Dossier zur Nutzenbewertung gemäß § 35a SGB V

Pembrolizumab (KEYTRUDA®)

MSD Sharp & Dohme GmbH

Modul 4A

Anhang 4-G: Weitere Ergebnisse

Behandlung des nicht resezierbaren nicht-epitheloiden malignen Pleuramesothelioms

Stand: 23.04.2025

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Anhang 4-G: Weitere Ergebnisse

Alle Ergebnisse beziehen sich auf den Datenschnitt vom 16.09.2022, außer für den Endpunkt Gesamtüberleben auf den Datenschnitt vom 31.01.2022.

Anhang 4-G1: Rücklaufquoten des EORTC QLQ-C30, EORTC QLQ-LC13 und EQ-5D VAS

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 die Rücklaufquoten des EORTC QLQ-C30, EORTC QLQ-LC13 und EQ-5D VAS dargestellt.

Anhang 4-G1.1: Rücklaufquoten des EORTC QLQ-C30

Table 4.1-1
Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
BASELINE	**Expected to Complete Questionnaires**	**45**	**(100.0)**	**47**	**(100.0)**
	Completed	45	(100.0)	47	(100.0)
	Compliance (% in those expected to complete questionnaires)	45	(100.0)	47	(100.0)
	Not completed	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**0**	**(0.0)**	**0**	**(0.0)**
	Discontinued due to progressive disease (objective)	0	(0.0)	0	(0.0)
	Discontinued due to symptomatic progression	0	(0.0)	0	(0.0)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 3	**Expected to Complete Questionnaires**	**42**	**(93.3)**	**44**	**(93.6)**

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 3	Completed	41	(91.1)	43	(91.5)
	Compliance (% in those expected to complete questionnaires)	41	(97.6)	43	(97.7)
	Not completed	1	(2.2)	1	(2.1)
	Other	1	(2.2)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**3**	**(6.7)**	**3**	**(6.4)**
	Discontinued due to progressive disease (objective)	0	(0.0)	2	(4.3)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(6.7)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 6	**Expected to Complete Questionnaires**	**37**	**(82.2)**	**40**	**(85.1)**
	Completed	37	(82.2)	38	(80.9)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 6	Compliance (% in those expected to complete questionnaires)	37	(100.0)	38	(95.0)
	Not completed	0	(0.0)	2	(4.3)
	Other	0	(0.0)	2	(4.3)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**8**	**(17.8)**	**7**	**(14.9)**
	Discontinued due to progressive disease (objective)	1	(2.2)	6	(12.8)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	1	(2.2)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	1	(2.2)	0	(0.0)
	Visit not scheduled	5	(11.1)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 9	**Expected to Complete Questionnaires**	**38**	**(84.4)**	**34**	**(72.3)**
	Completed	35	(77.8)	33	(70.2)
	Compliance (% in those expected to complete questionnaires)	35	(92.1)	33	(97.1)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 9	Not completed	3	(6.7)	1	(2.1)
	Other	3	(6.7)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**7**	**(15.6)**	**13**	**(27.7)**
	Discontinued due to progressive disease (objective)	2	(4.4)	7	(14.9)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	1	(2.1)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	1	(2.1)
	Visit not scheduled	3	(6.7)	1	(2.1)
	National, regional or local emergency situation	1	(2.2)	1	(2.1)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 12	**Expected to Complete Questionnaires**	**37**	**(82.2)**	**26**	**(55.3)**
	Completed	37	(82.2)	24	(51.1)
	Compliance (% in those expected to complete questionnaires)	37	(100.0)	24	(92.3)
	Not completed	0	(0.0)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 12	Other	0	(0.0)	1	(2.1)
	With visit, no record	0	(0.0)	1	(2.1)
	Missing by Design	**8**	**(17.8)**	**21**	**(44.7)**
	Discontinued due to progressive disease (objective)	4	(8.9)	9	(19.1)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	2	(4.4)	1	(2.1)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	7	(14.9)
	Visit not scheduled	1	(2.2)	2	(4.3)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 15	**Expected to Complete Questionnaires**	**29**	**(64.4)**	**31**	**(66.0)**
	Completed	27	(60.0)	29	(61.7)
	Compliance (% in those expected to complete questionnaires)	27	(93.1)	29	(93.5)
	Not completed	2	(4.4)	2	(4.3)
	Other	1	(2.2)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 15	With visit, no record	1	(2.2)	0	(0.0)
	Missing by Design	**16**	**(35.6)**	**16**	**(34.0)**
	Discontinued due to progressive disease (objective)	4	(8.9)	10	(21.3)
	Discontinued due to symptomatic progression	1	(2.2)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	4	(8.9)	1	(2.1)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	1	(2.1)
	Completed study treatment	1	(2.2)	1	(2.1)
	Visit not scheduled	5	(11.1)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 18	**Expected to Complete Questionnaires**	**34**	**(75.6)**	**17**	**(36.2)**
	Completed	32	(71.1)	16	(34.0)
	Compliance (% in those expected to complete questionnaires)	32	(94.1)	16	(94.1)
	Not completed	2	(4.4)	1	(2.1)
	Other	1	(2.2)	1	(2.1)
	With visit, no record	1	(2.2)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 18	**Missing by Design**	**11**	**(24.4)**	**30**	**(63.8)**
	Discontinued due to progressive disease (objective)	6	(13.3)	11	(23.4)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	1	(2.2)	2	(4.3)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	0	(0.0)	12	(25.5)
	Visit not scheduled	2	(4.4)	0	(0.0)
	National, regional or local emergency situation	1	(2.2)	1	(2.1)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 21	**Expected to Complete Questionnaires**	**29**	**(64.4)**	**10**	**(21.3)**
	Completed	27	(60.0)	8	(17.0)
	Compliance (% in those expected to complete questionnaires)	27	(93.1)	8	(80.0)
	Not completed	2	(4.4)	2	(4.3)
	Other	2	(4.4)	2	(4.3)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**16**	**(35.6)**	**37**	**(78.7)**

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 21	Discontinued due to progressive disease (objective)	7	(15.6)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	2	(4.3)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	0	(0.0)	18	(38.3)
	Visit not scheduled	1	(2.2)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 24	**Expected to Complete Questionnaires**	**28**	**(62.2)**	**12**	**(25.5)**
	Completed	24	(53.3)	7	(14.9)
	Compliance (% in those expected to complete questionnaires)	24	(85.7)	7	(58.3)
	Not completed	4	(8.9)	5	(10.6)
	Other	4	(8.9)	5	(10.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**17**	**(37.8)**	**35**	**(74.5)**
	Discontinued due to progressive disease (objective)	8	(17.8)	12	(25.5)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 24	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	14	(29.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	1	(2.1)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 27	**Expected to Complete Questionnaires**	**26**	**(57.8)**	**3**	**(6.4)**
	Completed	24	(53.3)	2	(4.3)
	Compliance (% in those expected to complete questionnaires)	24	(92.3)	2	(66.7)
	Not completed	2	(4.4)	1	(2.1)
	Other	2	(4.4)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**19**	**(42.2)**	**44**	**(93.6)**
	Discontinued due to progressive disease (objective)	9	(20.0)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 27	Discontinued due to adverse events related to protocol therapy	5	(11.1)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	1	(2.1)
	Completed study treatment	1	(2.2)	24	(51.1)
	Visit not scheduled	1	(2.2)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 30	**Expected to Complete Questionnaires**	**23**	**(51.1)**	**5**	**(10.6)**
	Completed	21	(46.7)	5	(10.6)
	Compliance (% in those expected to complete questionnaires)	21	(91.3)	5	(100.0)
	Not completed	2	(4.4)	0	(0.0)
	Other	2	(4.4)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**22**	**(48.9)**	**42**	**(89.4)**
	Discontinued due to progressive disease (objective)	15	(33.3)	13	(27.7)
	Discontinued due to symptomatic progression	0	(0.0)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	3	(6.4)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 30	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	0	(0.0)	19	(40.4)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.2)	2	(4.3)
WEEK 33	**Expected to Complete Questionnaires**	**23**	**(51.1)**	**5**	**(10.6)**
	Completed	22	(48.9)	4	(8.5)
	Compliance (% in those expected to complete questionnaires)	22	(95.7)	4	(80.0)
	Not completed	1	(2.2)	1	(2.1)
	Other	1	(2.2)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**22**	**(48.9)**	**42**	**(89.4)**
	Discontinued due to progressive disease (objective)	13	(28.9)	13	(27.7)
	Discontinued due to symptomatic progression	1	(2.2)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	6	(13.3)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 33	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	0	(0.0)	20	(42.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	1	(2.2)	0	(0.0)
	Not required - other	0	(0.0)	1	(2.1)
WEEK 36	**Expected to Complete Questionnaires**	**21**	**(46.7)**	**4**	**(8.5)**
	Completed	20	(44.4)	1	(2.1)
	Compliance (% in those expected to complete questionnaires)	20	(95.2)	1	(25.0)
	Not completed	1	(2.2)	3	(6.4)
	Other	1	(2.2)	3	(6.4)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**24**	**(53.3)**	**43**	**(91.5)**
	Discontinued due to progressive disease (objective)	16	(35.6)	12	(25.5)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	2	(4.3)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

		Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
Treatment Visit	Category	n	(%)	n	(%)
WEEK 36	Completed study treatment	0	(0.0)	22	(46.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	2	(4.3)
WEEK 39	**Expected to Complete Questionnaires**	**16**	**(35.6)**	**0**	**(0.0)**
	Completed	14	(31.1)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	14	(87.5)	0	(0.0)
	Not completed	2	(4.4)	0	(0.0)
	Other	1	(2.2)	0	(0.0)
	With visit, no record	1	(2.2)	0	(0.0)
	Missing by Design	**29**	**(64.4)**	**47**	**(100.0)**
	Discontinued due to progressive disease (objective)	18	(40.0)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	7	(15.6)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	25	(53.2)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 39	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	1	(2.1)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 42	**Expected to Complete Questionnaires**	**12**	**(26.7)**	**5**	**(10.6)**
	Completed	10	(22.2)	4	(8.5)
	Compliance (% in those expected to complete questionnaires)	10	(83.3)	4	(80.0)
	Not completed	2	(4.4)	1	(2.1)
	Other	2	(4.4)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**33**	**(73.3)**	**42**	**(89.4)**
	Discontinued due to progressive disease (objective)	20	(44.4)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	7	(15.6)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	2	(4.4)	21	(44.7)
	Visit not scheduled	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 42	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.2)	0	(0.0)
WEEK 45	**Expected to Complete Questionnaires**	**16**	**(35.6)**	**3**	**(6.4)**
	Completed	14	(31.1)	3	(6.4)
	Compliance (% in those expected to complete questionnaires)	14	(87.5)	3	(100.0)
	Not completed	2	(4.4)	0	(0.0)
	Other	2	(4.4)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**29**	**(64.4)**	**44**	**(93.6)**
	Discontinued due to progressive disease (objective)	20	(44.4)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	22	(46.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 45	Not required - other	0	(0.0)	1	(2.1)
WEEK 48	**Expected to Complete Questionnaires**	**15**	**(33.3)**	**2**	**(4.3)**
	Completed	13	(28.9)	2	(4.3)
	Compliance (% in those expected to complete questionnaires)	13	(86.7)	2	(100.0)
	Not completed	2	(4.4)	0	(0.0)
	Other	2	(4.4)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**30**	**(66.7)**	**45**	**(95.7)**
	Discontinued due to progressive disease (objective)	18	(40.0)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	7	(15.6)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	22	(46.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.2)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 51	**Expected to Complete Questionnaires**	**12**	**(26.7)**	**0**	**(0.0)**
	Completed	12	(26.7)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	12	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**33**	**(73.3)**	**47**	**(100.0)**
	Discontinued due to progressive disease (objective)	22	(48.9)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	6	(13.3)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	26	(55.3)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.2)	0	(0.0)
WEEK 54	**Expected to Complete Questionnaires**	**11**	**(24.4)**	**1**	**(2.1)**

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 54	Completed	10	(22.2)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	10	(90.9)	0	(0.0)
	Not completed	1	(2.2)	1	(2.1)
	Other	1	(2.2)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**34**	**(75.6)**	**46**	**(97.9)**
	Discontinued due to progressive disease (objective)	23	(51.1)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	6	(13.3)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	24	(51.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-C30 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

		Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
Treatment Visit	Category	n	(%)	n	(%)
WEEK 54	Not required - other	1	(2.2)	1	(2.1)

Expected to complete questionnaire includes all subjects who do not have missing data due to a missing by design reason.
Compliance is the proportion of subjects who completed the PRO questionnaire among those who are **expected to complete the questionnaire** at this time point, excluding those missing by design. All the other categories are defined as the proportion of subjects in the analysis population (N).
Database Cutoff Date: 16SEP2022

Anhang 4-G1.2: Rücklaufquoten des EORTC QLQ-LC13

Table 4.1-2
Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
BASELINE	**Expected to Complete Questionnaires**	**45**	**(100.0)**	**47**	**(100.0)**
	Completed	45	(100.0)	47	(100.0)
	Compliance (% in those expected to complete questionnaires)	45	(100.0)	47	(100.0)
	Not completed	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**0**	**(0.0)**	**0**	**(0.0)**
	Discontinued due to progressive disease (objective)	0	(0.0)	0	(0.0)
	Discontinued due to symptomatic progression	0	(0.0)	0	(0.0)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 3	**Expected to Complete Questionnaires**	**42**	**(93.3)**	**44**	**(93.6)**

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 3	Completed	41	(91.1)	43	(91.5)
	Compliance (% in those expected to complete questionnaires)	41	(97.6)	43	(97.7)
	Not completed	1	(2.2)	1	(2.1)
	Other	1	(2.2)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**3**	**(6.7)**	**3**	**(6.4)**
	Discontinued due to progressive disease (objective)	0	(0.0)	2	(4.3)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(6.7)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 6	**Expected to Complete Questionnaires**	**37**	**(82.2)**	**40**	**(85.1)**
	Completed	37	(82.2)	38	(80.9)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 6	Compliance (% in those expected to complete questionnaires)	37	(100.0)	38	(95.0)
	Not completed	0	(0.0)	2	(4.3)
	Other	0	(0.0)	2	(4.3)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**8**	**(17.8)**	**7**	**(14.9)**
	Discontinued due to progressive disease (objective)	1	(2.2)	6	(12.8)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	1	(2.2)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	1	(2.2)	0	(0.0)
	Visit not scheduled	5	(11.1)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 9	**Expected to Complete Questionnaires**	**38**	**(84.4)**	**34**	**(72.3)**
	Completed	35	(77.8)	33	(70.2)
	Compliance (% in those expected to complete questionnaires)	35	(92.1)	33	(97.1)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 9	Not completed	3	(6.7)	1	(2.1)
	Other	3	(6.7)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**7**	**(15.6)**	**13**	**(27.7)**
	Discontinued due to progressive disease (objective)	2	(4.4)	7	(14.9)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	1	(2.1)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	1	(2.1)
	Visit not scheduled	3	(6.7)	1	(2.1)
	National, regional or local emergency situation	1	(2.2)	1	(2.1)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 12	**Expected to Complete Questionnaires**	**37**	**(82.2)**	**26**	**(55.3)**
	Completed	37	(82.2)	24	(51.1)
	Compliance (% in those expected to complete questionnaires)	37	(100.0)	24	(92.3)
	Not completed	0	(0.0)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 12	Other	0	(0.0)	1	(2.1)
	With visit, no record	0	(0.0)	1	(2.1)
	Missing by Design	**8**	**(17.8)**	**21**	**(44.7)**
	Discontinued due to progressive disease (objective)	4	(8.9)	9	(19.1)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	2	(4.4)	1	(2.1)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	7	(14.9)
	Visit not scheduled	1	(2.2)	2	(4.3)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 15	**Expected to Complete Questionnaires**	**29**	**(64.4)**	**31**	**(66.0)**
	Completed	27	(60.0)	29	(61.7)
	Compliance (% in those expected to complete questionnaires)	27	(93.1)	29	(93.5)
	Not completed	2	(4.4)	2	(4.3)
	Other	1	(2.2)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 15	With visit, no record	1	(2.2)	0	(0.0)
	Missing by Design	**16**	**(35.6)**	**16**	**(34.0)**
	Discontinued due to progressive disease (objective)	4	(8.9)	10	(21.3)
	Discontinued due to symptomatic progression	1	(2.2)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	4	(8.9)	1	(2.1)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	1	(2.1)
	Completed study treatment	1	(2.2)	1	(2.1)
	Visit not scheduled	5	(11.1)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 18	**Expected to Complete Questionnaires**	**34**	**(75.6)**	**17**	**(36.2)**
	Completed	32	(71.1)	16	(34.0)
	Compliance (% in those expected to complete questionnaires)	32	(94.1)	16	(94.1)
	Not completed	2	(4.4)	1	(2.1)
	Other	1	(2.2)	1	(2.1)
	With visit, no record	1	(2.2)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 18	**Missing by Design**	**11**	**(24.4)**	**30**	**(63.8)**
	Discontinued due to progressive disease (objective)	6	(13.3)	11	(23.4)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	1	(2.2)	2	(4.3)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	0	(0.0)	12	(25.5)
	Visit not scheduled	2	(4.4)	0	(0.0)
	National, regional or local emergency situation	1	(2.2)	1	(2.1)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 21	**Expected to Complete Questionnaires**	**29**	**(64.4)**	**10**	**(21.3)**
	Completed	27	(60.0)	8	(17.0)
	Compliance (% in those expected to complete questionnaires)	27	(93.1)	8	(80.0)
	Not completed	2	(4.4)	2	(4.3)
	Other	2	(4.4)	2	(4.3)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**16**	**(35.6)**	**37**	**(78.7)**

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 21	Discontinued due to progressive disease (objective)	7	(15.6)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	1	(2.1)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	2	(4.3)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	0	(0.0)	18	(38.3)
	Visit not scheduled	1	(2.2)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 24	**Expected to Complete Questionnaires**	**28**	**(62.2)**	**12**	**(25.5)**
	Completed	24	(53.3)	7	(14.9)
	Compliance (% in those expected to complete questionnaires)	24	(85.7)	7	(58.3)
	Not completed	4	(8.9)	5	(10.6)
	Other	4	(8.9)	5	(10.6)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**17**	**(37.8)**	**35**	**(74.5)**
	Discontinued due to progressive disease (objective)	8	(17.8)	12	(25.5)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

		Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
Treatment Visit	Category	n	(%)	n	(%)
WEEK 24	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	14	(29.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	1	(2.1)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 27	**Expected to Complete Questionnaires**	**26**	**(57.8)**	**3**	**(6.4)**
	Completed	24	(53.3)	2	(4.3)
	Compliance (% in those expected to complete questionnaires)	24	(92.3)	2	(66.7)
	Not completed	2	(4.4)	1	(2.1)
	Other	2	(4.4)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**19**	**(42.2)**	**44**	**(93.6)**
	Discontinued due to progressive disease (objective)	9	(20.0)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 27	Discontinued due to adverse events related to protocol therapy	5	(11.1)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	1	(2.1)
	Completed study treatment	1	(2.2)	24	(51.1)
	Visit not scheduled	1	(2.2)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 30	**Expected to Complete Questionnaires**	**23**	**(51.1)**	**5**	**(10.6)**
	Completed	21	(46.7)	5	(10.6)
	Compliance (% in those expected to complete questionnaires)	21	(91.3)	5	(100.0)
	Not completed	2	(4.4)	0	(0.0)
	Other	2	(4.4)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**22**	**(48.9)**	**42**	**(89.4)**
	Discontinued due to progressive disease (objective)	15	(33.3)	13	(27.7)
	Discontinued due to symptomatic progression	0	(0.0)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	3	(6.4)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 30	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	0	(0.0)	19	(40.4)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.2)	2	(4.3)
WEEK 33	**Expected to Complete Questionnaires**	**23**	**(51.1)**	**5**	**(10.6)**
	Completed	22	(48.9)	4	(8.5)
	Compliance (% in those expected to complete questionnaires)	22	(95.7)	4	(80.0)
	Not completed	1	(2.2)	1	(2.1)
	Other	1	(2.2)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**22**	**(48.9)**	**42**	**(89.4)**
	Discontinued due to progressive disease (objective)	13	(28.9)	13	(27.7)
	Discontinued due to symptomatic progression	1	(2.2)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	6	(13.3)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 33	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	0	(0.0)	20	(42.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	1	(2.2)	0	(0.0)
	Not required - other	0	(0.0)	1	(2.1)
WEEK 36	**Expected to Complete Questionnaires**	**21**	**(46.7)**	**4**	**(8.5)**
	Completed	20	(44.4)	1	(2.1)
	Compliance (% in those expected to complete questionnaires)	20	(95.2)	1	(25.0)
	Not completed	1	(2.2)	3	(6.4)
	Other	1	(2.2)	3	(6.4)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**24**	**(53.3)**	**43**	**(91.5)**
	Discontinued due to progressive disease (objective)	16	(35.6)	12	(25.5)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	2	(4.3)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 36	Completed study treatment	0	(0.0)	22	(46.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	2	(4.3)
WEEK 39	**Expected to Complete Questionnaires**	**16**	**(35.6)**	**0**	**(0.0)**
	Completed	14	(31.1)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	14	(87.5)	0	(0.0)
	Not completed	2	(4.4)	0	(0.0)
	Other	1	(2.2)	0	(0.0)
	With visit, no record	1	(2.2)	0	(0.0)
	Missing by Design	**29**	**(64.4)**	**47**	**(100.0)**
	Discontinued due to progressive disease (objective)	18	(40.0)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	7	(15.6)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	25	(53.2)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 39	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	1	(2.1)
	Not required - other	0	(0.0)	0	(0.0)
WEEK 42	**Expected to Complete Questionnaires**	**12**	**(26.7)**	**5**	**(10.6)**
	Completed	10	(22.2)	4	(8.5)
	Compliance (% in those expected to complete questionnaires)	10	(83.3)	4	(80.0)
	Not completed	2	(4.4)	1	(2.1)
	Other	2	(4.4)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**33**	**(73.3)**	**42**	**(89.4)**
	Discontinued due to progressive disease (objective)	20	(44.4)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	7	(15.6)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	2	(4.4)	21	(44.7)
	Visit not scheduled	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 42	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.2)	0	(0.0)
WEEK 45	**Expected to Complete Questionnaires**	**16**	**(35.6)**	**3**	**(6.4)**
	Completed	14	(31.1)	3	(6.4)
	Compliance (% in those expected to complete questionnaires)	14	(87.5)	3	(100.0)
	Not completed	2	(4.4)	0	(0.0)
	Other	2	(4.4)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**29**	**(64.4)**	**44**	**(93.6)**
	Discontinued due to progressive disease (objective)	20	(44.4)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	5	(11.1)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	22	(46.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 45	Not required - other	0	(0.0)	1	(2.1)
WEEK 48	**Expected to Complete Questionnaires**	**15**	**(33.3)**	**2**	**(4.3)**
	Completed	13	(28.9)	2	(4.3)
	Compliance (% in those expected to complete questionnaires)	13	(86.7)	2	(100.0)
	Not completed	2	(4.4)	0	(0.0)
	Other	2	(4.4)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**30**	**(66.7)**	**45**	**(95.7)**
	Discontinued due to progressive disease (objective)	18	(40.0)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	7	(15.6)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	22	(46.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.2)	2	(4.3)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 51	**Expected to Complete Questionnaires**	**12**	**(26.7)**	**0**	**(0.0)**
	Completed	12	(26.7)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	12	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**33**	**(73.3)**	**47**	**(100.0)**
	Discontinued due to progressive disease (objective)	22	(48.9)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	6	(13.3)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	26	(55.3)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.2)	0	(0.0)
WEEK 54	**Expected to Complete Questionnaires**	**11**	**(24.4)**	**1**	**(2.1)**

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
		n	(%)	n	(%)
WEEK 54	Completed	10	(22.2)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	10	(90.9)	0	(0.0)
	Not completed	1	(2.2)	1	(2.1)
	Other	1	(2.2)	1	(2.1)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**34**	**(75.6)**	**46**	**(97.9)**
	Discontinued due to progressive disease (objective)	23	(51.1)	13	(27.7)
	Discontinued due to symptomatic progression	2	(4.4)	2	(4.3)
	Discontinued due to adverse events related to protocol therapy	6	(13.3)	3	(6.4)
	Discontinued due to death	1	(2.2)	1	(2.1)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.3)
	Completed study treatment	1	(2.2)	24	(51.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EORTC QLQ-LC13 by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

		Pembrolizumab + Chemotherapy N=45		Chemotherapy N=47	
Treatment Visit	Category	n	(%)	n	(%)
WEEK 54	Not required - other	1	(2.2)	1	(2.1)

Expected to complete questionnaire includes all subjects who do not have missing data due to a missing by design reason.
Compliance is the proportion of subjects who completed the PRO questionnaire among those who are **expected to complete the questionnaire** at this time point, excluding those missing by design. All the other categories are defined as the proportion of subjects in the analysis population (N).
Database Cutoff Date: 16SEP2022

Anhang 4-G1.3: Rücklaufquoten des EQ-5D VAS

Table 4.1-3
Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
BASELINE	**Expected to Complete Questionnaires**	**38**	**(100.0)**	**44**	**(97.8)**
	Completed	38	(100.0)	44	(97.8)
	Compliance (% in those expected to complete questionnaires)	38	(100.0)	44	(100.0)
	Not completed	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**0**	**(0.0)**	**1**	**(2.2)**
	Discontinued due to progressive disease (objective)	0	(0.0)	0	(0.0)
	Discontinued due to symptomatic progression	0	(0.0)	0	(0.0)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	0	(0.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	1	(2.2)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 3	**Expected to Complete Questionnaires**	**35**	**(92.1)**	**42**	**(93.3)**
	Completed	33	(86.8)	39	(86.7)
	Compliance (% in those expected to complete questionnaires)	33	(94.3)	39	(92.9)
	Not completed	2	(5.3)	3	(6.7)
	Other	2	(5.3)	3	(6.7)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**3**	**(7.9)**	**3**	**(6.7)**
	Discontinued due to progressive disease (objective)	0	(0.0)	2	(4.4)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.2)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(7.9)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 6	**Expected to Complete Questionnaires**	**31**	**(81.6)**	**36**	**(80.0)**
	Completed	29	(76.3)	34	(75.6)
	Compliance (% in those expected to complete questionnaires)	29	(93.5)	34	(94.4)
	Not completed	2	(5.3)	2	(4.4)
	Other	1	(2.6)	1	(2.2)
	With visit, no record	1	(2.6)	1	(2.2)
	Missing by Design	**7**	**(18.4)**	**9**	**(20.0)**
	Discontinued due to progressive disease (objective)	1	(2.6)	7	(15.6)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.2)
	Discontinued due to adverse events related to protocol therapy	1	(2.6)	0	(0.0)
	Discontinued due to death	0	(0.0)	0	(0.0)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	1	(2.6)	0	(0.0)
	Visit not scheduled	4	(10.5)	1	(2.2)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 9	**Expected to Complete Questionnaires**	**31**	**(81.6)**	**31**	**(68.9)**
	Completed	29	(76.3)	30	(66.7)
	Compliance (% in those expected to complete questionnaires)	29	(93.5)	30	(96.8)
	Not completed	2	(5.3)	1	(2.2)
	Other	2	(5.3)	1	(2.2)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**7**	**(18.4)**	**14**	**(31.1)**
	Discontinued due to progressive disease (objective)	2	(5.3)	8	(17.8)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.2)
	Discontinued due to adverse events related to protocol therapy	0	(0.0)	1	(2.2)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	1	(2.2)
	Visit not scheduled	3	(7.9)	1	(2.2)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	1	(2.6)	1	(2.2)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 12	**Expected to Complete Questionnaires**	**30**	**(78.9)**	**24**	**(53.3)**
	Completed	30	(78.9)	22	(48.9)
	Compliance (% in those expected to complete questionnaires)	30	(100.0)	22	(91.7)
	Not completed	0	(0.0)	2	(4.4)
	Other	0	(0.0)	1	(2.2)
	With visit, no record	0	(0.0)	1	(2.2)
	Missing by Design	**8**	**(21.1)**	**21**	**(46.7)**
	Discontinued due to progressive disease (objective)	4	(10.5)	10	(22.2)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.2)
	Discontinued due to adverse events related to protocol therapy	2	(5.3)	1	(2.2)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	0	(0.0)
	Completed study treatment	0	(0.0)	6	(13.3)
	Visit not scheduled	1	(2.6)	2	(4.4)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 15	**Expected to Complete Questionnaires**	**25**	**(65.8)**	**27**	**(60.0)**
	Completed	23	(60.5)	24	(53.3)
	Compliance (% in those expected to complete questionnaires)	23	(92.0)	24	(88.9)
	Not completed	2	(5.3)	3	(6.7)
	Other	1	(2.6)	3	(6.7)
	With visit, no record	1	(2.6)	0	(0.0)
	Missing by Design	**13**	**(34.2)**	**18**	**(40.0)**
	Discontinued due to progressive disease (objective)	3	(7.9)	10	(22.2)
	Discontinued due to symptomatic progression	1	(2.6)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	2	(5.3)	2	(4.4)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	1	(2.2)
	Completed study treatment	0	(0.0)	2	(4.4)
	Visit not scheduled	6	(15.8)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 18	**Expected to Complete Questionnaires**	**27**	**(71.1)**	**16**	**(35.6)**
	Completed	25	(65.8)	15	(33.3)
	Compliance (% in those expected to complete questionnaires)	25	(92.6)	15	(93.8)
	Not completed	2	(5.3)	1	(2.2)
	Other	1	(2.6)	1	(2.2)
	With visit, no record	1	(2.6)	0	(0.0)
	Missing by Design	**11**	**(28.9)**	**29**	**(64.4)**
	Discontinued due to progressive disease (objective)	6	(15.8)	12	(26.7)
	Discontinued due to symptomatic progression	0	(0.0)	1	(2.2)
	Discontinued due to adverse events related to protocol therapy	1	(2.6)	2	(4.4)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	1	(2.6)	10	(22.2)
	Visit not scheduled	1	(2.6)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	1	(2.6)	1	(2.2)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 21	**Expected to Complete Questionnaires**	**23**	**(60.5)**	**10**	**(22.2)**
	Completed	22	(57.9)	8	(17.8)
	Compliance (% in those expected to complete questionnaires)	22	(95.7)	8	(80.0)
	Not completed	1	(2.6)	2	(4.4)
	Other	1	(2.6)	2	(4.4)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**15**	**(39.5)**	**35**	**(77.8)**
	Discontinued due to progressive disease (objective)	6	(15.8)	14	(31.1)
	Discontinued due to symptomatic progression	2	(5.3)	1	(2.2)
	Discontinued due to adverse events related to protocol therapy	3	(7.9)	2	(4.4)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	1	(2.6)	15	(33.3)
	Visit not scheduled	1	(2.6)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	1	(2.6)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 24	**Expected to Complete Questionnaires**	**22**	**(57.9)**	**9**	**(20.0)**
	Completed	19	(50.0)	5	(11.1)
	Compliance (% in those expected to complete questionnaires)	19	(86.4)	5	(55.6)
	Not completed	3	(7.9)	4	(8.9)
	Other	3	(7.9)	4	(8.9)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**16**	**(42.1)**	**36**	**(80.0)**
	Discontinued due to progressive disease (objective)	7	(18.4)	13	(28.9)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	3	(7.9)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	2	(5.3)	14	(31.1)
	Visit not scheduled	1	(2.6)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	1	(2.2)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 27	**Expected to Complete Questionnaires**	**23**	**(60.5)**	**3**	**(6.7)**
	Completed	21	(55.3)	2	(4.4)
	Compliance (% in those expected to complete questionnaires)	21	(91.3)	2	(66.7)
	Not completed	2	(5.3)	1	(2.2)
	Other	2	(5.3)	1	(2.2)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**15**	**(39.5)**	**42**	**(93.3)**
	Discontinued due to progressive disease (objective)	7	(18.4)	14	(31.1)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	3	(7.9)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	1	(2.2)
	Completed study treatment	1	(2.6)	21	(46.7)
	Visit not scheduled	1	(2.6)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 30	**Expected to Complete Questionnaires**	**21**	**(55.3)**	**5**	**(11.1)**
	Completed	18	(47.4)	5	(11.1)
	Compliance (% in those expected to complete questionnaires)	18	(85.7)	5	(100.0)
	Not completed	3	(7.9)	0	(0.0)
	Other	2	(5.3)	0	(0.0)
	With visit, no record	1	(2.6)	0	(0.0)
	Missing by Design	**17**	**(44.7)**	**40**	**(88.9)**
	Discontinued due to progressive disease (objective)	12	(31.6)	14	(31.1)
	Discontinued due to symptomatic progression	0	(0.0)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	4	(10.5)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	0	(0.0)	16	(35.6)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	2	(4.4)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 33	**Expected to Complete Questionnaires**	**19**	**(50.0)**	**5**	**(11.1)**
	Completed	18	(47.4)	4	(8.9)
	Compliance (% in those expected to complete questionnaires)	18	(94.7)	4	(80.0)
	Not completed	1	(2.6)	1	(2.2)
	Other	1	(2.6)	1	(2.2)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**19**	**(50.0)**	**40**	**(88.9)**
	Discontinued due to progressive disease (objective)	11	(28.9)	14	(31.1)
	Discontinued due to symptomatic progression	1	(2.6)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	4	(10.5)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	1	(2.6)	18	(40.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	1	(2.6)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 36	**Expected to Complete Questionnaires**	**19**	**(50.0)**	**4**	**(8.9)**
	Completed	18	(47.4)	1	(2.2)
	Compliance (% in those expected to complete questionnaires)	18	(94.7)	1	(25.0)
	Not completed	1	(2.6)	3	(6.7)
	Other	1	(2.6)	3	(6.7)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**19**	**(50.0)**	**41**	**(91.1)**
	Discontinued due to progressive disease (objective)	13	(34.2)	13	(28.9)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	3	(7.9)	2	(4.4)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	0	(0.0)	19	(42.2)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	2	(4.4)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 39	**Expected to Complete Questionnaires**	**15**	**(39.5)**	**0**	**(0.0)**
	Completed	15	(39.5)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	15	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**23**	**(60.5)**	**45**	**(100.0)**
	Discontinued due to progressive disease (objective)	14	(36.8)	14	(31.1)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	5	(13.2)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	1	(2.6)	22	(48.9)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	1	(2.2)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 42	**Expected to Complete Questionnaires**	**11**	**(28.9)**	**5**	**(11.1)**
	Completed	10	(26.3)	4	(8.9)
	Compliance (% in those expected to complete questionnaires)	10	(90.9)	4	(80.0)
	Not completed	1	(2.6)	1	(2.2)
	Other	1	(2.6)	1	(2.2)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**27**	**(71.1)**	**40**	**(88.9)**
	Discontinued due to progressive disease (objective)	16	(42.1)	14	(31.1)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	5	(13.2)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	2	(5.3)	18	(40.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.6)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 45	**Expected to Complete Questionnaires**	**15**	**(39.5)**	**3**	**(6.7)**
	Completed	13	(34.2)	3	(6.7)
	Compliance (% in those expected to complete questionnaires)	13	(86.7)	3	(100.0)
	Not completed	2	(5.3)	0	(0.0)
	Other	2	(5.3)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**23**	**(60.5)**	**42**	**(93.3)**
	Discontinued due to progressive disease (objective)	16	(42.1)	14	(31.1)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	3	(7.9)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	1	(2.6)	19	(42.2)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	1	(2.2)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 48	**Expected to Complete Questionnaires**	**14**	**(36.8)**	**2**	**(4.4)**
	Completed	12	(31.6)	2	(4.4)
	Compliance (% in those expected to complete questionnaires)	12	(85.7)	2	(100.0)
	Not completed	2	(5.3)	0	(0.0)
	Other	2	(5.3)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**24**	**(63.2)**	**43**	**(95.6)**
	Discontinued due to progressive disease (objective)	14	(36.8)	14	(31.1)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	5	(13.2)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	1	(2.6)	19	(42.2)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	1	(2.6)	2	(4.4)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 51	**Expected to Complete Questionnaires**	**11**	**(28.9)**	**0**	**(0.0)**
	Completed	11	(28.9)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	11	(100.0)	0	(0.0)
	Not completed	0	(0.0)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**27**	**(71.1)**	**45**	**(100.0)**
	Discontinued due to progressive disease (objective)	18	(47.4)	14	(31.1)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	5	(13.2)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	1	(2.6)	23	(51.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)
	Not required - other	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 54	**Expected to Complete Questionnaires**	**10**	**(26.3)**	**1**	**(2.2)**
	Completed	9	(23.7)	0	(0.0)
	Compliance (% in those expected to complete questionnaires)	9	(90.0)	0	(0.0)
	Not completed	1	(2.6)	1	(2.2)
	Other	1	(2.6)	1	(2.2)
	With visit, no record	0	(0.0)	0	(0.0)
	Missing by Design	**28**	**(73.7)**	**44**	**(97.8)**
	Discontinued due to progressive disease (objective)	19	(50.0)	14	(31.1)
	Discontinued due to symptomatic progression	2	(5.3)	2	(4.4)
	Discontinued due to adverse events related to protocol therapy	4	(10.5)	3	(6.7)
	Discontinued due to death	1	(2.6)	1	(2.2)
	Discontinued due to patient refusal (not related to adverse event)	0	(0.0)	2	(4.4)
	Completed study treatment	1	(2.6)	21	(46.7)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Not required - patient randomized prior to amendment	0	(0.0)	0	(0.0)
	National, regional or local emergency situation	0	(0.0)	0	(0.0)

Completion and Compliance Percentages for EQ-5D by Visit (up to Week 54)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

Treatment Visit	Category	Pembrolizumab + Chemotherapy N=38		Chemotherapy N=45	
		n	(%)	n	(%)
WEEK 54	Not required - other	1	(2.6)	1	(2.2)

Expected to complete questionnaire includes all subjects who do not have missing data due to a missing by design reason.
Compliance is the proportion of subjects who completed the PRO questionnaire among those who are **expected to complete the questionnaire** at this time point, excluding those missing by design. All the other categories are defined as the proportion of subjects in the analysis population (N).
Database Cutoff Date: 16SEP2022

Anhang 4-G2: Ergebnisse der Auswertungen über den Studienverlauf für die Endpunkte Krankheitssymptomatik und Gesundheitszustand anhand von EORTC QLQ-C30, EORTC QLQ-LC13 und EQ-5D VAS der Studie KEYNOTE 483

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 die Auswertungen über den Studienverlauf des EORTC QLQ-C30, EORTC QLQ-LC13 und der EQ-5D VAS dargestellt.

Anhang 4-G2.1: EORTC QLQ-C30

4.1.1.1 Fatigue

Table 4.2-1
Descriptive Summary of EORTC QLQ-C30 Fatigue by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Fatigue	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	37.8 (27.2)	33.6 (22.6)
Median (Q1; Q3)	44.4 (22.2; 55.6)	33.3 (22.2; 44.4)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	38.2 (22.5)	38.8 (22.3)
Median (Q1; Q3)	33.3 (22.2; 55.6)	33.3 (22.2; 55.6)
Min; Max	0.0; 88.9	0.0; 100.0
Week 6		
N[d]	37	38
Mean (SD)	38.7 (26.9)	38.9 (26.7)
Median (Q1; Q3)	33.3 (22.2; 55.6)	33.3 (22.2; 55.6)
Min; Max	0.0; 100.0	0.0; 100.0
Week 9		
N[d]	35	33
Mean (SD)	33.3 (20.2)	39.1 (26.4)
Median (Q1; Q3)	33.3 (22.2; 44.4)	33.3 (22.2; 55.6)
Min; Max	0.0; 66.7	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	35.1 (23.1)	37.3 (21.9)
Median (Q1; Q3)	33.3 (22.2; 44.4)	33.3 (22.2; 50.0)
Min; Max	0.0; 100.0	0.0; 88.9
Week 15		
N[d]	27	29
Mean (SD)	39.9 (27.3)	37.2 (18.8)
Median (Q1; Q3)	33.3 (22.2; 66.7)	33.3 (33.3; 44.4)
Min; Max	0.0; 100.0	0.0; 77.8
Week 18		
N[d]	32	16
Mean (SD)	33.7 (26.7)	43.1 (25.0)
Median (Q1; Q3)	33.3 (11.1; 50.0)	33.3 (33.3; 61.1)
Min; Max	0.0; 100.0	0.0; 100.0

Week 21		
N[d]	27	8
Mean (SD)	40.7 (31.6)	36.1 (32.9)
Median (Q1; Q3)	33.3 (11.1; 66.7)	33.3 (11.1; 50.0)
Min; Max	0.0; 100.0	0.0; 100.0

Descriptive Summary of EORTC QLQ-C30 Fatigue by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

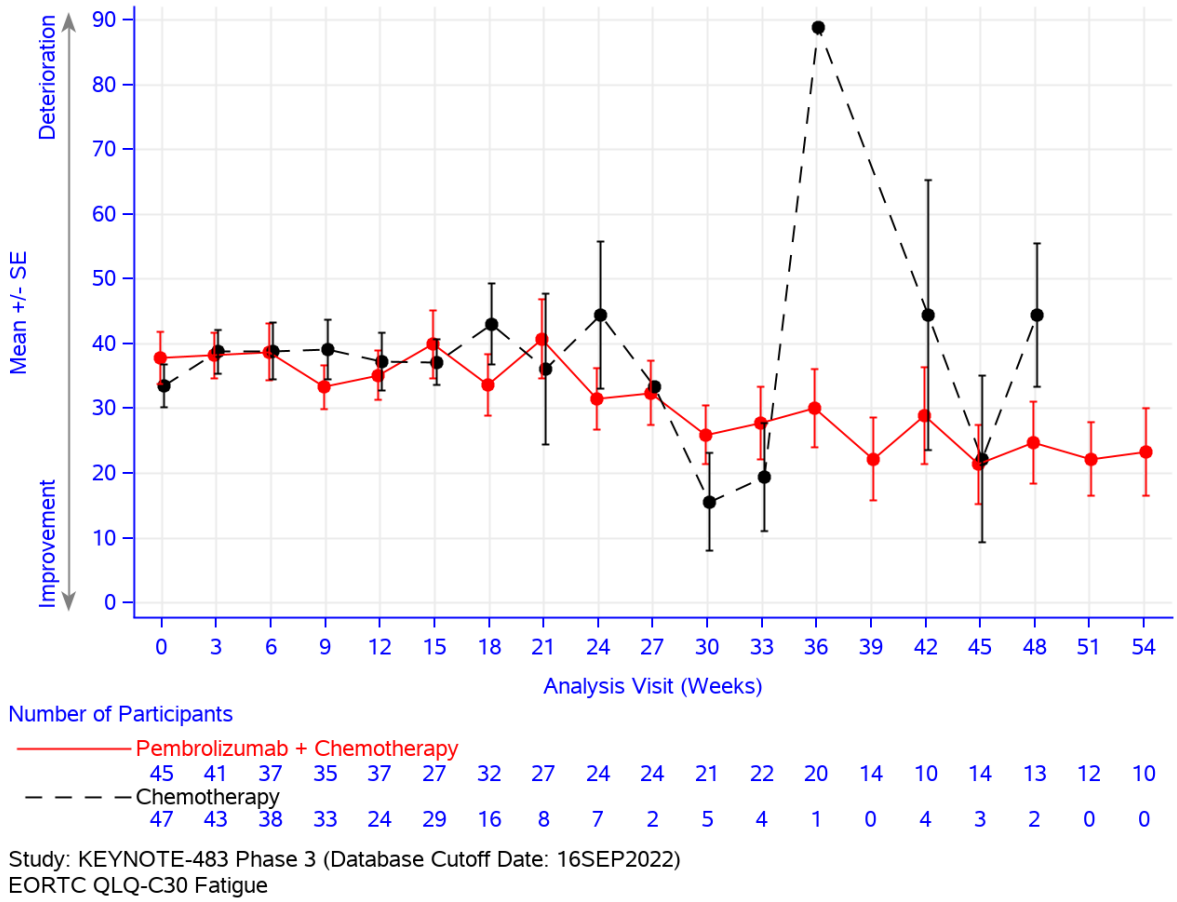
EORTC QLQ-C30 Fatigue	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	31.5 (23.3)	44.4 (30.1)
Median (Q1; Q3)	33.3 (16.7; 33.3)	33.3 (22.2; 66.7)
Min; Max	0.0; 88.9	11.1; 100.0
Week 27		
N[d]	24	2
Mean (SD)	32.4 (24.5)	33.3 (0.0)
Median (Q1; Q3)	33.3 (16.7; 44.4)	33.3 (33.3; 33.3)
Min; Max	0.0; 77.8	33.3; 33.3
Week 30		
N[d]	21	5
Mean (SD)	25.9 (20.9)	15.6 (16.9)
Median (Q1; Q3)	22.2 (11.1; 33.3)	11.1 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 33		
N[d]	22	4
Mean (SD)	27.8 (26.1)	19.4 (16.7)
Median (Q1; Q3)	27.8 (0.0; 33.3)	22.2 (5.6; 33.3)
Min; Max	0.0; 88.9	0.0; 33.3
Week 36		
N[d]	20	1
Mean (SD)	30.0 (27.0)	88.9 (-)
Median (Q1; Q3)	33.3 (0.0; 44.4)	88.9 (88.9; 88.9)
Min; Max	0.0; 88.9	88.9; 88.9
Week 39		
N[d]	14	0
Mean (SD)	22.2 (23.9)	- (-)
Median (Q1; Q3)	22.2 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	28.9 (23.5)	44.4 (41.6)
Median (Q1; Q3)	27.8 (11.1; 33.3)	38.9 (16.7; 72.2)
Min; Max	0.0; 66.7	0.0; 100.0
Week 45		
N[d]	14	3
Mean (SD)	21.4 (22.8)	22.2 (22.2)
Median (Q1; Q3)	22.2 (0.0; 33.3)	22.2 (0.0; 44.4)
Min; Max	0.0; 66.7	0.0; 44.4

Descriptive Summary of EORTC QLQ-C30 Fatigue by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Fatigue	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	24.8 (22.8)	44.4 (15.7)
Median (Q1; Q3)	33.3 (0.0; 33.3)	44.4 (33.3; 55.6)
Min; Max	0.0; 66.7	33.3; 55.6
Week 51		
N[d]	12	0
Mean (SD)	22.2 (19.5)	- (-)
Median (Q1; Q3)	27.8 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 55.6	-; -
Week 54		
N[d]	10	0
Mean (SD)	23.3 (21.2)	- (-)
Median (Q1; Q3)	27.8 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-1
Empirical Mean +/- SE of EORTC QLQ-C30 Fatigue Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Fatigue

4.1.1.2 Nausea and Vomiting

Table 4.2-2
Descriptive Summary of EORTC QLQ-C30 Nausea and Vomiting by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Nausea and Vomiting	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	46
Mean (SD)	6.7 (12.5)	3.6 (7.8)
Median (Q1; Q3)	0.0 (0.0; 16.7)	0.0 (0.0; 0.0)
Min; Max	0.0; 50.0	0.0; 33.3
Week 3		
N[d]	41	43
Mean (SD)	8.5 (13.5)	7.0 (9.8)
Median (Q1; Q3)	0.0 (0.0; 16.7)	0.0 (0.0; 16.7)
Min; Max	0.0; 50.0	0.0; 33.3
Week 6		
N[d]	37	38
Mean (SD)	9.5 (13.9)	9.6 (13.2)
Median (Q1; Q3)	0.0 (0.0; 16.7)	0.0 (0.0; 16.7)
Min; Max	0.0; 33.3	0.0; 50.0
Week 9		
N[d]	35	33
Mean (SD)	9.5 (14.2)	15.2 (20.1)
Median (Q1; Q3)	0.0 (0.0; 16.7)	16.7 (0.0; 16.7)
Min; Max	0.0; 50.0	0.0; 83.3
Week 12		
N[d]	37	24
Mean (SD)	12.2 (11.6)	15.3 (12.0)
Median (Q1; Q3)	16.7 (0.0; 16.7)	16.7 (0.0; 16.7)
Min; Max	0.0; 33.3	0.0; 33.3
Week 15		
N[d]	27	29
Mean (SD)	16.0 (18.2)	12.6 (18.2)
Median (Q1; Q3)	16.7 (0.0; 16.7)	0.0 (0.0; 16.7)
Min; Max	0.0; 66.7	0.0; 66.7
Week 18		
N[d]	32	16
Mean (SD)	12.0 (22.5)	11.5 (19.0)
Median (Q1; Q3)	0.0 (0.0; 16.7)	0.0 (0.0; 16.7)
Min; Max	0.0; 100.0	0.0; 66.7
Week 21		
N[d]	27	8
Mean (SD)	11.7 (16.5)	10.4 (12.4)
Median (Q1; Q3)	0.0 (0.0; 16.7)	8.3 (0.0; 16.7)
Min; Max	0.0; 50.0	0.0; 33.3

Descriptive Summary of EORTC QLQ-C30 Nausea and Vomiting by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Nausea and Vomiting	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	2.1 (5.6)	11.9 (24.9)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 16.7)
Min; Max	0.0; 16.7	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	2.8 (8.0)	16.7 (23.6)
Median (Q1; Q3)	0.0 (0.0; 0.0)	16.7 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 30		
N[d]	21	5
Mean (SD)	0.8 (3.6)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 16.7	0.0; 0.0
Week 33		
N[d]	22	4
Mean (SD)	3.0 (6.6)	8.3 (9.6)
Median (Q1; Q3)	0.0 (0.0; 0.0)	8.3 (0.0; 16.7)
Min; Max	0.0; 16.7	0.0; 16.7
Week 36		
N[d]	20	1
Mean (SD)	3.3 (11.6)	0.0 (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 50.0	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	0.0 (0.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 0.0	-; -
Week 42		
N[d]	10	4
Mean (SD)	3.3 (10.5)	4.2 (8.3)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 8.3)
Min; Max	0.0; 33.3	0.0; 16.7
Week 45		
N[d]	14	3
Mean (SD)	1.2 (4.5)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 16.7	0.0; 0.0

Descriptive Summary of EORTC QLQ-C30 Nausea and Vomiting by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Nausea and Vomiting	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	2.6 (9.2)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 51		
N[d]	12	0
Mean (SD)	0.0 (0.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 0.0	-; -
Week 54		
N[d]	10	0
Mean (SD)	0.0 (0.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 0.0	-; -

a: Database Cutoff Date: 16SEP2022

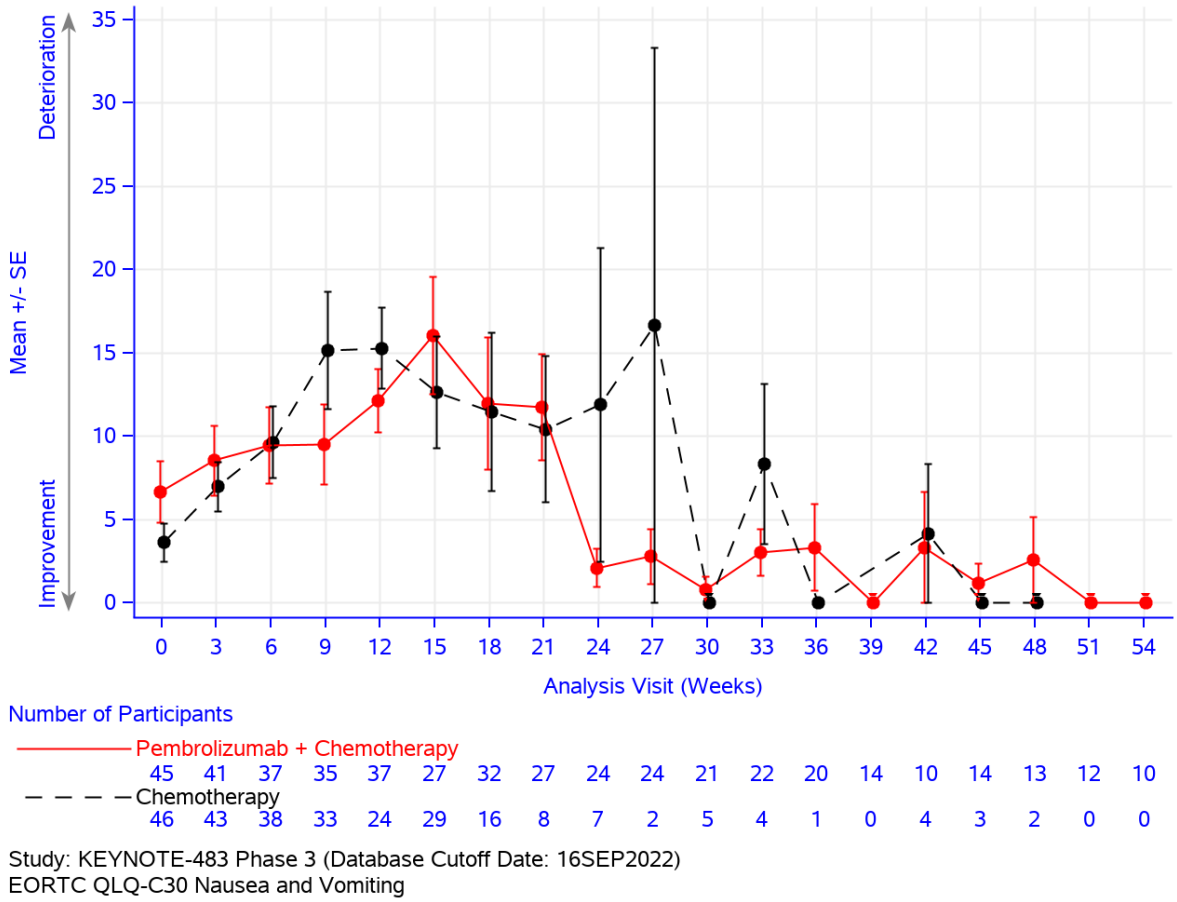
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-2
Empirical Mean +/- SE of EORTC QLQ-C30 Nausea and Vomiting Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Nausea and Vomiting

