Dossier zur Nutzenbewertung gemäß § 35a SGB V

Pembrolizumab (KEYTRUDA®)

MSD Sharp & Dohme GmbH

Modul 4A

Anhang 4-G: Weitere Ergebnisse

KEYTRUDA® ist in Kombination mit Radiochemotherapie (perkutane Strahlentherapie, gefolgt von einer Brachytherapie) zur Behandlung des lokal fortgeschrittenen Zervixkarzinoms (Stadium III bis IVA gemäß FIGO 2014) bei Erwachsenen, die keine vorherige definitive Therapie erhalten haben, angezeigt.

Stand: 14.11.2024

Inhaltsverzeichnis

Seite

Tabellenverzeichnis

Abbildungsverzeichnis

Es konnten keine Einträge für ein Abbildungsverzeichnis gefunden werden.

Anhang 4-G: Weitere Ergebnisse

Anhang 4-G1: Rücklaufquoten des EORTC QLQ-C30, EORTC QLQ-CX24, PGI-S, PGI-C 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-CX24, PGI-C, PGI-S und EQ-5D VAS dargestellt.

Alle Ergebnisse beziehen sich auf den Datenschnitt vom 08.01.2024.

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

Tabelle 4G-1: Gründe für das Fehlen von Werten im EORTC QLQ-C30

		Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
Treatment Visit	Category	n	(%)	n	(%)
Baseline	**Expected to Complete Questionnaires**	**266**	**(97.8)**	**277**	**(97.9)**
	Completed	261	(96.0)	270	(95.4)
	Compliance (% in those expected to complete questionnaires)	261	(98.1)	270	(97.5)
	Not completed	5	(1.8)	7	(2.5)
	Other	1	(0.4)	2	(0.7)
	With visit, no record	4	(1.5)	5	(1.8)
	Missing by Design	**6**	**(2.2)**	**6**	**(2.1)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	6	(2.2)	6	(2.1)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 3	**Expected to Complete Questionnaires**	**262**	**(96.3)**	**268**	**(94.7)**
	Completed	256	(94.1)	263	(92.9)
	Compliance (% in those expected to complete questionnaires)	256	(97.7)	263	(98.1)
	Not completed	6	(2.2)	5	(1.8)
	Other	1	(0.4)	1	(0.4)
	With visit, no record	5	(1.8)	4	(1.4)
	Missing by Design	**10**	**(3.7)**	**15**	**(5.3)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 3	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	2	(0.7)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	10	(3.7)	12	(4.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 6	**Expected to Complete Questionnaires**	**253**	**(93.0)**	**254**	**(89.8)**
	Completed	239	(87.9)	244	(86.2)
	Compliance (% in those expected to complete questionnaires)	239	(94.5)	244	(96.1)
	Not completed	14	(5.1)	10	(3.5)
	Other	4	(1.5)	5	(1.8)
	With visit, no record	10	(3.7)	5	(1.8)
	Missing by Design	**19**	**(7.0)**	**29**	**(10.2)**
	Discontinued due to adverse event	2	(0.7)	3	(1.1)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	1	(0.4)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	1	(0.4)	3	(1.1)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	15	(5.5)	22	(7.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 9	**Expected to Complete Questionnaires**	**247**	**(90.8)**	**260**	**(91.9)**
	Completed	238	(87.5)	255	(90.1)
	Compliance (% in those expected to complete questionnaires)	238	(96.4)	255	(98.1)
	Not completed	9	(3.3)	5	(1.8)
	Other	5	(1.8)	3	(1.1)
	With visit, no record	4	(1.5)	2	(0.7)
	Missing by Design	**25**	**(9.2)**	**23**	**(8.1)**
	Discontinued due to adverse event	3	(1.1)	3	(1.1)
	Discontinued due to clinical progression	1	(0.4)	2	(0.7)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 9	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	1	(0.4)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	2	(0.7)	4	(1.4)
	Discontinued due to radiographic progression	1	(0.4)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	15	(5.5)	14	(4.9)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 12	**Expected to Complete Questionnaires**	**249**	**(91.5)**	**259**	**(91.5)**
	Completed	240	(88.2)	253	(89.4)
	Compliance (% in those expected to complete questionnaires)	240	(96.4)	253	(97.7)
	Not completed	9	(3.3)	6	(2.1)
	Other	5	(1.8)	0	(0.0)
	With visit, no record	4	(1.5)	6	(2.1)
	Missing by Design	**23**	**(8.5)**	**24**	**(8.5)**
	Discontinued due to adverse event	5	(1.8)	4	(1.4)
	Discontinued due to clinical progression	1	(0.4)	3	(1.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	1	(0.4)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	2	(0.7)	4	(1.4)
	Discontinued due to radiographic progression	3	(1.1)	3	(1.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	8	(2.9)	9	(3.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 18	**Expected to Complete Questionnaires**	**254**	**(93.4)**	**263**	**(92.9)**
	Completed	249	(91.5)	260	(91.9)
	Compliance (% in those expected to complete questionnaires)	249	(98.0)	260	(98.9)
	Not completed	5	(1.8)	3	(1.1)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	5	(1.8)	3	(1.1)
	Missing by Design	**18**	**(6.6)**	**20**	**(7.1)**
	Discontinued due to adverse event	3	(1.1)	5	(1.8)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 18	Discontinued due to clinical progression	1	(0.4)	3	(1.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	3	(1.1)	5	(1.8)
	Discontinued due to radiographic progression	4	(1.5)	3	(1.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(1.1)	4	(1.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 24	**Expected to Complete Questionnaires**	**231**	**(84.9)**	**242**	**(85.5)**
	Completed	217	(79.8)	235	(83.0)
	Compliance (% in those expected to complete questionnaires)	217	(93.9)	235	(97.1)
	Not completed	14	(5.1)	7	(2.5)
	Other	7	(2.6)	1	(0.4)
	With visit, no record	7	(2.6)	6	(2.1)
	Missing by Design	**41**	**(15.1)**	**41**	**(14.5)**
	Discontinued due to adverse event	11	(4.0)	6	(2.1)
	Discontinued due to clinical progression	2	(0.7)	4	(1.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	3	(1.1)	2	(0.7)
	Discontinued due to progressive disease	0	(0.0)	1	(0.4)
	Discontinued due to withdrawal by subject	3	(1.1)	7	(2.5)
	Discontinued due to radiographic progression	10	(3.7)	12	(4.2)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	8	(2.9)	9	(3.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 30	**Expected to Complete Questionnaires**	**220**	**(80.9)**	**223**	**(78.8)**
	Completed	207	(76.1)	212	(74.9)
	Compliance (% in those expected to complete questionnaires)	207	(94.1)	212	(95.1)
	Not completed	13	(4.8)	11	(3.9)
	Other	8	(2.9)	4	(1.4)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**52**	**(19.1)**	**60**	**(21.2)**

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 30	Discontinued due to adverse event	8	(2.9)	5	(1.8)
	Discontinued due to clinical progression	2	(0.7)	5	(1.8)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	1	(0.4)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	2	(0.7)	8	(2.8)
	Discontinued due to radiographic progression	21	(7.7)	28	(9.9)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	11	(4.0)	11	(3.9)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 36	**Expected to Complete Questionnaires**	**212**	**(77.9)**	**211**	**(74.6)**
	Completed	200	(73.5)	198	(70.0)
	Compliance (% in those expected to complete questionnaires)	200	(94.3)	198	(93.8)
	Not completed	12	(4.4)	13	(4.6)
	Other	5	(1.8)	5	(1.8)
	With visit, no record	7	(2.6)	8	(2.8)
	Missing by Design	**60**	**(22.1)**	**72**	**(25.4)**
	Discontinued due to adverse event	16	(5.9)	6	(2.1)
	Discontinued due to clinical progression	2	(0.7)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	3	(1.1)	10	(3.5)
	Discontinued due to radiographic progression	25	(9.2)	41	(14.5)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	6	(2.2)	4	(1.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 42	**Expected to Complete Questionnaires**	**210**	**(77.2)**	**194**	**(68.6)**
	Completed	198	(72.8)	183	(64.7)
	Compliance (% in those expected to complete questionnaires)	198	(94.3)	183	(94.3)
	Not completed	12	(4.4)	11	(3.9)
	Other	8	(2.9)	3	(1.1)
	With visit, no record	4	(1.5)	8	(2.8)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 42	**Missing by Design**	**62**	**(22.8)**	**89**	**(31.4)**
	Discontinued due to adverse event	11	(4.0)	7	(2.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	10	(3.5)
	Discontinued due to radiographic progression	28	(10.3)	52	(18.4)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	7	(2.6)	8	(2.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 48	**Expected to Complete Questionnaires**	**200**	**(73.5)**	**188**	**(66.4)**
	Completed	189	(69.5)	178	(62.9)
	Compliance (% in those expected to complete questionnaires)	189	(94.5)	178	(94.7)
	Not completed	11	(4.0)	10	(3.5)
	Other	3	(1.1)	4	(1.4)
	With visit, no record	8	(2.9)	6	(2.1)
	Missing by Design	**72**	**(26.5)**	**95**	**(33.6)**
	Discontinued due to adverse event	20	(7.4)	7	(2.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	4	(1.5)	10	(3.5)
	Discontinued due to radiographic progression	33	(12.1)	62	(21.9)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(1.1)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 54	**Expected to Complete Questionnaires**	**200**	**(73.5)**	**174**	**(61.5)**
	Completed	189	(69.5)	165	(58.3)
	Compliance (% in those expected to complete questionnaires)	189	(94.5)	165	(94.8)
	Not completed	11	(4.0)	9	(3.2)
	Other	5	(1.8)	4	(1.4)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 54	With visit, no record	6	(2.2)	5	(1.8)
	Missing by Design	**72**	**(26.5)**	**109**	**(38.5)**
	Discontinued due to adverse event	13	(4.8)	9	(3.2)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	10	(3.5)
	Discontinued due to radiographic progression	38	(14.0)	68	(24.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	5	(1.8)	9	(3.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 60	**Expected to Complete Questionnaires**	**191**	**(70.2)**	**176**	**(62.2)**
	Completed	177	(65.1)	166	(58.7)
	Compliance (% in those expected to complete questionnaires)	177	(92.7)	166	(94.3)
	Not completed	14	(5.1)	10	(3.5)
	Other	7	(2.6)	3	(1.1)
	With visit, no record	7	(2.6)	7	(2.5)
	Missing by Design	**81**	**(29.8)**	**107**	**(37.8)**
	Discontinued due to adverse event	18	(6.6)	6	(2.1)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	10	(3.5)
	Discontinued due to radiographic progression	39	(14.3)	68	(24.0)
	Visit not reached	4	(1.5)	4	(1.4)
	Visit not scheduled	4	(1.5)	7	(2.5)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 66	**Expected to Complete Questionnaires**	**179**	**(65.8)**	**161**	**(56.9)**
	Completed	161	(59.2)	149	(52.7)
	Compliance (% in those expected to complete questionnaires)	161	(89.9)	149	(92.5)
	Not completed	18	(6.6)	12	(4.2)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 66	Other	8	(2.9)	8	(2.8)
	With visit, no record	10	(3.7)	4	(1.4)
	Missing by Design	**93**	**(34.2)**	**122**	**(43.1)**
	Discontinued due to adverse event	16	(5.9)	10	(3.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	7	(2.6)	11	(3.9)
	Discontinued due to radiographic progression	42	(15.4)	73	(25.8)
	Visit not reached	11	(4.0)	15	(5.3)
	Visit not scheduled	6	(2.2)	0	(0.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 72	**Expected to Complete Questionnaires**	**170**	**(62.5)**	**152**	**(53.7)**
	Completed	151	(55.5)	143	(50.5)
	Compliance (% in those expected to complete questionnaires)	151	(88.8)	143	(94.1)
	Not completed	19	(7.0)	9	(3.2)
	Other	7	(2.6)	5	(1.8)
	With visit, no record	12	(4.4)	4	(1.4)
	Missing by Design	**102**	**(37.5)**	**131**	**(46.3)**
	Discontinued due to adverse event	23	(8.5)	10	(3.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	11	(3.9)
	Discontinued due to radiographic progression	42	(15.4)	74	(26.1)
	Visit not reached	17	(6.3)	21	(7.4)
	Visit not scheduled	1	(0.4)	2	(0.7)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 78	**Expected to Complete Questionnaires**	**161**	**(59.2)**	**138**	**(48.8)**
	Completed	145	(53.3)	130	(45.9)
	Compliance (% in those expected to complete questionnaires)	145	(90.1)	130	(94.2)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 78	Not completed	16	(5.9)	8	(2.8)
	Other	8	(2.9)	4	(1.4)
	With visit, no record	8	(2.9)	4	(1.4)
	Missing by Design	**111**	**(40.8)**	**145**	**(51.2)**
	Discontinued due to adverse event	21	(7.7)	10	(3.5)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	6	(2.2)	11	(3.9)
	Discontinued due to radiographic progression	46	(16.9)	82	(29.0)
	Visit not reached	25	(9.2)	28	(9.9)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 84	**Expected to Complete Questionnaires**	**152**	**(55.9)**	**125**	**(44.2)**
	Completed	141	(51.8)	115	(40.6)
	Compliance (% in those expected to complete questionnaires)	141	(92.8)	115	(92.0)
	Not completed	11	(4.0)	10	(3.5)
	Other	4	(1.5)	3	(1.1)
	With visit, no record	7	(2.6)	7	(2.5)
	Missing by Design	**120**	**(44.1)**	**158**	**(55.8)**
	Discontinued due to adverse event	26	(9.6)	12	(4.2)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	12	(4.2)
	Discontinued due to radiographic progression	46	(16.9)	83	(29.3)
	Visit not reached	29	(10.7)	35	(12.4)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 90	**Expected to Complete Questionnaires**	**149**	**(54.8)**	**116**	**(41.0)**
	Completed	139	(51.1)	109	(38.5)
	Compliance (% in those expected to complete	139	(93.3)	109	(94.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
	questionnaires)				
Week 90	Not completed	10	(3.7)	7	(2.5)
	Other	7	(2.6)	4	(1.4)
	With visit, no record	3	(1.1)	3	(1.1)
	Missing by Design	**123**	**(45.2)**	**167**	**(59.0)**
	Discontinued due to adverse event	21	(7.7)	11	(3.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	6	(2.2)	13	(4.6)
	Discontinued due to radiographic progression	49	(18.0)	88	(31.1)
	Visit not reached	32	(11.8)	39	(13.8)
	Visit not scheduled	1	(0.4)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 96	**Expected to Complete Questionnaires**	**131**	**(48.2)**	**106**	**(37.5)**
	Completed	125	(46.0)	95	(33.6)
	Compliance (% in those expected to complete questionnaires)	125	(95.4)	95	(89.6)
	Not completed	6	(2.2)	11	(3.9)
	Other	2	(0.7)	6	(2.1)
	With visit, no record	4	(1.5)	5	(1.8)
	Missing by Design	**141**	**(51.8)**	**177**	**(62.5)**
	Discontinued due to adverse event	29	(10.7)	13	(4.6)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	8	(2.9)	13	(4.6)
	Discontinued due to radiographic progression	50	(18.4)	89	(31.4)
	Visit not reached	39	(14.3)	47	(16.6)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 102	**Expected to Complete Questionnaires**	**130**	**(47.8)**	**103**	**(36.4)**
	Completed	120	(44.1)	88	(31.1)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 102	Compliance (% in those expected to complete questionnaires)	120	(92.3)	88	(85.4)
	Not completed	10	(3.7)	15	(5.3)
	Other	2	(0.7)	3	(1.1)
	With visit, no record	8	(2.9)	12	(4.2)
	Missing by Design	**142**	**(52.2)**	**180**	**(63.6)**
	Discontinued due to adverse event	25	(9.2)	12	(4.2)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	13	(4.6)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.2)
	Visit not reached	43	(15.8)	48	(17.0)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 114	**Expected to Complete Questionnaires**	**115**	**(42.3)**	**94**	**(33.2)**
	Completed	55	(20.2)	50	(17.7)
	Compliance (% in those expected to complete questionnaires)	55	(47.8)	50	(53.2)
	Not completed	60	(22.1)	44	(15.5)
	Other	13	(4.8)	18	(6.4)
	With visit, no record	47	(17.3)	26	(9.2)
	Missing by Design	**157**	**(57.7)**	**189**	**(66.8)**
	Discontinued due to adverse event	27	(9.9)	11	(3.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	2	(0.7)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	13	(4.6)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.2)
	Visit not reached	43	(15.8)	48	(17.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	15	(5.5)	13	(4.6)
Week 126	**Expected to Complete Questionnaires**	**88**	**(32.4)**	**68**	**(24.0)**

