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1LCI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Coughing by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Coughing				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.5057
Male	Osimertinib	53	34 (64.2)	1.5	(0.9, 6.5)	1.41	(0.78, 2.56)	0.2555
	Placebo	31	16 (51.6)	5.5	(0.9, NC)			
Female	Osimertinib	90	65 (72.2)	1.1	(0.9, 1.6)	1.10	(0.71, 1.70)	0.6623
	Placebo	42	30 (71.4)	1.6	(0.6, 2.3)			
Age	Osimertinib						Interaction test:	0.9175
< 65 years	Osimertinib	81	57 (70.4)	1.1	(0.9, 1.4)	1.21	(0.75, 1.93)	0.4342
	Placebo	39	25 (64.1)	1.7	(0.9, 4.6)			
>= 65 years	Osimertinib	62	42 (67.7)	1.6	(1.0, 2.8)	1.25	(0.74, 2.12)	0.3998
	Placebo	34	21 (61.8)	3.7	(0.8, 13.7)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1LCI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Coughing by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Coughing				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.2634
Current/former	Osimertinib	41	27 (65.9)	1.6	(0.9, 5.6)	1.61	(0.83, 3.12)	0.1601
	Placebo	24	13 (54.2)	12.0	(0.9, NC)			
Never	Osimertinib	102	72 (70.6)	1.1	(0.9, 1.5)	1.03	(0.68, 1.56)	0.8715
	Placebo	49	33 (67.3)	1.5	(0.6, 3.7)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.5867
CCRT	Osimertinib	131	90 (68.7)	1.3	(0.9, 1.8)	1.20	(0.83, 1.76)	0.3343
	Placebo	62	39 (62.9)	1.8	(0.9, 5.5)			
SCRT	Osimertinib	12	9 (75.0)	1.2	(0.2, 2.8)	1.61	(0.60, 4.33)	0.3428
	Placebo	11	7 (63.6)	1.8	(0.5, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1LCI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Coughing by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Coughing				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.6465
IIIA	Osimertinib	52	35 (67.3)	1.8	(0.9, 2.8)	1.40	(0.75, 2.60)	0.2932
	Placebo	24	14 (58.3)	4.8	(0.9, NC)			
IIIB/IIIC	Osimertinib	91	64 (70.3)	1.1	(0.9, 1.5)	1.17	(0.76, 1.79)	0.4675
	Placebo	49	32 (65.3)	1.7	(0.8, 8.6)			
Race	Osimertinib						Interaction test:	0.6929
Asian	Osimertinib	116	83 (71.6)	1.3	(0.9, 1.8)	1.20	(0.82, 1.75)	0.3464
	Placebo	62	40 (64.5)	1.8	(0.9, 8.6)			
Non-Asian	Osimertinib	27	16 (59.3)	1.3	(0.7, 2.7)	1.47	(0.57, 3.76)	0.4230
	Placebo	11	6 (54.5)	5.5	(0.4, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1LCI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Coughing by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Coughing				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.1188
Yes	Osimertinib	27	18 (66.7)	1.9	(0.9, 8.3)	0.68	(0.31, 1.52)	0.3471
	Placebo	13	9 (69.2)	1.5	(0.4, 4.6)			
No	Osimertinib	116	81 (69.8)	1.1	(0.9, 1.5)	1.41	(0.96, 2.09)	0.0818
	Placebo	60	37 (61.7)	1.8	(0.9, 12.0)			
Response to prior CRT	Osimertinib						Interaction test:	0.5609
CR+PR	Osimertinib	71	47 (66.2)	1.3	(0.9, 1.9)	1.33	(0.77, 2.29)	0.3088
	Placebo	30	18 (60.0)	1.8	(0.8, NC)			
SD	Osimertinib	61	46 (75.4)	1.3	(0.9, 1.9)	1.07	(0.66, 1.74)	0.7938
	Placebo	37	25 (67.6)	1.8	(0.6, 5.5)			
NE	Osimertinib	11	6 (54.5)	0.9	(0.2, NC)	2.24	(0.56, 8.98)	0.2538
	Placebo	6	3 (50.0)	4.6	(1.5, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Table LT1LCI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Coughing by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Coughing				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.2556
Asia	Osimertinib	120	87 (72.5)	1.3	(0.9, 1.8)	1.22	(0.84, 1.78)	0.2895
	Placebo	64	41 (64.1)	1.8	(0.9, 5.5)			
Europe	Osimertinib	11	5 (45.5)	1.3	(0.5, NC)	0.65	(0.17, 2.43)	0.5234
	Placebo	7	4 (57.1)	0.7	(0.4, NC)			
Rest of the World	Osimertinib	12	7 (58.3)	0.9	(0.4, 2.7)	4.34	(0.53, 35.35)	0.1700
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.2634
Positive	Osimertinib	10	5 (50.0)	1.3	(0.4, NC)	0.42	(0.10, 1.75)	0.2312
	Placebo	4	3 (75.0)	0.4	(0.4, NC)			
Negative	Osimertinib	113	80 (70.8)	1.3	(0.9, 1.8)	1.24	(0.84, 1.83)	0.2873
	Placebo	58	37 (63.8)	1.8	(0.9, 8.6)			
Unknown	Osimertinib	20	14 (70.0)	1.2	(0.5, 2.7)	1.85	(0.71, 4.83)	0.2064
	Placebo	11	6 (54.5)	3.7	(0.4, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Table LT1LCI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Coughing by main subgroups
 Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Coughing				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.3782				
Ex19Del	Osimertinib	74	51 (68.9)	1.3	(0.9, 2.7)	1.09	(0.69, 1.71)	0.7228
	Placebo	43	30 (69.8)	1.8	(0.8, 5.5)			
L858R	Osimertinib	68	47 (69.1)	1.1	(0.9, 1.9)	1.50	(0.85, 2.65)	0.1620
	Placebo	30	16 (53.3)	3.0	(0.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1LHI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Haemoptysis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.0223 #
Male	Osimertinib	53	16 (30.2)	NC		0.67	(0.31, 1.46)	0.3147
	Placebo	31	11 (35.5)	NC				
Female	Osimertinib	90	33 (36.7)	28.6	(17.4, NC)	2.51	(1.05, 6.02)	0.0389 *
	Placebo	42	6 (14.3)	NC				
Age	Osimertinib						Interaction test:	0.0696
< 65 years	Osimertinib	81	30 (37.0)	29.4	(17.4, NC)	0.87	(0.45, 1.69)	0.6762
	Placebo	39	13 (33.3)	13.9	(9.1, NC)			
>= 65 years	Osimertinib	62	19 (30.6)	33.1	(24.8, NC)	2.65	(0.90, 7.79)	0.0773
	Placebo	34	4 (11.8)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1LHI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Haemoptysis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.0047 #
Current/former	Osimertinib	41	10 (24.4)	NC		0.47	(0.19, 1.14)	0.0942
	Placebo	24	10 (41.7)	13.9	(5.5, NC)			
Never	Osimertinib	102	39 (38.2)	28.6	(14.7, NC)	2.53	(1.13, 5.69)	0.0246 *
	Placebo	49	7 (14.3)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.0096 #
CCRT	Osimertinib	131	44 (33.6)	33.1	(24.8, NC)	1.08	(0.61, 1.90)	0.7982
	Placebo	62	17 (27.4)	NC				
SCRT	Osimertinib	12	5 (41.7)	7.4	(0.6, NC)	NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1LHI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Haemoptysis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.7958
IIIA	Osimertinib	52	17 (32.7)	33.1	(15.6, NC)	1.20	(0.47, 3.06)	0.6990
	Placebo	24	6 (25.0)	NC				
IIIB/IIIC	Osimertinib	91	32 (35.2)	29.4	(17.4, NC)	1.40	(0.70, 2.80)	0.3398
	Placebo	49	11 (22.4)	NC				
Race	Osimertinib						Interaction test:	0.1638
Asian	Osimertinib	116	40 (34.5)	NC		1.14	(0.63, 2.05)	0.6656
	Placebo	62	16 (25.8)	NC				
Non-Asian	Osimertinib	27	9 (33.3)	8.2	(1.8, NC)	4.28	(0.54, 33.84)	0.1678
	Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Table LT1LHI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Haemoptysis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.9465
Yes	Osimertinib	27	13 (48.1)	5.6	(1.7, NC)	1.24	(0.40, 3.81)	0.7125
	Placebo	13	4 (30.8)	NC				
No	Osimertinib	116	36 (31.0)	NC		1.29	(0.68, 2.46)	0.4356
	Placebo	60	13 (21.7)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.1736
CR+PR	Osimertinib	71	29 (40.8)	23.0	(10.2, NC)	1.79	(0.78, 4.10)	0.1689
	Placebo	30	7 (23.3)	NC				
SD	Osimertinib	61	18 (29.5)	NC		1.23	(0.51, 2.98)	0.6388
	Placebo	37	7 (18.9)	NC				
NE	Osimertinib	11	2 (18.2)	NC		0.28	(0.05, 1.67)	0.1612
	Placebo	6	3 (50.0)	2.7	(0.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Haemoptysis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.4826
Asia	Osimertinib	120	42 (35.0)	NC		1.20	(0.67, 2.16)	0.5352
	Placebo	64	16 (25.0)	NC				
Europe	Osimertinib	11	2 (18.2)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	5 (41.7)	7.4	(1.3, 23.0)	1.52	(0.18, 13.06)	0.7008
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.0730
Positive	Osimertinib	10	4 (40.0)	27.6	(1.8, NC)	NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	35 (31.0)	NC		1.01	(0.55, 1.83)	0.9820
	Placebo	58	16 (27.6)	NC				
Unknown	Osimertinib	20	10 (50.0)	8.2	(1.8, NC)	5.42	(0.69, 42.36)	0.1074
	Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1LHI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups
 Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Haemoptysis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib			Interaction test: 0.4975			
Ex19Del	Osimertinib	74	29 (39.2)	28.6	(11.9, NC)	1.59	(0.77, 3.29)	0.2120
	Placebo	43	10 (23.3)	NC				
L858R	Osimertinib	68	20 (29.4)	33.1	(24.8, NC)	1.07	(0.45, 2.55)	0.8700
	Placebo	30	7 (23.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LPI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dysphagia by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dysphagia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.1622
Male	Osimertinib	53	22 (41.5)	NC		0.69	(0.35, 1.35)	0.2737
	Placebo	31	14 (45.2)	9.2	(1.3, NC)			
Female	Osimertinib	90	40 (44.4)	19.3	(7.3, NC)	1.31	(0.71, 2.42)	0.3866
	Placebo	42	14 (33.3)	NC				
Age	Osimertinib						Interaction test:	0.4126
< 65 years	Osimertinib	81	34 (42.0)	20.2	(5.5, NC)	0.83	(0.46, 1.52)	0.5548
	Placebo	39	16 (41.0)	NC				
>= 65 years	Osimertinib	62	28 (45.2)	19.3	(7.3, NC)	1.22	(0.62, 2.39)	0.5722
	Placebo	34	12 (35.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1LPI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dysphagia by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dysphagia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.1285
Current/former	Osimertinib	41	17 (41.5)	NC		0.63	(0.31, 1.31)	0.2153
	Placebo	24	13 (54.2)	6.6	(1.3, NC)			
Never	Osimertinib	102	45 (44.1)	19.3	(7.3, NC)	1.30	(0.72, 2.34)	0.3792
	Placebo	49	15 (30.6)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.9603
CCRT	Osimertinib	131	58 (44.3)	19.3	(8.2, NC)	0.98	(0.61, 1.58)	0.9311
	Placebo	62	24 (38.7)	NC				
SCRT	Osimertinib	12	4 (33.3)	28.5	(0.2, NC)	0.94	(0.24, 3.79)	0.9346
	Placebo	11	4 (36.4)	13.0	(1.4, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LPI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dysphagia by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dysphagia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.0522
IIIA	Osimertinib	52	21 (40.4)	26.7	(4.6, NC)	2.10	(0.79, 5.57)	0.1370
	Placebo	24	5 (20.8)	NC				
IIIB/IIIC	Osimertinib	91	41 (45.1)	19.3	(7.3, NC)	0.74	(0.44, 1.25)	0.2632
	Placebo	49	23 (46.9)	8.3	(1.7, NC)			
Race	Osimertinib						Interaction test:	0.4695
Asian	Osimertinib	116	50 (43.1)	26.7	(11.0, NC)	0.93	(0.57, 1.51)	0.7609
	Placebo	62	24 (38.7)	NC				
Non-Asian	Osimertinib	27	12 (44.4)	2.7	(1.1, 8.2)	1.45	(0.47, 4.48)	0.5240
	Placebo	11	4 (36.4)	13.0	(0.4, NC)			

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dysphagia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.0697
Yes	Osimertinib	27	7 (25.9)	NC		0.39	(0.13, 1.16)	0.0891
	Placebo	13	6 (46.2)	6.6	(0.6, NC)			
No	Osimertinib	116	55 (47.4)	15.7	(6.5, 28.5)	1.20	(0.73, 1.98)	0.4641
	Placebo	60	22 (36.7)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.0214 #
CR+PR	Osimertinib	71	33 (46.5)	11.1	(4.5, NC)	2.07	(0.92, 4.70)	0.0806
	Placebo	30	7 (23.3)	NC				
SD	Osimertinib	61	25 (41.0)	28.5	(11.0, NC)	0.72	(0.39, 1.36)	0.3165
	Placebo	37	16 (43.2)	13.0	(2.7, NC)			
NE	Osimertinib	11	4 (36.4)	NC		0.30	(0.08, 1.12)	0.0735
	Placebo	6	5 (83.3)	1.7	(0.5, 6.6)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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The CI for median time was calculated based on Brookmeyer/Crowley.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dysphagia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.4154
Asia	Osimertinib	120	52 (43.3)	20.3	(11.0, NC)	0.93	(0.57, 1.50)	0.7534
	Placebo	64	25 (39.1)	NC				
Europe	Osimertinib	11	4 (36.4)	1.8	(0.2, NC)	2.83	(0.32, 25.43)	0.3522
	Placebo	7	1 (14.3)	NC				
Rest of the World	Osimertinib	12	6 (50.0)	1.5	(1.1, 8.2)	0.49	(0.10, 2.42)	0.3777
	Placebo	2	2 (100.0)	1.6	(0.4, 2.8)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.1679
Positive	Osimertinib	10	6 (60.0)	7.3	(0.5, NC)	0.91	(0.18, 4.52)	0.9071
	Placebo	4	2 (50.0)	NC				
Negative	Osimertinib	113	46 (40.7)	26.7	(11.0, NC)	0.82	(0.50, 1.36)	0.4464
	Placebo	58	24 (41.4)	NC				
Unknown	Osimertinib	20	10 (50.0)	5.5	(1.1, NC)	3.28	(0.72, 15.00)	0.1251
	Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LPI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dysphagia by main subgroups
 Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dysphagia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.6162				
Ex19Del	Osimertinib	74	29 (39.2)	28.5	(7.3, NC)	0.90	(0.49, 1.64)	0.7269
	Placebo	43	17 (39.5)	NC				
L858R	Osimertinib	68	33 (48.5)	18.5	(5.5, NC)	1.13	(0.57, 2.25)	0.7225
	Placebo	30	11 (36.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1LEI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.3596
Male	Osimertinib	53	39 (73.6)	6.4	(1.5, 11.9)	1.81	(0.96, 3.39)	0.0653
	Placebo	31	13 (41.9)	13.8	(3.6, NC)			
Female	Osimertinib	90	54 (60.0)	3.6	(1.4, 5.6)	1.24	(0.75, 2.06)	0.3996
	Placebo	42	21 (50.0)	6.4	(0.8, NC)			
Age	Osimertinib						Interaction test:	0.3259
< 65 years	Osimertinib	81	55 (67.9)	2.9	(1.5, 5.6)	1.19	(0.71, 1.99)	0.5042
	Placebo	39	20 (51.3)	4.5	(0.5, NC)			
≥ 65 years	Osimertinib	62	38 (61.3)	5.6	(1.4, 16.7)	1.78	(0.96, 3.28)	0.0662
	Placebo	34	14 (41.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1LEI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.3059
Current/former	Osimertinib	41	26 (63.4)	9.2	(1.5, 25.7)	1.92	(0.90, 4.10)	0.0929
	Placebo	24	9 (37.5)	NC				
Never	Osimertinib	102	67 (65.7)	3.6	(1.4, 5.5)	1.22	(0.77, 1.93)	0.4055
	Placebo	49	25 (51.0)	4.6	(0.8, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.7075
CCRT	Osimertinib	131	87 (66.4)	4.6	(1.6, 6.4)	1.48	(0.97, 2.25)	0.0688
	Placebo	62	29 (46.8)	8.7	(3.6, NC)			
SCRT	Osimertinib	12	6 (50.0)	3.7	(0.4, NC)	1.16	(0.35, 3.81)	0.8067
	Placebo	11	5 (45.5)	8.2	(0.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.3233
IIIA	Osimertinib	52	32 (61.5)	5.6	(3.6, 9.2)	1.97	(0.94, 4.12)	0.0733
	Placebo	24	9 (37.5)	NC				
IIIB/IIIC	Osimertinib	91	61 (67.0)	2.7	(1.1, 8.2)	1.27	(0.80, 2.04)	0.3126
	Placebo	49	25 (51.0)	8.3	(0.9, NC)			
Race	Osimertinib						Interaction test:	0.8574
Asian	Osimertinib	116	83 (71.6)	4.6	(1.8, 6.5)	1.48	(0.97, 2.25)	0.0666
	Placebo	62	30 (48.4)	8.3	(3.6, NC)			
Non-Asian	Osimertinib	27	10 (37.0)	1.6	(0.9, NC)	1.32	(0.41, 4.21)	0.6391
	Placebo	11	4 (36.4)	10.1	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.6510
Yes	Osimertinib	27	19 (70.4)	3.6	(0.9, 9.1)	1.79	(0.67, 4.82)	0.2474
	Placebo	13	5 (38.5)	8.7	(3.6, NC)			
No	Osimertinib	116	74 (63.8)	5.5	(1.5, 8.2)	1.40	(0.91, 2.16)	0.1229
	Placebo	60	29 (48.3)	8.3	(1.1, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.9197
CR+PR	Osimertinib	71	43 (60.6)	4.6	(1.1, 6.4)	1.52	(0.83, 2.78)	0.1748
	Placebo	30	14 (46.7)	8.7	(0.9, NC)			
SD	Osimertinib	61	44 (72.1)	3.6	(1.4, 10.1)	1.47	(0.84, 2.58)	0.1755
	Placebo	37	17 (45.9)	10.1	(1.9, NC)			
NE	Osimertinib	11	6 (54.5)	8.2	(0.4, NC)	1.11	(0.28, 4.42)	0.8872
	Placebo	6	3 (50.0)	8.3	(0.5, NC)			

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.6718
Asia	Osimertinib	120	85 (70.8)	4.6	(1.8, 6.4)	1.53	(1.01, 2.33)	0.0443 *
	Placebo	64	30 (46.9)	8.7	(3.6, NC)			
Europe	Osimertinib	11	3 (27.3)	NC		0.85	(0.14, 5.11)	0.8601
	Placebo	7	2 (28.6)	NC				
Rest of the World	Osimertinib	12	5 (41.7)	1.1	(0.3, NC)	0.83	(0.16, 4.31)	0.8293
	Placebo	2	2 (100.0)	5.5	(0.9, 10.1)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.6214
Positive	Osimertinib	10	7 (70.0)	2.7	(0.4, 22.1)	1.82	(0.38, 8.79)	0.4558
	Placebo	4	2 (50.0)	8.7	(0.4, NC)			
Negative	Osimertinib	113	74 (65.5)	5.5	(1.9, 9.1)	1.33	(0.86, 2.07)	0.1948
	Placebo	58	28 (48.3)	8.3	(1.9, NC)			
Unknown	Osimertinib	20	12 (60.0)	1.1	(0.5, 8.3)	2.34	(0.75, 7.25)	0.1414
	Placebo	11	4 (36.4)	NC				

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in arm/shoulder				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.9357
Ex19Del	Osimertinib	74	50 (67.6)	5.5	(1.5, 9.1)	1.44	(0.86, 2.40)	0.1655
	Placebo	43	21 (48.8)	10.1	(1.9, NC)			
L858R	Osimertinib	68	42 (61.8)	4.6	(1.4, 8.2)	1.48	(0.80, 2.77)	0.2132
	Placebo	30	13 (43.3)	8.7	(1.1, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1LOI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in other parts by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in other parts				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.0644
Male	Osimertinib	53	39 (73.6)	1.9	(1.1, 5.5)	1.28	(0.73, 2.25)	0.3861
	Placebo	31	18 (58.1)	6.4	(1.1, NC)			
Female	Osimertinib	90	45 (50.0)	11.0	(1.2, 23.9)	0.65	(0.40, 1.04)	0.0716
	Placebo	42	28 (66.7)	1.7	(0.7, 5.6)			
Age	Osimertinib						Interaction test:	0.6427
< 65 years	Osimertinib	81	53 (65.4)	1.5	(0.9, 3.6)	0.92	(0.57, 1.48)	0.7211
	Placebo	39	25 (64.1)	1.7	(0.8, 5.5)			
>= 65 years	Osimertinib	62	31 (50.0)	12.9	(1.8, 30.3)	0.77	(0.44, 1.34)	0.3579
	Placebo	34	21 (61.8)	7.3	(1.3, 10.2)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Time to increase by at least 10 points in QLQ-LC13 Pain in other parts				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.1854
Current/former	Osimertinib	41	28 (68.3)	1.6	(0.6, 12.9)	1.21	(0.65, 2.24)	0.5420
	Placebo	24	16 (66.7)	6.4	(0.9, 10.2)			
Never	Osimertinib	102	56 (54.9)	3.7	(1.5, 22.0)	0.73	(0.46, 1.14)	0.1653
	Placebo	49	30 (61.2)	2.9	(0.8, 5.9)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.1895
CCRT	Osimertinib	131	79 (60.3)	3.6	(1.3, 11.0)	0.94	(0.63, 1.39)	0.7524
	Placebo	62	38 (61.3)	4.4	(1.3, 8.2)			
SCRT	Osimertinib	12	5 (41.7)	NC		0.43	(0.14, 1.33)	0.1417
	Placebo	11	8 (72.7)	4.5	(0.4, 8.2)			

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Time to increase by at least 10 points in QLQ-LC13 Pain in other parts				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.0534
IIIA	Osimertinib	52	35 (67.3)	2.7	(1.2, 12.9)	1.38	(0.74, 2.57)	0.3066
	Placebo	24	14 (58.3)	8.2	(4.5, 10.2)			
IIIB/IIIC	Osimertinib	91	49 (53.8)	3.7	(1.1, 30.3)	0.66	(0.42, 1.03)	0.0697
	Placebo	49	32 (65.3)	1.4	(0.8, 5.6)			
Race	Osimertinib						Interaction test:	0.6415
Asian	Osimertinib	116	73 (62.9)	2.7	(1.3, 11.0)	0.84	(0.57, 1.24)	0.3751
	Placebo	62	41 (66.1)	2.3	(1.1, 7.4)			
Non-Asian	Osimertinib	27	11 (40.7)	5.5	(0.6, NC)	1.09	(0.38, 3.15)	0.8699
	Placebo	11	5 (45.5)	6.4	(0.7, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.6094
Yes	Osimertinib	27	15 (55.6)	3.6	(0.5, NC)	0.70	(0.30, 1.66)	0.4217
	Placebo	13	8 (61.5)	1.4	(0.5, NC)			
No	Osimertinib	116	69 (59.5)	2.8	(1.3, 12.9)	0.90	(0.60, 1.35)	0.6147
	Placebo	60	38 (63.3)	5.3	(1.1, 8.2)			
Response to prior CRT	Osimertinib						Interaction test:	0.4333
CR+PR	Osimertinib	71	34 (47.9)	5.6	(1.6, NC)	0.67	(0.39, 1.18)	0.1642
	Placebo	30	20 (66.7)	5.3	(0.9, 9.2)			
SD	Osimertinib	61	43 (70.5)	1.8	(1.1, 11.0)	1.11	(0.66, 1.88)	0.6909
	Placebo	37	21 (56.8)	5.5	(0.9, NC)			
NE	Osimertinib	11	7 (63.6)	0.7	(0.2, 24.9)	0.93	(0.29, 2.93)	0.8953
	Placebo	6	5 (83.3)	1.3	(0.6, 4.4)			

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Time to increase by at least 10 points in QLQ-LC13 Pain in other parts				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.8352
Asia	Osimertinib	120	76 (63.3)	2.7	(1.3, 11.0)	0.85	(0.58, 1.25)	0.4068
	Placebo	64	42 (65.6)	2.9	(1.1, 7.4)			
Europe	Osimertinib	11	4 (36.4)	23.9	(0.4, NC)	0.83	(0.18, 3.71)	0.8022
	Placebo	7	3 (42.9)	7.3	(0.7, 7.3)			
Rest of the World	Osimertinib	12	4 (33.3)	5.5	(0.3, NC)	1.61	(0.18, 14.45)	0.6689
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.1766
Positive	Osimertinib	10	7 (70.0)	3.7	(0.7, 35.8)	0.26	(0.07, 0.89)	0.0315 *
	Placebo	4	4 (100.0)	0.4	(0.4, 5.6)			
Negative	Osimertinib	113	66 (58.4)	2.7	(1.2, 11.0)	0.96	(0.63, 1.45)	0.8392
	Placebo	58	35 (60.3)	5.3	(1.3, 9.2)			
Unknown	Osimertinib	20	11 (55.0)	5.5	(0.6, 30.3)	0.78	(0.30, 2.03)	0.6160
	Placebo	11	7 (63.6)	1.7	(0.5, 7.3)			

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Table LT1LOI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in other parts by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in other parts				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.3552
Ex19Del	Osimertinib	74	45 (60.8)	1.9	(1.1, 12.9)	0.99	(0.61, 1.61)	0.9784
	Placebo	43	27 (62.8)	5.5	(0.9, 10.2)			
L858R	Osimertinib	68	38 (55.9)	5.5	(1.6, 24.9)	0.70	(0.40, 1.22)	0.2117
	Placebo	30	19 (63.3)	1.4	(0.7, 7.4)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1LBI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in chest by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in chest				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.9137
Male	Osimertinib	53	37 (69.8)	1.8	(0.7, 11.0)	1.27	(0.72, 2.23)	0.4141
	Placebo	31	18 (58.1)	4.1	(1.1, 16.5)			
Female	Osimertinib	90	49 (54.4)	2.7	(1.3, 10.2)	1.32	(0.77, 2.27)	0.3131
	Placebo	42	18 (42.9)	NC				
Age	Osimertinib						Interaction test:	0.4689
< 65 years	Osimertinib	81	50 (61.7)	1.5	(0.9, 4.7)	1.10	(0.66, 1.84)	0.7134
	Placebo	39	21 (53.8)	3.6	(0.9, NC)			
>= 65 years	Osimertinib	62	36 (58.1)	6.4	(1.4, 19.3)	1.47	(0.81, 2.69)	0.2085
	Placebo	34	15 (44.1)	16.5	(2.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1LBI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in chest by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in chest				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.6879
Current/former	Osimertinib	41	25 (61.0)	10.0	(1.8, 34.0)	1.13	(0.58, 2.22)	0.7184
	Placebo	24	13 (54.2)	10.5	(1.1, NC)			
Never	Osimertinib	102	61 (59.8)	1.5	(1.1, 6.4)	1.34	(0.83, 2.17)	0.2321
	Placebo	49	23 (46.9)	8.3	(1.1, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.9816
CCRT	Osimertinib	131	79 (60.3)	2.8	(1.5, 8.3)	1.30	(0.85, 1.98)	0.2271
	Placebo	62	30 (48.4)	8.7	(1.2, NC)			
SCRT	Osimertinib	12	7 (58.3)	1.3	(0.4, NC)	1.28	(0.43, 3.81)	0.6580
	Placebo	11	6 (54.5)	3.6	(0.4, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LBI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in chest by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in chest				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.2481
IIIA	Osimertinib	52	32 (61.5)	2.7	(0.7, 8.3)	1.75	(0.88, 3.49)	0.1089
	Placebo	24	11 (45.8)	11.1	(3.6, NC)			
IIIB/IIIC	Osimertinib	91	54 (59.3)	2.8	(1.4, 11.0)	1.08	(0.67, 1.74)	0.7521
	Placebo	49	25 (51.0)	3.6	(0.9, NC)			
Race	Osimertinib						Interaction test:	0.0850
Asian	Osimertinib	116	72 (62.1)	3.7	(1.5, 10.2)	1.12	(0.74, 1.70)	0.5785
	Placebo	62	33 (53.2)	6.0	(1.1, NC)			
Non-Asian	Osimertinib	27	14 (51.9)	1.1	(0.8, 1.5)	3.26	(0.94, 11.37)	0.0633
	Placebo	11	3 (27.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LBI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in chest by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in chest				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.8385
Yes	Osimertinib	27	19 (70.4)	1.4	(0.9, 6.4)	1.17	(0.49, 2.78)	0.7288
	Placebo	13	7 (53.8)	3.6	(0.5, NC)			
No	Osimertinib	116	67 (57.8)	2.8	(1.4, 10.2)	1.29	(0.83, 2.00)	0.2535
	Placebo	60	29 (48.3)	8.3	(1.2, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.5936
CR+PR	Osimertinib	71	36 (50.7)	6.4	(1.1, NC)	1.03	(0.56, 1.88)	0.9307
	Placebo	30	15 (50.0)	6.0	(1.1, NC)			
SD	Osimertinib	61	43 (70.5)	1.8	(1.3, 7.4)	1.51	(0.87, 2.62)	0.1442
	Placebo	37	18 (48.6)	11.1	(1.1, NC)			
NE	Osimertinib	11	7 (63.6)	0.6	(0.4, NC)	1.75	(0.45, 6.79)	0.4156
	Placebo	6	3 (50.0)	2.8	(0.5, NC)			