4.1.1.3 Pain

Table 4.2-3
Descriptive Summary of EORTC QLQ-C30 Pain by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Pain	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	32.2 (31.7)	38.7 (26.9)
Median (Q1; Q3)	16.7 (0.0; 66.7)	33.3 (16.7; 50.0)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	21.5 (21.5)	32.9 (25.3)
Median (Q1; Q3)	16.7 (0.0; 33.3)	33.3 (16.7; 50.0)
Min; Max	0.0; 83.3	0.0; 100.0
Week 6		
N[d]	37	38
Mean (SD)	22.5 (24.3)	36.4 (32.2)
Median (Q1; Q3)	16.7 (0.0; 33.3)	25.0 (16.7; 66.7)
Min; Max	0.0; 100.0	0.0; 100.0
Week 9		
N[d]	35	33
Mean (SD)	16.7 (20.2)	33.3 (27.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (16.7; 50.0)
Min; Max	0.0; 66.7	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	22.1 (22.2)	28.5 (27.1)
Median (Q1; Q3)	16.7 (0.0; 33.3)	25.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 83.3
Week 15		
N[d]	27	29
Mean (SD)	29.6 (31.8)	31.0 (27.0)
Median (Q1; Q3)	16.7 (0.0; 50.0)	33.3 (16.7; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 18		
N[d]	32	16
Mean (SD)	30.2 (29.2)	41.7 (23.6)
Median (Q1; Q3)	25.0 (0.0; 50.0)	33.3 (25.0; 66.7)
Min; Max	0.0; 100.0	0.0; 83.3
Week 21		
N[d]	27	8
Mean (SD)	30.2 (27.4)	25.0 (17.8)
Median (Q1; Q3)	16.7 (0.0; 50.0)	16.7 (16.7; 41.7)
Min; Max	0.0; 100.0	0.0; 50.0

Descriptive Summary of EORTC QLQ-C30 Pain by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Pain	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	31.3 (23.7)	40.5 (34.5)
Median (Q1; Q3)	33.3 (16.7; 50.0)	33.3 (16.7; 66.7)
Min; Max	0.0; 66.7	0.0; 100.0
Week 27		
N[d]	24	2
Mean (SD)	27.1 (26.8)	41.7 (11.8)
Median (Q1; Q3)	16.7 (0.0; 41.7)	41.7 (33.3; 50.0)
Min; Max	0.0; 83.3	33.3; 50.0
Week 30		
N[d]	21	5
Mean (SD)	27.0 (25.0)	20.0 (21.7)
Median (Q1; Q3)	16.7 (16.7; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 50.0
Week 33		
N[d]	22	4
Mean (SD)	28.8 (30.9)	25.0 (16.7)
Median (Q1; Q3)	16.7 (0.0; 33.3)	16.7 (16.7; 33.3)
Min; Max	0.0; 100.0	16.7; 50.0
Week 36		
N[d]	20	1
Mean (SD)	26.7 (24.4)	83.3 (-)
Median (Q1; Q3)	25.0 (0.0; 41.7)	83.3 (83.3; 83.3)
Min; Max	0.0; 83.3	83.3; 83.3
Week 39		
N[d]	14	0
Mean (SD)	28.6 (30.3)	- (-)
Median (Q1; Q3)	33.3 (0.0; 50.0)	- (-; -)
Min; Max	0.0; 83.3	-; -
Week 42		
N[d]	10	4
Mean (SD)	33.3 (30.4)	41.7 (34.7)
Median (Q1; Q3)	33.3 (16.7; 33.3)	41.7 (16.7; 66.7)
Min; Max	0.0; 100.0	0.0; 83.3
Week 45		
N[d]	14	3
Mean (SD)	26.2 (24.2)	16.7 (0.0)
Median (Q1; Q3)	33.3 (0.0; 33.3)	16.7 (16.7; 16.7)
Min; Max	0.0; 66.7	16.7; 16.7

Descriptive Summary of EORTC QLQ-C30 Pain by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Pain	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	**Chemotherapy[b]** N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	17.9 (17.3)	50.0 (23.6)
Median (Q1; Q3)	16.7 (0.0; 33.3)	50.0 (33.3; 66.7)
Min; Max	0.0; 50.0	33.3; 66.7
Week 51		
N[d]	12	0
Mean (SD)	25.0 (19.5)	- (-)
Median (Q1; Q3)	33.3 (8.3; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	26.7 (17.9)	- (-)
Median (Q1; Q3)	33.3 (16.7; 33.3)	- (-; -)
Min; Max	0.0; 50.0	-; -

a: Database Cutoff Date: 16SEP2022

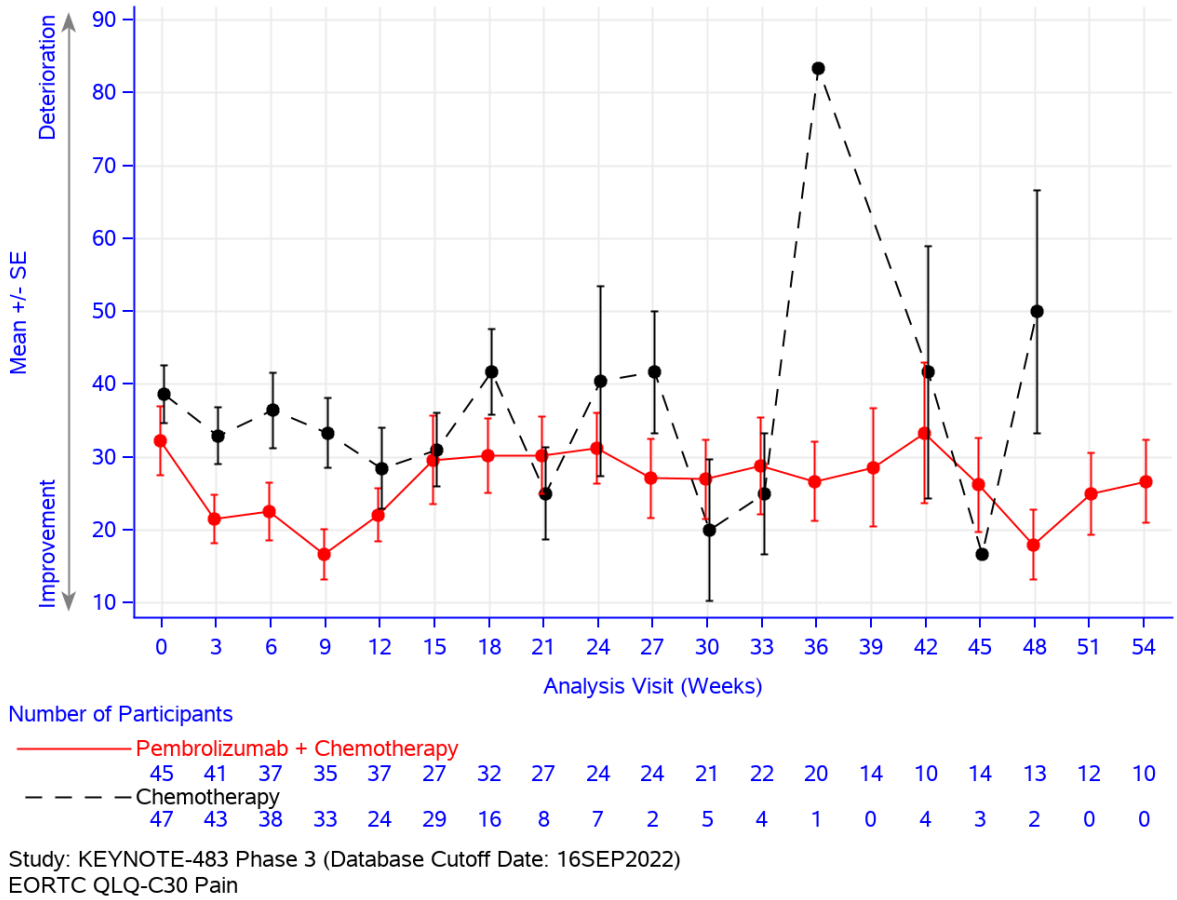
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-3
Empirical Mean +/- SE of EORTC QLQ-C30 Pain Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Pain

4.1.1.4 Dyspnoea

Table 4.2-4
Descriptive Summary of EORTC QLQ-C30 Dyspnoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Dyspnoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	41.5 (33.5)	31.2 (28.2)
Median (Q1; Q3)	33.3 (33.3; 66.7)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	30.9 (30.2)	27.9 (29.0)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 6		
N[d]	37	37
Mean (SD)	27.9 (22.9)	31.5 (31.4)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 9		
N[d]	35	33
Mean (SD)	32.4 (24.9)	34.3 (30.6)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 12		
N[d]	37	23
Mean (SD)	30.6 (27.6)	31.9 (23.5)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 15		
N[d]	27	29
Mean (SD)	28.4 (31.6)	33.3 (28.2)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 66.7)
Min; Max	0.0; 100.0	0.0; 100.0
Week 18		
N[d]	32	16
Mean (SD)	24.0 (29.6)	31.3 (33.3)
Median (Q1; Q3)	16.7 (0.0; 33.3)	33.3 (0.0; 66.7)
Min; Max	0.0; 100.0	0.0; 100.0
Week 21		
N[d]	27	8
Mean (SD)	35.8 (27.6)	45.8 (35.4)
Median (Q1; Q3)	33.3 (0.0; 66.7)	33.3 (33.3; 66.7)
Min; Max	0.0; 100.0	0.0; 100.0

Descriptive Summary of EORTC QLQ-C30 Dyspnoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Dyspnoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	29.2 (20.4)	38.1 (35.6)
Median (Q1; Q3)	33.3 (16.7; 33.3)	33.3 (0.0; 66.7)
Min; Max	0.0; 66.7	0.0; 100.0
Week 27		
N[d]	24	2
Mean (SD)	29.2 (22.7)	33.3 (0.0)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (33.3; 33.3)
Min; Max	0.0; 66.7	33.3; 33.3
Week 30		
N[d]	21	5
Mean (SD)	28.6 (19.1)	13.3 (18.3)
Median (Q1; Q3)	33.3 (33.3; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 33		
N[d]	22	4
Mean (SD)	30.3 (25.0)	33.3 (27.2)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (16.7; 50.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 36		
N[d]	20	1
Mean (SD)	28.3 (27.1)	66.7 (-)
Median (Q1; Q3)	33.3 (0.0; 33.3)	66.7 (66.7; 66.7)
Min; Max	0.0; 100.0	66.7; 66.7
Week 39		
N[d]	14	0
Mean (SD)	19.0 (21.5)	- (-)
Median (Q1; Q3)	16.7 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	26.7 (21.1)	25.0 (16.7)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (16.7; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 45		
N[d]	14	2
Mean (SD)	28.6 (22.1)	16.7 (23.6)
Median (Q1; Q3)	33.3 (0.0; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3

Descriptive Summary of EORTC QLQ-C30 Dyspnoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Dyspnoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	28.2 (26.7)	83.3 (23.6)
Median (Q1; Q3)	33.3 (0.0; 33.3)	83.3 (66.7; 100.0)
Min; Max	0.0; 66.7	66.7; 100.0
Week 51		
N[d]	12	0
Mean (SD)	30.6 (17.2)	- (-)
Median (Q1; Q3)	33.3 (33.3; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	30.0 (24.6)	- (-)
Median (Q1; Q3)	33.3 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

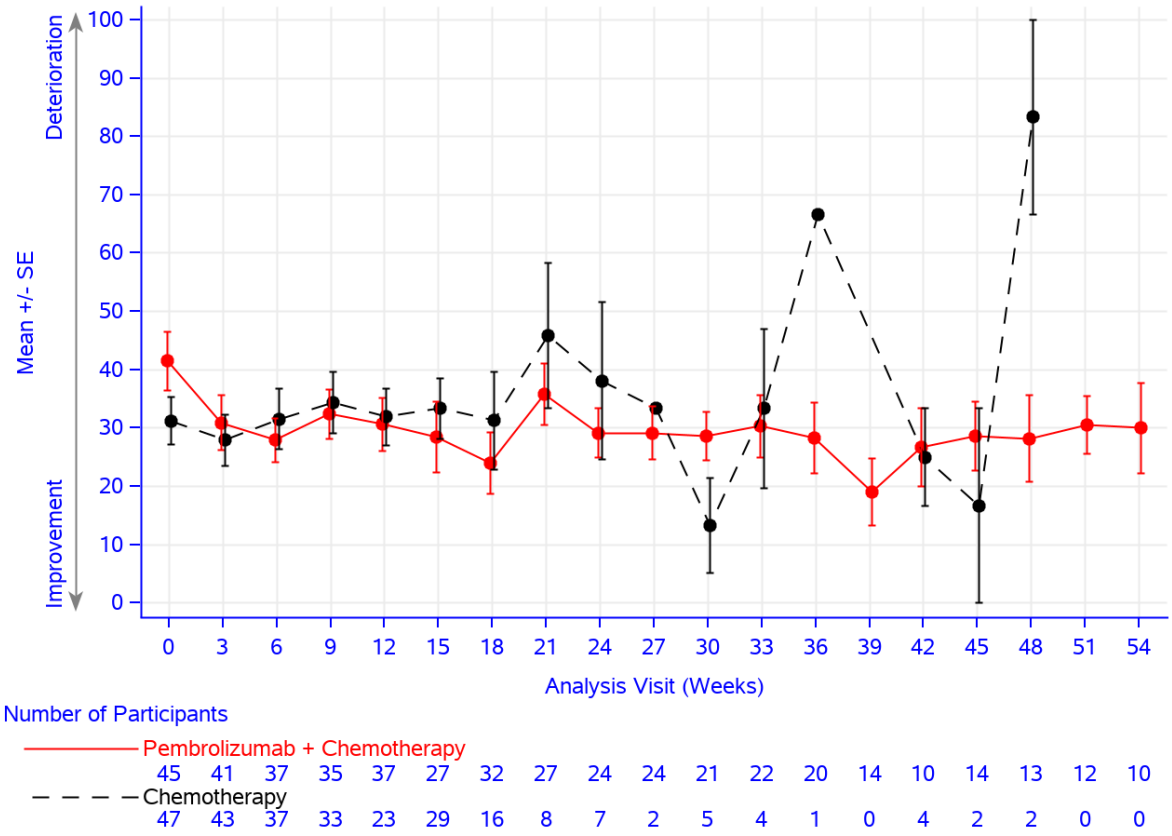
c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-4

Empirical Mean +/- SE of EORTC QLQ-C30 Dyspnoea Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Dyspnoea

4.1.1.5 Insomnia

Table 4.2-5
Descriptive Summary of EORTC QLQ-C30 Insomnia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Insomnia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	35.6 (35.1)	35.5 (31.4)
Median (Q1; Q3)	33.3 (0.0; 66.7)	33.3 (0.0; 66.7)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	32.5 (32.9)	23.3 (28.7)
Median (Q1; Q3)	33.3 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 6		
N[d]	37	38
Mean (SD)	23.4 (29.3)	35.1 (36.3)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 66.7)
Min; Max	0.0; 100.0	0.0; 100.0
Week 9		
N[d]	35	33
Mean (SD)	22.9 (25.3)	24.2 (30.4)
Median (Q1; Q3)	33.3 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	26.1 (31.6)	20.8 (23.7)
Median (Q1; Q3)	0.0 (0.0; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 15		
N[d]	27	29
Mean (SD)	22.2 (26.1)	19.5 (22.7)
Median (Q1; Q3)	33.3 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 18		
N[d]	32	16
Mean (SD)	24.0 (31.9)	22.9 (23.5)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 21		
N[d]	27	8
Mean (SD)	22.2 (24.5)	33.3 (39.8)
Median (Q1; Q3)	33.3 (0.0; 33.3)	16.7 (0.0; 66.7)
Min; Max	0.0; 66.7	0.0; 100.0

Descriptive Summary of EORTC QLQ-C30 Insomnia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

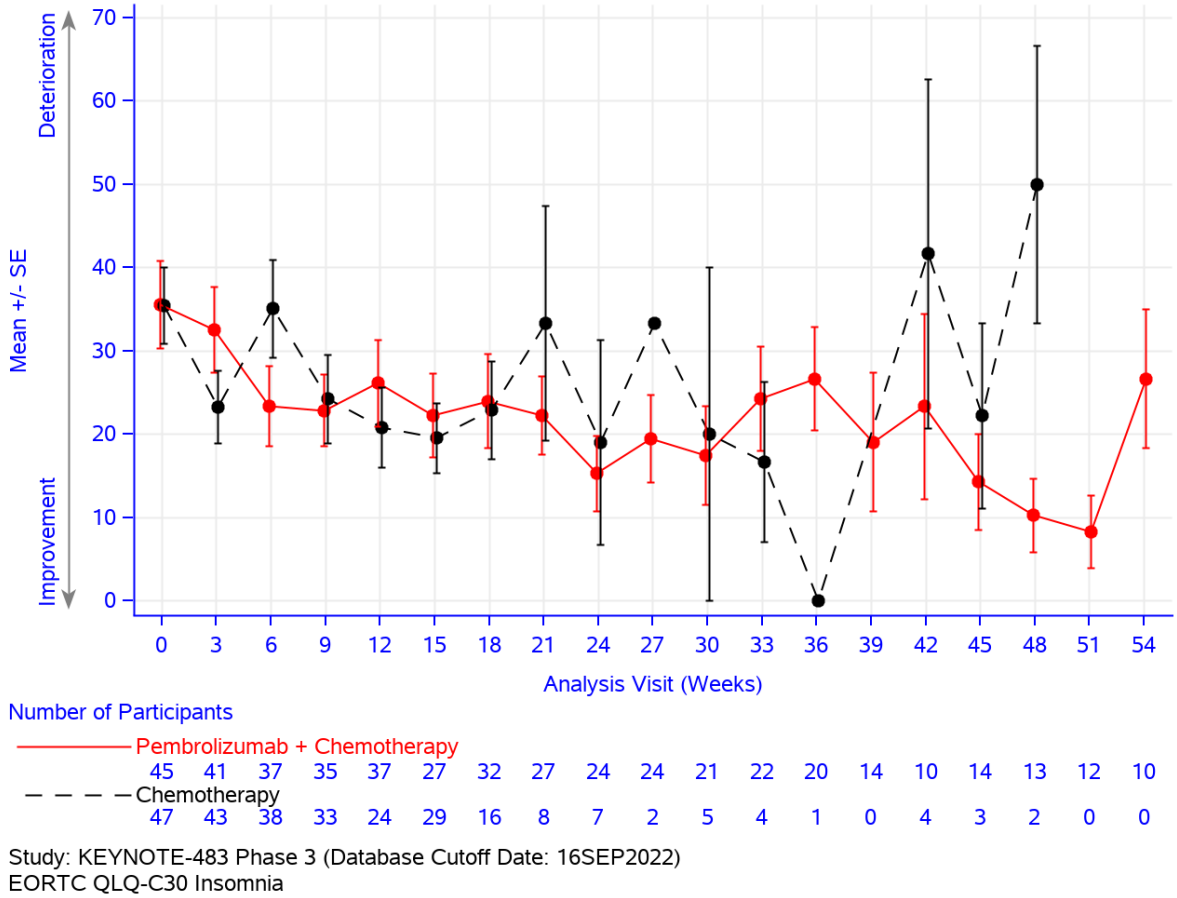
EORTC QLQ-C30 Insomnia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	15.3 (21.9)	19.0 (32.5)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 66.7)
Min; Max	0.0; 66.7	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	19.4 (25.9)	33.3 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (33.3; 33.3)
Min; Max	0.0; 100.0	33.3; 33.3
Week 30		
N[d]	21	5
Mean (SD)	17.5 (27.1)	20.0 (44.7)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 100.0
Week 33		
N[d]	22	4
Mean (SD)	24.2 (29.4)	16.7 (19.2)
Median (Q1; Q3)	16.7 (0.0; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 33.3
Week 36		
N[d]	20	1
Mean (SD)	26.7 (27.8)	0.0 (-)
Median (Q1; Q3)	33.3 (0.0; 50.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	19.0 (31.3)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 100.0	-; -
Week 42		
N[d]	10	4
Mean (SD)	23.3 (35.3)	41.7 (41.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (16.7; 66.7)
Min; Max	0.0; 100.0	0.0; 100.0
Week 45		
N[d]	14	3
Mean (SD)	14.3 (21.5)	22.2 (19.2)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3

Descriptive Summary of EORTC QLQ-C30 Insomnia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Insomnia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	10.3 (16.0)	50.0 (23.6)
Median (Q1; Q3)	0.0 (0.0; 33.3)	50.0 (33.3; 66.7)
Min; Max	0.0; 33.3	33.3; 66.7
Week 51		
N[d]	12	0
Mean (SD)	8.3 (15.1)	- (-)
Median (Q1; Q3)	0.0 (0.0; 16.7)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 54		
N[d]	10	0
Mean (SD)	26.7 (26.3)	- (-)
Median (Q1; Q3)	33.3 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-5
Empirical Mean +/- SE of EORTC QLQ-C30 Insomnia Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Insomnia

4.1.1.6 Appetite Loss

Table 4.2-6
Descriptive Summary of EORTC QLQ-C30 Appetite Loss by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Appetite Loss	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	46
Mean (SD)	26.7 (29.8)	15.9 (23.0)
Median (Q1; Q3)	33.3 (0.0; 66.7)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 3		
N[d]	41	43
Mean (SD)	19.5 (26.8)	17.1 (22.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 6		
N[d]	37	38
Mean (SD)	22.5 (29.5)	19.3 (22.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 9		
N[d]	35	32
Mean (SD)	20.0 (25.8)	24.0 (31.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	20.7 (28.7)	16.7 (22.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 15		
N[d]	27	29
Mean (SD)	24.7 (31.5)	19.5 (32.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 18		
N[d]	32	16
Mean (SD)	24.0 (34.1)	18.8 (27.1)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 21		
N[d]	27	8
Mean (SD)	25.9 (33.8)	16.7 (25.2)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7

Descriptive Summary of EORTC QLQ-C30 Appetite Loss by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Appetite Loss	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	9.7 (15.5)	28.6 (30.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 66.7)
Min; Max	0.0; 33.3	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	11.1 (18.8)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 30		
N[d]	21	5
Mean (SD)	4.8 (12.0)	6.7 (14.9)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 33.3
Week 33		
N[d]	22	4
Mean (SD)	9.1 (18.3)	8.3 (16.7)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 16.7)
Min; Max	0.0; 66.7	0.0; 33.3
Week 36		
N[d]	20	1
Mean (SD)	5.0 (12.2)	100.0 (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	100.0 (100.0; 100.0)
Min; Max	0.0; 33.3	100.0; 100.0
Week 39		
N[d]	14	0
Mean (SD)	7.1 (19.3)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	13.3 (23.3)	33.3 (47.1)
Median (Q1; Q3)	0.0 (0.0; 33.3)	16.7 (0.0; 66.7)
Min; Max	0.0; 66.7	0.0; 100.0
Week 45		
N[d]	14	3
Mean (SD)	9.5 (20.4)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0

Descriptive Summary of EORTC QLQ-C30 Appetite Loss by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Appetite Loss	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	7.7 (14.6)	16.7 (23.6)
Median (Q1; Q3)	0.0 (0.0; 0.0)	16.7 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 51		
N[d]	12	0
Mean (SD)	11.1 (21.7)	- (-)
Median (Q1; Q3)	0.0 (0.0; 16.7)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	3.3 (10.5)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -

a: Database Cutoff Date: 16SEP2022

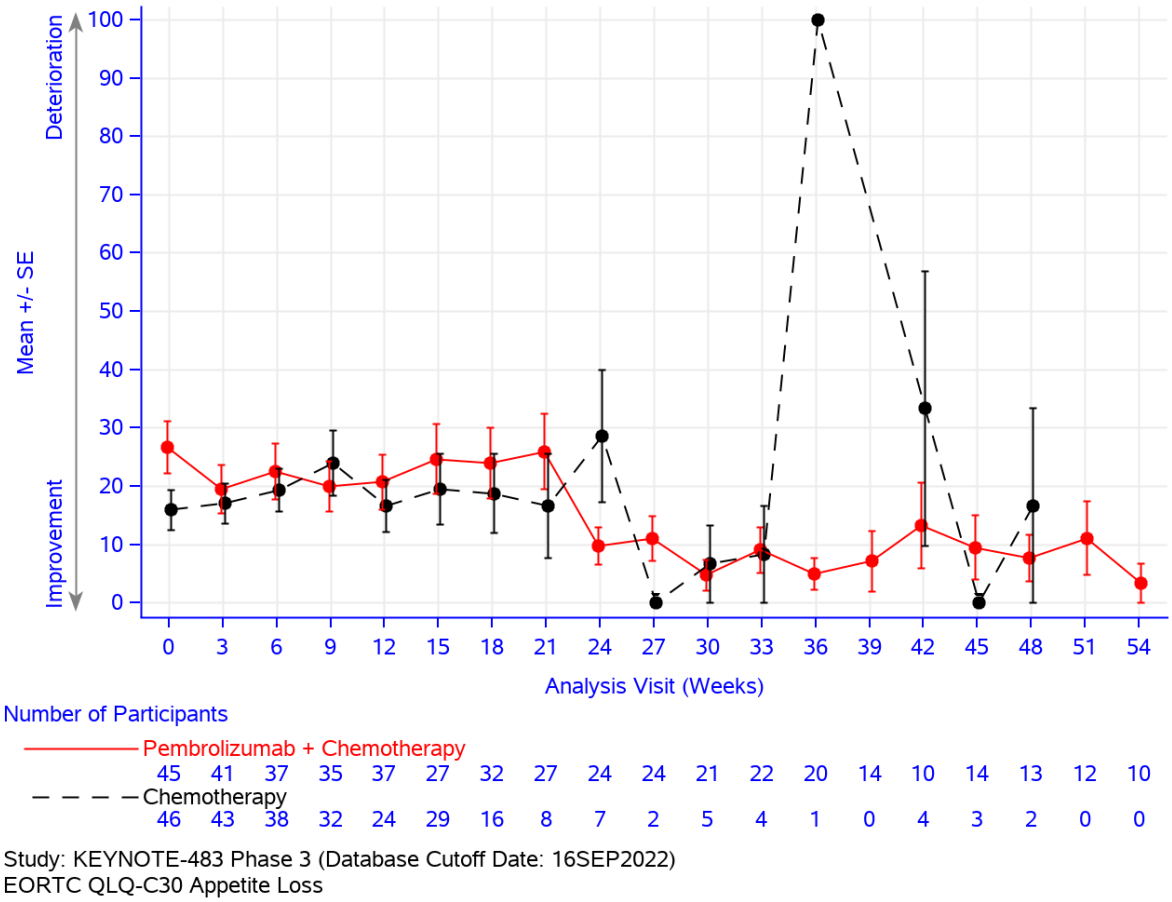
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-6
Empirical Mean +/- SE of EORTC QLQ-C30 Appetite Loss Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Appetite Loss

4.1.1.7 Constipation

Table 4.2-7
Descriptive Summary of EORTC QLQ-C30 Constipation by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Constipation	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	46
Mean (SD)	27.4 (34.3)	23.2 (31.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	33.3 (30.7)	23.3 (28.7)
Median (Q1; Q3)	33.3 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 6		
N[d]	37	38
Mean (SD)	21.6 (23.9)	28.1 (26.3)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 9		
N[d]	35	33
Mean (SD)	21.0 (26.9)	26.3 (27.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	23.4 (25.9)	22.2 (25.4)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 15		
N[d]	27	29
Mean (SD)	14.8 (23.3)	19.5 (24.4)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 18		
N[d]	32	15
Mean (SD)	26.0 (30.2)	17.8 (21.3)
Median (Q1; Q3)	33.3 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 21		
N[d]	27	8
Mean (SD)	19.8 (26.6)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 0.0

Descriptive Summary of EORTC QLQ-C30 Constipation by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Constipation	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	12.5 (19.2)	19.0 (26.2)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	15.3 (21.9)	16.7 (23.6)
Median (Q1; Q3)	0.0 (0.0; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 30		
N[d]	21	5
Mean (SD)	17.5 (22.7)	13.3 (18.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 33		
N[d]	22	4
Mean (SD)	10.6 (18.9)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 36		
N[d]	20	1
Mean (SD)	13.3 (22.7)	100.0 (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	100.0 (100.0; 100.0)
Min; Max	0.0; 66.7	100.0; 100.0
Week 39		
N[d]	14	0
Mean (SD)	11.9 (21.1)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	6.7 (21.1)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 45		
N[d]	14	3
Mean (SD)	9.5 (20.4)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0

Descriptive Summary of EORTC QLQ-C30 Constipation by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Constipation	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	5.1 (12.5)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 51		
N[d]	12	0
Mean (SD)	11.1 (21.7)	- (-)
Median (Q1; Q3)	0.0 (0.0; 16.7)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	10.0 (22.5)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 66.7	-; -

a: Database Cutoff Date: 16SEP2022

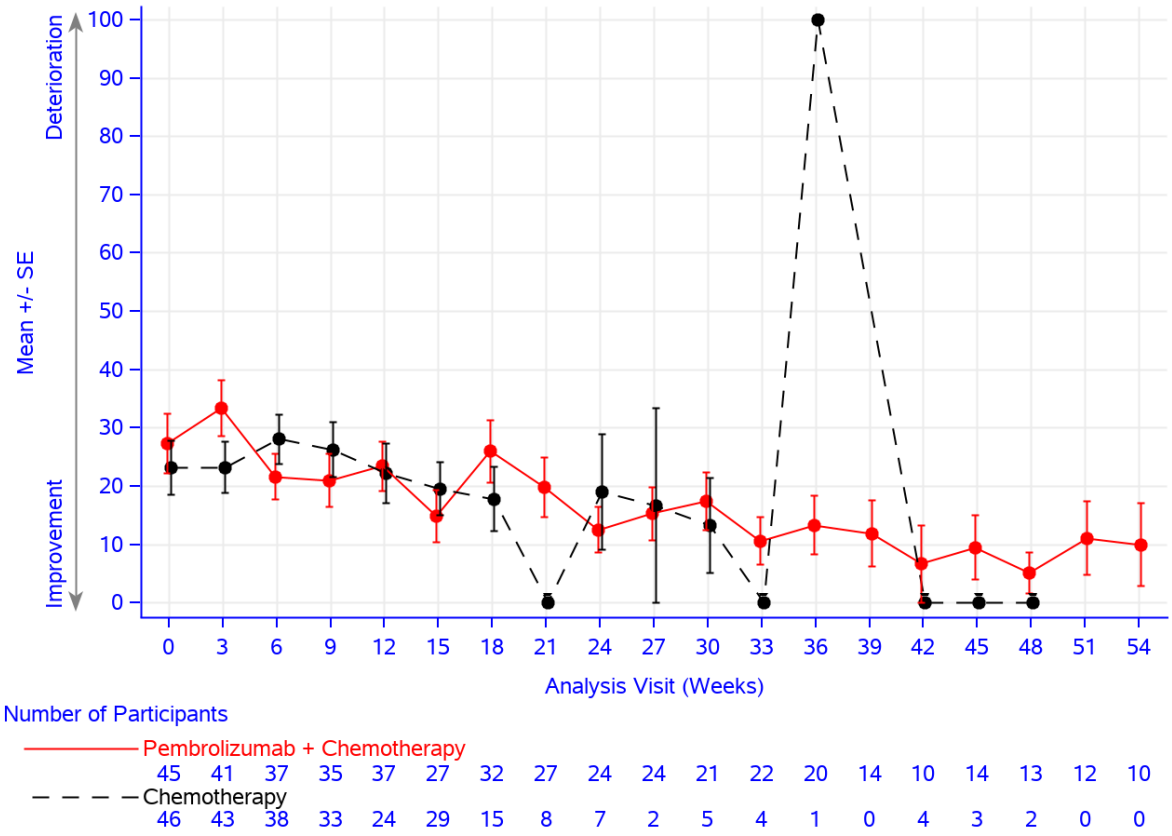
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-7
Empirical Mean +/- SE of EORTC QLQ-C30 Constipation Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Constipation

4.1.1.8 Diarrhoea

Table 4.2-8
Descriptive Summary of EORTC QLQ-C30 Diarrhoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Diarrhoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	46
Mean (SD)	4.4 (13.5)	1.4 (6.9)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 33.3
Week 3		
N[d]	41	43
Mean (SD)	4.9 (17.6)	5.4 (17.7)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 6		
N[d]	37	38
Mean (SD)	3.6 (10.5)	2.6 (9.1)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 33.3
Week 9		
N[d]	35	33
Mean (SD)	0.0 (0.0)	4.0 (11.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 33.3
Week 12		
N[d]	37	24
Mean (SD)	4.5 (17.9)	2.8 (9.4)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 33.3
Week 15		
N[d]	27	29
Mean (SD)	6.2 (16.1)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 18		
N[d]	32	15
Mean (SD)	3.1 (9.9)	2.2 (8.6)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 33.3
Week 21		
N[d]	27	8
Mean (SD)	3.7 (10.7)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0

Descriptive Summary of EORTC QLQ-C30 Diarrhoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Diarrhoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	5.6 (12.7)	19.0 (17.8)
Median (Q1; Q3)	0.0 (0.0; 0.0)	33.3 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 27		
N[d]	24	2
Mean (SD)	5.6 (16.1)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 30		
N[d]	21	5
Mean (SD)	7.9 (18.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 33		
N[d]	22	4
Mean (SD)	6.1 (16.7)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 36		
N[d]	20	1
Mean (SD)	1.7 (7.5)	0.0 (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	2.4 (8.9)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 42		
N[d]	10	4
Mean (SD)	6.7 (21.1)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 45		
N[d]	14	3
Mean (SD)	4.8 (17.8)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0

Descriptive Summary of EORTC QLQ-C30 Diarrhoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Diarrhoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	2.6 (9.2)	16.7 (23.6)
Median (Q1; Q3)	0.0 (0.0; 0.0)	16.7 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 51		
N[d]	12	0
Mean (SD)	5.6 (13.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 54		
N[d]	10	0
Mean (SD)	3.3 (10.5)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -

a: Database Cutoff Date: 16SEP2022

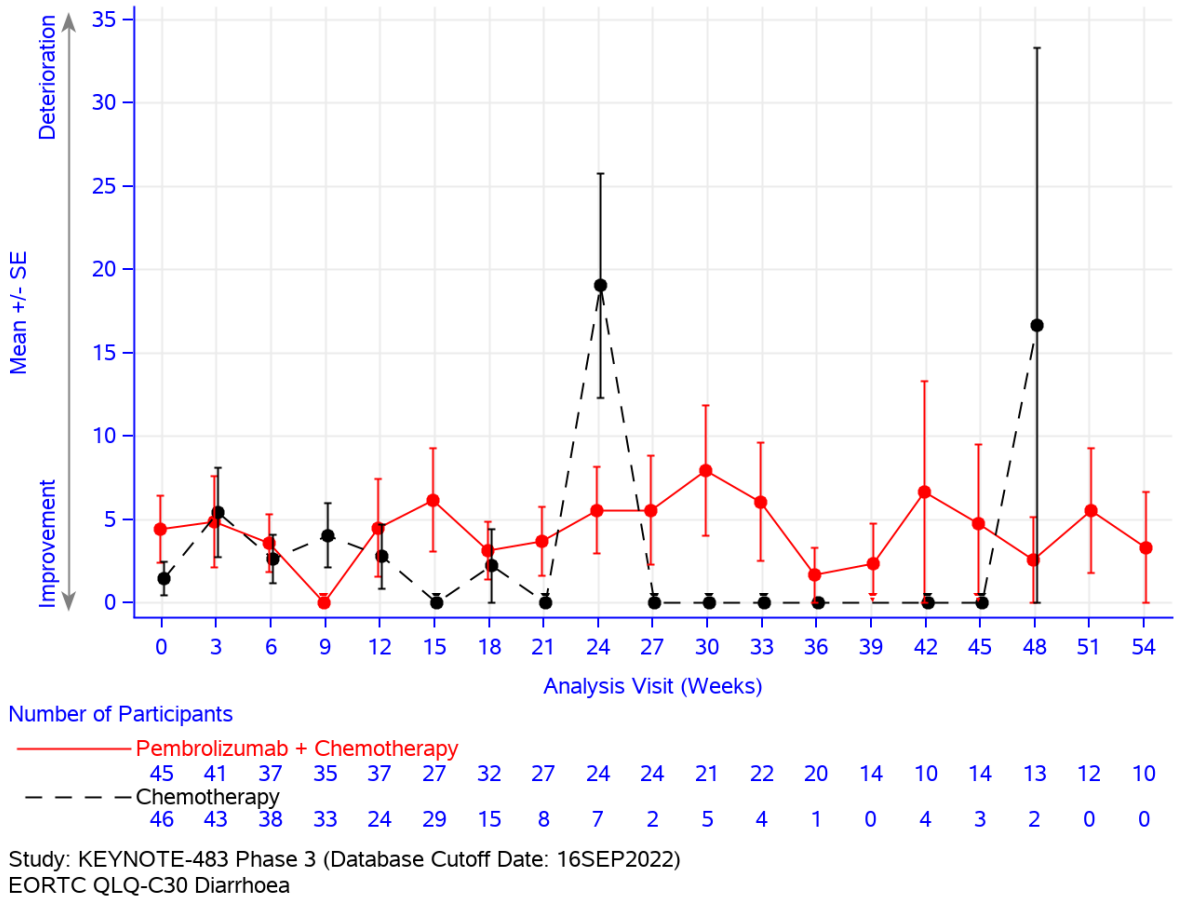
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-8
Empirical Mean +/- SE of EORTC QLQ-C30 Diarrhoea Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Diarrhoea

Anhang 4-G2.2: EORTC QLQ-LC13

4.1.1.9 Dyspnoea

Table 4.2-9
Descriptive Summary of EORTC QLQ-LC13 Dyspnoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Dyspnoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	27.9 (24.0)	25.3 (19.8)
Median (Q1; Q3)	22.2 (11.1; 44.4)	22.2 (11.1; 33.3)
Min; Max	0.0; 77.8	0.0; 77.8
Week 3		
N[d]	41	43
Mean (SD)	26.8 (20.6)	22.0 (16.7)
Median (Q1; Q3)	22.2 (11.1; 33.3)	22.2 (11.1; 33.3)
Min; Max	0.0; 66.7	0.0; 55.6
Week 6		
N[d]	37	38
Mean (SD)	26.1 (18.9)	25.4 (19.7)
Median (Q1; Q3)	22.2 (11.1; 33.3)	22.2 (11.1; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 9		
N[d]	35	33
Mean (SD)	23.2 (17.7)	26.3 (22.4)
Median (Q1; Q3)	22.2 (11.1; 33.3)	22.2 (11.1; 33.3)
Min; Max	0.0; 66.7	0.0; 77.8
Week 12		
N[d]	37	24
Mean (SD)	23.1 (18.6)	27.3 (19.4)
Median (Q1; Q3)	22.2 (11.1; 33.3)	22.2 (11.1; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 15		
N[d]	27	29
Mean (SD)	29.6 (20.0)	28.4 (18.2)
Median (Q1; Q3)	33.3 (11.1; 44.4)	22.2 (11.1; 44.4)
Min; Max	0.0; 66.7	0.0; 77.8
Week 18		
N[d]	32	16
Mean (SD)	24.7 (23.1)	26.4 (29.2)
Median (Q1; Q3)	22.2 (0.0; 33.3)	16.7 (5.6; 38.9)
Min; Max	0.0; 88.9	0.0; 100.0
Week 21		
N[d]	27	8
Mean (SD)	28.4 (23.5)	30.6 (22.8)
Median (Q1; Q3)	33.3 (11.1; 44.4)	22.2 (22.2; 38.9)
Min; Max	0.0; 88.9	0.0; 77.8

Descriptive Summary of EORTC QLQ-LC13 Dyspnoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Dyspnoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	27.3 (17.9)	38.1 (24.7)
Median (Q1; Q3)	22.2 (16.7; 44.4)	33.3 (22.2; 66.7)
Min; Max	0.0; 55.6	11.1; 77.8
Week 27		
N[d]	24	2
Mean (SD)	26.4 (20.1)	27.8 (7.9)
Median (Q1; Q3)	22.2 (11.1; 44.4)	27.8 (22.2; 33.3)
Min; Max	0.0; 66.7	22.2; 33.3
Week 30		
N[d]	21	5
Mean (SD)	21.2 (14.4)	4.4 (9.9)
Median (Q1; Q3)	22.2 (11.1; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 55.6	0.0; 22.2
Week 33		
N[d]	22	4
Mean (SD)	26.8 (21.6)	22.2 (15.7)
Median (Q1; Q3)	22.2 (11.1; 33.3)	16.7 (11.1; 33.3)
Min; Max	0.0; 88.9	11.1; 44.4
Week 36		
N[d]	19	1
Mean (SD)	25.7 (18.9)	55.6 (-)
Median (Q1; Q3)	22.2 (11.1; 33.3)	55.6 (55.6; 55.6)
Min; Max	0.0; 66.7	55.6; 55.6
Week 39		
N[d]	13	0
Mean (SD)	22.2 (18.7)	- (-)
Median (Q1; Q3)	22.2 (11.1; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	23.3 (19.2)	25.0 (16.7)
Median (Q1; Q3)	22.2 (11.1; 33.3)	33.3 (16.7; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 45		
N[d]	14	3
Mean (SD)	21.4 (20.2)	22.2 (22.2)
Median (Q1; Q3)	22.2 (0.0; 22.2)	22.2 (0.0; 44.4)
Min; Max	0.0; 66.7	0.0; 44.4

Descriptive Summary of EORTC QLQ-LC13 Dyspnoea by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Dyspnoea	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	**Chemotherapy[b]** N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	23.1 (17.3)	44.4 (0.0)
Median (Q1; Q3)	22.2 (11.1; 33.3)	44.4 (44.4; 44.4)
Min; Max	0.0; 55.6	44.4; 44.4
Week 51		
N[d]	12	0
Mean (SD)	28.7 (13.8)	- (-)
Median (Q1; Q3)	33.3 (22.2; 38.9)	- (-; -)
Min; Max	0.0; 44.4	-; -
Week 54		
N[d]	10	0
Mean (SD)	27.8 (16.8)	- (-)
Median (Q1; Q3)	33.3 (11.1; 33.3)	- (-; -)
Min; Max	0.0; 55.6	-; -

a: Database Cutoff Date: 16SEP2022

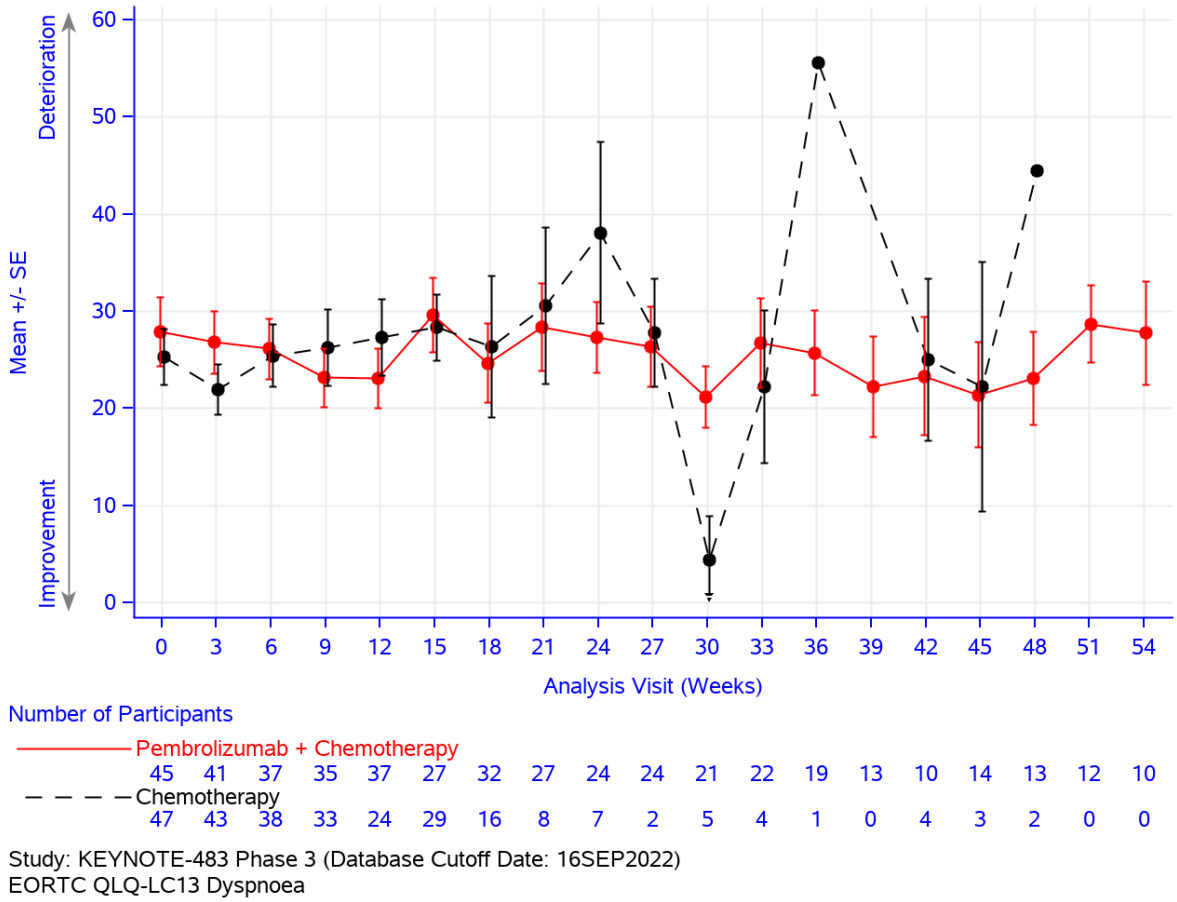
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-9
Empirical Mean +/- SE of EORTC QLQ-LC13 Dyspnoea Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Dyspnoea

4.1.1.10 Coughing

Table 4.2-10
Descriptive Summary of EORTC QLQ-LC13 Coughing by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Coughing	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	20.0 (24.0)	22.0 (24.4)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	24.4 (25.8)	20.2 (22.0)
Median (Q1; Q3)	33.3 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 6		
N[d]	37	38
Mean (SD)	18.9 (18.5)	17.5 (20.1)
Median (Q1; Q3)	33.3 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 9		
N[d]	35	32
Mean (SD)	17.1 (20.4)	18.8 (25.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	18.9 (27.8)	26.4 (27.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 50.0)
Min; Max	0.0; 100.0	0.0; 66.7
Week 15		
N[d]	27	29
Mean (SD)	18.5 (23.3)	19.5 (20.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 18		
N[d]	32	16
Mean (SD)	19.8 (22.2)	16.7 (27.2)
Median (Q1; Q3)	16.7 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 21		
N[d]	27	8
Mean (SD)	17.3 (21.4)	33.3 (30.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (16.7; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0

Descriptive Summary of EORTC QLQ-LC13 Coughing by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

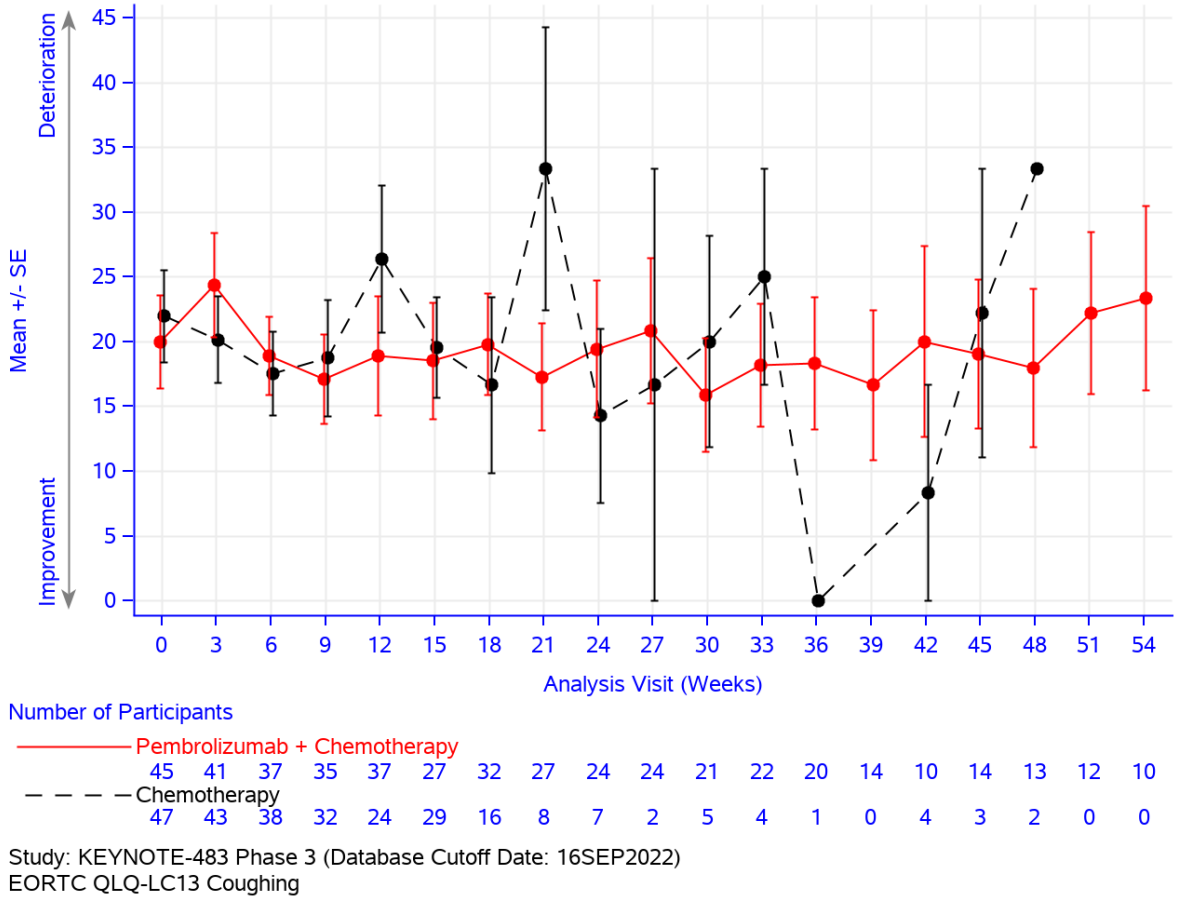
EORTC QLQ-LC13 Coughing	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	19.4 (25.9)	14.3 (17.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 27		
N[d]	24	2
Mean (SD)	20.8 (27.5)	16.7 (23.6)
Median (Q1; Q3)	0.0 (0.0; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 33.3
Week 30		
N[d]	21	5
Mean (SD)	15.9 (20.1)	20.0 (18.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 33		
N[d]	22	4
Mean (SD)	18.2 (22.4)	25.0 (16.7)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (16.7; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 36		
N[d]	20	1
Mean (SD)	18.3 (22.9)	0.0 (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	16.7 (21.7)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	20.0 (23.3)	8.3 (16.7)
Median (Q1; Q3)	16.7 (0.0; 33.3)	0.0 (0.0; 16.7)
Min; Max	0.0; 66.7	0.0; 33.3
Week 45		
N[d]	14	3
Mean (SD)	19.0 (21.5)	22.2 (19.2)
Median (Q1; Q3)	16.7 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3

Descriptive Summary of EORTC QLQ-LC13 Coughing by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Coughing	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	17.9 (22.0)	33.3 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (33.3; 33.3)
Min; Max	0.0; 66.7	33.3; 33.3
Week 51		
N[d]	12	0
Mean (SD)	22.2 (21.7)	- (-)
Median (Q1; Q3)	33.3 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	23.3 (22.5)	- (-)
Median (Q1; Q3)	33.3 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-10
Empirical Mean +/- SE of EORTC QLQ-LC13 Coughing Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Coughing