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 126	Completed	69	(25.4)	59	(20.8)
	Compliance (% in those expected to complete questionnaires)	69	(78.4)	59	(86.8)
	Not completed	19	(7.0)	9	(3.2)
	Other	3	(1.1)	0	(0.0)
	With visit, no record	16	(5.9)	9	(3.2)
	Missing by Design	**184**	**(67.6)**	**215**	**(76.0)**
	Discontinued due to adverse event	22	(8.1)	12	(4.2)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	13	(4.6)
	Discontinued due to radiographic progression	51	(18.8)	90	(31.8)
	Visit not reached	46	(16.9)	50	(17.7)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	42	(15.4)	35	(12.4)
Week 138	**Expected to Complete Questionnaires**	**17**	**(6.3)**	**11**	**(3.9)**
	Completed	14	(5.1)	7	(2.5)
	Compliance (% in those expected to complete questionnaires)	14	(82.4)	7	(63.6)
	Not completed	3	(1.1)	4	(1.4)
	Other	1	(0.4)	0	(0.0)
	With visit, no record	2	(0.7)	4	(1.4)
	Missing by Design	**255**	**(93.8)**	**272**	**(96.1)**
	Discontinued due to adverse event	28	(10.3)	14	(4.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	13	(4.6)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.2)
	Visit not reached	47	(17.3)	51	(18.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	106	(39.0)	88	(31.1)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 150	**Expected to Complete Questionnaires**	**35**	**(12.9)**	**31**	**(11.0)**
	Completed	34	(12.5)	31	(11.0)
	Compliance (% in those expected to complete questionnaires)	34	(97.1)	31	(100.0)
	Not completed	1	(0.4)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	1	(0.4)	0	(0.0)
	Missing by Design	**237**	**(87.1)**	**252**	**(89.0)**
	Discontinued due to adverse event	27	(9.9)	12	(4.2)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	13	(4.6)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.2)
	Visit not reached	47	(17.3)	51	(18.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	88	(32.4)	70	(24.7)
Week 162	**Expected to Complete Questionnaires**	**1**	**(0.4)**	**2**	**(0.7)**
	Completed	1	(0.4)	2	(0.7)
	Compliance (% in those expected to complete questionnaires)	1	(100.0)	2	(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	**271**	**(99.6)**	**281**	**(99.3)**
	Discontinued due to adverse event	29	(10.7)	14	(4.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	13	(4.6)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.2)
	Visit not reached	47	(17.3)	51	(18.0)
	Visit not scheduled	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=283	
		n	(%)	n	(%)
Week 162	Completed treatment and no visit scheduled	120	(44.1)	97	(34.3)

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).

Missing by design includes: death, disease progression, other discontinuations (reasons may include unacceptable AEs, withdrawal of consent, intercurrent illness that prevents further administration of treatment, investigator's decision to discontinue the participant, noncompliance with study treatment or procedure requirements or administrative reasons requiring cessation of treatment), and translation not available