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Table LT1LBI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in chest by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in chest				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.2539
Asia	Osimertinib	120	75 (62.5)	2.8	(1.5, 10.0)	1.14	(0.76, 1.72)	0.5169
	Placebo	64	34 (53.1)	5.5	(1.1, NC)			
Europe	Osimertinib	11	5 (45.5)	0.8	(0.4, NC)	4.46	(0.52, 38.11)	0.1722
	Placebo	7	1 (14.3)	NC				
Rest of the World	Osimertinib	12	6 (50.0)	1.1	(0.4, 1.5)	3.06	(0.37, 25.47)	0.3015
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.2489
Positive	Osimertinib	10	5 (50.0)	6.9	(1.3, NC)	0.59	(0.14, 2.46)	0.4670
	Placebo	4	3 (75.0)	3.2	(0.6, NC)			
Negative	Osimertinib	113	69 (61.1)	2.8	(1.3, 10.0)	1.22	(0.80, 1.88)	0.3595
	Placebo	58	30 (51.7)	8.3	(1.1, NC)			
Unknown	Osimertinib	20	12 (60.0)	1.1	(0.6, 19.4)	2.80	(0.79, 9.93)	0.1107
	Placebo	11	3 (27.3)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1LBI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Pain in chest by main subgroups
 Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Pain in chest				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.6900				
Ex19Del	Osimertinib	74	43 (58.1)	1.5	(0.9, 19.4)	1.37	(0.81, 2.32)	0.2375
	Placebo	43	21 (48.8)	8.7	(2.8, NC)			
L858R	Osimertinib	68	43 (63.2)	3.7	(1.4, 10.0)	1.17	(0.65, 2.10)	0.6044
	Placebo	30	15 (50.0)	2.8	(1.0, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LSI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Sore mouth by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Sore mouth				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.4662
Male	Osimertinib	53	34 (64.2)	1.2	(0.7, 9.2)	1.13	(0.64, 1.99)	0.6695
	Placebo	31	19 (61.3)	4.8	(1.5, 12.0)			
Female	Osimertinib	90	56 (62.2)	1.5	(0.9, 5.5)	1.50	(0.90, 2.48)	0.1181
	Placebo	42	21 (50.0)	7.4	(2.7, NC)			
Age	Osimertinib						Interaction test:	0.0333 #
< 65 years	Osimertinib	81	57 (70.4)	1.1	(0.6, 2.7)	1.92	(1.14, 3.24)	0.0146 *
	Placebo	39	19 (48.7)	11.3	(3.6, NC)			
>= 65 years	Osimertinib	62	33 (53.2)	6.5	(1.1, 22.9)	0.85	(0.49, 1.46)	0.5490
	Placebo	34	21 (61.8)	6.8	(1.3, 11.4)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1LSI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Sore mouth by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Sore mouth				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.1329
Current/former	Osimertinib	41	27 (65.9)	6.5	(0.7, 16.7)	0.92	(0.50, 1.67)	0.7771
	Placebo	24	18 (75.0)	3.2	(0.9, 12.0)			
Never	Osimertinib	102	63 (61.8)	1.2	(0.9, 4.5)	1.66	(1.02, 2.70)	0.0432 *
	Placebo	49	22 (44.9)	9.2	(2.8, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.7037
CCRT	Osimertinib	131	84 (64.1)	1.5	(0.9, 5.5)	1.27	(0.86, 1.88)	0.2338
	Placebo	62	36 (58.1)	6.8	(2.7, 11.4)			
SCRT	Osimertinib	12	6 (50.0)	2.9	(0.4, NC)	1.64	(0.46, 5.82)	0.4445
	Placebo	11	4 (36.4)	13.0	(0.8, 13.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Sore mouth				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.6274
IIIA	Osimertinib	52	32 (61.5)	1.3	(0.6, 11.1)	1.50	(0.79, 2.87)	0.2152
	Placebo	24	13 (54.2)	11.4	(2.8, 20.6)			
IIIB/IIIC	Osimertinib	91	58 (63.7)	1.5	(0.9, 5.6)	1.24	(0.78, 1.96)	0.3620
	Placebo	49	27 (55.1)	6.8	(1.3, 12.0)			
Race	Osimertinib						Interaction test:	0.7691
Asian	Osimertinib	116	78 (67.2)	1.3	(0.9, 4.6)	1.30	(0.87, 1.94)	0.1960
	Placebo	62	36 (58.1)	7.3	(2.7, 11.4)			
Non-Asian	Osimertinib	27	12 (44.4)	4.6	(0.7, 11.1)	1.55	(0.50, 4.82)	0.4464
	Placebo	11	4 (36.4)	13.0	(0.8, 13.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1LSI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Sore mouth by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Sore mouth				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.9976
Yes	Osimertinib	27	18 (66.7)	0.8	(0.5, 33.1)	1.33	(0.52, 3.36)	0.5500
	Placebo	13	6 (46.2)	3.6	(0.4, NC)			
No	Osimertinib	116	72 (62.1)	1.5	(1.0, 5.6)	1.33	(0.88, 2.00)	0.1784
	Placebo	60	34 (56.7)	7.4	(2.8, 12.0)			
Response to prior CRT	Osimertinib						Interaction test:	0.9183
CR+PR	Osimertinib	71	47 (66.2)	1.5	(0.9, 5.5)	1.38	(0.79, 2.42)	0.2552
	Placebo	30	17 (56.7)	5.9	(1.6, 11.4)			
SD	Osimertinib	61	37 (60.7)	1.5	(0.9, 19.3)	1.21	(0.70, 2.09)	0.4908
	Placebo	37	20 (54.1)	7.3	(1.8, 20.6)			
NE	Osimertinib	11	6 (54.5)	0.6	(0.4, NC)	1.55	(0.39, 6.20)	0.5389
	Placebo	6	3 (50.0)	9.2	(0.5, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Table LT1LSI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Sore mouth by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Sore mouth				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.9736
Asia	Osimertinib	120	80 (66.7)	1.3	(0.9, 4.6)	1.32	(0.89, 1.95)	0.1716
	Placebo	64	37 (57.8)	7.3	(2.7, 12.0)			
Europe	Osimertinib	11	5 (45.5)	1.1	(0.2, NC)	1.53	(0.30, 7.95)	0.6109
	Placebo	7	2 (28.6)	NC				
Rest of the World	Osimertinib	12	5 (41.7)	5.5	(0.3, NC)	1.56	(0.18, 13.35)	0.6852
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.7694
Positive	Osimertinib	10	5 (50.0)	9.2	(0.4, NC)	1.13	(0.22, 5.82)	0.8874
	Placebo	4	2 (50.0)	NC				
Negative	Osimertinib	113	73 (64.6)	1.5	(0.9, 4.6)	1.27	(0.84, 1.92)	0.2479
	Placebo	58	34 (58.6)	7.3	(2.7, 12.0)			
Unknown	Osimertinib	20	12 (60.0)	1.3	(0.4, 32.3)	1.93	(0.62, 6.01)	0.2545
	Placebo	11	4 (36.4)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LSI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Sore mouth by main subgroups
 Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Sore mouth				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.9937				
Ex19Del	Osimertinib	74	46 (62.2)	1.2	(0.5, 5.5)	1.34	(0.82, 2.17)	0.2410
	Placebo	43	26 (60.5)	7.3	(2.7, 13.0)			
L858R	Osimertinib	68	43 (63.2)	3.7	(1.1, 9.2)	1.33	(0.73, 2.44)	0.3516
	Placebo	30	14 (46.7)	10.4	(1.1, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1LDI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dyspnoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.5199
Male	Osimertinib	53	40 (75.5)	1.2	(0.6, 2.7)	1.28	(0.75, 2.20)	0.3652
	Placebo	31	20 (64.5)	2.3	(0.7, 11.3)			
Female	Osimertinib	90	70 (77.8)	1.0	(0.8, 1.3)	1.61	(1.04, 2.51)	0.0345 *
	Placebo	42	28 (66.7)	1.8	(0.6, 6.5)			
Age	Osimertinib						Interaction test:	0.3863
< 65 years	Osimertinib	81	64 (79.0)	0.9	(0.6, 1.3)	1.69	(1.05, 2.73)	0.0314 *
	Placebo	39	23 (59.0)	1.8	(0.7, 11.1)			
>= 65 years	Osimertinib	62	46 (74.2)	1.1	(0.9, 1.5)	1.25	(0.77, 2.04)	0.3674
	Placebo	34	25 (73.5)	1.9	(0.6, 8.3)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1LDI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dyspnoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.8584
Current/former	Osimertinib	41	31 (75.6)	1.4	(0.6, 2.7)	1.39	(0.76, 2.54)	0.2914
	Placebo	24	16 (66.7)	6.4	(0.7, 18.4)			
Never	Osimertinib	102	79 (77.5)	0.9	(0.7, 1.2)	1.48	(0.98, 2.24)	0.0624
	Placebo	49	32 (65.3)	1.4	(0.6, 3.7)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.5641
CCRT	Osimertinib	131	101 (77.1)	1.1	(0.9, 1.3)	1.46	(1.01, 2.12)	0.0459 *
	Placebo	62	39 (62.9)	1.9	(0.7, 6.4)			
SCRT	Osimertinib	12	9 (75.0)	0.7	(0.4, 1.0)	1.96	(0.78, 4.96)	0.1546
	Placebo	11	9 (81.8)	1.4	(0.6, 10.1)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

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Table LT1LDI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dyspnoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.3823
IIIA	Osimertinib	52	41 (78.8)	0.9	(0.6, 1.2)	1.80	(1.01, 3.22)	0.0472 *
	Placebo	24	16 (66.7)	4.6	(0.7, 8.3)			
IIIB/IIIC	Osimertinib	91	69 (75.8)	1.1	(0.7, 1.5)	1.31	(0.86, 2.00)	0.2073
	Placebo	49	32 (65.3)	1.1	(0.6, 5.6)			
Race	Osimertinib						Interaction test:	0.9970
Asian	Osimertinib	116	96 (82.8)	1.0	(0.7, 1.3)	1.47	(1.02, 2.13)	0.0404 *
	Placebo	62	41 (66.1)	1.8	(0.8, 6.4)			
Non-Asian	Osimertinib	27	14 (51.9)	1.1	(0.5, 1.5)	1.47	(0.59, 3.65)	0.4088
	Placebo	11	7 (63.6)	6.4	(0.4, 10.1)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LDI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dyspnoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.5231
Yes	Osimertinib	27	22 (81.5)	0.6	(0.4, 1.5)	1.17	(0.55, 2.47)	0.6877
	Placebo	13	10 (76.9)	1.1	(0.4, 5.6)			
No	Osimertinib	116	88 (75.9)	1.2	(0.9, 1.3)	1.54	(1.05, 2.26)	0.0277 *
	Placebo	60	38 (63.3)	2.3	(0.8, 10.1)			
Response to prior CRT	Osimertinib						Interaction test:	0.0928
CR+PR	Osimertinib	71	52 (73.2)	0.9	(0.6, 1.4)	1.63	(0.96, 2.76)	0.0701
	Placebo	30	19 (63.3)	1.9	(0.8, 10.1)			
SD	Osimertinib	61	51 (83.6)	1.2	(0.9, 1.4)	1.58	(0.97, 2.58)	0.0665
	Placebo	37	24 (64.9)	5.0	(0.6, 11.1)			
NE	Osimertinib	11	7 (63.6)	0.7	(0.4, NC)	0.38	(0.12, 1.22)	0.1044
	Placebo	6	5 (83.3)	0.5	(0.4, 1.8)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LDI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dyspnoea by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.4917
Asia	Osimertinib	120	99 (82.5)	1.0	(0.7, 1.3)	1.47	(1.02, 2.11)	0.0369 *
	Placebo	64	43 (67.2)	1.8	(0.7, 6.4)			
Europe	Osimertinib	11	6 (54.5)	0.9	(0.2, 1.3)	2.64	(0.66, 10.59)	0.1703
	Placebo	7	3 (42.9)	10.1	(0.4, 10.1)			
Rest of the World	Osimertinib	12	5 (41.7)	1.5	(0.4, NC)	0.70	(0.14, 3.61)	0.6681
	Placebo	2	2 (100.0)	3.5	(0.6, 6.4)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.9357
Positive	Osimertinib	10	9 (90.0)	1.2	(0.5, 2.8)	1.29	(0.39, 4.19)	0.6768
	Placebo	4	4 (100.0)	3.2	(0.4, 5.6)			
Negative	Osimertinib	113	88 (77.9)	1.1	(0.7, 1.3)	1.45	(0.98, 2.13)	0.0621
	Placebo	58	37 (63.8)	1.1	(0.6, 6.4)			
Unknown	Osimertinib	20	13 (65.0)	1.0	(0.4, 1.5)	1.67	(0.67, 4.21)	0.2730
	Placebo	11	7 (63.6)	6.0	(0.4, 18.4)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1LDI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Dyspnoea by main subgroups
 Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Dyspnoea				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.9978				
Ex19Del	Osimertinib	74	57 (77.0)	1.1	(0.7, 1.4)	1.46	(0.93, 2.28)	0.1015
	Placebo	43	29 (67.4)	2.7	(0.7, 6.5)			
L858R	Osimertinib	68	52 (76.5)	1.1	(0.7, 1.4)	1.46	(0.86, 2.47)	0.1613
	Placebo	30	19 (63.3)	1.7	(0.5, 11.1)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

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Table LT1LNI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.4844
Male	Osimertinib	53	34 (64.2)	4.6	(2.7, 9.2)	1.25	(0.69, 2.23)	0.4605
	Placebo	31	17 (54.8)	9.1	(2.8, 20.6)			
Female	Osimertinib	90	53 (58.9)	4.6	(1.2, 6.4)	1.65	(0.97, 2.82)	0.0661
	Placebo	42	18 (42.9)	14.7	(2.7, NC)			
Age	Osimertinib						Interaction test:	0.2318
< 65 years	Osimertinib	81	49 (60.5)	3.6	(1.5, 6.5)	1.16	(0.69, 1.95)	0.5852
	Placebo	39	20 (51.3)	7.9	(1.7, 20.6)			
>= 65 years	Osimertinib	62	38 (61.3)	5.5	(1.3, 9.3)	1.88	(1.03, 3.41)	0.0393 *
	Placebo	34	15 (44.1)	14.7	(4.5, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LNI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.7040
Current/former	Osimertinib	41	26 (63.4)	6.5	(2.7, 12.9)	1.31	(0.68, 2.51)	0.4208
	Placebo	24	14 (58.3)	9.2	(3.6, NC)			
Never	Osimertinib	102	61 (59.8)	3.6	(1.3, 6.4)	1.53	(0.93, 2.52)	0.0922
	Placebo	49	21 (42.9)	9.9	(1.9, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.2068
CCRT	Osimertinib	131	80 (61.1)	4.6	(2.7, 6.5)	1.34	(0.89, 2.02)	0.1662
	Placebo	62	32 (51.6)	9.1	(4.5, 20.6)			
SCRT	Osimertinib	12	7 (58.3)	2.4	(0.2, NC)	3.21	(0.83, 12.43)	0.0910
	Placebo	11	3 (27.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.0943
IIIA	Osimertinib	52	33 (63.5)	4.6	(1.4, 9.1)	2.37	(1.14, 4.97)	0.0216 *
	Placebo	24	9 (37.5)	20.6	(4.5, NC)			
IIIB/IIIC	Osimertinib	91	54 (59.3)	4.6	(1.4, 9.2)	1.15	(0.72, 1.84)	0.5624
	Placebo	49	26 (53.1)	6.5	(1.8, 14.7)			
Race	Osimertinib						Interaction test:	0.6551
Asian	Osimertinib	116	78 (67.2)	4.6	(1.6, 6.4)	1.51	(0.996, 2.29)	0.0524
	Placebo	62	31 (50.0)	9.9	(4.5, NC)			
Non-Asian	Osimertinib	27	9 (33.3)	5.6	(1.1, NC)	1.13	(0.35, 3.67)	0.8373
	Placebo	11	4 (36.4)	6.4	(0.6, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1LNI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.6116
Yes	Osimertinib	27	19 (70.4)	5.1	(0.8, 18.4)	1.89	(0.64, 5.57)	0.2500
	Placebo	13	4 (30.8)	NC				
No	Osimertinib	116	68 (58.6)	4.6	(1.6, 6.5)	1.41	(0.92, 2.15)	0.1168
	Placebo	60	31 (51.7)	9.2	(4.5, 20.6)			
Response to prior CRT	Osimertinib						Interaction test:	0.6905
CR+PR	Osimertinib	71	36 (50.7)	6.4	(3.6, 14.7)	1.51	(0.78, 2.90)	0.2186
	Placebo	30	12 (40.0)	NC				
SD	Osimertinib	61	45 (73.8)	2.7	(1.3, 5.5)	1.63	(0.96, 2.77)	0.0682
	Placebo	37	20 (54.1)	6.5	(1.8, 20.6)			
NE	Osimertinib	11	6 (54.5)	6.5	(0.2, NC)	0.83	(0.21, 3.34)	0.7953
	Placebo	6	3 (50.0)	2.8	(0.5, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.4015
Asia	Osimertinib	120	80 (66.7)	3.7	(1.6, 6.4)	1.57	(1.04, 2.38)	0.0336 *
	Placebo	64	31 (48.4)	9.9	(4.5, NC)			
Europe	Osimertinib	11	4 (36.4)	5.6	(0.4, NC)	1.20	(0.22, 6.55)	0.8335
	Placebo	7	2 (28.6)	NC				
Rest of the World	Osimertinib	12	3 (25.0)	10.1	(0.5, NC)	0.41	(0.07, 2.49)	0.3353
	Placebo	2	2 (100.0)	5.5	(4.5, 6.4)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.9708
Positive	Osimertinib	10	7 (70.0)	2.7	(0.4, 11.9)	1.38	(0.29, 6.67)	0.6862
	Placebo	4	2 (50.0)	NC				
Negative	Osimertinib	113	71 (62.8)	4.6	(1.6, 6.5)	1.43	(0.93, 2.20)	0.0994
	Placebo	58	30 (51.7)	9.2	(4.5, 20.6)			
Unknown	Osimertinib	20	9 (45.0)	6.4	(0.9, NC)	1.69	(0.46, 6.24)	0.4328
	Placebo	11	3 (27.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Peripheral neuropathy				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.4112
Ex19Del	Osimertinib	74	49 (66.2)	1.6	(1.1, 5.6)	1.70	(1.03, 2.82)	0.0392 *
	Placebo	43	22 (51.2)	9.9	(6.4, 20.6)			
L858R	Osimertinib	68	37 (54.4)	6.4	(3.6, 9.3)	1.21	(0.64, 2.28)	0.5563
	Placebo	30	13 (43.3)	9.2	(1.7, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1LAI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Alopecia by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Alopecia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.8135
Male	Osimertinib	53	15 (28.3)	NC		0.91	(0.39, 2.17)	0.8382
	Placebo	31	8 (25.8)	NC				
Female	Osimertinib	90	29 (32.2)	47.5	(13.8, NC)	1.04	(0.53, 2.05)	0.9043
	Placebo	42	12 (28.6)	NC				
Age	Osimertinib						Interaction test:	0.6954
< 65 years	Osimertinib	81	29 (35.8)	47.5	(14.7, 47.5)	0.89	(0.46, 1.74)	0.7375
	Placebo	39	13 (33.3)	15.5	(11.0, NC)			
>= 65 years	Osimertinib	62	15 (24.2)	NC		1.11	(0.45, 2.73)	0.8150
	Placebo	34	7 (20.6)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1LAI10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Alopecia by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Alopecia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.4193
Current/former	Osimertinib	41	9 (22.0)	NC		0.69	(0.25, 1.85)	0.4573
	Placebo	24	7 (29.2)	NC				
Never	Osimertinib	102	35 (34.3)	47.5	(13.8, NC)	1.12	(0.59, 2.12)	0.7362
	Placebo	49	13 (26.5)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.1042
CCRT	Osimertinib	131	38 (29.0)	47.5	(30.4, NC)	0.88	(0.50, 1.54)	0.6447
	Placebo	62	18 (29.0)	NC				
SCRT	Osimertinib	12	6 (50.0)	8.2	(0.5, NC)	3.27	(0.66, 16.26)	0.1473
	Placebo	11	2 (18.2)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Alopecia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.1571
IIIA	Osimertinib	52	21 (40.4)	21.2	(7.4, NC)	1.63	(0.66, 4.06)	0.2903
	Placebo	24	6 (25.0)	NC				
IIIB/IIIC	Osimertinib	91	23 (25.3)	47.5	(47.5, NC)	0.74	(0.38, 1.44)	0.3716
	Placebo	49	14 (28.6)	NC				
Race	Osimertinib						Interaction test:	0.5729
Asian	Osimertinib	116	35 (30.2)	47.5	(30.4, NC)	0.93	(0.52, 1.67)	0.8051
	Placebo	62	17 (27.4)	NC				
Non-Asian	Osimertinib	27	9 (33.3)	7.4	(2.8, NC)	1.39	(0.38, 5.14)	0.6211
	Placebo	11	3 (27.3)	8.9	(1.1, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Alopecia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.4154
Yes	Osimertinib	27	14 (51.9)	8.2	(2.7, NC)	1.44	(0.47, 4.38)	0.5243
	Placebo	13	4 (30.8)	12.3	(1.5, NC)			
No	Osimertinib	116	30 (25.9)	47.5	(47.5, NC)	0.86	(0.47, 1.59)	0.6276
	Placebo	60	16 (26.7)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.9742
CR+PR	Osimertinib	71	18 (25.4)	NC		0.96	(0.41, 2.22)	0.9193
	Placebo	30	8 (26.7)	NC				
SD	Osimertinib	61	23 (37.7)	47.5	(14.7, NC)	1.08	(0.51, 2.28)	0.8417
	Placebo	37	10 (27.0)	NC				
NE	Osimertinib	11	3 (27.3)	30.4	(0.4, 30.4)	0.94	(0.16, 5.61)	0.9427
	Placebo	6	2 (33.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Time to increase by at least 10 points in QLQ-LC13 Alopecia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.7203
Asia	Osimertinib	120	37 (30.8)	47.5	(30.4, NC)	0.99	(0.55, 1.76)	0.9601
	Placebo	64	17 (26.6)	NC				
Europe	Osimertinib	11	3 (27.3)	NC		1.62	(0.17, 15.64)	0.6755
	Placebo	7	1 (14.3)	NC				
Rest of the World	Osimertinib	12	4 (33.3)	5.5	(1.1, NC)	0.53	(0.10, 2.92)	0.4684
	Placebo	2	2 (100.0)	4.7	(1.1, 8.2)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.9392
Positive	Osimertinib	10	3 (30.0)	47.5	(0.6, 47.5)	0.89	(0.09, 8.63)	0.9179
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	35 (31.0)	NC		0.98	(0.55, 1.76)	0.9465
	Placebo	58	17 (29.3)	NC				
Unknown	Osimertinib	20	6 (30.0)	NC		1.30	(0.26, 6.49)	0.7451
	Placebo	11	2 (18.2)	NC				

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The CI for median time was calculated based on Brookmeyer/Crowley.

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 Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Alopecia				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.8034				
Ex19Del	Osimertinib	74	26 (35.1)	47.5	(18.9, NC)	0.99	(0.51, 1.92)	0.9835
	Placebo	43	14 (32.6)	NC				
L858R	Osimertinib	68	18 (26.5)	NC		1.15	(0.45, 2.89)	0.7739
	Placebo	30	6 (20.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1LT110T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	4 (7.5)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	3 (3.3)	NC		NC		NC
	Placebo	42	1 (2.4)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	3 (3.7)	NC		NC		NC
	Placebo	39	1 (2.6)	NC				
>= 65 years	Osimertinib	62	4 (6.5)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1LT110T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	5 (12.2)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	2 (2.0)	NC		NC		NC
	Placebo	49	1 (2.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	6 (4.6)	NC		NC		NC
	Placebo	62	1 (1.6)	NC				
SCRT	Osimertinib	12	1 (8.3)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas

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Table LT1LTII10T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	7 (7.7)	NC		NC		NC
	Placebo	49	1 (2.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	6 (5.2)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	1 (3.7)	NC		NC		NC
	Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1LT110T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	1 (3.7)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	6 (5.2)	NC		NC		NC
	Placebo	60	1 (1.7)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	4 (5.6)	NC		NC		NC
	Placebo	30	1 (3.3)	NC				
SD	Osimertinib	61	3 (4.9)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1LT110T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain by main subgroups
Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	7 (5.8)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	1 (14.3)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	0 (0.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	7 (6.2)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

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 Program Name: LT1_APRO_TTE_TS.sas
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Table LT1LT110T_SFTM: Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain by main subgroups
 Full Analysis Set

Time to increase by at least 10 points in QLQ-LC13 Take any medicine for pain				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	NC
Ex19Del	Osimertinib	74	1 (1.4)	NC		NC		NC
	Placebo	43	1 (2.3)	NC				
L858R	Osimertinib	68	6 (8.8)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APRO_TTE_KS.sas

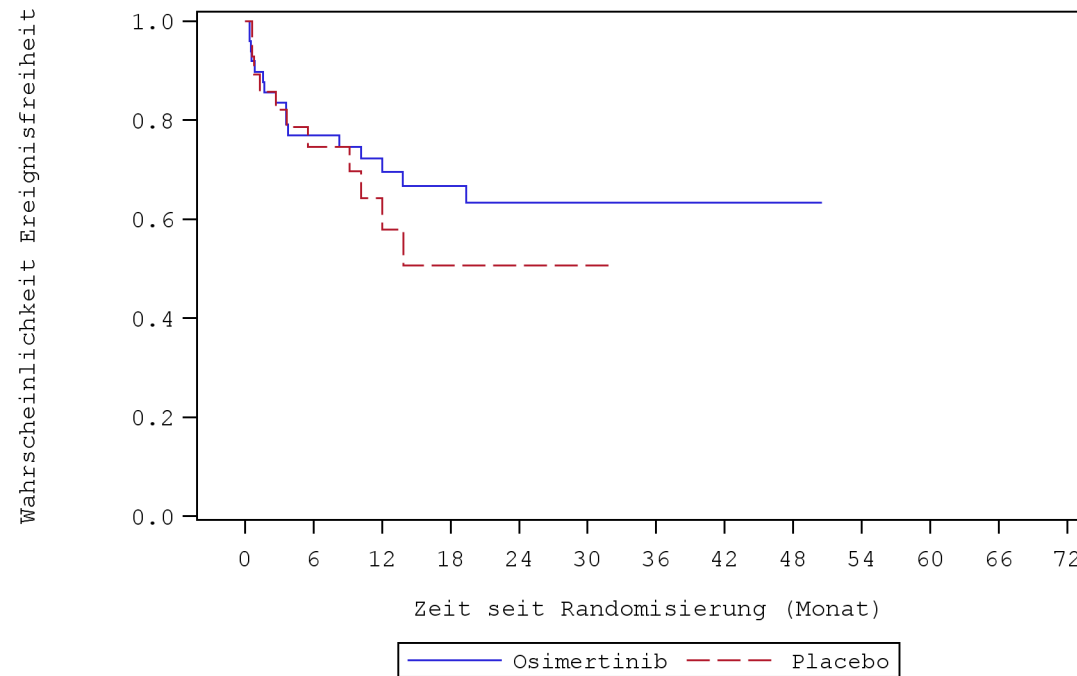
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Figure LF1LHI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups

Full Analysis Set

Study: LAURA

Sex: Male



Osimertinib	53	34	25	23	16	11	7	3	1	0
Placebo	31	19	9	4	1	1	0			

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LHI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APRO_TTE_KS.sas

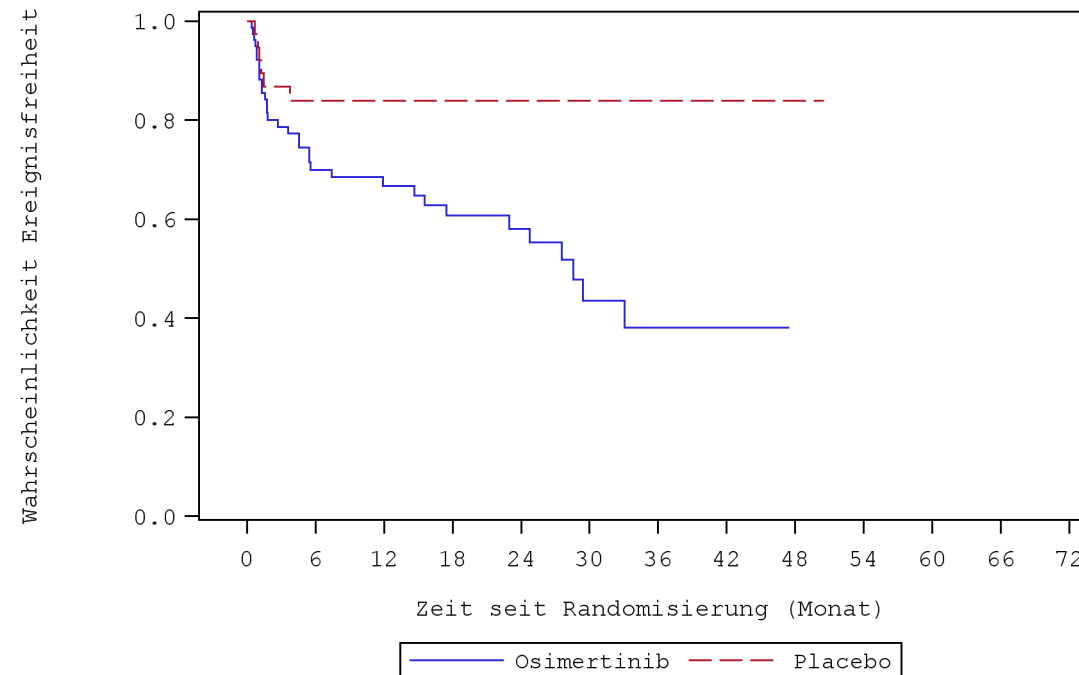
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Figure LF1LHI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups

Full Analysis Set

Study: LAURA

Sex: Female



Osimertinib	90	46	37	29	21	10	6	2	0
Placebo	42	29	16	5	2	2	1	1	1

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LHI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

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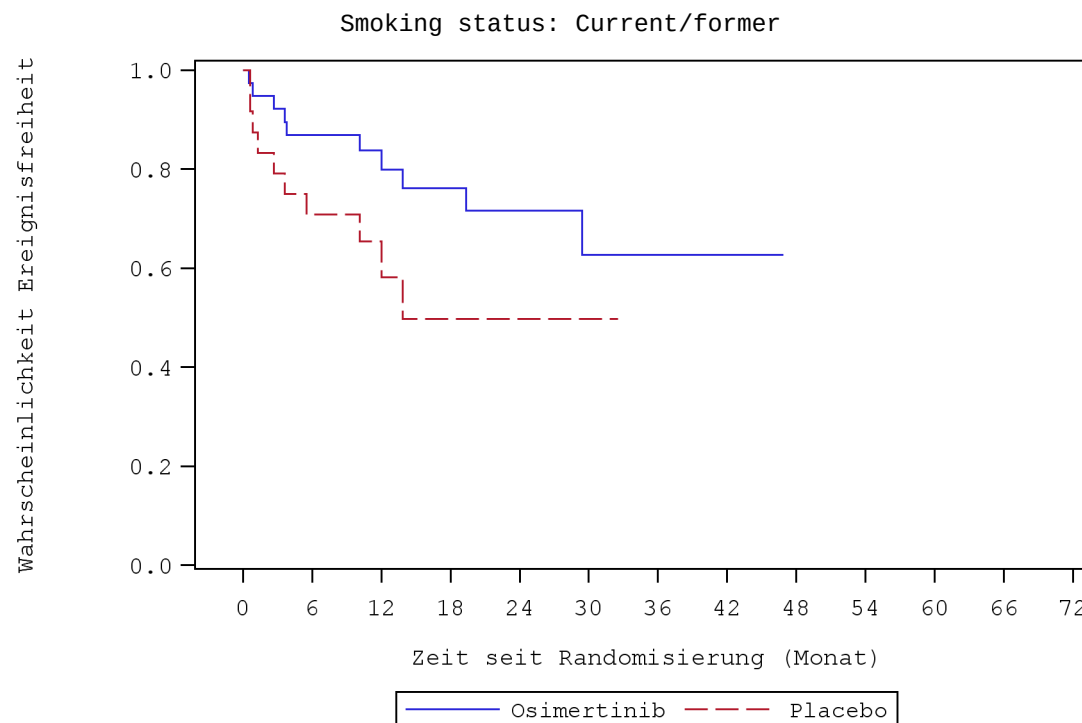
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Figure LF1LHI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups

Full Analysis Set

Study: LAURA



Osimertinib	41	30	21	18	12	7	4	1	0
Placebo	24	17	8	4	1	1	0		

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LHI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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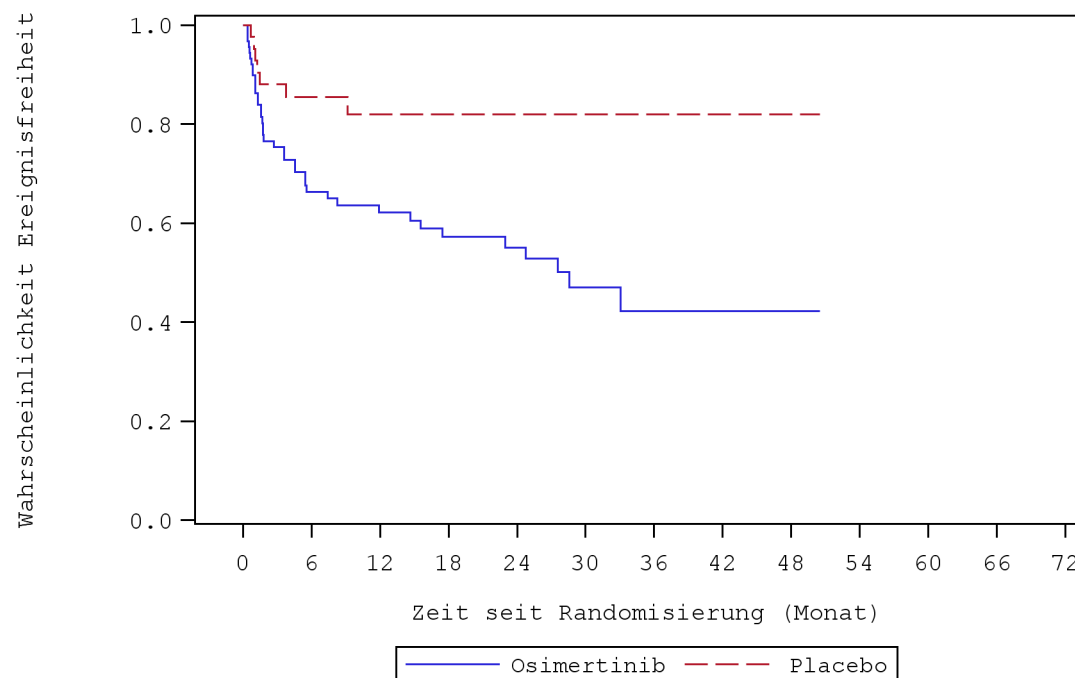
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Figure LF1LHI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups

Full Analysis Set

Study: LAURA

Smoking status: Never



Osimertinib	102	50	41	34	25	14	9	4	1	0
Placebo	49	31	17	5	2	2	1	1	1	0

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LHI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

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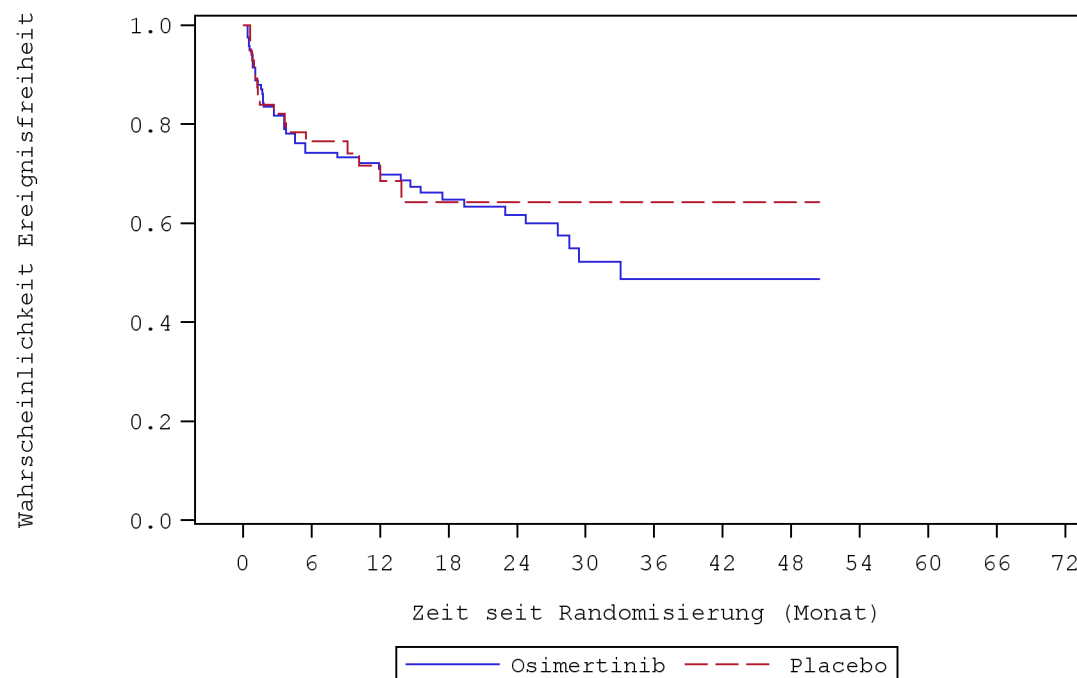
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Figure LF1LHI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups

Full Analysis Set

Study: LAURA

Prior chemoradiation strategy: CCRT



Osimertinib	131	76	59	49	35	19	12	4	1	0
Placebo	62	41	22	8	3	3	1	1	1	0

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LHI10T_SFTM

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Program Name: LF1_APRO_TTE_KS.sas

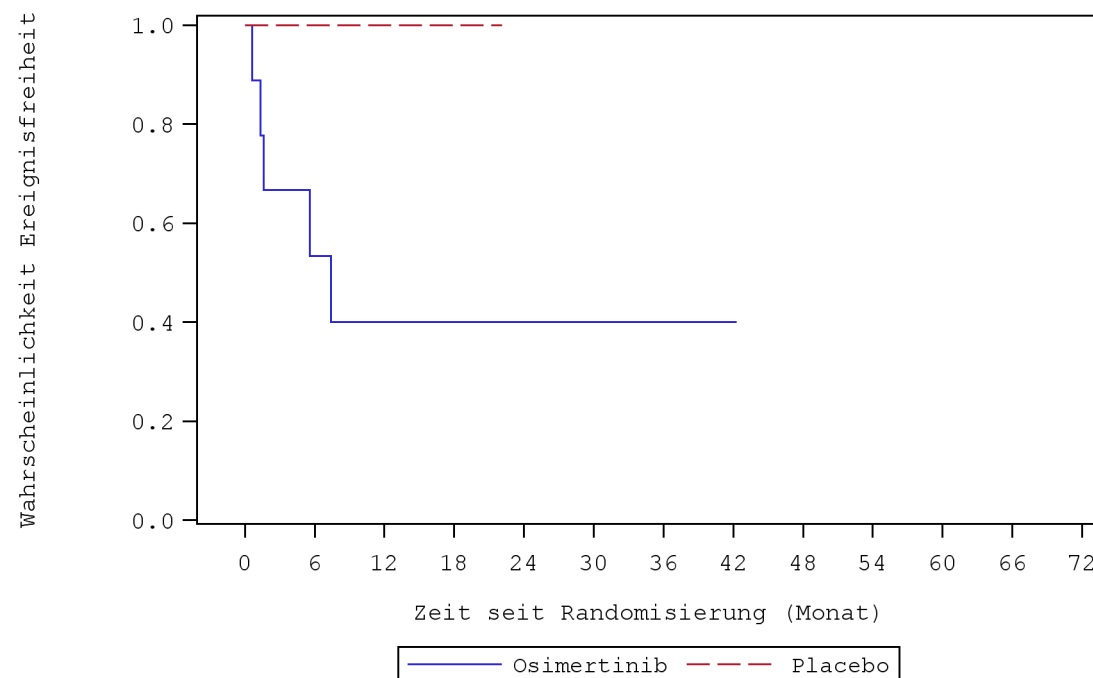
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Figure LF1LHI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Haemoptysis by main subgroups

Full Analysis Set

Study: LAURA

Prior chemoradiation strategy: SCRT



Osimertinib	12	4	3	3	2	2	1	1	0
Placebo	11	7	3	1	0				

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LHI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

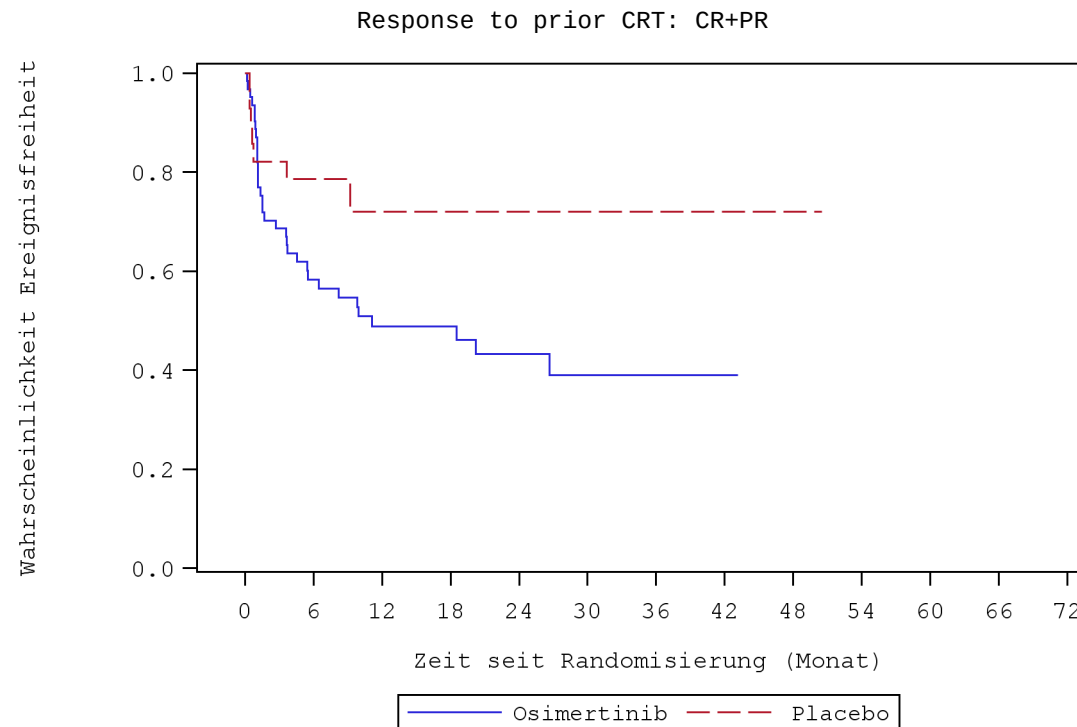
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Program Name: LF1_APRO_TTE_KS.sas

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Figure LF1LPI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Dysphagia by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	71	32	23	19	14	8	3	1	0
Placebo	30	18	8	3	1	1	1	1	0

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.
Reference table: LT1LPI10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

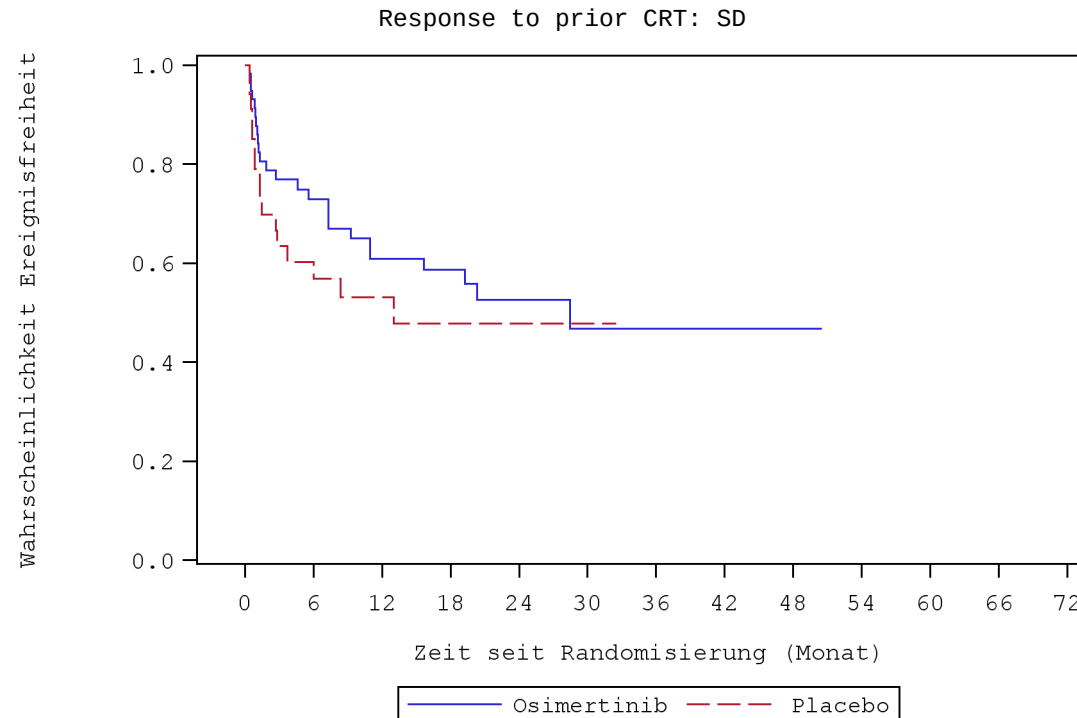
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Program Name: LF1_APRO_TTE_KS.sas

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Figure LF1LPI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Dysphagia by main subgroups
Full Analysis Set
Study: LAURA



Osimertinib	61	37	28	25	15	7	6	3	1	0
Placebo	37	18	10	3	1	1	0			

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.
Reference table: LT1LPI10T_SFkm

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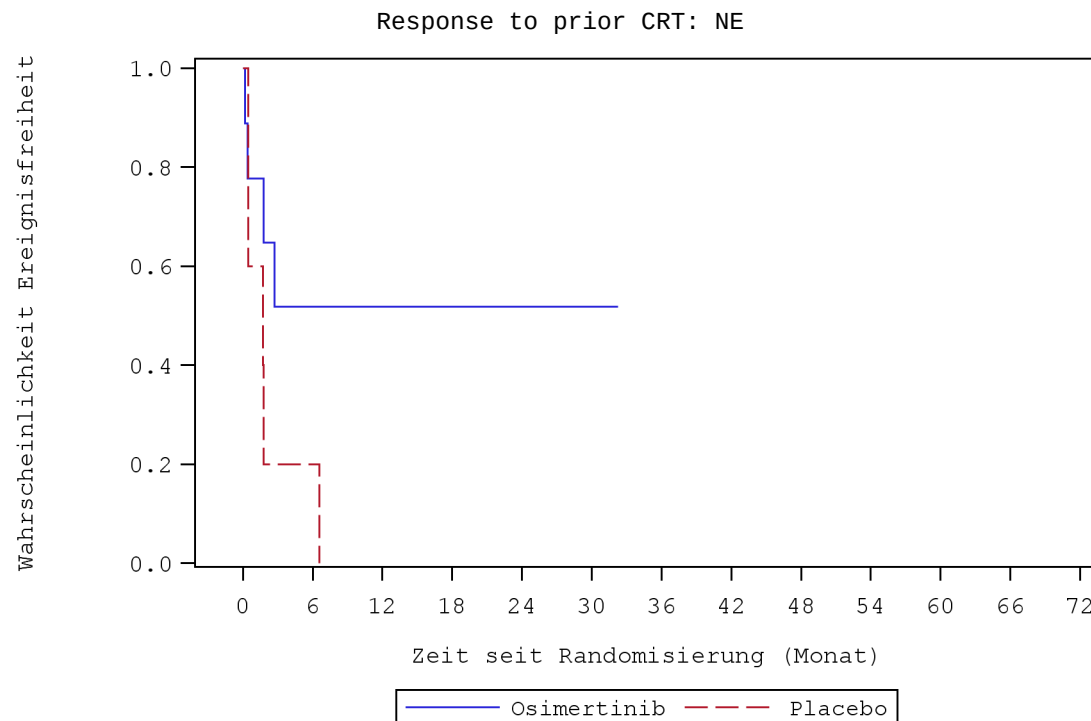
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Run Date: 27SEP2024:11:28:15

Figure LF1LPI10T_SFkm: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Dysphagia by main subgroups

Full Analysis Set

Study: LAURA



Osimertinib	11	3	1	1	1	1	0
Placebo	6	1	0				

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LPI10T_SFTM

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Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_APRO_TTE_KS.sas

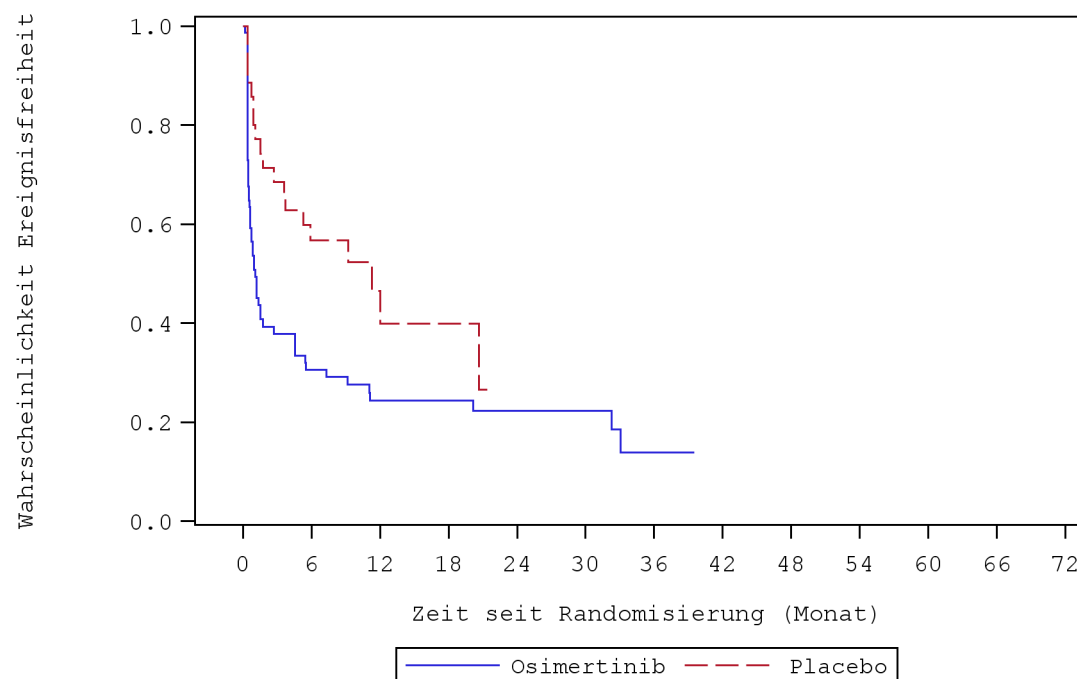
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Figure LF1LSI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Sore mouth by main subgroups

Full Analysis Set

Study: LAURA

Age: < 65 years



Osimertinib	81	21	15	13	10	6	3	0
Placebo	39	18	6	3	0			

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LSI10T_SFTM

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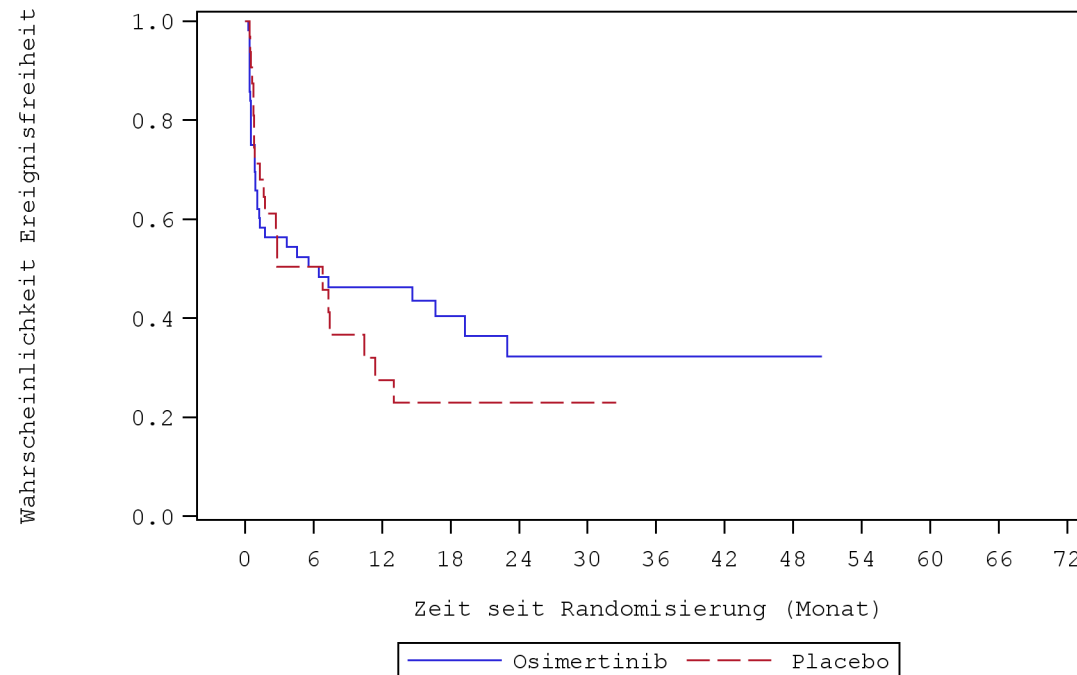
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Figure LF1LSI10T_SFKM: Kaplan Meier plot for time to increase by at least 10 points in QLQ-LC13 Sore mouth by main subgroups

Full Analysis Set

Study: LAURA

Age: >= 65 years



Osimertinib	62	25	18	12	8	6	5	2	1	0
Placebo	34	12	6	1	1	1	0			

QLQ-LC13: EORTC Cancer Quality of Life Questionnaire – Lung Cancer 13 items.

Reference table: LT1LSI10T_SFTM

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1EVD15T_SFTM: Time to decrease by at least 15 points in EQ-5D VAS by main subgroups
Full Analysis Set

Time to decrease by at least 15 points in EQ-5D VAS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.0751
Male	Osimertinib	53	24 (45.3)	33.1	(3.7, NC)	2.38	(0.97, 5.83)	0.0585
	Placebo	31	6 (19.4)	NC				
Female	Osimertinib	90	48 (53.3)	6.4	(3.7, 33.1)	0.97	(0.58, 1.62)	0.8973
	Placebo	42	21 (50.0)	5.6	(3.7, NC)			
Age	Osimertinib						Interaction test:	0.1854
< 65 years	Osimertinib	81	38 (46.9)	33.1	(5.5, NC)	1.00	(0.55, 1.81)	0.9960
	Placebo	39	16 (41.0)	11.0	(4.2, NC)			
>= 65 years	Osimertinib	62	34 (54.8)	6.4	(1.9, 22.0)	1.83	(0.93, 3.62)	0.0822
	Placebo	34	11 (32.4)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

EQ-5D VAS: EuroQoL 5-Dimension visual analogue scale.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1EVD15T_SFTM: Time to decrease by at least 15 points in EQ-5D VAS by main subgroups
Full Analysis Set

Time to decrease by at least 15 points in EQ-5D VAS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.0769
Current/former	Osimertinib	41	23 (56.1)	9.2	(1.9, NC)	2.44	(0.99, 6.02)	0.0519
	Placebo	24	6 (25.0)	NC				
Never	Osimertinib	102	49 (48.0)	16.7	(3.8, 38.6)	0.99	(0.59, 1.67)	0.9848
	Placebo	49	21 (42.9)	7.3	(3.9, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.1688
CCRT	Osimertinib	131	68 (51.9)	9.1	(5.5, 33.1)	1.47	(0.90, 2.38)	0.1224
	Placebo	62	22 (35.5)	NC				
SCRT	Osimertinib	12	4 (33.3)	NC		0.55	(0.15, 2.06)	0.3725
	Placebo	11	5 (45.5)	5.7	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

EQ-5D VAS: EuroQoL 5-Dimension visual analogue scale.

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Table LT1EVD15T_SFTM: Time to decrease by at least 15 points in EQ-5D VAS by main subgroups
Full Analysis Set

Time to decrease by at least 15 points in EQ-5D VAS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.7315
IIIA	Osimertinib	52	31 (59.6)	6.4	(3.7, 22.0)	1.44	(0.70, 2.93)	0.3214
	Placebo	24	10 (41.7)	11.0	(4.9, NC)			
IIIB/IIIC	Osimertinib	91	41 (45.1)	33.1	(3.7, NC)	1.22	(0.69, 2.17)	0.4887
	Placebo	49	17 (34.7)	NC				
Race	Osimertinib						Interaction test:	0.5368
Asian	Osimertinib	116	62 (53.4)	9.2	(3.8, 38.6)	1.25	(0.78, 2.00)	0.3514
	Placebo	62	25 (40.3)	NC				
Non-Asian	Osimertinib	27	10 (37.0)	6.4	(1.8, NC)	2.02	(0.44, 9.23)	0.3641
	Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Table LT1EVD15T_SFTM: Time to decrease by at least 15 points in EQ-5D VAS by main subgroups
Full Analysis Set

Time to decrease by at least 15 points in EQ-5D VAS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.0716
Yes	Osimertinib	27	9 (33.3)	NC		0.53	(0.19, 1.51)	0.2351
	Placebo	13	6 (46.2)	5.6	(1.9, 11.0)			
No	Osimertinib	116	63 (54.3)	5.5	(3.7, 22.0)	1.59	(0.97, 2.61)	0.0687
	Placebo	60	21 (35.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.2048
CR+PR	Osimertinib	71	38 (53.5)	9.2	(3.7, 38.6)	1.54	(0.78, 3.02)	0.2111
	Placebo	30	11 (36.7)	NC				
SD	Osimertinib	61	33 (54.1)	5.5	(3.7, NC)	1.33	(0.71, 2.50)	0.3678
	Placebo	37	14 (37.8)	NC				
NE	Osimertinib	11	1 (9.1)	NC		0.17	(0.02, 1.89)	0.1492
	Placebo	6	2 (33.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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EQ-5D VAS: EuroQoL 5-Dimension visual analogue scale.

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Table LT1EVD15T_SFTM: Time to decrease by at least 15 points in EQ-5D VAS by main subgroups
Full Analysis Set

Time to decrease by at least 15 points in EQ-5D VAS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.2348
Asia	Osimertinib	120	64 (53.3)	9.2	(3.8, 33.1)	1.23	(0.78, 1.96)	0.3719
	Placebo	64	26 (40.6)	NC				
Europe	Osimertinib	11	3 (27.3)	NC		1.18	(0.12, 11.34)	0.8875
	Placebo	7	1 (14.3)	NC				
Rest of the World	Osimertinib	12	5 (41.7)	5.5	(0.9, NC)	NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.1521
Positive	Osimertinib	10	8 (80.0)	4.6	(0.9, 38.6)	3.57	(0.44, 28.57)	0.2312
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	55 (48.7)	9.2	(3.8, NC)	1.08	(0.67, 1.74)	0.7435
	Placebo	58	25 (43.1)	11.0	(4.2, NC)			
Unknown	Osimertinib	20	9 (45.0)	16.7	(1.0, NC)	4.66	(0.59, 36.79)	0.1448
	Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1EVD15T_SFTM: Time to decrease by at least 15 points in EQ-5D VAS by main subgroups
Full Analysis Set

Time to decrease by at least 15 points in EQ-5D VAS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.1335				
Ex19Del	Osimertinib	74	40 (54.1)	5.5	(3.7, 38.6)	1.79	(0.97, 3.29)	0.0620
	Placebo	43	14 (32.6)	NC				
L858R	Osimertinib	68	32 (47.1)	20.3	(3.7, NC)	0.90	(0.47, 1.73)	0.7581
	Placebo	30	13 (43.3)	11.0	(3.6, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1IIII1T_SFTM: Time to increase by at least 1 point in PGIS by main subgroups
Full Analysis Set

Time to increase by at least 1 point in PGIS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.4277
Male	Osimertinib	53	29 (54.7)	12.9	(3.6, NC)	0.50	(0.29, 0.87)	0.0138 *
	Placebo	31	25 (80.6)	3.6	(1.9, 5.6)			
Female	Osimertinib	90	44 (48.9)	9.1	(3.6, 36.7)	0.68	(0.41, 1.10)	0.1153
	Placebo	42	26 (61.9)	3.7	(1.9, 5.9)			
Age	Osimertinib						Interaction test:	0.6926
< 65 years	Osimertinib	81	42 (51.9)	12.8	(3.6, 36.7)	0.55	(0.34, 0.91)	0.0187 *
	Placebo	39	27 (69.2)	3.6	(1.9, 5.6)			
>= 65 years	Osimertinib	62	31 (50.0)	9.2	(3.6, NC)	0.64	(0.37, 1.09)	0.1024
	Placebo	34	24 (70.6)	3.7	(1.9, 7.4)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

PGIS: Patients Global Impression of Severity.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1III1T_SFTM: Time to increase by at least 1 point in PGIS by main subgroups
Full Analysis Set

Time to increase by at least 1 point in PGIS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.9989
Current/former	Osimertinib	41	23 (56.1)	7.4	(1.9, NC)	0.59	(0.32, 1.10)	0.0959
	Placebo	24	19 (79.2)	3.7	(1.9, 7.4)			
Never	Osimertinib	102	50 (49.0)	12.8	(3.7, 36.7)	0.59	(0.38, 0.93)	0.0231 *
	Placebo	49	32 (65.3)	3.7	(1.9, 5.6)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.4418
CCRT	Osimertinib	131	70 (53.4)	9.2	(3.7, 22.0)	0.60	(0.41, 0.88)	0.0086 *
	Placebo	62	45 (72.6)	3.6	(1.9, 5.5)			
SCRT	Osimertinib	12	3 (25.0)	NC		0.35	(0.09, 1.39)	0.1344
	Placebo	11	6 (54.5)	4.8	(1.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Table LT1IIII1T_SFTM: Time to increase by at least 1 point in PGIS by main subgroups
Full Analysis Set

Time to increase by at least 1 point in PGIS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.8067
IIIA	Osimertinib	52	23 (44.2)	20.3	(3.6, NC)	0.56	(0.29, 1.07)	0.0804
	Placebo	24	15 (62.5)	4.3	(1.9, 11.0)			
IIIB/IIIC	Osimertinib	91	50 (54.9)	7.4	(3.6, 25.8)	0.62	(0.40, 0.95)	0.0298 *
	Placebo	49	36 (73.5)	3.7	(1.9, 5.6)			
Race	Osimertinib						Interaction test:	0.5703
Asian	Osimertinib	116	64 (55.2)	9.2	(3.7, 35.4)	0.61	(0.42, 0.91)	0.0137 *
	Placebo	62	46 (74.2)	3.7	(2.0, 5.6)			
Non-Asian	Osimertinib	27	9 (33.3)	11.0	(1.9, NC)	0.44	(0.15, 1.31)	0.1394
	Placebo	11	5 (45.5)	3.6	(1.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1IIII1T_SFTM: Time to increase by at least 1 point in PGIS by main subgroups
Full Analysis Set