4.1.1.11 Haemoptysis

Table 4.2-11
Descriptive Summary of EORTC QLQ-LC13 Haemoptysis by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Haemoptysis	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 3		
N[d]	41	43
Mean (SD)	0.8 (5.2)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 6		
N[d]	37	38
Mean (SD)	0.9 (5.5)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 9		
N[d]	35	33
Mean (SD)	1.0 (5.6)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 12		
N[d]	37	24
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 15		
N[d]	27	28
Mean (SD)	1.2 (6.4)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 18		
N[d]	32	16
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 21		
N[d]	27	8
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0

Descriptive Summary of EORTC QLQ-LC13 Haemoptysis by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Haemoptysis	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	1.4 (6.8)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 27		
N[d]	24	2
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 30		
N[d]	21	5
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 33		
N[d]	22	4
Mean (SD)	3.0 (9.8)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 36		
N[d]	20	1
Mean (SD)	1.7 (7.5)	0.0 (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 39		
N[d]	13	0
Mean (SD)	0.0 (0.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 0.0	-; -
Week 42		
N[d]	10	4
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 45		
N[d]	14	3
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0

Descriptive Summary of EORTC QLQ-LC13 Haemoptysis by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Haemoptysis	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	**Chemotherapy[b]** N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 51		
N[d]	12	0
Mean (SD)	0.0 (0.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 0.0	-; -
Week 54		
N[d]	10	0
Mean (SD)	0.0 (0.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 0.0	-; -

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

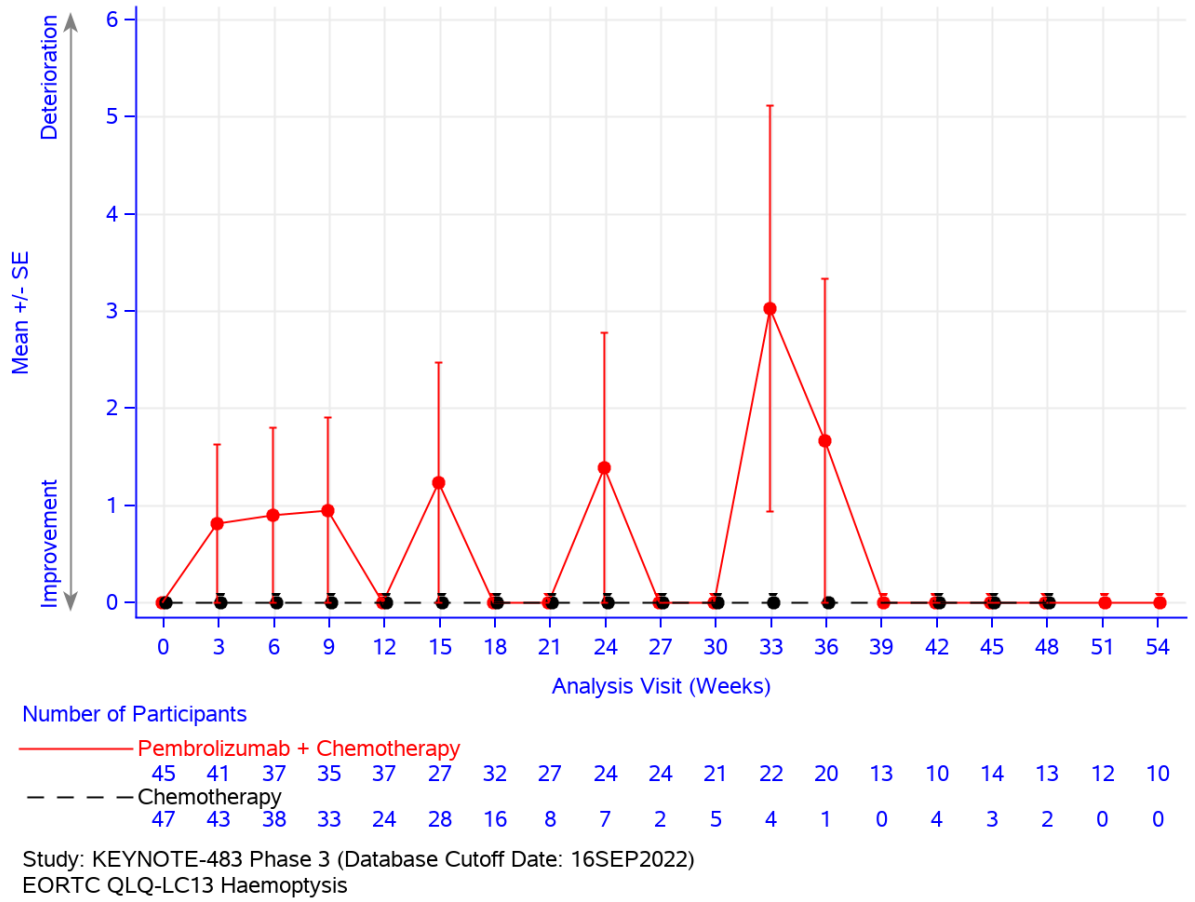
c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-11

Empirical Mean +/- SE of EORTC QLQ-LC13 Haemoptysis Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Haemoptysis

4.1.1.12 Sore Mouth

Table 4.2-12
Descriptive Summary of EORTC QLQ-LC13 Sore Mouth by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Sore Mouth	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	1.5 (6.9)	1.4 (6.8)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 33.3
Week 3		
N[d]	40	43
Mean (SD)	13.3 (28.0)	4.7 (13.8)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 66.7
Week 6		
N[d]	37	38
Mean (SD)	9.0 (20.3)	3.5 (10.4)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 33.3
Week 9		
N[d]	35	33
Mean (SD)	6.7 (15.8)	5.1 (12.1)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 33.3
Week 12		
N[d]	37	24
Mean (SD)	9.0 (20.3)	8.3 (14.7)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 16.7)
Min; Max	0.0; 66.7	0.0; 33.3
Week 15		
N[d]	27	29
Mean (SD)	4.9 (15.2)	4.6 (11.7)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 33.3
Week 18		
N[d]	32	16
Mean (SD)	7.3 (16.4)	8.3 (19.2)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 21		
N[d]	27	8
Mean (SD)	11.1 (22.6)	4.2 (11.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 33.3

Descriptive Summary of EORTC QLQ-LC13 Sore Mouth by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

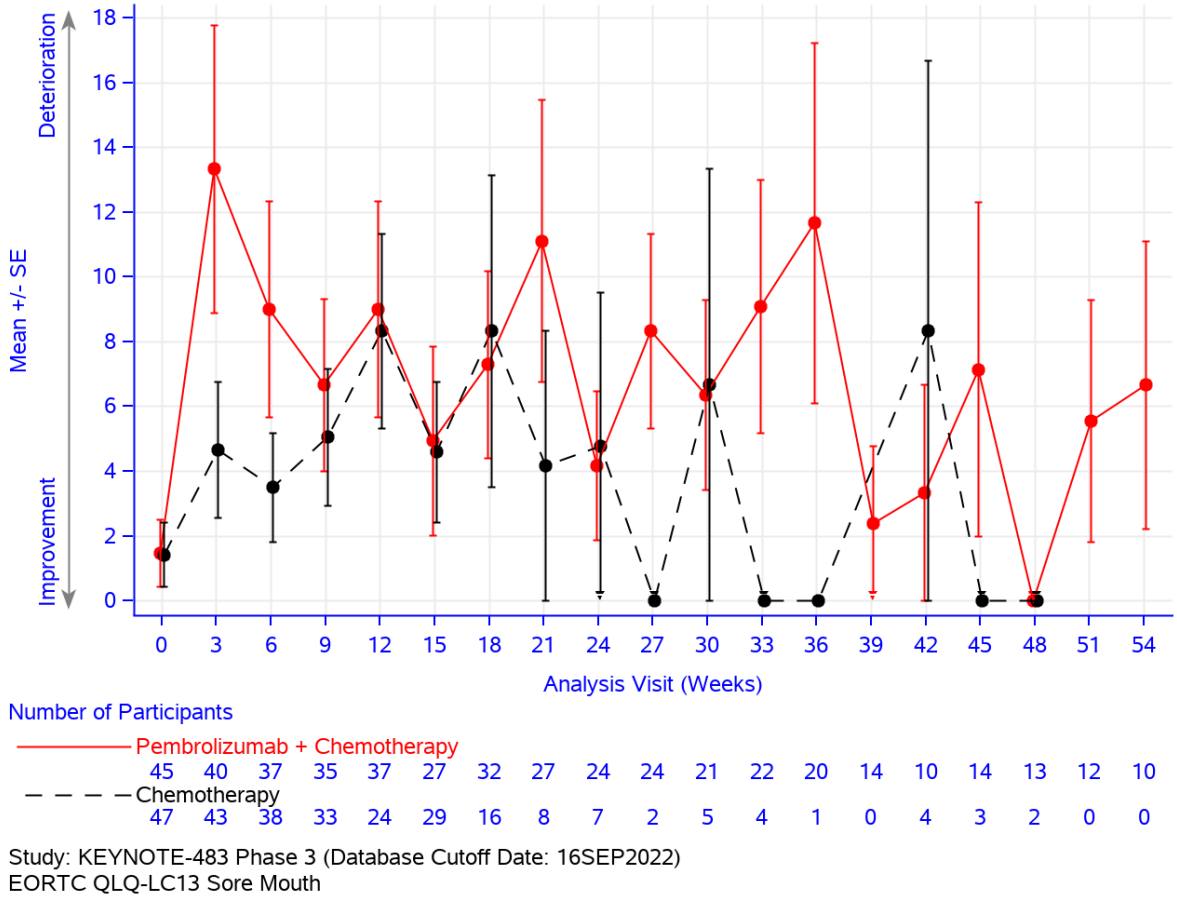
EORTC QLQ-LC13 Sore Mouth	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	4.2 (11.3)	4.8 (12.6)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 33.3
Week 27		
N[d]	24	2
Mean (SD)	8.3 (14.7)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 16.7)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 30		
N[d]	21	5
Mean (SD)	6.3 (13.4)	6.7 (14.9)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 33.3
Week 33		
N[d]	22	4
Mean (SD)	9.1 (18.3)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 36		
N[d]	20	1
Mean (SD)	11.7 (24.8)	0.0 (-)
Median (Q1; Q3)	0.0 (0.0; 16.7)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	2.4 (8.9)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 42		
N[d]	10	4
Mean (SD)	3.3 (10.5)	8.3 (16.7)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 16.7)
Min; Max	0.0; 33.3	0.0; 33.3
Week 45		
N[d]	14	3
Mean (SD)	7.1 (19.3)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0

Descriptive Summary of EORTC QLQ-LC13 Sore Mouth by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Sore Mouth	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 51		
N[d]	12	0
Mean (SD)	5.6 (13.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 54		
N[d]	10	0
Mean (SD)	6.7 (14.1)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-12
Empirical Mean +/- SE of EORTC QLQ-LC13 Sore Mouth Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Sore Mouth

4.1.1.13 Dysphagia

Table 4.2-13
Descriptive Summary of EORTC QLQ-LC13 Dysphagia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Dysphagia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	5.2 (12.2)	7.1 (18.3)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 66.7
Week 3		
N[d]	41	43
Mean (SD)	10.6 (20.3)	7.8 (16.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 6		
N[d]	37	38
Mean (SD)	8.1 (21.4)	9.6 (18.8)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 66.7
Week 9		
N[d]	35	33
Mean (SD)	8.6 (16.8)	11.1 (18.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 12		
N[d]	37	24
Mean (SD)	6.3 (13.2)	12.5 (16.5)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 15		
N[d]	27	29
Mean (SD)	8.6 (17.5)	10.3 (22.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 18		
N[d]	32	16
Mean (SD)	7.3 (16.4)	18.8 (27.1)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 21		
N[d]	27	8
Mean (SD)	11.1 (20.7)	12.5 (17.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3

Descriptive Summary of EORTC QLQ-LC13 Dysphagia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

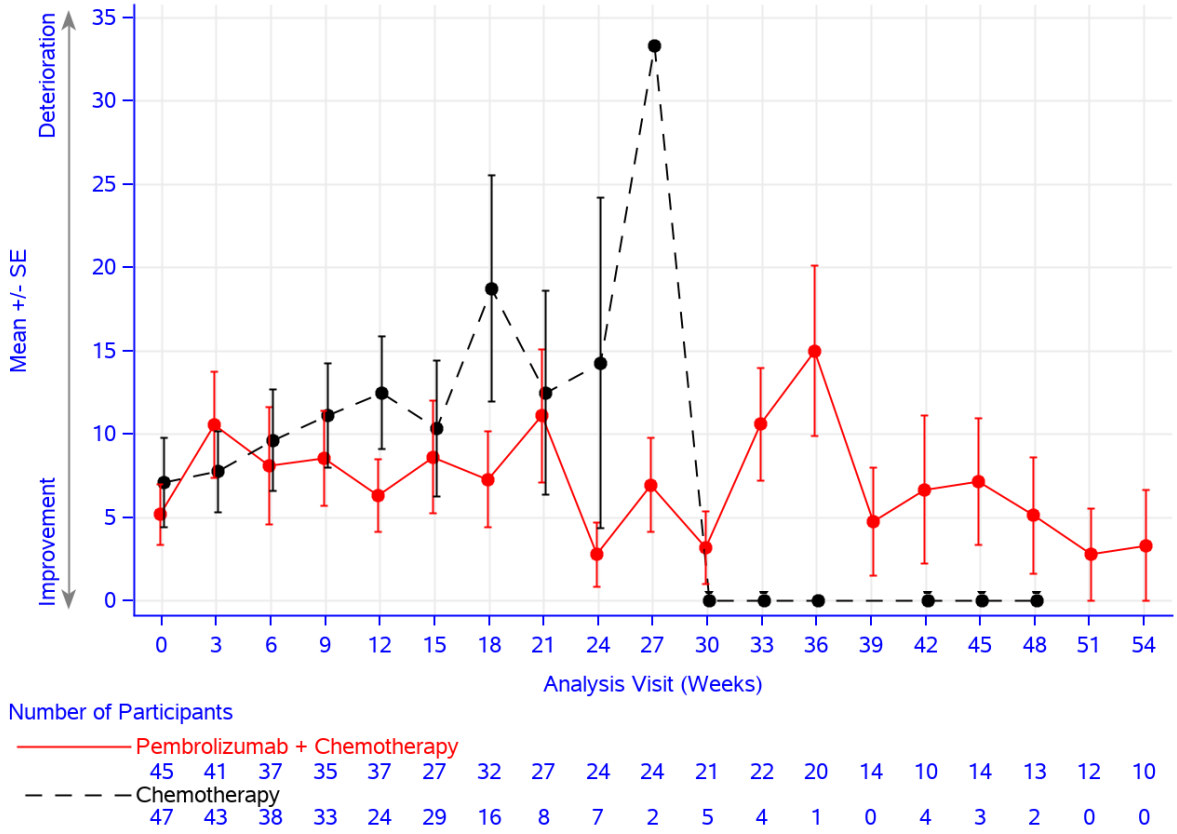
EORTC QLQ-LC13 Dysphagia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	2.8 (9.4)	14.3 (26.2)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	6.9 (13.8)	33.3 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	33.3 (33.3; 33.3)
Min; Max	0.0; 33.3	33.3; 33.3
Week 30		
N[d]	21	5
Mean (SD)	3.2 (10.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 33		
N[d]	22	4
Mean (SD)	10.6 (15.9)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 36		
N[d]	20	1
Mean (SD)	15.0 (22.9)	0.0 (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	4.8 (12.1)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 42		
N[d]	10	4
Mean (SD)	6.7 (14.1)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 45		
N[d]	14	3
Mean (SD)	7.1 (14.2)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0

Descriptive Summary of EORTC QLQ-LC13 Dysphagia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Dysphagia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	**Chemotherapy[b]** N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	5.1 (12.5)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 51		
N[d]	12	0
Mean (SD)	2.8 (9.6)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 54		
N[d]	10	0
Mean (SD)	3.3 (10.5)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-13
Empirical Mean +/- SE of EORTC QLQ-LC13 Dysphagia Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Dysphagia

4.1.1.14 Peripheral Neuropathy

Table 4.2-14
Descriptive Summary of EORTC QLQ-LC13 Peripheral Neuropathy by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Peripheral Neuropathy	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	6.7 (15.2)	5.7 (14.4)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 3		
N[d]	40	43
Mean (SD)	6.7 (13.5)	3.9 (10.8)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 33.3
Week 6		
N[d]	37	38
Mean (SD)	5.4 (16.7)	9.6 (18.8)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 9		
N[d]	35	33
Mean (SD)	4.8 (11.8)	13.1 (18.5)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 66.7
Week 12		
N[d]	37	24
Mean (SD)	7.2 (16.0)	8.3 (14.7)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 16.7)
Min; Max	0.0; 66.7	0.0; 33.3
Week 15		
N[d]	27	28
Mean (SD)	8.6 (17.5)	10.7 (18.3)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 18		
N[d]	32	16
Mean (SD)	12.5 (20.3)	8.3 (19.2)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 21		
N[d]	27	8
Mean (SD)	8.6 (17.5)	12.5 (17.3)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3

Descriptive Summary of EORTC QLQ-LC13 Peripheral Neuropathy by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Peripheral Neuropathy	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	13.9 (23.9)	19.0 (17.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3
Week 27		
N[d]	24	2
Mean (SD)	15.3 (19.6)	33.3 (47.1)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 66.7)
Min; Max	0.0; 66.7	0.0; 66.7
Week 30		
N[d]	21	5
Mean (SD)	12.7 (19.7)	6.7 (14.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 33.3
Week 33		
N[d]	22	4
Mean (SD)	18.2 (24.6)	25.0 (50.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 50.0)
Min; Max	0.0; 66.7	0.0; 100.0
Week 36		
N[d]	20	1
Mean (SD)	20.0 (22.7)	100.0 (-)
Median (Q1; Q3)	16.7 (0.0; 33.3)	100.0 (100.0; 100.0)
Min; Max	0.0; 66.7	100.0; 100.0
Week 39		
N[d]	14	0
Mean (SD)	19.0 (25.2)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	23.3 (27.4)	8.3 (16.7)
Median (Q1; Q3)	16.7 (0.0; 33.3)	0.0 (0.0; 16.7)
Min; Max	0.0; 66.7	0.0; 33.3
Week 45		
N[d]	14	3
Mean (SD)	21.4 (24.8)	22.2 (19.2)
Median (Q1; Q3)	16.7 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3

Descriptive Summary of EORTC QLQ-LC13 Peripheral Neuropathy by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Peripheral Neuropathy	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	10.3 (21.0)	33.3 (47.1)
Median (Q1; Q3)	0.0 (0.0; 0.0)	33.3 (0.0; 66.7)
Min; Max	0.0; 66.7	0.0; 66.7
Week 51		
N[d]	12	0
Mean (SD)	8.3 (20.7)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	16.7 (23.6)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

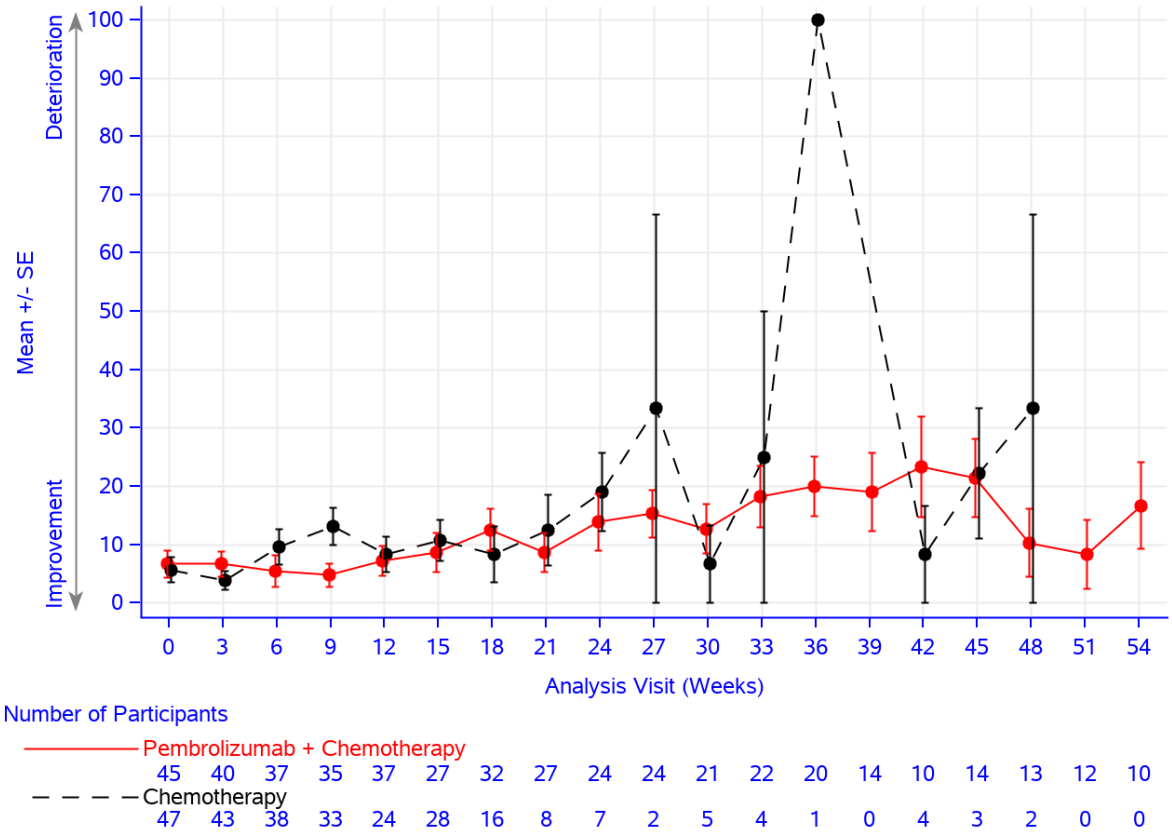
c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-14

Empirical Mean +/- SE of EORTC QLQ-LC13 Peripheral Neuropathy Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Peripheral Neuropathy

4.1.1.15 Alopecia

Table 4.2-15
Descriptive Summary of EORTC QLQ-LC13 Alopecia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Alopecia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	0.0 (0.0)	0.7 (4.9)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 33.3
Week 3		
N[d]	41	43
Mean (SD)	4.9 (14.1)	1.6 (7.1)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 33.3
Week 6		
N[d]	37	38
Mean (SD)	6.3 (13.2)	9.6 (15.3)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 9		
N[d]	35	33
Mean (SD)	8.6 (14.8)	13.1 (16.5)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 12		
N[d]	37	24
Mean (SD)	5.4 (12.5)	13.9 (21.8)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 66.7
Week 15		
N[d]	27	29
Mean (SD)	9.9 (18.1)	12.6 (18.7)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 18		
N[d]	32	16
Mean (SD)	10.4 (15.7)	12.5 (16.7)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 21		
N[d]	27	8
Mean (SD)	13.6 (19.1)	8.3 (15.4)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 16.7)
Min; Max	0.0; 66.7	0.0; 33.3

Descriptive Summary of EORTC QLQ-LC13 Alopecia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

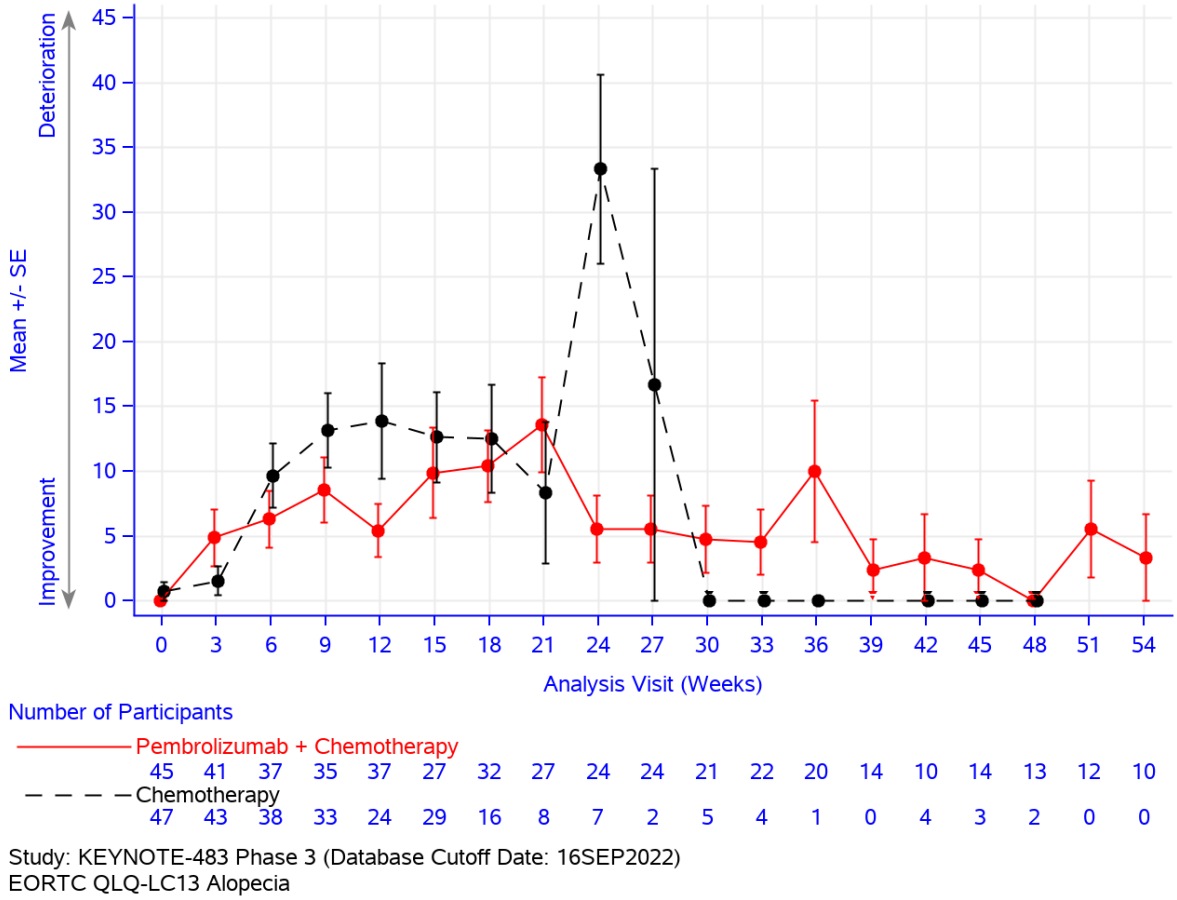
EORTC QLQ-LC13 Alopecia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	5.6 (12.7)	33.3 (19.2)
Median (Q1; Q3)	0.0 (0.0; 0.0)	33.3 (33.3; 33.3)
Min; Max	0.0; 33.3	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	5.6 (12.7)	16.7 (23.6)
Median (Q1; Q3)	0.0 (0.0; 0.0)	16.7 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 33.3
Week 30		
N[d]	21	5
Mean (SD)	4.8 (12.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 33		
N[d]	22	4
Mean (SD)	4.5 (11.7)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 36		
N[d]	20	1
Mean (SD)	10.0 (24.4)	0.0 (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 100.0	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	2.4 (8.9)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 42		
N[d]	10	4
Mean (SD)	3.3 (10.5)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 45		
N[d]	14	3
Mean (SD)	2.4 (8.9)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0

Descriptive Summary of EORTC QLQ-LC13 Alopecia by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Alopecia	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	**Chemotherapy[b]** N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	0.0 (0.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)
Min; Max	0.0; 0.0	0.0; 0.0
Week 51		
N[d]	12	0
Mean (SD)	5.6 (13.0)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 54		
N[d]	10	0
Mean (SD)	3.3 (10.5)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 33.3	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-15
Empirical Mean +/- SE of EORTC QLQ-LC13 Alopecia Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Alopecia

4.1.1.16 Pain in Chest

Table 4.2-16
Descriptive Summary of EORTC QLQ-LC13 Pain in Chest by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Chest	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	46
Mean (SD)	20.7 (27.8)	26.1 (28.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	42
Mean (SD)	15.4 (24.8)	24.6 (27.6)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 6		
N[d]	37	38
Mean (SD)	13.5 (21.5)	25.4 (32.4)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 9		
N[d]	35	33
Mean (SD)	7.6 (16.3)	23.2 (28.2)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	12.6 (19.8)	16.7 (22.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 15		
N[d]	27	29
Mean (SD)	18.5 (28.2)	21.8 (24.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 18		
N[d]	32	16
Mean (SD)	15.6 (22.4)	20.8 (20.6)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 21		
N[d]	26	8
Mean (SD)	17.9 (25.4)	16.7 (17.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3

Descriptive Summary of EORTC QLQ-LC13 Pain in Chest by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Chest	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	11.1 (16.1)	28.6 (23.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 33.3	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	13.9 (16.8)	33.3 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (33.3; 33.3)
Min; Max	0.0; 33.3	33.3; 33.3
Week 30		
N[d]	21	5
Mean (SD)	14.3 (19.9)	20.0 (29.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 66.7
Week 33		
N[d]	22	4
Mean (SD)	15.2 (19.9)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 36		
N[d]	20	1
Mean (SD)	11.7 (16.3)	0.0 (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	9.5 (20.4)	- (-)
Median (Q1; Q3)	0.0 (0.0; 0.0)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	13.3 (17.2)	33.3 (47.1)
Median (Q1; Q3)	0.0 (0.0; 33.3)	16.7 (0.0; 66.7)
Min; Max	0.0; 33.3	0.0; 100.0
Week 45		
N[d]	14	2
Mean (SD)	9.5 (20.4)	16.7 (23.6)
Median (Q1; Q3)	0.0 (0.0; 0.0)	16.7 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 33.3

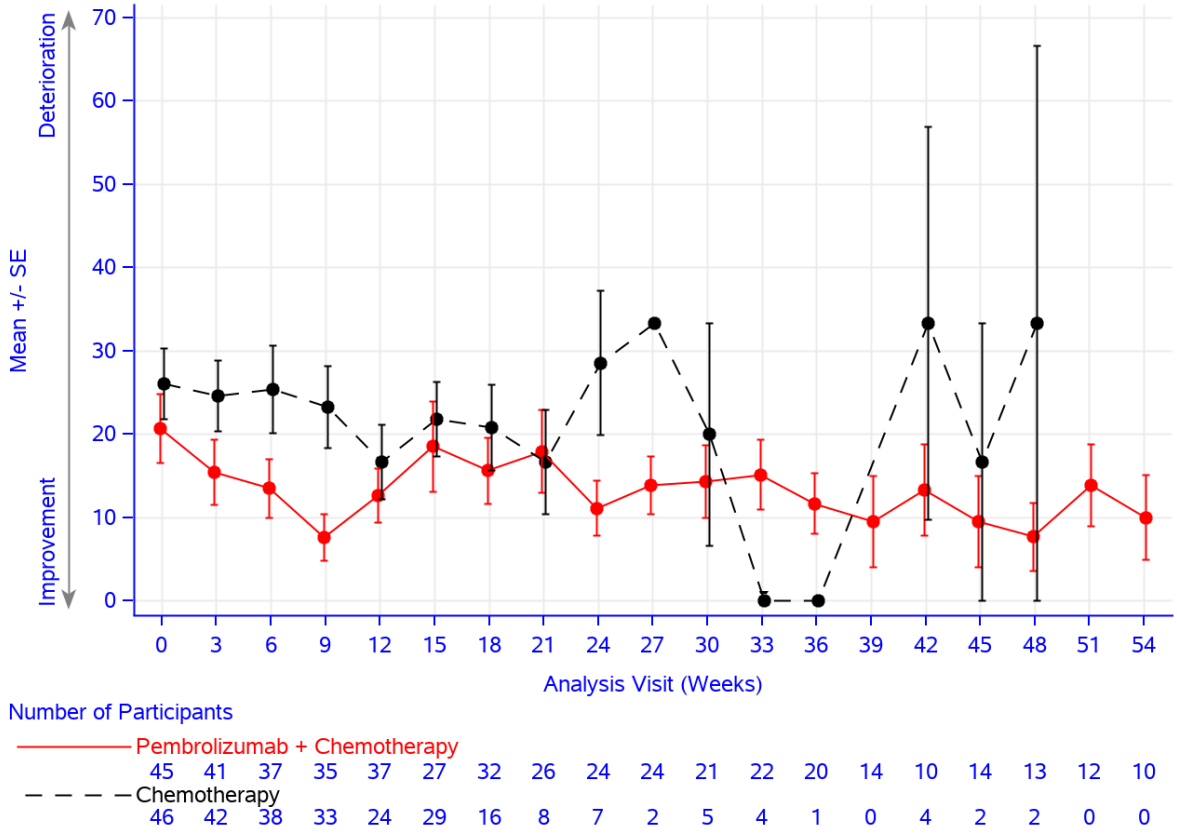
Descriptive Summary of EORTC QLQ-LC13 Pain in Chest by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Chest	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	7.7 (14.6)	33.3 (47.1)
Median (Q1; Q3)	0.0 (0.0; 0.0)	33.3 (0.0; 66.7)
Min; Max	0.0; 33.3	0.0; 66.7
Week 51		
N[d]	12	0
Mean (SD)	13.9 (17.2)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 33.3	-; -
Week 54		
N[d]	10	0
Mean (SD)	10.0 (16.1)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 33.3	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-16

Empirical Mean +/- SE of EORTC QLQ-LC13 Pain in Chest Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Pain in Chest

4.1.1.17 Pain in Arm or Shoulders

Table 4.2-17
Descriptive Summary of EORTC QLQ-LC13 Pain in Arm or Shoulder by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Arm or Shoulder	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	19.3 (25.1)	24.1 (28.4)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	17.1 (27.0)	21.7 (29.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 6		
N[d]	36	38
Mean (SD)	14.8 (23.2)	27.2 (32.7)
Median (Q1; Q3)	0.0 (0.0; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 9		
N[d]	35	33
Mean (SD)	9.5 (19.1)	21.2 (31.0)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	10.8 (17.7)	20.8 (29.2)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 15		
N[d]	27	29
Mean (SD)	9.9 (22.3)	20.7 (30.1)
Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 18		
N[d]	32	16
Mean (SD)	12.5 (22.0)	27.1 (34.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 66.7)
Min; Max	0.0; 66.7	0.0; 100.0
Week 21		
N[d]	27	8
Mean (SD)	13.6 (24.9)	20.8 (35.4)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0

Descriptive Summary of EORTC QLQ-LC13 Pain in Arm or Shoulder by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Arm or Shoulder	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	12.5 (21.6)	33.3 (27.2)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 66.7)
Min; Max	0.0; 66.7	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	13.9 (16.8)	50.0 (23.6)
Median (Q1; Q3)	0.0 (0.0; 33.3)	50.0 (33.3; 66.7)
Min; Max	0.0; 33.3	33.3; 66.7
Week 30		
N[d]	21	5
Mean (SD)	17.5 (27.1)	26.7 (43.5)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 33		
N[d]	22	4
Mean (SD)	19.7 (28.5)	16.7 (33.3)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 36		
N[d]	20	1
Mean (SD)	15.0 (20.2)	66.7 (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	66.7 (66.7; 66.7)
Min; Max	0.0; 66.7	66.7; 66.7
Week 39		
N[d]	14	0
Mean (SD)	21.4 (21.1)	- (-)
Median (Q1; Q3)	33.3 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	23.3 (31.6)	41.7 (50.0)
Median (Q1; Q3)	16.7 (0.0; 33.3)	33.3 (0.0; 83.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 45		
N[d]	14	3
Mean (SD)	16.7 (28.5)	11.1 (19.2)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 33.3

Descriptive Summary of EORTC QLQ-LC13 Pain in Arm or Shoulder by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Arm or Shoulder	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	10.3 (16.0)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 33.3	0.0; 0.0
Week 51		
N[d]	12	0
Mean (SD)	25.0 (20.7)	- (-)
Median (Q1; Q3)	33.3 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	23.3 (16.1)	- (-)
Median (Q1; Q3)	33.3 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 33.3	-; -

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

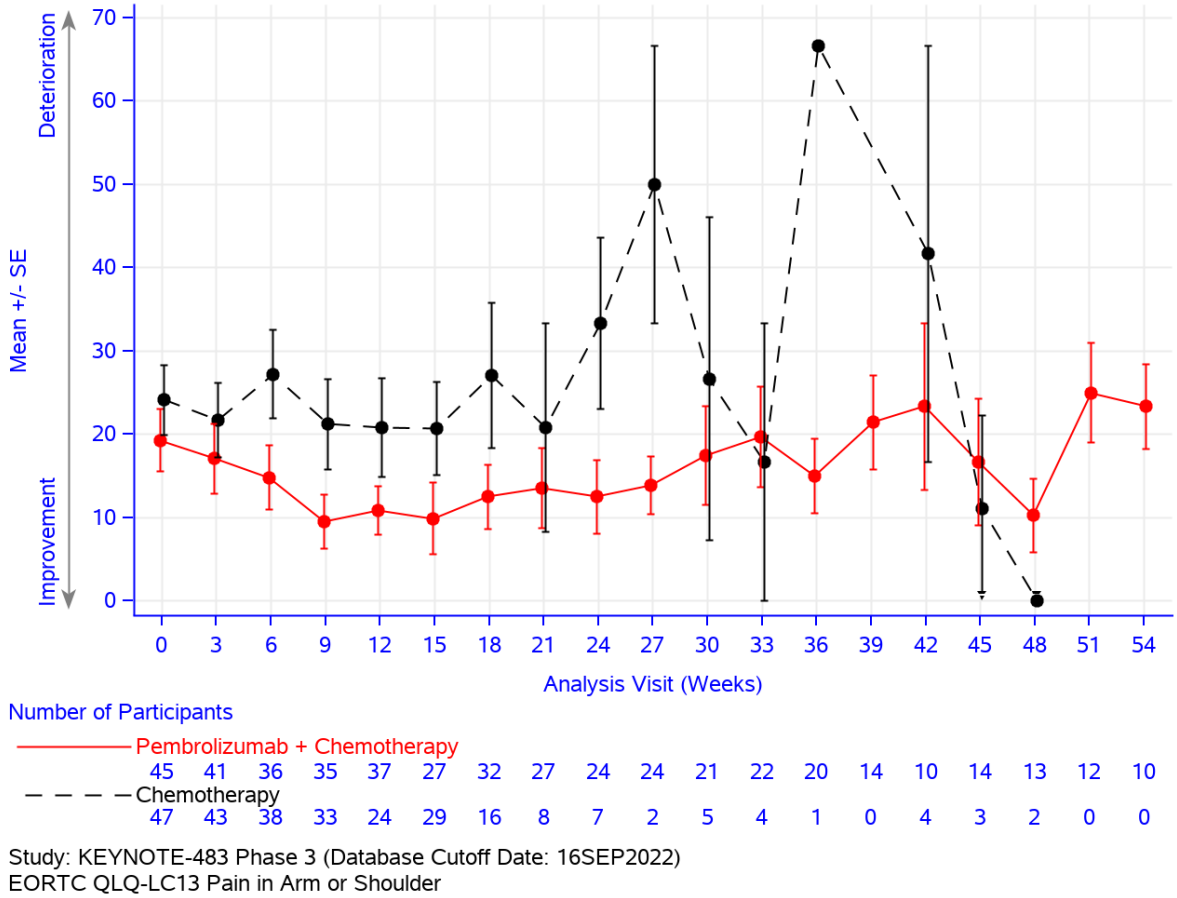
c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-17

Empirical Mean +/- SE of EORTC QLQ-LC13 Pain in Arm or Shoulder Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Pain in Arm or Shoulder

4.1.1.18 Pain in Other Parts

Table 4.2-18
Descriptive Summary of EORTC QLQ-LC13 Pain in Other Parts by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Other Parts	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	44	44
Mean (SD)	25.0 (31.4)	22.7 (27.6)
Median (Q1; Q3)	0.0 (0.0; 33.3)	16.7 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	38	41
Mean (SD)	14.9 (25.3)	19.5 (27.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 6		
N[d]	36	37
Mean (SD)	18.5 (21.7)	27.0 (34.1)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 9		
N[d]	33	30
Mean (SD)	17.2 (25.2)	22.2 (30.7)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 12		
N[d]	34	21
Mean (SD)	12.7 (20.1)	15.9 (27.1)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 66.7	0.0; 100.0
Week 15		
N[d]	25	28
Mean (SD)	14.7 (25.6)	19.0 (24.7)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 18		
N[d]	30	15
Mean (SD)	22.2 (30.7)	26.7 (25.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 21		
N[d]	21	8
Mean (SD)	17.5 (29.1)	25.0 (23.6)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7

Descriptive Summary of EORTC QLQ-LC13 Pain in Other Parts by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Other Parts	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	21	6
Mean (SD)	17.5 (27.1)	16.7 (27.9)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 33.3)
Min; Max	0.0; 100.0	0.0; 66.7
Week 27		
N[d]	24	2
Mean (SD)	11.1 (18.8)	0.0 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 0.0
Week 30		
N[d]	20	5
Mean (SD)	11.7 (19.6)	13.3 (29.8)
Median (Q1; Q3)	0.0 (0.0; 33.3)	0.0 (0.0; 0.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 33		
N[d]	20	3
Mean (SD)	21.7 (29.2)	44.4 (19.2)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (33.3; 66.7)
Min; Max	0.0; 100.0	33.3; 66.7
Week 36		
N[d]	15	1
Mean (SD)	22.2 (27.2)	100.0 (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	100.0 (100.0; 100.0)
Min; Max	0.0; 66.7	100.0; 100.0
Week 39		
N[d]	13	0
Mean (SD)	20.5 (25.6)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 42		
N[d]	10	4
Mean (SD)	20.0 (23.3)	25.0 (31.9)
Median (Q1; Q3)	16.7 (0.0; 33.3)	16.7 (0.0; 50.0)
Min; Max	0.0; 66.7	0.0; 66.7
Week 45		
N[d]	13	3
Mean (SD)	15.4 (22.0)	33.3 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (33.3; 33.3)
Min; Max	0.0; 66.7	33.3; 33.3

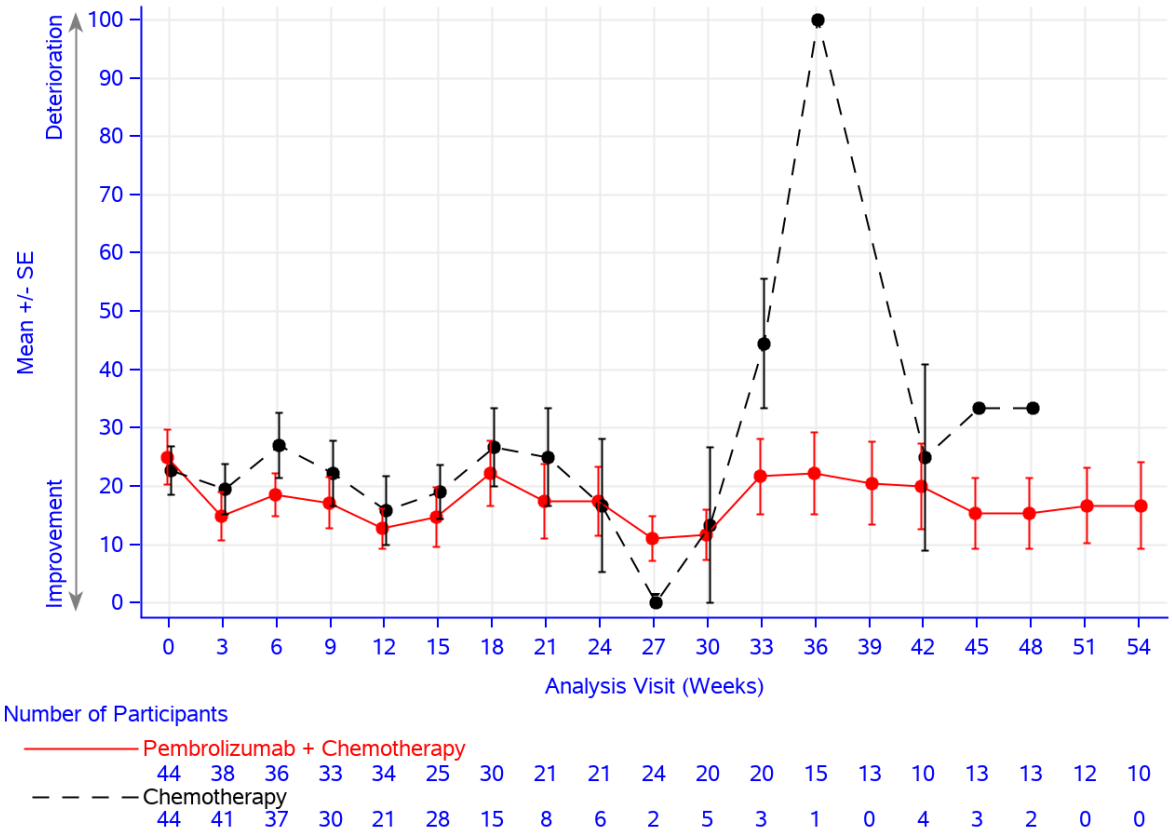
Descriptive Summary of EORTC QLQ-LC13 Pain in Other Parts by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-LC13 Pain in Other Parts	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	15.4 (22.0)	33.3 (0.0)
Median (Q1; Q3)	0.0 (0.0; 33.3)	33.3 (33.3; 33.3)
Min; Max	0.0; 66.7	33.3; 33.3
Week 51		
N[d]	12	0
Mean (SD)	16.7 (22.5)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	16.7 (23.6)	- (-)
Median (Q1; Q3)	0.0 (0.0; 33.3)	- (-; -)
Min; Max	0.0; 66.7	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-18

Empirical Mean +/- SE of EORTC QLQ-LC13 Pain in Other Parts Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-LC13 Pain in Other Parts

Anhang 4-G2.3: EQ-5D VAS

4.1.2 EQ-5D VAS

Table 4.2-25
Descriptive Summary of EQ-5D VAS by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EQ-5D VAS	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=38	Chemotherapy[b] N[c]=45
Baseline		
N[d]	38	44
Mean (SD)	63.4 (15.3)	66.5 (20.9)
Median (Q1; Q3)	60.0 (50.0; 75.0)	67.5 (50.0; 82.5)
Min; Max	35.0; 90.0	10.0; 100.0
Week 3		
N[d]	33	39
Mean (SD)	65.2 (15.2)	68.1 (18.9)
Median (Q1; Q3)	70.0 (50.0; 80.0)	70.0 (55.0; 80.0)
Min; Max	40.0; 90.0	10.0; 100.0
Week 6		
N[d]	29	34
Mean (SD)	69.7 (11.9)	63.6 (19.2)
Median (Q1; Q3)	70.0 (60.0; 80.0)	67.5 (50.0; 75.0)
Min; Max	50.0; 90.0	30.0; 100.0
Week 9		
N[d]	29	30
Mean (SD)	67.2 (14.4)	64.9 (21.1)
Median (Q1; Q3)	70.0 (55.0; 75.0)	70.0 (50.0; 80.0)
Min; Max	40.0; 95.0	10.0; 100.0
Week 12		
N[d]	30	22
Mean (SD)	69.7 (14.6)	68.4 (18.2)
Median (Q1; Q3)	70.0 (60.0; 80.0)	70.0 (60.0; 80.0)
Min; Max	30.0; 95.0	20.0; 100.0
Week 15		
N[d]	23	24
Mean (SD)	65.7 (15.9)	66.0 (15.1)
Median (Q1; Q3)	70.0 (55.0; 80.0)	65.0 (50.0; 77.5)
Min; Max	30.0; 92.0	40.0; 100.0
Week 18		
N[d]	25	15
Mean (SD)	67.0 (21.7)	61.7 (22.7)
Median (Q1; Q3)	75.0 (60.0; 80.0)	65.0 (50.0; 80.0)
Min; Max	10.0; 95.0	10.0; 92.0
Week 21		
N[d]	22	8
Mean (SD)	67.6 (15.6)	55.9 (18.7)
Median (Q1; Q3)	67.5 (60.0; 80.0)	50.0 (42.5; 70.0)
Min; Max	40.0; 95.0	35.0; 87.0

Descriptive Summary of EQ-5D VAS by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

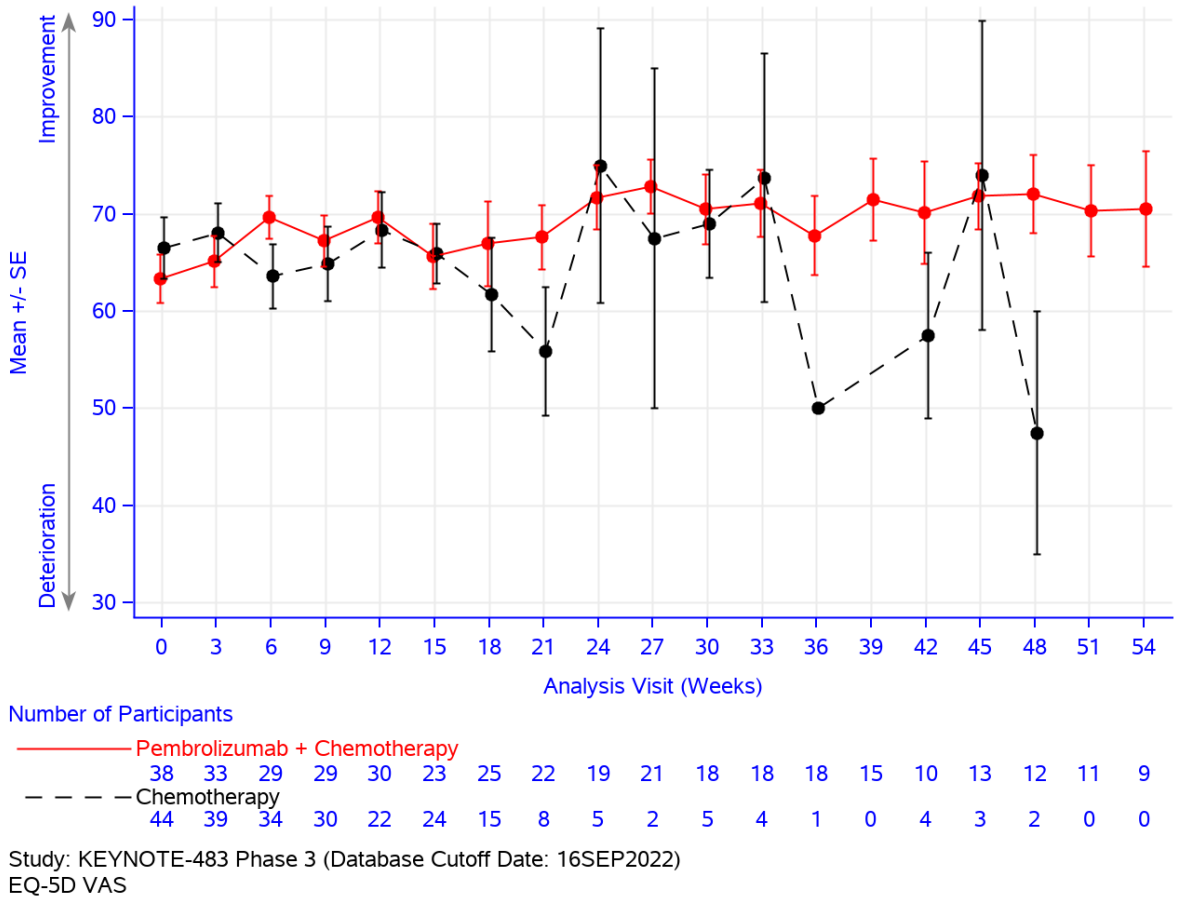
EQ-5D VAS	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=38	Chemotherapy[b] N[c]=45
Week 24		
N[d]	19	5
Mean (SD)	71.7 (14.4)	75.0 (31.6)
Median (Q1; Q3)	70.0 (60.0; 85.0)	85.0 (80.0; 90.0)
Min; Max	40.0; 95.0	20.0; 100.0
Week 27		
N[d]	21	2
Mean (SD)	72.9 (12.7)	67.5 (24.7)
Median (Q1; Q3)	75.0 (70.0; 80.0)	67.5 (50.0; 85.0)
Min; Max	40.0; 95.0	50.0; 85.0
Week 30		
N[d]	18	5
Mean (SD)	70.5 (15.2)	69.0 (12.4)
Median (Q1; Q3)	75.0 (65.0; 80.0)	70.0 (65.0; 80.0)
Min; Max	35.0; 95.0	50.0; 80.0
Week 33		
N[d]	18	4
Mean (SD)	71.1 (14.8)	73.8 (25.6)
Median (Q1; Q3)	72.5 (65.0; 80.0)	75.0 (52.5; 95.0)
Min; Max	30.0; 95.0	45.0; 100.0
Week 36		
N[d]	18	1
Mean (SD)	67.8 (17.3)	50.0 (-)
Median (Q1; Q3)	70.0 (65.0; 80.0)	50.0 (50.0; 50.0)
Min; Max	15.0; 95.0	50.0; 50.0
Week 39		
N[d]	15	0
Mean (SD)	71.5 (16.3)	- (-)
Median (Q1; Q3)	75.0 (65.0; 80.0)	- (-; -)
Min; Max	30.0; 95.0	-; -
Week 42		
N[d]	10	4
Mean (SD)	70.2 (16.6)	57.5 (17.1)
Median (Q1; Q3)	70.0 (70.0; 80.0)	55.0 (45.0; 70.0)
Min; Max	30.0; 95.0	40.0; 80.0
Week 45		
N[d]	13	3
Mean (SD)	71.8 (12.2)	74.0 (27.6)
Median (Q1; Q3)	70.0 (65.0; 80.0)	77.0 (45.0; 100.0)
Min; Max	50.0; 90.0	45.0; 100.0

Descriptive Summary of EQ-5D VAS by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EQ-5D VAS	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=38	Chemotherapy[b] N[c]=45
Week 48		
N[d]	12	2
Mean (SD)	72.1 (14.0)	47.5 (17.7)
Median (Q1; Q3)	72.5 (62.5; 82.5)	47.5 (35.0; 60.0)
Min; Max	45.0; 93.0	35.0; 60.0
Week 51		
N[d]	11	0
Mean (SD)	70.4 (15.7)	- (-)
Median (Q1; Q3)	74.0 (55.0; 80.0)	- (-; -)
Min; Max	45.0; 93.0	-; -
Week 54		
N[d]	9	0
Mean (SD)	70.6 (17.8)	- (-)
Median (Q1; Q3)	74.0 (61.0; 80.0)	- (-; -)
Min; Max	40.0; 95.0	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EQ-5D: European Quality of Life 5 Dimensions; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation; VAS: Visual Analogue Scale

Figure 4.2-25
Empirical Mean +/- SE of EQ-5D VAS Over Time by Treatment Group
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EQ-5D VAS

Anhang 4-G3: Auswertungen über den Studienverlauf für den Endpunkt Gesundheitsbezogene Lebensqualität anhand von EORTC QLQ-C30 der Studie KEYNOT 483

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.3.1 die Auswertungen über den Studienverlauf des EORTC QLQ-C30 dargestellt.