a: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

Database Cutoff Date: 08JAN2024

Anhang 4-G1.2: Rücklaufquoten des EORTC QLQ-CX24

Tabelle 4G-2: Gründe für das Fehlen von Werten im EORTC QLQ-CX24

		Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
Treatment Visit	Category	n	(%)	n	(%)
Baseline	**Expected to Complete Questionnaires**	**265**	**(97.4)**	**274**	**(97.5)**
	Completed	259	(95.2)	267	(95.0)
	Compliance (% in those expected to complete questionnaires)	259	(97.7)	267	(97.4)
	Not completed	6	(2.2)	7	(2.5)
	Other	1	(0.4)	2	(0.7)
	With visit, no record	5	(1.8)	5	(1.8)
	Missing by Design	**7**	**(2.6)**	**7**	**(2.5)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	7	(2.6)	7	(2.5)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 3	**Expected to Complete Questionnaires**	**260**	**(95.6)**	**266**	**(94.7)**
	Completed	251	(92.3)	262	(93.2)
	Compliance (% in those expected to complete questionnaires)	251	(96.5)	262	(98.5)
	Not completed	9	(3.3)	4	(1.4)
	Other	1	(0.4)	1	(0.4)
	With visit, no record	8	(2.9)	3	(1.1)
	Missing by Design	**12**	**(4.4)**	**15**	**(5.3)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	1	(0.4)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 3	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	12	(4.4)	13	(4.6)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 6	**Expected to Complete Questionnaires**	**252**	**(92.6)**	**252**	**(89.7)**
	Completed	236	(86.8)	243	(86.5)
	Compliance (% in those expected to complete questionnaires)	236	(93.7)	243	(96.4)
	Not completed	16	(5.9)	9	(3.2)
	Other	4	(1.5)	5	(1.8)
	With visit, no record	12	(4.4)	4	(1.4)
	Missing by Design	**20**	**(7.4)**	**29**	**(10.3)**
	Discontinued due to adverse event	2	(0.7)	3	(1.1)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	1	(0.4)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	1	(0.4)	2	(0.7)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	16	(5.9)	23	(8.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 9	**Expected to Complete Questionnaires**	**246**	**(90.4)**	**259**	**(92.2)**
	Completed	237	(87.1)	254	(90.4)
	Compliance (% in those expected to complete questionnaires)	237	(96.3)	254	(98.1)
	Not completed	9	(3.3)	5	(1.8)
	Other	5	(1.8)	3	(1.1)
	With visit, no record	4	(1.5)	2	(0.7)
	Missing by Design	**26**	**(9.6)**	**22**	**(7.8)**
	Discontinued due to adverse event	3	(1.1)	3	(1.1)
	Discontinued due to clinical progression	1	(0.4)	2	(0.7)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	1	(0.4)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	2	(0.7)	3	(1.1)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 9	Discontinued due to radiographic progression	1	(0.4)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	16	(5.9)	14	(5.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 12	**Expected to Complete Questionnaires**	**249**	**(91.5)**	**256**	**(91.1)**
	Completed	239	(87.9)	249	(88.6)
	Compliance (% in those expected to complete questionnaires)	239	(96.0)	249	(97.3)
	Not completed	10	(3.7)	7	(2.5)
	Other	5	(1.8)	0	(0.0)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**23**	**(8.5)**	**25**	**(8.9)**
	Discontinued due to adverse event	5	(1.8)	4	(1.4)
	Discontinued due to clinical progression	1	(0.4)	3	(1.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	1	(0.4)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	2	(0.7)	3	(1.1)
	Discontinued due to radiographic progression	3	(1.1)	3	(1.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	8	(2.9)	11	(3.9)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 18	**Expected to Complete Questionnaires**	**253**	**(93.0)**	**261**	**(92.9)**
	Completed	248	(91.2)	259	(92.2)
	Compliance (% in those expected to complete questionnaires)	248	(98.0)	259	(99.2)
	Not completed	5	(1.8)	2	(0.7)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	5	(1.8)	2	(0.7)
	Missing by Design	**19**	**(7.0)**	**20**	**(7.1)**
	Discontinued due to adverse event	3	(1.1)	5	(1.8)
	Discontinued due to clinical progression	1	(0.4)	3	(1.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 18	Discontinued due to withdrawal by subject	3	(1.1)	4	(1.4)
	Discontinued due to radiographic progression	4	(1.5)	3	(1.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	4	(1.5)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 24	**Expected to Complete Questionnaires**	**231**	**(84.9)**	**240**	**(85.4)**
	Completed	217	(79.8)	234	(83.3)
	Compliance (% in those expected to complete questionnaires)	217	(93.9)	234	(97.5)
	Not completed	14	(5.1)	6	(2.1)
	Other	7	(2.6)	1	(0.4)
	With visit, no record	7	(2.6)	5	(1.8)
	Missing by Design	**41**	**(15.1)**	**41**	**(14.6)**
	Discontinued due to adverse event	11	(4.0)	6	(2.1)
	Discontinued due to clinical progression	2	(0.7)	4	(1.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	3	(1.1)	2	(0.7)
	Discontinued due to progressive disease	0	(0.0)	1	(0.4)
	Discontinued due to withdrawal by subject	3	(1.1)	6	(2.1)
	Discontinued due to radiographic progression	10	(3.7)	12	(4.3)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	8	(2.9)	10	(3.6)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 30	**Expected to Complete Questionnaires**	**220**	**(80.9)**	**221**	**(78.6)**
	Completed	207	(76.1)	210	(74.7)
	Compliance (% in those expected to complete questionnaires)	207	(94.1)	210	(95.0)
	Not completed	13	(4.8)	11	(3.9)
	Other	8	(2.9)	4	(1.4)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**52**	**(19.1)**	**60**	**(21.4)**
	Discontinued due to adverse event	8	(2.9)	5	(1.8)
	Discontinued due to clinical progression	2	(0.7)	5	(1.8)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	1	(0.4)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 30	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	2	(0.7)	7	(2.5)
	Discontinued due to radiographic progression	21	(7.7)	28	(10.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	11	(4.0)	12	(4.3)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 36	**Expected to Complete Questionnaires**	**212**	**(77.9)**	**209**	**(74.4)**
	Completed	200	(73.5)	197	(70.1)
	Compliance (% in those expected to complete questionnaires)	200	(94.3)	197	(94.3)
	Not completed	12	(4.4)	12	(4.3)
	Other	5	(1.8)	5	(1.8)
	With visit, no record	7	(2.6)	7	(2.5)
	Missing by Design	**60**	**(22.1)**	**72**	**(25.6)**
	Discontinued due to adverse event	16	(5.9)	6	(2.1)
	Discontinued due to clinical progression	2	(0.7)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	3	(1.1)	9	(3.2)
	Discontinued due to radiographic progression	25	(9.2)	41	(14.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	6	(2.2)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 42	**Expected to Complete Questionnaires**	**210**	**(77.2)**	**193**	**(68.7)**
	Completed	197	(72.4)	183	(65.1)
	Compliance (% in those expected to complete questionnaires)	197	(93.8)	183	(94.8)
	Not completed	13	(4.8)	10	(3.6)
	Other	8	(2.9)	3	(1.1)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**62**	**(22.8)**	**88**	**(31.3)**
	Discontinued due to adverse event	11	(4.0)	7	(2.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 42	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	28	(10.3)	52	(18.5)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	7	(2.6)	8	(2.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 48	**Expected to Complete Questionnaires**	**200**	**(73.5)**	**187**	**(66.5)**
	Completed	189	(69.5)	178	(63.3)
	Compliance (% in those expected to complete questionnaires)	189	(94.5)	178	(95.2)
	Not completed	11	(4.0)	9	(3.2)
	Other	3	(1.1)	3	(1.1)
	With visit, no record	8	(2.9)	6	(2.1)
	Missing by Design	**72**	**(26.5)**	**94**	**(33.5)**
	Discontinued due to adverse event	20	(7.4)	7	(2.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	4	(1.5)	9	(3.2)
	Discontinued due to radiographic progression	33	(12.1)	62	(22.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(1.1)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 54	**Expected to Complete Questionnaires**	**200**	**(73.5)**	**173**	**(61.6)**
	Completed	189	(69.5)	165	(58.7)
	Compliance (% in those expected to complete questionnaires)	189	(94.5)	165	(95.4)
	Not completed	11	(4.0)	8	(2.8)
	Other	5	(1.8)	4	(1.4)
	With visit, no record	6	(2.2)	4	(1.4)
	Missing by Design	**72**	**(26.5)**	**108**	**(38.4)**
	Discontinued due to adverse event	13	(4.8)	9	(3.2)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study	3	(1.1)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
	drug				
Week 54	Discontinued due to physician decision	4	(1.5)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	38	(14.0)	68	(24.2)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	5	(1.8)	9	(3.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 60	**Expected to Complete Questionnaires**	**191**	**(70.2)**	**175**	**(62.3)**
	Completed	177	(65.1)	166	(59.1)
	Compliance (% in those expected to complete questionnaires)	177	(92.7)	166	(94.9)
	Not completed	14	(5.1)	9	(3.2)
	Other	7	(2.6)	3	(1.1)
	With visit, no record	7	(2.6)	6	(2.1)
	Missing by Design	**81**	**(29.8)**	**106**	**(37.7)**
	Discontinued due to adverse event	18	(6.6)	6	(2.1)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	39	(14.3)	68	(24.2)
	Visit not reached	4	(1.5)	4	(1.4)
	Visit not scheduled	4	(1.5)	7	(2.5)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 66	**Expected to Complete Questionnaires**	**179**	**(65.8)**	**160**	**(56.9)**
	Completed	161	(59.2)	149	(53.0)
	Compliance (% in those expected to complete questionnaires)	161	(89.9)	149	(93.1)
	Not completed	18	(6.6)	11	(3.9)
	Other	8	(2.9)	8	(2.8)
	With visit, no record	10	(3.7)	3	(1.1)
	Missing by Design	**93**	**(34.2)**	**121**	**(43.1)**
	Discontinued due to adverse event	16	(5.9)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 66	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	7	(2.6)	10	(3.6)
	Discontinued due to radiographic progression	42	(15.4)	73	(26.0)
	Visit not reached	11	(4.0)	15	(5.3)
	Visit not scheduled	6	(2.2)	0	(0.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 72	**Expected to Complete Questionnaires**	**170**	**(62.5)**	**151**	**(53.7)**
	Completed	151	(55.5)	143	(50.9)
	Compliance (% in those expected to complete questionnaires)	151	(88.8)	143	(94.7)
	Not completed	19	(7.0)	8	(2.8)
	Other	7	(2.6)	5	(1.8)
	With visit, no record	12	(4.4)	3	(1.1)
	Missing by Design	**102**	**(37.5)**	**130**	**(46.3)**
	Discontinued due to adverse event	23	(8.5)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	10	(3.6)
	Discontinued due to radiographic progression	42	(15.4)	74	(26.3)
	Visit not reached	17	(6.3)	21	(7.5)
	Visit not scheduled	1	(0.4)	2	(0.7)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 78	**Expected to Complete Questionnaires**	**161**	**(59.2)**	**137**	**(48.8)**
	Completed	145	(53.3)	130	(46.3)