Time to increase by at least 1 point in PGIS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.0877
Yes	Osimertinib	27	9 (33.3)	NC		0.28	(0.11, 0.72)	0.0080 *
	Placebo	13	9 (69.2)	3.6	(1.8, 7.4)			
No	Osimertinib	116	64 (55.2)	7.4	(3.7, 20.3)	0.69	(0.46, 1.02)	0.0616
	Placebo	60	42 (70.0)	3.7	(1.9, 5.6)			
Response to prior CRT	Osimertinib						Interaction test:	0.3983
CR+PR	Osimertinib	71	36 (50.7)	7.4	(1.9, 36.7)	0.75	(0.44, 1.29)	0.3019
	Placebo	30	21 (70.0)	5.3	(1.9, 5.9)			
SD	Osimertinib	61	32 (52.5)	14.7	(4.4, NC)	0.46	(0.27, 0.77)	0.0035 *
	Placebo	37	26 (70.3)	3.6	(1.8, 7.3)			
NE	Osimertinib	11	5 (45.5)	8.4	(1.8, NC)	0.76	(0.20, 2.84)	0.6851
	Placebo	6	4 (66.7)	3.6	(1.9, 9.2)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1IIII1T_SFTM: Time to increase by at least 1 point in PGIS by main subgroups
Full Analysis Set

Time to increase by at least 1 point in PGIS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.5110
Asia	Osimertinib	120	67 (55.8)	9.1	(3.7, 25.8)	0.63	(0.43, 0.92)	0.0169 *
	Placebo	64	47 (73.4)	3.7	(2.0, 5.6)			
Europe	Osimertinib	11	2 (18.2)	NC		0.23	(0.03, 1.66)	0.1456
	Placebo	7	2 (28.6)	5.3	(1.8, NC)			
Rest of the World	Osimertinib	12	4 (33.3)	5.5	(1.8, NC)	0.33	(0.06, 1.83)	0.2065
	Placebo	2	2 (100.0)	2.7	(1.8, 3.6)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.8677
Positive	Osimertinib	10	7 (70.0)	16.6	(1.8, 36.7)	0.60	(0.15, 2.32)	0.4554
	Placebo	4	3 (75.0)	3.6	(1.8, NC)			
Negative	Osimertinib	113	57 (50.4)	11.0	(3.8, 35.4)	0.57	(0.38, 0.85)	0.0066 *
	Placebo	58	41 (70.7)	3.6	(1.9, 5.6)			
Unknown	Osimertinib	20	9 (45.0)	5.5	(1.8, NC)	0.76	(0.28, 2.04)	0.5840
	Placebo	11	7 (63.6)	5.6	(1.8, 32.5)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

PGIS: Patients Global Impression of Severity.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_APRO_TTE_TS.sas
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Table LT1III1T_SFTM: Time to increase by at least 1 point in PGIS by main subgroups
 Full Analysis Set

Time to increase by at least 1 point in PGIS				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.2741				
Ex19Del	Osimertinib	74	39 (52.7)	9.1	(1.9, 36.7)	0.70	(0.43, 1.15)	0.1603
	Placebo	43	27 (62.8)	3.9	(1.9, 11.0)			
L858R	Osimertinib	68	33 (48.5)	11.0	(3.6, NC)	0.47	(0.27, 0.80)	0.0054 *
	Placebo	30	24 (80.0)	3.7	(1.9, 5.6)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

PGIS: Patients Global Impression of Severity.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QGD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.6808
Male	Osimertinib	53	27 (50.9)	11.0	(1.8, NC)	1.08	(0.56, 2.06)	0.8257
	Placebo	31	14 (45.2)	10.2	(4.2, NC)			
Female	Osimertinib	90	57 (63.3)	1.9	(1.0, 7.3)	1.27	(0.78, 2.07)	0.3289
	Placebo	42	23 (54.8)	5.6	(1.9, 7.4)			
Age	Osimertinib						Interaction test:	0.0707
< 65 years	Osimertinib	81	44 (54.3)	11.0	(1.8, 25.8)	0.88	(0.52, 1.49)	0.6364
	Placebo	39	21 (53.8)	5.6	(1.9, 12.0)			
≥ 65 years	Osimertinib	62	40 (64.5)	1.9	(1.0, 5.6)	1.81	(1.01, 3.23)	0.0458 *
	Placebo	34	16 (47.1)	7.4	(3.7, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QGD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.1523
Current/former	Osimertinib	41	26 (63.4)	1.9	(1.0, 12.8)	1.84	(0.89, 3.82)	0.1021
	Placebo	24	10 (41.7)	12.0	(4.2, NC)			
Never	Osimertinib	102	58 (56.9)	5.5	(1.8, 18.5)	0.99	(0.62, 1.57)	0.9672
	Placebo	49	27 (55.1)	5.5	(1.9, 6.6)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.9800
CCRT	Osimertinib	131	76 (58.0)	4.3	(1.8, 12.8)	1.25	(0.82, 1.90)	0.3068
	Placebo	62	31 (50.0)	6.2	(4.9, NC)			
SCRT	Osimertinib	12	8 (66.7)	1.0	(0.9, 16.7)	1.26	(0.44, 3.66)	0.6648
	Placebo	11	6 (54.5)	1.8	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1QGD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.4069
IIIA	Osimertinib	52	35 (67.3)	3.8	(1.0, 16.7)	1.51	(0.77, 2.98)	0.2320
	Placebo	24	11 (45.8)	6.6	(1.8, NC)			
IIIB/IIIC	Osimertinib	91	49 (53.8)	5.5	(1.8, 25.8)	1.07	(0.66, 1.73)	0.7870
	Placebo	49	26 (53.1)	5.6	(3.8, NC)			
Race	Osimertinib						Interaction test:	0.1491
Asian	Osimertinib	116	69 (59.5)	4.3	(1.8, 18.5)	1.30	(0.85, 1.99)	0.2339
	Placebo	62	31 (50.0)	6.6	(5.5, NC)			
Non-Asian	Osimertinib	27	15 (55.6)	3.6	(1.0, 11.0)	0.58	(0.22, 1.51)	0.2655
	Placebo	11	6 (54.5)	1.8	(0.9, 3.8)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1QGD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.1569
Yes	Osimertinib	27	10 (37.0)	NC		0.61	(0.22, 1.69)	0.3449
	Placebo	13	6 (46.2)	6.2	(1.0, NC)			
No	Osimertinib	116	74 (63.8)	1.9	(1.8, 7.3)	1.39	(0.91, 2.12)	0.1285
	Placebo	60	31 (51.7)	5.6	(3.8, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.1941
CR+PR	Osimertinib	71	43 (60.6)	1.9	(1.0, 9.2)	1.02	(0.60, 1.73)	0.9533
	Placebo	30	20 (66.7)	4.9	(1.9, 5.6)			
SD	Osimertinib	61	40 (65.6)	5.5	(1.8, 16.7)	1.61	(0.89, 2.92)	0.1171
	Placebo	37	15 (40.5)	12.0	(3.6, NC)			
NE	Osimertinib	11	1 (9.1)	NC		0.23	(0.02, 2.58)	0.2354
	Placebo	6	2 (33.3)	6.2	(1.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1QGD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.4694
Asia	Osimertinib	120	72 (60.0)	5.5	(1.8, 16.7)	1.27	(0.83, 1.93)	0.2736
	Placebo	64	32 (50.0)	6.6	(4.9, NC)			
Europe	Osimertinib	11	6 (54.5)	3.8	(1.0, NC)	0.49	(0.12, 1.96)	0.3112
	Placebo	7	3 (42.9)	1.1	(0.9, 3.8)			
Rest of the World	Osimertinib	12	6 (50.0)	1.0	(0.9, 20.3)	1.03	(0.21, 5.14)	0.9708
	Placebo	2	2 (100.0)	2.7	(1.8, 3.6)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.2719
Positive	Osimertinib	10	8 (80.0)	10.2	(0.9, 25.8)	3.76	(0.47, 30.16)	0.2120
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	63 (55.8)	5.5	(1.8, 12.8)	1.05	(0.69, 1.62)	0.8142
	Placebo	58	32 (55.2)	5.6	(3.8, 12.0)			
Unknown	Osimertinib	20	13 (65.0)	1.4	(0.9, 20.3)	1.91	(0.62, 5.87)	0.2594
	Placebo	11	4 (36.4)	3.8	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1QGD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL by main subgroups
 Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Global Health Status/QoL				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.0758
Ex19Del	Osimertinib	74	41 (55.4)	5.6	(1.9, 25.8)	0.89	(0.54, 1.47)	0.6587
	Placebo	43	25 (58.1)	5.5	(1.8, 12.0)			
L858R	Osimertinib	68	42 (61.8)	1.8	(1.0, 11.0)	1.84	(0.97, 3.51)	0.0639
	Placebo	30	12 (40.0)	10.2	(4.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QYD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Physical Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Physical Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.7566
Male	Osimertinib	53	28 (52.8)	11.1	(3.6, NC)	1.07	(0.55, 2.06)	0.8472
	Placebo	31	13 (41.9)	14.8	(1.0, NC)			
Female	Osimertinib	90	47 (52.2)	5.5	(3.7, 22.0)	1.22	(0.71, 2.11)	0.4714
	Placebo	42	18 (42.9)	NC				
Age	Osimertinib						Interaction test:	0.8137
< 65 years	Osimertinib	81	41 (50.6)	7.3	(3.7, NC)	1.11	(0.62, 1.98)	0.7274
	Placebo	39	16 (41.0)	NC				
>= 65 years	Osimertinib	62	34 (54.8)	9.2	(3.7, 14.8)	1.23	(0.67, 2.25)	0.5097
	Placebo	34	15 (44.1)	14.8	(1.1, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Table LT1QYD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Physical Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Physical Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.3209
Current/former	Osimertinib	41	25 (61.0)	5.5	(1.9, 14.8)	1.58	(0.74, 3.39)	0.2393
	Placebo	24	9 (37.5)	NC				
Never	Osimertinib	102	50 (49.0)	9.3	(3.7, 40.4)	1.00	(0.61, 1.66)	0.9935
	Placebo	49	22 (44.9)	6.6	(1.9, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.7855
CCRT	Osimertinib	131	69 (52.7)	7.4	(4.0, 22.0)	1.15	(0.73, 1.79)	0.5453
	Placebo	62	27 (43.5)	14.8	(5.5, NC)			
SCRT	Osimertinib	12	6 (50.0)	1.9	(0.9, NC)	1.38	(0.39, 4.91)	0.6161
	Placebo	11	4 (36.4)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1QYD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Physical Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Physical Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.4894
IIIA	Osimertinib	52	28 (53.8)	11.1	(3.7, 40.4)	1.44	(0.68, 3.05)	0.3451
	Placebo	24	9 (37.5)	NC				
IIIB/IIIC	Osimertinib	91	47 (51.6)	5.5	(3.7, NC)	1.05	(0.63, 1.74)	0.8609
	Placebo	49	22 (44.9)	14.8	(1.8, NC)			
Race	Osimertinib						Interaction test:	0.5176
Asian	Osimertinib	116	63 (54.3)	9.2	(3.7, 29.4)	1.20	(0.76, 1.89)	0.4309
	Placebo	62	27 (43.5)	14.8	(5.6, NC)			
Non-Asian	Osimertinib	27	12 (44.4)	5.5	(1.8, NC)	0.79	(0.26, 2.46)	0.6891
	Placebo	11	4 (36.4)	1.1	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1QYD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Physical Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Physical Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.2997
Yes	Osimertinib	27	10 (37.0)	NC		0.68	(0.23, 1.99)	0.4808
	Placebo	13	5 (38.5)	NC				
No	Osimertinib	116	65 (56.0)	6.4	(3.7, 12.9)	1.28	(0.81, 2.02)	0.2862
	Placebo	60	26 (43.3)	14.8	(4.9, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.0541
CR+PR	Osimertinib	71	39 (54.9)	7.3	(3.7, 14.8)	1.37	(0.73, 2.56)	0.3309
	Placebo	30	13 (43.3)	NC				
SD	Osimertinib	61	35 (57.4)	5.5	(3.6, NC)	1.24	(0.68, 2.28)	0.4800
	Placebo	37	15 (40.5)	NC				
NE	Osimertinib	11	1 (9.1)	NC		0.10	(0.01, 0.95)	0.0448 *
	Placebo	6	3 (50.0)	1.0	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QYD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Physical Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Physical Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.4725
Asia	Osimertinib	120	67 (55.8)	7.4	(3.7, 22.0)	1.21	(0.77, 1.88)	0.4063
	Placebo	64	28 (43.8)	14.8	(5.5, NC)			
Europe	Osimertinib	11	2 (18.2)	NC		0.34	(0.05, 2.40)	0.2778
	Placebo	7	2 (28.6)	NC				
Rest of the World	Osimertinib	12	6 (50.0)	3.6	(1.0, 12.9)	1.41	(0.17, 11.74)	0.7505
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.5124
Positive	Osimertinib	10	8 (80.0)	3.7	(0.9, 9.3)	1.53	(0.33, 7.22)	0.5890
	Placebo	4	2 (50.0)	5.6	(0.9, NC)			
Negative	Osimertinib	113	58 (51.3)	9.2	(3.7, 40.4)	1.03	(0.65, 1.63)	0.8986
	Placebo	58	27 (46.6)	14.8	(1.9, NC)			
Unknown	Osimertinib	20	9 (45.0)	6.4	(0.9, NC)	2.36	(0.51, 10.94)	0.2719
	Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QYD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Physical Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Physical Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.4283
Ex19Del	Osimertinib	74	40 (54.1)	5.5	(3.7, 29.4)	1.35	(0.76, 2.38)	0.3046
	Placebo	43	17 (39.5)	NC				
L858R	Osimertinib	68	34 (50.0)	9.3	(3.6, NC)	0.96	(0.51, 1.79)	0.8906
	Placebo	30	14 (46.7)	14.8	(1.1, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Program Name: LT1_APRO_TTE_TS.sas
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Table LT1QRD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Role Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Role Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.5256
Male	Osimertinib	53	31 (58.5)	11.1	(3.7, 37.3)	1.00	(0.54, 1.87)	0.9875
	Placebo	31	15 (48.4)	9.2	(5.5, 27.0)			
Female	Osimertinib	90	55 (61.1)	3.7	(2.0, 10.0)	0.78	(0.49, 1.25)	0.3053
	Placebo	42	26 (61.9)	3.7	(1.0, 5.6)			
Age	Osimertinib						Interaction test:	0.6854
< 65 years	Osimertinib	81	46 (56.8)	7.3	(3.6, 22.0)	0.83	(0.49, 1.41)	0.4842
	Placebo	39	20 (51.3)	5.5	(1.8, NC)			
>= 65 years	Osimertinib	62	40 (64.5)	7.4	(3.6, 11.1)	0.97	(0.57, 1.64)	0.8964
	Placebo	34	21 (61.8)	5.6	(3.6, 14.8)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QRD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Role Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Role Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.0585
Current/former	Osimertinib	41	27 (65.9)	8.0	(1.9, 20.3)	1.51	(0.73, 3.13)	0.2653
	Placebo	24	10 (41.7)	27.0	(5.5, 27.0)			
Never	Osimertinib	102	59 (57.8)	6.4	(3.6, 11.1)	0.68	(0.44, 1.06)	0.0864
	Placebo	49	31 (63.3)	3.7	(1.1, 5.6)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.8777
CCRT	Osimertinib	131	79 (60.3)	6.4	(3.6, 11.1)	0.91	(0.61, 1.37)	0.6649
	Placebo	62	34 (54.8)	5.6	(3.6, 14.8)			
SCRT	Osimertinib	12	7 (58.3)	7.4	(0.9, NC)	0.84	(0.29, 2.39)	0.7397
	Placebo	11	7 (63.6)	3.7	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Table LT1QRD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Role Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Role Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.1351
IIIA	Osimertinib	52	37 (71.2)	6.4	(3.6, 11.1)	1.29	(0.67, 2.48)	0.4403
	Placebo	24	12 (50.0)	5.6	(3.7, NC)			
IIIB/IIIC	Osimertinib	91	49 (53.8)	8.0	(2.1, 23.9)	0.71	(0.44, 1.13)	0.1489
	Placebo	49	29 (59.2)	3.7	(1.9, 7.4)			
Race	Osimertinib						Interaction test:	0.2154
Asian	Osimertinib	116	71 (61.2)	8.0	(3.6, 14.8)	0.92	(0.61, 1.38)	0.6848
	Placebo	62	35 (56.5)	5.6	(3.7, 27.0)			
Non-Asian	Osimertinib	27	15 (55.6)	6.4	(1.8, 11.0)	0.47	(0.18, 1.21)	0.1160
	Placebo	11	6 (54.5)	1.1	(0.9, 7.3)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1QRD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Role Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Role Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.1544
Yes	Osimertinib	27	10 (37.0)	NC		0.46	(0.17, 1.21)	0.1169
	Placebo	13	7 (53.8)	6.2	(1.0, NC)			
No	Osimertinib	116	76 (65.5)	5.5	(3.6, 9.2)	1.00	(0.67, 1.51)	0.9900
	Placebo	60	34 (56.7)	5.5	(3.6, 14.8)			
Response to prior CRT	Osimertinib						Interaction test:	0.8280
CR+PR	Osimertinib	71	42 (59.2)	5.5	(3.6, 11.1)	0.80	(0.46, 1.38)	0.4164
	Placebo	30	19 (63.3)	4.9	(1.1, 9.2)			
SD	Osimertinib	61	41 (67.2)	7.4	(1.9, 14.8)	0.99	(0.58, 1.69)	0.9649
	Placebo	37	20 (54.1)	5.6	(2.3, 27.0)			
NE	Osimertinib	11	3 (27.3)	11.1	(0.9, NC)	0.69	(0.11, 4.12)	0.6818
	Placebo	6	2 (33.3)	6.2	(1.0, NC)			

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Table LT1QRD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Role Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Role Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.3628
Asia	Osimertinib	120	75 (62.5)	5.5	(3.6, 11.1)	0.94	(0.63, 1.41)	0.7633
	Placebo	64	36 (56.3)	5.6	(3.7, 14.8)			
Europe	Osimertinib	11	5 (45.5)	11.0	(1.9, NC)	0.34	(0.08, 1.44)	0.1441
	Placebo	7	3 (42.9)	1.1	(0.9, 7.3)			
Rest of the World	Osimertinib	12	6 (50.0)	5.5	(0.9, 12.9)	0.50	(0.10, 2.46)	0.3908
	Placebo	2	2 (100.0)	3.2	(0.9, 5.5)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.7071
Positive	Osimertinib	10	7 (70.0)	1.9	(1.0, NC)	1.53	(0.32, 7.38)	0.5984
	Placebo	4	2 (50.0)	NC				
Negative	Osimertinib	113	66 (58.4)	9.1	(3.6, 20.2)	0.83	(0.54, 1.26)	0.3759
	Placebo	58	33 (56.9)	5.5	(2.3, 14.8)			
Unknown	Osimertinib	20	13 (65.0)	5.5	(0.9, 12.9)	1.02	(0.39, 2.68)	0.9694
	Placebo	11	6 (54.5)	3.7	(0.9, 27.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

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Table LT1QRD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Role Functioning by main subgroups
 Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Role Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.3193
Ex19Del	Osimertinib	74	44 (59.5)	9.2	(3.6, 20.3)	0.75	(0.46, 1.22)	0.2414
	Placebo	43	26 (60.5)	5.5	(1.0, 7.4)			
L858R	Osimertinib	68	41 (60.3)	7.3	(3.6, 11.1)	1.10	(0.61, 1.99)	0.7556
	Placebo	30	15 (50.0)	5.6	(3.6, 27.0)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QTD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.7505
Male	Osimertinib	53	31 (58.5)	7.4	(3.6, 41.0)	1.05	(0.56, 1.99)	0.8750
	Placebo	31	14 (45.2)	11.1	(1.8, NC)			
Female	Osimertinib	90	51 (56.7)	7.4	(3.7, 12.8)	0.92	(0.56, 1.51)	0.7536
	Placebo	42	23 (54.8)	6.6	(1.8, 20.9)			
Age	Osimertinib						Interaction test:	0.5286
< 65 years	Osimertinib	81	52 (64.2)	7.3	(3.6, 11.0)	1.07	(0.63, 1.82)	0.7914
	Placebo	39	19 (48.7)	8.2	(1.8, 20.9)			
>= 65 years	Osimertinib	62	30 (48.4)	7.4	(3.6, NC)	0.83	(0.46, 1.50)	0.5426
	Placebo	34	18 (52.9)	5.6	(1.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1QTD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.4522
Current/former	Osimertinib	41	21 (51.2)	11.0	(5.6, NC)	0.77	(0.38, 1.57)	0.4747
	Placebo	24	12 (50.0)	10.2	(1.0, NC)			
Never	Osimertinib	102	61 (59.8)	7.3	(3.6, 11.0)	1.07	(0.67, 1.71)	0.7757
	Placebo	49	25 (51.0)	7.4	(1.9, 20.9)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.8505
CCRT	Osimertinib	131	74 (56.5)	7.4	(5.6, 11.1)	1.01	(0.66, 1.54)	0.9736
	Placebo	62	31 (50.0)	8.9	(1.9, 20.9)			
SCRT	Osimertinib	12	8 (66.7)	3.7	(1.0, 18.5)	0.90	(0.31, 2.61)	0.8494
	Placebo	11	6 (54.5)	1.9	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Table LT1QTD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.9416
IIIA	Osimertinib	52	27 (51.9)	9.2	(1.9, 22.0)	0.96	(0.48, 1.89)	0.9001
	Placebo	24	12 (50.0)	6.6	(1.8, NC)			
IIIB/IIIC	Osimertinib	91	55 (60.4)	7.3	(5.5, 11.0)	0.99	(0.61, 1.59)	0.9589
	Placebo	49	25 (51.0)	8.9	(1.8, 20.9)			
Race	Osimertinib						Interaction test:	0.4039
Asian	Osimertinib	116	71 (61.2)	7.4	(5.5, 11.1)	1.03	(0.68, 1.57)	0.8815
	Placebo	62	32 (51.6)	7.4	(1.9, 20.9)			
Non-Asian	Osimertinib	27	11 (40.7)	7.3	(3.6, NC)	0.63	(0.22, 1.81)	0.3894
	Placebo	11	5 (45.5)	1.9	(0.9, NC)			

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.6256
Yes	Osimertinib	27	15 (55.6)	11.0	(1.8, 22.0)	0.78	(0.30, 2.02)	0.6137
	Placebo	13	6 (46.2)	1.9	(0.9, NC)			
No	Osimertinib	116	67 (57.8)	7.3	(5.5, 11.0)	1.02	(0.66, 1.56)	0.9353
	Placebo	60	31 (51.7)	8.9	(1.9, 20.9)			
Response to prior CRT	Osimertinib						Interaction test:	0.5881
CR+PR	Osimertinib	71	35 (49.3)	7.3	(3.6, NC)	1.05	(0.56, 1.96)	0.8748
	Placebo	30	14 (46.7)	10.2	(1.8, NC)			
SD	Osimertinib	61	45 (73.8)	7.3	(3.6, 11.0)	1.01	(0.60, 1.70)	0.9584
	Placebo	37	21 (56.8)	3.7	(1.8, 20.9)			
NE	Osimertinib	11	2 (18.2)	NC		0.35	(0.05, 2.51)	0.2989
	Placebo	6	2 (33.3)	NC				

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Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.3762
Asia	Osimertinib	120	75 (62.5)	7.3	(5.5, 11.0)	1.03	(0.69, 1.56)	0.8702
	Placebo	64	33 (51.6)	7.4	(1.8, 20.9)			
Europe	Osimertinib	11	3 (27.3)	NC		0.32	(0.06, 1.58)	0.1609
	Placebo	7	3 (42.9)	5.0	(0.9, 8.9)			
Rest of the World	Osimertinib	12	4 (33.3)	3.7	(0.9, NC)	1.33	(0.15, 11.93)	0.7976
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.1698
Positive	Osimertinib	10	7 (70.0)	10.2	(0.9, NC)	0.46	(0.12, 1.80)	0.2673
	Placebo	4	3 (75.0)	1.9	(0.9, NC)			
Negative	Osimertinib	113	64 (56.6)	7.4	(5.6, 12.8)	0.91	(0.59, 1.41)	0.6793
	Placebo	58	31 (53.4)	7.4	(1.8, 20.9)			
Unknown	Osimertinib	20	11 (55.0)	3.6	(0.9, NC)	2.50	(0.70, 8.96)	0.1599
	Placebo	11	3 (27.3)	8.9	(1.1, NC)			

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 Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Cognitive Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.5210
Ex19Del	Osimertinib	74	45 (60.8)	7.3	(1.9, 11.0)	1.11	(0.67, 1.86)	0.6813
	Placebo	43	22 (51.2)	8.9	(1.8, 20.9)			
L858R	Osimertinib	68	37 (54.4)	8.2	(5.5, 18.5)	0.86	(0.47, 1.57)	0.6207
	Placebo	30	15 (50.0)	5.6	(1.8, NC)			

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Table LT1QED10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Emotional Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Emotional Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.6133
Male	Osimertinib	53	25 (47.2)	20.2	(5.6, NC)	0.97	(0.48, 1.99)	0.9427
	Placebo	31	11 (35.5)	NC				
Female	Osimertinib	90	52 (57.8)	7.4	(2.6, 18.5)	1.22	(0.73, 2.05)	0.4465
	Placebo	42	20 (47.6)	9.2	(3.9, NC)			
Age	Osimertinib						Interaction test:	0.0172 #
< 65 years	Osimertinib	81	43 (53.1)	9.3	(3.7, 31.2)	0.71	(0.42, 1.20)	0.2000
	Placebo	39	21 (53.8)	5.3	(1.9, NC)			
>= 65 years	Osimertinib	62	34 (54.8)	12.9	(5.6, 25.8)	2.01	(0.99, 4.08)	0.0524
	Placebo	34	10 (29.4)	34.9	(9.2, NC)			

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Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Emotional Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.8856
Current/former	Osimertinib	41	20 (48.8)	20.2	(3.6, NC)	1.07	(0.48, 2.35)	0.8751
	Placebo	24	9 (37.5)	NC				
Never	Osimertinib	102	57 (55.9)	9.3	(5.5, 18.5)	1.14	(0.70, 1.87)	0.6012
	Placebo	49	22 (44.9)	9.2	(3.8, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.4186
CCRT	Osimertinib	131	70 (53.4)	12.8	(5.5, 20.2)	1.23	(0.77, 1.94)	0.3867
	Placebo	62	25 (40.3)	34.9	(6.6, NC)			
SCRT	Osimertinib	12	7 (58.3)	14.7	(1.0, 28.3)	0.75	(0.25, 2.24)	0.6051
	Placebo	11	6 (54.5)	3.8	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Emotional Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.1796
IIIA	Osimertinib	52	30 (57.7)	12.9	(5.5, 20.2)	1.72	(0.78, 3.75)	0.1761
	Placebo	24	8 (33.3)	NC				
IIIB/IIIC	Osimertinib	91	47 (51.6)	12.8	(3.7, 27.5)	0.92	(0.56, 1.53)	0.7556
	Placebo	49	23 (46.9)	9.2	(1.9, 34.9)			
Race	Osimertinib						Interaction test:	0.4570
Asian	Osimertinib	116	63 (54.3)	16.5	(5.5, 27.5)	1.15	(0.73, 1.83)	0.5470
	Placebo	62	26 (41.9)	34.9	(6.6, NC)			
Non-Asian	Osimertinib	27	14 (51.9)	6.4	(1.0, 12.9)	0.74	(0.27, 2.07)	0.5719
	Placebo	11	5 (45.5)	2.8	(0.9, NC)			

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.4167
Yes	Osimertinib	27	12 (44.4)	16.5	(1.9, NC)	0.75	(0.26, 2.15)	0.5956
	Placebo	13	5 (38.5)	7.3	(0.9, NC)			
No	Osimertinib	116	65 (56.0)	12.8	(5.5, 20.2)	1.22	(0.77, 1.93)	0.3914
	Placebo	60	26 (43.3)	34.9	(4.9, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.1220
CR+PR	Osimertinib	71	36 (50.7)	6.5	(2.1, NC)	0.73	(0.41, 1.30)	0.2857
	Placebo	30	18 (60.0)	3.9	(1.8, NC)			
SD	Osimertinib	61	39 (63.9)	12.8	(5.5, 25.8)	1.78	(0.93, 3.40)	0.0831
	Placebo	37	12 (32.4)	34.9	(7.3, 34.9)			
NE	Osimertinib	11	2 (18.2)	NC		0.81	(0.07, 8.93)	0.8620
	Placebo	6	1 (16.7)	NC				

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.2131
Asia	Osimertinib	120	67 (55.8)	14.7	(5.5, 25.8)	1.17	(0.74, 1.84)	0.4989
	Placebo	64	27 (42.2)	34.9	(5.5, NC)			
Europe	Osimertinib	11	4 (36.4)	6.4	(1.9, NC)	0.29	(0.07, 1.32)	0.1104
	Placebo	7	3 (42.9)	1.8	(0.9, 3.8)			
Rest of the World	Osimertinib	12	6 (50.0)	1.0	(0.9, 14.7)	2.07	(0.25, 17.21)	0.5006
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.4012
Positive	Osimertinib	10	9 (90.0)	6.4	(0.9, 23.9)	2.99	(0.38, 23.62)	0.2995
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	56 (49.6)	16.5	(5.5, 31.2)	0.98	(0.61, 1.57)	0.9268
	Placebo	58	26 (44.8)	34.9	(5.3, NC)			
Unknown	Osimertinib	20	12 (60.0)	1.9	(0.9, 20.2)	1.59	(0.51, 4.93)	0.4224
	Placebo	11	4 (36.4)	3.8	(0.9, NC)			