4.1.3 EORTC QLQ-C30 Global Health Status Endpoints and Functional Scales

4.1.3.1 Global Health Status

Table 4.2-19
Descriptive Summary of EORTC QLQ-C30 Global Health Status/QoL by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Global Health Status/QoL	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	59.1 (20.8)	60.1 (21.1)
Median (Q1; Q3)	58.3 (50.0; 83.3)	66.7 (50.0; 83.3)
Min; Max	16.7; 91.7	8.3; 100.0
Week 3		
N[d]	41	43
Mean (SD)	61.0 (15.3)	57.4 (18.7)
Median (Q1; Q3)	58.3 (50.0; 66.7)	58.3 (41.7; 66.7)
Min; Max	33.3; 83.3	16.7; 100.0
Week 6		
N[d]	37	37
Mean (SD)	67.3 (17.5)	57.9 (22.6)
Median (Q1; Q3)	66.7 (58.3; 83.3)	66.7 (50.0; 66.7)
Min; Max	16.7; 100.0	0.0; 100.0
Week 9		
N[d]	35	33
Mean (SD)	64.0 (18.8)	54.8 (20.7)
Median (Q1; Q3)	66.7 (50.0; 83.3)	50.0 (41.7; 66.7)
Min; Max	16.7; 100.0	8.3; 100.0
Week 12		
N[d]	37	24
Mean (SD)	62.6 (15.7)	59.4 (18.4)
Median (Q1; Q3)	66.7 (50.0; 75.0)	58.3 (50.0; 66.7)
Min; Max	33.3; 91.7	16.7; 100.0
Week 15		
N[d]	27	29
Mean (SD)	59.0 (21.0)	57.5 (16.1)
Median (Q1; Q3)	66.7 (50.0; 75.0)	58.3 (50.0; 66.7)
Min; Max	16.7; 83.3	16.7; 83.3
Week 18		
N[d]	32	16
Mean (SD)	63.0 (17.1)	55.2 (26.0)
Median (Q1; Q3)	66.7 (50.0; 75.0)	54.2 (37.5; 75.0)
Min; Max	25.0; 91.7	8.3; 100.0

Week 21		
N[d]	27	8
Mean (SD)	62.7 (17.0)	55.2 (18.9)
Median (Q1; Q3)	66.7 (50.0; 83.3)	58.3 (41.7; 66.7)
Min; Max	16.7; 83.3	25.0; 83.3

Descriptive Summary of EORTC QLQ-C30 Global Health Status/QoL by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Global Health Status/QoL	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	67.7 (15.6)	60.7 (33.9)
Median (Q1; Q3)	66.7 (50.0; 83.3)	66.7 (33.3; 91.7)
Min; Max	41.7; 91.7	8.3; 100.0
Week 27		
N[d]	24	2
Mean (SD)	69.1 (16.2)	66.7 (23.6)
Median (Q1; Q3)	70.8 (54.2; 83.3)	66.7 (50.0; 83.3)
Min; Max	33.3; 91.7	50.0; 83.3
Week 30		
N[d]	21	5
Mean (SD)	67.9 (19.2)	63.3 (21.7)
Median (Q1; Q3)	66.7 (66.7; 83.3)	66.7 (50.0; 83.3)
Min; Max	16.7; 100.0	33.3; 83.3
Week 33		
N[d]	22	4
Mean (SD)	61.7 (23.2)	68.8 (25.8)
Median (Q1; Q3)	66.7 (50.0; 83.3)	75.0 (50.0; 87.5)
Min; Max	16.7; 83.3	33.3; 91.7
Week 36		
N[d]	20	1
Mean (SD)	68.3 (15.9)	33.3 (-)
Median (Q1; Q3)	66.7 (66.7; 83.3)	33.3 (33.3; 33.3)
Min; Max	33.3; 83.3	33.3; 33.3
Week 39		
N[d]	14	0
Mean (SD)	69.0 (15.8)	- (-)
Median (Q1; Q3)	66.7 (66.7; 83.3)	- (-; -)
Min; Max	33.3; 83.3	-; -
Week 42		
N[d]	10	4
Mean (SD)	71.7 (18.9)	47.9 (30.7)
Median (Q1; Q3)	75.0 (66.7; 83.3)	50.0 (29.2; 66.7)
Min; Max	33.3; 100.0	8.3; 83.3
Week 45		
N[d]	14	3
Mean (SD)	72.0 (10.6)	72.2 (19.2)
Median (Q1; Q3)	70.8 (66.7; 83.3)	83.3 (50.0; 83.3)
Min; Max	50.0; 83.3	50.0; 83.3

Descriptive Summary of EORTC QLQ-C30 Global Health Status/QoL by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Global Health Status/QoL	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	68.6 (18.7)	58.3 (35.4)
Median (Q1; Q3)	66.7 (50.0; 83.3)	58.3 (33.3; 83.3)
Min; Max	41.7; 100.0	33.3; 83.3
Week 51		
N[d]	12	0
Mean (SD)	70.8 (14.0)	- (-)
Median (Q1; Q3)	66.7 (62.5; 83.3)	- (-; -)
Min; Max	50.0; 91.7	-; -
Week 54		
N[d]	10	0
Mean (SD)	68.3 (14.1)	- (-)
Median (Q1; Q3)	66.7 (58.3; 83.3)	- (-; -)
Min; Max	50.0; 83.3	-; -

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

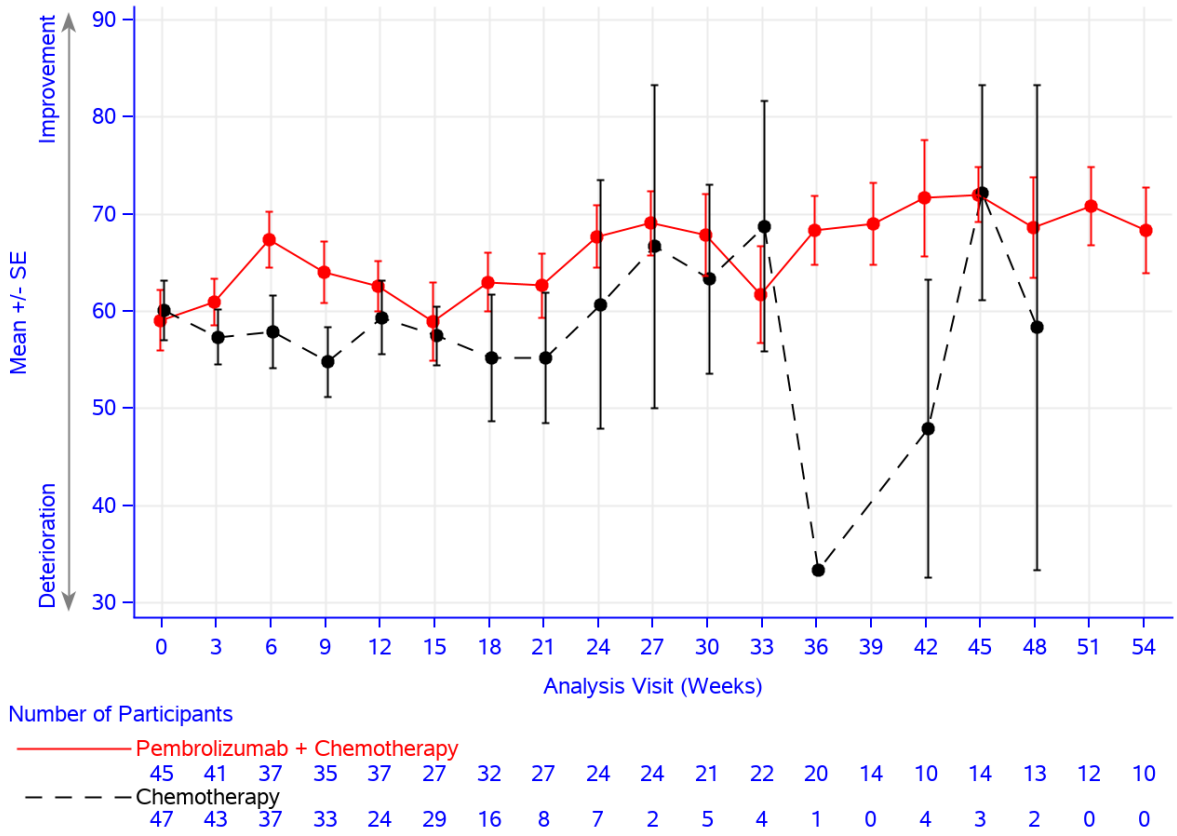
c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; QoL: Quality of Life; SD: Standard Deviation

Figure 4.2-19

Empirical Mean +/- SE of EORTC QLQ-C30 Global Health Status/QoL Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Global Health Status/QoL

4.1.3.2 Physical Functioning

Table 4.2-20
Descriptive Summary of EORTC QLQ-C30 Physical Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Physical Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	72.1 (23.1)	75.9 (21.6)
Median (Q1; Q3)	73.3 (60.0; 86.7)	80.0 (66.7; 93.3)
Min; Max	20.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	73.0 (22.3)	74.7 (17.0)
Median (Q1; Q3)	73.3 (60.0; 93.3)	80.0 (66.7; 86.7)
Min; Max	13.3; 100.0	26.7; 100.0
Week 6		
N[d]	37	37
Mean (SD)	72.8 (23.2)	74.4 (19.8)
Median (Q1; Q3)	73.3 (60.0; 93.3)	73.3 (66.7; 93.3)
Min; Max	13.3; 100.0	13.3; 100.0
Week 9		
N[d]	35	33
Mean (SD)	76.4 (17.1)	71.9 (22.7)
Median (Q1; Q3)	80.0 (66.7; 86.7)	73.3 (60.0; 86.7)
Min; Max	26.7; 100.0	20.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	73.2 (21.4)	71.7 (20.7)
Median (Q1; Q3)	73.3 (60.0; 86.7)	73.3 (60.0; 86.7)
Min; Max	13.3; 100.0	20.0; 100.0
Week 15		
N[d]	27	29
Mean (SD)	75.6 (22.0)	73.7 (21.1)
Median (Q1; Q3)	80.0 (60.0; 93.3)	80.0 (60.0; 86.7)
Min; Max	20.0; 100.0	6.7; 100.0
Week 18		
N[d]	32	16
Mean (SD)	74.0 (24.9)	72.1 (24.9)
Median (Q1; Q3)	80.0 (56.7; 100.0)	80.0 (66.7; 90.0)
Min; Max	20.0; 100.0	20.0; 100.0
Week 21		
N[d]	27	8
Mean (SD)	68.9 (25.7)	65.8 (28.6)
Median (Q1; Q3)	66.7 (46.7; 93.3)	76.7 (43.3; 83.3)
Min; Max	13.3; 100.0	20.0; 100.0

Descriptive Summary of EORTC QLQ-C30 Physical Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Physical Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	76.9 (22.0)	73.1 (28.7)
Median (Q1; Q3)	86.7 (60.0; 96.7)	80.0 (46.7; 100.0)
Min; Max	26.7; 100.0	25.0; 100.0
Week 27		
N[d]	24	2
Mean (SD)	77.2 (20.4)	70.0 (14.1)
Median (Q1; Q3)	80.0 (63.3; 93.3)	70.0 (60.0; 80.0)
Min; Max	33.3; 100.0	60.0; 80.0
Week 30		
N[d]	21	5
Mean (SD)	77.6 (22.7)	88.0 (11.9)
Median (Q1; Q3)	86.7 (66.7; 93.3)	86.7 (80.0; 100.0)
Min; Max	16.7; 100.0	73.3; 100.0
Week 33		
N[d]	22	4
Mean (SD)	74.2 (24.6)	83.3 (17.6)
Median (Q1; Q3)	83.3 (66.7; 93.3)	86.7 (70.0; 96.7)
Min; Max	13.3; 100.0	60.0; 100.0
Week 36		
N[d]	20	1
Mean (SD)	77.0 (20.1)	33.3 (-)
Median (Q1; Q3)	80.0 (66.7; 93.3)	33.3 (33.3; 33.3)
Min; Max	33.3; 100.0	33.3; 33.3
Week 39		
N[d]	14	0
Mean (SD)	78.6 (25.9)	- (-)
Median (Q1; Q3)	86.7 (80.0; 100.0)	- (-; -)
Min; Max	20.0; 100.0	-; -
Week 42		
N[d]	10	4
Mean (SD)	79.3 (27.5)	80.0 (17.2)
Median (Q1; Q3)	93.3 (73.3; 100.0)	80.0 (66.7; 93.3)
Min; Max	26.7; 100.0	60.0; 100.0
Week 45		
N[d]	14	3
Mean (SD)	76.7 (22.6)	88.9 (19.2)
Median (Q1; Q3)	86.7 (60.0; 93.3)	100.0 (66.7; 100.0)
Min; Max	33.3; 100.0	66.7; 100.0

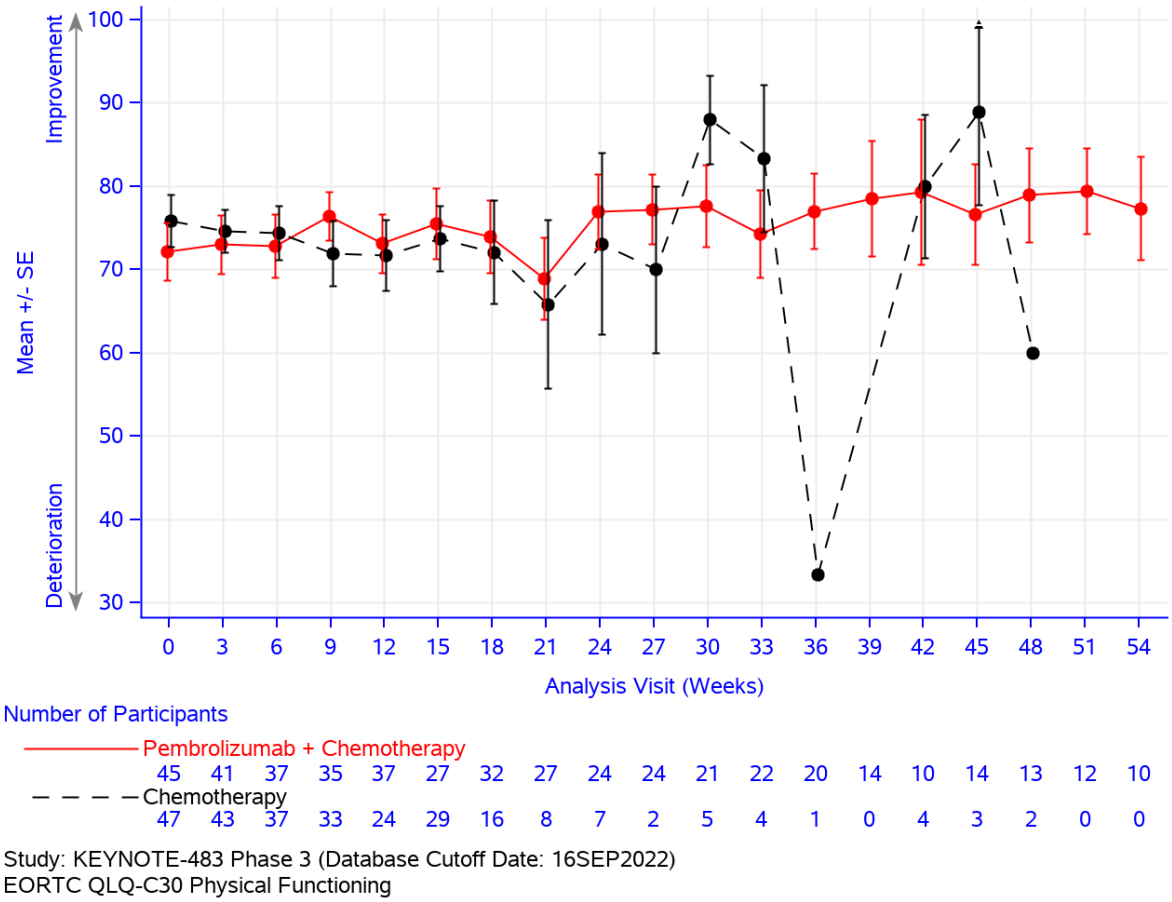
Descriptive Summary of EORTC QLQ-C30 Physical Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Physical Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	79.0 (20.3)	60.0 (0.0)
Median (Q1; Q3)	86.7 (66.7; 93.3)	60.0 (60.0; 60.0)
Min; Max	33.3; 100.0	60.0; 60.0
Week 51		
N[d]	12	0
Mean (SD)	79.4 (17.9)	- (-)
Median (Q1; Q3)	83.3 (73.3; 93.3)	- (-; -)
Min; Max	40.0; 100.0	-; -
Week 54		
N[d]	10	0
Mean (SD)	77.3 (19.7)	- (-)
Median (Q1; Q3)	80.0 (66.7; 93.3)	- (-; -)
Min; Max	40.0; 100.0	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-20

Empirical Mean +/- SE of EORTC QLQ-C30 Physical Functioning Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Physical Functioning

4.1.3.3 Role Functioning

Table 4.2-21
Descriptive Summary of EORTC QLQ-C30 Role Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Role Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	66.3 (29.4)	64.2 (30.1)
Median (Q1; Q3)	66.7 (33.3; 100.0)	66.7 (50.0; 83.3)
Min; Max	16.7; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	66.3 (30.4)	66.3 (27.3)
Median (Q1; Q3)	66.7 (50.0; 100.0)	66.7 (50.0; 83.3)
Min; Max	0.0; 100.0	0.0; 100.0
Week 6		
N[d]	37	37
Mean (SD)	67.6 (30.4)	68.5 (28.8)
Median (Q1; Q3)	66.7 (66.7; 100.0)	66.7 (50.0; 100.0)
Min; Max	0.0; 100.0	0.0; 100.0
Week 9		
N[d]	35	33
Mean (SD)	70.0 (24.9)	63.1 (32.2)
Median (Q1; Q3)	66.7 (50.0; 100.0)	66.7 (50.0; 100.0)
Min; Max	16.7; 100.0	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	67.1 (27.1)	68.8 (26.2)
Median (Q1; Q3)	66.7 (50.0; 100.0)	66.7 (41.7; 100.0)
Min; Max	0.0; 100.0	33.3; 100.0
Week 15		
N[d]	27	29
Mean (SD)	62.3 (32.6)	67.2 (30.7)
Median (Q1; Q3)	66.7 (33.3; 100.0)	66.7 (50.0; 100.0)
Min; Max	0.0; 100.0	0.0; 100.0
Week 18		
N[d]	32	16
Mean (SD)	67.2 (31.8)	62.5 (35.7)
Median (Q1; Q3)	66.7 (50.0; 100.0)	66.7 (33.3; 100.0)
Min; Max	0.0; 100.0	0.0; 100.0
Week 21		
N[d]	27	8
Mean (SD)	61.1 (33.7)	56.3 (26.6)
Median (Q1; Q3)	66.7 (33.3; 100.0)	66.7 (33.3; 66.7)
Min; Max	0.0; 100.0	16.7; 100.0

Descriptive Summary of EORTC QLQ-C30 Role Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Role Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	70.8 (24.7)	66.7 (31.9)
Median (Q1; Q3)	66.7 (50.0; 100.0)	66.7 (33.3; 100.0)
Min; Max	16.7; 100.0	16.7; 100.0
Week 27		
N[d]	24	2
Mean (SD)	66.7 (25.1)	66.7 (0.0)
Median (Q1; Q3)	66.7 (50.0; 83.3)	66.7 (66.7; 66.7)
Min; Max	16.7; 100.0	66.7; 66.7
Week 30		
N[d]	21	5
Mean (SD)	71.4 (24.2)	90.0 (14.9)
Median (Q1; Q3)	66.7 (66.7; 100.0)	100.0 (83.3; 100.0)
Min; Max	16.7; 100.0	66.7; 100.0
Week 33		
N[d]	22	4
Mean (SD)	68.9 (30.6)	75.0 (21.5)
Median (Q1; Q3)	66.7 (50.0; 100.0)	75.0 (58.3; 91.7)
Min; Max	0.0; 100.0	50.0; 100.0
Week 36		
N[d]	20	1
Mean (SD)	69.2 (24.9)	0.0 (-)
Median (Q1; Q3)	66.7 (50.0; 91.7)	0.0 (0.0; 0.0)
Min; Max	16.7; 100.0	0.0; 0.0
Week 39		
N[d]	14	0
Mean (SD)	70.2 (28.6)	- (-)
Median (Q1; Q3)	66.7 (50.0; 100.0)	- (-; -)
Min; Max	16.7; 100.0	-; -
Week 42		
N[d]	10	4
Mean (SD)	71.7 (33.4)	83.3 (19.2)
Median (Q1; Q3)	83.3 (50.0; 100.0)	83.3 (66.7; 100.0)
Min; Max	16.7; 100.0	66.7; 100.0
Week 45		
N[d]	14	3
Mean (SD)	65.5 (34.3)	72.2 (25.5)
Median (Q1; Q3)	66.7 (33.3; 100.0)	66.7 (50.0; 100.0)
Min; Max	0.0; 100.0	50.0; 100.0

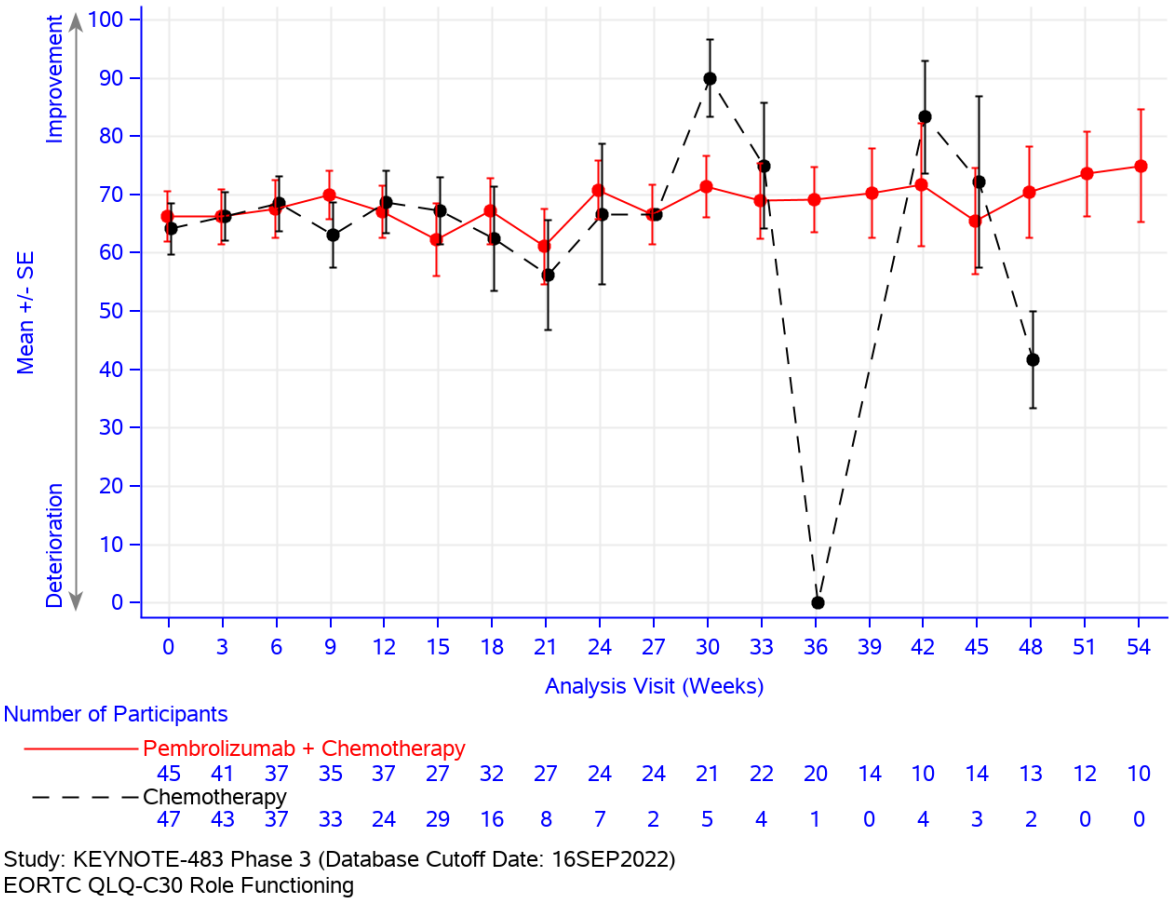
Descriptive Summary of EORTC QLQ-C30 Role Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Role Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	70.5 (28.2)	41.7 (11.8)
Median (Q1; Q3)	66.7 (66.7; 100.0)	41.7 (33.3; 50.0)
Min; Max	16.7; 100.0	33.3; 50.0
Week 51		
N[d]	12	0
Mean (SD)	73.6 (25.1)	- (-)
Median (Q1; Q3)	66.7 (66.7; 100.0)	- (-; -)
Min; Max	16.7; 100.0	-; -
Week 54		
N[d]	10	0
Mean (SD)	75.0 (30.7)	- (-)
Median (Q1; Q3)	83.3 (66.7; 100.0)	- (-; -)
Min; Max	16.7; 100.0	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-21

Empirical Mean +/- SE of EORTC QLQ-C30 Role Functioning Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Role Functioning

4.1.3.4 Emotional Functioning

Table 4.2-22
Descriptive Summary of EORTC QLQ-C30 Emotional Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Emotional Functioning	Study: KEYNOTE-483 Phase 3a	
	Pembrolizumab + Chemotherapyb Nc=45	Chemotherapyb Nc=47
Baseline		
Nd	45	47
Mean (SD)	71.9 (23.1)	71.8 (22.1)
Median (Q1; Q3)	75.0 (58.3; 91.7)	75.0 (66.7; 91.7)
Min; Max	8.3; 100.0	25.0; 100.0
Week 3		
Nd	41	43
Mean (SD)	79.1 (19.6)	78.7 (19.1)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (66.7; 91.7)
Min; Max	16.7; 100.0	25.0; 100.0
Week 6		
Nd	37	38
Mean (SD)	79.1 (21.4)	73.2 (20.6)
Median (Q1; Q3)	83.3 (66.7; 100.0)	75.0 (66.7; 91.7)
Min; Max	16.7; 100.0	25.0; 100.0
Week 9		
Nd	35	33
Mean (SD)	79.5 (21.3)	75.3 (22.1)
Median (Q1; Q3)	75.0 (66.7; 100.0)	75.0 (66.7; 91.7)
Min; Max	33.3; 100.0	25.0; 100.0
Week 12		
Nd	37	24
Mean (SD)	78.2 (18.1)	76.4 (19.9)
Median (Q1; Q3)	83.3 (66.7; 91.7)	79.2 (66.7; 91.7)
Min; Max	33.3; 100.0	16.7; 100.0
Week 15		
Nd	27	29
Mean (SD)	73.8 (25.0)	76.2 (18.6)
Median (Q1; Q3)	83.3 (66.7; 91.7)	75.0 (66.7; 91.7)
Min; Max	16.7; 100.0	33.3; 100.0
Week 18		
Nd	32	16
Mean (SD)	81.5 (17.9)	77.6 (17.7)
Median (Q1; Q3)	83.3 (66.7; 100.0)	75.0 (66.7; 95.8)
Min; Max	33.3; 100.0	41.7; 100.0
Week 21		
Nd	27	8
Mean (SD)	78.1 (19.4)	71.9 (14.0)
Median (Q1; Q3)	83.3 (66.7; 100.0)	66.7 (62.5; 79.2)
Min; Max	33.3; 100.0	58.3; 100.0

Descriptive Summary of EORTC QLQ-C30 Emotional Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Emotional Functioning	Study: KEYNOTE-483 Phase 3a	
	Pembrolizumab + Chemotherapyb Nc=45	**Chemotherapyb** Nc=47
Week 24		
Nd	24	7
Mean (SD)	79.5 (20.8)	77.4 (24.9)
Median (Q1; Q3)	79.2 (66.7; 100.0)	83.3 (50.0; 100.0)
Min; Max	8.3; 100.0	41.7; 100.0
Week 27		
Nd	24	2
Mean (SD)	80.2 (17.5)	79.2 (5.9)
Median (Q1; Q3)	75.0 (66.7; 100.0)	79.2 (75.0; 83.3)
Min; Max	50.0; 100.0	75.0; 83.3
Week 30		
Nd	21	5
Mean (SD)	80.6 (18.9)	88.3 (13.9)
Median (Q1; Q3)	83.3 (66.7; 100.0)	91.7 (83.3; 100.0)
Min; Max	41.7; 100.0	66.7; 100.0
Week 33		
Nd	22	4
Mean (SD)	75.8 (22.4)	81.3 (8.0)
Median (Q1; Q3)	70.8 (66.7; 100.0)	79.2 (75.0; 87.5)
Min; Max	33.3; 100.0	75.0; 91.7
Week 36		
Nd	20	1
Mean (SD)	75.4 (21.4)	83.3 (-)
Median (Q1; Q3)	75.0 (66.7; 95.8)	83.3 (83.3; 83.3)
Min; Max	33.3; 100.0	83.3; 83.3
Week 39		
Nd	14	0
Mean (SD)	77.4 (23.4)	- (-)
Median (Q1; Q3)	79.2 (66.7; 100.0)	- (-; -)
Min; Max	33.3; 100.0	-; -
Week 42		
Nd	10	4
Mean (SD)	75.0 (20.4)	83.3 (13.6)
Median (Q1; Q3)	75.0 (66.7; 91.7)	83.3 (75.0; 91.7)
Min; Max	33.3; 100.0	66.7; 100.0
Week 45		
Nd	14	3
Mean (SD)	77.4 (20.8)	66.7 (8.3)
Median (Q1; Q3)	79.2 (58.3; 100.0)	66.7 (58.3; 75.0)
Min; Max	41.7; 100.0	58.3; 75.0

Descriptive Summary of EORTC QLQ-C30 Emotional Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Emotional Functioning	Study: KEYNOTE-483 Phase 3a	
	Pembrolizumab + Chemotherapyb Nc=45	**Chemotherapyb** Nc=47
Week 48		
Nd	13	2
Mean (SD)	75.0 (20.1)	79.2 (5.9)
Median (Q1; Q3)	66.7 (66.7; 100.0)	79.2 (75.0; 83.3)
Min; Max	33.3; 100.0	75.0; 83.3
Week 51		
Nd	12	0
Mean (SD)	82.6 (15.7)	- (-)
Median (Q1; Q3)	83.3 (66.7; 100.0)	- (-; -)
Min; Max	58.3; 100.0	-; -
Week 54		
Nd	10	0
Mean (SD)	81.7 (16.6)	- (-)
Median (Q1; Q3)	83.3 (66.7; 100.0)	- (-; -)
Min; Max	58.3; 100.0	-; -

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

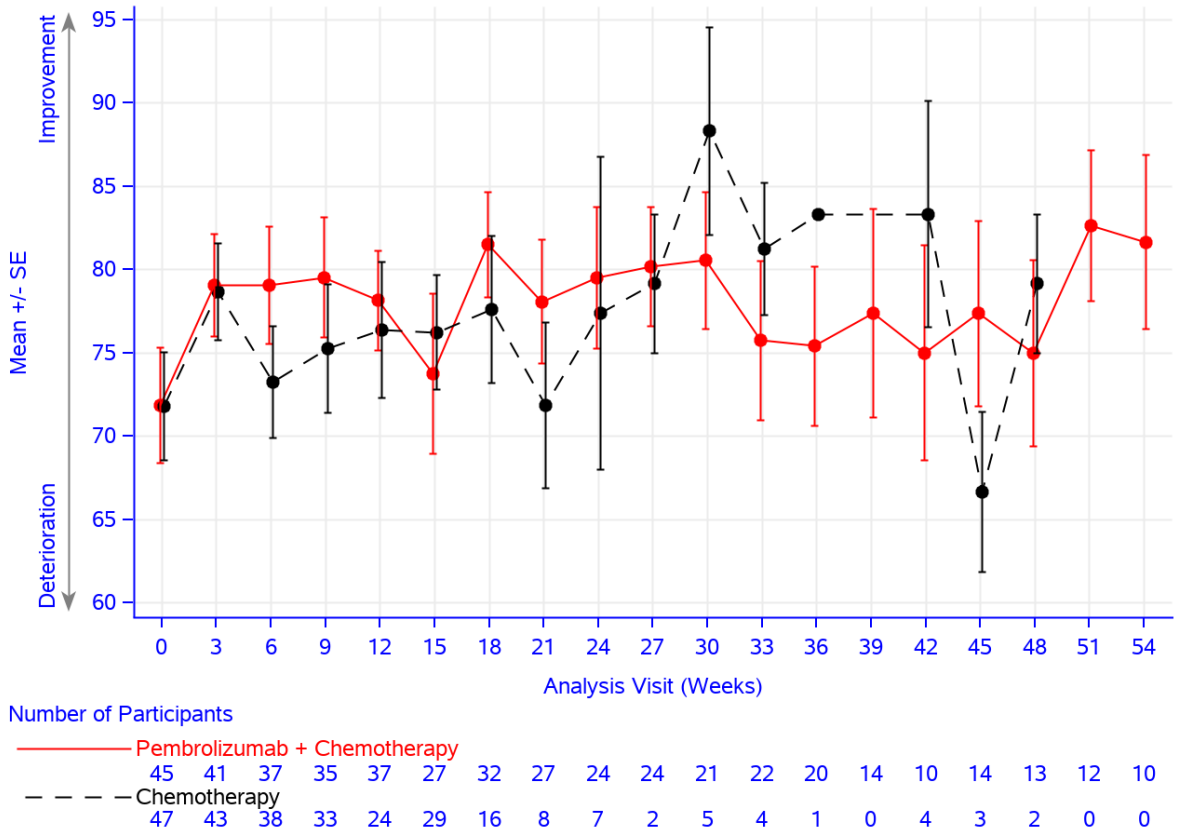
c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-22

Empirical Mean +/- SE of EORTC QLQ-C30 Emotional Functioning Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Emotional Functioning

4.1.3.5 Cognitive Functioning

Table 4.2-23
Descriptive Summary of EORTC QLQ-C30 Cognitive Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Cognitive Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	83.7 (20.9)	85.8 (18.1)
Median (Q1; Q3)	83.3 (83.3; 100.0)	83.3 (83.3; 100.0)
Min; Max	0.0; 100.0	16.7; 100.0
Week 3		
N[d]	41	43
Mean (SD)	84.6 (14.6)	89.9 (13.7)
Median (Q1; Q3)	83.3 (66.7; 100.0)	100.0 (83.3; 100.0)
Min; Max	50.0; 100.0	50.0; 100.0
Week 6		
N[d]	37	38
Mean (SD)	82.4 (20.4)	84.2 (19.7)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (83.3; 100.0)
Min; Max	16.7; 100.0	16.7; 100.0
Week 9		
N[d]	35	33
Mean (SD)	81.9 (19.5)	86.4 (19.3)
Median (Q1; Q3)	83.3 (66.7; 100.0)	100.0 (66.7; 100.0)
Min; Max	33.3; 100.0	33.3; 100.0
Week 12		
N[d]	37	24
Mean (SD)	82.0 (19.4)	86.8 (16.3)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (83.3; 100.0)
Min; Max	33.3; 100.0	33.3; 100.0
Week 15		
N[d]	27	29
Mean (SD)	82.7 (23.3)	87.4 (17.6)
Median (Q1; Q3)	100.0 (66.7; 100.0)	100.0 (83.3; 100.0)
Min; Max	16.7; 100.0	33.3; 100.0
Week 18		
N[d]	32	16
Mean (SD)	80.2 (23.4)	86.5 (19.5)
Median (Q1; Q3)	91.7 (66.7; 100.0)	100.0 (75.0; 100.0)
Min; Max	33.3; 100.0	33.3; 100.0
Week 21		
N[d]	27	8
Mean (SD)	85.2 (18.7)	91.7 (12.6)
Median (Q1; Q3)	100.0 (66.7; 100.0)	100.0 (83.3; 100.0)
Min; Max	33.3; 100.0	66.7; 100.0

Descriptive Summary of EORTC QLQ-C30 Cognitive Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Cognitive Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	79.9 (22.0)	76.2 (23.3)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (66.7; 100.0)
Min; Max	16.7; 100.0	33.3; 100.0
Week 27		
N[d]	24	2
Mean (SD)	84.0 (17.4)	83.3 (0.0)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (83.3; 83.3)
Min; Max	50.0; 100.0	83.3; 83.3
Week 30		
N[d]	21	5
Mean (SD)	83.3 (21.1)	100.0 (0.0)
Median (Q1; Q3)	83.3 (66.7; 100.0)	100.0 (100.0; 100.0)
Min; Max	33.3; 100.0	100.0; 100.0
Week 33		
N[d]	22	4
Mean (SD)	78.8 (20.7)	79.2 (8.3)
Median (Q1; Q3)	75.0 (66.7; 100.0)	83.3 (75.0; 83.3)
Min; Max	33.3; 100.0	66.7; 83.3
Week 36		
N[d]	20	1
Mean (SD)	76.7 (22.6)	50.0 (-)
Median (Q1; Q3)	83.3 (66.7; 100.0)	50.0 (50.0; 50.0)
Min; Max	33.3; 100.0	50.0; 50.0
Week 39		
N[d]	14	0
Mean (SD)	85.7 (18.3)	- (-)
Median (Q1; Q3)	100.0 (66.7; 100.0)	- (-; -)
Min; Max	50.0; 100.0	-; -
Week 42		
N[d]	10	4
Mean (SD)	78.3 (26.1)	83.3 (13.6)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (75.0; 91.7)
Min; Max	16.7; 100.0	66.7; 100.0
Week 45		
N[d]	14	3
Mean (SD)	83.3 (19.6)	72.2 (9.6)
Median (Q1; Q3)	91.7 (66.7; 100.0)	66.7 (66.7; 83.3)
Min; Max	50.0; 100.0	66.7; 83.3

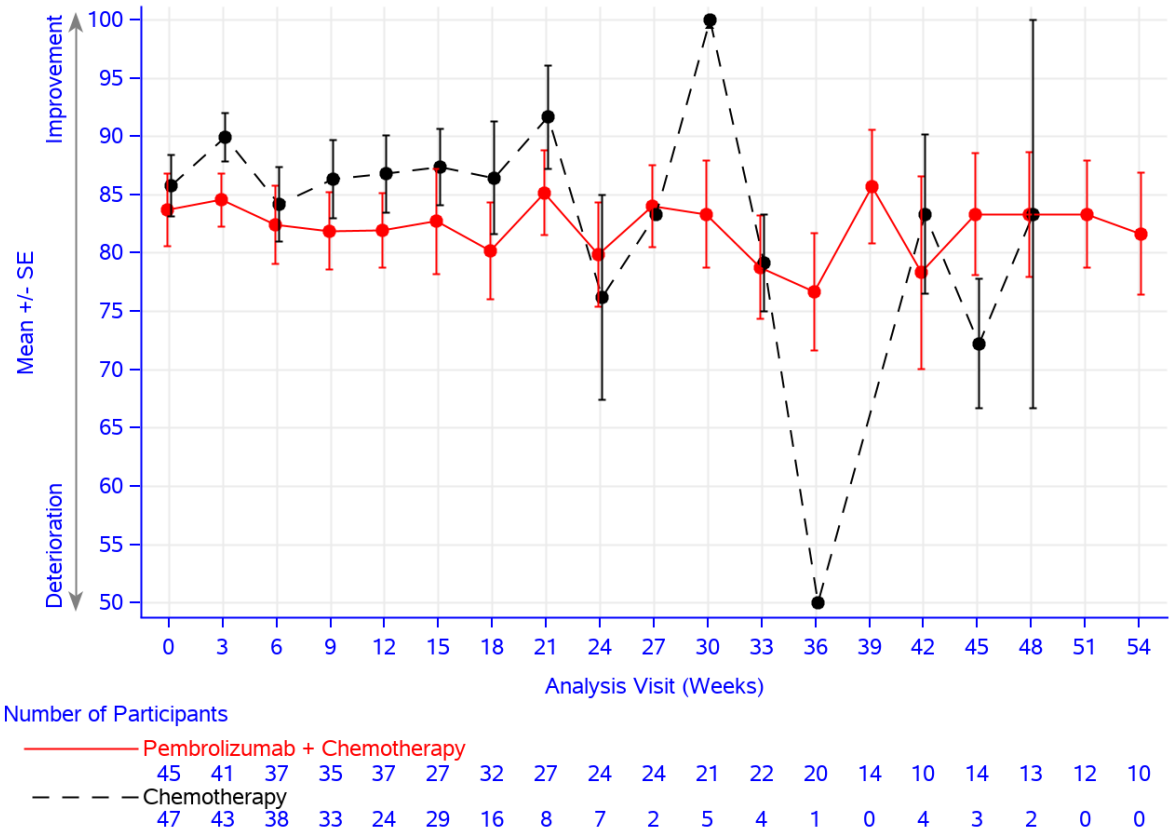
Descriptive Summary of EORTC QLQ-C30 Cognitive Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Cognitive Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	83.3 (19.2)	83.3 (23.6)
Median (Q1; Q3)	100.0 (66.7; 100.0)	83.3 (66.7; 100.0)
Min; Max	50.0; 100.0	66.7; 100.0
Week 51		
N[d]	12	0
Mean (SD)	83.3 (15.9)	- (-)
Median (Q1; Q3)	83.3 (66.7; 100.0)	- (-; -)
Min; Max	66.7; 100.0	-; -
Week 54		
N[d]	10	0
Mean (SD)	81.7 (16.6)	- (-)
Median (Q1; Q3)	75.0 (66.7; 100.0)	- (-; -)
Min; Max	66.7; 100.0	-; -

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3, non-epithelioid
d: Number of observations at each time point
CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-23

Empirical Mean +/- SE of EORTC QLQ-C30 Cognitive Functioning Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Cognitive Functioning

4.1.3.6 Social Functioning

Table 4.2-24
Descriptive Summary of EORTC QLQ-C30 Social Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Social Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Baseline		
N[d]	45	47
Mean (SD)	78.1 (25.8)	75.2 (27.6)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (66.7; 100.0)
Min; Max	0.0; 100.0	0.0; 100.0
Week 3		
N[d]	41	43
Mean (SD)	74.0 (24.7)	79.8 (22.0)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (66.7; 100.0)
Min; Max	0.0; 100.0	0.0; 100.0
Week 6		
N[d]	37	37
Mean (SD)	76.6 (25.6)	76.1 (23.7)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (66.7; 100.0)
Min; Max	33.3; 100.0	16.7; 100.0
Week 9		
N[d]	35	33
Mean (SD)	78.1 (22.1)	73.2 (27.6)
Median (Q1; Q3)	83.3 (66.7; 100.0)	66.7 (66.7; 100.0)
Min; Max	33.3; 100.0	0.0; 100.0
Week 12		
N[d]	37	24
Mean (SD)	78.8 (22.1)	76.4 (23.5)
Median (Q1; Q3)	83.3 (66.7; 100.0)	75.0 (66.7; 100.0)
Min; Max	0.0; 100.0	16.7; 100.0
Week 15		
N[d]	27	29
Mean (SD)	77.8 (24.9)	77.6 (24.1)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (66.7; 100.0)
Min; Max	16.7; 100.0	16.7; 100.0
Week 18		
N[d]	32	16
Mean (SD)	73.4 (29.3)	77.1 (27.1)
Median (Q1; Q3)	83.3 (50.0; 100.0)	83.3 (66.7; 100.0)
Min; Max	0.0; 100.0	16.7; 100.0
Week 21		
N[d]	27	8
Mean (SD)	77.2 (26.6)	75.0 (28.2)
Median (Q1; Q3)	83.3 (66.7; 100.0)	83.3 (50.0; 100.0)
Min; Max	0.0; 100.0	33.3; 100.0

Descriptive Summary of EORTC QLQ-C30 Social Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Social Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 24		
N[d]	24	7
Mean (SD)	76.4 (26.9)	81.0 (31.1)
Median (Q1; Q3)	66.7 (66.7; 100.0)	100.0 (66.7; 100.0)
Min; Max	0.0; 100.0	16.7; 100.0
Week 27		
N[d]	24	2
Mean (SD)	79.2 (23.7)	66.7 (0.0)
Median (Q1; Q3)	91.7 (66.7; 100.0)	66.7 (66.7; 66.7)
Min; Max	33.3; 100.0	66.7; 66.7
Week 30		
N[d]	21	5
Mean (SD)	75.4 (27.7)	86.7 (18.3)
Median (Q1; Q3)	66.7 (66.7; 100.0)	100.0 (66.7; 100.0)
Min; Max	0.0; 100.0	66.7; 100.0
Week 33		
N[d]	22	4
Mean (SD)	78.8 (26.8)	91.7 (9.6)
Median (Q1; Q3)	91.7 (66.7; 100.0)	91.7 (83.3; 100.0)
Min; Max	0.0; 100.0	83.3; 100.0
Week 36		
N[d]	20	1
Mean (SD)	79.2 (27.5)	33.3 (-)
Median (Q1; Q3)	100.0 (66.7; 100.0)	33.3 (33.3; 33.3)
Min; Max	0.0; 100.0	33.3; 33.3
Week 39		
N[d]	14	0
Mean (SD)	76.2 (26.7)	- (-)
Median (Q1; Q3)	83.3 (50.0; 100.0)	- (-; -)
Min; Max	33.3; 100.0	-; -
Week 42		
N[d]	10	4
Mean (SD)	81.7 (21.4)	83.3 (23.6)
Median (Q1; Q3)	91.7 (66.7; 100.0)	91.7 (66.7; 100.0)
Min; Max	50.0; 100.0	50.0; 100.0
Week 45		
N[d]	14	3
Mean (SD)	78.6 (19.0)	83.3 (16.7)
Median (Q1; Q3)	75.0 (66.7; 100.0)	83.3 (66.7; 100.0)
Min; Max	50.0; 100.0	66.7; 100.0

Descriptive Summary of EORTC QLQ-C30 Social Functioning by Timepoint
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3)

EORTC QLQ-C30 Social Functioning	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c]=45	Chemotherapy[b] N[c]=47
Week 48		
N[d]	13	2
Mean (SD)	84.6 (20.9)	66.7 (0.0)
Median (Q1; Q3)	100.0 (66.7; 100.0)	66.7 (66.7; 66.7)
Min; Max	33.3; 100.0	66.7; 66.7
Week 51		
N[d]	12	0
Mean (SD)	81.9 (18.1)	- (-)
Median (Q1; Q3)	83.3 (66.7; 100.0)	- (-; -)
Min; Max	50.0; 100.0	-; -
Week 54		
N[d]	10	0
Mean (SD)	80.0 (18.9)	- (-)
Median (Q1; Q3)	75.0 (66.7; 100.0)	- (-; -)
Min; Max	50.0; 100.0	-; -

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

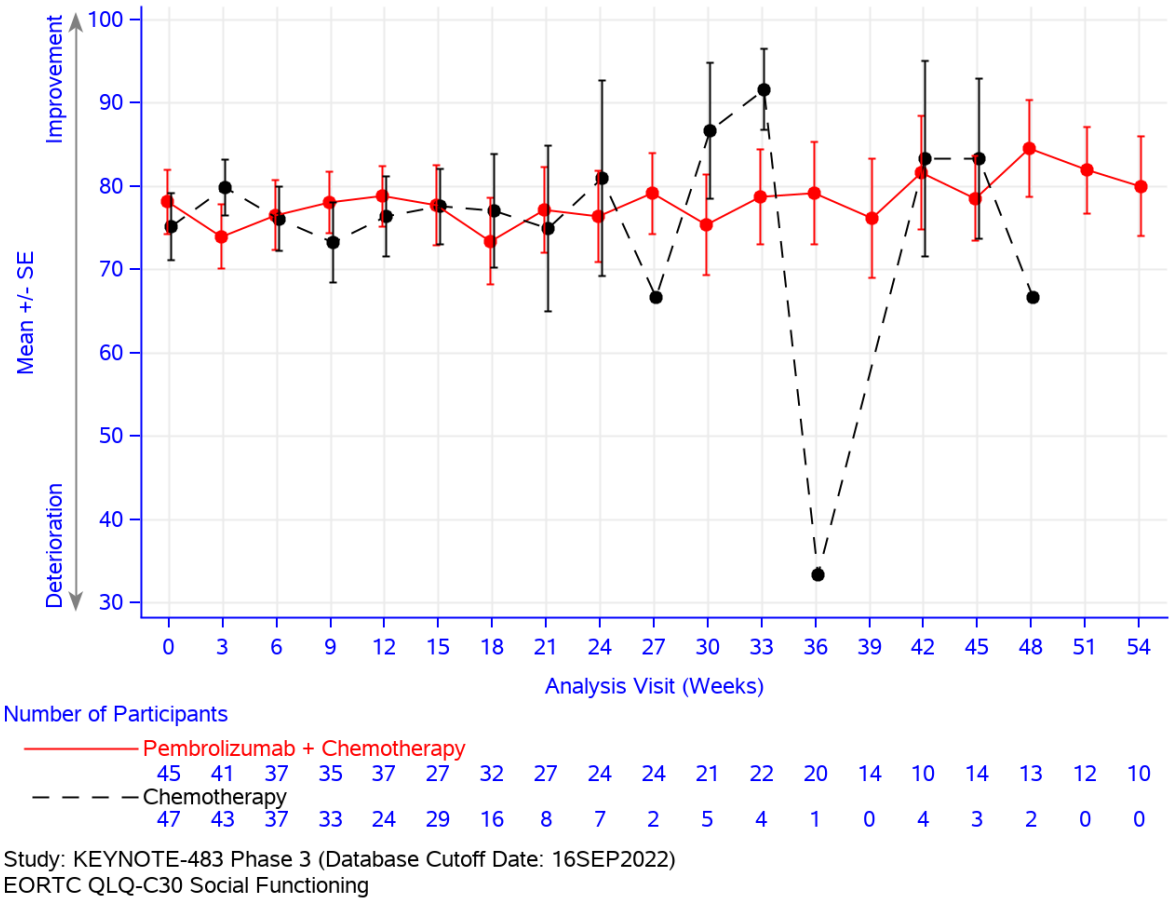
c: Number of participants: full-analysis-set, phase 3, non-epithelioid

d: Number of observations at each time point

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Figure 4.2-24

Empirical Mean +/- SE of EORTC QLQ-C30 Social Functioning Over Time by Treatment Group Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3)



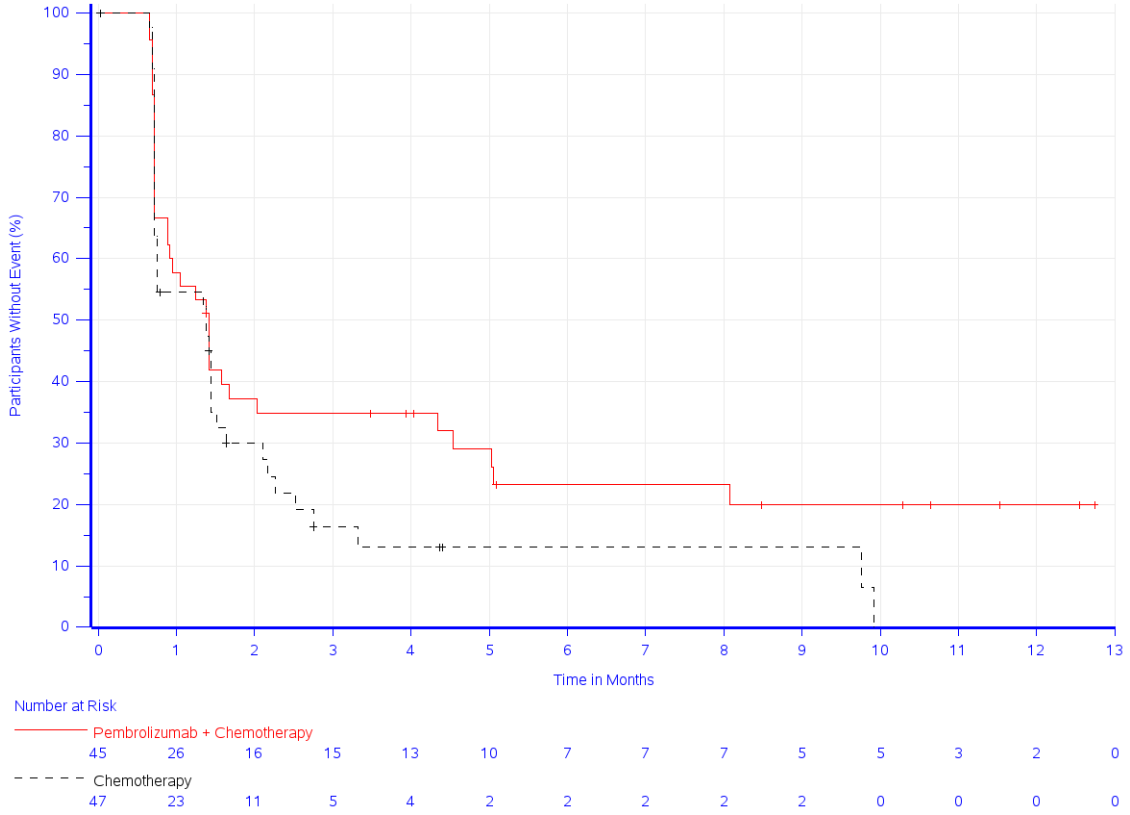
Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
EORTC QLQ-C30 Social Functioning

Anhang 4-G4: Analyse der Endpunktkategorien Krankheitssymptomatik und Gesundheitszustand und Gesundheitsbezogene Lebensqualität anhand von EORTC QLQ-C30, EORTC QLQ-LC13 und EQ-5D VAS – Kaplan-Meier-Kurven der statistisch nicht signifikanten (p ≥ 0,05) Symptom- und Funktionsskalen bzw. der EQ-5D VAS

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.1.2.2 und Abschnitt 4.3.1.3.1.3.1 die Kaplan-Meier-Kurven der nicht signifikanten (p ≥ 0,05) Symptom- und Funktionsskalen des EORTC QLQ-C30, EORTC QLQ-LC13 und der EQ-5D VAS dargestellt.