	Compliance (% in those expected to complete questionnaires)	145	(90.1)	130	(94.9)
	Not completed	16	(5.9)	7	(2.5)
	Other	8	(2.9)	4	(1.4)
	With visit, no record	8	(2.9)	3	(1.1)
	Missing by Design	**111**	**(40.8)**	**144**	**(51.2)**
	Discontinued due to adverse event	21	(7.7)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 78	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	6	(2.2)	10	(3.6)
	Discontinued due to radiographic progression	46	(16.9)	82	(29.2)
	Visit not reached	25	(9.2)	28	(10.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 84	**Expected to Complete Questionnaires**	**152**	**(55.9)**	**124**	**(44.1)**
	Completed	141	(51.8)	115	(40.9)
	Compliance (% in those expected to complete questionnaires)	141	(92.8)	115	(92.7)
	Not completed	11	(4.0)	9	(3.2)
	Other	4	(1.5)	3	(1.1)
	With visit, no record	7	(2.6)	6	(2.1)
	Missing by Design	**120**	**(44.1)**	**157**	**(55.9)**
	Discontinued due to adverse event	26	(9.6)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	11	(3.9)
	Discontinued due to radiographic progression	46	(16.9)	83	(29.5)
	Visit not reached	29	(10.7)	35	(12.5)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 90	**Expected to Complete Questionnaires**	**149**	**(54.8)**	**115**	**(40.9)**
	Completed	139	(51.1)	108	(38.4)
	Compliance (% in those expected to complete questionnaires)	139	(93.3)	108	(93.9)
	Not completed	10	(3.7)	7	(2.5)
	Other	7	(2.6)	4	(1.4)
	With visit, no record	3	(1.1)	3	(1.1)
	Missing by Design	**123**	**(45.2)**	**166**	**(59.1)**
	Discontinued due to adverse event	21	(7.7)	11	(3.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 90	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	6	(2.2)	12	(4.3)
	Discontinued due to radiographic progression	49	(18.0)	88	(31.3)
	Visit not reached	32	(11.8)	39	(13.9)
	Visit not scheduled	1	(0.4)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 96	**Expected to Complete Questionnaires**	**131**	**(48.2)**	**105**	**(37.4)**
	Completed	125	(46.0)	95	(33.8)
	Compliance (% in those expected to complete questionnaires)	125	(95.4)	95	(90.5)
	Not completed	6	(2.2)	10	(3.6)
	Other	2	(0.7)	6	(2.1)
	With visit, no record	4	(1.5)	4	(1.4)
	Missing by Design	**141**	**(51.8)**	**176**	**(62.6)**
	Discontinued due to adverse event	29	(10.7)	13	(4.6)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	8	(2.9)	12	(4.3)
	Discontinued due to radiographic progression	50	(18.4)	89	(31.7)
	Visit not reached	39	(14.3)	47	(16.7)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 102	**Expected to Complete Questionnaires**	**130**	**(47.8)**	**102**	**(36.3)**
	Completed	120	(44.1)	88	(31.3)
	Compliance (% in those expected to complete questionnaires)	120	(92.3)	88	(86.3)
	Not completed	10	(3.7)	14	(5.0)
	Other	2	(0.7)	2	(0.7)
	With visit, no record	8	(2.9)	12	(4.3)
	Missing by Design	**142**	**(52.2)**	**179**	**(63.7)**
	Discontinued due to adverse event	25	(9.2)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 102	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	43	(15.8)	48	(17.1)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 114	**Expected to Complete Questionnaires**	**115**	**(42.3)**	**93**	**(33.1)**
	Completed	55	(20.2)	50	(17.8)
	Compliance (% in those expected to complete questionnaires)	55	(47.8)	50	(53.8)
	Not completed	60	(22.1)	43	(15.3)
	Other	13	(4.8)	18	(6.4)
	With visit, no record	47	(17.3)	25	(8.9)
	Missing by Design	**157**	**(57.7)**	**188**	**(66.9)**
	Discontinued due to adverse event	27	(9.9)	11	(3.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	2	(0.7)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	43	(15.8)	48	(17.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	15	(5.5)	13	(4.6)
Week 126	**Expected to Complete Questionnaires**	**88**	**(32.4)**	**68**	**(24.2)**
	Completed	69	(25.4)	59	(21.0)
	Compliance (% in those expected to complete questionnaires)	69	(78.4)	59	(86.8)
	Not completed	19	(7.0)	9	(3.2)
	Other	3	(1.1)	0	(0.0)
	With visit, no record	16	(5.9)	9	(3.2)
	Missing by Design	**184**	**(67.6)**	**213**	**(75.8)**
	Discontinued due to adverse event	22	(8.1)	12	(4.3)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 126	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	90	(32.0)
	Visit not reached	46	(16.9)	50	(17.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	42	(15.4)	34	(12.1)
Week 138	**Expected to Complete Questionnaires**	**17**	**(6.3)**	**11**	**(3.9)**
	Completed	13	(4.8)	7	(2.5)
	Compliance (% in those expected to complete questionnaires)	13	(76.5)	7	(63.6)
	Not completed	4	(1.5)	4	(1.4)
	Other	1	(0.4)	0	(0.0)
	With visit, no record	3	(1.1)	4	(1.4)
	Missing by Design	**255**	**(93.8)**	**270**	**(96.1)**
	Discontinued due to adverse event	28	(10.3)	14	(5.0)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	106	(39.0)	87	(31.0)
Week 150	**Expected to Complete Questionnaires**	**35**	**(12.9)**	**31**	**(11.0)**
	Completed	34	(12.5)	31	(11.0)
	Compliance (% in those expected to complete questionnaires)	34	(97.1)	31	(100.0)
	Not completed	1	(0.4)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	1	(0.4)	0	(0.0)
	Missing by Design	**237**	**(87.1)**	**250**	**(89.0)**

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 150	Discontinued due to adverse event	27	(9.9)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	88	(32.4)	69	(24.6)
Week 162	**Expected to Complete Questionnaires**	**1**	**(0.4)**	**2**	**(0.7)**
	Completed	1	(0.4)	2	(0.7)
	Compliance (% in those expected to complete questionnaires)	1	(100.0)	2	(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	**271**	**(99.6)**	**279**	**(99.3)**
	Discontinued due to adverse event	29	(10.7)	14	(5.0)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	120	(44.1)	96	(34.2)

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).

Missing by design includes: death, disease progression, other discontinuations (reasons may include unacceptable AEs, withdrawal of consent, intercurrent illness that prevents further administration of treatment, investigator's decision to discontinue the participant, noncompliance with study treatment or

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272 n (%)	Placebo + CCRT[a] N=281 n (%)
procedure requirements or administrative reasons requiring cessation of treatment), and translation not available			
a: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]			
Database Cutoff Date: 08JAN2024			

Anhang 4-G1.3: Rücklaufquoten des PGI-C

Tabelle 4G-3: Gründe für das Fehlen von Werten im PGI-C

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=254		Placebo + CCRT[a] N=265	
		n	(%)	n	(%)
Week 9	**Expected to Complete Questionnaires**	**252**	**(99.2)**	**264**	**(99.6)**
	Completed	251	(98.8)	260	(98.1)
	Compliance (% in those expected to complete questionnaires)	251	(99.6)	260	(98.5)
	Not completed	1	(0.4)	4	(1.5)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	1	(0.4)	4	(1.5)
	Missing by Design	**2**	**(0.8)**	**1**	**(0.4)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not scheduled	2	(0.8)	1	(0.4)
Week 24	**Expected to Complete Questionnaires**	**224**	**(88.2)**	**228**	**(86.0)**
	Completed	212	(83.5)	221	(83.4)
	Compliance (% in those expected to complete questionnaires)	212	(94.6)	221	(96.9)
	Not completed	12	(4.7)	7	(2.6)
	Other	2	(0.8)	0	(0.0)
	With visit, no record	10	(3.9)	7	(2.6)
	Missing by Design	**30**	**(11.8)**	**37**	**(14.0)**
	Discontinued due to adverse event	8	(3.1)	2	(0.8)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to physician decision	2	(0.8)	1	(0.4)
	Discontinued due to progressive disease	0	(0.0)	2	(0.8)
	Discontinued due to withdrawal by subject	1	(0.4)	1	(0.4)
	Discontinued due to radiographic progression	13	(5.1)	19	(7.2)
	Visit not scheduled	6	(2.4)	11	(4.2)
Week 30	**Expected to Complete Questionnaires**	**205**	**(80.7)**	**215**	**(81.1)**
	Completed	181	(71.3)	184	(69.4)
	Compliance (% in those expected to complete questionnaires)	181	(88.3)	184	(85.6)
	Not completed	24	(9.4)	31	(11.7)
	Other	7	(2.8)	4	(1.5)
	With visit, no record	17	(6.7)	27	(10.2)
	Missing by Design	**49**	**(19.3)**	**50**	**(18.9)**
	Discontinued due to adverse event	11	(4.3)	2	(0.8)
	Discontinued due to clinical progression	1	(0.4)	2	(0.8)
	Discontinued due to physician decision	3	(1.2)	1	(0.4)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=254		Placebo + CCRT[a] N=265	
		n	(%)	n	(%)
Week 30	Discontinued due to progressive disease	0	(0.0)	2	(0.8)
	Discontinued due to withdrawal by subject	1	(0.4)	2	(0.8)
	Discontinued due to radiographic progression	21	(8.3)	30	(11.3)
	Visit not scheduled	12	(4.7)	11	(4.2)
Week 42	**Expected to Complete Questionnaires**	**193**	**(76.0)**	**190**	**(71.7)**
	Completed	178	(70.1)	183	(69.1)
	Compliance (% in those expected to complete questionnaires)	178	(92.2)	183	(96.3)
	Not completed	15	(5.9)	7	(2.6)
	Other	3	(1.2)	0	(0.0)
	With visit, no record	12	(4.7)	7	(2.6)
	Missing by Design	**61**	**(24.0)**	**75**	**(28.3)**
	Discontinued due to adverse event	15	(5.9)	3	(1.1)
	Discontinued due to clinical progression	2	(0.8)	3	(1.1)
	Discontinued due to physician decision	3	(1.2)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.8)
	Discontinued due to withdrawal by subject	2	(0.8)	4	(1.5)
	Discontinued due to radiographic progression	29	(11.4)	55	(20.8)
	Visit not scheduled	10	(3.9)	5	(1.9)
Week 48	**Expected to Complete Questionnaires**	**192**	**(75.6)**	**179**	**(67.5)**
	Completed	183	(72.0)	169	(63.8)
	Compliance (% in those expected to complete questionnaires)	183	(95.3)	169	(94.4)
	Not completed	9	(3.5)	10	(3.8)
	Other	3	(1.2)	3	(1.1)
	With visit, no record	6	(2.4)	7	(2.6)
	Missing by Design	**62**	**(24.4)**	**86**	**(32.5)**
	Discontinued due to adverse event	17	(6.7)	4	(1.5)
	Discontinued due to clinical progression	2	(0.8)	3	(1.1)
	Discontinued due to physician decision	4	(1.6)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	2	(0.8)	4	(1.5)
	Discontinued due to radiographic progression	33	(13.0)	62	(23.4)
	Visit not scheduled	4	(1.6)	7	(2.6)
Week 54	**Expected to Complete Questionnaires**	**188**	**(74.0)**	**179**	**(67.5)**
	Completed	169	(66.5)	158	(59.6)
	Compliance (% in those expected to complete questionnaires)	169	(89.9)	158	(88.3)
	Not completed	19	(7.5)	21	(7.9)
	Other	5	(2.0)	1	(0.4)
	With visit, no record	14	(5.5)	20	(7.5)
	Missing by Design	**66**	**(26.0)**	**86**	**(32.5)**
	Discontinued due to adverse event	17	(6.7)	5	(1.9)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=254		Placebo + CCRT[a] N=265	
		n	(%)	n	(%)
Week 54	Discontinued due to clinical progression	2	(0.8)	3	(1.1)
	Discontinued due to physician decision	4	(1.6)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	2	(0.8)	4	(1.5)
	Discontinued due to radiographic progression	37	(14.6)	66	(24.9)
	Visit not scheduled	4	(1.6)	2	(0.8)