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.5855
Ex19Del	Osimertinib	74	40 (54.1)	7.4	(3.7, 27.5)	1.02	(0.59, 1.75)	0.9414
	Placebo	43	20 (46.5)	9.2	(3.8, NC)			
L858R	Osimertinib	68	36 (52.9)	14.7	(3.7, 28.3)	1.30	(0.66, 2.55)	0.4543
	Placebo	30	11 (36.7)	34.9	(3.8, 34.9)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QSD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Social Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Social Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.8665
Male	Osimertinib	53	32 (60.4)	11.0	(3.6, 24.0)	1.40	(0.72, 2.74)	0.3225
	Placebo	31	12 (38.7)	NC				
Female	Osimertinib	90	56 (62.2)	5.8	(1.9, 10.0)	1.31	(0.79, 2.16)	0.3006
	Placebo	42	21 (50.0)	7.3	(3.7, NC)			
Age	Osimertinib						Interaction test:	0.4043
< 65 years	Osimertinib	81	55 (67.9)	3.7	(1.8, 11.0)	1.55	(0.90, 2.69)	0.1149
	Placebo	39	17 (43.6)	9.3	(3.9, NC)			
>= 65 years	Osimertinib	62	33 (53.2)	9.2	(3.6, 24.0)	1.10	(0.60, 2.01)	0.7514
	Placebo	34	16 (47.1)	9.1	(3.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QSD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Social Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Social Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.2925
Current/former	Osimertinib	41	28 (68.3)	3.6	(1.8, 14.7)	1.86	(0.88, 3.97)	0.1055
	Placebo	24	9 (37.5)	NC				
Never	Osimertinib	102	60 (58.8)	9.2	(2.1, 12.9)	1.16	(0.72, 1.88)	0.5312
	Placebo	49	24 (49.0)	7.3	(3.8, NC)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.3054
CCRT	Osimertinib	131	82 (62.6)	6.4	(3.6, 11.0)	1.46	(0.94, 2.27)	0.0891
	Placebo	62	27 (43.5)	9.2	(5.5, NC)			
SCRT	Osimertinib	12	6 (50.0)	11.0	(0.9, NC)	0.77	(0.25, 2.41)	0.6573
	Placebo	11	6 (54.5)	7.3	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QSD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Social Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Social Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.8872
IIIA	Osimertinib	52	31 (59.6)	9.2	(3.6, 24.0)	1.41	(0.69, 2.89)	0.3420
	Placebo	24	10 (41.7)	9.2	(5.5, NC)			
IIIB/IIIC	Osimertinib	91	57 (62.6)	3.8	(1.9, 11.0)	1.33	(0.82, 2.17)	0.2538
	Placebo	49	23 (46.9)	7.3	(3.8, NC)			
Race	Osimertinib						Interaction test:	0.2949
Asian	Osimertinib	116	73 (62.9)	6.9	(3.6, 14.7)	1.42	(0.91, 2.20)	0.1215
	Placebo	62	28 (45.2)	9.3	(5.6, NC)			
Non-Asian	Osimertinib	27	15 (55.6)	6.4	(1.0, 11.0)	0.77	(0.28, 2.12)	0.6081
	Placebo	11	5 (45.5)	3.8	(0.9, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QSD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Social Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Social Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.8941
Yes	Osimertinib	27	20 (74.1)	3.6	(1.8, 14.7)	1.26	(0.53, 2.99)	0.5980
	Placebo	13	7 (53.8)	3.7	(1.8, NC)			
No	Osimertinib	116	68 (58.6)	9.1	(3.6, 12.9)	1.35	(0.85, 2.13)	0.2003
	Placebo	60	26 (43.3)	9.2	(5.6, NC)			
Response to prior CRT	Osimertinib						Interaction test:	0.9788
CR+PR	Osimertinib	71	42 (59.2)	5.8	(1.8, 11.0)	1.38	(0.75, 2.52)	0.3039
	Placebo	30	14 (46.7)	9.2	(3.8, NC)			
SD	Osimertinib	61	40 (65.6)	11.0	(1.9, 14.8)	1.29	(0.73, 2.29)	0.3799
	Placebo	37	17 (45.9)	9.2	(5.5, NC)			
NE	Osimertinib	11	6 (54.5)	3.6	(1.8, 12.9)	1.50	(0.30, 7.46)	0.6171
	Placebo	6	2 (33.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QSD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Social Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Social Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.2515
Asia	Osimertinib	120	77 (64.2)	6.9	(3.6, 11.1)	1.43	(0.93, 2.20)	0.1036
	Placebo	64	29 (45.3)	9.2	(5.6, NC)			
Europe	Osimertinib	11	6 (54.5)	7.8	(1.0, NC)	0.96	(0.19, 4.75)	0.9562
	Placebo	7	2 (28.6)	3.8	(0.9, NC)			
Rest of the World	Osimertinib	12	5 (41.7)	1.0	(0.9, NC)	0.29	(0.06, 1.53)	0.1456
	Placebo	2	2 (100.0)	1.4	(0.9, 1.9)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.9861
Positive	Osimertinib	10	8 (80.0)	8.0	(0.9, 33.1)	1.48	(0.31, 7.00)	0.6190
	Placebo	4	2 (50.0)	NC				
Negative	Osimertinib	113	68 (60.2)	7.4	(3.6, 11.1)	1.32	(0.84, 2.07)	0.2210
	Placebo	58	27 (46.6)	9.2	(5.5, NC)			
Unknown	Osimertinib	20	12 (60.0)	5.0	(0.9, 25.8)	1.41	(0.45, 4.41)	0.5510
	Placebo	11	4 (36.4)	9.1	(1.9, 9.1)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_APRO_TTE_TS.sas
Run Date: 24OCT2024:12:15:20

Table LT1QSD10T_SFTM: Time to decrease by at least 10 points in QLQ-C30 Social Functioning by main subgroups
Full Analysis Set

Time to decrease by at least 10 points in QLQ-C30 Social Functioning				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib							Interaction test: 0.9341
Ex19Del	Osimertinib	74	44 (59.5)	6.9	(1.8, 14.7)	1.34	(0.79, 2.28)	0.2837
	Placebo	43	20 (46.5)	9.2	(3.9, NC)			
L858R	Osimertinib	68	43 (63.2)	6.4	(2.1, 12.9)	1.38	(0.74, 2.58)	0.3068
	Placebo	30	13 (43.3)	9.1	(3.8, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

QLQ-C30: EORTC Quality of Life Questionnaire - Core 30 items.

Source Data: APRO_TTE, created on: 19SEP2024

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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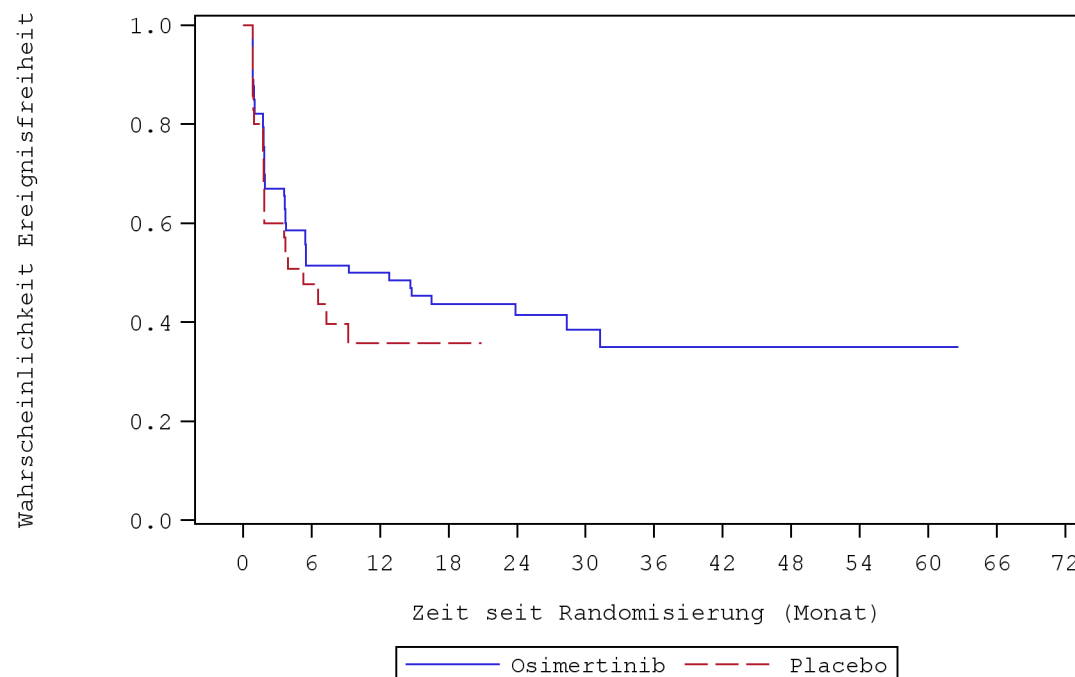
Program Name: LF1_APRO_TTE_KS.sas

Run Date: 27SEP2024:11:28:15

Figure LF1QED10T_SFKM: Kaplan Meier plot for time to decrease by at least 10 points in QLQ-C30 Emotional Functioning by main

subgroups
Full Analysis Set
Study: LAURA

Age: < 65 years



Osimertinib	81	35	32	26	17	12	7	3	1	1	1	0
Placebo	39	14	4	2	0							

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.

Reference table: LT1QED10T_SFTM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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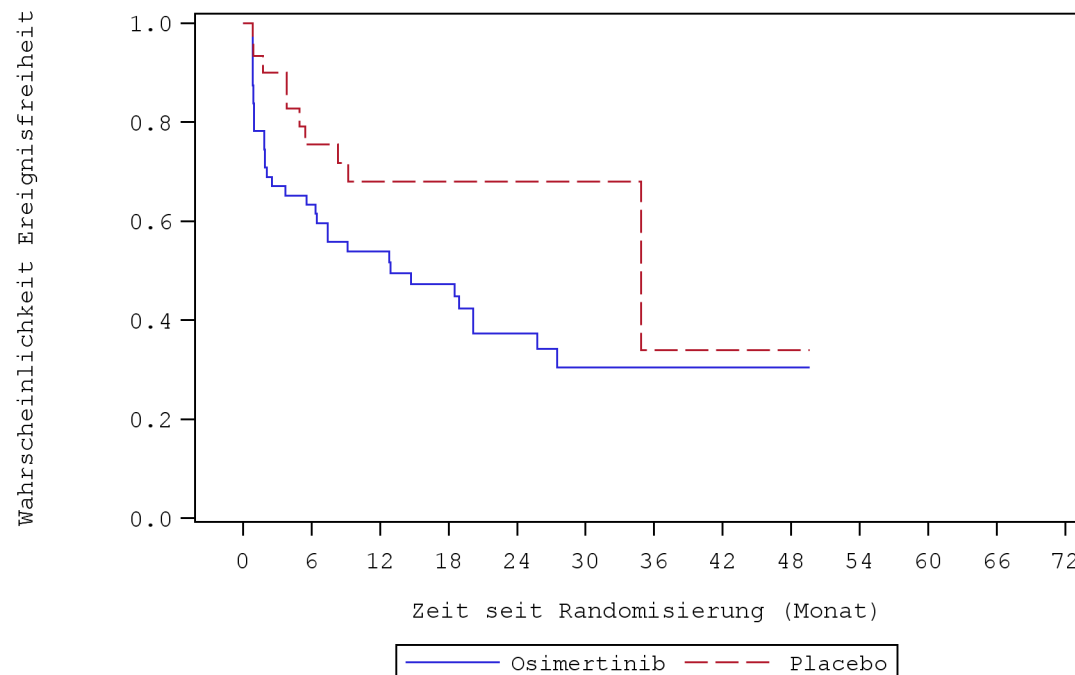
Program Name: LF1_APRO_TTE_KS.sas

Run Date: 27SEP2024:11:28:15

Figure LF1QED10T_SFKM: Kaplan Meier plot for time to decrease by at least 10 points in QLQ-C30 Emotional Functioning by main

subgroups
Full Analysis Set
Study: LAURA

Age: >= 65 years



Osimertinib	62	34	25	20	13	6	5	1	1	0
Placebo	34	21	15	6	3	3	1	1	1	0

QLQ-C30: EORTC Quality of Life Questionnaire – Core 30 items.
Reference table: LT1QED10T_SFTM

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1A_SSTM: Time to any AE by main subgroups
Safety Set

Time to any AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.3365
Male	Osimertinib	53	51 (96.2)	0.5	(0.3, 0.6)	1.44	(0.91, 2.26)	0.1162
	Placebo	31	30 (96.8)	0.7	(0.4, 1.6)			
Female	Osimertinib	90	89 (98.9)	0.6	(0.5, 0.8)	1.93	(1.29, 2.89)	0.0013 *
	Placebo	42	34 (81.0)	1.5	(0.7, 1.9)			
Age	Osimertinib						Interaction test:	0.6208
< 65 years	Osimertinib	81	79 (97.5)	0.5	(0.4, 0.6)	1.82	(1.20, 2.76)	0.0048 *
	Placebo	39	32 (82.1)	1.6	(0.5, 1.8)			
>= 65 years	Osimertinib	62	61 (98.4)	0.5	(0.4, 0.7)	1.57	(1.02, 2.41)	0.0423 *
	Placebo	34	32 (94.1)	0.7	(0.5, 1.6)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1A_SSTM: Time to any AE by main subgroups
Safety Set

Time to any AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.8233
Current/former	Osimertinib	41	40 (97.6)	0.4	(0.3, 0.5)	1.63	(0.97, 2.75)	0.0674
	Placebo	24	22 (91.7)	0.6	(0.3, 1.6)			
Never	Osimertinib	102	100 (98.0)	0.6	(0.5, 0.8)	1.75	(1.22, 2.53)	0.0026 *
	Placebo	49	42 (85.7)	1.5	(0.7, 1.8)			
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.9247
CCRT	Osimertinib	131	128 (97.7)	0.5	(0.4, 0.6)	1.66	(1.20, 2.28)	0.0020 *
	Placebo	62	55 (88.7)	1.0	(0.5, 1.7)			
SCRT	Osimertinib	12	12 (100.0)	0.8	(0.2, 1.0)	1.73	(0.73, 4.13)	0.2139
	Placebo	11	9 (81.8)	1.9	(0.4, 3.7)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event.

Source Data: AAE_TTE, created on: 08OCT2024

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Value Dossier Analysis: D5160C00048
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Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1A_SSTM: Time to any AE by main subgroups
Safety Set

Time to any AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.2922
IIIA	Osimertinib	52	52 (100.0)	0.5	(0.4, 0.7)	2.10	(1.26, 3.51)	0.0047 *
	Placebo	24	21 (87.5)	1.7	(0.4, 2.8)			
IIIB/IIIC	Osimertinib	91	88 (96.7)	0.5	(0.4, 0.7)	1.50	(1.04, 2.17)	0.0298 *
	Placebo	49	43 (87.8)	0.9	(0.5, 1.6)			
Race	Osimertinib						Interaction test:	0.7440
Asian	Osimertinib	116	115 (99.1)	0.5	(0.5, 0.7)	1.72	(1.24, 2.39)	0.0012 *
	Placebo	62	54 (87.1)	1.0	(0.6, 1.7)			
Non-Asian	Osimertinib	27	25 (92.6)	0.4	(0.2, 0.6)	1.50	(0.72, 3.15)	0.2774
	Placebo	11	10 (90.9)	1.0	(0.1, 2.8)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Table LT1A_SSTM: Time to any AE by main subgroups
Safety Set

Time to any AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.9147
Yes	Osimertinib	27	26 (96.3)	0.9	(0.4, 1.7)	1.66	(0.80, 3.45)	0.1748
	Placebo	13	10 (76.9)	1.8	(0.5, 2.9)			
No	Osimertinib	116	114 (98.3)	0.5	(0.4, 0.6)	1.73	(1.25, 2.41)	0.0011 *
	Placebo	60	54 (90.0)	0.9	(0.5, 1.6)			
Response to prior CRT	Osimertinib						Interaction test:	0.9771
CR+PR	Osimertinib	71	71 (100.0)	0.5	(0.3, 0.5)	1.63	(1.05, 2.53)	0.0292 *
	Placebo	30	28 (93.3)	0.8	(0.4, 1.7)			
SD	Osimertinib	61	59 (96.7)	0.7	(0.5, 0.9)	1.65	(1.06, 2.56)	0.0262 *
	Placebo	37	31 (83.8)	1.2	(0.5, 1.9)			
NE	Osimertinib	11	10 (90.9)	0.4	(0.2, 1.7)	1.85	(0.63, 5.42)	0.2618
	Placebo	6	5 (83.3)	1.7	(0.3, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event.

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Table LT1A_SSTM: Time to any AE by main subgroups
Safety Set

Time to any AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.5541
Asia	Osimertinib	120	118 (98.3)	0.5	(0.5, 0.7)	1.66	(1.20, 2.30)	0.0020 *
	Placebo	64	56 (87.5)	1.0	(0.6, 1.7)			
Europe	Osimertinib	11	11 (100.0)	0.4	(0.1, 0.8)	2.50	(0.92, 6.82)	0.0726
	Placebo	7	6 (85.7)	1.0	(0.1, 3.7)			
Rest of the World	Osimertinib	12	11 (91.7)	0.4	(0.1, 0.6)	0.91	(0.20, 4.13)	0.9014
	Placebo	2	2 (100.0)	0.6	(0.0, 1.2)			
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.5369
Positive	Osimertinib	10	9 (90.0)	0.6	(0.1, 0.9)	1.04	(0.32, 3.41)	0.9471
	Placebo	4	4 (100.0)	1.2	(0.5, 1.9)			
Negative	Osimertinib	113	112 (99.1)	0.5	(0.4, 0.6)	1.63	(1.17, 2.29)	0.0042 *
	Placebo	58	51 (87.9)	0.8	(0.5, 1.6)			
Unknown	Osimertinib	20	19 (95.0)	0.7	(0.1, 1.6)	2.31	(1.04, 5.11)	0.0395 *
	Placebo	11	9 (81.8)	2.9	(0.8, 3.7)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Table LT1A_SSTM: Time to any AE by main subgroups
Safety Set

Time to any AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.0055 #				
Ex19Del	Osimertinib	74	72 (97.3)	0.6	(0.5, 0.8)	1.17	(0.80, 1.73)	0.4176
	Placebo	43	41 (95.3)	0.9	(0.4, 1.6)			
L858R	Osimertinib	68	67 (98.5)	0.5	(0.3, 0.6)	2.77	(1.71, 4.49)	<0.0001 *
	Placebo	30	23 (76.7)	1.7	(0.6, 2.8)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Sex	Osimertinib							
		Placebo							
	Male	Osimertinib	53	32 (60.4)	3.7	(0.9, 35.8)	1.49	(0.79, 2.80)	0.2181
		Placebo	31	14 (45.2)	13.8	(5.5, NC)			
	Female	Osimertinib	90	52 (57.8)	15.2	(3.7, 26.9)	2.23	(1.13, 4.42)	0.0212 *
		Placebo	42	10 (23.8)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

Only significant SOC/PT combinations from the main analysis are reported. The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Age	Osimertinib							
		Placebo							
	< 65 years	Osimertinib	81	45 (55.6)	16.5	(3.7, 35.9)	1.57	(0.84, 2.93)	0.1537
		Placebo	39	13 (33.3)	NC				
	>= 65 years	Osimertinib	62	39 (62.9)	3.7	(1.0, 25.1)	2.02	(1.03, 3.98)	0.0408 *
		Placebo	34	11 (32.4)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Smoking status	Osimertinib							
								Interaction test:	0.9241
	Current/former	Osimertinib	41	26 (63.4)	3.6	(0.7, 17.4)	1.77	(0.85, 3.67)	0.1275
		Placebo	24	10 (41.7)	12.8	(3.7, NC)			
	Never	Osimertinib	102	58 (56.9)	17.9	(3.7, 26.9)	1.85	(1.02, 3.34)	0.0418 *
		Placebo	49	14 (28.6)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.8770
	CCRT	Osimertinib	131	78 (59.5)	9.4	(2.8, 19.3)	1.68	(1.04, 2.71)	0.0334 *
		Placebo	62	22 (35.5)	NC				
	SCRT	Osimertinib	12	6 (50.0)	26.9	(0.7, NC)	1.92	(0.37, 9.96)	0.4365
		Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Disease stage prior to chemoradiation	Osimertinib							
		Placebo							
	IIIA	Osimertinib	52	40 (76.9)	1.8	(1.0, 7.0)	3.28	(1.47, 7.34)	0.0038 *
		Placebo	24	7 (29.2)	NC				
	IIIB/IIIC	Osimertinib	91	44 (48.4)	24.4	(12.5, 38.7)	1.20	(0.68, 2.12)	0.5336
		Placebo	49	17 (34.7)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
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Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Race	Osimertinib							Interaction test: 0.6936
		Placebo							
	Asian	Osimertinib	116	67 (57.8)	13.2	(3.6, 25.1)	1.69	(1.03, 2.78)	0.0372 *
		Placebo	62	21 (33.9)	NC				
		Osimertinib	27	17 (63.0)	3.7	(0.7, NC)	2.20	(0.64, 7.57)	0.2111
		Placebo	11	3 (27.3)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	China Cohort	Osimertinib							Interaction test: 0.1761
	Yes	Osimertinib	27	12 (44.4)	26.9	(1.0, NC)	5.53	(0.72, 42.59)	0.1003
		Placebo	13	1 (7.7)	NC				
	No	Osimertinib	116	72 (62.1)	7.0	(2.6, 18.9)	1.60	(0.995, 2.58)	0.0522
		Placebo	60	23 (38.3)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Response to prior CRT	Osimertinib						Interaction test:	0.8148
	CR+PR	Osimertinib	71	43 (60.6)	4.7	(1.0, 24.4)	1.60	(0.84, 3.06)	0.1557
		Placebo	30	12 (40.0)	13.8	(4.7, NC)			
	SD	Osimertinib	61	36 (59.0)	17.4	(3.4, 35.8)	1.76	(0.89, 3.47)	0.1013
		Placebo	37	11 (29.7)	NC				
	NE	Osimertinib	11	5 (45.5)	3.6	(0.3, NC)	3.17	(0.37, 27.17)	0.2918
		Placebo	6	1 (16.7)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Region	Osimertinib						Interaction test:	0.8424
	Asia	Osimertinib	120	67 (55.8)	16.5	(3.7, 25.5)	1.67	(1.02, 2.74)	0.0433 *
		Placebo	64	21 (32.8)	NC				
	Europe	Osimertinib	11	7 (63.6)	19.3	(0.5, NC)	1.34	(0.27, 6.69)	0.7202
		Placebo	7	2 (28.6)	NC				
	Rest of the World	Osimertinib	12	10 (83.3)	0.7	(0.3, 1.6)	2.80	(0.36, 21.90)	0.3271
		Placebo	2	1 (50.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							Interaction test: 0.6583
	Positive	Osimertinib	10	5 (50.0)	24.4	(0.9, NC)	1.25	(0.15, 10.78)	0.8382
		Placebo	4	1 (25.0)	NC				
	Negative	Osimertinib	113	68 (60.2)	7.0	(2.7, 18.9)	1.67	(1.01, 2.74)	0.0440 *
		Placebo	58	21 (36.2)	NC				
	Unknown	Osimertinib	20	11 (55.0)	19.3	(0.7, 38.7)	3.22	(0.71, 14.55)	0.1292
		Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Gastrointestinal disorders	Tissue EGFR mutation at screening	Osimertinib							
		Placebo							
	Ex19Del	Osimertinib	74	41 (55.4)	17.9	(3.7, 38.7)	1.33	(0.74, 2.39)	0.3343
		Placebo	43	16 (37.2)	NC				
	L858R	Osimertinib	68	42 (61.8)	3.7	(0.9, 25.1)	2.61	(1.22, 5.60)	0.0134 *
		Placebo	30	8 (26.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Sex	Osimertinib							Interaction test: 0.1859
	Male	Osimertinib	53	20 (37.7)	NC		1.85	(0.78, 4.39)	0.1610
		Placebo	31	7 (22.6)	NC				
	Female	Osimertinib	90	31 (34.4)	NC		4.81	(1.47, 15.75)	0.0095
		Placebo	42	3 (7.1)	NC				

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The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Age	Osimertinib							Interaction test: 0.4510
	< 65 years	Osimertinib	81	27 (33.3)	NC		2.14	(0.88, 5.20)	0.0933
		Placebo	39	6 (15.4)	NC				
	>= 65 years	Osimertinib	62	24 (38.7)	NC		3.62	(1.25, 10.44)	0.0174 *
		Placebo	34	4 (11.8)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Smoking status	Osimertinib							
								Interaction test:	0.5845
	Current/former	Osimertinib	41	16 (39.0)	NC		3.59	(1.04, 12.32)	0.0425 *
		Placebo	24	3 (12.5)	NC				
	Never	Osimertinib	102	35 (34.3)	NC		2.39	(1.06, 5.40)	0.0358 *
		Placebo	49	7 (14.3)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.9068
	CCRT	Osimertinib	131	48 (36.6)	NC		2.68	(1.31, 5.47)	0.0069 *
		Placebo	62	9 (14.5)	NC				
	SCRT	Osimertinib	12	3 (25.0)	38.7	(17.9, NC)	2.32	(0.24, 22.30)	0.4672
		Placebo	11	1 (9.1)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Disease stage prior to chemoradiation	Osimertinib							
		Placebo							
	IIIA	Osimertinib	52	22 (42.3)	NC		3.71	(1.11, 12.41)	0.0334 *
		Placebo	24	3 (12.5)	NC				
	IIIB/IIIC	Osimertinib	91	29 (31.9)	NC		2.25	(0.99, 5.16)	0.0543
		Placebo	49	7 (14.3)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Race	Osimertinib							Interaction test: 0.5583
	Asian	Osimertinib	116	42 (36.2)	NC		2.97	(1.39, 6.33)	0.0050
		Placebo	62	8 (12.9)	NC				
	Non-Asian	Osimertinib	27	9 (33.3)	NC		1.75	(0.38, 8.10)	0.4759
		Placebo	11	2 (18.2)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	China Cohort	Osimertinib							
								Interaction test:	0.0991
	Yes	Osimertinib	27	8 (29.6)	NC		NC		NC
		Placebo	13	0 (0.0)	NC				
	No	Osimertinib	116	43 (37.1)	NC		2.34	(1.17, 4.67)	0.0157 *
		Placebo	60	10 (16.7)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Response to prior CRT	Osimertinib						Interaction test:	0.1306
	CR+PR	Osimertinib	71	26 (36.6)	NC		1.69	(0.73, 3.91)	0.2203
		Placebo	30	7 (23.3)	NC				
	SD	Osimertinib	61	20 (32.8)	NC		3.79	(1.12, 12.77)	0.0316
		Placebo	37	3 (8.1)	NC				
	NE	Osimertinib	11	5 (45.5)	3.6	(0.5, NC)	NC		NC
		Placebo	6	0 (0.0)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Region	Osimertinib							Interaction test: 0.2164
	Asia	Osimertinib	120	42 (35.0)	NC		2.94	(1.38, 6.28)	0.0053 *
		Placebo	64	8 (12.5)	NC				
	Europe	Osimertinib	11	3 (27.3)	NC		0.67	(0.11, 4.03)	0.6619
		Placebo	7	2 (28.6)	NC				
	Rest of the World	Osimertinib	12	6 (50.0)	NC		NC		NC
		Placebo	2	0 (0.0)	NC				

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							
		Placebo							
	Positive	Osimertinib	10	2 (20.0)	NC		NC		NC
		Placebo	4	0 (0.0)	NC				
	Negative	Osimertinib	113	43 (38.1)	NC		3.01	(1.41, 6.41)	0.0044 *
		Placebo	58	8 (13.8)	NC				
	Unknown	Osimertinib	20	6 (30.0)	NC		1.58	(0.32, 7.84)	0.5756
		Placebo	11	2 (18.2)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Diarrhoea	Tissue EGFR mutation at screening	Osimertinib							
		Placebo							
	Ex19Del	Osimertinib	74	23 (31.1)	NC		2.65	(1.004, 6.97)	0.0492 *
		Placebo	43	5 (11.6)	NC				
	L858R	Osimertinib	68	28 (41.2)	NC		2.70	(1.04, 7.01)	0.0408 *
		Placebo	30	5 (16.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Sex	Osimertinib							
		Placebo							
	Male	Osimertinib	53	36 (67.9)	9.1	(2.0, 19.3)	1.90	(0.96, 3.75)	0.0644
		Placebo	31	11 (35.5)	NC				
	Female	Osimertinib	90	57 (63.3)	7.3	(5.1, 13.6)	1.85	(1.01, 3.38)	0.0468 *
		Placebo	42	13 (31.0)	15.8	(7.5, NC)			

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
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Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Age	Osimertinib							Interaction test: 0.0462 #
	< 65 years	Osimertinib	81	56 (69.1)	5.6	(4.1, 9.2)	3.10	(1.47, 6.52)	0.0029 *
		Placebo	39	8 (20.5)	NC				
	>= 65 years	Osimertinib	62	37 (59.7)	13.4	(4.7, 22.7)	1.21	(0.67, 2.19)	0.5206
		Placebo	34	16 (47.1)	13.6	(6.6, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Smoking status	Osimertinib							
								Interaction test:	0.5600
	Current/former	Osimertinib	41	27 (65.9)	5.5	(1.4, 22.7)	2.28	(1.03, 5.04)	0.0411 *
		Placebo	24	8 (33.3)	NC				
	Never	Osimertinib	102	66 (64.7)	7.4	(5.4, 13.4)	1.72	(0.99, 2.98)	0.0533
		Placebo	49	16 (32.7)	15.8	(7.5, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.1391
	CCRT	Osimertinib	131	84 (64.1)	7.3	(5.2, 13.6)	2.24	(1.33, 3.79)	0.0025 *
		Placebo	62	17 (27.4)	NC				
	SCRT	Osimertinib	12	9 (75.0)	6.5	(1.5, 24.9)	0.95	(0.35, 2.57)	0.9225
		Placebo	11	7 (63.6)	9.5	(1.7, 15.8)			

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Disease stage prior to chemoradiation	Osimertinib							
		Placebo							
	IIIA	Osimertinib	52	34 (65.4)	7.4	(3.7, 14.5)	2.09	(0.96, 4.52)	0.0617
		Placebo	24	8 (33.3)	NC				
	IIIB/IIIC	Osimertinib	91	59 (64.8)	6.5	(5.1, 15.6)	1.74	(1.0005, 3.04)	0.0498 *
		Placebo	49	16 (32.7)	15.8	(13.6, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Race	Osimertinib						Interaction test:	0.1857
	Asian	Osimertinib	116	74 (63.8)	8.2	(5.4, 15.6)	2.16	(1.27, 3.67)	0.0045 *
		Placebo	62	17 (27.4)	NC				
	Non-Asian	Osimertinib	27	19 (70.4)	5.6	(1.8, 13.4)	1.07	(0.45, 2.54)	0.8851
		Placebo	11	7 (63.6)	6.9	(1.0, 15.8)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	China Cohort	Osimertinib							Interaction test: 0.9969
	Yes	Osimertinib	27	12 (44.4)	15.7	(6.5, NC)	1.93	(0.43, 8.65)	0.3912
		Placebo	13	2 (15.4)	NC				
	No	Osimertinib	116	81 (69.8)	5.7	(4.1, 9.1)	1.94	(1.21, 3.11)	0.0063 *
		Placebo	60	22 (36.7)	15.8	(9.5, NC)			

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Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Response to prior CRT	Osimertinib						Interaction test:	0.6320
	CR+PR	Osimertinib	71	39 (54.9)	9.5	(5.4, 24.9)	1.58	(0.76, 3.29)	0.2189
		Placebo	30	9 (30.0)	15.8	(6.9, 15.8)			
	SD	Osimertinib	61	48 (78.7)	6.3	(3.6, 9.2)	2.38	(1.26, 4.49)	0.0074 *
		Placebo	37	12 (32.4)	NC				
	NE	Osimertinib	11	6 (54.5)	3.7	(0.3, NC)	1.38	(0.34, 5.54)	0.6482
		Placebo	6	3 (50.0)	13.6	(2.8, NC)			