4.1.3.7 EORTC QLQ-C30 Fatigue

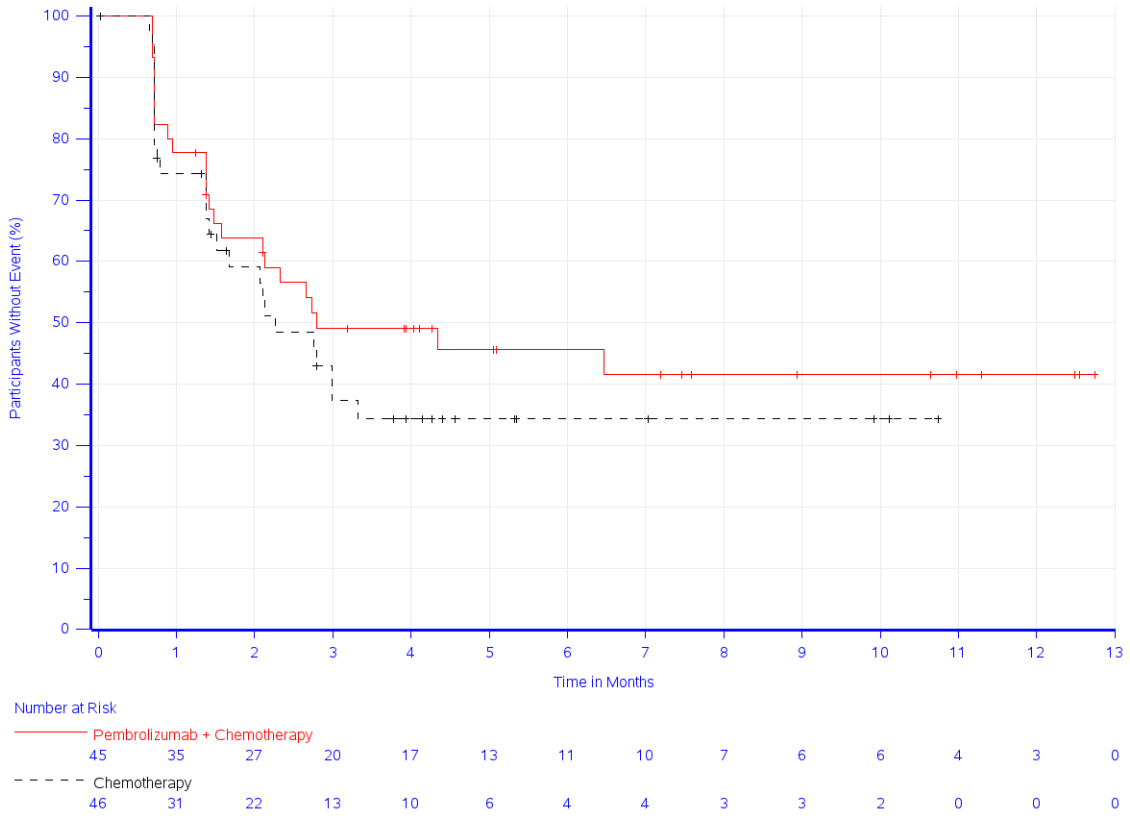
Figure 4.3-1
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Fatigue (10 Points)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Fatigue (10 Points)

4.1.3.8 EORTC QLQ-C30 Nausea and Vomiting

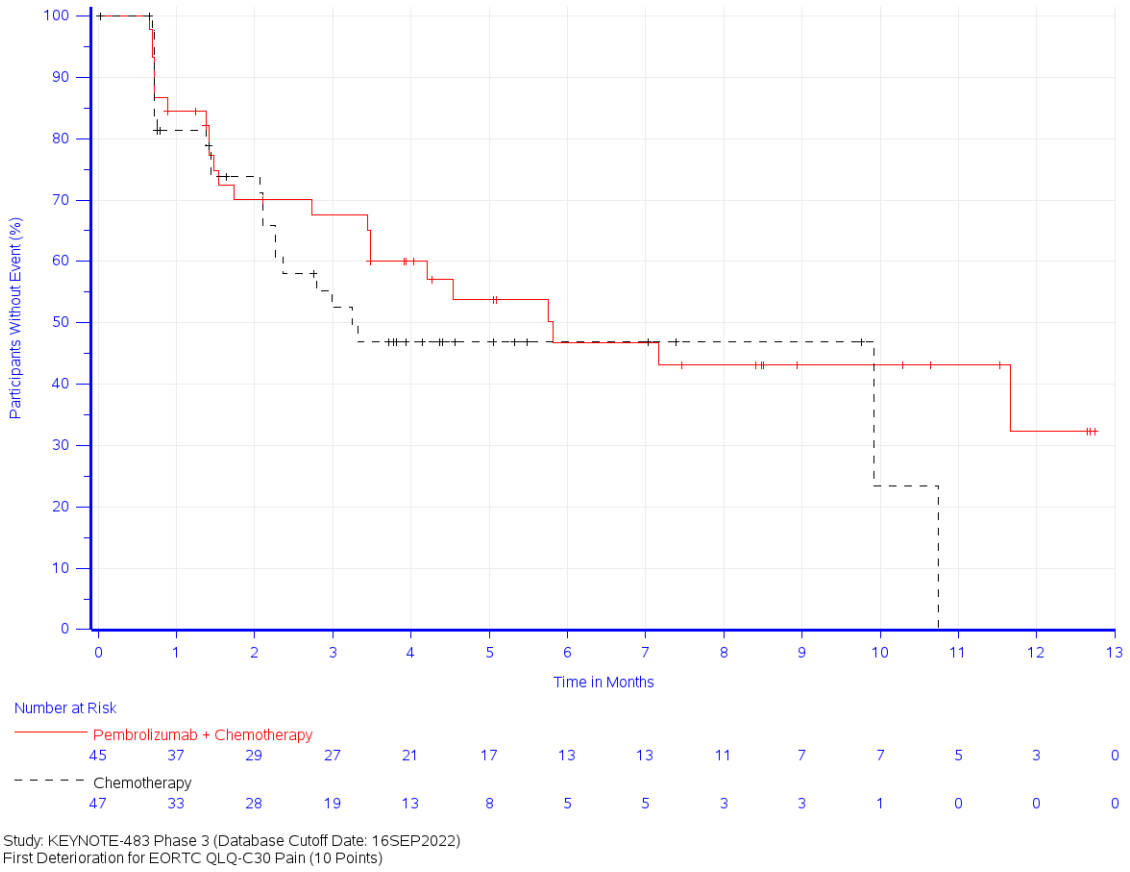
Figure 4.3-2
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Nausea and Vomiting (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Nausea and Vomiting (10 Points)

4.1.3.9 EORTC QLQ-C30 Pain

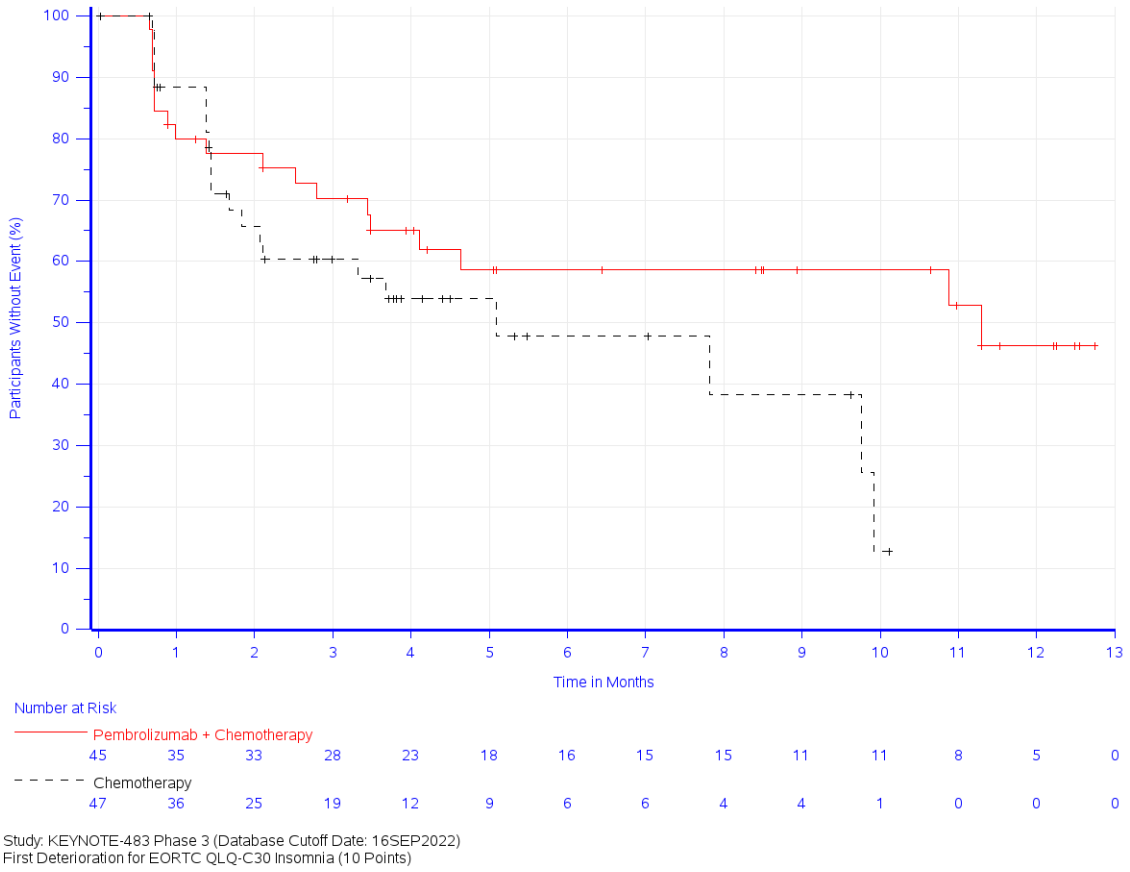
Figure 4.3-3
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Pain (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Pain (10 Points)

4.1.3.10 EORTC QLQ-C30 Insomnia

Figure 4.3-5
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Insomnia (10 Points)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

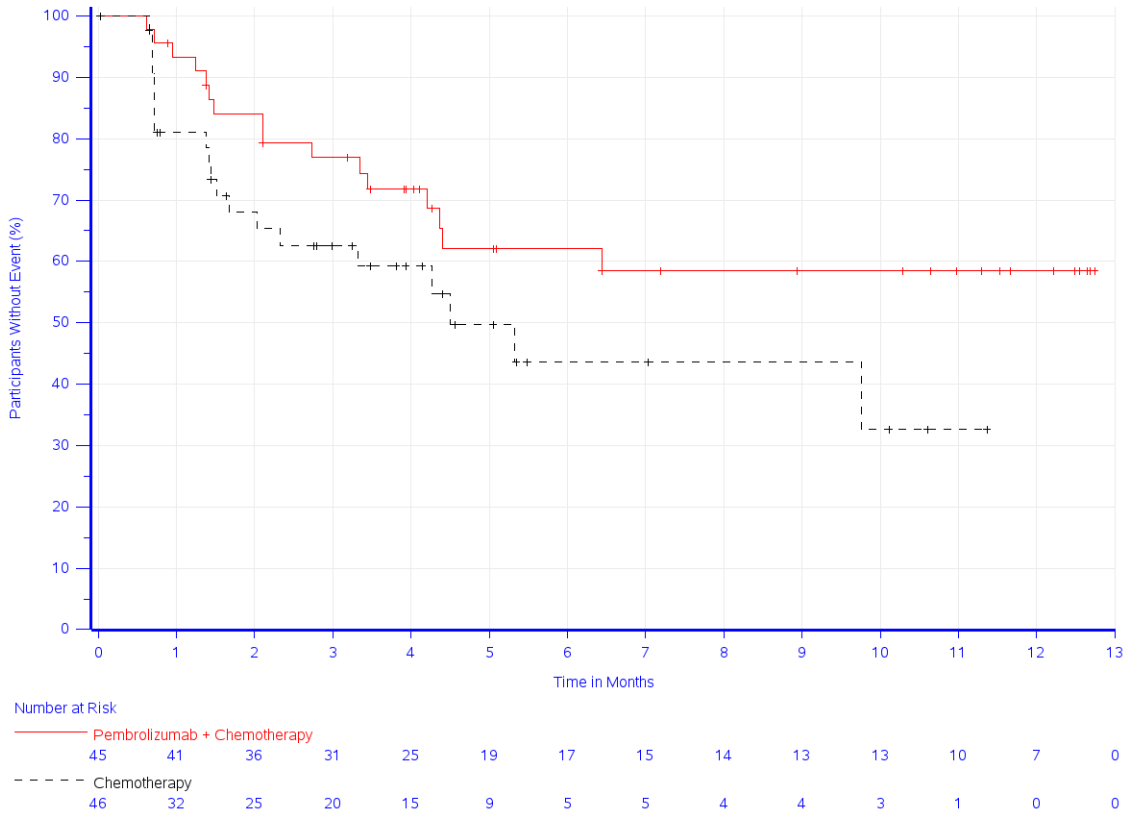


Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Insomnia (10 Points)

4.1.3.11 EORTC QLQ-C30 Appetite Loss

Figure 4.3-6

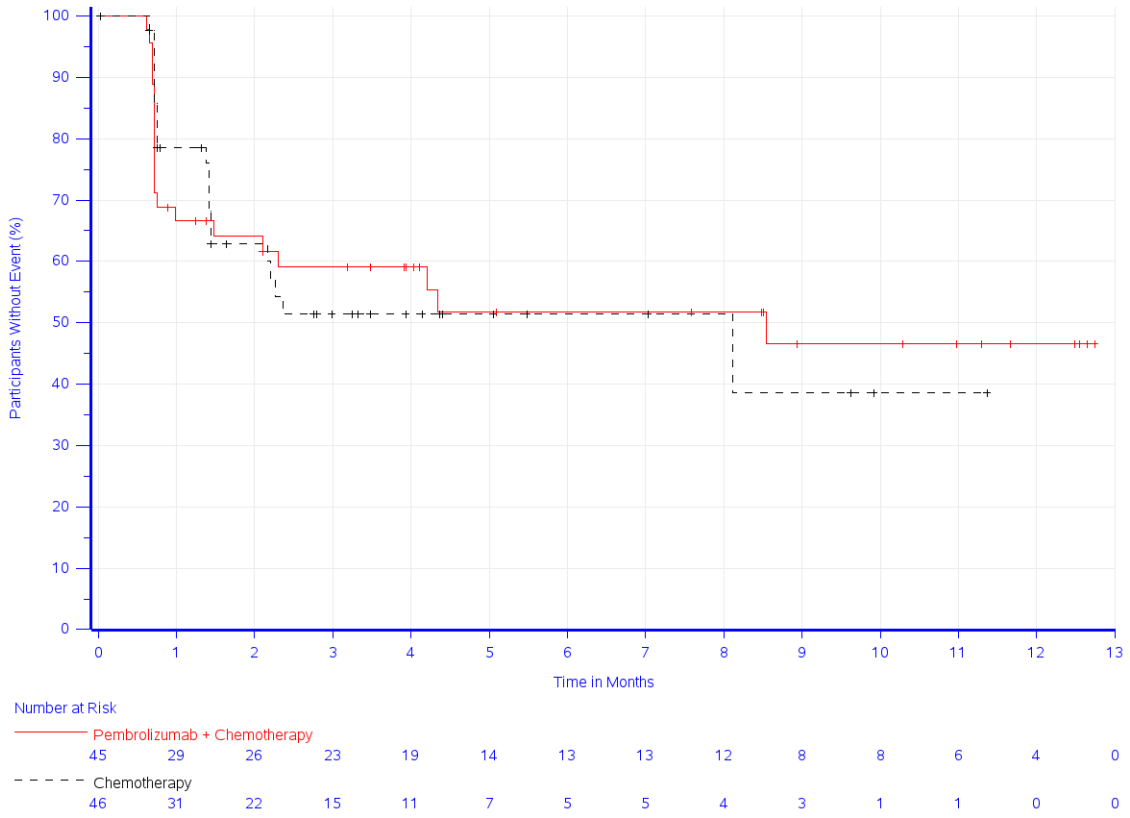
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Appetite Loss (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Appetite Loss (10 Points)

4.1.3.12 EORTC QLQ-C30 Constipation

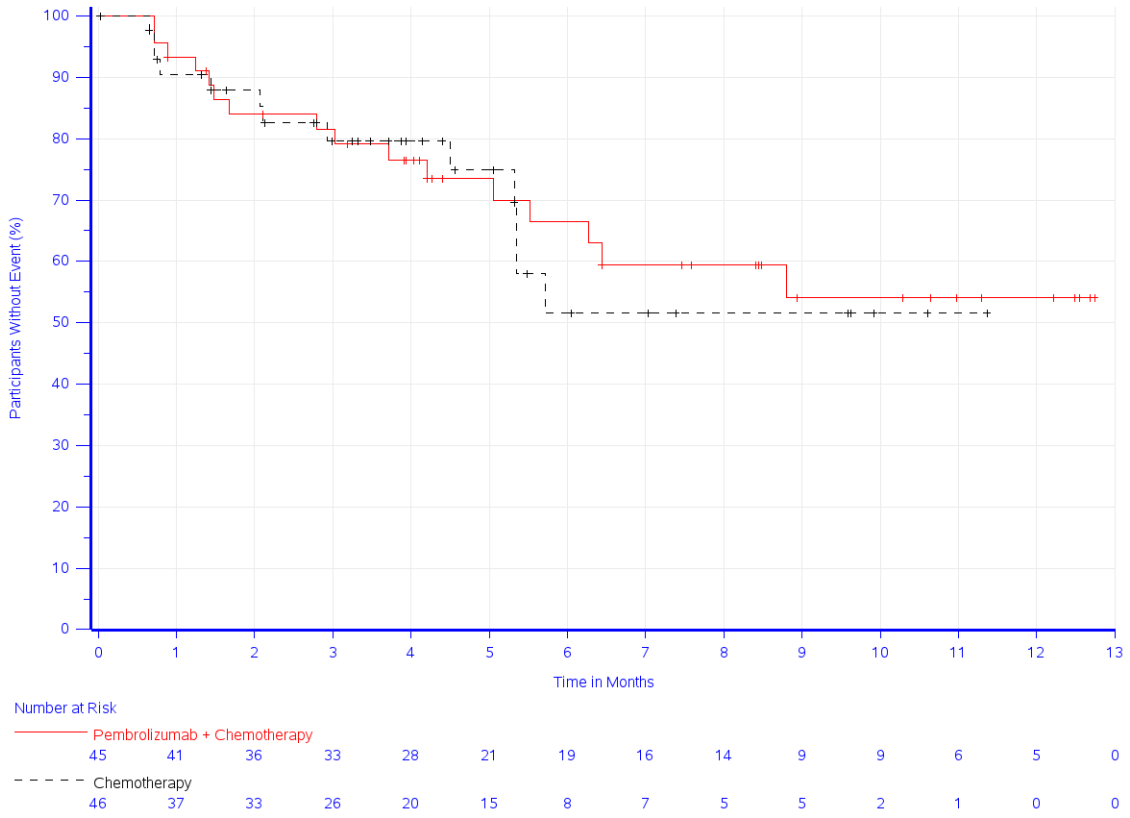
Figure 4.3-7
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Constipation (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Constipation (10 Points)

4.1.3.13 EORTC QLQ-C30 Diarrhoea

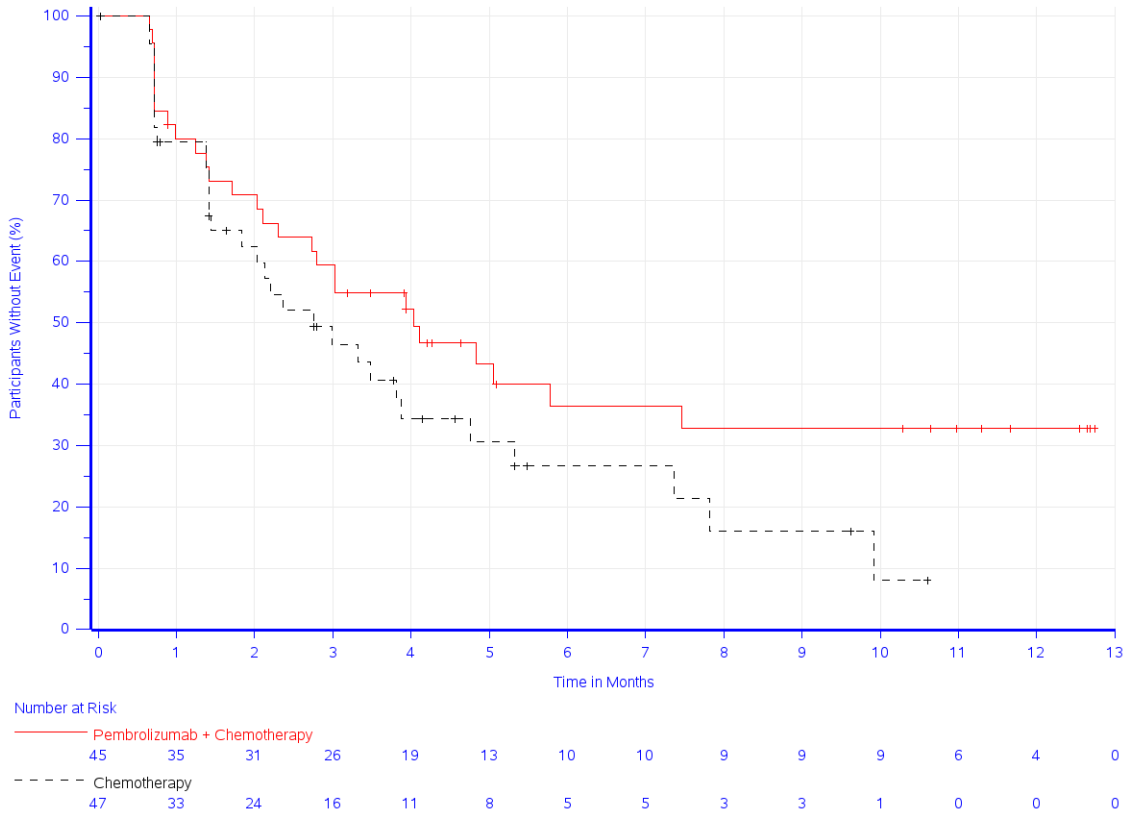
Figure 4.3-8
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Diarrhoea (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Diarrhoea (10 Points)

4.1.3.14 EORTC QLQ-LC13 Dyspnoea

Figure 4.3-9
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-LC13 Dyspnoea (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)

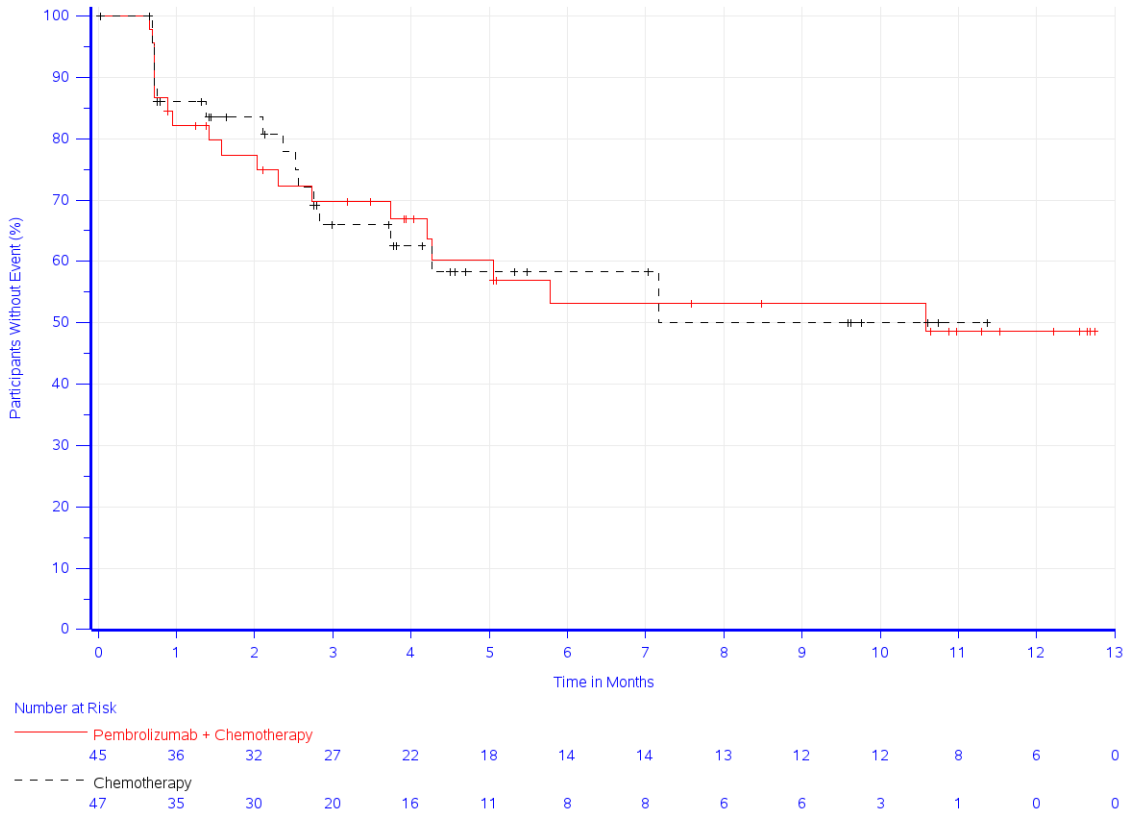


Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-LC13 Dyspnoea (10 Points)

4.1.3.15 EORTC QLQ-LC13 Coughing

Figure 4.3-10

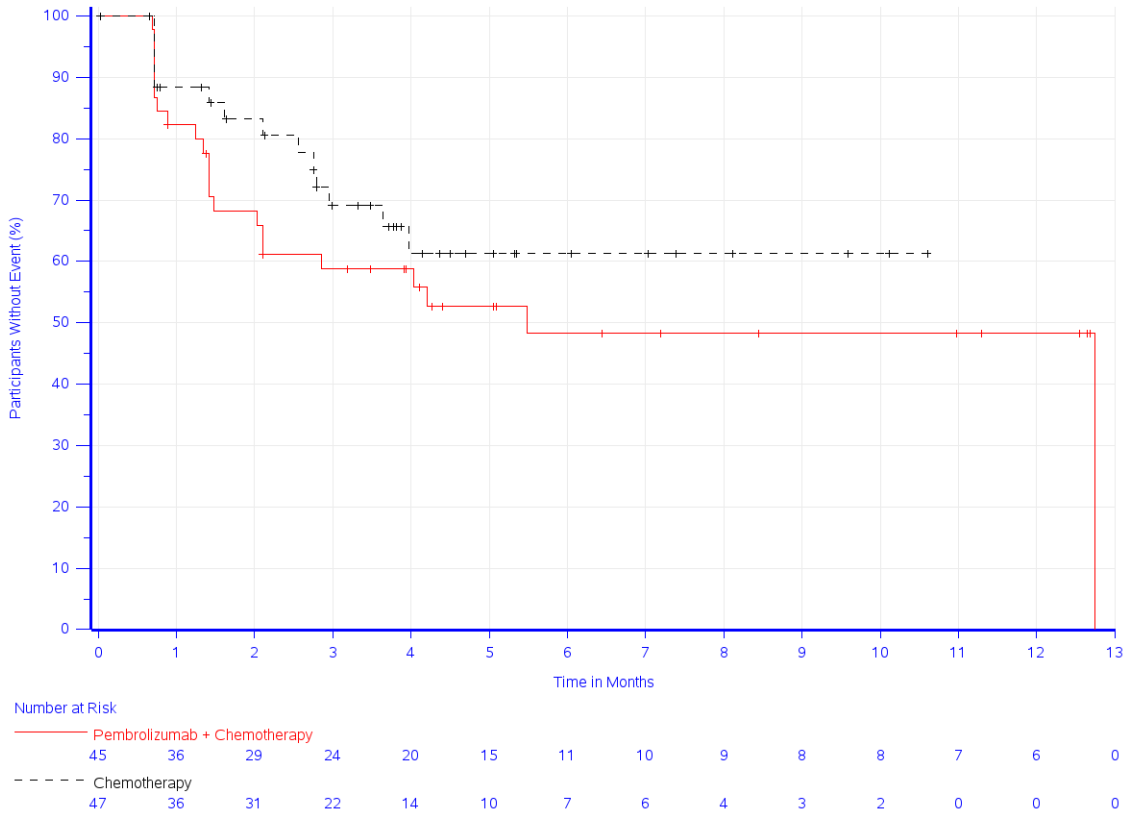
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-LC13 Coughing (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-LC13 Coughing (10 Points)

4.1.3.16 EORTC QLQ-LC1 Sore Mouth

Figure 4.3-12
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-LC13 Sore Mouth (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)

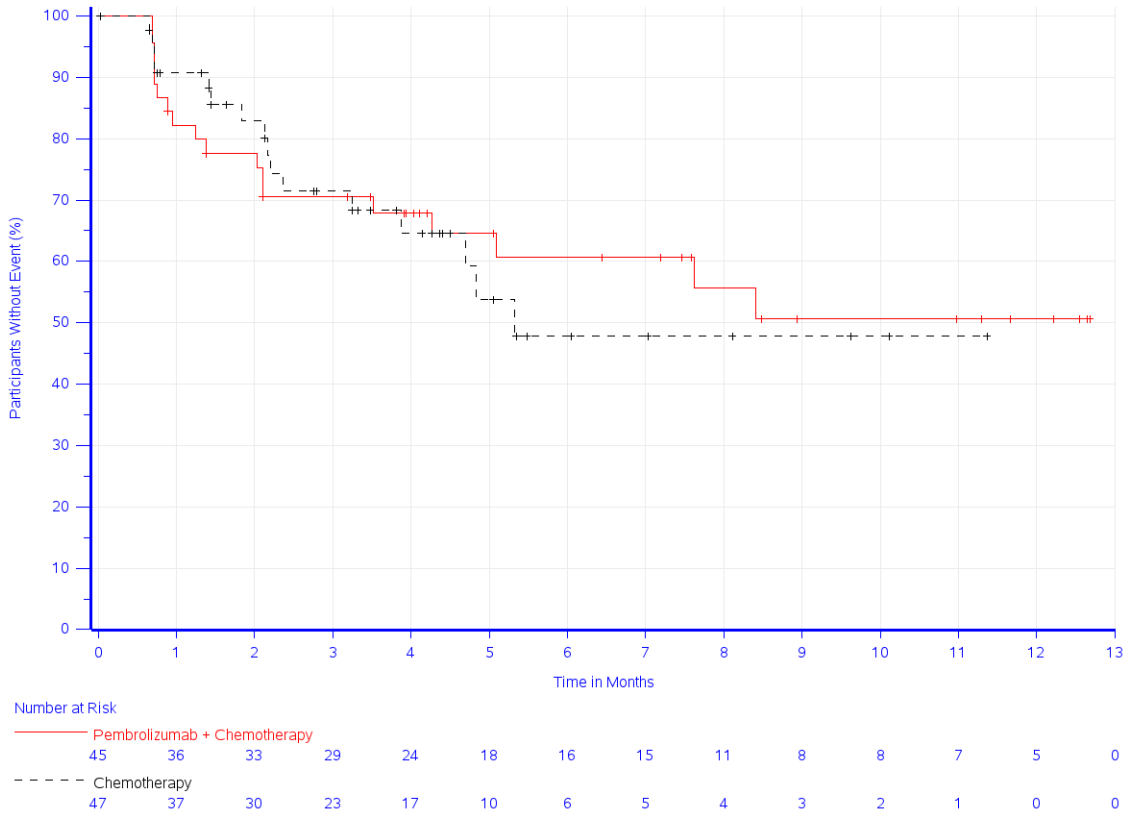


Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-LC13 Sore Mouth (10 Points)

4.1.3.17 EORTC QLQ-LC1 Dysphagia

Figure 4.3-13

Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-LC13 Dysphagia (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)

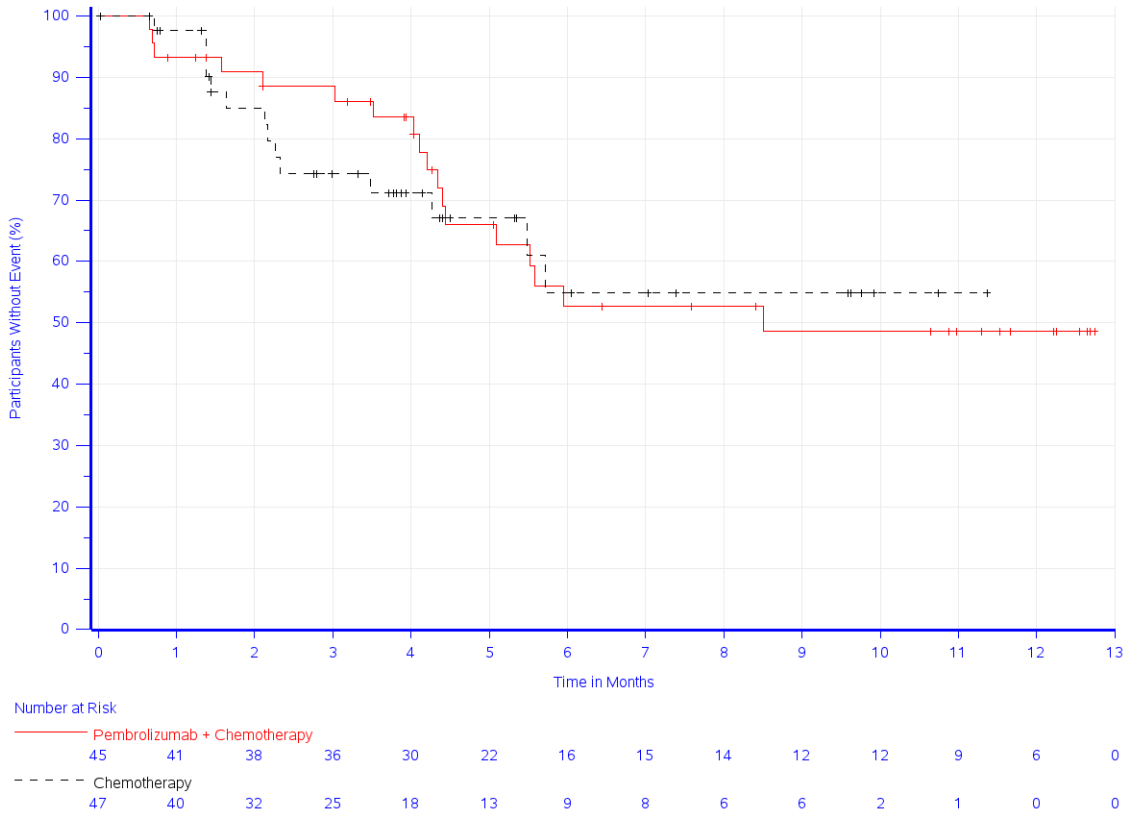


Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-LC13 Dysphagia (10 Points)

4.1.3.18 EORTC QLQ-LC1 Peripheral Neuropathy

Figure 4.3-14

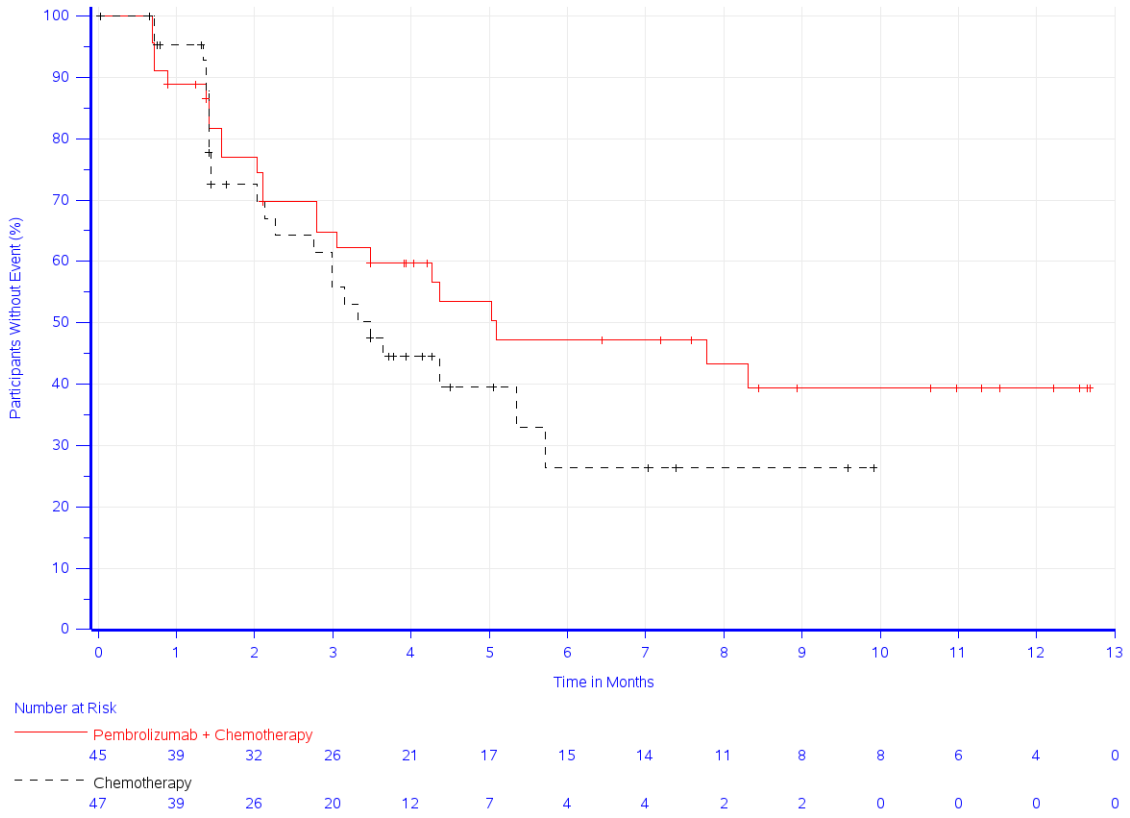
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-LC13 Peripheral Neuropathy (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-LC13 Peripheral Neuropathy (10 Points)

4.1.3.19 EORTC QLQ-LC1 Alopecia

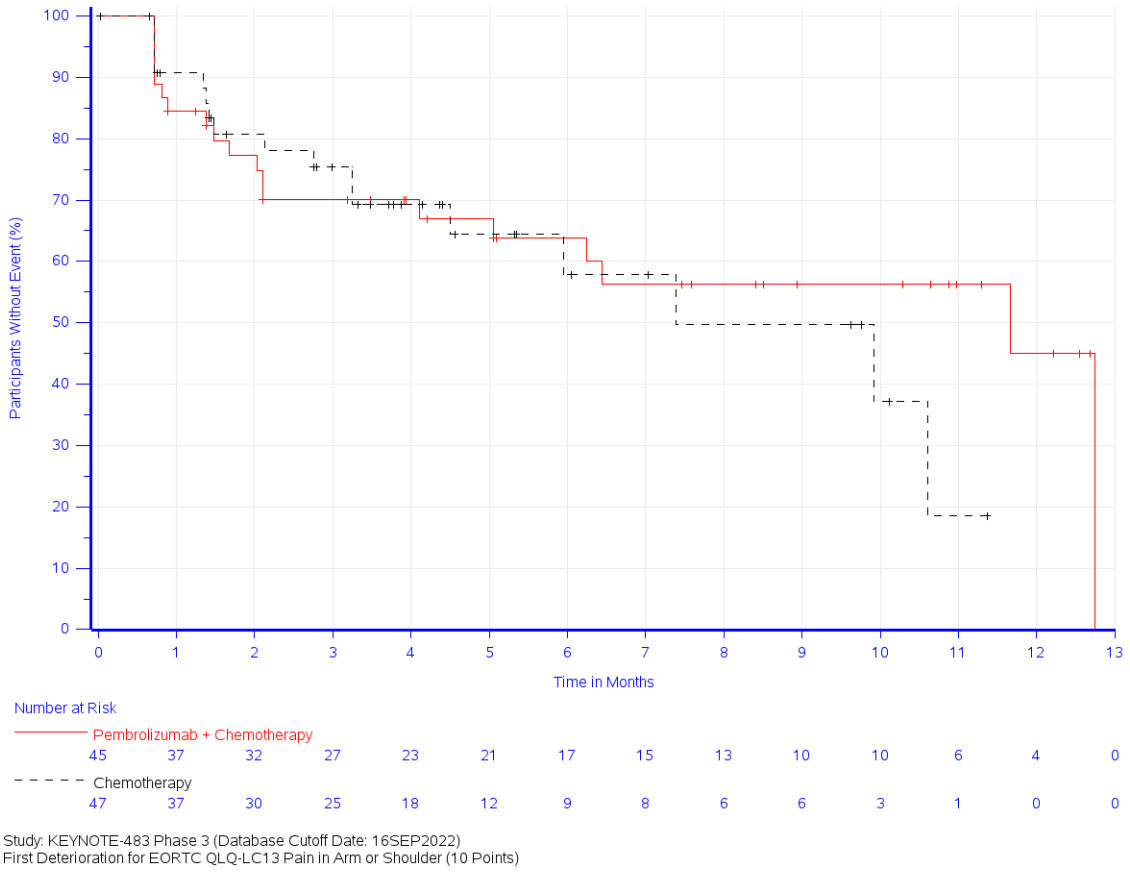
Figure 4.3-15
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-LC13 Alopecia (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-LC13 Alopecia (10 Points)

4.1.3.20 EORTC QLQ-LC1 Pain in Arm or Shoulders

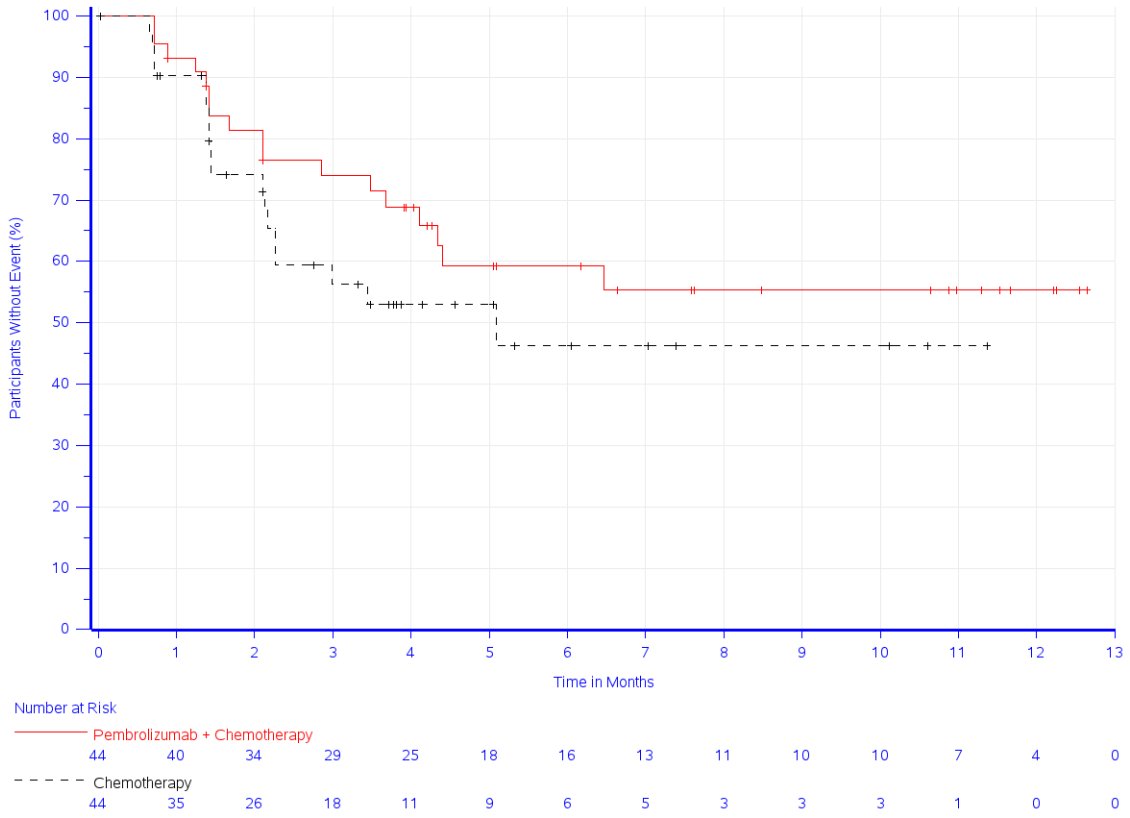
Figure 4.3-17
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-LC13 Pain in Arm or Shoulder (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-LC13 Pain in Arm or Shoulder (10 Points)

4.1.3.21 EORTC QLQ-LC13 Pain in Other Parts

Figure 4.3-18
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-LC13 Pain in Other Parts (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)

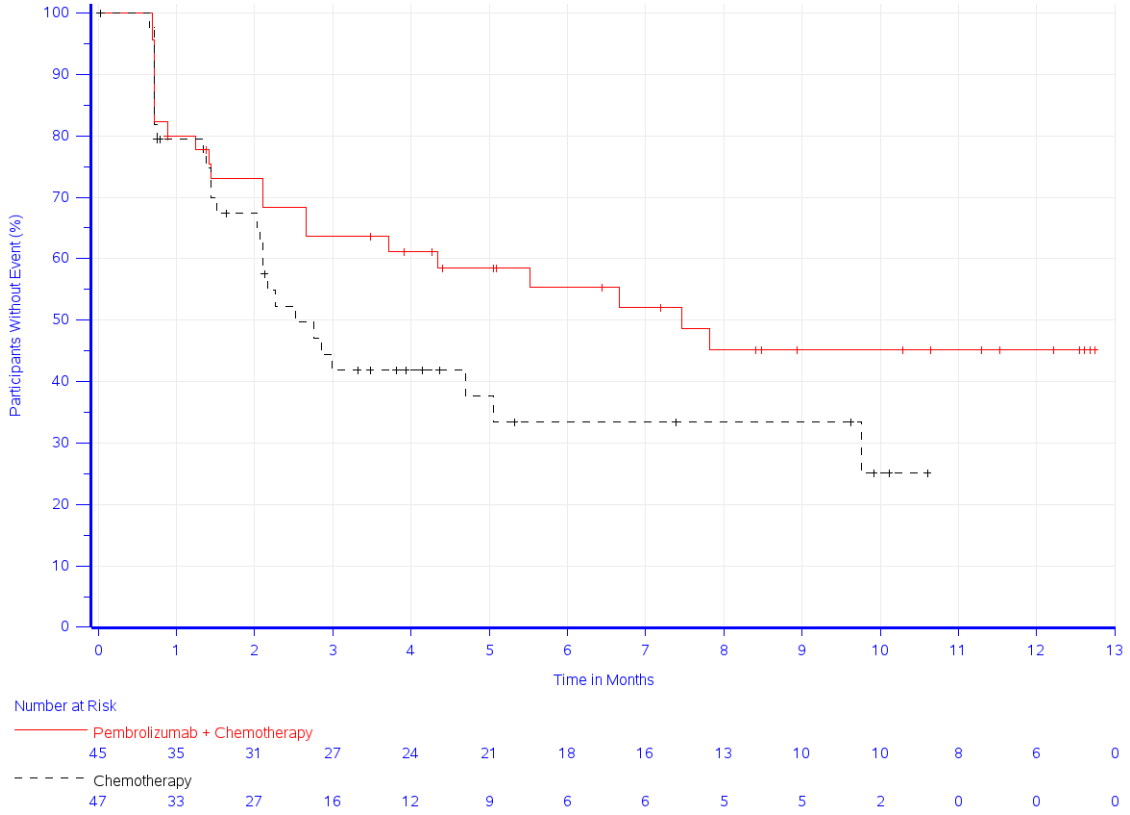


Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-LC13 Pain in Other Parts (10 Points)

4.1.3.22 EORTC QLQ-C30 Physical Functioning

Figure 4.4-2

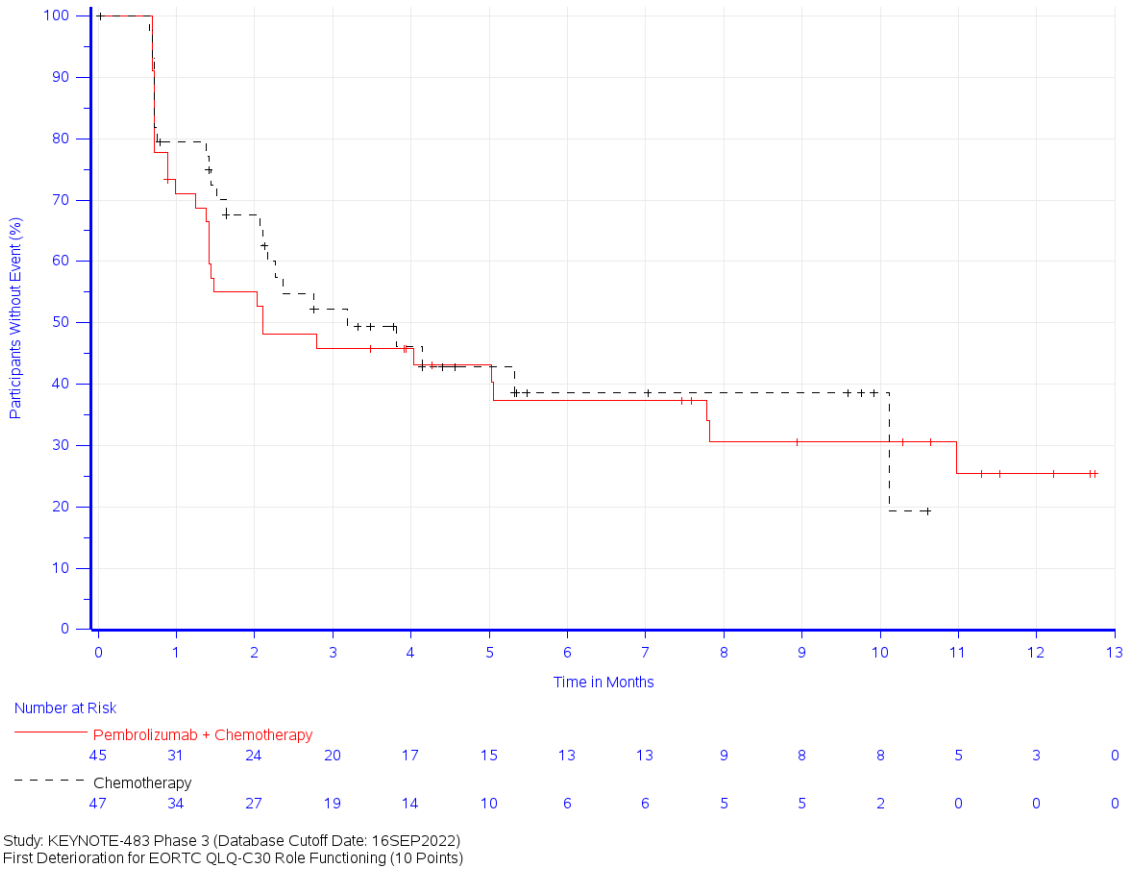
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Physical Functioning (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Physical Functioning (10 Points)