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).

Missing by design includes: death, disease progression, other discontinuations (reasons may include unacceptable AEs, withdrawal of consent, intercurrent illness that prevents further administration of treatment, investigator's decision to discontinue the participant, noncompliance with study treatment or procedure requirements or administrative reasons requiring cessation of treatment), and translation not available

a: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

Database Cutoff Date: 08JAN2024

Anhang 4-G1.4: Rücklaufquoten des PGI-S

Tabelle 4G-4: Gründe für das Fehlen von Werten im PGI-S

		Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
Treatment Visit	Category	n	(%)	n	(%)
Baseline	**Expected to Complete Questionnaires**	**265**	**(97.4)**	**274**	**(97.5)**
	Completed	259	(95.2)	267	(95.0)
	Compliance (% in those expected to complete questionnaires)	259	(97.7)	267	(97.4)
	Not completed	6	(2.2)	7	(2.5)
	Other	1	(0.4)	2	(0.7)
	With visit, no record	5	(1.8)	5	(1.8)
	Missing by Design	**7**	**(2.6)**	**7**	**(2.5)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	7	(2.6)	7	(2.5)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 3	**Expected to Complete Questionnaires**	**260**	**(95.6)**	**266**	**(94.7)**
	Completed	250	(91.9)	262	(93.2)
	Compliance (% in those expected to complete questionnaires)	250	(96.2)	262	(98.5)
	Not completed	10	(3.7)	4	(1.4)
	Other	1	(0.4)	1	(0.4)
	With visit, no record	9	(3.3)	3	(1.1)
	Missing by Design	**12**	**(4.4)**	**15**	**(5.3)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	1	(0.4)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 3	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	12	(4.4)	13	(4.6)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 6	**Expected to Complete Questionnaires**	**252**	**(92.6)**	**252**	**(89.7)**
	Completed	236	(86.8)	243	(86.5)
	Compliance (% in those expected to complete questionnaires)	236	(93.7)	243	(96.4)
	Not completed	16	(5.9)	9	(3.2)
	Other	4	(1.5)	5	(1.8)
	With visit, no record	12	(4.4)	4	(1.4)
	Missing by Design	**20**	**(7.4)**	**29**	**(10.3)**
	Discontinued due to adverse event	2	(0.7)	3	(1.1)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	1	(0.4)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	1	(0.4)	2	(0.7)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	16	(5.9)	23	(8.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 9	**Expected to Complete Questionnaires**	**246**	**(90.4)**	**259**	**(92.2)**
	Completed	237	(87.1)	254	(90.4)
	Compliance (% in those expected to complete questionnaires)	237	(96.3)	254	(98.1)
	Not completed	9	(3.3)	5	(1.8)
	Other	5	(1.8)	3	(1.1)
	With visit, no record	4	(1.5)	2	(0.7)
	Missing by Design	**26**	**(9.6)**	**22**	**(7.8)**
	Discontinued due to adverse event	3	(1.1)	3	(1.1)
	Discontinued due to clinical progression	1	(0.4)	2	(0.7)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	1	(0.4)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	2	(0.7)	3	(1.1)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 9	Discontinued due to radiographic progression	1	(0.4)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	16	(5.9)	14	(5.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 12	**Expected to Complete Questionnaires**	**249**	**(91.5)**	**255**	**(90.7)**
	Completed	239	(87.9)	248	(88.3)
	Compliance (% in those expected to complete questionnaires)	239	(96.0)	248	(97.3)
	Not completed	10	(3.7)	7	(2.5)
	Other	5	(1.8)	0	(0.0)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**23**	**(8.5)**	**26**	**(9.3)**
	Discontinued due to adverse event	5	(1.8)	4	(1.4)
	Discontinued due to clinical progression	1	(0.4)	3	(1.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	1	(0.4)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	2	(0.7)	3	(1.1)
	Discontinued due to radiographic progression	3	(1.1)	3	(1.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	8	(2.9)	12	(4.3)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 18	**Expected to Complete Questionnaires**	**252**	**(92.6)**	**261**	**(92.9)**
	Completed	247	(90.8)	259	(92.2)
	Compliance (% in those expected to complete questionnaires)	247	(98.0)	259	(99.2)
	Not completed	5	(1.8)	2	(0.7)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	5	(1.8)	2	(0.7)
	Missing by Design	**20**	**(7.4)**	**20**	**(7.1)**
	Discontinued due to adverse event	3	(1.1)	5	(1.8)
	Discontinued due to clinical progression	1	(0.4)	3	(1.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 18	Discontinued due to withdrawal by subject	3	(1.1)	4	(1.4)
	Discontinued due to radiographic progression	4	(1.5)	3	(1.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	4	(1.5)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 24	**Expected to Complete Questionnaires**	**230**	**(84.6)**	**240**	**(85.4)**
	Completed	216	(79.4)	234	(83.3)
	Compliance (% in those expected to complete questionnaires)	216	(93.9)	234	(97.5)
	Not completed	14	(5.1)	6	(2.1)
	Other	7	(2.6)	1	(0.4)
	With visit, no record	7	(2.6)	5	(1.8)
	Missing by Design	**42**	**(15.4)**	**41**	**(14.6)**
	Discontinued due to adverse event	11	(4.0)	6	(2.1)
	Discontinued due to clinical progression	2	(0.7)	4	(1.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	3	(1.1)	2	(0.7)
	Discontinued due to progressive disease	0	(0.0)	1	(0.4)
	Discontinued due to withdrawal by subject	3	(1.1)	6	(2.1)
	Discontinued due to radiographic progression	10	(3.7)	12	(4.3)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	9	(3.3)	10	(3.6)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 30	**Expected to Complete Questionnaires**	**220**	**(80.9)**	**221**	**(78.6)**
	Completed	207	(76.1)	210	(74.7)
	Compliance (% in those expected to complete questionnaires)	207	(94.1)	210	(95.0)
	Not completed	13	(4.8)	11	(3.9)
	Other	8	(2.9)	4	(1.4)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**52**	**(19.1)**	**60**	**(21.4)**
	Discontinued due to adverse event	8	(2.9)	5	(1.8)
	Discontinued due to clinical progression	2	(0.7)	5	(1.8)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	1	(0.4)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 30	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	2	(0.7)	7	(2.5)
	Discontinued due to radiographic progression	21	(7.7)	28	(10.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	11	(4.0)	12	(4.3)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 36	**Expected to Complete Questionnaires**	**212**	**(77.9)**	**209**	**(74.4)**
	Completed	200	(73.5)	197	(70.1)
	Compliance (% in those expected to complete questionnaires)	200	(94.3)	197	(94.3)
	Not completed	12	(4.4)	12	(4.3)
	Other	5	(1.8)	5	(1.8)
	With visit, no record	7	(2.6)	7	(2.5)
	Missing by Design	**60**	**(22.1)**	**72**	**(25.6)**
	Discontinued due to adverse event	16	(5.9)	6	(2.1)
	Discontinued due to clinical progression	2	(0.7)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	3	(1.1)	9	(3.2)
	Discontinued due to radiographic progression	25	(9.2)	41	(14.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	6	(2.2)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 42	**Expected to Complete Questionnaires**	**210**	**(77.2)**	**192**	**(68.3)**
	Completed	197	(72.4)	182	(64.8)
	Compliance (% in those expected to complete questionnaires)	197	(93.8)	182	(94.8)
	Not completed	13	(4.8)	10	(3.6)
	Other	8	(2.9)	3	(1.1)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**62**	**(22.8)**	**89**	**(31.7)**
	Discontinued due to adverse event	11	(4.0)	7	(2.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 42	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	28	(10.3)	52	(18.5)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	7	(2.6)	9	(3.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 48	**Expected to Complete Questionnaires**	**200**	**(73.5)**	**187**	**(66.5)**
	Completed	189	(69.5)	178	(63.3)
	Compliance (% in those expected to complete questionnaires)	189	(94.5)	178	(95.2)
	Not completed	11	(4.0)	9	(3.2)
	Other	3	(1.1)	3	(1.1)
	With visit, no record	8	(2.9)	6	(2.1)
	Missing by Design	**72**	**(26.5)**	**94**	**(33.5)**
	Discontinued due to adverse event	20	(7.4)	7	(2.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	4	(1.5)	9	(3.2)
	Discontinued due to radiographic progression	33	(12.1)	62	(22.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(1.1)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 54	**Expected to Complete Questionnaires**	**200**	**(73.5)**	**173**	**(61.6)**
	Completed	189	(69.5)	165	(58.7)
	Compliance (% in those expected to complete questionnaires)	189	(94.5)	165	(95.4)
	Not completed	11	(4.0)	8	(2.8)
	Other	5	(1.8)	4	(1.4)
	With visit, no record	6	(2.2)	4	(1.4)
	Missing by Design	**72**	**(26.5)**	**108**	**(38.4)**
	Discontinued due to adverse event	13	(4.8)	9	(3.2)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study	3	(1.1)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
	drug				
Week 54	Discontinued due to physician decision	4	(1.5)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	38	(14.0)	68	(24.2)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	5	(1.8)	9	(3.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 60	**Expected to Complete Questionnaires**	**191**	**(70.2)**	**175**	**(62.3)**
	Completed	177	(65.1)	165	(58.7)
	Compliance (% in those expected to complete questionnaires)	177	(92.7)	165	(94.3)
	Not completed	14	(5.1)	10	(3.6)
	Other	7	(2.6)	3	(1.1)
	With visit, no record	7	(2.6)	7	(2.5)
	Missing by Design	**81**	**(29.8)**	**106**	**(37.7)**
	Discontinued due to adverse event	18	(6.6)	6	(2.1)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	39	(14.3)	68	(24.2)
	Visit not reached	4	(1.5)	4	(1.4)
	Visit not scheduled	4	(1.5)	7	(2.5)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 66	**Expected to Complete Questionnaires**	**179**	**(65.8)**	**160**	**(56.9)**
	Completed	161	(59.2)	149	(53.0)
	Compliance (% in those expected to complete questionnaires)	161	(89.9)	149	(93.1)
	Not completed	18	(6.6)	11	(3.9)
	Other	8	(2.9)	8	(2.8)
	With visit, no record	10	(3.7)	3	(1.1)
	Missing by Design	**93**	**(34.2)**	**121**	**(43.1)**
	Discontinued due to adverse event	16	(5.9)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 66	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	7	(2.6)	10	(3.6)
	Discontinued due to radiographic progression	42	(15.4)	73	(26.0)
	Visit not reached	11	(4.0)	15	(5.3)
	Visit not scheduled	6	(2.2)	0	(0.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 72	**Expected to Complete Questionnaires**	**170**	**(62.5)**	**151**	**(53.7)**
	Completed	151	(55.5)	143	(50.9)
	Compliance (% in those expected to complete questionnaires)	151	(88.8)	143	(94.7)
	Not completed	19	(7.0)	8	(2.8)
	Other	7	(2.6)	5	(1.8)
	With visit, no record	12	(4.4)	3	(1.1)
	Missing by Design	**102**	**(37.5)**	**130**	**(46.3)**
	Discontinued due to adverse event	23	(8.5)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	10	(3.6)
	Discontinued due to radiographic progression	42	(15.4)	74	(26.3)
	Visit not reached	17	(6.3)	21	(7.5)
	Visit not scheduled	1	(0.4)	2	(0.7)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 78	**Expected to Complete Questionnaires**	**161**	**(59.2)**	**137**	**(48.8)**
	Completed	145	(53.3)	130	(46.3)
	Compliance (% in those expected to complete questionnaires)	145	(90.1)	130	(94.9)
	Not completed	16	(5.9)	7	(2.5)
	Other	8	(2.9)	4	(1.4)
	With visit, no record	8	(2.9)	3	(1.1)
	Missing by Design	**111**	**(40.8)**	**144**	**(51.2)**
	Discontinued due to adverse event	21	(7.7)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 78	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	6	(2.2)	10	(3.6)
	Discontinued due to radiographic progression	46	(16.9)	82	(29.2)
	Visit not reached	25	(9.2)	28	(10.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 84	**Expected to Complete Questionnaires**	**152**	**(55.9)**	**124**	**(44.1)**
	Completed	141	(51.8)	115	(40.9)
	Compliance (% in those expected to complete questionnaires)	141	(92.8)	115	(92.7)
	Not completed	11	(4.0)	9	(3.2)
	Other	4	(1.5)	3	(1.1)
	With visit, no record	7	(2.6)	6	(2.1)
	Missing by Design	**120**	**(44.1)**	**157**	**(55.9)**
	Discontinued due to adverse event	26	(9.6)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	11	(3.9)
	Discontinued due to radiographic progression	46	(16.9)	83	(29.5)
	Visit not reached	29	(10.7)	35	(12.5)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 90	**Expected to Complete Questionnaires**	**149**	**(54.8)**	**115**	**(40.9)**
	Completed	139	(51.1)	109	(38.8)
	Compliance (% in those expected to complete questionnaires)	139	(93.3)	109	(94.8)
	Not completed	10	(3.7)	6	(2.1)
	Other	7	(2.6)	4	(1.4)
	With visit, no record	3	(1.1)	2	(0.7)
	Missing by Design	**123**	**(45.2)**	**166**	**(59.1)**
	Discontinued due to adverse event	21	(7.7)	11	(3.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 90	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	6	(2.2)	12	(4.3)
	Discontinued due to radiographic progression	49	(18.0)	88	(31.3)
	Visit not reached	32	(11.8)	39	(13.9)
	Visit not scheduled	1	(0.4)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 96	**Expected to Complete Questionnaires**	**131**	**(48.2)**	**105**	**(37.4)**
	Completed	125	(46.0)	95	(33.8)
	Compliance (% in those expected to complete questionnaires)	125	(95.4)	95	(90.5)
	Not completed	6	(2.2)	10	(3.6)
	Other	2	(0.7)	6	(2.1)
	With visit, no record	4	(1.5)	4	(1.4)
	Missing by Design	**141**	**(51.8)**	**176**	**(62.6)**
	Discontinued due to adverse event	29	(10.7)	13	(4.6)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	8	(2.9)	12	(4.3)
	Discontinued due to radiographic progression	50	(18.4)	89	(31.7)
	Visit not reached	39	(14.3)	47	(16.7)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 102	**Expected to Complete Questionnaires**	**130**	**(47.8)**	**102**	**(36.3)**
	Completed	120	(44.1)	88	(31.3)
	Compliance (% in those expected to complete questionnaires)	120	(92.3)	88	(86.3)
	Not completed	10	(3.7)	14	(5.0)
	Other	2	(0.7)	2	(0.7)
	With visit, no record	8	(2.9)	12	(4.3)
	Missing by Design	**142**	**(52.2)**	**179**	**(63.7)**
	Discontinued due to adverse event	25	(9.2)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 102	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	43	(15.8)	48	(17.1)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 114	**Expected to Complete Questionnaires**	**115**	**(42.3)**	**93**	**(33.1)**
	Completed	55	(20.2)	50	(17.8)
	Compliance (% in those expected to complete questionnaires)	55	(47.8)	50	(53.8)
	Not completed	60	(22.1)	43	(15.3)
	Other	13	(4.8)	18	(6.4)
	With visit, no record	47	(17.3)	25	(8.9)
	Missing by Design	**157**	**(57.7)**	**188**	**(66.9)**
	Discontinued due to adverse event	27	(9.9)	11	(3.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	2	(0.7)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	43	(15.8)	48	(17.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	15	(5.5)	13	(4.6)
Week 126	**Expected to Complete Questionnaires**	**88**	**(32.4)**	**68**	**(24.2)**
	Completed	69	(25.4)	59	(21.0)
	Compliance (% in those expected to complete questionnaires)	69	(78.4)	59	(86.8)
	Not completed	19	(7.0)	9	(3.2)
	Other	3	(1.1)	0	(0.0)
	With visit, no record	16	(5.9)	9	(3.2)
	Missing by Design	**184**	**(67.6)**	**213**	**(75.8)**
	Discontinued due to adverse event	22	(8.1)	12	(4.3)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 126	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	90	(32.0)
	Visit not reached	46	(16.9)	50	(17.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	42	(15.4)	34	(12.1)
Week 138	**Expected to Complete Questionnaires**	**17**	**(6.3)**	**11**	**(3.9)**
	Completed	13	(4.8)	7	(2.5)
	Compliance (% in those expected to complete questionnaires)	13	(76.5)	7	(63.6)
	Not completed	4	(1.5)	4	(1.4)
	Other	1	(0.4)	0	(0.0)
	With visit, no record	3	(1.1)	4	(1.4)
	Missing by Design	**255**	**(93.8)**	**270**	**(96.1)**
	Discontinued due to adverse event	28	(10.3)	14	(5.0)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	106	(39.0)	87	(31.0)
Week 150	**Expected to Complete Questionnaires**	**35**	**(12.9)**	**31**	**(11.0)**
	Completed	34	(12.5)	31	(11.0)
	Compliance (% in those expected to complete questionnaires)	34	(97.1)	31	(100.0)
	Not completed	1	(0.4)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	1	(0.4)	0	(0.0)
	Missing by Design	**237**	**(87.1)**	**250**	**(89.0)**