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Region	Osimertinib						Interaction test:	0.6955
	Asia	Osimertinib	120	76 (63.3)	8.3	(5.4, 15.6)	1.96	(1.18, 3.25)	0.0096
		Placebo	64	19 (29.7)	NC				*
	Europe	Osimertinib	11	8 (72.7)	7.3	(0.2, 24.9)	1.10	(0.33, 3.67)	0.8783
		Placebo	7	4 (57.1)	6.9	(1.0, 15.8)			
	Rest of the World	Osimertinib	12	9 (75.0)	3.6	(0.6, 7.1)	2.06	(0.26, 16.27)	0.4938
		Placebo	2	1 (50.0)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							Interaction test: 0.8928
	Positive	Osimertinib	10	7 (70.0)	5.8	(0.6, NC)	2.43	(0.30, 19.80)	0.4072
		Placebo	4	1 (25.0)	NC				
	Negative	Osimertinib	113	73 (64.6)	9.0	(5.4, 15.6)	1.92	(1.14, 3.23)	0.0141
		Placebo	58	18 (31.0)	NC				
	Unknown	Osimertinib	20	13 (65.0)	5.6	(1.8, NC)	1.51	(0.54, 4.26)	0.4311
Placebo		11	5 (45.5)	15.4	(1.7, NC)				

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Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Infections and infestations	Tissue EGFR mutation at screening	Osimertinib							
		Placebo							
	Ex19Del	Osimertinib	74	46 (62.2)	8.3	(4.1, 19.3)	1.20	(0.69, 2.08)	0.5195
		Placebo	43	18 (41.9)	15.4	(3.7, NC)			
	L858R	Osimertinib	68	47 (69.1)	6.3	(4.3, 10.2)	3.93	(1.68, 9.20)	0.0016
		Placebo	30	6 (20.0)	NC				

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Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Sex	Osimertinib							Interaction test: 0.2424
	Male	Osimertinib	53	10 (18.9)	NC		NC		NC
		Placebo	31	0 (0.0)	NC				
	Female	Osimertinib	90	14 (15.6)	NC		5.44	(0.71, 41.53)	0.1026
		Placebo	42	1 (2.4)	NC				

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Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Age	Osimertinib							Interaction test: 0.2763
	< 65 years	Osimertinib	81	13 (16.0)	NC		NC		NC
		Placebo	39	0 (0.0)	NC				
	>= 65 years	Osimertinib	62	11 (17.7)	NC		5.97	(0.77, 46.37)	0.0875
		Placebo	34	1 (2.9)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Smoking status	Osimertinib							Interaction test: 0.2986
		Placebo							
	Current/former	Osimertinib	41	8 (19.5)	NC		NC		NC
		Placebo	24	0 (0.0)	NC				
	Never	Osimertinib	102	16 (15.7)	NC		6.40	(0.85, 48.50)	0.0722
		Placebo	49	1 (2.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.5936
		Placebo							
	CCRT	Osimertinib	131	22 (16.8)	NC		9.31	(1.25, 69.34)	0.0293 *
		Placebo	62	1 (1.6)	NC				
	SCRT	Osimertinib	12	2 (16.7)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Disease stage prior to chemoradiation	Osimertinib							
		Placebo							
	IIIA	Osimertinib	52	9 (17.3)	NC		3.92	(0.49, 31.02)	0.1958
		Placebo	24	1 (4.2)	NC				
	IIIB/IIIC	Osimertinib	91	15 (16.5)	NC		NC		NC
		Placebo	49	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Race	Osimertinib							Interaction test: 0.5990
		Placebo							
	Asian	Osimertinib	116	20 (17.2)	NC		9.46	(1.26, 70.79)	0.0287
		Placebo	62	1 (1.6)	NC				
	Non-Asian	Osimertinib	27	4 (14.8)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	China Cohort	Osimertinib							
								Interaction test:	0.8079
	Yes	Osimertinib	27	1 (3.7)	NC		NC		NC
		Placebo	13	0 (0.0)	NC				
	No	Osimertinib	116	23 (19.8)	NC		11.01	(1.48, 81.85)	0.0191 *
		Placebo	60	1 (1.7)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Response to prior CRT	Osimertinib							Interaction test: 0.3113
	CR+PR	Osimertinib	71	9 (12.7)	NC		3.35	(0.42, 26.61)	0.2521
		Placebo	30	1 (3.3)	NC				
	SD	Osimertinib	61	14 (23.0)	NC		NC		NC
		Placebo	37	0 (0.0)	NC				
	NE	Osimertinib	11	1 (9.1)	NC		NC		NC
		Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Region	Osimertinib							Interaction test: 0.6938
	Asia	Osimertinib	120	20 (16.7)	NC		9.31	(1.24, 69.78)	0.0299 *
		Placebo	64	1 (1.6)	NC				
	Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
		Placebo	7	0 (0.0)	NC				
	Rest of the World	Osimertinib	12	4 (33.3)	NC		NC		NC
		Placebo	2	0 (0.0)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							Interaction test: 0.8312
	Positive	Osimertinib	10	2 (20.0)	NC		NC		NC
		Placebo	4	0 (0.0)	NC				
	Negative	Osimertinib	113	19 (16.8)	NC		8.93	(1.19, 66.94)	0.0332
		Placebo	58	1 (1.7)	NC				
	Unknown	Osimertinib	20	3 (15.0)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Paronychia	Tissue EGFR mutation at screening	Osimertinib							
		Placebo							
	Ex19Del	Osimertinib	74	16 (21.6)	NC		8.29	(1.09, 62.79)	0.0407 *
		Placebo	43	1 (2.3)	NC				
	L858R	Osimertinib	68	8 (11.8)	NC		NC		NC
		Placebo	30	0 (0.0)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Sex	Osimertinib						Interaction test:	0.4212
	Male	Osimertinib	53	16 (30.2)	NC		4.13	(0.95, 18.02)	0.0592
		Placebo	31	2 (6.5)	NC				
	Female	Osimertinib	90	29 (32.2)	NC		2.06	(0.79, 5.35)	0.1386
		Placebo	42	5 (11.9)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Age	Osimertinib						Interaction test:	0.2889
	< 65 years	Osimertinib	81	27 (33.3)	35.9	(27.7, NC)	1.86	(0.71, 4.88)	0.2088
		Placebo	39	5 (12.8)	NC				
	>= 65 years	Osimertinib	62	18 (29.0)	NC		4.61	(1.07, 19.90)	0.0406 *
		Placebo	34	2 (5.9)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Smoking status	Osimertinib						Interaction test:	0.8582
	Current/former	Osimertinib	41	11 (26.8)	NC		2.97	(0.66, 13.40)	0.1576
		Placebo	24	2 (8.3)	NC				
	Never	Osimertinib	102	34 (33.3)	NC		2.53	(0.98, 6.51)	0.0547
		Placebo	49	5 (10.2)	NC				

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Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.2227
	CCRT	Osimertinib	131	42 (32.1)	NC		3.33	(1.31, 8.46)	0.0114 *
		Placebo	62	5 (8.1)	NC				
	SCRT	Osimertinib	12	3 (25.0)	NC		0.90	(0.15, 5.47)	0.9126
		Placebo	11	2 (18.2)	NC				

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Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Disease stage prior to chemoradiation	Osimertinib							Interaction test: 0.5886
	IIIA	Osimertinib	52	18 (34.6)	NC		3.64	(0.84, 15.73)	0.0831
		Placebo	24	2 (8.3)	NC				
	IIIB/IIIC	Osimertinib	91	27 (29.7)	NC		2.28	(0.87, 5.96)	0.0935
		Placebo	49	5 (10.2)	NC				

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Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Race	Osimertinib						Interaction test:	0.6124
	Asian	Osimertinib	116	40 (34.5)	35.9	(27.7, NC)	2.96	(1.24, 7.03)	0.0140
		Placebo	62	6 (9.7)	NC				
	Non-Asian	Osimertinib	27	5 (18.5)	NC		1.57	(0.18, 13.48)	0.6791
		Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	China Cohort	Osimertinib							Interaction test: 0.8805
	Yes	Osimertinib	27	19 (70.4)	4.5	(1.0, 16.9)	2.89	(0.85, 9.77)	0.0885
		Placebo	13	3 (23.1)	NC				
	No	Osimertinib	116	26 (22.4)	NC		2.55	(0.88, 7.36)	0.0835
		Placebo	60	4 (6.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Response to prior CRT	Osimertinib						Interaction test:	0.4819
	CR+PR	Osimertinib	71	19 (26.8)	NC		3.19	(0.74, 13.77)	0.1193
		Placebo	30	2 (6.7)	NC				
	SD	Osimertinib	61	23 (37.7)	35.6	(27.6, NC)	2.22	(0.84, 5.88)	0.1080
		Placebo	37	5 (13.5)	NC				
	NE	Osimertinib	11	3 (27.3)	NC		NC		NC
		Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Region	Osimertinib						Interaction test:	0.6155
	Asia	Osimertinib	120	40 (33.3)	NC		2.50	(1.11, 5.61)	0.0271 *
		Placebo	64	7 (10.9)	NC				
	Europe	Osimertinib	11	2 (18.2)	NC		NC		NC
		Placebo	7	0 (0.0)	NC				
	Rest of the World	Osimertinib	12	3 (25.0)	NC		NC		NC
		Placebo	2	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE			Kaplan-Meier analysis				Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							Interaction test: 0.3951
	Positive	Osimertinib	10	5 (50.0)	35.6	(1.8, 35.9)	0.98	(0.11, 8.53)	0.9885
		Placebo	4	1 (25.0)	NC				
	Negative	Osimertinib	113	36 (31.9)	NC	2.60	(1.09, 6.21)	0.0313	
		Placebo	58	6 (10.3)	NC				
	Unknown	Osimertinib	20	4 (20.0)	NC	NC	NC		
Placebo		11	0 (0.0)	NC					

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Investigations	Tissue EGFR mutation at screening	Osimertinib							Interaction test: 0.6945
		Placebo							
	Ex19Del	Osimertinib	74	27 (36.5)	35.6	(27.6, NC)	2.44	(0.93, 6.39)	0.0688
		Placebo	43	5 (11.6)	NC				
	L858R	Osimertinib	68	18 (26.5)	NC		3.45	(0.80, 14.88)	0.0975
		Placebo	30	2 (6.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Sex	Osimertinib						Interaction test:	NC
		Placebo							
	Male	Osimertinib	53	1 (1.9)	NC		NC		NC
		Placebo	31	4 (12.9)	NC				
	Female	Osimertinib	90	4 (4.4)	NC		NC		NC
		Placebo	42	5 (11.9)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Age	Osimertinib							
		Placebo							
	< 65 years	Osimertinib	81	3 (3.7)	NC		NC		NC
		Placebo	39	5 (12.8)	NC				
	>= 65 years	Osimertinib	62	2 (3.2)	NC		NC		NC
		Placebo	34	4 (11.8)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Smoking status	Osimertinib							Interaction test: 0.3945
		Placebo							
	Current/former	Osimertinib	41	0 (0.0)	NC		NC		NC
		Placebo	24	1 (4.2)	NC				
	Never	Osimertinib	102	5 (4.9)	NC		0.23	(0.07, 0.74)	0.0131 *
		Placebo	49	8 (16.3)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.4244
		Placebo							
	CCRT	Osimertinib	131	5 (3.8)	NC		0.25	(0.08, 0.77)	0.0158 *
		Placebo	62	8 (12.9)	NC				
		Osimertinib	12	0 (0.0)	NC		NC		NC
		Placebo	11	1 (9.1)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Disease stage prior to chemoradiation	Osimertinib							
		Placebo							
	IIIA	Osimertinib	52	3 (5.8)	NC		NC		NC
		Placebo	24	3 (12.5)	NC				
	IIIB/IIIC	Osimertinib	91	2 (2.2)	NC		NC		NC
		Placebo	49	6 (12.2)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Race	Osimertinib						Interaction test:	0.0388 #
	Asian	Osimertinib	116	3 (2.6)	NC		0.14	(0.04, 0.54)	0.0040 *
		Placebo	62	9 (14.5)	NC				
	Non-Asian	Osimertinib	27	2 (7.4)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	China Cohort	Osimertinib							Interaction test: 0.1467
	Yes	Osimertinib	27	1 (3.7)	NC		NC		NC
		Placebo	13	0 (0.0)	NC				
	No	Osimertinib	116	4 (3.4)	NC		0.19	(0.06, 0.62)	0.0063 *
		Placebo	60	9 (15.0)	NC				

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Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Response to prior CRT	Osimertinib						Interaction test:	NC
	CR+PR	Osimertinib	71	3 (4.2)	NC		NC		NC
		Placebo	30	5 (16.7)	NC				
	SD	Osimertinib	61	1 (1.6)	NC		NC		NC
		Placebo	37	3 (8.1)	NC				
	NE	Osimertinib	11	1 (9.1)	NC		NC		NC
		Placebo	6	1 (16.7)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Region	Osimertinib							
		Placebo							
	Asia	Osimertinib	120	3 (2.5)	NC		0.14	(0.04, 0.53)	0.0038 *
		Placebo	64	9 (14.1)	NC				
	Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
		Placebo	7	0 (0.0)	NC				
	Rest of the World	Osimertinib	12	2 (16.7)	NC		NC		NC
		Placebo	2	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							Interaction test: 0.1805
	Positive	Osimertinib	10	1 (10.0)	NC		NC		NC
		Placebo	4	0 (0.0)	NC				
	Negative	Osimertinib	113	4 (3.5)	NC		0.25	(0.07, 0.88)	0.0304
		Placebo	58	7 (12.1)	NC				
	Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
		Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Musculoskeletal chest pain	Tissue EGFR mutation at screening	Osimertinib							
		Placebo							
	Ex19Del	Osimertinib	74	3 (4.1)	NC		NC		NC
		Placebo	43	5 (11.6)	NC				
	L858R	Osimertinib	68	2 (2.9)	NC		NC		NC
		Placebo	30	4 (13.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Sex	Osimertinib						Interaction test:	0.9059
	Male	Osimertinib	53	32 (60.4)	2.8	(1.6, 14.6)	2.30	(1.13, 4.69)	0.0217 *
		Placebo	31	10 (32.3)	NC				
	Female	Osimertinib	90	47 (52.2)	19.0	(4.6, NC)	2.45	(1.20, 5.00)	0.0143 *
		Placebo	42	9 (21.4)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Age	Osimertinib							Interaction test: 0.0710
	< 65 years	Osimertinib	81	45 (55.6)	8.1	(2.8, NC)	3.96	(1.69, 9.31)	0.0016 *
		Placebo	39	6 (15.4)	NC				
	>= 65 years	Osimertinib	62	34 (54.8)	5.6	(2.8, NC)	1.53	(0.81, 2.90)	0.1945
		Placebo	34	13 (38.2)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Smoking status	Osimertinib							
								Interaction test:	0.3123
	Current/former	Osimertinib	41	23 (56.1)	6.5	(1.6, NC)	1.69	(0.78, 3.66)	0.1821
		Placebo	24	9 (37.5)	7.5	(5.6, NC)			
	Never	Osimertinib	102	56 (54.9)	8.1	(3.0, 33.2)	2.87	(1.46, 5.64)	0.0022 *
		Placebo	49	10 (20.4)	NC				

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.5950
		Placebo							
	CCRT	Osimertinib	131	75 (57.3)	7.5	(3.0, 19.6)	2.12	(1.27, 3.56)	0.0043 *
		Placebo	62	18 (29.0)	NC				
	SCRT	Osimertinib	12	4 (33.3)	NC		3.79	(0.42, 33.95)	0.2330
		Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Disease stage prior to chemoradiation	Osimertinib							Interaction test: 0.3131
	IIIA	Osimertinib	52	27 (51.9)	11.1	(2.6, NC)	1.64	(0.74, 3.62)	0.2221
		Placebo	24	8 (33.3)	NC				
	IIIB/IIIC	Osimertinib	91	52 (57.1)	7.5	(3.0, 19.8)	2.79	(1.45, 5.35)	0.0020 *
		Placebo	49	11 (22.4)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Race	Osimertinib						Interaction test:	0.9705
	Asian	Osimertinib	116	65 (56.0)	8.1	(3.2, 22.2)	2.31	(1.33, 4.00)	0.0029 *
		Placebo	62	16 (25.8)	NC				
	Non-Asian	Osimertinib	27	14 (51.9)	4.3	(2.3, NC)	2.25	(0.65, 7.83)	0.2028
		Placebo	11	3 (27.3)	NC				

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The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	China Cohort	Osimertinib							Interaction test: 0.0589
	Yes	Osimertinib	27	10 (37.0)	NC		NC		NC
		Placebo	13	0 (0.0)	NC				
	No	Osimertinib	116	69 (59.5)	4.7	(2.6, 9.2)	2.13	(1.28, 3.55)	0.0037 *
		Placebo	60	19 (31.7)	NC				

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Response to prior CRT	Osimertinib							Interaction test: 0.2317
	CR+PR	Osimertinib	71	42 (59.2)	4.3	(2.3, 19.6)	1.73	(0.89, 3.37)	0.1080
		Placebo	30	11 (36.7)	NC				
	SD	Osimertinib	61	34 (55.7)	9.2	(3.0, NC)	3.65	(1.53, 8.70)	0.0035 *
		Placebo	37	6 (16.2)	NC				
	NE	Osimertinib	11	3 (27.3)	NC		0.85	(0.14, 5.11)	0.8624
		Placebo	6	2 (33.3)	11.1	(0.3, NC)			

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Region	Osimertinib							Interaction test: 0.9806
	Asia	Osimertinib	120	65 (54.2)	8.5	(3.4, 33.2)	2.28	(1.32, 3.96)	0.0033 *
		Placebo	64	16 (25.0)	NC				
	Europe	Osimertinib	11	6 (54.5)	3.0	(0.8, NC)	1.92	(0.39, 9.53)	0.4240
		Placebo	7	2 (28.6)	NC				
	Rest of the World	Osimertinib	12	8 (66.7)	2.8	(0.1, NC)	2.20	(0.28, 17.65)	0.4568
		Placebo	2	1 (50.0)	7.5	(NC, NC)			

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Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

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Table LT1A_SSUM: Time to any AE by SOC/PT by main subgroups
 Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							Interaction test: 0.4570
	Positive	Osimertinib	10	5 (50.0)	19.8	(0.4, NC)	NC		NC
		Placebo	4	0 (0.0)	NC				
	Negative	Osimertinib	113	66 (58.4)	6.5	(2.8, 14.6)	2.18	(1.28, 3.73)	0.0043 *
		Placebo	58	17 (29.3)	NC				
	Unknown	Osimertinib	20	8 (40.0)	NC		2.34	(0.50, 11.03)	0.2828
		Placebo	11	2 (18.2)	NC				

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Safety Set

Time to any AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Skin and subcutaneous tissue disorders	Tissue EGFR mutation at screening	Osimertinib							Interaction test: 0.5797
	Ex19Del	Osimertinib	74	40 (54.1)	8.5	(1.8, NC)	2.58	(1.29, 5.17)	0.0077 *
		Placebo	43	10 (23.3)	NC				
	L858R	Osimertinib	68	38 (55.9)	7.6	(2.8, 33.2)	1.94	(0.94, 4.02)	0.0741
		Placebo	30	9 (30.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

Only significant SOC/PT combinations from the main analysis are reported. The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

Source Data: AAES_TTE, created on: 08OCT2024

AstraZeneca

Value Dossier Analysis: D5160C00048

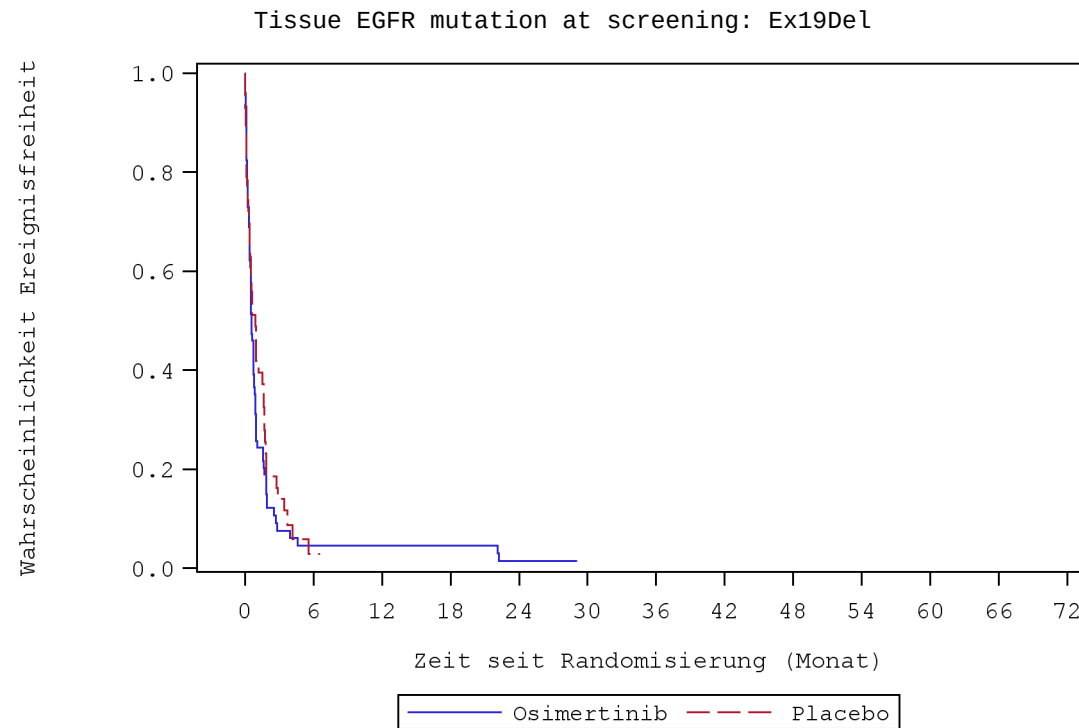
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_KS.sas

Run Date: 27SEP2024:11:25:50

Figure LF1A_SSKM: Kaplan Meier plot for time to any AE by main subgroups
Safety Set
Study: LAURA



Osimertinib	74	3	3	3	1	0
Placebo	43	1	0			

AE = Adverse Event.

Reference table: LT1A_SSTM

AstraZeneca

Value Dossier Analysis: D5160C00048

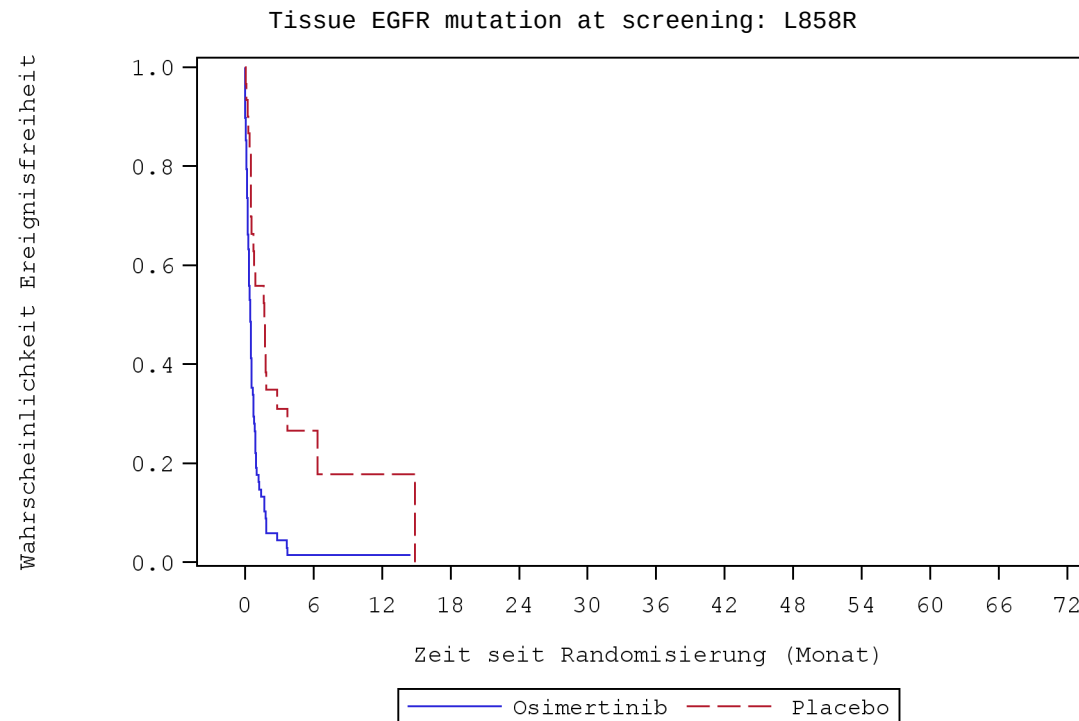
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAE_TTE_KS.sas

Run Date: 27SEP2024:11:25:50

Figure LF1A_SSKM: Kaplan Meier plot for time to any AE by main subgroups
Safety Set
Study: LAURA



Osimertinib	68	1	1	0
Placebo	30	5	1	0

AE = Adverse Event.

Reference table: LT1A_SSTM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAES_TTE_VS.sas

Run Date: 09OCT2024:10:55:47

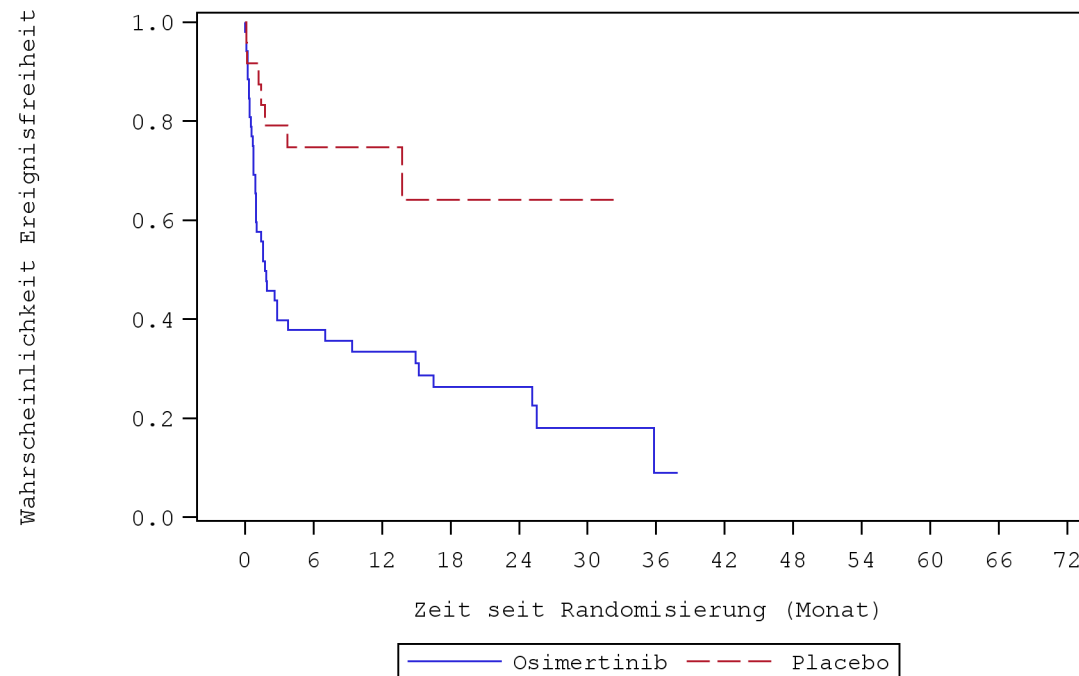
Figure LF1A_SSVM: Kaplan Meier plot for time to any AE by SOC/PT by main subgroups

Safety Set
Study: LAURA

SOC: Gastrointestinal disorders

PT: ALL PTs

Disease stage prior to chemoradiation: IIIA



Osimertinib	52	18	15	11	7	4	1	0
Placebo	24	14	7	3	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_SSUM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAES_TTE_VS.sas

Run Date: 09OCT2024:10:55:47

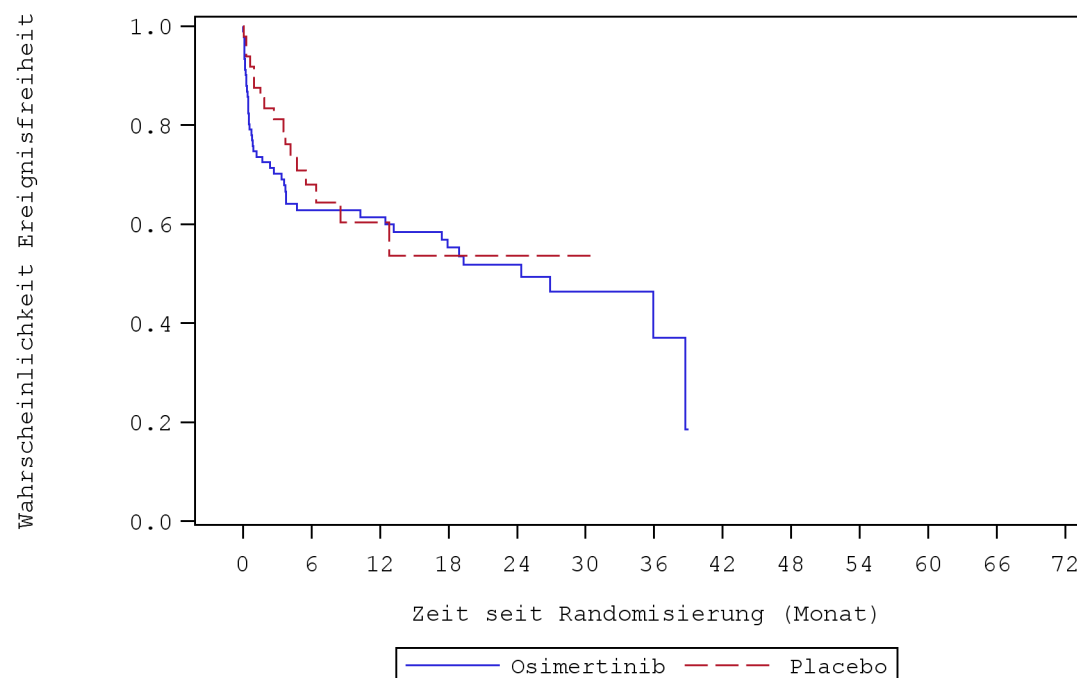
Figure LF1A_SSVM: Kaplan Meier plot for time to any AE by SOC/PT by main subgroups

Safety Set
Study: LAURA

SOC: Gastrointestinal disorders

PT: All PTs

Disease stage prior to chemoradiation: IIIB/IIIC



Osimertinib	91	46	42	35	22	10	4	0
Placebo	49	21	10	3	1	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_SSUM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAES_TTE_VS.sas