4.1.3.23 EORTC QLQ-C30 Role Functioning

Figure 4.4-3
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Role Functioning (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)

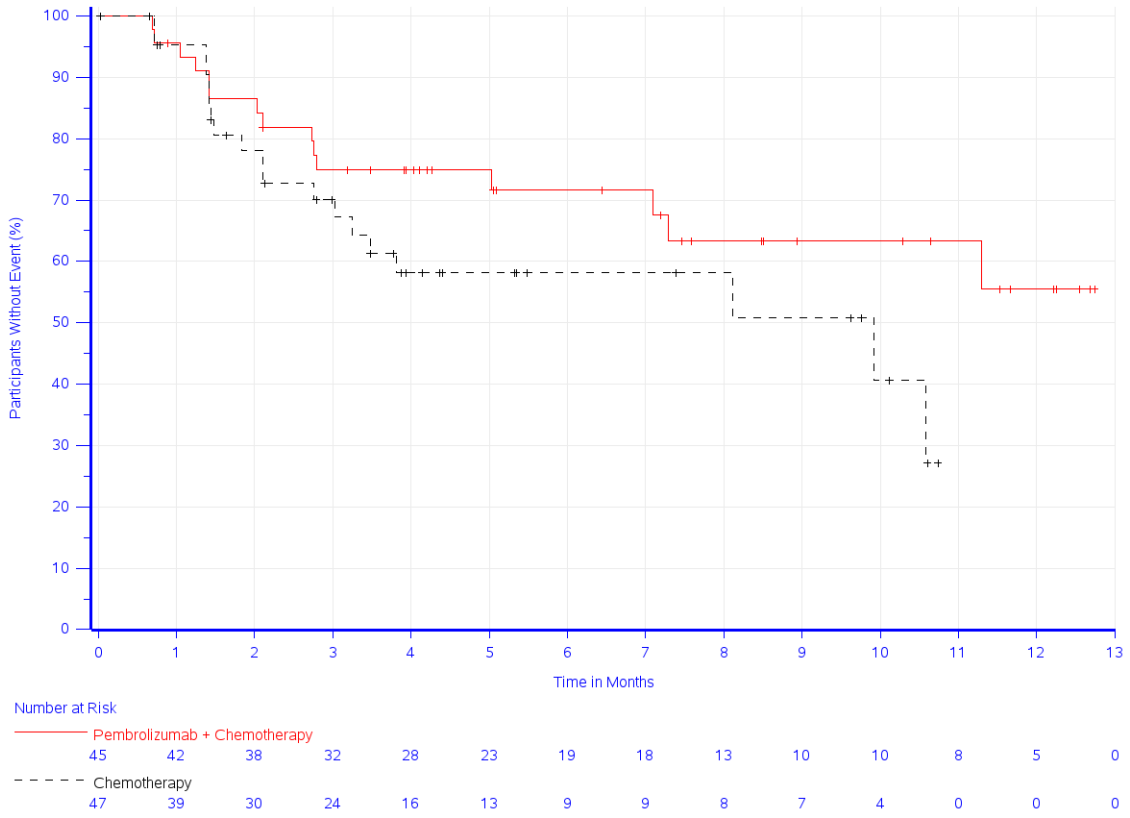


Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Role Functioning (10 Points)

4.1.3.24 EORTC QLQ-C30 Emotional Functioning

Figure 4.4-4

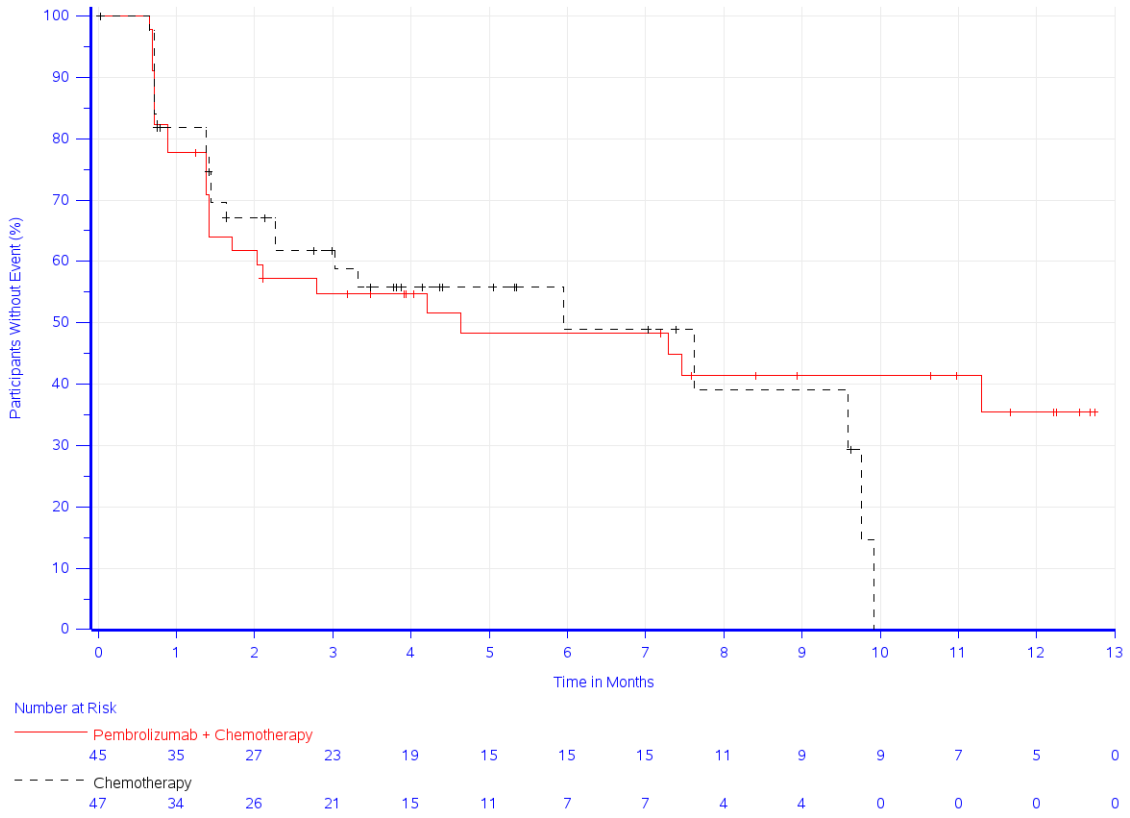
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Emotional Functioning (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Emotional Functioning (10 Points)

4.1.3.25 EORTC QLQ-C30 Cognitive Functioning

Figure 4.4-5
Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Cognitive Functioning (10 Points) Subpopulation of Participants, Non-epithelioid (Full-Analysis-Set Population, Phase 3 With Baseline)

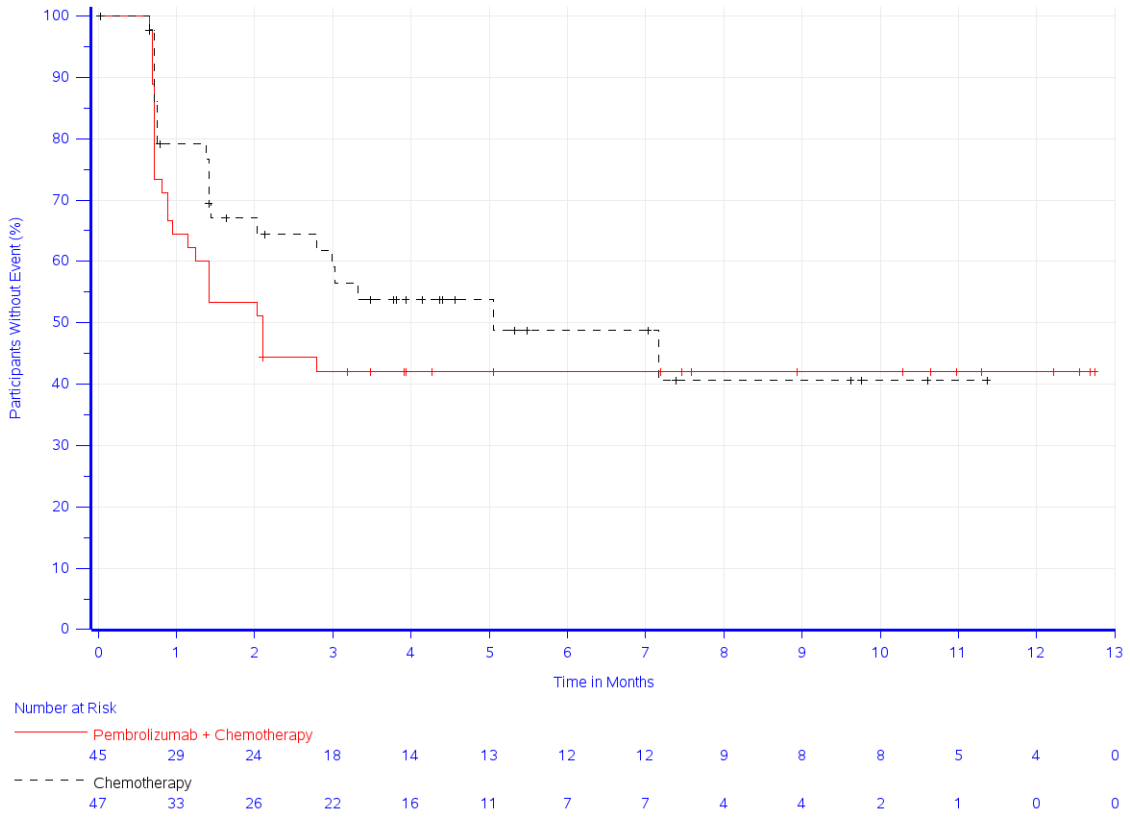


Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Cognitive Functioning (10 Points)

4.1.3.26 EORTC QLQ-C30 Social Functioning

Figure 4.4-6

Kaplan-Meier Curve of Time to First Deterioration for EORTC QLQ-C30 Social Functioning (10 Points)
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 (Database Cutoff Date: 16SEP2022)
First Deterioration for EORTC QLQ-C30 Social Functioning (10 Points)

Anhang 4-G5: Kaplan-Meier-Kurven der Subgruppen mit signifikantem Interaktionstest (p < 0,05)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.2 die Kaplan-Meier-Kurven der Subgruppenanalysen, für die ein signifikanter Interaktionstest (p < 0,05) vorliegt, dargestellt.

Anhang 4-G5.1: Mortalität

Keine vorhanden.

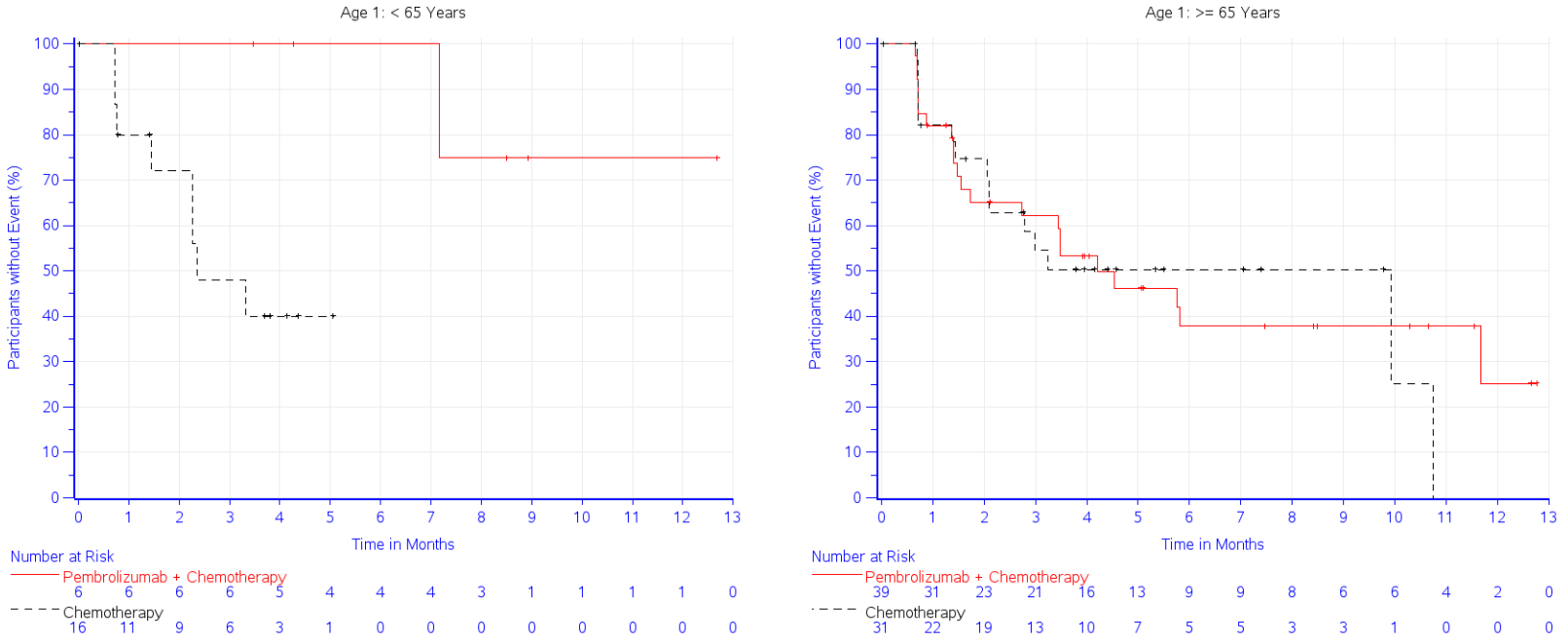
Anhang 4-G5.2: Morbidität

Progressionsfreies Überleben

Keine vorhanden

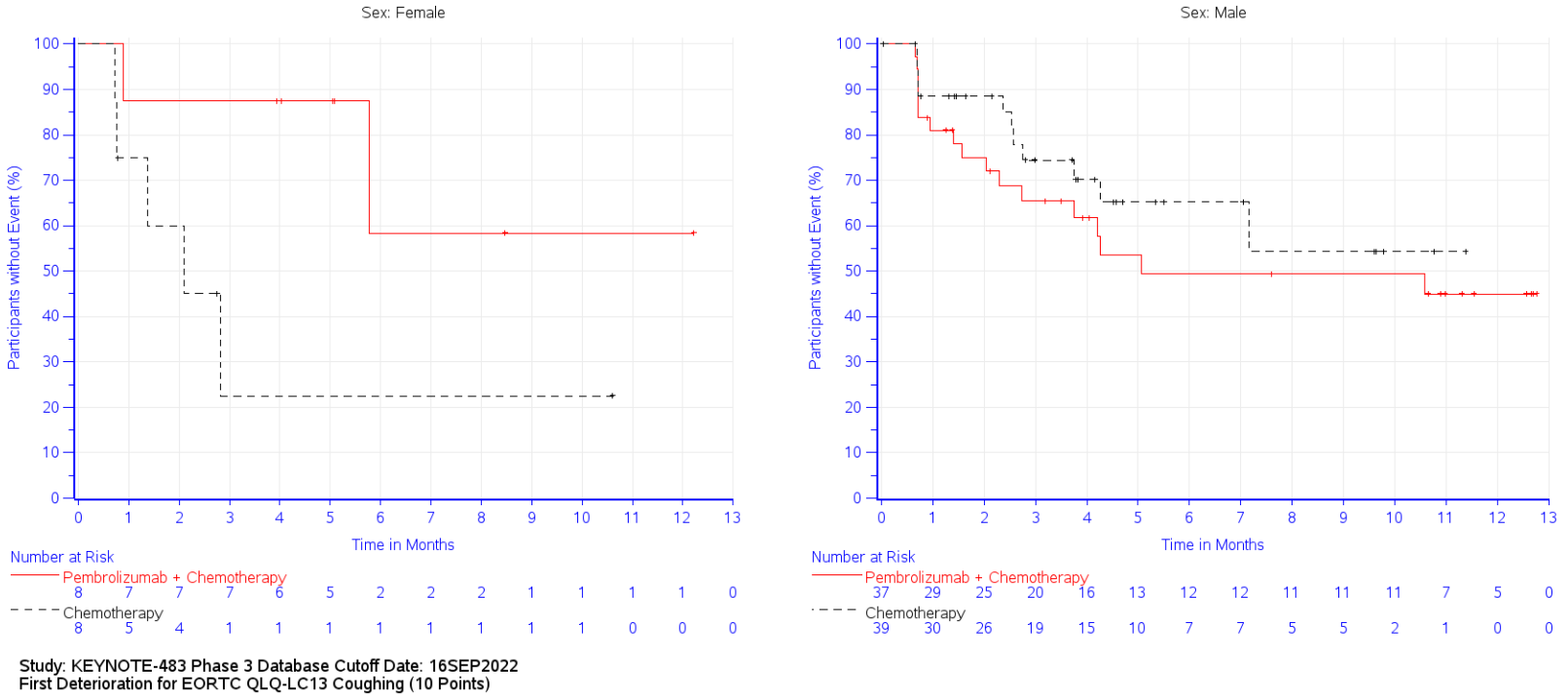
Figure 4.3-20

Kaplan-Meier Curves of Time to First Deterioration for EORTC QLQ-C30 Pain (10 Points) by Subgroups With p-Value for Interaction Test < 0.05
Age 1
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)



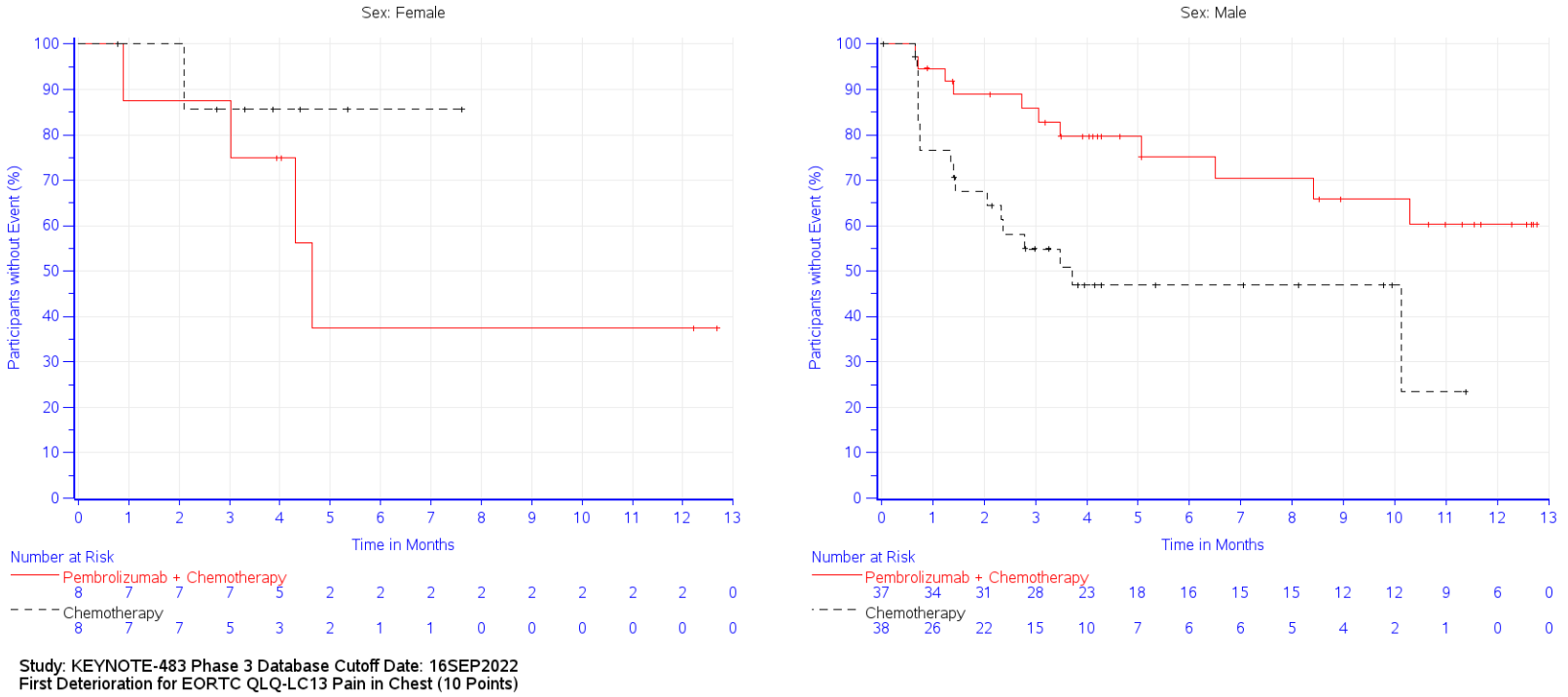
Study: KEYNOTE-483 Phase 3 Database Cutoff Date: 16SEP2022
First Deterioration for EORTC QLQ-C30 Pain (10 Points)

Figure 4.3-21
Kaplan-Meier Curves of Time to First Deterioration for EORTC QLQ-LC13 Coughing (10 Points) by Subgroups With p-Value for Interaction Test < 0.05
Sex
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 Database Cutoff Date: 16SEP2022
First Deterioration for EORTC QLQ-LC13 Coughing (10 Points)

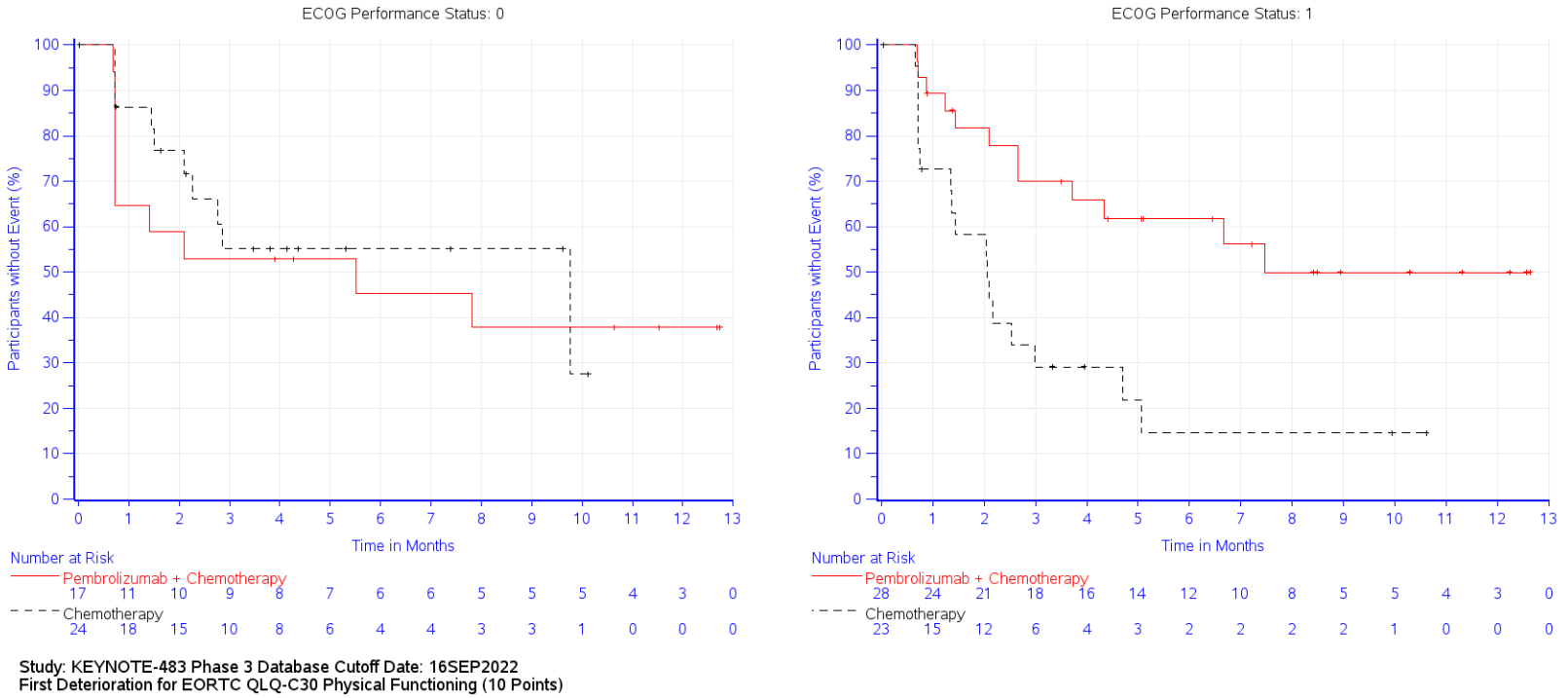
Figure 4.3-22
Kaplan-Meier Curves of Time to First Deterioration for EORTC QLQ-LC13 Pain in Chest (10 Points) by Subgroups With p-Value for Interaction Test < 0.05
Sex
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 Database Cutoff Date: 16SEP2022
First Deterioration for EORTC QLQ-LC13 Pain in Chest (10 Points)

Anhang 4-G5.3: Gesundheitsbezogene Lebensqualität

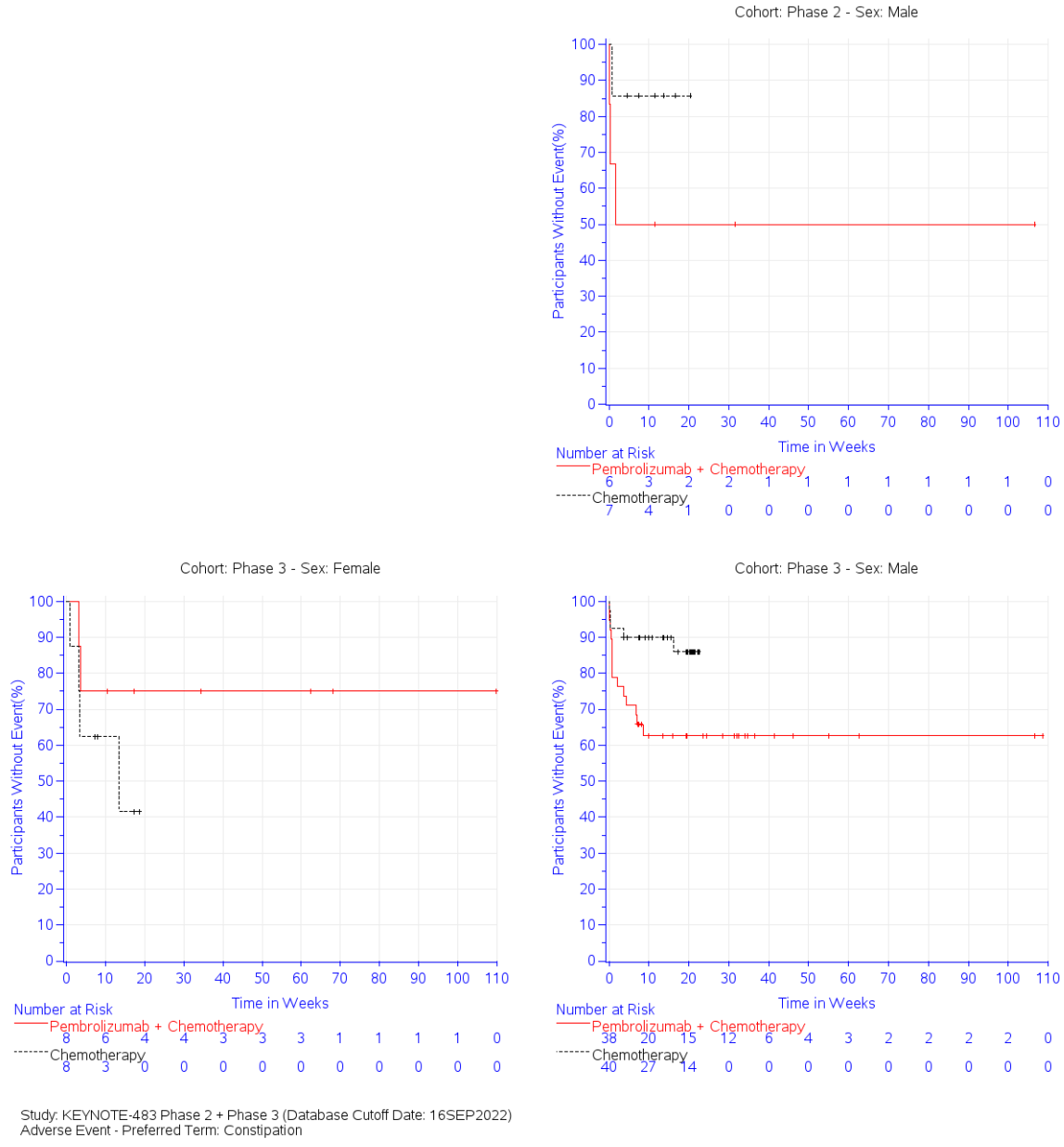
Figure 4.4-7
Kaplan-Meier Curves of Time to First Deterioration for EORTC QLQ-C30 Physical Functioning (10 Points) by Subgroups With p-Value for Interaction Test < 0.05
ECOG Performance Status
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)



Study: KEYNOTE-483 Phase 3 Database Cutoff Date: 16SEP2022
First Deterioration for EORTC QLQ-C30 Physical Functioning (10 Points)

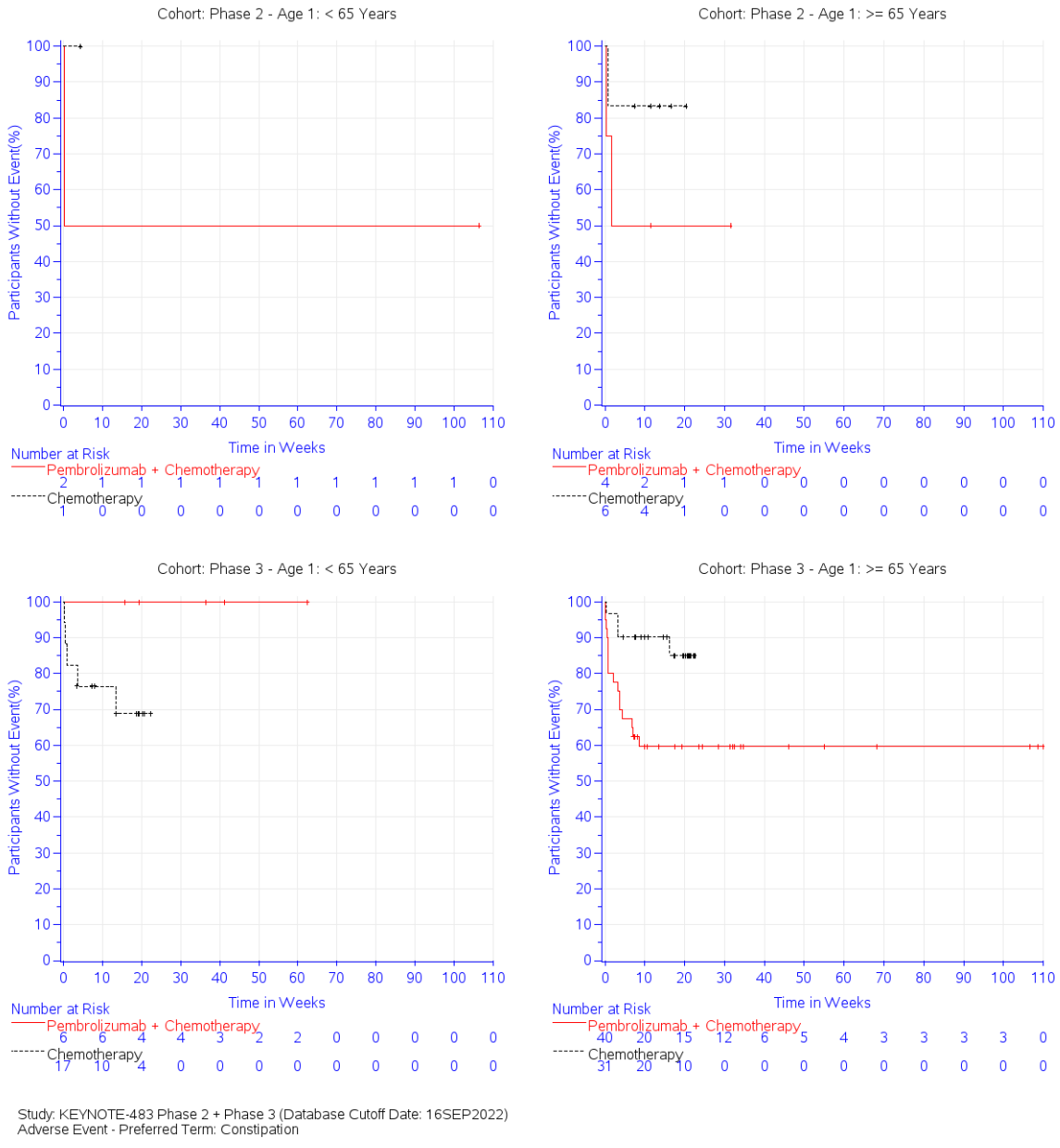
Anhang 4-G5.4: Nebenwirkungen

Figure 4.1-79
Analysis of Time to Adverse Event by Subgroup
With p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for Preferred Term: Constipation
Sex
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)



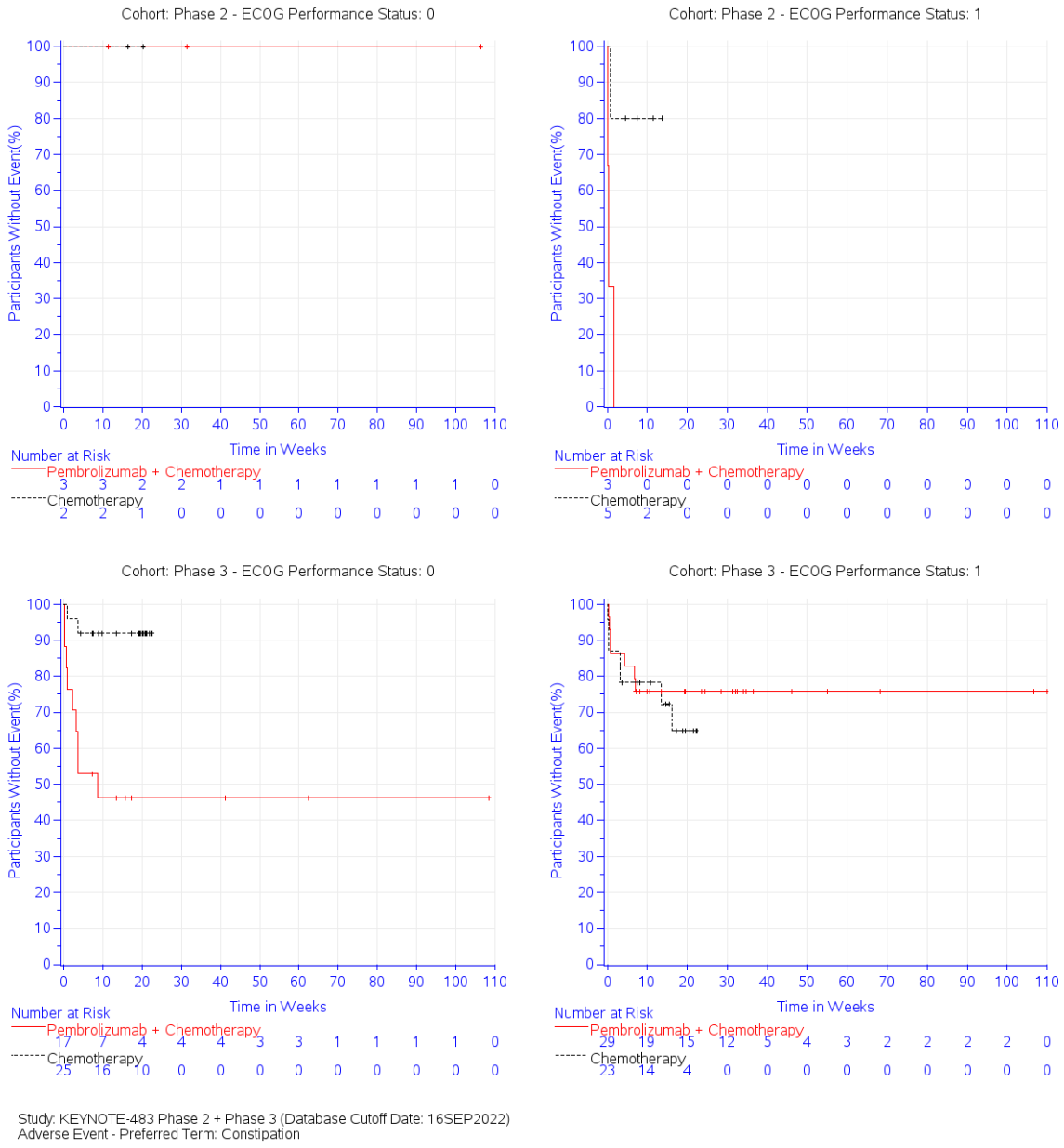
Study: KEYNOTE-483 Phase 2 + Phase 3 (Database Cutoff Date: 16SEP2022)
Adverse Event - Preferred Term: Constipation

Figure 4.1-81
Analysis of Time to Adverse Event by Subgroup
With p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for Preferred Term: Constipation
Age 1
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)



Study: KEYNOTE-483 Phase 2 + Phase 3 (Database Cutoff Date: 16SEP2022)
Adverse Event - Preferred Term: Constipation

Figure 4.1-83
Analysis of Time to Adverse Event by Subgroup
With p-Value for Interaction Test < 0.05 - Kaplan-Meier Curve
for Preferred Term: Constipation
ECOG Performance Status
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)



Study: KEYNOTE-483 Phase 2 + Phase 3 (Database Cutoff Date: 16SEP2022)
Adverse Event - Preferred Term: Constipation

Anhang 4-G6: Ergebnisse der Subgruppen mit nicht signifikantem Interaktionstest ($p \geq 0,05$)

Im Folgenden werden ergänzend zu Abschnitt 4.3.1.3.2.2 die Ergebnisse der Subgruppenanalysen, für die ein nicht signifikanter Interaktionstest ($p \geq 0,05$) vorliegt, dargestellt.

Anhang 4-G6.1: Mortalität

Gesamtüberleben

Table 4.1.4-5
Analyses of Overall Survival
for Subgroups With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Intention-to-Treat Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	Pembrolizumab + Chemotherapy[b]			Chemotherapy[b]			Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]		
Overall Survival	N[c]	Participants with Event n (%)	Median Time[d] in Months [95 %-CI]	N[c]	Participants with Event n (%)	Median Time[d] in Months [95 %-CI]	Hazard Ratio [95 %-CI][e]	p-Value[e,f]	p-Value for Interaction Test[g]
Sex									
Female	8	6 (75.0)	18.1 [6.4; -]	8	8 (100.0)	7.0 [4.0; 14.2]	0.32 [0.10; 1.00]	0.050[j]	0.261
Male	44	35 (79.5)	11.3 [8.1; 19.3]	48	43 (89.6)	8.2 [5.6; 10.8]	0.61 [0.39; 0.95]	0.031	
Age 1									
< 65 Years	8	6 (75.0)	12.2 [7.0; -]	18	17 (94.4)	8.0 [4.6; 19.9]	0.73 [0.26; 2.04]	0.546	0.735
≥ 65 Years	44	35 (79.5)	11.9 [8.1; 21.2]	38	34 (89.5)	7.9 [5.6; 9.4]	0.52 [0.32; 0.85]	0.010	
Age 2									
< 65 Years	8	6 (75.0)	12.2 [7.0; -]	18	17 (94.4)	8.0 [4.6; 19.9]	0.73 [0.26; 2.04]	0.546	0.479
65 - 74 Years	25	21 (84.0)	9.8 [6.9; 25.7]	25	22 (88.0)	8.5 [5.6; 11.3]	0.62 [0.33; 1.15]	0.130	
≥ 75 Years	19	14 (73.7)	12.2 [7.8; 25.4]	13	12 (92.3)	4.9 [1.4; 13.6]	0.41 [0.19; 0.92]	0.031	
ECOG Performance Status									
0	20	15 (75.0)	16.0 [7.0; 28.1]	27	25 (92.6)	8.5 [6.1; 14.2]	0.52 [0.27; 1.01]	0.053	0.985
1	32	26 (81.3)	11.3 [7.8; 14.6]	29	26 (89.7)	5.6 [4.0; 10.8]	0.55 [0.32; 0.96]	0.036	
Region									
EU	36	27 (75.0)	11.7 [7.6; 24.0]	34	30 (88.2)	8.5 [6.3; 11.4]	0.56 [0.33; 0.95]	0.032	0.923
Non-EU	16	14 (87.5)	11.9 [7.8; 25.1]	22	21 (95.5)	5.7 [3.7; 11.3]	0.56 [0.28; 1.13]	0.107	
Initial Choice Of Platinum Chemotherapy									
Cisplatin[h]	29	24 (82.8)	9.3 [7.0; 14.6]	38	35 (92.1)	8.3 [5.6; 11.3]	0.63 [0.37; 1.09]	0.100	0.267
Carboplatin	23	17 (73.9)	14.4 [10.3; 25.4]	17	16 (94.1)	6.3 [4.0; 15.0]	0.40 [0.20; 0.83]	0.013	

Analyses of Overall Survival
for Subgroups With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Intention-to-Treat Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	Pembrolizumab + Chemotherapy[b]			Chemotherapy[b]			Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]		p-Value for Interaction Test[g]
Overall Survival	N[c]	Participants with Event n (%)	Median Time[d] in Months [95 %-CI]	N[c]	Participants with Event n (%)	Median Time[d] in Months [95 %-CI]	Hazard Ratio [95 %-CI][e]	p-Value[e,f]	
PD-L1 CPS									
CPS ≥ 1	28	23 (82.1)	12.1 [7.0; 24.0]	33	30 (90.9)	6.5 [5.2; 10.8]	0.56 [0.32; 0.98]	0.041	0.749
CPS < 1	8	6 (75.0)	13.3 [7.6; -]	10	9 (90.0)	8.5 [7.7; 26.9]	0.65 [0.23; 1.84]	0.416	
Missing[i]	16	12 (75.0)	9.8 [7.5; 25.1]	13	12 (92.3)	5.8 [1.4; 14.2]	0.35 [0.14; 0.85]	0.021	
Smoking History									
Never	20	15 (75.0)	17.9 [8.1; 28.1]	20	19 (95.0)	7.8 [4.6; 8.6]	0.38 [0.18; 0.79]	0.010	0.260
Current/Former	30	24 (80.0)	10.4 [7.8; 19.3]	36	32 (88.9)	9.2 [5.4; 13.6]	0.63 [0.36; 1.07]	0.089	
Race									
White	45	35 (77.8)	9.8 [7.8; 14.6]	49	45 (91.8)	6.7 [5.6; 8.5]	0.51 [0.32; 0.80]	0.003	0.329
All Others	7	6 (85.7)	19.3 [10.3; 28.1]	7	6 (85.7)	15.0 [2.8; 28.9]	0.93 [0.29; 2.92]	0.898	

a: Database Cutoff Date: 31JAN2022 (phase 2), 16SEP2022 (phase 3)

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: intention-to-treat, phase 2 and phase 3, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate stratified by cohort (phase 2 vs phase 3)

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) stratified by cohort (phase 2 vs phase 3)

h: This category consists of participants who received cisplatin only and participants who switched from cisplatin to carboplatin

i: This category consists of participants with PD-L1 CPS status unknown and not done

j: Unrounded p-value > 0.050

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1

Anhang 4-G6.2: Morbidität

Progressionsfreies Überleben

Table 4.3.8-4
Analyses of Progression-Free Survival Based on BICR Assessment per mRECIST
for Subgroups With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Intention-to-Treat Population, Phase 3)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
Progression-Free Survival (BICR Primary Analysis)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	6 (75.0)	12.3 [2.5; -]	8	6 (75.0)	4.0 [1.3; -]	0.31 [0.09; 1.15]	0.081	0.617
Male	38	30 (78.9)	7.1 [4.0; 9.7]	41	32 (78.0)	5.2 [4.1; 6.5]	0.51 [0.30; 0.87]	0.013	
Age 1									
< 65 Years	6	4 (66.7)	9.8 [3.4; -]	17	10 (58.8)	6.4 [2.8; 9.0]	0.54 [0.15; 1.86]	0.327	0.747
≥ 65 Years	40	32 (80.0)	6.9 [4.5; 9.7]	32	28 (87.5)	4.3 [2.3; 5.6]	0.46 [0.27; 0.80]	0.005	
Age 2									
< 65 Years	6	4 (66.7)	9.8 [3.4; -]	17	10 (58.8)	6.4 [2.8; 9.0]	0.54 [0.15; 1.86]	0.327	0.646
65 - 74 Years	21	18 (85.7)	6.9 [2.8; 9.9]	20	17 (85.0)	4.5 [3.6; 5.6]	0.55 [0.27; 1.12]	0.098	
≥ 75 Years	19	14 (73.7)	7.0 [4.0; 18.0]	12	11 (91.7)	2.3 [1.3; 8.2]	0.41 [0.18; 0.94]	0.035	
ECOG Performance Status									
0	17	14 (82.4)	6.9 [3.4; 9.8]	25	19 (76.0)	4.5 [2.3; 6.4]	0.52 [0.25; 1.09]	0.085	0.792
1	29	22 (75.9)	7.6 [4.5; 10.0]	24	19 (79.2)	5.2 [2.6; 8.2]	0.47 [0.25; 0.91]	0.025	
Region									
EU	33	24 (72.7)	6.9 [3.9; 9.8]	32	25 (78.1)	4.2 [2.3; 5.6]	0.38 [0.20; 0.72]	0.003	0.133
Non-EU	13	12 (92.3)	7.6 [4.5; 18.0]	17	13 (76.5)	5.6 [4.1; 9.8]	0.59 [0.25; 1.39]	0.225	
Initial Choice Of Platinum Chemotherapy									
Cisplatin[h]	23	17 (73.9)	9.3 [3.9; 9.8]	32	24 (75.0)	4.5 [2.8; 6.5]	0.50 [0.26; 0.97]	0.040	0.683
Carboplatin	23	19 (82.6)	7.1 [4.0; 12.3]	16	14 (87.5)	4.2 [2.3; 8.1]	0.48 [0.23; 1.01]	0.053	

Analyses of Progression-Free Survival Based on BICR Assessment per mRECIST
for Subgroups With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Intention-to-Treat Population, Phase 3)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
Progression-Free Survival (BICR Primary Analysis)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
PD-L1 CPS									
CPS ≥ 1	28	22 (78.6)	6.9 [2.8; 12.3]	33	27 (81.8)	4.5 [2.6; 6.4]	0.47 [0.26; 0.87]	0.016	0.434
CPS < 1	8	7 (87.5)	9.3 [5.1; 9.7]	10	7 (70.0)	6.8 [3.6; -]	0.25 [0.06; 1.01]	0.051	
Smoking History									
Never	20	15 (75.0)	6.9 [3.9; 12.3]	18	14 (77.8)	4.3 [1.4; 6.8]	0.48 [0.22; 1.04]	0.063	0.739
Current/Former	24	19 (79.2)	9.3 [3.4; 10.0]	31	24 (77.4)	5.2 [2.6; 8.1]	0.44 [0.23; 0.84]	0.014	
Race									
White	39	30 (76.9)	7.6 [4.5; 9.8]	42	31 (73.8)	4.5 [3.6; 5.6]	0.45 [0.26; 0.77]	0.004	0.481
All Others	7	6 (85.7)	6.9 [2.8; 10.0]	7	7 (100.0)	6.4 [1.1; 9.7]	0.65 [0.20; 2.06]	0.460	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: intention-to-treat, phase 3, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

h: This category consists of participants who received cisplatin only and participants who switched from cisplatin to carboplatin

BICR: Blinded Independent Central Review; CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; CPS: Combined Positive Score; ECOG: Eastern Cooperative Oncology Group; PD-L1: Programmed Cell Death - Ligand 1

4.1.3.26.1 **EORTC QLQ-C30 Fatigue**

Table 4.3-6
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Fatigue (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Fatigue (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	5 (62.5)	1.4 [0.7; -]	8	5 (62.5)	2.1 [0.7; -]	0.90 [0.26; 3.14]	0.871	0.701
Male	37	29 (78.4)	1.4 [0.7; 2.0]	39	33 (84.6)	1.4 [0.7; 1.4]	0.67 [0.40; 1.12]	0.126	
Age 1									
< 65 Years	6	5 (83.3)	1.4 [0.7; -]	16	12 (75.0)	1.4 [0.7; 2.8]	1.00 [0.35; 2.84]	0.994	0.510
≥ 65 Years	39	29 (74.4)	1.4 [0.7; 4.3]	31	26 (83.9)	1.3 [0.7; 1.4]	0.67 [0.39; 1.15]	0.151	
ECOG Performance Status									
0	17	13 (76.5)	1.0 [0.7; 1.4]	24	18 (75.0)	1.4 [0.7; 2.2]	1.07 [0.52; 2.21]	0.849	0.341
1	28	21 (75.0)	1.6 [0.9; 5.0]	23	20 (87.0)	1.3 [0.7; 1.6]	0.54 [0.29; 1.01]	0.056	
Region									
EU	33	26 (78.8)	1.2 [0.7; 1.4]	30	22 (73.3)	1.4 [0.7; 2.1]	0.96 [0.54; 1.70]	0.883	0.079
Non-EU	12	8 (66.7)	2.0 [0.7; -]	17	16 (94.1)	0.8 [0.7; 1.4]	0.32 [0.12; 0.86]	0.023	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.2 **EORTC QLQ-C30 Nausea and Vomiting**

Table 4.3-7
Subgroup Analysis of Time to First Deterioration for EORTC QLQ-C30 Nausea and Vomiting (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Nausea and Vomiting (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	4 (50.0)	Not reached [0.7; -]	8	6 (75.0)	2.4 [0.7; -]	0.64 [0.18; 2.27]	0.489	0.702
Male	37	20 (54.1)	2.8 [1.4; -]	38	20 (52.6)	2.3 [1.4; -]	0.83 [0.45; 1.55]	0.561	
Age 1									
< 65 Years	6	4 (66.7)	1.2 [0.7; -]	16	10 (62.5)	1.5 [0.8; -]	1.20 [0.37; 3.83]	0.761	0.563
≥ 65 Years	39	20 (51.3)	4.3 [2.1; -]	30	16 (53.3)	2.8 [1.7; -]	0.77 [0.40; 1.48]	0.427	
ECOG Performance Status									
0	17	8 (47.1)	Not reached [0.7; -]	24	11 (45.8)	2.8 [1.4; -]	0.95 [0.38; 2.37]	0.913	0.611
1	28	16 (57.1)	2.7 [1.5; -]	22	15 (68.2)	2.1 [0.8; 3.3]	0.64 [0.32; 1.31]	0.225	
Region									
EU	33	17 (51.5)	2.8 [1.6; -]	30	16 (53.3)	2.1 [0.8; -]	0.73 [0.37; 1.44]	0.363	0.668
Non-EU	12	7 (58.3)	2.7 [0.7; -]	16	10 (62.5)	2.3 [1.4; -]	0.91 [0.35; 2.40]	0.847	

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid
d: From product-limit (Kaplan-Meier) method for censored data
e: Based on Cox regression model with treatment as a covariate
f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.3 **EORTC QLQ-C30 Pain**