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 150	Discontinued due to adverse event	27	(9.9)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	88	(32.4)	69	(24.6)
Week 162	**Expected to Complete Questionnaires**	**1**	**(0.4)**	**2**	**(0.7)**
	Completed	1	(0.4)	2	(0.7)
	Compliance (% in those expected to complete questionnaires)	1	(100.0)	2	(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	**271**	**(99.6)**	**279**	**(99.3)**
	Discontinued due to adverse event	29	(10.7)	14	(5.0)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	120	(44.1)	96	(34.2)

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).

Missing by design includes: death, disease progression, other discontinuations (reasons may include unacceptable AEs, withdrawal of consent, intercurrent illness that prevents further administration of treatment, investigator's decision to discontinue the participant, noncompliance with study treatment or

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272 n (%)	Placebo + CCRT[a] N=281 n (%)
procedure requirements or administrative reasons requiring cessation of treatment), and translation not available			
a: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]			
Database Cutoff Date: 08JAN2024			

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

Tabelle 4G-5: Gründe für das Fehlen von Werten im EQ-5D VAS

		Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
Treatment Visit	Category	n	(%)	n	(%)
Baseline	**Expected to Complete Questionnaires**	**264**	**(97.1)**	**274**	**(97.5)**
	Completed	258	(94.9)	266	(94.7)
	Compliance (% in those expected to complete questionnaires)	258	(97.7)	266	(97.1)
	Not completed	6	(2.2)	8	(2.8)
	Other	1	(0.4)	2	(0.7)
	With visit, no record	5	(1.8)	6	(2.1)
	Missing by Design	**8**	**(2.9)**	**7**	**(2.5)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	0	(0.0)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	0	(0.0)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	8	(2.9)	7	(2.5)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 3	**Expected to Complete Questionnaires**	**260**	**(95.6)**	**265**	**(94.3)**
	Completed	250	(91.9)	260	(92.5)
	Compliance (% in those expected to complete questionnaires)	250	(96.2)	260	(98.1)
	Not completed	10	(3.7)	5	(1.8)
	Other	1	(0.4)	1	(0.4)
	With visit, no record	9	(3.3)	4	(1.4)
	Missing by Design	**12**	**(4.4)**	**16**	**(5.7)**
	Discontinued due to adverse event	0	(0.0)	0	(0.0)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	0	(0.0)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	0	(0.0)	1	(0.4)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 3	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	12	(4.4)	14	(5.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 6	**Expected to Complete Questionnaires**	**252**	**(92.6)**	**252**	**(89.7)**
	Completed	236	(86.8)	242	(86.1)
	Compliance (% in those expected to complete questionnaires)	236	(93.7)	242	(96.0)
	Not completed	16	(5.9)	10	(3.6)
	Other	4	(1.5)	5	(1.8)
	With visit, no record	12	(4.4)	5	(1.8)
	Missing by Design	**20**	**(7.4)**	**29**	**(10.3)**
	Discontinued due to adverse event	2	(0.7)	3	(1.1)
	Discontinued due to clinical progression	0	(0.0)	1	(0.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	0	(0.0)	0	(0.0)
	Discontinued due to non-compliance with study drug	1	(0.4)	0	(0.0)
	Discontinued due to physician decision	0	(0.0)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	1	(0.4)	2	(0.7)
	Discontinued due to radiographic progression	0	(0.0)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	16	(5.9)	23	(8.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 9	**Expected to Complete Questionnaires**	**246**	**(90.4)**	**259**	**(92.2)**
	Completed	237	(87.1)	253	(90.0)
	Compliance (% in those expected to complete questionnaires)	237	(96.3)	253	(97.7)
	Not completed	9	(3.3)	6	(2.1)
	Other	5	(1.8)	3	(1.1)
	With visit, no record	4	(1.5)	3	(1.1)
	Missing by Design	**26**	**(9.6)**	**22**	**(7.8)**
	Discontinued due to adverse event	3	(1.1)	3	(1.1)
	Discontinued due to clinical progression	1	(0.4)	2	(0.7)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	1	(0.4)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	2	(0.7)	3	(1.1)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 9	Discontinued due to radiographic progression	1	(0.4)	0	(0.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	16	(5.9)	14	(5.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 12	**Expected to Complete Questionnaires**	**249**	**(91.5)**	**256**	**(91.1)**
	Completed	239	(87.9)	249	(88.6)
	Compliance (% in those expected to complete questionnaires)	239	(96.0)	249	(97.3)
	Not completed	10	(3.7)	7	(2.5)
	Other	5	(1.8)	0	(0.0)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**23**	**(8.5)**	**25**	**(8.9)**
	Discontinued due to adverse event	5	(1.8)	4	(1.4)
	Discontinued due to clinical progression	1	(0.4)	3	(1.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	1	(0.4)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)
	Discontinued due to withdrawal by subject	2	(0.7)	3	(1.1)
	Discontinued due to radiographic progression	3	(1.1)	3	(1.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	8	(2.9)	11	(3.9)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 18	**Expected to Complete Questionnaires**	**253**	**(93.0)**	**261**	**(92.9)**
	Completed	248	(91.2)	259	(92.2)
	Compliance (% in those expected to complete questionnaires)	248	(98.0)	259	(99.2)
	Not completed	5	(1.8)	2	(0.7)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	5	(1.8)	2	(0.7)
	Missing by Design	**19**	**(7.0)**	**20**	**(7.1)**
	Discontinued due to adverse event	3	(1.1)	5	(1.8)
	Discontinued due to clinical progression	1	(0.4)	3	(1.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	2	(0.7)	0	(0.0)
	Discontinued due to physician decision	1	(0.4)	0	(0.0)
	Discontinued due to progressive disease	0	(0.0)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 18	Discontinued due to withdrawal by subject	3	(1.1)	4	(1.4)
	Discontinued due to radiographic progression	4	(1.5)	3	(1.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	4	(1.5)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 24	**Expected to Complete Questionnaires**	**230**	**(84.6)**	**240**	**(85.4)**
	Completed	216	(79.4)	234	(83.3)
	Compliance (% in those expected to complete questionnaires)	216	(93.9)	234	(97.5)
	Not completed	14	(5.1)	6	(2.1)
	Other	7	(2.6)	1	(0.4)
	With visit, no record	7	(2.6)	5	(1.8)
	Missing by Design	**42**	**(15.4)**	**41**	**(14.6)**
	Discontinued due to adverse event	11	(4.0)	6	(2.1)
	Discontinued due to clinical progression	2	(0.7)	4	(1.4)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	3	(1.1)	2	(0.7)
	Discontinued due to progressive disease	0	(0.0)	1	(0.4)
	Discontinued due to withdrawal by subject	3	(1.1)	6	(2.1)
	Discontinued due to radiographic progression	10	(3.7)	12	(4.3)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	9	(3.3)	10	(3.6)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 30	**Expected to Complete Questionnaires**	**220**	**(80.9)**	**221**	**(78.6)**
	Completed	207	(76.1)	208	(74.0)
	Compliance (% in those expected to complete questionnaires)	207	(94.1)	208	(94.1)
	Not completed	13	(4.8)	13	(4.6)
	Other	8	(2.9)	4	(1.4)
	With visit, no record	5	(1.8)	9	(3.2)
	Missing by Design	**52**	**(19.1)**	**60**	**(21.4)**
	Discontinued due to adverse event	8	(2.9)	5	(1.8)
	Discontinued due to clinical progression	2	(0.7)	5	(1.8)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	1	(0.4)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 30	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	2	(0.7)	7	(2.5)
	Discontinued due to radiographic progression	21	(7.7)	28	(10.0)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	11	(4.0)	12	(4.3)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 36	**Expected to Complete Questionnaires**	**212**	**(77.9)**	**209**	**(74.4)**
	Completed	200	(73.5)	197	(70.1)
	Compliance (% in those expected to complete questionnaires)	200	(94.3)	197	(94.3)
	Not completed	12	(4.4)	12	(4.3)
	Other	5	(1.8)	5	(1.8)
	With visit, no record	7	(2.6)	7	(2.5)
	Missing by Design	**60**	**(22.1)**	**72**	**(25.6)**
	Discontinued due to adverse event	16	(5.9)	6	(2.1)
	Discontinued due to clinical progression	2	(0.7)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	3	(1.1)	9	(3.2)
	Discontinued due to radiographic progression	25	(9.2)	41	(14.6)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	6	(2.2)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 42	**Expected to Complete Questionnaires**	**210**	**(77.2)**	**192**	**(68.3)**
	Completed	197	(72.4)	182	(64.8)
	Compliance (% in those expected to complete questionnaires)	197	(93.8)	182	(94.8)
	Not completed	13	(4.8)	10	(3.6)
	Other	8	(2.9)	3	(1.1)
	With visit, no record	5	(1.8)	7	(2.5)
	Missing by Design	**62**	**(22.8)**	**89**	**(31.7)**
	Discontinued due to adverse event	11	(4.0)	7	(2.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 42	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	28	(10.3)	52	(18.5)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	7	(2.6)	9	(3.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 48	**Expected to Complete Questionnaires**	**200**	**(73.5)**	**187**	**(66.5)**
	Completed	189	(69.5)	178	(63.3)
	Compliance (% in those expected to complete questionnaires)	189	(94.5)	178	(95.2)
	Not completed	11	(4.0)	9	(3.2)
	Other	3	(1.1)	3	(1.1)
	With visit, no record	8	(2.9)	6	(2.1)
	Missing by Design	**72**	**(26.5)**	**94**	**(33.5)**
	Discontinued due to adverse event	20	(7.4)	7	(2.5)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	2	(0.7)
	Discontinued due to withdrawal by subject	4	(1.5)	9	(3.2)
	Discontinued due to radiographic progression	33	(12.1)	62	(22.1)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	3	(1.1)	5	(1.8)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 54	**Expected to Complete Questionnaires**	**200**	**(73.5)**	**173**	**(61.6)**
	Completed	189	(69.5)	164	(58.4)
	Compliance (% in those expected to complete questionnaires)	189	(94.5)	164	(94.8)
	Not completed	11	(4.0)	9	(3.2)
	Other	5	(1.8)	4	(1.4)
	With visit, no record	6	(2.2)	5	(1.8)
	Missing by Design	**72**	**(26.5)**	**108**	**(38.4)**
	Discontinued due to adverse event	13	(4.8)	9	(3.2)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study	3	(1.1)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
	drug				
Week 54	Discontinued due to physician decision	4	(1.5)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	38	(14.0)	68	(24.2)
	Visit not reached	0	(0.0)	0	(0.0)
	Visit not scheduled	5	(1.8)	9	(3.2)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 60	**Expected to Complete Questionnaires**	**191**	**(70.2)**	**175**	**(62.3)**
	Completed	177	(65.1)	165	(58.7)
	Compliance (% in those expected to complete questionnaires)	177	(92.7)	165	(94.3)
	Not completed	14	(5.1)	10	(3.6)
	Other	7	(2.6)	3	(1.1)
	With visit, no record	7	(2.6)	7	(2.5)
	Missing by Design	**81**	**(29.8)**	**106**	**(37.7)**
	Discontinued due to adverse event	18	(6.6)	6	(2.1)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	5	(1.8)	9	(3.2)
	Discontinued due to radiographic progression	39	(14.3)	68	(24.2)
	Visit not reached	4	(1.5)	4	(1.4)
	Visit not scheduled	4	(1.5)	7	(2.5)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 66	**Expected to Complete Questionnaires**	**179**	**(65.8)**	**160**	**(56.9)**
	Completed	161	(59.2)	149	(53.0)
	Compliance (% in those expected to complete questionnaires)	161	(89.9)	149	(93.1)
	Not completed	18	(6.6)	11	(3.9)
	Other	8	(2.9)	8	(2.8)
	With visit, no record	10	(3.7)	3	(1.1)
	Missing by Design	**93**	**(34.2)**	**121**	**(43.1)**
	Discontinued due to adverse event	16	(5.9)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 66	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	4	(1.5)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	3	(1.1)
	Discontinued due to withdrawal by subject	7	(2.6)	10	(3.6)
	Discontinued due to radiographic progression	42	(15.4)	73	(26.0)
	Visit not reached	11	(4.0)	15	(5.3)
	Visit not scheduled	6	(2.2)	0	(0.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 72	**Expected to Complete Questionnaires**	**170**	**(62.5)**	**151**	**(53.7)**
	Completed	151	(55.5)	143	(50.9)
	Compliance (% in those expected to complete questionnaires)	151	(88.8)	143	(94.7)
	Not completed	19	(7.0)	8	(2.8)
	Other	7	(2.6)	5	(1.8)
	With visit, no record	12	(4.4)	3	(1.1)
	Missing by Design	**102**	**(37.5)**	**130**	**(46.3)**
	Discontinued due to adverse event	23	(8.5)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	6	(2.1)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	10	(3.6)
	Discontinued due to radiographic progression	42	(15.4)	74	(26.3)
	Visit not reached	17	(6.3)	21	(7.5)
	Visit not scheduled	1	(0.4)	2	(0.7)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 78	**Expected to Complete Questionnaires**	**161**	**(59.2)**	**137**	**(48.8)**
	Completed	145	(53.3)	130	(46.3)
	Compliance (% in those expected to complete questionnaires)	145	(90.1)	130	(94.9)
	Not completed	16	(5.9)	7	(2.5)
	Other	8	(2.9)	4	(1.4)
	With visit, no record	8	(2.9)	3	(1.1)
	Missing by Design	**111**	**(40.8)**	**144**	**(51.2)**
	Discontinued due to adverse event	21	(7.7)	10	(3.6)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 78	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	6	(2.2)	10	(3.6)
	Discontinued due to radiographic progression	46	(16.9)	82	(29.2)
	Visit not reached	25	(9.2)	28	(10.0)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 84	**Expected to Complete Questionnaires**	**152**	**(55.9)**	**124**	**(44.1)**
	Completed	141	(51.8)	115	(40.9)
	Compliance (% in those expected to complete questionnaires)	141	(92.8)	115	(92.7)
	Not completed	11	(4.0)	9	(3.2)
	Other	4	(1.5)	3	(1.1)
	With visit, no record	7	(2.6)	6	(2.1)
	Missing by Design	**120**	**(44.1)**	**157**	**(55.9)**
	Discontinued due to adverse event	26	(9.6)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	0	(0.0)	0	(0.0)
	Discontinued due to excluded medication	0	(0.0)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	11	(3.9)
	Discontinued due to radiographic progression	46	(16.9)	83	(29.5)
	Visit not reached	29	(10.7)	35	(12.5)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 90	**Expected to Complete Questionnaires**	**149**	**(54.8)**	**115**	**(40.9)**
	Completed	139	(51.1)	108	(38.4)
	Compliance (% in those expected to complete questionnaires)	139	(93.3)	108	(93.9)
	Not completed	10	(3.7)	7	(2.5)
	Other	7	(2.6)	4	(1.4)
	With visit, no record	3	(1.1)	3	(1.1)
	Missing by Design	**123**	**(45.2)**	**166**	**(59.1)**
	Discontinued due to adverse event	21	(7.7)	11	(3.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 90	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	6	(2.2)	12	(4.3)
	Discontinued due to radiographic progression	49	(18.0)	88	(31.3)
	Visit not reached	32	(11.8)	39	(13.9)
	Visit not scheduled	1	(0.4)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 96	**Expected to Complete Questionnaires**	**131**	**(48.2)**	**105**	**(37.4)**
	Completed	125	(46.0)	95	(33.8)
	Compliance (% in those expected to complete questionnaires)	125	(95.4)	95	(90.5)
	Not completed	6	(2.2)	10	(3.6)
	Other	2	(0.7)	6	(2.1)
	With visit, no record	4	(1.5)	4	(1.4)
	Missing by Design	**141**	**(51.8)**	**176**	**(62.6)**
	Discontinued due to adverse event	29	(10.7)	13	(4.6)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	3	(1.1)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	8	(2.9)	12	(4.3)
	Discontinued due to radiographic progression	50	(18.4)	89	(31.7)
	Visit not reached	39	(14.3)	47	(16.7)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 102	**Expected to Complete Questionnaires**	**130**	**(47.8)**	**102**	**(36.3)**
	Completed	120	(44.1)	88	(31.3)
	Compliance (% in those expected to complete questionnaires)	120	(92.3)	88	(86.3)
	Not completed	10	(3.7)	14	(5.0)
	Other	2	(0.7)	2	(0.7)
	With visit, no record	8	(2.9)	12	(4.3)
	Missing by Design	**142**	**(52.2)**	**179**	**(63.7)**
	Discontinued due to adverse event	25	(9.2)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 102	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	43	(15.8)	48	(17.1)
	Visit not scheduled	0	(0.0)	1	(0.4)
	Completed treatment and no visit scheduled	0	(0.0)	0	(0.0)
Week 114	**Expected to Complete Questionnaires**	**115**	**(42.3)**	**93**	**(33.1)**
	Completed	55	(20.2)	49	(17.4)
	Compliance (% in those expected to complete questionnaires)	55	(47.8)	49	(52.7)
	Not completed	60	(22.1)	44	(15.7)
	Other	13	(4.8)	19	(6.8)
	With visit, no record	47	(17.3)	25	(8.9)
	Missing by Design	**157**	**(57.7)**	**188**	**(66.9)**
	Discontinued due to adverse event	27	(9.9)	11	(3.9)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	2	(0.7)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	7	(2.6)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	43	(15.8)	48	(17.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	15	(5.5)	13	(4.6)
Week 126	**Expected to Complete Questionnaires**	**88**	**(32.4)**	**68**	**(24.2)**
	Completed	69	(25.4)	59	(21.0)
	Compliance (% in those expected to complete questionnaires)	69	(78.4)	59	(86.8)
	Not completed	19	(7.0)	9	(3.2)
	Other	3	(1.1)	0	(0.0)
	With visit, no record	16	(5.9)	9	(3.2)
	Missing by Design	**184**	**(67.6)**	**213**	**(75.8)**
	Discontinued due to adverse event	22	(8.1)	12	(4.3)

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 126	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	90	(32.0)
	Visit not reached	46	(16.9)	50	(17.8)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	42	(15.4)	34	(12.1)
Week 138	**Expected to Complete Questionnaires**	**17**	**(6.3)**	**11**	**(3.9)**
	Completed	13	(4.8)	7	(2.5)
	Compliance (% in those expected to complete questionnaires)	13	(76.5)	7	(63.6)
	Not completed	4	(1.5)	4	(1.4)
	Other	1	(0.4)	0	(0.0)
	With visit, no record	3	(1.1)	4	(1.4)
	Missing by Design	**255**	**(93.8)**	**270**	**(96.1)**
	Discontinued due to adverse event	28	(10.3)	14	(5.0)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	5	(1.8)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	106	(39.0)	87	(31.0)
Week 150	**Expected to Complete Questionnaires**	**35**	**(12.9)**	**31**	**(11.0)**
	Completed	34	(12.5)	31	(11.0)
	Compliance (% in those expected to complete questionnaires)	34	(97.1)	31	(100.0)
	Not completed	1	(0.4)	0	(0.0)
	Other	0	(0.0)	0	(0.0)
	With visit, no record	1	(0.4)	0	(0.0)
	Missing by Design	**237**	**(87.1)**	**250**	**(89.0)**

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272		Placebo + CCRT[a] N=281	
		n	(%)	n	(%)
Week 150	Discontinued due to adverse event	27	(9.9)	12	(4.3)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	88	(32.4)	69	(24.6)
Week 162	**Expected to Complete Questionnaires**	**1**	**(0.4)**	**2**	**(0.7)**
	Completed	1	(0.4)	2	(0.7)
	Compliance (% in those expected to complete questionnaires)	1	(100.0)	2	(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	**271**	**(99.6)**	**279**	**(99.3)**
	Discontinued due to adverse event	29	(10.7)	14	(5.0)
	Discontinued due to clinical progression	3	(1.1)	7	(2.5)
	Discontinued due to lost to follow-up	1	(0.4)	0	(0.0)
	Discontinued due to excluded medication	1	(0.4)	0	(0.0)
	Discontinued due to non-study anti-cancer therapy	1	(0.4)	0	(0.0)
	Discontinued due to non-compliance with study drug	3	(1.1)	0	(0.0)
	Discontinued due to physician decision	6	(2.2)	4	(1.4)
	Discontinued due to progressive disease	0	(0.0)	4	(1.4)
	Discontinued due to withdrawal by subject	9	(3.3)	12	(4.3)
	Discontinued due to radiographic progression	51	(18.8)	91	(32.4)
	Visit not reached	47	(17.3)	51	(18.1)
	Visit not scheduled	0	(0.0)	0	(0.0)
	Completed treatment and no visit scheduled	120	(44.1)	96	(34.2)

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).