Run Date: 09OCT2024:10:55:47

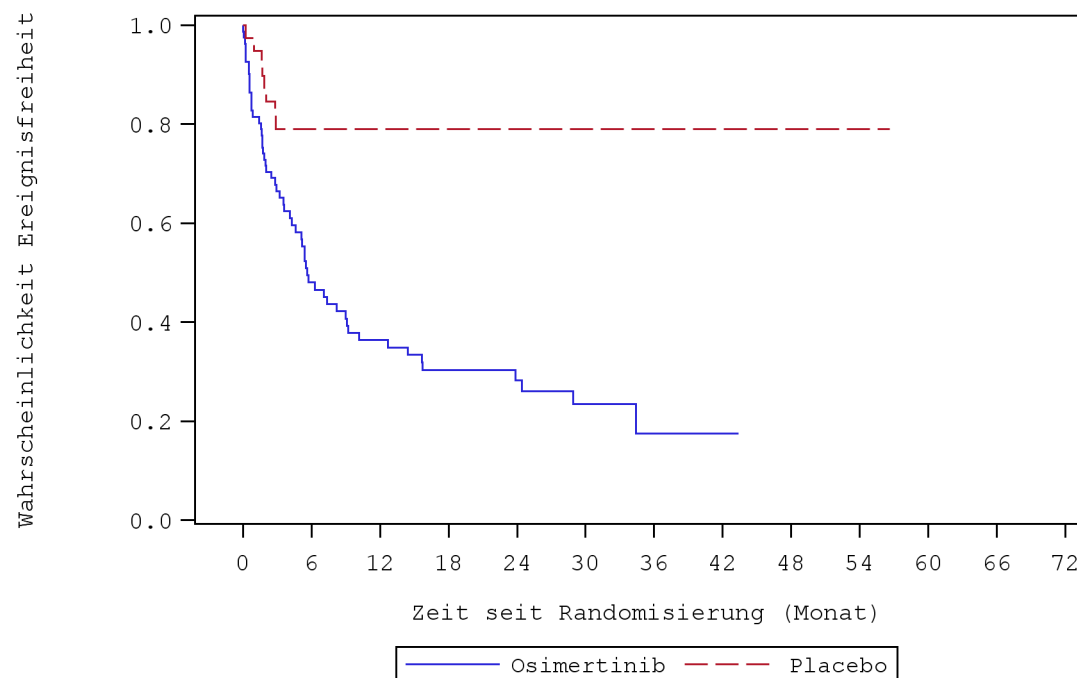
Figure LF1A_SSVM: Kaplan Meier plot for time to any AE by SOC/PT by main subgroups

Safety Set
Study: LAURA

SOC: Infections and infestations

PT: All PTs

Age: < 65 years



Osimertinib	81	33	25	18	13	8	2	1	0		
Placebo	39	16	5	2	1	1	1	1	1	1	0

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_SSUM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAES_TTE_VS.sas

Run Date: 09OCT2024:10:55:47

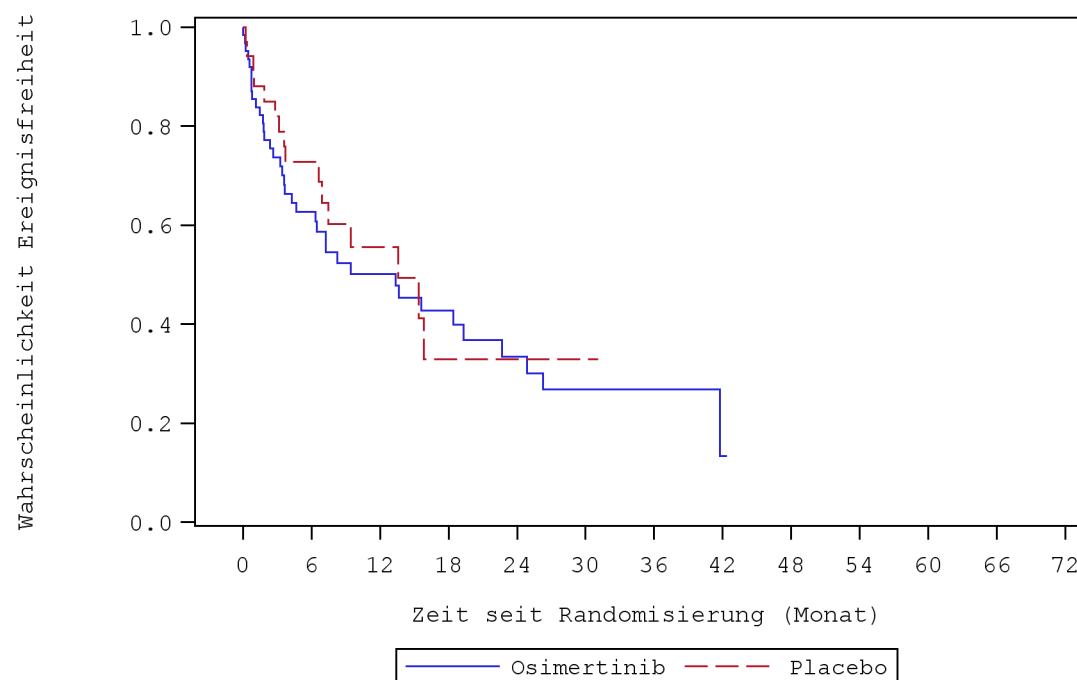
Figure LF1A_SSVM: Kaplan Meier plot for time to any AE by SOC/PT by main subgroups

Safety Set
Study: LAURA

SOC: Infections and infestations

PT: All PTs

Age: >= 65 years



Osimertinib	62	33	21	15	10	7	6	1	0
Placebo	34	21	9	2	2	1	0		

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_SSUM

AstraZeneca

Value Dossier Analysis: D5160C00048

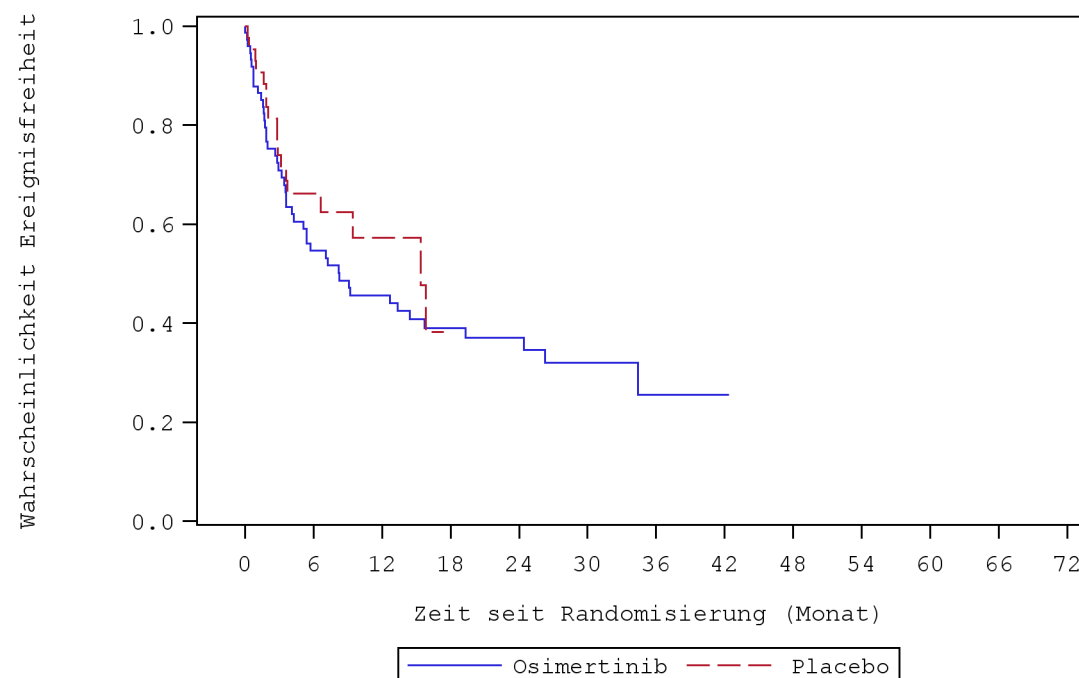
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAES_TTE_VS.sas

Run Date: 09OCT2024:10:55:47

Figure LF1A_SSVM: Kaplan Meier plot for time to any AE by SOC/PT by main subgroups

Safety Set
Study: LAURASOC: Infections and infestations
PT: All PTs
Tissue EGFR mutation at screening: Ex19Del

Osimertinib	74	37	29	21	15	9	3	1	0
Placebo	43	19	7	0					

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_SSUM

AstraZeneca

Value Dossier Analysis: D5160C00048

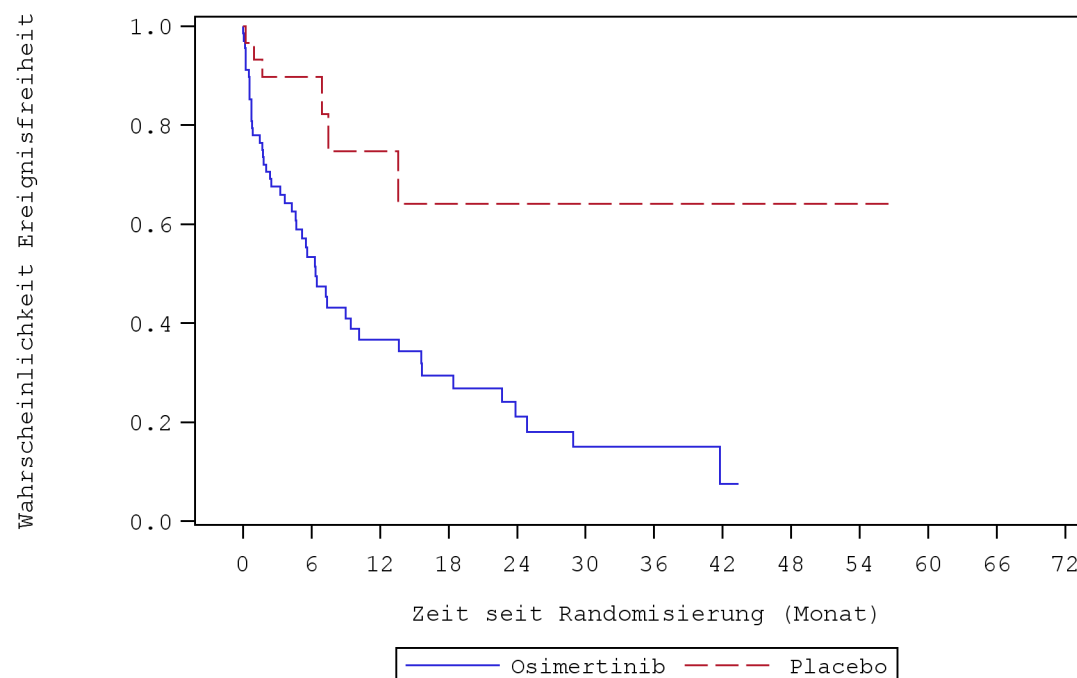
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAES_TTE_VS.sas

Run Date: 09OCT2024:10:55:47

Figure LF1A_SSVM: Kaplan Meier plot for time to any AE by SOC/PT by main subgroups

Safety Set
Study: LAURASOC: Infections and infestations
PT: All PTs
Tissue EGFR mutation at screening: L858R

Osimertinib	68	28	16	11	7	5	5	1	0	
Placebo	30	18	7	4	3	2	1	1	1	0

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.
Reference table: LT1A_SSUM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAES_TTE_VS.sas

Run Date: 09OCT2024:10:55:47

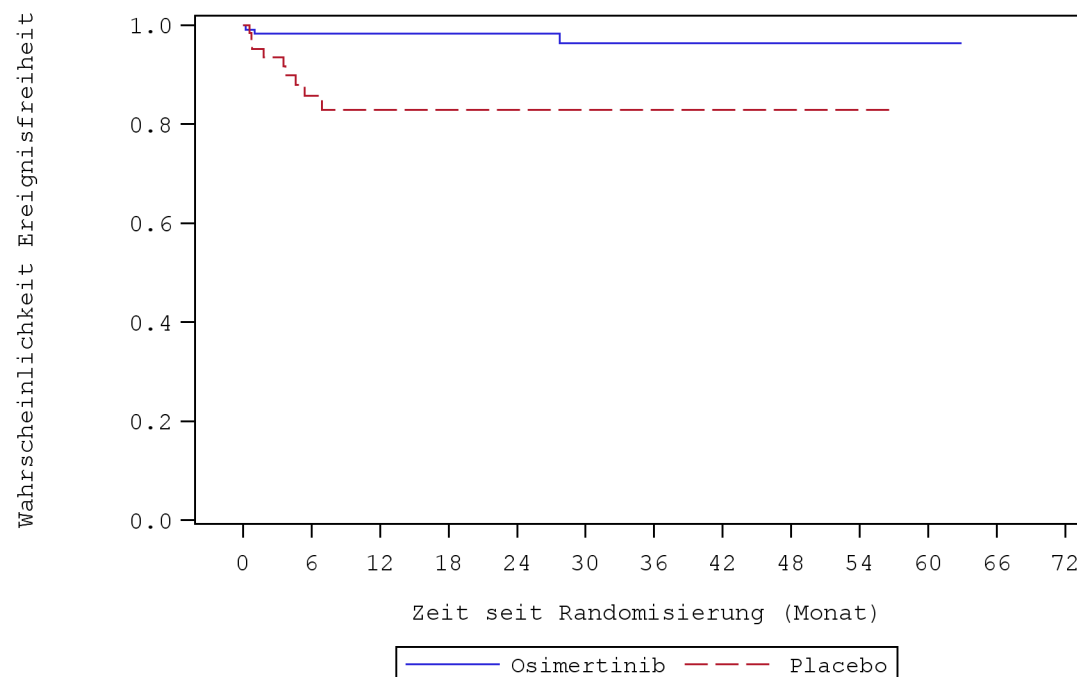
Figure LF1A_SSVM: Kaplan Meier plot for time to any AE by SOC/PT by main subgroups

Safety Set
Study: LAURA

SOC: Musculoskeletal and connective tissue disorders

PT: Musculoskeletal chest pain

Race: Asian



Osimertinib	116	94	86	80	61	43	26	12	4	1	1	0
Placebo	62	35	16	8	6	4	2	2	2	1	0	

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_SSUM

AstraZeneca

Value Dossier Analysis: D5160C00048

Cutoff Date (Interim): 05/Jan/2024

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Program Name: LF1_AAES_TTE_VS.sas

Run Date: 09OCT2024:10:55:47

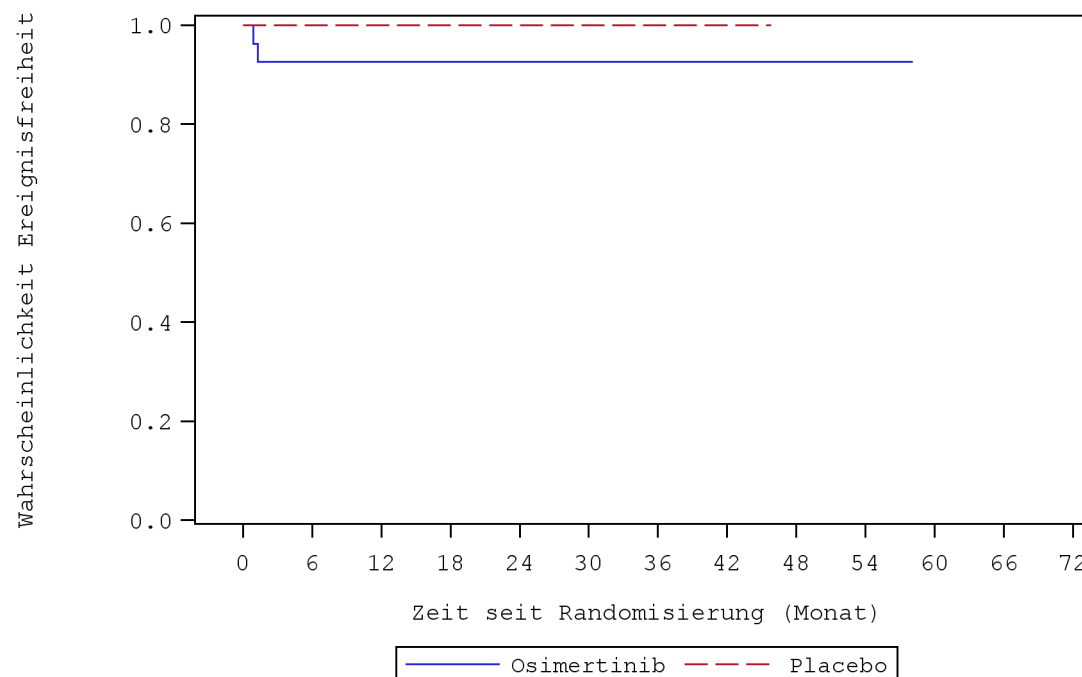
Figure LF1A_SSVM: Kaplan Meier plot for time to any AE by SOC/PT by main subgroups

Safety Set
Study: LAURA

SOC: Musculoskeletal and connective tissue disorders

PT: Musculoskeletal chest pain

Race: Non-Asian



Osimertinib	27	22	19	16	10	5	4	2	1	1	0
Placebo	11	9	6	3	1	1	1	1	0		

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

Reference table: LT1A_SSUM

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1AC_SSTM: Time to any severe AE by main subgroups
Safety Set

Time to any severe AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.6537
Male	Osimertinib	53	20 (37.7)	34.5	(28.0, NC)	1.97	(0.73, 5.28)	0.1789
	Placebo	31	5 (16.1)	NC				
Female	Osimertinib	90	30 (33.3)	NC		2.73	(0.95, 7.79)	0.0610
	Placebo	42	4 (9.5)	NC				
Age	Osimertinib						Interaction test:	0.5381
< 65 years	Osimertinib	81	27 (33.3)	NC		1.84	(0.70, 4.84)	0.2159
	Placebo	39	5 (12.8)	NC				
>= 65 years	Osimertinib	62	23 (37.1)	38.1	(31.5, NC)	2.88	(0.99, 8.36)	0.0519
	Placebo	34	4 (11.8)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event. Severe = maximum CTCAE grade >= 3. CTCAE = Common terminology criteria for adverse events.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1AC_SSTM: Time to any severe AE by main subgroups
Safety Set

Time to any severe AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.9633
Current/former	Osimertinib	41	14 (34.1)	NC		2.35	(0.67, 8.23)	0.1812
	Placebo	24	3 (12.5)	NC				
Never	Osimertinib	102	36 (35.3)	38.1	(33.0, NC)	2.27	(0.95, 5.42)	0.0657
	Placebo	49	6 (12.2)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.2673
CCRT	Osimertinib	131	45 (34.4)	NC		2.91	(1.23, 6.86)	0.0149 *
	Placebo	62	6 (9.7)	NC				
SCRT	Osimertinib	12	5 (41.7)	38.1	(1.8, NC)	1.11	(0.26, 4.67)	0.8897
	Placebo	11	3 (27.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event. Severe = maximum CTCAE grade $\geq$ 3. CTCAE = Common terminology criteria for adverse events.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1AC_SSTM: Time to any severe AE by main subgroups
Safety Set

Time to any severe AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.2023
IIIA	Osimertinib	52	21 (40.4)	34.5	(21.8, NC)	4.57	(1.07, 19.54)	0.0405 *
	Placebo	24	2 (8.3)	NC				
IIIB/IIIC	Osimertinib	91	29 (31.9)	NC		1.65	(0.71, 3.80)	0.2436
	Placebo	49	7 (14.3)	NC				
Race	Osimertinib						Interaction test:	0.8208
Asian	Osimertinib	116	39 (33.6)	NC		2.36	(1.04, 5.34)	0.0389 *
	Placebo	62	7 (11.3)	NC				
Non-Asian	Osimertinib	27	11 (40.7)	38.1	(6.1, NC)	1.93	(0.43, 8.73)	0.3913
	Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event. Severe = maximum CTCAE grade $\geq$ 3. CTCAE = Common terminology criteria for adverse events.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1AC_SSTM: Time to any severe AE by main subgroups
Safety Set

Time to any severe AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.8573
Yes	Osimertinib	27	8 (29.6)	NC		2.74	(0.34, 21.98)	0.3431
	Placebo	13	1 (7.7)	NC				
No	Osimertinib	116	42 (36.2)	38.1	(31.5, NC)	2.25	(1.04, 4.83)	0.0384 *
	Placebo	60	8 (13.3)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.8143
CR+PR	Osimertinib	71	24 (33.8)	NC		2.89	(0.86, 9.64)	0.0849
	Placebo	30	3 (10.0)	NC				
SD	Osimertinib	61	21 (34.4)	NC		1.84	(0.69, 4.93)	0.2241
	Placebo	37	5 (13.5)	NC				
NE	Osimertinib	11	5 (45.5)	8.5	(1.4, NC)	3.08	(0.36, 26.42)	0.3043
	Placebo	6	1 (16.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event. Severe = maximum CTCAE grade ≥ 3 . CTCAE = Common terminology criteria for adverse events.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

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Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1AC_SSTM: Time to any severe AE by main subgroups
Safety Set

Time to any severe AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.5033
Asia	Osimertinib	120	40 (33.3)	NC		2.46	(1.09, 5.56)	0.0298 *
	Placebo	64	7 (10.9)	NC				
Europe	Osimertinib	11	5 (45.5)	38.1	(2.0, NC)	1.12	(0.22, 5.77)	0.8946
	Placebo	7	2 (28.6)	NC				
Rest of the World	Osimertinib	12	5 (41.7)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.2507
Positive	Osimertinib	10	2 (20.0)	NC		0.35	(0.03, 3.93)	0.3957
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	42 (37.2)	38.1	(31.5, NC)	3.08	(1.30, 7.29)	0.0107 *
	Placebo	58	6 (10.3)	NC				
Unknown	Osimertinib	20	6 (30.0)	NC		1.23	(0.25, 6.10)	0.8020
	Placebo	11	2 (18.2)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event. Severe = maximum CTCAE grade $\geq$ 3. CTCAE = Common terminology criteria for adverse events.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
 Value Dossier Analysis: D5160C00048
 Cutoff Date (Interim): 05/Jan/2024

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 Program Name: LT1_AAE_TTE_TS.sas
 Run Date: 24OCT2024:12:00:50

Table LT1AC_SSTM: Time to any severe AE by main subgroups
 Safety Set

Time to any severe AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	0.8680
Ex19Del	Osimertinib	74	27 (36.5)	34.5	(29.2, NC)	2.43	(0.93, 6.37)	0.0699
	Placebo	43	5 (11.6)	NC				
L858R	Osimertinib	68	23 (33.8)	NC		2.16	(0.74, 6.27)	0.1587
	Placebo	30	4 (13.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event. Severe = maximum CTCAE grade $\geq$ 3. CTCAE = Common terminology criteria for adverse events.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
Cutoff Date (Interim): 05/Jan/2024

Page 1 of 6
Program Name: LT1_AAE_TTE_TS.sas
Run Date: 24OCT2024:12:00:50

Table LT1AS_SSTM: Time to any serious AE by main subgroups
Safety Set

Time to any serious AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.2876
Male	Osimertinib	53	18 (34.0)	NC		1.36	(0.53, 3.45)	0.5216
	Placebo	31	6 (19.4)	NC				
Female	Osimertinib	90	37 (41.1)	38.1	(21.3, NC)	2.76	(1.08, 7.07)	0.0342 *
	Placebo	42	5 (11.9)	NC				
Age	Osimertinib						Interaction test:	0.5712
< 65 years	Osimertinib	81	30 (37.0)	NC		1.68	(0.69, 4.10)	0.2507
	Placebo	39	6 (15.4)	NC				
>= 65 years	Osimertinib	62	25 (40.3)	38.1	(18.0, NC)	2.45	(0.93, 6.44)	0.0684
	Placebo	34	5 (14.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event.

Source Data: AAE_TTE, created on: 08OCT2024

AstraZeneca
Value Dossier Analysis: D5160C00048
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Table LT1AS_SSTM: Time to any serious AE by main subgroups
Safety Set

Time to any serious AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.9742
Current/former	Osimertinib	41	13 (31.7)	NC		1.97	(0.56, 6.96)	0.2916
	Placebo	24	3 (12.5)	NC				
Never	Osimertinib	102	42 (41.2)	38.1	(21.8, NC)	2.02	(0.94, 4.34)	0.0712
	Placebo	49	8 (16.3)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.9266
CCRT	Osimertinib	131	47 (35.9)	NC		2.22	(1.04, 4.73)	0.0396 *
	Placebo	62	8 (12.9)	NC				
SCRT	Osimertinib	12	8 (66.7)	13.4	(0.8, NC)	2.06	(0.54, 7.84)	0.2883
	Placebo	11	3 (27.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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AE = Adverse Event.

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Table LT1AS_SSTM: Time to any serious AE by main subgroups
Safety Set

Time to any serious AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.3739
IIIA	Osimertinib	52	22 (42.3)	34.3	(18.0, NC)	3.07	(0.92, 10.29)	0.0688
	Placebo	24	3 (12.5)	NC				
IIIB/IIIC	Osimertinib	91	33 (36.3)	NC		1.63	(0.75, 3.58)	0.2200
	Placebo	49	8 (16.3)	NC				
Race	Osimertinib						Interaction test:	0.5058
Asian	Osimertinib	116	44 (37.9)	NC		1.86	(0.92, 3.73)	0.0830
	Placebo	62	10 (16.1)	NC				
Non-Asian	Osimertinib	27	11 (40.7)	38.1	(8.5, NC)	3.67	(0.47, 28.44)	0.2134
	Placebo	11	1 (9.1)	NC				

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Table LT1AS_SSTM: Time to any serious AE by main subgroups
Safety Set

Time to any serious AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.5421
Yes	Osimertinib	27	11 (40.7)	NC		1.40	(0.39, 5.05)	0.6079
	Placebo	13	3 (23.1)	NC				
No	Osimertinib	116	44 (37.9)	38.1	(29.2, NC)	2.25	(1.05, 4.81)	0.0377 *
	Placebo	60	8 (13.3)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.5610
CR+PR	Osimertinib	71	26 (36.6)	NC		3.08	(0.93, 10.21)	0.0663
	Placebo	30	3 (10.0)	NC				
SD	Osimertinib	61	24 (39.3)	NC		1.48	(0.63, 3.48)	0.3663
	Placebo	37	7 (18.9)	NC				
NE	Osimertinib	11	5 (45.5)	8.5	(1.7, NC)	2.98	(0.35, 25.49)	0.3196
	Placebo	6	1 (16.7)	NC				

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Safety Set

Time to any serious AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.6874
Asia	Osimertinib	120	46 (38.3)	NC		1.97	(0.98, 3.95)	0.0563
	Placebo	64	10 (15.6)	NC				
Europe	Osimertinib	11	4 (36.4)	NC		1.67	(0.19, 15.01)	0.6449
	Placebo	7	1 (14.3)	NC				
Rest of the World	Osimertinib	12	5 (41.7)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.2872
Positive	Osimertinib	10	5 (50.0)	26.0	(0.4, NC)	0.48	(0.09, 2.54)	0.3907
	Placebo	4	2 (50.0)	NC				
Negative	Osimertinib	113	43 (38.1)	38.1	(30.4, NC)	2.27	(1.06, 4.88)	0.0353 *
	Placebo	58	8 (13.8)	NC				
Unknown	Osimertinib	20	7 (35.0)	NC		2.92	(0.36, 23.79)	0.3161
	Placebo	11	1 (9.1)	NC				

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Safety Set

Time to any serious AE				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.9482				
Ex19Del	Osimertinib	74	28 (37.8)	NC		2.08	(0.85, 5.05)	0.1076
	Placebo	43	6 (14.0)	NC				
L858R	Osimertinib	68	27 (39.7)	38.1	(26.0, NC)	1.99	(0.76, 5.20)	0.1606
	Placebo	30	5 (16.7)	NC				

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Table LT1AS_SSUM: Time to any serious AE by SOC/PT by main subgroups
Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Sex	Osimertinib							
		Placebo							
	Male	Osimertinib	53	6 (11.3)	NC		3.21	(0.38, 26.82)	0.2815
		Placebo	31	1 (3.2)	NC				
	Female	Osimertinib	90	13 (14.4)	NC		5.36	(0.70, 41.23)	0.1068
		Placebo	42	1 (2.4)	NC				

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The CI for median time was calculated based on Brookmeyer/Crowley.