Table 4.3-8
Subgroup Analysis of Time to First Deterioration for EORTC QLQ-C30 Pain (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Pain (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	4 (50.0)	Not reached [0.9; -]	8	5 (62.5)	2.8 [0.8; -]	0.55 [0.14; 2.16]	0.396	0.575
Male	37	19 (51.4)	5.8 [3.4; -]	39	18 (46.2)	9.9 [2.1; -]	0.78 [0.40; 1.51]	0.459	
ECOG Performance Status									
0	17	7 (41.2)	Not reached [1.4; -]	24	8 (33.3)	Not reached [2.3; -]	0.96 [0.34; 2.69]	0.935	0.835
1	28	16 (57.1)	4.5 [1.5; -]	23	15 (65.2)	2.8 [1.4; 9.9]	0.63 [0.30; 1.29]	0.205	
Region									
EU	33	19 (57.6)	4.5 [2.7; 11.7]	30	13 (43.3)	9.9 [1.4; -]	0.93 [0.45; 1.90]	0.833	0.227
Non-EU	12	4 (33.3)	Not reached [0.7; -]	17	10 (58.8)	3.0 [2.1; -]	0.52 [0.16; 1.66]	0.269	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.4 **EORTC QLQ-C30 Dyspnoea**

Table 4.3-9
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Dyspnoea (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Dyspnoea (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	5 (62.5)	4.1 [0.7; -]	8	4 (50.0)	3.7 [0.8; -]	0.95 [0.25; 3.61]	0.942	0.137
Male	37	11 (29.7)	Not reached [6.3; -]	39	21 (53.8)	3.3 [2.0; 7.8]	0.35 [0.17; 0.75]	0.006	
Age 1									
< 65 Years	6	3 (50.0)	Not reached [0.7; -]	16	6 (37.5)	5.7 [2.8; -]	1.46 [0.36; 5.85]	0.597	0.082
≥ 65 Years	39	13 (33.3)	Not reached [4.9; -]	31	19 (61.3)	2.4 [1.4; 7.8]	0.34 [0.17; 0.69]	0.003	
ECOG Performance Status									
0	17	5 (29.4)	Not reached [3.0; -]	24	10 (41.7)	5.3 [2.4; -]	0.55 [0.19; 1.62]	0.279	0.635
1	28	11 (39.3)	Not reached [3.4; -]	23	15 (65.2)	2.1 [1.4; 7.8]	0.38 [0.17; 0.84]	0.016	
Region									
EU	33	10 (30.3)	Not reached [4.9; -]	30	14 (46.7)	5.3 [2.2; -]	0.43 [0.19; 0.99]	0.047	0.751
Non-EU	12	6 (50.0)	4.6 [0.7; -]	17	11 (64.7)	2.8 [0.8; 7.8]	0.58 [0.21; 1.59]	0.290	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.5 **EORTC QLQ-C30 Insomnia**

Table 4.3-10
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Insomnia (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Insomnia (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	2 (25.0)	11.3 [0.9; -]	8	4 (50.0)	3.3 [0.7; -]	0.18 [0.02; 1.60]	0.123	0.267
Male	37	17 (45.9)	10.9 [2.8; -]	39	18 (46.2)	7.8 [1.7; 9.9]	0.74 [0.38; 1.47]	0.396	
Age 1									
< 65 Years	6	3 (50.0)	11.3 [0.7; -]	16	6 (37.5)	5.1 [2.1; -]	0.62 [0.12; 3.18]	0.567	0.477
≥ 65 Years	39	16 (41.0)	Not reached [3.4; -]	31	16 (51.6)	7.8 [1.4; -]	0.55 [0.27; 1.13]	0.103	
ECOG Performance Status									
0	17	6 (35.3)	11.3 [2.5; -]	24	6 (25.0)	9.8 [3.7; -]	0.71 [0.20; 2.59]	0.608	0.263
1	28	13 (46.4)	4.6 [2.8; -]	23	16 (69.6)	1.8 [1.4; 5.1]	0.46 [0.22; 0.98]	0.044	
Region									
EU	33	11 (33.3)	Not reached [4.6; -]	30	13 (43.3)	5.1 [2.1; -]	0.41 [0.17; 0.99]	0.047	0.172
Non-EU	12	8 (66.7)	2.1 [0.7; -]	17	9 (52.9)	2.1 [1.4; -]	1.27 [0.49; 3.34]	0.624	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.6 **EORTC QLQ-C30 Appetite Loss**

Table 4.3-11
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Appetite Loss (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Appetite Loss (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	4 (50.0)	4.4 [1.4; -]	8	3 (37.5)	Not reached [1.4; -]	1.04 [0.23; 4.64]	0.962	0.326
Male	37	12 (32.4)	Not reached [4.4; -]	38	17 (44.7)	4.5 [1.7; -]	0.47 [0.22; 1.00]	0.050[h]	
Age 1									
< 65 Years	6	1 (16.7)	Not reached [1.0; -]	16	8 (50.0)	3.3 [0.7; -]	0.23 [0.03; 1.85]	0.168	0.160
≥ 65 Years	39	15 (38.5)	Not reached [4.2; -]	30	12 (40.0)	5.3 [2.3; -]	0.70 [0.33; 1.51]	0.365	
ECOG Performance Status									
0	17	6 (35.3)	Not reached [2.1; -]	24	11 (45.8)	5.3 [1.4; -]	0.47 [0.17; 1.29]	0.144	0.706
1	28	10 (35.7)	Not reached [3.4; -]	22	9 (40.9)	4.5 [2.0; -]	0.65 [0.26; 1.61]	0.351	
Region									
EU	33	12 (36.4)	Not reached [4.2; -]	30	15 (50.0)	4.5 [1.4; -]	0.47 [0.22; 1.03]	0.059	0.521
Non-EU	12	4 (33.3)	Not reached [3.4; -]	16	5 (31.3)	Not reached [1.4; -]	0.74 [0.20; 2.79]	0.660	

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid
d: From product-limit (Kaplan-Meier) method for censored data
e: Based on Cox regression model with treatment as a covariate
f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
h: Unrounded p-value < 0.050
CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.7 **EORTC QLQ-C30 Constipation**

Table 4.3-12
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Constipation (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Constipation (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	4 (50.0)	8.5 [0.7; -]	8	4 (50.0)	1.4 [0.7; -]	0.81 [0.18; 3.64]	0.784	0.840
Male	37	17 (45.9)	4.3 [1.0; -]	38	16 (42.1)	8.1 [1.4; -]	1.01 [0.51; 2.01]	0.977	
Age 1									
< 65 Years	6	3 (50.0)	Not reached [0.7; -]	16	9 (56.3)	2.2 [0.8; -]	0.82 [0.22; 3.04]	0.767	0.512
≥ 65 Years	39	18 (46.2)	8.5 [1.0; -]	30	11 (36.7)	8.1 [1.4; -]	1.17 [0.55; 2.49]	0.680	
ECOG Performance Status									
0	17	10 (58.8)	2.1 [0.7; -]	24	11 (45.8)	2.3 [1.4; -]	1.46 [0.62; 3.45]	0.388	0.338
1	28	11 (39.3)	Not reached [1.5; -]	22	9 (40.9)	8.1 [0.8; -]	0.77 [0.32; 1.87]	0.564	
Region									
EU	33	17 (51.5)	4.2 [0.8; -]	30	12 (40.0)	Not reached [1.4; -]	1.24 [0.59; 2.60]	0.572	0.246
Non-EU	12	4 (33.3)	Not reached [0.7; -]	16	8 (50.0)	2.2 [1.4; -]	0.52 [0.15; 1.77]	0.297	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.8 **EORTC QLQ-C30 Diarrhoea**

Table 4.3-13
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Diarrhoea (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Diarrhoea (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	3 (37.5)	Not reached [0.9; -]	8	2 (25.0)	Not reached [0.8; -]	1.42 [0.24; 8.49]	0.703	0.642
Male	37	13 (35.1)	Not reached [5.5; -]	38	11 (28.9)	5.7 [5.3; -]	0.83 [0.37; 1.88]	0.660	
Age 1									
< 65 Years	6	3 (50.0)	6.3 [1.4; -]	16	7 (43.8)	5.4 [2.1; -]	0.46 [0.11; 1.93]	0.289	0.418
≥ 65 Years	39	13 (33.3)	Not reached [5.1; -]	30	6 (20.0)	Not reached [5.4; -]	1.34 [0.51; 3.52]	0.558	
ECOG Performance Status									
0	17	6 (35.3)	6.4 [4.2; -]	24	6 (25.0)	5.7 [5.3; -]	0.86 [0.27; 2.71]	0.799	0.930
1	28	10 (35.7)	Not reached [3.7; -]	22	7 (31.8)	Not reached [4.5; -]	0.97 [0.37; 2.54]	0.946	
Region									
EU	33	13 (39.4)	8.8 [4.2; -]	30	6 (20.0)	Not reached [4.5; -]	1.58 [0.60; 4.18]	0.358	0.077
Non-EU	12	3 (25.0)	Not reached [5.1; -]	16	7 (43.8)	5.4 [1.4; -]	0.32 [0.08; 1.29]	0.110	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.9 **EORTC QLQ-LC13 Dyspnoea**

Table 4.3-14
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Dyspnoea (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-LC13 Dyspnoea (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	6 (75.0)	3.5 [0.7; -]	8	5 (62.5)	3.3 [0.8; -]	1.00 [0.30; 3.35]	0.994	0.331
Male	37	21 (56.8)	4.1 [2.1; -]	39	26 (66.7)	2.8 [1.4; 4.8]	0.59 [0.33; 1.05]	0.074	
Age 1									
< 65 Years	6	3 (50.0)	5.8 [1.7; -]	16	10 (62.5)	3.3 [1.4; -]	0.48 [0.13; 1.78]	0.270	0.724
≥ 65 Years	39	24 (61.5)	4.0 [2.1; 7.5]	31	21 (67.7)	2.4 [1.4; 5.3]	0.69 [0.38; 1.24]	0.216	
ECOG Performance Status									
0	17	10 (58.8)	4.8 [0.7; -]	24	13 (54.2)	3.9 [2.2; 7.4]	0.91 [0.39; 2.08]	0.817	0.219
1	28	17 (60.7)	4.0 [2.0; -]	23	18 (78.3)	1.4 [0.7; 3.0]	0.48 [0.24; 0.93]	0.031	
Region									
EU	33	17 (51.5)	5.8 [1.7; -]	30	19 (63.3)	3.3 [1.4; 4.8]	0.63 [0.32; 1.22]	0.167	0.588
Non-EU	12	10 (83.3)	4.1 [1.4; 7.5]	17	12 (70.6)	2.8 [0.8; 7.4]	0.77 [0.33; 1.79]	0.538	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items

4.1.3.26.10 **EORTC QLQ-LC13 Coughing**

Table 4.3-15
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Coughing (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-LC13 Coughing (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Age 1									
< 65 Years	6	4 (66.7)	4.3 [0.7; -]	16	6 (37.5)	3.7 [1.4; -]	1.17 [0.31; 4.40]	0.813	0.691
≥ 65 Years	39	15 (38.5)	Not reached [3.7; -]	31	10 (32.3)	Not reached [2.6; -]	1.02 [0.46; 2.27]	0.966	
ECOG Performance Status									
0	17	5 (29.4)	Not reached [4.2; -]	24	6 (25.0)	Not reached [3.7; -]	0.77 [0.23; 2.57]	0.670	0.620
1	28	14 (50.0)	5.1 [1.6; -]	23	10 (43.5)	7.2 [2.5; -]	1.11 [0.49; 2.49]	0.808	
Region									
EU	33	12 (36.4)	Not reached [4.3; -]	30	9 (30.0)	Not reached [2.4; -]	0.81 [0.33; 1.96]	0.638	0.332
Non-EU	12	7 (58.3)	2.3 [0.7; -]	17	7 (41.2)	4.3 [2.5; -]	1.83 [0.64; 5.26]	0.259	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items

4.1.3.26.11 **EORTC QLQ-LC13 Haemoptysis**

Table 4.3-16
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Haemoptysis (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3a	**Pembrolizumab + Chemotherapyb**			**Chemotherapyb**			**Pembrolizumab + Chemotherapyb vs. Chemotherapyb**		
EORTC QLQ-LC13 Haemoptysis (10 Points)	**Nc**	**Participants with Event n (%)**	**Median Timed in Months [95 %-CI]**	**Nc**	**Participants with Event n (%)**	**Median Timed in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Valuee[f]**	**p-Value for Interaction Testg**
Sex									
Female	8	0 (0.0)	n.c.	8	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Male	37	7 (18.9)	n.c.	39	0 (0.0)	n.c.	n.c.	n.c.	
Age 1									
< 65 Years	6	1 (16.7)	n.c.	16	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65 Years	39	6 (15.4)	n.c.	31	0 (0.0)	n.c.	n.c.	n.c.	
ECOG Performance Status									
0	17	2 (11.8)	n.c.	24	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1	28	5 (17.9)	n.c.	23	0 (0.0)	n.c.	n.c.	n.c.	
Region									
EU	33	3 (9.1)	n.c.	30	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-EU	12	4 (33.3)	n.c.	17	0 (0.0)	n.c.	n.c.	n.c.	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary)

4.1.3.26.12 **EORTC QLQ-LC13 Sore Mouth**

Table 4.3-17
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Sore Mouth (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-LC13 Sore Mouth (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	4 (50.0)	Not reached [0.7; -]	8	1 (12.5)	Not reached [2.8; -]	4.95 [0.55; 44.42]	0.153	0.164
Male	37	18 (48.6)	5.5 [2.1; -]	39	13 (33.3)	Not reached [3.0; -]	1.19 [0.58; 2.46]	0.634	
Age 1									
< 65 Years	6	2 (33.3)	Not reached [1.3; -]	16	2 (12.5)	Not reached [-; -]	2.20 [0.31; 15.64]	0.432	0.544
≥ 65 Years	39	20 (51.3)	5.5 [1.5; -]	31	12 (38.7)	4.0 [2.8; -]	1.17 [0.57; 2.41]	0.674	
ECOG Performance Status									
0	17	9 (52.9)	4.2 [1.4; -]	24	6 (25.0)	Not reached [2.8; -]	1.63 [0.57; 4.72]	0.365	0.776
1	28	13 (46.4)	5.5 [1.4; -]	23	8 (34.8)	Not reached [2.6; -]	1.34 [0.56; 3.25]	0.512	
Region									
EU	33	16 (48.5)	12.7 [1.5; -]	30	10 (33.3)	Not reached [2.6; -]	1.21 [0.54; 2.70]	0.637	0.411
Non-EU	12	6 (50.0)	5.5 [1.3; -]	17	4 (23.5)	Not reached [3.0; -]	2.09 [0.58; 7.50]	0.258	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items

4.1.3.26.13 **EORTC QLQ-LC13 Dysphagia**

Table 4.3-18
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Dysphagia (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-LC13 Dysphagia (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	3 (37.5)	Not reached [0.7; -]	8	2 (25.0)	Not reached [3.9; -]	1.20 [0.20; 7.26]	0.845	0.666
Male	37	15 (40.5)	8.4 [3.5; -]	39	14 (35.9)	5.3 [2.2; -]	0.90 [0.43; 1.87]	0.772	
Age 1									
< 65 Years	6	2 (33.3)	Not reached [1.0; -]	16	4 (25.0)	5.3 [3.9; -]	0.85 [0.15; 4.72]	0.849	0.929
≥ 65 Years	39	16 (41.0)	8.4 [3.5; -]	31	12 (38.7)	4.8 [2.2; -]	0.85 [0.40; 1.80]	0.667	
ECOG Performance Status									
0	17	9 (52.9)	4.3 [0.8; -]	24	8 (33.3)	5.3 [2.2; -]	1.49 [0.57; 3.91]	0.414	0.260
1	28	9 (32.1)	Not reached [5.1; -]	23	8 (34.8)	Not reached [1.8; -]	0.67 [0.26; 1.77]	0.423	
Region									
EU	33	14 (42.4)	8.4 [3.5; -]	30	9 (30.0)	5.3 [2.4; -]	1.12 [0.48; 2.62]	0.798	0.540
Non-EU	12	4 (33.3)	Not reached [1.4; -]	17	7 (41.2)	4.8 [2.2; -]	0.68 [0.20; 2.34]	0.544	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items

4.1.3.26.14 **EORTC QLQ-LC13 Peripheral Neuropathy**

Table 4.3-19
Subgroup Analysis of Time to First Deterioration for EORTC QLQ-LC13 Peripheral Neuropathy (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-LC13 Peripheral Neuropathy (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	3 (37.5)	Not reached [1.6; -]	8	1 (12.5)	Not reached [3.5; -]	2.90 [0.30; 27.94]	0.356	0.310
Male	37	15 (40.5)	8.5 [4.4; -]	39	13 (33.3)	Not reached [2.3; -]	0.82 [0.39; 1.74]	0.612	
Age 1									
< 65 Years	6	3 (50.0)	5.8 [5.5; -]	16	4 (25.0)	5.7 [2.3; -]	0.77 [0.16; 3.67]	0.740	0.885
≥ 65 Years	39	15 (38.5)	Not reached [4.3; -]	31	10 (32.3)	Not reached [3.5; -]	0.93 [0.42; 2.08]	0.867	
ECOG Performance Status									
0	17	5 (29.4)	Not reached [4.2; -]	24	6 (25.0)	Not reached [5.7; -]	0.86 [0.26; 2.84]	0.802	0.773
1	28	13 (46.4)	5.9 [4.1; -]	23	8 (34.8)	5.5 [2.3; -]	0.97 [0.40; 2.34]	0.943	
Region									
EU	33	9 (27.3)	Not reached [5.5; -]	30	6 (20.0)	Not reached [-; -]	0.96 [0.34; 2.70]	0.931	0.639
Non-EU	12	9 (75.0)	4.3 [0.7; 8.5]	17	8 (47.1)	5.5 [1.4; -]	1.24 [0.48; 3.24]	0.659	

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid
d: From product-limit (Kaplan-Meier) method for censored data
e: Based on Cox regression model with treatment as a covariate
f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items

4.1.3.26.15 **EORTC QLQ-LC13 Alopecia**

Table 4.3-20
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Alopecia (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-LC13 Alopecia (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	6 (75.0)	2.1 [0.7; -]	8	7 (87.5)	1.4 [0.7; 2.8]	0.49 [0.15; 1.58]	0.232	0.357
Male	37	17 (45.9)	7.8 [3.1; -]	39	17 (43.6)	4.4 [3.0; -]	0.75 [0.38; 1.48]	0.403	
Age 1									
< 65 Years	6	3 (50.0)	7.8 [2.8; -]	16	9 (56.3)	3.3 [1.4; -]	0.39 [0.10; 1.52]	0.176	0.529
≥ 65 Years	39	20 (51.3)	5.0 [2.1; -]	31	15 (48.4)	3.5 [2.0; -]	0.81 [0.41; 1.59]	0.539	
ECOG Performance Status									
0	17	9 (52.9)	7.8 [2.1; -]	24	13 (54.2)	3.5 [2.1; 5.7]	0.52 [0.21; 1.32]	0.171	0.773
1	28	14 (50.0)	5.0 [1.6; -]	23	11 (47.8)	3.3 [1.4; -]	0.81 [0.37; 1.81]	0.612	
Region									
EU	33	16 (48.5)	5.1 [2.8; -]	30	14 (46.7)	3.5 [2.3; -]	0.78 [0.38; 1.62]	0.511	0.727
Non-EU	12	7 (58.3)	4.4 [1.4; -]	17	10 (58.8)	3.0 [1.4; -]	0.54 [0.19; 1.53]	0.250	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items

4.1.3.26.16 **EORTC QLQ-LC13 Pain in Chest**

Table 4.3-21
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Pain in Chest (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-LC13 Pain in Chest (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Age 1									
< 65 Years	6	0 (0.0)	Not reached [-; -]	16	5 (31.3)	10.1 [2.8; -]	n.a. [n.a.; n.a.]	0.050[h]	0.095
≥ 65 Years	39	15 (38.5)	10.3 [4.6; -]	30	14 (46.7)	3.5 [1.3; -]	0.52 [0.25; 1.09]	0.084	
ECOG Performance Status									
0	17	3 (17.6)	Not reached [4.3; -]	23	11 (47.8)	3.7 [0.8; -]	0.22 [0.06; 0.83]	0.025	0.088
1	28	12 (42.9)	10.3 [4.6; -]	23	8 (34.8)	Not reached [2.1; -]	0.77 [0.31; 1.91]	0.569	
Region									
EU	33	10 (30.3)	Not reached [5.1; -]	30	13 (43.3)	3.7 [2.1; -]	0.41 [0.18; 0.97]	0.041	0.346
Non-EU	12	5 (41.7)	10.3 [2.7; -]	16	6 (37.5)	10.1 [1.3; -]	0.72 [0.22; 2.41]	0.597	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

h: Unrounded p-value > 0.050

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; n.a.: not applicable (when estimation not possible)

4.1.3.26.17 **EORTC QLQ-LC13 Pain in Arm or Shoulders**

Table 4.3-22
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Pain in Arm or Shoulder (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-LC13 Pain in Arm or Shoulder (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	3 (37.5)	Not reached [0.7; -]	8	1 (12.5)	10.6 [-; -]	2.69 [0.28; 26.40]	0.395	0.248
Male	37	16 (43.2)	11.7 [4.1; -]	39	16 (41.0)	5.9 [3.3; -]	0.70 [0.34; 1.45]	0.336	
Age 1									
< 65 Years	6	2 (33.3)	Not reached [0.7; -]	16	4 (25.0)	Not reached [2.1; -]	1.24 [0.23; 6.80]	0.801	0.908
≥ 65 Years	39	17 (43.6)	11.7 [4.1; -]	31	13 (41.9)	7.4 [3.3; 10.6]	0.74 [0.35; 1.55]	0.421	
ECOG Performance Status									
0	17	7 (41.2)	12.7 [2.1; -]	24	5 (20.8)	Not reached [7.4; -]	1.40 [0.42; 4.64]	0.580	0.316
1	28	12 (42.9)	11.7 [2.0; -]	23	12 (52.2)	4.5 [2.8; 10.6]	0.61 [0.27; 1.38]	0.237	
Region									
EU	33	12 (36.4)	12.7 [5.1; -]	30	10 (33.3)	7.4 [3.3; -]	0.72 [0.29; 1.76]	0.470	0.434
Non-EU	12	7 (58.3)	6.2 [1.4; -]	17	7 (41.2)	5.9 [1.4; -]	1.21 [0.40; 3.62]	0.735	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items

4.1.3.26.18 **EORTC QLQ-LC13 Pain in Other Parts**

Table 4.3-23
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-LC13 Pain in Other Parts (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3a	**Pembrolizumab + Chemotherapyb**			**Chemotherapyb**			**Pembrolizumab + Chemotherapyb vs. Chemotherapyb**		
EORTC QLQ-LC13 Pain in Other Parts (10 Points)	**Nc**	**Participants with Event n (%)**	**Median Timed in Months [95 %-CI]**	**Nc**	**Participants with Event n (%)**	**Median Timed in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Valuee[f]**	**p-Value for Interaction Testg**
Sex									
Female	8	2 (25.0)	Not reached [0.7; -]	7	2 (28.6)	Not reached [1.4; -]	0.93 [0.13; 6.61]	0.943	0.851
Male	36	15 (41.7)	Not reached [3.7; -]	37	16 (43.2)	5.1 [2.1; -]	0.66 [0.32; 1.34]	0.247	
Age 1									
< 65 Years	6	4 (66.7)	3.2 [0.7; -]	16	6 (37.5)	5.1 [2.1; -]	1.54 [0.44; 5.48]	0.501	0.136
≥ 65 Years	38	13 (34.2)	Not reached [4.3; -]	28	12 (42.9)	3.0 [1.4; -]	0.55 [0.25; 1.20]	0.134	
ECOG Performance Status									
0	17	6 (35.3)	Not reached [2.1; -]	22	5 (22.7)	Not reached [2.3; -]	1.37 [0.42; 4.50]	0.603	0.111
1	27	11 (40.7)	Not reached [4.1; -]	22	13 (59.1)	2.1 [1.4; -]	0.43 [0.19; 0.97]	0.043	
Region									
EU	32	13 (40.6)	Not reached [3.5; -]	28	10 (35.7)	5.1 [2.2; -]	0.83 [0.36; 1.91]	0.663	0.377
Non-EU	12	4 (33.3)	Not reached [1.4; -]	16	8 (50.0)	3.0 [1.4; -]	0.45 [0.13; 1.51]	0.198	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items

4.1.3.26.19 **EQ-5D VAS**

Table 4.3-24
Subgroup Analysis of Time to First Deterioration for
EQ-5D VAS (15 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EQ-5D VAS (15 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	7	1 (14.3)	Not reached [3.0; -]	7	2 (28.6)	Not reached [2.3; -]	0.35 [0.03; 3.90]	0.394	0.907
Male	31	8 (25.8)	Not reached [8.0; -]	37	16 (43.2)	5.1 [3.5; -]	0.36 [0.15; 0.86]	0.022	
Age 1									
< 65 Years	4	0 (0.0)	Not reached [-; -]	14	4 (28.6)	5.1 [2.1; -]	n.a. [n.a.; n.a.]	0.075	0.193
≥ 65 Years	34	9 (26.5)	Not reached [8.0; -]	30	14 (46.7)	4.7 [1.4; -]	0.38 [0.16; 0.90]	0.027	
ECOG Performance Status									
0	12	1 (8.3)	Not reached [-; -]	23	7 (30.4)	Not reached [2.3; -]	0.21 [0.03; 1.69]	0.141	0.308
1	26	8 (30.8)	Not reached [4.5; -]	21	11 (52.4)	5.1 [1.4; -]	0.40 [0.16; 1.01]	0.053	
Region									
EU	28	5 (17.9)	Not reached [8.0; -]	29	10 (34.5)	9.9 [2.8; -]	0.29 [0.09; 0.88]	0.029	0.409
Non-EU	10	4 (40.0)	Not reached [0.7; -]	15	8 (53.3)	4.7 [1.4; -]	0.58 [0.18; 1.95]	0.382	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EQ-5D: European Quality of Life 5 Dimensions; n.a.: not applicable (when estimation not possible); VAS: Visual Analogue Scale

Anhang 4-G6.3: Gesundheitsbezogene Lebensqualität

4.1.3.26.20 EORTC QLQ-C30 Global Health Status

Table 4.4-4
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Global Health Status/QoL (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Global Health Status/QoL (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	6 (75.0)	3.5 [0.7; -]	8	4 (50.0)	2.8 [0.7; -]	1.17 [0.32; 4.21]	0.814	0.112
Male	37	18 (48.6)	7.5 [3.8; -]	39	26 (66.7)	1.6 [0.7; 2.2]	0.39 [0.20; 0.73]	0.003	
Age 1									
< 65 Years	6	2 (33.3)	Not reached [1.4; -]	16	7 (43.8)	3.4 [0.7; -]	0.60 [0.12; 2.91]	0.527	0.670
≥ 65 Years	39	22 (56.4)	4.6 [3.0; 11.0]	31	23 (74.2)	1.4 [0.7; 2.1]	0.38 [0.20; 0.70]	0.002	
ECOG Performance Status									
0	17	10 (58.8)	3.9 [0.8; -]	24	13 (54.2)	2.3 [0.8; -]	0.82 [0.35; 1.92]	0.644	0.120
1	28	14 (50.0)	7.5 [3.8; -]	23	17 (73.9)	1.4 [0.7; 2.1]	0.29 [0.14; 0.64]	0.002	
Region									
EU	33	18 (54.5)	4.5 [2.1; -]	30	18 (60.0)	1.6 [0.7; 4.2]	0.58 [0.29; 1.13]	0.108	0.534
Non-EU	12	6 (50.0)	10.6 [1.4; -]	17	12 (70.6)	2.1 [0.7; 3.4]	0.31 [0.11; 0.91]	0.033	

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid
d: From product-limit (Kaplan-Meier) method for censored data
e: Based on Cox regression model with treatment as a covariate
f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; QoL: Quality of Life

4.1.3.26.21 **EORTC QLQ-C30 Physical Functioning**

Table 4.4-5
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Physical Functioning (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Physical Functioning (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	3 (37.5)	Not reached [0.7; -]	8	5 (62.5)	2.3 [0.7; -]	0.55 [0.13; 2.33]	0.419	0.536
Male	37	19 (51.4)	6.7 [2.7; -]	39	22 (56.4)	2.9 [1.5; 9.8]	0.66 [0.35; 1.22]	0.185	
Age 1									
< 65 Years	6	1 (16.7)	Not reached [5.5; -]	16	7 (43.8)	2.3 [0.8; -]	0.17 [0.02; 1.52]	0.112	0.233
≥ 65 Years	39	21 (53.8)	6.7 [2.1; -]	31	20 (64.5)	2.5 [1.4; 5.1]	0.66 [0.35; 1.22]	0.183	
Region									
EU	33	15 (45.5)	Not reached [2.1; -]	30	14 (46.7)	9.8 [1.4; -]	0.79 [0.38; 1.65]	0.531	0.568
Non-EU	12	7 (58.3)	7.5 [0.9; -]	17	13 (76.5)	2.3 [1.3; 4.7]	0.44 [0.17; 1.11]	0.082	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.22 **EORTC QLQ-C30 Role Functioning**

Table 4.4-6
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Role Functioning (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Role Functioning (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	5 (62.5)	1.8 [0.7; -]	8	2 (25.0)	Not reached [2.1; -]	3.56 [0.68; 18.57]	0.132	0.212
Male	37	25 (67.6)	2.8 [1.2; 7.8]	39	23 (59.0)	2.8 [1.4; 5.3]	0.95 [0.53; 1.69]	0.855	
Age 1									
< 65 Years	6	2 (33.3)	Not reached [1.4; -]	16	7 (43.8)	10.1 [1.5; -]	0.44 [0.09; 2.18]	0.315	0.324
≥ 65 Years	39	28 (71.8)	2.0 [1.0; 5.0]	31	18 (58.1)	2.4 [1.4; -]	1.19 [0.66; 2.17]	0.565	
ECOG Performance Status									
0	17	10 (58.8)	7.8 [0.7; -]	24	11 (45.8)	5.3 [1.5; -]	1.02 [0.42; 2.47]	0.962	0.964
1	28	20 (71.4)	2.0 [1.2; 5.1]	23	14 (60.9)	2.2 [1.4; -]	1.08 [0.54; 2.16]	0.824	
Region									
EU	33	21 (63.6)	2.1 [1.2; 11.0]	30	13 (43.3)	5.3 [1.6; -]	1.43 [0.71; 2.89]	0.318	0.488
Non-EU	12	9 (75.0)	3.1 [0.7; 7.8]	17	12 (70.6)	2.8 [0.7; 10.1]	0.91 [0.38; 2.17]	0.834	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.23 **EORTC QLQ-C30 Emotional Functioning**

Table 4.4-7
Subgroup Analysis of Time to First Deterioration for EORTC QLQ-C30 Emotional Functioning (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Emotional Functioning (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	1 (12.5)	Not reached [7.1; -]	8	3 (37.5)	Not reached [1.4; -]	0.18 [0.02; 1.82]	0.146	0.276
Male	37	14 (37.8)	Not reached [5.0; -]	39	16 (41.0)	8.1 [3.3; -]	0.66 [0.32; 1.38]	0.269	
Age 1									
< 65 Years	6	1 (16.7)	Not reached [1.4; -]	16	6 (37.5)	Not reached [1.5; -]	0.33 [0.04; 2.76]	0.308	0.438
≥ 65 Years	39	14 (35.9)	Not reached [7.1; -]	31	13 (41.9)	9.9 [2.1; -]	0.62 [0.29; 1.33]	0.219	
ECOG Performance Status									
0	17	5 (29.4)	Not reached [2.1; -]	24	6 (25.0)	Not reached [3.0; -]	0.83 [0.23; 2.96]	0.780	0.405
1	28	10 (35.7)	Not reached [5.0; -]	23	13 (56.5)	3.5 [1.5; 10.6]	0.46 [0.20; 1.06]	0.069	
Region									
EU	33	10 (30.3)	Not reached [7.1; -]	30	13 (43.3)	9.9 [2.1; -]	0.46 [0.20; 1.07]	0.071	0.216
Non-EU	12	5 (41.7)	11.3 [1.4; -]	17	6 (35.3)	10.6 [2.1; -]	0.91 [0.25; 3.24]	0.880	

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid
d: From product-limit (Kaplan-Meier) method for censored data
e: Based on Cox regression model with treatment as a covariate
f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.24 **EORTC QLQ-C30 Cognitive Functioning**

Table 4.4-8
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Cognitive Functioning (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Cognitive Functioning (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	4 (50.0)	Not reached [0.9; -]	8	3 (37.5)	7.6 [0.7; -]	1.18 [0.26; 5.33]	0.831	0.835
Male	37	21 (56.8)	4.6 [1.4; -]	39	20 (51.3)	5.9 [1.4; 9.8]	0.86 [0.46; 1.62]	0.648	
Age 1									
< 65 Years	6	3 (50.0)	Not reached [0.7; -]	16	6 (37.5)	9.6 [2.3; -]	1.24 [0.30; 5.06]	0.765	0.690
≥ 65 Years	39	22 (56.4)	4.6 [1.4; -]	31	17 (54.8)	5.9 [1.4; 9.8]	0.79 [0.41; 1.51]	0.481	
ECOG Performance Status									
0	17	10 (58.8)	4.2 [0.7; -]	24	7 (29.2)	9.8 [3.0; -]	1.77 [0.65; 4.82]	0.264	0.061
1	28	15 (53.6)	7.3 [1.4; -]	23	16 (69.6)	2.3 [0.7; 7.6]	0.57 [0.28; 1.16]	0.122	
Region									
EU	33	15 (45.5)	7.3 [1.7; -]	30	14 (46.7)	9.6 [1.6; -]	0.78 [0.37; 1.63]	0.504	0.271
Non-EU	12	10 (83.3)	1.7 [0.7; 7.5]	17	9 (52.9)	5.9 [0.8; -]	1.26 [0.49; 3.23]	0.637	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

4.1.3.26.25 **EORTC QLQ-C30 Social Functioning**

Table 4.4-9
Subgroup Analysis of Time to First Deterioration for
EORTC QLQ-C30 Social Functioning (10 Points) With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(Full-Analysis-Set Population, Phase 3 With Baseline)

Study: KEYNOTE-483 Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
EORTC QLQ-C30 Social Functioning (10 Points)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Months [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	5 (62.5)	1.8 [0.7; -]	8	5 (62.5)	1.4 [0.7; -]	0.83 [0.24; 2.86]	0.762	0.458
Male	37	21 (56.8)	2.1 [0.9; -]	39	16 (41.0)	7.2 [2.8; -]	1.46 [0.76; 2.80]	0.255	
Age 1									
< 65 Years	6	2 (33.3)	Not reached [1.0; -]	16	8 (50.0)	3.3 [1.4; -]	0.46 [0.10; 2.20]	0.333	0.170
≥ 65 Years	39	24 (61.5)	1.4 [0.8; -]	31	13 (41.9)	7.2 [1.4; -]	1.56 [0.79; 3.06]	0.199	
ECOG Performance Status									
0	17	10 (58.8)	2.1 [0.7; -]	24	7 (29.2)	Not reached [1.4; -]	2.29 [0.87; 6.04]	0.093	0.122
1	28	16 (57.1)	2.1 [0.9; -]	23	14 (60.9)	2.8 [1.4; 7.2]	0.87 [0.42; 1.79]	0.709	
Region									
EU	33	18 (54.5)	2.1 [1.0; -]	30	11 (36.7)	7.2 [2.8; -]	1.62 [0.76; 3.44]	0.209	0.595
Non-EU	12	8 (66.7)	1.6 [0.7; -]	17	10 (58.8)	2.0 [0.8; -]	1.14 [0.45; 2.90]	0.781	

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: full-analysis-set, phase 3 with baseline, non-epithelioid
d: From product-limit (Kaplan-Meier) method for censored data
e: Based on Cox regression model with treatment as a covariate
f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term)
CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items

Anhang 4-G6.4: Nebenwirkungen

Table 4.1-13
Analyses of Time to Adverse Event by Subgroups
With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	Pembrolizumab + Chemotherapy[b]			Chemotherapy[b]			Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]		
Adverse Events	N[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	N[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][e]	p-Value[e,f]	p-Value for Interaction Test[g]
Sex									
Female	8	8 (100.0)	0.6 [0.1; 3.1]	8	7 (87.5)	0.8 [0.1; 5.0]	1.49 [0.51; 4.32]	0.463	0.215
Male	44	43 (97.7)	0.7 [0.4; 1.0]	47	45 (95.7)	0.3 [0.1; 0.4]	0.67 [0.44; 1.03]	0.068	
Age 1									
< 65 Years	8	8 (100.0)	2.0 [0.1; 3.4]	18	17 (94.4)	0.4 [0.1; 0.9]	0.58 [0.23; 1.43]	0.233	0.994
≥ 65 Years	44	43 (97.7)	0.6 [0.4; 1.0]	37	35 (94.6)	0.3 [0.1; 0.4]	0.69 [0.43; 1.08]	0.104	
ECOG Performance Status									
0	20	20 (100.0)	0.9 [0.4; 2.0]	27	24 (88.9)	0.4 [0.1; 2.6]	1.15 [0.62; 2.13]	0.666	0.052
1	32	31 (96.9)	0.6 [0.3; 1.0]	28	28 (100.0)	0.1 [0.1; 0.4]	0.50 [0.29; 0.85]	0.012	
Region									
EU	36	35 (97.2)	0.9 [0.6; 2.0]	33	30 (90.9)	0.4 [0.1; 0.9]	0.88 [0.54; 1.44]	0.607	0.316
Non-EU	16	16 (100.0)	0.5 [0.1; 0.6]	22	22 (100.0)	0.1 [0.1; 0.4]	0.55 [0.27; 1.09]	0.087	

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid
d: From product-limit (Kaplan-Meier) method for censored data
e: Based on Cox regression model with treatment as a covariate stratified by cohort (phase 2 vs phase 3)
f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)
g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) stratified by cohort (phase 2 vs phase 3)
CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group

Table 4.1-14
Analyses of Time to Serious Adverse Event by Subgroups
With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	Pembrolizumab + Chemotherapy[b]			Chemotherapy[b]			Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]		
Serious Adverse Events	N[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	N[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][e]	p-Value[e,f]	p-Value for Interaction Test[g]
Sex									
Female	8	2 (25.0)	Not reached [14.3; -]	8	3 (37.5)	Not reached [9.9; -]	0.54 [0.09; 3.22]	0.495	0.456
Male	44	17 (38.6)	Not reached [26.0; -]	47	13 (27.7)	Not reached [-; -]	1.11 [0.52; 2.34]	0.794	
Age 1									
< 65 Years	8	2 (25.0)	Not reached [0.1; -]	18	5 (27.8)	Not reached [9.9; -]	0.67 [0.12; 3.75]	0.650	0.600
≥ 65 Years	44	17 (38.6)	Not reached [26.0; -]	37	11 (29.7)	Not reached [17.1; -]	1.05 [0.48; 2.29]	0.907	
ECOG Performance Status									
0	20	7 (35.0)	Not reached [13.9; -]	27	4 (14.8)	Not reached [-; -]	2.05 [0.59; 7.10]	0.258	0.117
1	32	12 (37.5)	Not reached [26.0; -]	28	12 (42.9)	Not reached [9.9; -]	0.62 [0.26; 1.47]	0.278	
Region									
EU	36	9 (25.0)	Not reached [-; -]	33	9 (27.3)	Not reached [-; -]	0.79 [0.31; 2.00]	0.623	0.317
Non-EU	16	10 (62.5)	29.1 [6.9; -]	22	7 (31.8)	Not reached [9.9; -]	1.46 [0.51; 4.21]	0.483	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate stratified by cohort (phase 2 vs phase 3)

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) stratified by cohort (phase 2 vs phase 3)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group

Table 4.1-15
Analyses of Time to Severe Adverse Event (CTCAE-Grade 3-5) by Subgroups
With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
Severe Adverse Events (CTCAE-Grade 3-5)	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
Sex									
Female	8	1 (12.5)	Not reached [0.4; -]	8	3 (37.5)	Not reached [5.4; -]	0.31 [0.03; 2.99]	0.310	0.220
Male	44	19 (43.2)	57.3 [19.9; -]	47	17 (36.2)	Not reached [15.3; -]	0.85 [0.43; 1.68]	0.637	
Age 1									
< 65 Years	8	1 (12.5)	Not reached [1.1; -]	18	6 (33.3)	Not reached [10.0; -]	0.24 [0.03; 2.09]	0.195	0.228
≥ 65 Years	44	19 (43.2)	57.3 [19.9; -]	37	14 (37.8)	Not reached [15.3; -]	0.79 [0.38; 1.63]	0.523	
ECOG Performance Status									
0	20	6 (30.0)	Not reached [9.9; -]	27	4 (14.8)	Not reached [-; -]	1.86 [0.52; 6.65]	0.339	0.079
1	32	14 (43.8)	57.3 [19.9; -]	28	16 (57.1)	15.3 [5.1; -]	0.42 [0.19; 0.92]	0.031	
Region									
EU	36	10 (27.8)	Not reached [-; -]	33	9 (27.3)	Not reached [15.3; -]	0.90 [0.36; 2.21]	0.813	0.873
Non-EU	16	10 (62.5)	26.0 [7.1; -]	22	11 (50.0)	20.0 [4.0; -]	0.65 [0.25; 1.69]	0.374	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate stratified by cohort (phase 2 vs phase 3)

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) stratified by cohort (phase 2 vs phase 3)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events

Table 4.1-16
Analyses of Time to Adverse Event Leading to Treatment Discontinuation by Subgroups
With p-Value for Interaction Test ≥ 0.05 or not Calculated
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
Adverse Events Leading to Treatment Discontinuation[c]	**N[d]**	**Participants with Event n (%)**	**Median Time[e] in Weeks [95 %-CI]**	**N[d]**	**Participants with Event n (%)**	**Median Time[e] in Weeks [95 %-CI]**	**Hazard Ratio [95 %-CI][f]**	**p-Value[f,g]**	**p-Value for Interaction Test[h]**
Sex									
Female	8	4 (50.0)	60.9 [0.4; -]	8	2 (25.0)	Not reached [0.9; -]	1.42 [0.24; 8.55]	0.700	0.878
Male	44	14 (31.8)	Not reached [33.1; -]	47	9 (19.1)	Not reached [-; -]	1.17 [0.48; 2.81]	0.730	
Age 1									
< 65 Years	8	0 (0.0)	Not reached [-; -]	18	2 (11.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.356	0.070
≥ 65 Years	44	18 (40.9)	78.9 [19.9; -]	37	9 (24.3)	Not reached [-; -]	1.31 [0.56; 3.04]	0.531	
ECOG Performance Status									
0	20	6 (30.0)	Not reached [13.9; -]	27	4 (14.8)	Not reached [-; -]	1.88 [0.53; 6.73]	0.329	0.750
1	32	12 (37.5)	78.9 [21.7; -]	28	7 (25.0)	Not reached [17.6; -]	0.99 [0.35; 2.78]	0.982	
Region									
EU	36	9 (25.0)	Not reached [60.9; -]	33	5 (15.2)	Not reached [-; -]	1.24 [0.40; 3.84]	0.706	0.811
Non-EU	16	9 (56.3)	33.1 [7.1; -]	22	6 (27.3)	Not reached [17.6; -]	1.44 [0.47; 4.37]	0.520	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: The endpoint consists of drug-related adverse events, serious adverse events leading to treatment discontinuation and incidences of treatment discontinuation due to adverse events, which could not be linked to specific adverse events. For the incidences the date of last dose of study treatment is considered as the onset date for treatment discontinuations

d: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid

e: From product-limit (Kaplan-Meier) method for censored data

f: Based on Cox regression model with treatment as a covariate stratified by cohort (phase 2 vs phase 3)

g: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

h: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) stratified by cohort (phase 2 vs phase 3)

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible)

Table 4.1-19
Analyses of Time to Adverse Event by Subgroups
With p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants)
in One or More Treatment Groups)
For System Organ Classes
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
Adverse Events	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
SOC[h]: Psychiatric disorders									
Sex									
Female	8	1 (12.5)	Not reached [49.1; -]	8	2 (25.0)	Not reached [0.1; -]	n.a. [n.a.; n.a.]	0.998	0.626
Male	44	9 (20.5)	Not reached [57.9; -]	47	11 (23.4)	Not reached [-; -]	0.41 [0.14; 1.19]	0.101	
Age 1									
< 65 Years	8	1 (12.5)	Not reached [49.1; -]	18	3 (16.7)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.996	0.937
≥ 65 Years	44	9 (20.5)	Not reached [57.9; -]	37	10 (27.0)	Not reached [-; -]	0.33 [0.11; 0.99]	0.047	
ECOG Performance Status									
0	20	2 (10.0)	Not reached [49.1; -]	27	3 (11.1)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.996	0.772
1	32	8 (25.0)	Not reached [57.9; -]	28	10 (35.7)	Not reached [6.9; -]	0.33 [0.11; 0.98]	0.046	
Region									
EU	36	2 (5.6)	Not reached [49.1; -]	33	5 (15.2)	Not reached [-; -]	n.a. [n.a.; n.a.]	0.994	0.185
Non-EU	16	8 (50.0)	57.9 [7.1; -]	22	8 (36.4)	Not reached [3.0; -]	0.70 [0.23; 2.16]	0.539	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate stratified by cohort (phase 2 vs phase 3)

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) stratified by cohort (phase 2 vs phase 3)

h: A system organ class appears on this report only if its incidence ≥ 10% or (incidence ≥ 1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.a.: not applicable (when estimation not possible); SOC: System Organ Class

Table 4.1-20
Analyses of Time to Adverse Event by Subgroups
With p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 10% or (Incidence ≥ 1% and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	**Pembrolizumab + Chemotherapy[b]**			**Chemotherapy[b]**			**Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]**		
Adverse Events	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**N[c]**	**Participants with Event n (%)**	**Median Time[d] in Weeks [95 %-CI]**	**Hazard Ratio [95 %-CI][e]**	**p-Value[e,f]**	**p-Value for Interaction Test[g]**
SOC: Gastrointestinal disorders - PT[h]: Constipation									
Region									
EU	36	10 (27.8)	Not reached [-; -]	33	3 (9.1)	Not reached [-; -]	3.25 [0.89; 11.80]	0.074	0.683
Non-EU	16	9 (56.3)	4.3 [0.3; -]	22	7 (31.8)	Not reached [13.4; -]	2.35 [0.86; 6.41]	0.097	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate stratified by cohort (phase 2 vs phase 3)

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) stratified by cohort (phase 2 vs phase 3)

h: A specific adverse event appears on this report only if its incidence ≥ 10% or (incidence ≥ 1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; PT: Preferred Term; SOC: System Organ Class

Table 4.1-22
Analyses of Time to Serious Adverse Event by Subgroups
With p-Value for Interaction Test ≥ 0.05 or not Calculated
(Incidence ≥ 5% or (Incidence ≥ 1% and in at least 10 Participants)
in One or More Treatment Groups)
For Preferred Terms
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	Pembrolizumab + Chemotherapy[b]			Chemotherapy[b]			Pembrolizumab + Chemotherapy[b] vs. Chemotherapy[b]		
Serious Adverse Events	N[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	N[c]	Participants with Event n (%)	Median Time[d] in Weeks [95 %-CI]	Hazard Ratio [95 %-CI][e]	p-Value[e,f]	p-Value for Interaction Test[g]
SOC: Gastrointestinal disorders - PT[h]: Diarrhoea									
Sex									
Female	8	1 (12.5)	n.c.	8	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Male	44	4 (9.1)	n.c.	47	0 (0.0)	n.c.	n.c.	n.c.	
Age 1									
< 65 Years	8	1 (12.5)	n.c.	18	0 (0.0)	n.c.	n.c.	n.c.	n.c.
≥ 65 Years	44	4 (9.1)	n.c.	37	0 (0.0)	n.c.	n.c.	n.c.	
ECOG Performance Status									
0	20	2 (10.0)	n.c.	27	0 (0.0)	n.c.	n.c.	n.c.	n.c.
1	32	3 (9.4)	n.c.	28	0 (0.0)	n.c.	n.c.	n.c.	
Region									
EU	36	3 (8.3)	n.c.	33	0 (0.0)	n.c.	n.c.	n.c.	n.c.
Non-EU	16	2 (12.5)	n.c.	22	0 (0.0)	n.c.	n.c.	n.c.	