Missing by design includes: death, disease progression, other discontinuations (reasons may include unacceptable AEs, withdrawal of consent, intercurrent illness that prevents further administration of treatment, investigator's decision to discontinue the participant, noncompliance with study treatment or

Treatment Visit	Category	Pembrolizumab + CCRT[a] N=272 n (%)	Placebo + CCRT[a] N=281 n (%)
procedure requirements or administrative reasons requiring cessation of treatment), and translation not available			
a: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]			
Database Cutoff Date: 08JAN2024			

Anhang 4-G2: 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.

Alle Ergebnisse beziehen sich auf den Datenschnitt vom 08.01.2024.

Anhang 4-G2.1: Mortalität

Gesamtüberleben

Tabelle 4G-6: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Gesamtüberleben aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**			**Placebo + CCRT[b]**			**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[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]**
Age									
< 65	254	34 (13.4)	Not reached [-; -]	248	64 (25.8)	Not reached [-; -]	0.49 [0.32; 0.74]	< 0.001	0.060
≥ 65	42	9 (21.4)	Not reached [-; -]	57	9 (15.8)	Not reached [-; -]	1.31 [0.52; 3.30]	0.570	
ECOG Performance Status									
0	194	28 (14.4)	Not reached [-; -]	212	51 (24.1)	Not reached [-; -]	0.58 [0.36; 0.92]	0.019	0.936
1	102	15 (14.7)	Not reached [-; -]	93	22 (23.7)	Not reached [-; -]	0.57 [0.29; 1.09]	0.091	
Region									
Western Europe	52	7 (13.5)	Not reached [-; -]	55	11 (20.0)	Not reached [27.5; -]	0.64 [0.25; 1.64]	0.350	0.892
North America	14	4 (28.6)	Not reached [15.1; -]	17	6 (35.3)	Not reached [11.7; -]	0.79 [0.22; 2.81]	0.719	
RoW	230	32 (13.9)	Not reached [-; -]	233	56 (24.0)	Not reached [-; -]	0.55 [0.35; 0.84]	0.006	
Planned Type of EBRT									
IMRT or VMAT	255	37 (14.5)	Not reached [-; -]	264	64 (24.2)	Not reached [-; -]	0.56 [0.37; 0.84]	0.005	0.806
Non-IMRT and Non-VMAT	41	6 (14.6)	Not reached [34.0; -]	41	9 (22.0)	Not reached [-; -]	0.66 [0.23; 1.85]	0.430	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)									
< 70 Gy	32	5 (15.6)	Not reached [-; -]	29	7 (24.1)	Not reached [30.8; -]	0.70 [0.22; 2.20]	0.540	0.734
≥ 70 Gy	264	38 (14.4)	Not reached [-; -]	276	66 (23.9)	Not reached [-; -]	0.56 [0.37; 0.83]	0.004	
Race									
White	104	21 (20.2)	Not reached [-; -]	113	29 (25.7)	Not reached [-; -]	0.74 [0.42; 1.30]	0.294	0.243
All Others	192	22 (11.5)	Not reached [-; -]	192	44 (22.9)	Not reached [-; -]	0.47 [0.28; 0.78]	0.004	

a: Database Cutoff Date: 08JAN2024
b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]			Placebo + CCRT[b]			Pembrolizumab + CCRT[b] vs. Placebo + CCRT[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]
c: Number of participants: intention-to-treat population with FIGO III to IVA									
d: From product-limit (Kaplan-Meier) method for censored data									
e: Based on Cox regression model with treatment as a covariate using Wald confidence interval									
f: Two-sided p-value using Wald test									
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)									
CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy									

Anhang 4-G2.2: Morbidität

Progress als Scheitern des potenziell kurativen Therapieansatzes

Tabelle 4G-7: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0{,}05$) für den Endpunkt Progress als Scheitern des potenziell kurativen Therapieansatzes aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]			Placebo + CCRT[b]			Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Progression-Free 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]
Age									
< 65	254	66 (26.0)	Not reached [-; -]	248	104 (41.9)	Not reached [23.4; -]	0.56 [0.41; 0.76]	< 0.001	0.694
≥ 65	42	13 (31.0)	Not reached [30.4; -]	57	21 (36.8)	Not reached [16.9; -]	0.65 [0.32; 1.30]	0.222	
ECOG Performance Status									
0	194	53 (27.3)	Not reached [-; -]	212	88 (41.5)	Not reached [23.4; -]	0.61 [0.43; 0.85]	0.004	0.613
1	102	26 (25.5)	Not reached [34.9; -]	93	37 (39.8)	Not reached [18.7; -]	0.53 [0.32; 0.87]	0.012	
Region									
Western Europe	52	16 (30.8)	30.4 [23.3; -]	55	27 (49.1)	20.1 [11.2; -]	0.64 [0.34; 1.19]	0.159	0.984
North America	14	6 (42.9)	15.7 [6.9; -]	17	10 (58.8)	13.1 [4.5; -]	0.61 [0.22; 1.68]	0.337	
RoW	230	57 (24.8)	Not reached [-; -]	233	88 (37.8)	Not reached [29.7; -]	0.57 [0.41; 0.80]	0.001	
Planned Type of EBRT									
IMRT or VMAT	255	69 (27.1)	Not reached [-; -]	264	110 (41.7)	Not reached [23.2; -]	0.57 [0.42; 0.77]	< 0.001	0.956
Non-IMRT and Non-VMAT	41	10 (24.4)	Not reached [-; -]	41	15 (36.6)	Not reached [15.7; -]	0.60 [0.27; 1.34]	0.211	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)									
< 70 Gy	32	8 (25.0)	Not reached [-; -]	29	13 (44.8)	29.7 [12.9; -]	0.52 [0.22; 1.26]	0.147	0.814
≥ 70 Gy	264	71 (26.9)	Not reached [-; -]	276	112 (40.6)	Not reached [24.1; -]	0.58 [0.43; 0.78]	< 0.001	

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]			Placebo + CCRT[b]			Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Progression-Free 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]
Race									
White	104	35 (33.7)	Not reached [30.4; -]	113	58 (51.3)	18.8 [12.8; 32.0]	0.59 [0.39; 0.90]	0.015	0.956
All Others	192	44 (22.9)	Not reached [-; -]	192	67 (34.9)	Not reached [-; -]	0.57 [0.39; 0.84]	0.004	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: intention-to-treat population with FIGO III to IVA

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

e: Based on Cox regression model with treatment as a covariate using Wald confidence interval

f: Two-sided p-value using Wald test

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)

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Zeit bis zur palliativen Therapie als Übergang ins palliative Therapiesetting

Tabelle 4G-8: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0{,}05$) für den Endpunkt Zeit bis zur palliativen Therapie als Übergang ins palliative Setting aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]			Placebo + CCRT[b]			Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Subsequent Palliative Therapy or Death	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									
< 65	254	59 (23.2)	Not reached [37.4; -]	248	98 (39.5)	Not reached [32.0; -]	0.53 [0.38; 0.73]	< 0.001	0.513
≥ 65	42	12 (28.6)	Not reached [31.2; -]	57	20 (35.1)	Not reached [19.1; -]	0.68 [0.33; 1.40]	0.293	
ECOG Performance Status									
0	194	49 (25.3)	Not reached [-; -]	212	83 (39.2)	Not reached [31.4; -]	0.60 [0.42; 0.85]	0.004	0.468
1	102	22 (21.6)	Not reached [37.4; -]	93	35 (37.6)	Not reached [-; -]	0.48 [0.28; 0.81]	0.007	
Region									
Western Europe	52	15 (28.8)	32.3 [31.7; -]	55	24 (43.6)	32.0 [16.3; -]	0.66 [0.35; 1.27]	0.214	0.735
North America	14	7 (50.0)	17.6 [6.9; -]	17	10 (58.8)	16.4 [5.4; -]	0.74 [0.28; 1.96]	0.549	
RoW	230	49 (21.3)	Not reached [-; -]	233	84 (36.1)	Not reached [-; -]	0.52 [0.36; 0.74]	< 0.001	
Planned Type of EBRT									
IMRT or VMAT	255	62 (24.3)	Not reached [37.4; -]	264	103 (39.0)	Not reached [-; -]	0.55 [0.40; 0.75]	< 0.001	0.956
Non-IMRT and	41	9	Not reached	41	15	Not reached	0.56	0.167	

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]			Placebo + CCRT[b]			Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Subsequent Palliative Therapy or Death	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]
Non-VMAT		(22.0)	[-; -]		(36.6)	[16.9; -]	[0.24; 1.28]		
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)									
< 70 Gy	32	9 (28.1)	Not reached [37.4; -]	29	14 (48.3)	31.4 [14.1; -]	0.48 [0.20; 1.15]	0.100	0.939
≥ 70 Gy	264	62 (23.5)	Not reached [-; -]	276	104 (37.7)	Not reached [-; -]	0.55 [0.40; 0.76]	< 0.001	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: intention-to-treat population with FIGO III to IVA

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

e: Based on Cox regression model with treatment as a covariate using Wald confidence interval

f: Two-sided p-value using Wald test

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)

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Krankheitssymptomatik und Gesundheitszustand

EORTC QLQ-C30: Symptomskala Erschöpfung

Tabelle 4G-9: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Erschöpfung aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Fatigue	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	31.12 (25.32)	154	18.04 (21.07)	235	-10.18 [-13.29; -7.06]	0.74	0.721	-	0.220
Placebo + CCRT[b]	223	29.74 (22.03)	141	15.44 (19.28)	234	-10.92 [-14.14; -7.70]	[-3.33; 4.82]			
≥ 65										
Pembrolizumab + CCRT[b]	35	26.03 (20.69)	23	25.12 (18.72)	37	0.60 [-6.72; 7.92]	2.17	0.677	-	
Placebo + CCRT[b]	47	31.91 (26.58)	25	28.44 (22.70)	49	-1.57 [-10.14; 6.99]	[-8.06; 12.40]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	26.89 (22.36)	124	18.55 (20.37)	185	-6.86 [-10.22; -3.50]	0.38	0.864	-	0.826
Placebo + CCRT[b]	194	27.55 (21.38)	121	17.17 (18.98)	203	-7.24 [-10.56; -3.92]	[-3.98; 4.74]			
1										
Pembrolizumab + CCRT[b]	85	37.78 (27.87)	53	19.92 (22.15)	87	-13.14 [-18.74; -7.54]	2.37	0.558	-	
Placebo + CCRT[b]	76	36.70 (25.21)	45	18.02 (23.72)	80	-15.51 [-22.36; -8.67]	[-5.58; 10.32]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	40.74 (22.89)	5	15.55 (18.59)	13	-23.14 [-40.45; -5.83]	-11.11	0.339	-	0.333
Placebo + CCRT[b]	15	48.89 (31.65)	5	26.67 (25.58)	17	-12.03 [-33.17; 9.11]	[-33.99; 11.77]			
RoW										
Pembrolizumab + CCRT[b]	204	28.59 (24.09)	145	18.31 (19.71)	207	-7.59 [-10.72; -4.46]	0.99	0.635	-	
Placebo + CCRT[b]	206	27.61 (21.27)	133	16.04 (18.82)	213	-8.59 [-11.90; -5.28]	[-3.12; 5.11]			
Western Europe										
Pembrolizumab + CCRT[b]	45	36.05 (27.23)	27	23.04 (26.85)	52	-13.88 [-22.23; -5.54]	0.19	0.972	-	

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Fatigue	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	49	34.92 (23.24)	28	22.22 (25.30)	53	-14.07 [-21.42; -6.73]	[-10.43; 10.80]			
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	29.71 (24.78)	152	19.37 (21.72)	232	-8.34 [-11.58; -5.09]	1.66	0.451	-	0.070
Placebo + CCRT[b]	230	31.01 (23.34)	140	17.62 (20.82)	242	-9.99 [-13.43; -6.56]	[-2.65; 5.97]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	34.44 (24.63)	25	16.44 (14.74)	40	-11.74 [-17.65; -5.83]	-4.92	0.215	-	
Placebo + CCRT[b]	40	25.00 (19.29)	26	16.24 (17.56)	41	-6.82 [-13.20; -0.45]	[-12.69; 2.85]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	36.40 (26.54)	19	21.64 (20.11)	29	-8.42 [-17.21; 0.37]	0.72	0.888	-	0.245
Placebo + CCRT[b]	28	22.62 (19.00)	19	12.86 (13.99)	28	-9.14 [-16.06; -2.21]	[-9.30; 10.74]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	29.69 (24.50)	158	18.63 (20.99)	243	-8.99 [-12.08; -5.90]	0.59	0.779	-	
Placebo + CCRT[b]	242	30.99 (23.13)	147	17.99 (20.94)	255	-9.58 [-12.92; -6.25]	[-3.55; 4.74]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Symptomskala Übelkeit und Erbrechen