Only significant SOC/PT combinations from the main analysis are reported. The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning Age and procedural complications		Osimertinib							Interaction test: 0.1292
	< 65 years	Osimertinib	81	11 (13.6)	NC		2.35	(0.52, 10.67)	0.2702
		Placebo	39	2 (5.1)	NC				
	>= 65 years	Osimertinib	62	8 (12.9)	NC		NC		NC
		Placebo	34	0 (0.0)	NC				

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Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Smoking status	Osimertinib							Interaction test: 0.2991
		Placebo							
	Current/former	Osimertinib	41	4 (9.8)	NC		NC		NC
		Placebo	24	0 (0.0)	NC				
	Never	Osimertinib	102	15 (14.7)	NC		3.21	(0.73, 14.16)	0.1234
		Placebo	49	2 (4.1)	NC				

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Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.3937
		Placebo							
	CCRT	Osimertinib	131	17 (13.0)	NC		3.66	(0.84, 15.96)	0.0841
		Placebo	62	2 (3.2)	NC				
	SCRT	Osimertinib	12	2 (16.7)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

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Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.2442
		Placebo						Interaction test:	0.2442
	IIIA	Osimertinib	52	6 (11.5)	NC		NC		NC
		Placebo	24	0 (0.0)	NC				
	IIIB/IIIC	Osimertinib	91	13 (14.3)	NC		3.05	(0.68, 13.69)	0.1447
		Placebo	49	2 (4.1)	NC				

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Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Race	Osimertinib							Interaction test: NC
		Placebo							
	Asian	Osimertinib	116	19 (16.4)	NC		4.65	(1.07, 20.14)	0.0400 *
		Placebo	62	2 (3.2)	NC				
	Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	China Cohort	Osimertinib							
									Interaction test: 0.0735
	Yes	Osimertinib	27	8 (29.6)	NC		1.81	(0.38, 8.57)	0.4560
		Placebo	13	2 (15.4)	NC				
	No	Osimertinib	116	11 (9.5)	NC		NC		NC
		Placebo	60	0 (0.0)	NC				

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Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Response to prior CRT	Osimertinib						Interaction test:	0.6295
		Placebo						Interaction test:	0.6295
	CR+PR	Osimertinib	71	6 (8.5)	NC		2.25	(0.27, 18.78)	0.4549
		Placebo	30	1 (3.3)	NC				
	SD	Osimertinib	61	11 (18.0)	NC		5.88	(0.75, 45.89)	0.0909
		Placebo	37	1 (2.7)	NC				
	NE	Osimertinib	11	2 (18.2)	NC		NC		NC
		Placebo	6	0 (0.0)	NC				

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Table LT1AS_SSUM: Time to any serious AE by SOC/PT by main subgroups
Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Region	Osimertinib							
		Placebo							
	Asia	Osimertinib	120	19 (15.8)	NC		4.63	(1.07, 20.06)	0.0405 *
		Placebo	64	2 (3.1)	NC				
	Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
		Placebo	7	0 (0.0)	NC				
	Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
		Placebo	2	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

Only significant SOC/PT combinations from the main analysis are reported. The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

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Table LT1AS_SSUM: Time to any serious AE by SOC/PT by main subgroups
 Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							Interaction test: 0.3981
	Positive	Osimertinib	10	3 (30.0)	NC		0.97	(0.10, 9.52)	0.9818
		Placebo	4	1 (25.0)	NC				
	Negative	Osimertinib	113	14 (12.4)	NC		6.66	(0.87, 50.88)	0.0678
		Placebo	58	1 (1.7)	NC				
	Unknown	Osimertinib	20	2 (10.0)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1AS_SSUM: Time to any serious AE by SOC/PT by main subgroups
Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
SOC: Injury, poisoning and procedural complications	Tissue EGFR mutation at screening	Osimertinib							Interaction test: 0.6755
		Placebo							
	Ex19Del	Osimertinib	74	11 (14.9)	NC		5.85	(0.75, 45.58)	0.0919
		Placebo	43	1 (2.3)	NC				
	L858R	Osimertinib	68	8 (11.8)	NC		3.12	(0.39, 25.09)	0.2840
		Placebo	30	1 (3.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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 Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Sex	Osimertinib							Interaction test: 0.6258
	Male	Osimertinib	53	4 (7.5)	NC		2.46	(0.27, 21.99)	0.4212
		Placebo	31	1 (3.2)	NC				
	Female	Osimertinib	90	11 (12.2)	NC		5.21	(0.67, 40.35)	0.1142
		Placebo	42	1 (2.4)	NC				

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Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Age	Osimertinib							Interaction test: 0.1458
	< 65 years	Osimertinib	81	9 (11.1)	NC		2.20	(0.48, 10.20)	0.3128
		Placebo	39	2 (5.1)	NC				
	>= 65 years	Osimertinib	62	6 (9.7)	NC		NC		NC
		Placebo	34	0 (0.0)	NC				

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Table LT1AS_SSUM: Time to any serious AE by SOC/PT by main subgroups
 Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Smoking status	Osimertinib							Interaction test: 0.3181
	Current/former	Osimertinib	41	3 (7.3)	NC		NC		NC
		Placebo	24	0 (0.0)	NC				
	Never	Osimertinib	102	12 (11.8)	NC		2.95	(0.66, 13.18)	0.1568
		Placebo	49	2 (4.1)	NC				

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Table LT1AS_SSUM: Time to any serious AE by SOC/PT by main subgroups
Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Prior chemoradiation strategy	Osimertinib							Interaction test: 0.3313
	CCRT	Osimertinib	131	13 (9.9)	NC		3.18	(0.72, 14.10)	0.1277
		Placebo	62	2 (3.2)	NC				
	SCRT	Osimertinib	12	2 (16.7)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

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An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Safety Set

Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.3906
		Placebo						Interaction test:	0.3906
	IIIA	Osimertinib	52	3 (5.8)	NC		NC		NC
		Placebo	24	0 (0.0)	NC				
	IIIB/IIIC	Osimertinib	91	12 (13.2)	NC		3.32	(0.74, 14.82)	0.1167
		Placebo	49	2 (4.1)	NC				

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Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Race	Osimertinib							
							Interaction test:		NC
	Asian	Osimertinib	116	15 (12.9)	NC		4.23	(0.97, 18.49)	0.0555
		Placebo	62	2 (3.2)	NC				
	Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

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Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	China Cohort	Osimertinib						Interaction test:	0.1228
		Placebo						Interaction test:	0.1228
	Yes	Osimertinib	27	8 (29.6)	NC		2.02	(0.43, 9.55)	0.3731
		Placebo	13	2 (15.4)	NC				
	No	Osimertinib	116	7 (6.0)	NC		NC		NC
		Placebo	60	0 (0.0)	NC				

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Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Response to prior CRT	Osimertinib						Interaction test:	NC
	CR+PR	Osimertinib	71	5 (7.0)	NC		NC		NC
		Placebo	30	1 (3.3)	NC				
	SD	Osimertinib	61	8 (13.1)	NC		NC		NC
		Placebo	37	1 (2.7)	NC				
	NE	Osimertinib	11	2 (18.2)	NC		NC		NC
		Placebo	6	0 (0.0)	NC				

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Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Region	Osimertinib						Interaction test:	NC
	Asia	Osimertinib	120	15 (12.5)	NC		4.21	(0.96, 18.42)	0.0562
		Placebo	64	2 (3.1)	NC				
	Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
		Placebo	7	0 (0.0)	NC				
	Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
		Placebo	2	0 (0.0)	NC				

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Time to any serious AE					Kaplan-Meier analysis		Cox regression		
SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Central plasma ctDNA EGFR mutation status at screening	Osimertinib							Interaction test: 0.5513
	Positive	Osimertinib	10	3 (30.0)	NC		1.27	(0.13, 12.20)	0.8385
		Placebo	4	1 (25.0)	NC				
	Negative	Osimertinib	113	11 (9.7)	NC		5.93	(0.77, 45.92)	0.0885
		Placebo	58	1 (1.7)	NC				
	Unknown	Osimertinib	20	1 (5.0)	NC		NC		NC
		Placebo	11	0 (0.0)	NC				

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SOC/PT	Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
PT: Radiation pneumonitis	Tissue EGFR mutation at screening	Osimertinib							Interaction test: NC
	Ex19Del	Osimertinib	74	8 (10.8)	NC		NC		NC
		Placebo	43	1 (2.3)	NC				
	L858R	Osimertinib	68	7 (10.3)	NC		NC		NC
		Placebo	30	1 (3.3)	NC				

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The CI for median time was calculated based on Brookmeyer/Crowley.

Only significant SOC/PT combinations from the main analysis are reported. The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

AE = Adverse Event. SOC = System Organ Class. PT = Preferred Term.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

Source Data: AAES_TTE, created on: 08OCT2024

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Table LT1AT_SSTM: Time to AE leading to discontinuation of treatment by main subgroups
Safety Set

Time to any AE leading to discontinuation of treatment				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.9546
Male	Osimertinib	53	8 (15.1)	NC		1.79	(0.38, 8.54)	0.4635
	Placebo	31	2 (6.5)	NC				
Female	Osimertinib	90	10 (11.1)	NC		1.68	(0.36, 7.78)	0.5048
	Placebo	42	2 (4.8)	NC				
Age	Osimertinib						Interaction test:	0.8146
< 65 years	Osimertinib	81	7 (8.6)	NC		2.25	(0.27, 18.49)	0.4512
	Placebo	39	1 (2.6)	NC				
>= 65 years	Osimertinib	62	11 (17.7)	NC		1.68	(0.47, 6.10)	0.4269
	Placebo	34	3 (8.8)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event.

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Table LT1AT_SSTM: Time to AE leading to discontinuation of treatment by main subgroups
Safety Set

Time to any AE leading to discontinuation of treatment				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.5576
Current/former	Osimertinib	41	6 (14.6)	NC		2.81	(0.34, 23.51)	0.3407
	Placebo	24	1 (4.2)	NC				
Never	Osimertinib	102	12 (11.8)	NC		1.38	(0.38, 4.96)	0.6235
	Placebo	49	3 (6.1)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.7572
CCRT	Osimertinib	131	14 (10.7)	NC		1.67	(0.47, 5.88)	0.4255
	Placebo	62	3 (4.8)	NC				
SCRT	Osimertinib	12	4 (33.3)	NC		2.47	(0.27, 22.40)	0.4224
	Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AE = Adverse Event.

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Table LT1AT_SSTM: Time to AE leading to discontinuation of treatment by main subgroups
Safety Set

Time to any AE leading to discontinuation of treatment				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.8083
IIIA	Osimertinib	52	8 (15.4)	NC		1.47	(0.31, 7.00)	0.6266
	Placebo	24	2 (8.3)	NC				
IIIB/IIIC	Osimertinib	91	10 (11.0)	NC		1.93	(0.42, 8.91)	0.4015
	Placebo	49	2 (4.1)	NC				
Race	Osimertinib						Interaction test:	0.2853
Asian	Osimertinib	116	15 (12.9)	NC		1.46	(0.47, 4.48)	0.5131
	Placebo	62	4 (6.5)	NC				
Non-Asian	Osimertinib	27	3 (11.1)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1AT_SSTM: Time to AE leading to discontinuation of treatment by main subgroups
Safety Set

Time to any AE leading to discontinuation of treatment				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.6989
Yes	Osimertinib	27	4 (14.8)	NC		1.11	(0.12, 10.16)	0.9236
	Placebo	13	1 (7.7)	NC				
No	Osimertinib	116	14 (12.1)	NC		1.86	(0.53, 6.56)	0.3342
	Placebo	60	3 (5.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.8098
CR+PR	Osimertinib	71	8 (11.3)	NC		1.27	(0.27, 6.04)	0.7667
	Placebo	30	2 (6.7)	NC				
SD	Osimertinib	61	7 (11.5)	NC		2.93	(0.36, 24.05)	0.3167
	Placebo	37	1 (2.7)	NC				
NE	Osimertinib	11	3 (27.3)	NC		1.67	(0.17, 16.08)	0.6586
	Placebo	6	1 (16.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1AT_SSTM: Time to AE leading to discontinuation of treatment by main subgroups
Safety Set

Time to any AE leading to discontinuation of treatment				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.5496
Asia	Osimertinib	120	16 (13.3)	NC		1.55	(0.51, 4.74)	0.4421
	Placebo	64	4 (6.3)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	2 (16.7)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.5834
Positive	Osimertinib	10	1 (10.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	15 (13.3)	NC		1.49	(0.49, 4.56)	0.4857
	Placebo	58	4 (6.9)	NC				
Unknown	Osimertinib	20	2 (10.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

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Table LT1AT_SSTM: Time to AE leading to discontinuation of treatment by main subgroups
 Safety Set

Time to any AE leading to discontinuation of treatment				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test: 0.6898				
Ex19Del	Osimertinib	74	10 (13.5)	NC		2.10	(0.45, 9.73)	0.3419
	Placebo	43	2 (4.7)	NC				
L858R	Osimertinib	68	8 (11.8)	NC		1.35	(0.28, 6.42)	0.7059
	Placebo	30	2 (6.7)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

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Table LT1AEI_SSTM: Time to any AEI ILD and pneumonitis by main subgroups
Safety Set

Time to any AEI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	3 (5.7)	NC		NC		NC
	Placebo	31	1 (3.2)	NC				
Female	Osimertinib	90	8 (8.9)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	3 (3.7)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
≥ 65 years	Osimertinib	62	8 (12.9)	NC		NC		NC
	Placebo	34	1 (2.9)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AEI = Adverse Event of special interest. ILD = Interstitial lung disease.

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Table LT1AEI_SSTM: Time to any AEI ILD and pneumonitis by main subgroups
Safety Set

Time to any AEI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.6353
Current/former	Osimertinib	41	1 (2.4)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	10 (9.8)	NC		4.33	(0.55, 34.03)	0.1640
	Placebo	49	1 (2.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.5779
CCRT	Osimertinib	131	10 (7.6)	NC		4.36	(0.56, 34.27)	0.1611
	Placebo	62	1 (1.6)	NC				
SCRT	Osimertinib	12	1 (8.3)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AEI = Adverse Event of special interest. ILD = Interstitial lung disease.

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Table LT1AEI_SSTM: Time to any AEI ILD and pneumonitis by main subgroups
Safety Set

Time to any AEI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	3 (5.8)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	8 (8.8)	NC		NC		NC
	Placebo	49	1 (2.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	6 (5.2)	NC		NC		NC
	Placebo	62	1 (1.6)	NC				
Non-Asian	Osimertinib	27	5 (18.5)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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AEI = Adverse Event of special interest. ILD = Interstitial lung disease.

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Table LT1AEI_SSTM: Time to any AEI ILD and pneumonitis by main subgroups
Safety Set

Time to any AEI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.5712
Yes	Osimertinib	27	2 (7.4)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	9 (7.8)	NC		4.33	(0.55, 34.39)	0.1658
	Placebo	60	1 (1.7)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	7 (9.9)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	4 (6.6)	NC		NC		NC
	Placebo	37	1 (2.7)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

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Table LT1AEI_SSTM: Time to any AEI ILD and pneumonitis by main subgroups
Safety Set

Time to any AEI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	7 (5.8)	NC		NC		NC
	Placebo	64	1 (1.6)	NC				
Europe	Osimertinib	11	1 (9.1)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	3 (25.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.7390
Positive	Osimertinib	10	1 (10.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	10 (8.8)	NC		4.85	(0.62, 38.08)	0.1333
	Placebo	58	1 (1.7)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AEI = Adverse Event of special interest. ILD = Interstitial lung disease.

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Safety Set

Time to any AEI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	NC
Ex19Del	Osimertinib	74	7 (9.5)	NC		NC		NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	4 (5.9)	NC		NC		NC
	Placebo	30	1 (3.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AEI = Adverse Event of special interest. ILD = Interstitial lung disease.

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Table LT1AEIC_SSTM: Time to any severe AESI ILD and pneumonitis by main subgroups
Safety Set

Time to any severe AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	0 (0.0)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	3 (3.3)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	0 (0.0)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
>= 65 years	Osimertinib	62	3 (4.8)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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AESI = Adverse Event of special interest. ILD = Interstitial lung disease. Severe = maximum CTCAE grade >= 3. CTCAE = Common terminology criteria for adverse events.

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Safety Set

Time to any severe AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	1 (2.4)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	2 (2.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	3 (2.3)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Safety Set

Time to any severe AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	1 (1.9)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	2 (2.2)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	1 (0.9)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	2 (7.4)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Safety Set

Time to any severe AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	3 (2.6)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	3 (4.2)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	0 (0.0)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

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Safety Set

Time to any severe AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	1 (0.8)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	2 (16.7)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	0 (0.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	3 (2.7)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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 Safety Set

Time to any severe AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib			Interaction test:			NC
Ex19Del	Osimertinib	74	2 (2.7)	NC	NC			NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	1 (1.5)	NC	NC			NC
	Placebo	30	0 (0.0)	NC				

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Table LT1AEIS_SSTM: Time to any serious AESI ILD and pneumonitis by main subgroups
Safety Set

Time to any serious AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	0 (0.0)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	3 (3.3)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	0 (0.0)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
>= 65 years	Osimertinib	62	3 (4.8)	NC		NC		NC
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Time to any serious AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	1 (2.4)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	2 (2.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	3 (2.3)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Time to any serious AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	1 (1.9)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	2 (2.2)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	1 (0.9)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	2 (7.4)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Time to any serious AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	3 (2.6)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	3 (4.2)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	0 (0.0)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
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Time to any serious AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	1 (0.8)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	2 (16.7)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	0 (0.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	3 (2.7)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Safety Set

Time to any serious AESI ILD and pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test:				
Ex19Del	Osimertinib	74	2 (2.7)	NC		NC		NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	1 (1.5)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1AER_SSTM: Time to any AESI radiation pneumonitis by main subgroups
Safety Set

Time to any AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.7958
Male	Osimertinib	53	27 (50.9)	3.5	(1.9, NC)	1.45	(0.74, 2.87)	0.2824
	Placebo	31	12 (38.7)	NC				
Female	Osimertinib	90	42 (46.7)	NC		1.29	(0.73, 2.30)	0.3850
	Placebo	42	16 (38.1)	NC				
Age	Osimertinib						Interaction test:	0.7120
< 65 years	Osimertinib	81	41 (50.6)	22.2	(1.9, NC)	1.25	(0.71, 2.20)	0.4385
	Placebo	39	17 (43.6)	NC				
>= 65 years	Osimertinib	62	28 (45.2)	NC		1.48	(0.74, 2.98)	0.2698
	Placebo	34	11 (32.4)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Table LT1AER_SSTM: Time to any AESI radiation pneumonitis by main subgroups
Safety Set

Time to any AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.1365
Current/former	Osimertinib	41	24 (58.5)	1.9	(1.8, NC)	2.21	(0.99, 4.91)	0.0527
	Placebo	24	8 (33.3)	NC				
Never	Osimertinib	102	45 (44.1)	NC		1.08	(0.64, 1.83)	0.7732
	Placebo	49	20 (40.8)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.2037
CCRT	Osimertinib	131	65 (49.6)	22.2	(1.9, NC)	1.19	(0.76, 1.87)	0.4419
	Placebo	62	27 (43.5)	NC				
SCRT	Osimertinib	12	4 (33.3)	NC		4.43	(0.50, 39.64)	0.1830
	Placebo	11	1 (9.1)	NC				

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.5855
IIIA	Osimertinib	52	26 (50.0)	11.1	(2.1, NC)	1.61	(0.73, 3.56)	0.2372
	Placebo	24	8 (33.3)	NC				
IIIB/IIIC	Osimertinib	91	43 (47.3)	NC		1.24	(0.73, 2.11)	0.4276
	Placebo	49	20 (40.8)	NC				
Race	Osimertinib						Interaction test:	0.7984
Asian	Osimertinib	116	66 (56.9)	1.9	(1.9, NC)	1.49	(0.95, 2.33)	0.0822
	Placebo	62	27 (43.5)	NC				
Non-Asian	Osimertinib	27	3 (11.1)	NC		1.09	(0.11, 10.51)	0.9383
	Placebo	11	1 (9.1)	NC				

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Time to any AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.9566
Yes	Osimertinib	27	14 (51.9)	3.7	(1.7, NC)	1.38	(0.50, 3.83)	0.5361
	Placebo	13	5 (38.5)	NC				
No	Osimertinib	116	55 (47.4)	NC		1.34	(0.82, 2.18)	0.2415
	Placebo	60	23 (38.3)	NC				
Response to prior CRT	Osimertinib						Interaction test:	0.3333
CR+PR	Osimertinib	71	29 (40.8)	NC		0.95	(0.49, 1.83)	0.8827
	Placebo	30	13 (43.3)	NC				
SD	Osimertinib	61	36 (59.0)	2.8	(1.8, NC)	1.90	(1.01, 3.58)	0.0478 *
	Placebo	37	13 (35.1)	NC				
NE	Osimertinib	11	4 (36.4)	NC		1.27	(0.23, 6.94)	0.7821
	Placebo	6	2 (33.3)	NC				

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Time to any AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	0.1518
Asia	Osimertinib	120	66 (55.0)	2.5	(1.9, NC)	1.47	(0.94, 2.31)	0.0901
	Placebo	64	27 (42.2)	NC				
Europe	Osimertinib	11	2 (18.2)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	1 (8.3)	NC		0.13	(0.01, 2.07)	0.1480
	Placebo	2	1 (50.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.2574
Positive	Osimertinib	10	8 (80.0)	1.8	(0.4, 22.2)	1.18	(0.31, 4.45)	0.8094
	Placebo	4	3 (75.0)	1.8	(1.8, NC)			
Negative	Osimertinib	113	57 (50.4)	3.7	(1.9, NC)	1.28	(0.80, 2.04)	0.3087
	Placebo	58	25 (43.1)	NC				
Unknown	Osimertinib	20	4 (20.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Time to any AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib		Interaction test: 0.8273				
Ex19Del	Osimertinib	74	40 (54.1)	3.5	(1.9, NC)	1.42	(0.81, 2.48)	0.2166
	Placebo	43	18 (41.9)	NC				
L858R	Osimertinib	68	28 (41.2)	NC		1.28	(0.62, 2.64)	0.4989
	Placebo	30	10 (33.3)	NC				

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Time to any severe AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	1 (1.9)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	2 (2.2)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	1 (1.2)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
≥ 65 years	Osimertinib	62	2 (3.2)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

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Time to any severe AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	1 (2.4)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	2 (2.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	3 (2.3)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	2 (3.8)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	1 (1.1)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	3 (2.6)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	1 (3.7)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	2 (1.7)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	0 (0.0)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	2 (3.3)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	1 (9.1)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Time to any severe AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	3 (2.5)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	1 (10.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	2 (1.8)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	NC
Ex19Del	Osimertinib	74	2 (2.7)	NC		NC		NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	1 (1.5)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	0.6258
Male	Osimertinib	53	4 (7.5)	NC		2.46	(0.27, 21.99)	0.4212
	Placebo	31	1 (3.2)	NC				
Female	Osimertinib	90	11 (12.2)	NC		5.21	(0.67, 40.35)	0.1142
	Placebo	42	1 (2.4)	NC				
Age	Osimertinib						Interaction test:	0.1458
< 65 years	Osimertinib	81	9 (11.1)	NC		2.20	(0.48, 10.20)	0.3128
	Placebo	39	2 (5.1)	NC				
>= 65 years	Osimertinib	62	6 (9.7)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1AERS_SSTM: Time to any serious AESI radiation pneumonitis by main subgroups
Safety Set

Time to any serious AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	0.3181
Current/former	Osimertinib	41	3 (7.3)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	12 (11.8)	NC		2.95	(0.66, 13.18)	0.1568
	Placebo	49	2 (4.1)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	0.3313
CCRT	Osimertinib	131	13 (9.9)	NC		3.18	(0.72, 14.10)	0.1277
	Placebo	62	2 (3.2)	NC				
SCRT	Osimertinib	12	2 (16.7)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Time to any serious AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	0.3906
IIIA	Osimertinib	52	3 (5.8)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	12 (13.2)	NC		3.32	(0.74, 14.82)	0.1167
	Placebo	49	2 (4.1)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	15 (12.9)	NC		4.23	(0.97, 18.49)	0.0555
	Placebo	62	2 (3.2)	NC				
Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Safety Set

Time to any serious AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	0.1228
Yes	Osimertinib	27	8 (29.6)	NC		2.02	(0.43, 9.55)	0.3731
	Placebo	13	2 (15.4)	NC				
No	Osimertinib	116	7 (6.0)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	5 (7.0)	NC		NC		NC
	Placebo	30	1 (3.3)	NC				
SD	Osimertinib	61	8 (13.1)	NC		NC		NC
	Placebo	37	1 (2.7)	NC				
NE	Osimertinib	11	2 (18.2)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Safety Set

Time to any serious AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	15 (12.5)	NC		4.21	(0.96, 18.42)	0.0562
	Placebo	64	2 (3.1)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	0.5513
Positive	Osimertinib	10	3 (30.0)	NC		1.27	(0.13, 12.20)	0.8385
	Placebo	4	1 (25.0)	NC				
Negative	Osimertinib	113	11 (9.7)	NC		5.93	(0.77, 45.92)	0.0885
	Placebo	58	1 (1.7)	NC				
Unknown	Osimertinib	20	1 (5.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Safety Set

Time to any serious AESI Radiation pneumonitis				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	NC
Ex19Del	Osimertinib	74	8 (10.8)	NC		NC		NC
	Placebo	43	1 (2.3)	NC				
L858R	Osimertinib	68	7 (10.3)	NC		NC		NC
	Placebo	30	1 (3.3)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1AEQ_SSTM: Time to any AESI cardiac effects (QT) by main subgroups
Safety Set

Time to any AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	4 (7.5)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	1 (1.1)	NC		NC		NC
	Placebo	42	1 (2.4)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	1 (1.2)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
≥ 65 years	Osimertinib	62	4 (6.5)	NC		NC		NC
	Placebo	34	1 (2.9)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Safety Set

Time to any AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	3 (7.3)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	2 (2.0)	NC		NC		NC
	Placebo	49	1 (2.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	5 (3.8)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	11	1 (9.1)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Safety Set

Time to any AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	1 (1.9)	NC		NC		NC
	Placebo	24	1 (4.2)	NC				
IIIB/IIIC	Osimertinib	91	4 (4.4)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	5 (4.3)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	11	1 (9.1)	NC				

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Time to any AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	5 (4.3)	NC		NC		NC
	Placebo	60	1 (1.7)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	2 (2.8)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	2 (3.3)	NC		NC		NC
	Placebo	37	1 (2.7)	NC				
NE	Osimertinib	11	1 (9.1)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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Time to any AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	5 (4.2)	NC		NC		NC
	Placebo	64	1 (1.6)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	1 (10.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	4 (3.5)	NC		NC		NC
	Placebo	58	1 (1.7)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Time to any AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib			Interaction test:			NC
Ex19Del	Osimertinib	74	1 (1.4)	NC		NC		NC
	Placebo	43	1 (2.3)	NC				
L858R	Osimertinib	68	4 (5.9)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1AEQC_SSTM: Time to any severe AESI cardiac effects (QT) by main subgroups
Safety Set

Time to any severe AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	1 (1.9)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	0 (0.0)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	0 (0.0)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
>= 65 years	Osimertinib	62	1 (1.6)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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AESI = Adverse Event of special interest. Severe = maximum CTCAE grade >= 3. CTCAE = Common terminology criteria for adverse events.

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Table LT1AEQC_SSTM: Time to any severe AESI cardiac effects (QT) by main subgroups
Safety Set

Time to any severe AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	1 (2.4)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	0 (0.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	1 (0.8)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Time to any severe AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	1 (1.1)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	1 (0.9)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Safety Set

Time to any severe AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	1 (0.9)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	1 (1.4)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	0 (0.0)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

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Safety Set

Time to any severe AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	1 (0.8)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	0 (0.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	1 (0.9)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

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 Safety Set

Time to any severe AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening		Osimertinib			Interaction test:			NC
Ex19Del	Osimertinib	74	0 (0.0)	NC	NC			NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	1 (1.5)	NC	NC			NC
	Placebo	30	0 (0.0)	NC				

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Safety Set

Time to any serious AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	0 (0.0)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	0 (0.0)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	0 (0.0)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
>= 65 years	Osimertinib	62	0 (0.0)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

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Time to any serious AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	0 (0.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	0 (0.0)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
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Time to any serious AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	0 (0.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	0 (0.0)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
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Time to any serious AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	0 (0.0)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	0 (0.0)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	0 (0.0)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
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Time to any serious AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	0 (0.0)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	0 (0.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	0 (0.0)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
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Time to any serious AESI cardiac effects (QT)				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test:				
Ex19Del	Osimertinib	74	0 (0.0)	NC		NC		NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	0 (0.0)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				

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Table LT1AEF_SSTM: Time to any AESI cardiac failure by main subgroups
Safety Set

Time to any AESI cardiac failures				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	0 (0.0)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	1 (1.1)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	0 (0.0)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
>= 65 years	Osimertinib	62	1 (1.6)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

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Safety Set

Time to any AESI cardiac failures				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	1 (1.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	1 (0.8)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1AEF_SSTM: Time to any AESI cardiac failure by main subgroups
Safety Set

Time to any AESI cardiac failures				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	1 (1.1)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	1 (0.9)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Safety Set

Time to any AESI cardiac failures				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	1 (0.9)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	0 (0.0)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	1 (1.6)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

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Time to any AESI cardiac failures				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	1 (0.8)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	0 (0.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	1 (0.9)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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 Safety Set

Time to any AESI cardiac failures				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test:				
Ex19Del	Osimertinib	74	0 (0.0)	NC		NC		NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	1 (1.5)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				

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Table LT1AEFC_SSTM: Time to any severe AESI cardiac failure by main subgroups
Safety Set

Time to any severe AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	0 (0.0)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	0 (0.0)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	0 (0.0)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
≥ 65 years	Osimertinib	62	0 (0.0)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

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Safety Set

Time to any severe AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	0 (0.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	0 (0.0)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Time to any severe AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	0 (0.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	0 (0.0)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Time to any severe AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	0 (0.0)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	0 (0.0)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	0 (0.0)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

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Time to any severe AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	0 (0.0)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	0 (0.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	0 (0.0)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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 Safety Set

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Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening	Osimertinib						Interaction test:	NC
Ex19Del	Osimertinib	74	0 (0.0)	NC		NC		NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	0 (0.0)	NC		NC		NC
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Table LT1AEFS_SSTM: Time to any serious AESI cardiac failure by main subgroups
Safety Set

Time to any serious AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Sex	Osimertinib						Interaction test:	NC
Male	Osimertinib	53	0 (0.0)	NC		NC		NC
	Placebo	31	0 (0.0)	NC				
Female	Osimertinib	90	0 (0.0)	NC		NC		NC
	Placebo	42	0 (0.0)	NC				
Age	Osimertinib						Interaction test:	NC
< 65 years	Osimertinib	81	0 (0.0)	NC		NC		NC
	Placebo	39	0 (0.0)	NC				
>= 65 years	Osimertinib	62	0 (0.0)	NC		NC		NC
	Placebo	34	0 (0.0)	NC				

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Time to any serious AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Smoking status	Osimertinib						Interaction test:	NC
Current/former	Osimertinib	41	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
Never	Osimertinib	102	0 (0.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Prior chemoradiation strategy	Osimertinib						Interaction test:	NC
CCRT	Osimertinib	131	0 (0.0)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
SCRT	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

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Safety Set

Time to any serious AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Disease stage prior to chemoradiation	Osimertinib						Interaction test:	NC
IIIA	Osimertinib	52	0 (0.0)	NC		NC		NC
	Placebo	24	0 (0.0)	NC				
IIIB/IIIC	Osimertinib	91	0 (0.0)	NC		NC		NC
	Placebo	49	0 (0.0)	NC				
Race	Osimertinib						Interaction test:	NC
Asian	Osimertinib	116	0 (0.0)	NC		NC		NC
	Placebo	62	0 (0.0)	NC				
Non-Asian	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

The Cox model is only calculated in case at least 10 patients at each subgroup level combined for both arms and at least 10 events in at least 1 subgroup level combined for both arms are reported.

For subgroup levels with no events, the Cox model is not calculated, and the respective level is excluded from the interaction test due to expected convergence issues. If no events for a treatment group over all subgroup levels are observed, no Cox model and interaction test are calculated due to expected convergence issues.

CI = Confidence Interval. NC = Not calculated / Non convergence / Not evaluable. * = significant treatment effect. # = significant interaction.

AESI = Adverse Event of special interest.

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Table LT1AEFS_SSTM: Time to any serious AESI cardiac failure by main subgroups
Safety Set

Time to any serious AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
China Cohort	Osimertinib						Interaction test:	NC
Yes	Osimertinib	27	0 (0.0)	NC		NC		NC
	Placebo	13	0 (0.0)	NC				
No	Osimertinib	116	0 (0.0)	NC		NC		NC
	Placebo	60	0 (0.0)	NC				
Response to prior CRT	Osimertinib						Interaction test:	NC
CR+PR	Osimertinib	71	0 (0.0)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				
SD	Osimertinib	61	0 (0.0)	NC		NC		NC
	Placebo	37	0 (0.0)	NC				
NE	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	6	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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Table LT1AEFS_SSTM: Time to any serious AESI cardiac failure by main subgroups
Safety Set

Time to any serious AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Region	Osimertinib						Interaction test:	NC
Asia	Osimertinib	120	0 (0.0)	NC		NC		NC
	Placebo	64	0 (0.0)	NC				
Europe	Osimertinib	11	0 (0.0)	NC		NC		NC
	Placebo	7	0 (0.0)	NC				
Rest of the World	Osimertinib	12	0 (0.0)	NC		NC		NC
	Placebo	2	0 (0.0)	NC				
Central plasma ctDNA EGFR mutation status at screening	Osimertinib						Interaction test:	NC
Positive	Osimertinib	10	0 (0.0)	NC		NC		NC
	Placebo	4	0 (0.0)	NC				
Negative	Osimertinib	113	0 (0.0)	NC		NC		NC
	Placebo	58	0 (0.0)	NC				
Unknown	Osimertinib	20	0 (0.0)	NC		NC		NC
	Placebo	11	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

The CI for median time was calculated based on Brookmeyer/Crowley.

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Table LT1AEFS_SSTM: Time to any serious AESI cardiac failure by main subgroups
 Safety Set

Time to any serious AESI cardiac failure				Kaplan-Meier analysis		Cox regression		
Subgroup	Treatment	N	nev (%)	Median time (months)	95% CI	Hazard Ratio	95% CI	p-value
Tissue EGFR mutation at screening				Interaction test:				
Ex19Del	Osimertinib	74	0 (0.0)	NC		NC		NC
	Placebo	43	0 (0.0)	NC				
L858R	Osimertinib	68	0 (0.0)	NC		NC		NC
	Placebo	30	0 (0.0)	NC				

N = number of patients in analysis set. nev (%) = number of patients with at least one event.

An unstratified Cox proportional model was applied with factor treatment, subgroup and interaction term treatment*subgroup. The interaction test was performed by comparing the full model to the reduced model without the interaction term (likelihood-ratio test).

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