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid

d: From product-limit (Kaplan-Meier) method for censored data

e: Based on Cox regression model with treatment as a covariate stratified by cohort (phase 2 vs phase 3)

f: Two-sided p-value using Wald test (Score test in case of zero event in one treatment group)

g: Based on Cox model with treatment and subgroup as covariates, and treatment-by-subgroup interaction (p-value of likelihood ratio test for interaction term) stratified by cohort (phase 2 vs phase 3)

h: A specific adverse event appears on this report only if its incidence ≥ 5% or (incidence ≥ 1% and in at least 10 participants) in one or more treatment groups and p-value of main treatment effect is smaller than 0.05, and the interaction p-value is greater than or equal to 0.05 or not calculated

CCTG: Canadian Cancer Trials Group; CI: Confidence Interval; ECOG: Eastern Cooperative Oncology Group; n.c.: not calculated (at least 10 participants per subgroup category and at least 10 participants with events in one of the subgroup categories necessary); PT: Preferred Term; SOC: System Organ Class

Anhang 4-G7: Folgetherapien

Table 4.2.6-1
Summary of Participants by the Status
of Receiving Subsequent Oncologic Systemic or Radiation Therapy
Subpopulation of Participants, Non-epithelioid
(Intention-to-Treat Population, Phase 2)

First Subsequent Oncologic Therapy	Study: KEYNOTE-483 Phase 2[a]	
	Pembrolizumab + Chemotherapy[b] N[c] = 6	Chemotherapy[b] N[c] = 7
Status of First Subsequent Oncologic Therapy, n (%)		
Received first subsequent systemic therapy	3 (50.0)	0 (0.0)
Received first subsequent radiation therapy	0 (0.0)	2 (28.6)
Received first subsequent systemic and radiation therapy[d]	0 (0.0)	0 (0.0)
Died without receiving a subsequent therapy	3 (50.0)	5 (71.4)
Did not receive a subsequent therapy	0 (0.0)	0 (0.0)

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: intention-to-treat, phase 2, non-epithelioid
d: Participants receiving both systemic and radiation therapy (if any) are only counted in the combined category
CCTG: Canadian Cancer Trials Group

Table 4.3.6-1
Summary of Participants by the Status
of Receiving Subsequent Oncologic Systemic or Radiation Therapy
Subpopulation of Participants, Non-epithelioid
(Intention-to-Treat Population, Phase 3)

First Subsequent Oncologic Therapy	Study: KEYNOTE-483 Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] N[c] = 46	Chemotherapy[b] N[c] = 49
Status of First Subsequent Oncologic Therapy, n (%)		
Received first subsequent systemic therapy	22 (47.8)	20 (40.8)
Received first subsequent radiation therapy	3 (6.5)	9 (18.4)
Received first subsequent systemic and radiation therapy[d]	0 (0.0)	0 (0.0)
Died without receiving a subsequent therapy	18 (39.1)	18 (36.7)
Did not receive a subsequent therapy	3 (6.5)	2 (4.1)

a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: intention-to-treat, phase 3, non-epithelioid
d: Participants receiving both systemic and radiation therapy (if any) are only counted in the combined category
CCTG: Canadian Cancer Trials Group

Anhang 4-G8: Behandlungs- und Beobachtungsdauer

Table 4.2.4-1
Summary of Treatment Duration and Observation Period
Subpopulation of Participants, Non-epithelioid

Study: KEYNOTE-483 Phase 2[a]	Pembrolizumab + Chemotherapy[b]	Chemotherapy[b]
Duration of Treatment (Months)[c]		
N[d]	6	7
Mean (SD)	10.2 (8.3)	1.7 (1.3)
Median (Q1; Q3)	6.9 (5.1; 17.1)	1.6 (0.7; 2.8)
Min; Max	1.6; 23.5	0.0; 3.7
Observation Period		
Overall Survival (Months)[e]		
N[f]	6	7
Mean (SD)	24.4 (26.5)	7.6 (6.9)
Median (Q1; Q3)	9.1 (7.5; 55.0)	5.6 (3.4; 11.3)
Min; Max	3.9; 61.9	1.2; 21.5
Adverse Event (Months)[g]		
N[d]	6	7
Mean (SD)	11.1 (8.3)	2.7 (1.3)
Median (Q1; Q3)	7.8 (6.1; 18.0)	2.6 (1.7; 3.8)
Min; Max	2.6; 24.5	1.0; 4.7
Serious Adverse Event (Months)[g]		
N[d]	6	7
Mean (SD)	12.4 (8.8)	4.1 (1.8)
Median (Q1; Q3)	8.2 (7.5; 20.0)	3.7 (3.2; 5.7)
Min; Max	3.9; 26.4	1.2; 6.7

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Calculated from date of first dose until date of last dose

d: Number of participants: all-participants-as-treated, phase 2, non-epithelioid

e: Calculated from date of randomization until date of death, date of last contact, or the database cutoff date (i.e., 31JAN2022) if the participant is still alive

f: Number of participants: intention-to-treat, phase 2, non-epithelioid

g: Adverse event follow-up duration is defined as the time from first dose to the earliest of the last dose + planned safety follow-up time, date of death, date of last contact or the database cutoff date (i.e., 16SEP2022) if the participant is still alive

CCTG: Canadian Cancer Trials Group; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Table 4.3.4-1
Summary of Treatment Duration and Observation Period
Subpopulation of Participants, Non-epithelioid

Study: KEYNOTE-483 Phase 3[a]	Pembrolizumab + Chemotherapy[b]	Chemotherapy[b]
Duration of Treatment (Months)[c]		
N[d]	46	48
Mean (SD)	8.3 (7.1)	2.8 (1.3)
Median (Q1; Q3)	6.5 (3.0; 11.5)	3.5 (1.6; 3.8)
Min; Max	0.7; 24.3	0.0; 4.4
Observation Period		
Overall Survival (Months)[e]		
N[f]	46	49
Mean (SD)	18.3 (14.8)	11.3 (10.0)

Median (Q1; Q3)	12.3 (7.6; 25.7)	7.9 (4.0; 15.0)
Min; Max	1.7; 60.2	0.0; 38.6
Adverse Event (Months)[g]		
N[d]	46	48
Mean (SD)	9.3 (7.1)	3.7 (1.4)
Median (Q1; Q3)	7.4 (4.0; 12.5)	4.5 (2.4; 4.8)
Min; Max	1.6; 25.3	0.8; 5.4
Serious Adverse Event (Months)[g]		
N[d]	46	48
Mean (SD)	11.0 (7.2)	5.3 (1.8)
Median (Q1; Q3)	9.4 (5.7; 14.5)	6.4 (3.8; 6.7)
Min; Max	1.6; 27.2	0.8; 7.2
EORTC QLQ-C30 (Months)[h]		
N[i]	45	47
Mean (SD)	7.6 (3.9)	4.7 (3.2)
Median (Q1; Q3)	7.6 (4.1; 11.5)	4.1 (2.8; 6.0)
Min; Max	0.9; 12.7	0.0; 11.4
EORTC QLQ-LC13 (Months)[h]		
N[i]	45	47
Mean (SD)	7.6 (3.9)	4.7 (3.2)
Median (Q1; Q3)	7.6 (4.1; 11.5)	4.1 (2.8; 6.0)
Min; Max	0.9; 12.7	0.0; 11.4
EQ-5D VAS (Months)[h]		
N[i]	38	45
Mean (SD)	7.8 (4.1)	4.6 (3.3)
Median (Q1; Q3)	8.4 (4.0; 11.7)	3.9 (2.1; 6.0)
Min; Max	0.9; 12.7	0.0; 11.4

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Calculated from date of first dose until date of last dose

d: Number of participants: all-participants-as-treated, phase 3, non-epithelioid

e: Calculated from date of randomization until date of death, date of last contact, or the database cutoff date if the participant is still alive

f: Number of participants: intention-to-treat, phase 3, non-epithelioid

g: Adverse event follow-up duration is defined as the time from first dose to the earliest of the last dose + planned safety follow-up time, date of death, date of last contact or the database cutoff date if the participant is still alive

h: Calculated from date of first dose until date of last questionnaire assessment

i: Number of participants: full-analysis-set, phase 3, non-epithelioid

CCTG: Canadian Cancer Trials Group; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; EORTC QLQ-LC13: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Lung Cancer 13 items; EQ-5D: European Quality of Life 5 Dimensions; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation; VAS: Visual Analogue Scale

Table 4.1.3-1
Summary of Treatment Duration and Observation Period
Subpopulation of Participants, Non-epithelioid

Study: KEYNOTE-483 Phase 2 + Phase 3[a]	Pembrolizumab + Chemotherapy[b]	Chemotherapy[b]
Duration of Treatment (Months)[c]		
N[d]	52	55
Mean (SD)	8.5 (7.1)	2.6 (1.4)
Median (Q1; Q3)	6.5 (3.3; 11.6)	3.4 (1.4; 3.7)
Min; Max	0.7; 24.3	0.0; 4.4
Observation Period		
Overall Survival (Months)[e]		
N[f]	52	56
Mean (SD)	19.0 (16.3)	10.8 (9.7)
Median (Q1; Q3)	11.9 (7.5; 26.3)	7.6 (3.8; 14.6)
Min; Max	1.7; 61.9	0.0; 38.6
Adverse Event (Months)[g]		
N[d]	52	55
Mean (SD)	9.5 (7.2)	3.6 (1.4)
Median (Q1; Q3)	7.4 (4.2; 12.6)	4.4 (2.3; 4.7)
Min; Max	1.6; 25.3	0.8; 5.4
Serious Adverse Event (Months)[g]		
N[d]	52	55
Mean (SD)	11.2 (7.3)	5.1 (1.9)
Median (Q1; Q3)	9.3 (5.8; 14.6)	5.8 (3.7; 6.7)
Min; Max	1.6; 27.2	0.8; 7.2

a: Database Cutoff Date: 16SEP2022

b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)

c: Calculated from date of first dose until date of last dose

d: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid

e: Calculated from date of randomization until date of death, date of last contact, or the database cutoff date (i.e., 31JAN2022 for phase 2, 16SEP2022 for phase 3) if the participant is still alive

f: Number of participants: intention-to-treat, phase 2 and phase 3, non-epithelioid

g: Adverse event follow-up duration is defined as the time from first dose to the earliest of the last dose + planned safety follow-up time, date of death, date of last contact or the database cutoff date (i.e., 16SEP2022 for phase 2 and phase 3) if the participant is still alive

CCTG: Canadian Cancer Trials Group; Max: Maximum; Min: Minimum; Q1: First Quartile; Q3: Third Quartile; SD: Standard Deviation

Anhang 4-G9: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) anhand der zugeordneten PT

Table 4.7-1

AEOSI Preferred Terms, version 25 (24-Jul-2023)

MedDRA Version 26

AEOSI	Preferred Terms	Immune-mediated (Yes/No)
Pneumonitis	Acute interstitial pneumonitis, Autoimmune lung disease, Interstitial lung disease, Pneumonitis, Idiopathic pneumonia syndrome, Organising pneumonia, Immunemediated lung disease	Yes
Colitis	Colitis, Colitis microscopic, Enterocolitis, Enterocolitis haemorrhagic, Necrotising colitis, Colitis erosive, Autoimmune colitis, Immune-mediated enterocolitis	Yes
Hepatitis	Hepatitis, Immune-mediated hepatitis, Autoimmune hepatitis, Hepatitis acute, Hepatitis fulminant, Drug-induced liver injury	Yes
Nephritis	Nephritis, Autoimmune nephritis, Chronic autoimmune glomerulonephritis, Fibrillary glomerulonephritis, Focal segmental glomerulosclerosis, Glomerulonephritis, Glomerulonephritis acute, Glomerulonephritis membranoproliferative, Glomerulonephritis membranous, Glomerulonephritis minimal lesion, Glomerulonephritis proliferative, Glomerulonephritis rapidly progressive, Mesangioproliferative glomerulonephritis, Nephritis haemorrhagic, Tubulointerstitial nephritis, Nephrotic syndrome, Immune-mediated nephritis	Yes
Adrenal Insufficiency	Adrenal insufficiency, Adrenocortical insufficiency acute, Secondary adrenocortical insufficiency, Primary adrenal insufficiency, Addison's disease, immunemediated adrenal insufficiency	Yes
Hypophysitis	Hypophysitis, Hypopituitarism, Lymphocytic hypophysitis, Immune-mediated hypophysitis	Yes
Hyperthyroidism	Hyperthyroidism, Thyrotoxic crisis, Immune-mediated hyperthyroidism, Graves' disease	Yes
Hypothyroidism	Hypothyroidism, Hypothyroidic goitre, Myxoedema, Myxoedema coma, Primary hypothyroidism,	Yes

	Autoimmune hypothyroidism, Immune-mediated hypothyroidism	
Thyroiditis	Thyroid disorder, Thyroiditis, Autoimmune thyroiditis, Thyroiditis acute, Silent thyroiditis, Autoimmune thyroid disorder, Immune-mediated thyroiditis	Yes
Type 1 Diabetes Mellitus	Diabetic ketoacidosis, Diabetic ketoacidotic hyperglycaemic coma, Fulminant type 1 diabetes mellitus, Latent autoimmune diabetes in adults, Type 1 diabetes mellitus, Euglycaemic diabetic ketoacidosis, Diabetic ketosis, Ketosis-prone diabetes mellitus	Yes
Severe Skin Reactions Including Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN): or	Dermatitis bullous, Dermatitis exfoliative, Dermatitis exfoliative generalised, Epidermal necrosis, Erythema multiforme, Exfoliative rash, Pemphigoid, Mucous membrane pemphigoid, Pemphigus, Skin necrosis, Stevens-Johnson syndrome, Toxic epidermal necrolysis, Toxic skin eruption, SJS-TEN overlap, Lichen planus pemphigoides	Yes
Severe Skin (continued): **If grade 3 or higher**:	Rash, Rash erythematous, Rash maculo-papular, Rash pruritic, Rash pustular, Pruritus, Pruritus genital, Lichen planus, Oral lichen planus, Cutaneous vasculitis, Vasculitic rash	Yes
Uveitis	Iritis, Uveitis, Cyclitis, Autoimmune uveitis, Iridocyclitis, Vogt-Koyanagi-Harada disease, Chorioretinitis, Choroiditis, Immune-mediated uveitis, Choroidal effusion, Choroidal detachment, Serous retinal detachment	Yes
Pancreatitis	Pancreatitis, Autoimmune pancreatitis, Pancreatitis acute, Pancreatitis haemorrhagic, Pancreatitis necrotising, Immune-mediated pancreatitis	Yes
Myositis	Myositis, Necrotising myositis, Polymyositis, Immunemediated myositis, Rhabdomyolysis, Myopathy, Dermatomyositis, Autoimmune myositis	Yes
Guillain-Barre Syndrome	Demyelinating polyneuropathy, Guillain-Barre syndrome, Axonal neuropathy, Multifocal motor neuropathy, Polyneuropathy idiopathic progressive, Miller Fisher syndrome, Subacute inflammatory demyelinating polyneuropathy	Yes
Myocarditis	Myocarditis, Autoimmune myocarditis, Hypersensitivity myocarditis, Immune-mediated myocarditis	Yes
Encephalitis	Encephalitis, Encephalitis autoimmune, Limbic encephalitis, Noninfective encephalitis, Immunemediated encephalitis	Yes
Sarcoidosis	Sarcoidosis, Cutaneous sarcoidosis, Ocular sarcoidosis,	Yes

	Pulmonary sarcoidosis, Sarcoidosis of lymph node	
Infusion Reactions	Hypersensitivity, Drug hypersensitivity, Anaphylactic reaction, Anaphylactoid reaction, Cytokine release syndrome, Serum sickness, Serum sickness-like reaction, Infusion related reaction, Infusion related hypersensitivity reaction	No
Myasthenic Syndrome	Myasthenic syndrome, Myasthenia gravis, Myasthenia gravis crisis, Ocular myasthenia, Immune-mediated myasthenia gravis	Yes
Myelitis	Myelitis, Myelitis transverse, Acute necrotising myelitis, Immune-mediated myelitis	Yes
Vasculitis	Anti-neutrophil cytoplasmic antibody positive vasculitis, Aortitis, Arteritis, Arteritis coronary, Behcet's syndrome, Central nervous system vasculitis, Cerebral arteritis, Diffuse vasculitis, Eosinophilic granulomatosis with polyangiitis, Granulomatosis with polyangiitis, Haemorrhagic vasculitis, Hypersensitivity vasculitis, Microscopic polyangiitis, Ocular vasculitis, Polyarteritis nodosa, Pulmonary vasculitis, Renal arteritis, Renal vasculitis, Retinal vasculitis, Takayasu's arteritis, Giant cell arteritis, Vasculitis, Vasculitis gastrointestinal, Vasculitis necrotising	Yes
Cholangitis Sclerosing	Cholangitis sclerosing, Autoimmune cholangitis, Immune-mediated cholangitis	Yes
Hypoparathyroidism	Hypoparathyroidism, Primary hypoparathyroidism	Yes
Arthritis	Autoimmune arthritis, Immune-mediated arthritis	Yes
HLH	Haemophagocytic lymphohistiocytosis	Yes
Optic Neuritis	Optic neuritis, Immune-mediated optic neuritis	Yes
Gastritis	Gastritis, Gastritis erosive, Gastritis haemorrhagic, Haemorrhagic erosive gastritis, Immune-mediated gastritis, Ulcerative gastritis	**Yes**

Anhang 4-G10: Unerwünschte Ereignisse mit Abweichungen der Laborwerte

Table 7-69
Summary of Adverse Events Including Lab Abnormalities
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

	Study: KEYNOTE-483 Phase 2 + Phase 3[a]	
	Pembrolizumab + Chemotherapy[b] (N[c]=52) n (%)	**Chemotherapy[b] (N[c]=55) n (%)**
Any adverse event	51 (98.1)	52 (94.5)
Any adverse event including lab abnormalities[d]	52 (100.0)	53 (96.4)
Adverse events leading to treatment discontinuation	18 (34.6)	10 (18.2)
Adverse events leading to treatment discontinuation including lab abnormalities[e]	20 (38.5)	14 (25.5)

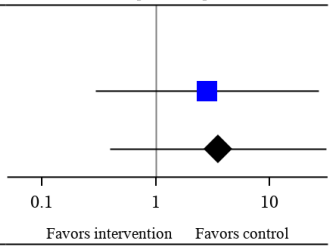
a: Database Cutoff Date: 16SEP2022
b: Chemotherapy: Cisplatin + Pemetrexed (or Carboplatin + Pemetrexed after CCTG approval)
c: Number of participants: all-participants-as-treated, phase 2 and phase 3, non-epithelioid
d: This category includes lab abnormalities leading to treatment interruption or discontinuation
e: This category includes lab abnormalities leading to treatment discontinuation
Every participant is counted a single time for each applicable row and column
Non-serious adverse events up to 30 days of last dose and serious adverse events up to 90 days of last dose are included
MedDRA preferred terms 'Neoplasm progression', 'Malignant neoplasm progression' and 'Disease progression' not related to the drug are excluded
CCTG: Canadian Cancer Trials Group; MedDRA: Medical Dictionary for Regulatory Activities

Anhang 4-G11: Analyse der Endpunkte Unerwünschte Ereignisse (gegliedert nach SOC und PT) – Meta-Analyse - Forest Plots der statistisch nicht signifikanten (p ≥ 0,05) Ergebnisse

Unerwünschte Ereignisse gesamt (SOC und PT)

Figure 4.1-5
Forest Plot of Time to Adverse Event in System Organ Class
Endocrine disorders
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

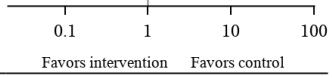
SOC: Endocrine disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	1 (16.7)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	6 (13.0)	48	1 (2.1)	2.81 [0.30; 26.84]	
Overall[c]	**52**	**7 (13.5)**	**55**	**1 (1.8)**	**3.52 [0.39; 31.43]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.260
Heterogeneity test, p-value: 0.621[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-6
Forest Plot of Time to Adverse Event in Preferred Term
Hypothyroidism
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

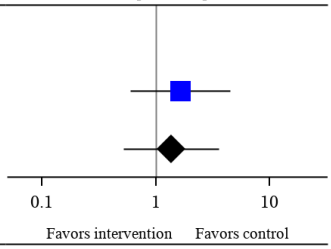
PT: Hypothyroidism	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	1 (16.7)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	5 (10.9)	48	0 (0.0)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**6 (11.5)**	**55**	**0 (0.0)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.108
Heterogeneity test, p-value: 0.997[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-7
Forest Plot of Time to Adverse Event in System Organ Class
Eye disorders
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

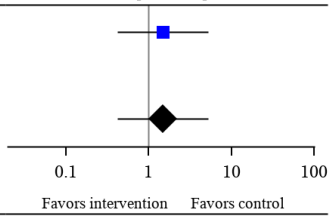
SOC: Eye disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	0 (0.0)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	10 (21.7)	48	6 (12.5)	1.63 [0.59; 4.50]	
Overall[c]	**52**	**10 (19.2)**	**55**	**7 (12.7)**	**1.37 [0.52; 3.60]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.524
Heterogeneity test, p-value: 0.150[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-8
Forest Plot of Time to Adverse Event in Preferred Term
Lacrimation increased
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Lacrimation increased	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	6 (13.0)	48	4 (8.3)	1.48 [0.42; 5.26]	
Overall[c]	**52**	**6 (11.5)**	**55**	**4 (7.3)**	**1.48 [0.42; 5.26]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.543

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

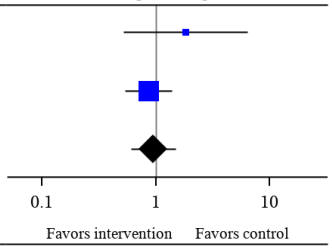
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Adverse Events by SOC and PT - Time to Event

Figure 4.1-9
Forest Plot of Time to Adverse Event in System Organ Class Gastrointestinal disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

SOC: Gastrointestinal disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	5 (83.3)	7	5 (71.4)	1.83 [0.52; 6.44]	
PHASE 3[b]	46	35 (76.1)	48	34 (70.8)	0.86 [0.53; 1.40]	
Overall[c]	**52**	**40 (76.9)**	**55**	**39 (70.9)**	**0.95 [0.60; 1.49]**	

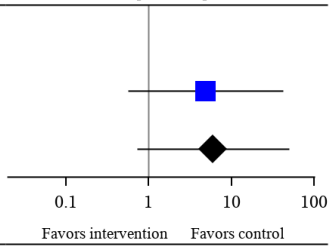


Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.817
Heterogeneity test, p-value: 0.273[d]

a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-10
Forest Plot of Time to Adverse Event in Preferred Term
Abdominal pain
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

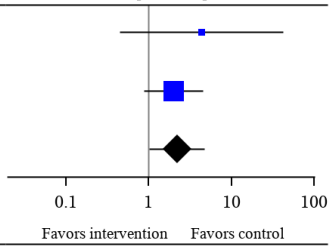
PT: Abdominal pain	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	2 (33.3)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	6 (13.0)	48	1 (2.1)	4.88 [0.57; 41.81]	
Overall[c]	**52**	**8 (15.4)**	**55**	**1 (1.8)**	**6.02 [0.72; 50.00]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.097
Heterogeneity test, p-value: 0.442[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-11
Forest Plot of Time to Adverse Event in Preferred Term
Constipation
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

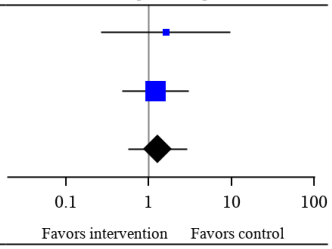
PT: Constipation	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	3 (50.0)	7	1 (14.3)	4.34 [0.45; 41.91]	
PHASE 3[b]	46	16 (34.8)	48	9 (18.8)	2.00 [0.88; 4.53]	
Overall[c]	**52**	**19 (36.5)**	**55**	**10 (18.2)**	**2.21 [1.03; 4.77]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.042
Heterogeneity test, p-value: 0.451[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-12
Forest Plot of Time to Adverse Event in Preferred Term
Diarrhoea
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

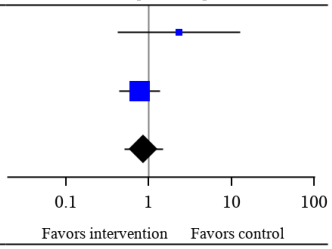
PT: Diarrhoea	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	4 (66.7)	7	2 (28.6)	1.61 [0.27; 9.62]	
PHASE 3[b]	46	11 (23.9)	48	8 (16.7)	1.21 [0.48; 3.08]	
Overall[c]	**52**	**15 (28.8)**	**55**	**10 (18.2)**	**1.29 [0.56; 2.94]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.547
Heterogeneity test, p-value: 0.568[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-13
Forest Plot of Time to Adverse Event in Preferred Term
Nausea
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

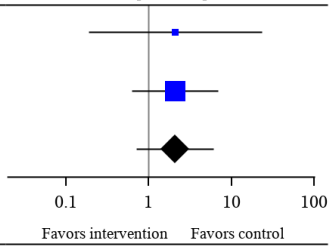
PT: Nausea	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	5 (83.3)	7	2 (28.6)	2.33 [0.43; 12.79]	
PHASE 3[b]	46	24 (52.2)	48	26 (54.2)	0.77 [0.44; 1.36]	
Overall[c]	**52**	**29 (55.8)**	**55**	**28 (50.9)**	**0.87 [0.51; 1.49]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.610
Heterogeneity test, p-value: 0.096[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-14
Forest Plot of Time to Adverse Event in Preferred Term
Stomatitis
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

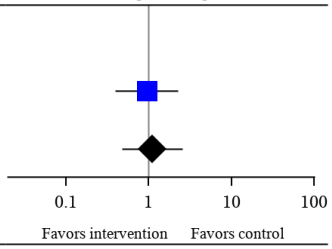
PT: Stomatitis	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	2 (33.3)	7	1 (14.3)	2.11 [0.19; 23.27]	
PHASE 3[b]	46	10 (21.7)	48	4 (8.3)	2.10 [0.64; 6.94]	
Overall [c]	**52**	**12 (23.1)**	**55**	**5 (9.1)**	**2.10 [0.72; 6.13]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.174
Heterogeneity test, p-value: 0.838[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-15
Forest Plot of Time to Adverse Event in Preferred Term
Vomiting
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Vomiting	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	2 (33.3)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	11 (23.9)	48	10 (20.8)	0.95 [0.39; 2.28]	
Overall[c]	**52**	**13 (25.0)**	**55**	**10 (18.2)**	**1.12 [0.48; 2.60]**	

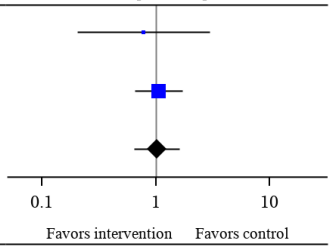


Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.795
Heterogeneity test, p-value: 0.090[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-16

Forest Plot of Time to Adverse Event in System Organ Class General disorders and administration site conditions Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

SOC: General disorders and administration site conditions	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	6 (100.0)	7	5 (71.4)	0.78 [0.20; 2.97]	
PHASE 3[b]	46	39 (84.8)	48	30 (62.5)	1.06 [0.65; 1.72]	
Overall[c]	**52**	**45 (86.5)**	**55**	**35 (63.6)**	**1.02 [0.65; 1.61]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.932

Heterogeneity test, p-value: 0.716[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

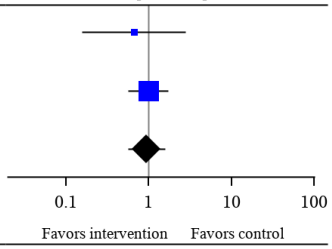
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Adverse Events by SOC and PT - Time to Event

Figure 4.1-17
Forest Plot of Time to Adverse Event in Preferred Term
Fatigue
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

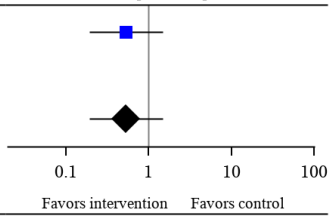
PT: Fatigue	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	5 (83.3)	7	5 (71.4)	0.67 [0.16; 2.79]	
PHASE 3[b]	46	29 (63.0)	48	24 (50.0)	1.00 [0.57; 1.74]	
Overall[c]	**52**	**34 (65.4)**	**55**	**29 (52.7)**	**0.94 [0.56; 1.58]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.829
Heterogeneity test, p-value: 0.587[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-18
Forest Plot of Time to Adverse Event in Preferred Term
Non-cardiac chest pain
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Non cardiac chest Cohort[a]	Pembrolizumab + Chemotherapy Participants with Event N	n (%)	Chemotherapy Participants with Event N	n (%)	Hazard Ratio [95% CI]	Hazard Ratio [95% CI]
PHASE 3[b]	46	8 (17.4)	48	9 (18.8)	0.54 [0.20; 1.48]	
Overall[c]	**52**	**8 (15.4)**	**55**	**9 (16.4)**	**0.54 [0.20; 1.48]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.229

Heterogeneity test, p-value: 0.998[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

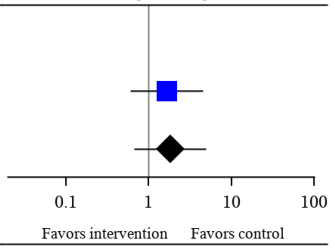
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Adverse Events by SOC and PT - Time to Event

Figure 4.1-19
Forest Plot of Time to Adverse Event in Preferred Term
Pyrexia
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

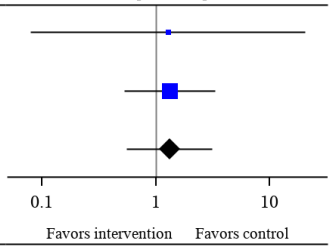
PT: Pyrexia	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	1 (16.7)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	12 (26.1)	48	6 (12.5)	1.66 [0.60; 4.56]	
Overall[c]	**52**	**13 (25.0)**	**55**	**6 (10.9)**	**1.82 [0.67; 4.93]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.237
Heterogeneity test, p-value: 0.408[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-20
Forest Plot of Time to Adverse Event in System Organ Class
Infections and infestations
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

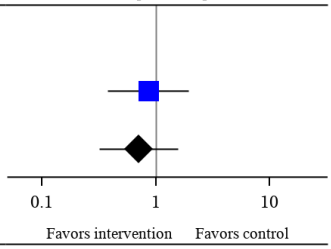
SOC: Infections and infestations	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	2 (33.3)	7	1 (14.3)	1.28 [0.08; 20.49]	
PHASE 3[b]	46	14 (30.4)	48	8 (16.7)	1.32 [0.53; 3.30]	
Overall[c]	**52**	**16 (30.8)**	**55**	**9 (16.4)**	**1.32 [0.55; 3.14]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.535
Heterogeneity test, p-value: 0.970[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-21
Forest Plot of Time to Adverse Event in System Organ Class Metabolism and nutrition disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

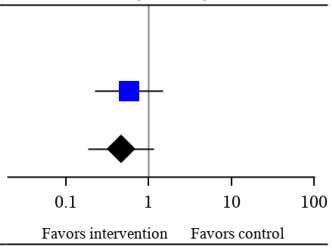
SOC: Metabolism and nutrition disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	3 (50.0)	7	2 (28.6)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	11 (23.9)	48	12 (25.0)	0.86 [0.38; 1.94]	
Overall[c]	**52**	**14 (26.9)**	**55**	**14 (25.5)**	**0.71 [0.32; 1.56]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.391
Heterogeneity test, p-value: 0.761[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-22
Forest Plot of Time to Adverse Event in Preferred Term
Decreased appetite
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

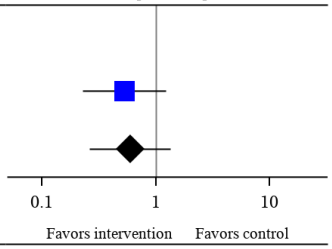
PT: Decreased appetite	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	3 (50.0)	7	2 (28.6)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	7 (15.2)	48	11 (22.9)	0.58 [0.22; 1.49]	
Overall[c]	**52**	**10 (19.2)**	**55**	**13 (23.6)**	**0.46 [0.18; 1.17]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.104
Heterogeneity test, p-value: 0.545[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-23
Forest Plot of Time to Adverse Event in System Organ Class Musculoskeletal and connective tissue disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

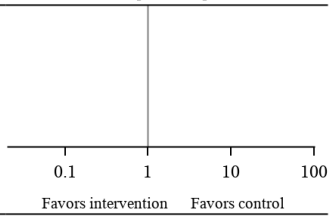
SOC: Musculoskeletal and connective tissue disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	2 (33.3)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	19 (41.3)	48	14 (29.2)	0.53 [0.23; 1.23]	
Overall[c]	**52**	**21 (40.4)**	**55**	**14 (25.5)**	**0.60 [0.26; 1.35]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.216
Heterogeneity test, p-value: 0.159[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-24
Forest Plot of Time to Adverse Event in Preferred Term
Arthralgia
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Arthralgia	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	7 (15.2)	48	0 (0.0)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**7 (13.5)**	**55**	**0 (0.0)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.288

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

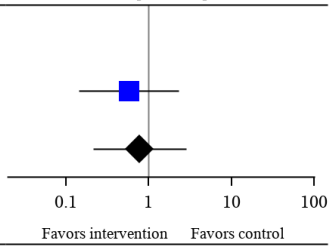
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Adverse Events by SOC and PT - Time to Event

Figure 4.1-25
Forest Plot of Time to Adverse Event in Preferred Term
Back pain
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

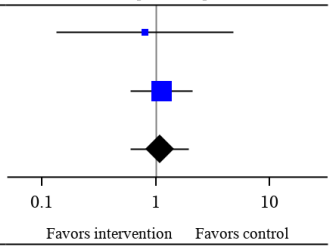
PT: Back pain	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	2 (33.3)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	6 (13.0)	48	5 (10.4)	0.58 [0.14; 2.32]	
Overall[c]	**52**	**8 (15.4)**	**55**	**5 (9.1)**	**0.78 [0.21; 2.83]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.703
Heterogeneity test, p-value: 0.115[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-26
Forest Plot of Time to Adverse Event in System Organ Class Nervous system disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

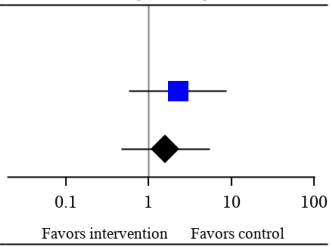
SOC: Nervous disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	2 (33.3)	7	3 (42.9)	0.80 [0.13; 4.78]	
PHASE 3[b]	46	21 (45.7)	48	18 (37.5)	1.12 [0.60; 2.11]	
Overall[c]	**52**	**23 (44.2)**	**55**	**21 (38.2)**	**1.08 [0.60; 1.95]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.800
Heterogeneity test, p-value: 0.466[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-27
Forest Plot of Time to Adverse Event in Preferred Term
Dizziness
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

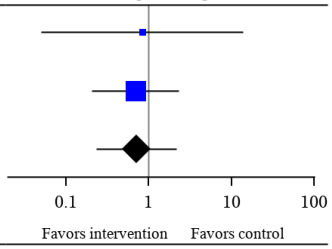
PT: Dizziness	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	0 (0.0)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	7 (15.2)	48	3 (6.3)	2.25 [0.58; 8.71]	
Overall[c]	**52**	**7 (13.5)**	**55**	**4 (7.3)**	**1.60 [0.47; 5.49]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.455
Heterogeneity test, p-value: 0.099[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-28
Forest Plot of Time to Adverse Event in Preferred Term
Dysgeusia
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

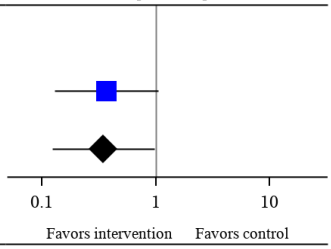
PT: Dysgeusia	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	1 (16.7)	7	1 (14.3)	0.84 [0.05; 13.90]	
PHASE 3[b]	46	5 (10.9)	48	6 (12.5)	0.69 [0.21; 2.32]	
Overall[c]	**52**	**6 (11.5)**	**55**	**7 (12.7)**	**0.71 [0.24; 2.17]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.552
Heterogeneity test, p-value: 0.911[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-29
Forest Plot of Time to Adverse Event in System Organ Class Psychiatric disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

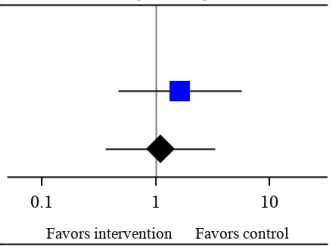
SOC: Psychiatric disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	1 (16.7)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	9 (19.6)	48	12 (25.0)	0.37 [0.13; 1.05]	
Overall[c]	**52**	**10 (19.2)**	**55**	**13 (23.6)**	**0.34 [0.12; 0.97]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.043
Heterogeneity test, p-value: 0.938[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-30
Forest Plot of Time to Adverse Event in System Organ Class Renal and urinary disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

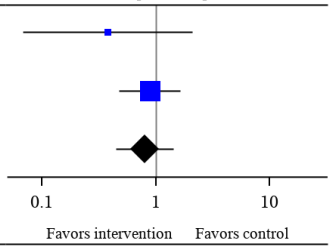
SOC: Renal and urinary disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	0 (0.0)	7	2 (28.6)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	8 (17.4)	48	4 (8.3)	1.62 [0.47; 5.63]	
Overall[c]	**52**	**8 (15.4)**	**55**	**6 (10.9)**	**1.09 [0.36; 3.32]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.873
Heterogeneity test, p-value: 0.038[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-31
Forest Plot of Time to Adverse Event in System Organ Class Respiratory, thoracic and mediastinal disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

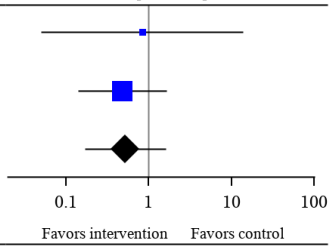
SOC: Respiratory, thoracic and mediastinal disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	2 (33.3)	7	4 (57.1)	0.38 [0.07; 2.08]	
PHASE 3[b]	46	23 (50.0)	48	20 (41.7)	0.89 [0.48; 1.65]	
Overall[c]	**52**	**25 (48.1)**	**55**	**24 (43.6)**	**0.80 [0.45; 1.42]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.440
Heterogeneity test, p-value: 0.250[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-32
Forest Plot of Time to Adverse Event in Preferred Term
Cough
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

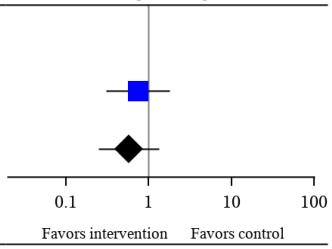
PT: Cough	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	1 (16.7)	7	1 (14.3)	0.84 [0.05; 13.90]	
PHASE 3[b]	46	7 (15.2)	48	7 (14.6)	0.48 [0.14; 1.65]	
Overall [c]	**52**	**8 (15.4)**	**55**	**8 (14.5)**	**0.53 [0.17; 1.62]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.262
Heterogeneity test, p-value: 0.765[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-33
Forest Plot of Time to Adverse Event in Preferred Term
Dyspnoea
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

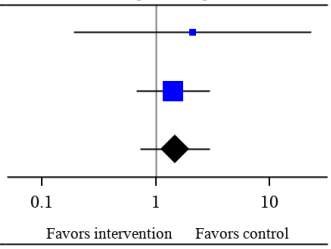
PT: Dyspnoea	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	2 (33.3)	7	3 (42.9)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	10 (21.7)	48	11 (22.9)	0.74 [0.31; 1.79]	
Overall[c]	**52**	**12 (23.1)**	**55**	**14 (25.5)**	**0.57 [0.25; 1.33]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.196
Heterogeneity test, p-value: 0.447[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-34
Forest Plot of Time to Adverse Event in System Organ Class
Skin and subcutaneous tissue disorders
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

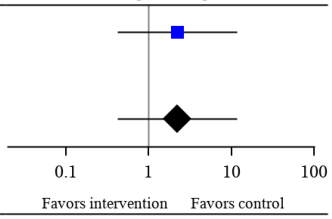
SOC: Skin and subcutaneous tissue disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	4 (66.7)	7	1 (14.3)	2.11 [0.19; 23.27]	
PHASE 3[b]	46	20 (43.5)	48	12 (25.0)	1.42 [0.68; 2.97]	
Overall[c]	**52**	**24 (46.2)**	**55**	**13 (23.6)**	**1.47 [0.72; 2.98]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.286
Heterogeneity test, p-value: 0.586[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-35
Forest Plot of Time to Adverse Event in Preferred Term
Pruritus
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Pruritus	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 3[b]	46	8 (17.4)	48	2 (4.2)	2.23 [0.43; 11.65]	
Overall[c]	**52**	**8 (15.4)**	**55**	**2 (3.6)**	**2.23 [0.43; 11.65]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.343

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

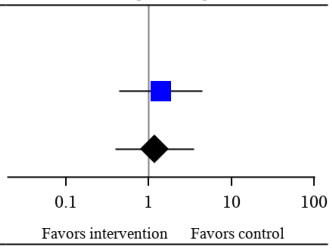
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Adverse Events by SOC and PT - Time to Event

Figure 4.1-36
Forest Plot of Time to Adverse Event in Preferred Term
Rash maculo-papular
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

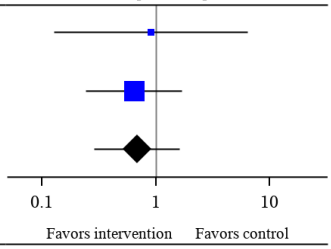
PT: Rash maculo papular	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	1 (16.7)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	8 (17.4)	48	5 (10.4)	1.40 [0.44; 4.41]	
Overall[c]	**52**	**9 (17.3)**	**55**	**6 (10.9)**	**1.18 [0.40; 3.51]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.769
Heterogeneity test, p-value: 0.639[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-37
Forest Plot of Time to Adverse Event in System Organ Class
Vascular disorders
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

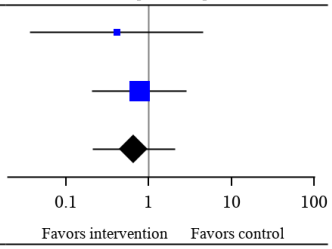
SOC: Vascular disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	2 (33.3)	7	2 (28.6)	0.90 [0.13; 6.43]	
PHASE 3[b]	46	8 (17.4)	48	10 (20.8)	0.64 [0.24; 1.68]	
Overall[c]	**52**	**10 (19.2)**	**55**	**12 (21.8)**	**0.68 [0.29; 1.63]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.391
Heterogeneity test, p-value: 0.842[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-38
Forest Plot of Time to Adverse Event in Preferred Term
Embolism
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

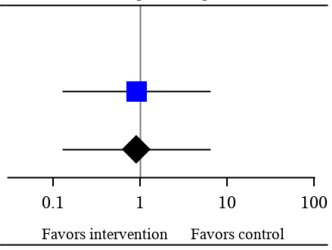
PT: Embolism	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	1 (16.7)	7	2 (28.6)	0.41 [0.04; 4.55]	
PHASE 3[b]	46	5 (10.9)	48	5 (10.4)	0.77 [0.21; 2.87]	
Overall[c]	**52**	**6 (11.5)**	**55**	**7 (12.7)**	**0.66 [0.21; 2.09]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.480
Heterogeneity test, p-value: 0.561[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Adverse Events by SOC and PT - Time to Event

Figure 4.1-39
Forest Plot of Time to Serious Adverse Event in System Organ Class Cardiac disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

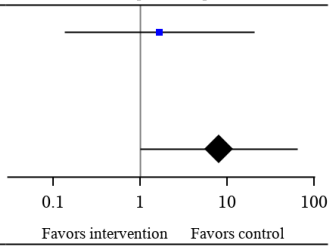
SOC: Cardiac disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	1 (16.7)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	2 (4.3)	48	2 (4.2)	0.90 [0.13; 6.40]	
Overall [c]	**52**	**3 (5.8)**	**55**	**2 (3.6)**	**0.90 [0.13; 6.40]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.916
Heterogeneity test, p-value: 0.330[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-40
Forest Plot of Time to Serious Adverse Event in System Organ Class Gastrointestinal disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

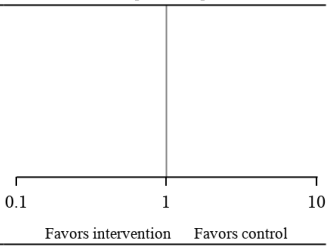
SOC: Gastrointestinal disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	2 (33.3)	7	1 (14.3)	1.66 [0.13; 20.71]	
PHASE 3[b]	46	7 (15.2)	48	0 (0.0)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**9 (17.3)**	**55**	**1 (1.8)**	**7.98 [0.99; 64.47]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.051
Heterogeneity test, p-value: 0.119[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-41
Forest Plot of Time to Serious Adverse Event in Preferred Term
Abdominal pain
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

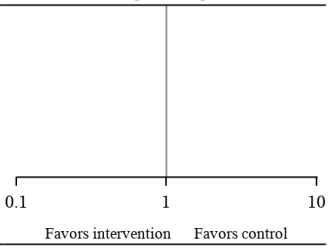
PT: Abdominal pain	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	1 (16.7)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	3 (6.5)	48	0 (0.0)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**4 (7.7)**	**55**	**0 (0.0)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.073
Heterogeneity test, p-value: 0.997[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-42
Forest Plot of Time to Serious Adverse Event in Preferred Term Diarrhoea
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

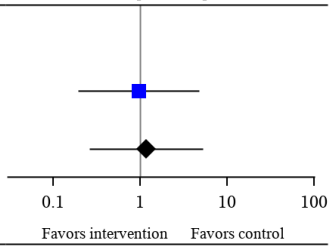
PT: Diarrhoea	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	2 (33.3)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	3 (6.5)	48	0 (0.0)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**5 (9.6)**	**55**	**0 (0.0)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.038
Heterogeneity test, p-value: 0.997[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-43
Forest Plot of Time to Serious Adverse Event in System Organ Class General disorders and administration site conditions Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

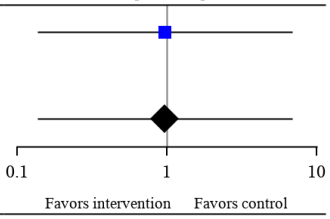
SOC: General disorders and administration site conditions	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	1 (16.7)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	4 (8.7)	48	3 (6.3)	0.95 [0.19; 4.74]	
Overall[c]	**52**	**5 (9.6)**	**55**	**3 (5.5)**	**1.17 [0.26; 5.26]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.841
Heterogeneity test, p-value: 0.342[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-44
Forest Plot of Time to Serious Adverse Event in Preferred Term Pyrexia
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Pyrexia	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 3[b]	46	3 (6.5)	48	2 (4.2)	0.97 [0.14; 6.90]	
Overall[c]	**52**	**3 (5.8)**	**55**	**2 (3.6)**	**0.97 [0.14; 6.90]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.976

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

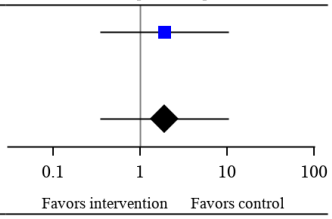
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-45
Forest Plot of Time to Serious Adverse Event in System Organ Class Infections and infestations Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

SOC: Infections and infestations	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	4 (8.7)	48	2 (4.2)	1.90 [0.35; 10.41]	
Overall[c]	**52**	**4 (7.7)**	**55**	**2 (3.6)**	**1.90 [0.35; 10.41]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.457

Heterogeneity test, p-value: 0.998[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

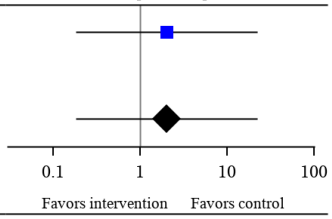
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-46
Forest Plot of Time to Serious Adverse Event in System Organ Class Psychiatric disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

SOC: Psychiatric disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	3 (6.5)	48	1 (2.1)	2.00 [0.18; 22.06]	
Overall[c]	**52**	**3 (5.8)**	**55**	**1 (1.8)**	**2.00 [0.18; 22.06]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.571

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

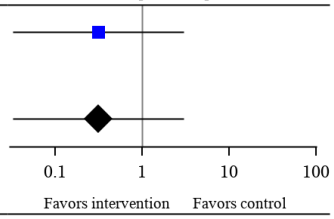
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-47
Forest Plot of Time to Serious Adverse Event in System Organ Class Respiratory, thoracic and mediastinal disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

SOC: Respiratory, thoracic and mediastinal disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	3 (6.5)	48	3 (6.3)	0.31 [0.03; 3.02]	
Overall[c]	**52**	**3 (5.8)**	**55**	**3 (5.5)**	**0.31 [0.03; 3.02]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.315

Heterogeneity test, p-value: 0.998[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

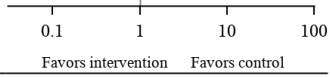
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-48
Forest Plot of Time to Serious Adverse Event in System Organ Class Vascular disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

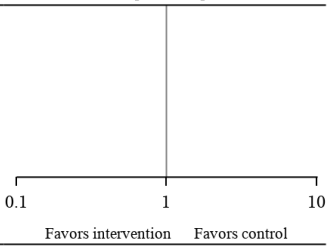
SOC: Vascular disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	0 (0.0)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	0 (0.0)	48	2 (4.2)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**0 (0.0)**	**55**	**3 (5.5)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.094
Heterogeneity test, p-value: 0.997[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-49
Forest Plot of Time to Serious Adverse Event in Preferred Term Embolism
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

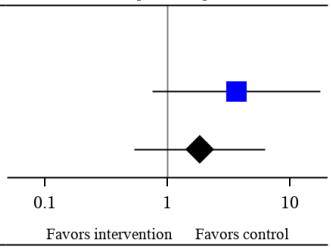
PT: Embolism	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	0 (0.0)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	0 (0.0)	48	2 (4.2)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**0 (0.0)**	**55**	**3 (5.5)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.094
Heterogeneity test, p-value: 0.997[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Serious Adverse Events by SOC and PT - Time to Event

Figure 4.1-50
Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in System Organ Class Gastrointestinal disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

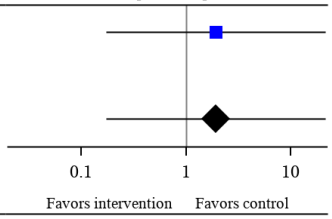
SOC: Gastrointestinal disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	1 (16.7)	7	2 (28.6)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	7 (15.2)	48	2 (4.2)	3.64 [0.76; 17.52]	
Overall [c]	**52**	**8 (15.4)**	**55**	**4 (7.3)**	**1.83 [0.54; 6.26]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.334
Heterogeneity test, p-value: 0.121[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-51
Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in Preferred Term Abdominal pain
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Abdominal pain	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	3 (6.5)	48	1 (2.1)	1.91 [0.17; 21.18]	
Overall[c]	**52**	**3 (5.8)**	**55**	**1 (1.8)**	**1.91 [0.17; 21.18]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.596

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

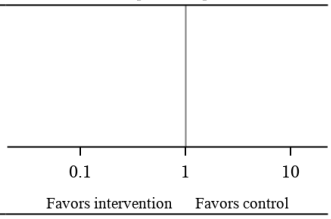
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-52
Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in Preferred Term Nausea
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Nausea	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	3 (6.5)	48	0 (0.0)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**3 (5.8)**	**55**	**0 (0.0)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.077
Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

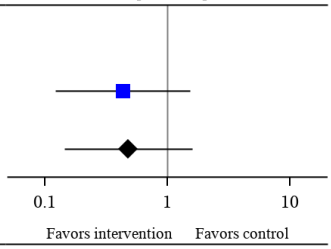
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-53
Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in System Organ Class General disorders and administration site conditions Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

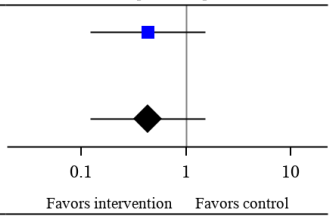
SOC: General disorders and administration site conditions	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	1 (16.7)	7	0 (0.0)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	4 (8.7)	48	7 (14.6)	0.43 [0.12; 1.52]	
Overall[c]	**52**	**5 (9.6)**	**55**	**7 (12.7)**	**0.48 [0.14; 1.59]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.230
Heterogeneity test, p-value: 0.232[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-54
Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in Preferred Term Fatigue
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Fatigue	Pembrolizumab + Chemotherapy Participants with Event		Chemotherapy Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 3[b]	46	4 (8.7)	48	7 (14.6)	0.43 [0.12; 1.52]	
Overall[c]	**52**	**4 (7.7)**	**55**	**7 (12.7)**	**0.43 [0.12; 1.52]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.192

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

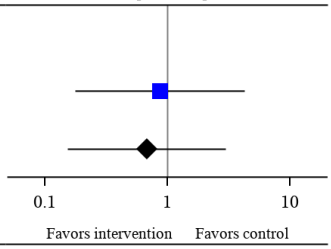
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-55
Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in System Organ Class Infections and infestations Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

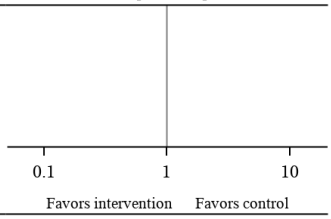
SOC: Infections and infestations	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	0 (0.0)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	5 (10.9)	48	3 (6.3)	0.86 [0.18; 4.23]	
Overall[c]	**52**	**5 (9.6)**	**55**	**4 (7.3)**	**0.68 [0.15; 2.99]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.608
Heterogeneity test, p-value: 0.130[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-56
Forest Plot of Time to Severe Adverse Event in System Organ Class Psychiatric disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

SOC: Psychiatric disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	3 (6.5)	48	0 (0.0)	n.a. [n.a.; n.a.]	
Overall[b]	**52**	**3 (5.8)**	**55**	**0 (0.0)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.160

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

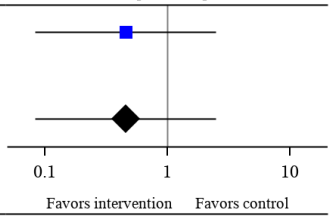
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-57

Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in System Organ Class Respiratory, thoracic and mediastinal disorders Subpopulation of Participants, Non-epithelioid (All-Participants-as-Treated Population, Phase 2 and Phase 3)

SOC: Respiratory, thoracic and mediastinal disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 3[b]	46	4 (8.7)	48	4 (8.3)	0.46 [0.08; 2.49]	
Overall[b]	**52**	**4 (7.7)**	**55**	**4 (7.3)**	**0.46 [0.08; 2.49]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.365

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

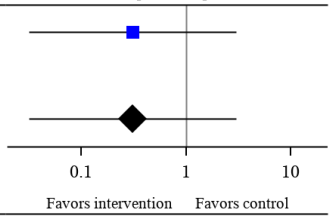
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-58

Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in Preferred Term Dyspnoea
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Dyspnoea	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 3[b]	46	2 (4.3)	48	3 (6.3)	0.31 [0.03; 2.98]	
Overall[c]	**52**	**2 (3.8)**	**55**	**3 (5.5)**	**0.31 [0.03; 2.98]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.310

Heterogeneity test, p-value: 0.997[d]

a: Database Cutoff Date: 16SEP2022

b: Based on Cox model with treatment as a covariate

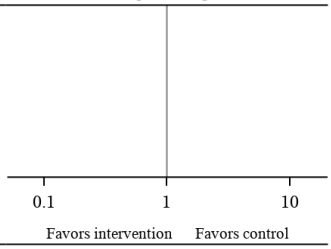
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)

d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)

Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-59
Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in System Organ Class Vascular disorders
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

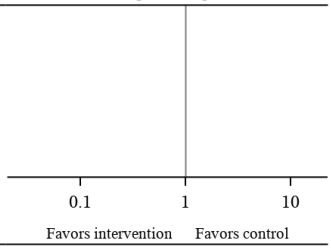
SOC: Vascular disorders	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	N	n (%)	N	n (%)	[95% CI]	[95% CI]
PHASE 2[b]	6	0 (0.0)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	1 (2.2)	48	6 (12.5)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**1 (1.9)**	**55**	**7 (12.7)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.993
Heterogeneity test, p-value: 0.539[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event

Figure 4.1-60
Forest Plot of Time to Severe Adverse Event (CTCAE-Grade 3-5) in Preferred Term Embolism
Subpopulation of Participants, Non-epithelioid
(All-Participants-as-Treated Population, Phase 2 and Phase 3)

PT: Embolism	Pembrolizumab + Chemotherapy		Chemotherapy			
	Participants with Event		Participants with Event		Hazard Ratio	Hazard Ratio
Cohort[a]	**N**	**n (%)**	**N**	**n (%)**	**[95% CI]**	**[95% CI]**
PHASE 2[b]	6	0 (0.0)	7	1 (14.3)	n.a. [n.a.; n.a.]	
PHASE 3[b]	46	1 (2.2)	48	4 (8.3)	n.a. [n.a.; n.a.]	
Overall[c]	**52**	**1 (1.9)**	**55**	**5 (9.1)**	**n.a. [n.a.; n.a.]**	



Test for overall effect based on KN483 phase 2 + phase 3, p-value: 0.994
Heterogeneity test, p-value: 0.466[d]
a: Database Cutoff Date: 16SEP2022
b: Based on Cox model with treatment as a covariate
c: Based on Cox model with treatment as a covariate and stratified by cohort (phase 2 vs phase 3)
d: Based on Cox model with treatment and cohort as covariates and treatment-by-cohort interaction (p-value of likelihood ratio test for interaction term)
Severe Adverse Events (CTCAE-Grade 3-5) by SOC and PT - Time to Event