Tabelle 4G-10: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Übelkeit und Erbrechen aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Nausea and Vomiting	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	9.44 (16.83)	154	4.65 (11.51)	235	-3.73 [-5.75; -1.72]	1.10	0.375	-	0.272
Placebo + CCRT[b]	223	9.04 (18.70)	141	2.01 (7.58)	234	-4.84 [-6.93; -2.75]	[-1.33; 3.54]			
≥ 65										
Pembrolizumab + CCRT[b]	35	3.33 (7.88)	23	6.52 (10.94)	37	3.33 [-1.04; 7.70]	-0.46	0.905	-	
Placebo + CCRT[b]	47	3.90 (9.96)	25	7.33 (16.02)	49	3.79 [-2.77; 10.35]	[-7.98; 7.06]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	7.67 (15.31)	124	4.30 (9.47)	185	-2.49 [-4.65; -0.34]	0.14	0.915	-	0.180
Placebo + CCRT[b]	194	7.04 (16.77)	121	3.44 (10.52)	203	-2.63 [-5.03; -0.23]	[-2.45; 2.74]			
1										
Pembrolizumab + CCRT[b]	85	10.59 (17.41)	53	6.29 (15.06)	87	-3.22 [-6.45; 0.02]	3.31	0.145	-	
Placebo + CCRT[b]	76	10.97 (19.35)	45	1.11 (5.50)	80	-6.53 [-10.07; -2.99]	[-1.14; 7.76]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	9.72 (16.60)	5	6.67 (9.13)	13	-21.89 [-38.93; -4.84]	-17.66	0.053	-	0.321
Placebo + CCRT[b]	15	27.78 (31.91)	5	6.67 (14.91)	17	-4.22 [-20.63; 12.19]	[-35.59; 0.26]			
RoW										
Pembrolizumab + CCRT[b]	204	8.66 (15.20)	145	4.48 (11.33)	207	-3.14 [-4.98; -1.30]	-0.11	0.933	-	
Placebo + CCRT[b]	206	7.69 (16.67)	133	3.26 (10.15)	213	-3.02 [-5.41; -0.64]	[-2.76; 2.53]			
Western Europe										
Pembrolizumab + CCRT[b]	45	8.15 (19.66)	27	6.79 (12.45)	52	1.40 [-3.74; 6.54]	6.45	0.006	0.39	
Placebo + CCRT[b]	49	4.08 (10.50)	28	0.00 (0.00)	53	-5.05 [-8.65; -1.45]	[1.85; 11.05]		[0.11; 0.67]	

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Nausea and Vomiting	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	4.60 (8.79)	19	0.88 (3.82)	29	0.01 [-3.75; 3.76]	1.69	0.552	-	0.211
Placebo + CCRT[b]	28	2.98 (9.13)	19	3.51 (8.92)	28	-1.68 [-7.12; 3.75]	[-3.88; 7.26]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	9.12 (16.68)	158	5.38 (11.94)	243	-2.63 [-4.64; -0.62]	1.49	0.251	-	
Placebo + CCRT[b]	242	8.75 (18.23)	147	2.72 (9.56)	255	-4.12 [-6.34; -1.91]	[-1.06; 4.04]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation

EORTC QLQ-C30: Symptomskala Schmerzen

Tabelle 4G-11: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schmerzen aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Pain	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	32.39 (30.06)	124	14.52 (23.76)	185	-16.38 [-20.45; -12.30]	-2.38	0.341	-	0.443
Placebo + CCRT[b]	194	31.10 (27.00)	121	13.09 (19.98)	203	-13.99 [-17.74; -10.24]	[-7.29; 2.52]			
1										
Pembrolizumab + CCRT[b]	85	43.14 (35.01)	53	18.87 (29.42)	87	-20.80 [-27.79; -13.80]	0.54	0.909	-	
Placebo + CCRT[b]	76	38.82 (31.43)	45	15.56 (22.02)	80	-21.33 [-29.53; -13.14]	[-8.69; 9.77]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	51.39 (39.86)	5	16.67 (28.87)	13	-41.17 [-72.11; -10.22]	-20.37	0.159	-	0.959
Placebo + CCRT[b]	15	55.55 (36.00)	5	20.00 (18.26)	17	-20.80 [-38.73; -2.86]	[-48.80; 8.07]			
RoW										
Pembrolizumab + CCRT[b]	204	35.29 (31.46)	145	14.71 (24.02)	207	-18.04 [-21.77; -14.31]	-2.58	0.280	-	
Placebo + CCRT[b]	206	31.80 (27.67)	133	13.41 (20.04)	213	-15.47 [-19.32; -11.61]	[-7.25; 2.10]			
Western Europe										
Pembrolizumab + CCRT[b]	45	34.44 (32.45)	27	21.61 (32.63)	52	-13.42 [-23.61; -3.23]	3.96	0.540	-	
Placebo + CCRT[b]	49	32.65 (26.99)	28	14.29 (23.45)	53	-17.37 [-27.31; -7.43]	[-8.71; 16.63]			
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	35.82 (32.84)	152	16.56 (26.12)	232	-17.22 [-21.20; -13.25]	-0.19	0.938	-	0.238
Placebo + CCRT[b]	230	34.28 (29.14)	140	13.69 (19.72)	242	-17.03 [-20.98; -13.08]	[-5.05; 4.67]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	36.25 (27.96)	25	11.33 (21.90)	40	-21.69 [-28.86; -14.51]	-11.34	0.021	-0.56	
Placebo + CCRT[b]	40	27.50 (23.74)	26	14.10 (24.81)	41	-10.35 [-17.93; -2.77]	[-21.00; -1.68]		[-1.03; -0.08]	

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Pain	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	41.95 (27.68)	19	15.79 (31.66)	29	-20.29 [-31.11; -9.47]	-2.42	0.717	-	0.200
Placebo + CCRT[b]	28	25.00 (21.99)	19	8.77 (17.00)	28	-17.86 [-26.79; -8.94]	[-15.57; 10.72]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	35.13 (32.57)	158	15.82 (24.87)	243	-17.39 [-21.16; -13.62]	-1.62	0.496	-	
Placebo + CCRT[b]	242	34.23 (29.01)	147	14.40 (20.89)	255	-15.77 [-19.62; -11.92]	[-6.30; 3.05]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Symptomskala Atemnot (Dyspnoe)

Tabelle 4G-12: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Atemnot (Dyspnoe) aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Dyspnoea	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	10.18 (19.36)	154	6.93 (15.09)	235	-1.79 [-4.47; 0.90]	0.94	0.531	-	0.397
Placebo + CCRT[b]	223	8.67 (18.57)	141	5.20 (12.78)	234	-2.73 [-4.98; -0.48]	[-2.01; 3.90]			
≥ 65										
Pembrolizumab + CCRT[b]	35	8.57 (16.85)	23	8.69 (14.96)	37	1.38 [-3.87; 6.64]	-1.78	0.659	-	
Placebo + CCRT[b]	47	9.93 (15.41)	25	13.33 (19.24)	49	3.17 [-3.14; 9.48]	[-9.71; 6.15]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	8.90 (16.80)	124	6.45 (14.52)	185	-1.49 [-4.38; 1.39]	-0.45	0.788	-	0.470
Placebo + CCRT[b]	194	9.11 (19.27)	121	6.61 (14.67)	203	-1.04 [-3.52; 1.45]	[-3.78; 2.87]			
1										
Pembrolizumab + CCRT[b]	85	12.16 (22.91)	53	8.80 (16.21)	87	-1.86 [-6.45; 2.72]	2.03	0.455	-	
Placebo + CCRT[b]	76	8.33 (14.53)	45	5.93 (12.89)	80	-3.90 [-8.17; 0.38]	[-3.30; 7.37]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	5.56 (12.97)	5	6.67 (14.91)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	8.89 (15.26)	5	6.67 (14.91)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	204	9.15 (18.51)	145	6.67 (14.49)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	206	8.09 (17.09)	133	5.76 (12.65)	213	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	45	14.81 (21.97)	27	9.88 (18.06)	52	- [-; -]	-	-	-	
Placebo + CCRT[b]	49	12.24 (22.25)	28	9.52 (19.99)	53	- [-; -]				

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Dyspnoea	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	8.60 (17.45)	152	7.02 (15.17)	232	-0.73 [-3.28; 1.83]	0.85	0.580	-	0.064
Placebo + CCRT[b]	230	8.55 (18.15)	140	5.95 (14.00)	242	-1.58 [-3.91; 0.75]	[-2.18; 3.88]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	17.50 (25.02)	25	8.00 (14.53)	40	-5.94 [-13.56; 1.69]	-2.59	0.520	-	
Placebo + CCRT[b]	40	10.83 (17.52)	26	8.97 (15.08)	41	-3.35 [-8.80; 2.10]	[-10.49; 5.32]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Symptomskala Schlaflosigkeit

Tabelle 4G-13: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Schlaflosigkeit aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Insomnia	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	32.01 (30.84)	154	15.58 (25.33)	235	-14.15 [-18.32; -9.98]	-0.93	0.715	-	0.106
Placebo + CCRT[b]	223	31.09 (29.85)	141	13.47 (21.81)	234	-13.22 [-17.19; -9.25]	[-5.94; 4.08]			
≥ 65										
Pembrolizumab + CCRT[b]	35	22.86 (27.74)	23	21.74 (19.09)	37	-3.86 [-12.77; 5.04]	5.12	0.371	-	
Placebo + CCRT[b]	47	34.04 (30.68)	25	22.67 (26.74)	49	-8.98 [-18.42; 0.46]	[-6.11; 16.35]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	26.70 (28.95)	124	16.13 (24.23)	185	-10.14 [-14.65; -5.64]	-0.70	0.804	-	0.231
Placebo + CCRT[b]	194	29.72 (29.06)	121	15.43 (23.19)	203	-9.44 [-13.80; -5.09]	[-6.23; 4.83]			
1										
Pembrolizumab + CCRT[b]	85	39.22 (32.19)	53	16.98 (25.84)	87	-18.34 [-25.51; -11.17]	2.11	0.615	-	
Placebo + CCRT[b]	76	36.40 (31.82)	45	13.33 (21.79)	80	-20.45 [-26.81; -14.09]	[-6.11; 10.33]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	47.22 (33.21)	5	20.00 (29.82)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	62.22 (33.02)	5	20.00 (18.26)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	204	28.43 (29.74)	145	15.63 (23.91)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	206	28.64 (28.22)	133	14.54 (23.34)	213	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	45	37.04 (31.96)	27	19.75 (28.13)	52	- [-; -]	-	-	-	
Placebo + CCRT[b]	49	34.69 (31.15)	28	15.48 (21.24)	53	- [-; -]				

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Insomnia	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	p-Value for Interaction Test[g]
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	30.47 (31.57)	152	16.67 (25.73)	232	-13.04 [-17.36; -8.72]	1.31	0.616	-	0.205
Placebo + CCRT[b]	230	33.04 (30.99)	140	14.29 (23.02)	242	-14.35 [-18.41; -10.29]	[-3.82; 6.45]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	32.50 (24.45)	25	14.67 (16.89)	40	-14.26 [-21.22; -7.29]	-11.48	0.014	-0.57	
Placebo + CCRT[b]	40	23.33 (21.62)	26	17.95 (21.56)	41	-2.78 [-9.92; 4.37]	[-20.60; -2.36]		[-1.02; -0.12]	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	39.08 (23.69)	19	17.54 (20.39)	29	-11.04 [-21.27; -0.82]	3.55	0.573	-	0.496
Placebo + CCRT[b]	28	23.81 (21.96)	19	12.28 (19.91)	28	-14.59 [-23.88; -5.31]	[-8.83; 15.93]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	29.74 (31.19)	158	16.24 (25.16)	243	-12.53 [-16.68; -8.39]	0.05	0.985	-	
Placebo + CCRT[b]	242	32.51 (30.66)	147	15.19 (23.16)	255	-12.58 [-16.54; -8.63]	[-4.92; 5.02]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Symptomskala Appetitlosigkeit

Tabelle 4G-14: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Appetitlosigkeit aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Appetite Loss	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	19.76 (26.16)	154	9.74 (20.85)	235	-9.13 [-12.76; -5.49]	3.64	0.058	-	0.106
Placebo + CCRT[b]	223	21.37 (28.59)	141	4.02 (12.26)	234	-12.76 [-15.69; -9.84]	[-0.12; 7.39]			
≥ 65										
Pembrolizumab + CCRT[b]	35	16.19 (23.39)	23	7.25 (14.06)	37	-11.03 [-18.37; -3.68]	-4.40	0.345	-	
Placebo + CCRT[b]	47	20.57 (27.41)	25	12.00 (18.95)	49	-6.63 [-15.90; 2.64]	[-13.54; 4.75]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	15.34 (22.50)	124	8.87 (19.06)	185	-6.39 [-10.15; -2.63]	2.35	0.258	-	0.293
Placebo + CCRT[b]	194	17.87 (25.65)	121	5.23 (13.61)	203	-8.74 [-12.05; -5.43]	[-1.72; 6.42]			
1										
Pembrolizumab + CCRT[b]	85	27.45 (30.07)	53	10.69 (22.43)	87	-14.93 [-21.21; -8.65]	4.94	0.164	-	
Placebo + CCRT[b]	76	29.82 (32.92)	45	5.18 (14.13)	80	-19.87 [-25.64; -14.10]	[-2.02; 11.90]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	22.22 (25.95)	5	6.67 (14.91)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	44.44 (34.89)	5	6.67 (14.91)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	204	18.79 (25.86)	145	9.20 (20.22)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	206	19.90 (27.89)	133	4.26 (12.59)	213	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	45	20.74 (25.91)	27	11.11 (20.67)	52	- [-; -]	-	-	-	
Placebo + CCRT[b]	49	19.73 (25.38)	28	9.52 (17.82)	53	- [-; -]				

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Appetite Loss	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	19.00 (26.80)	152	9.87 (20.96)	232	-8.56 [-12.17; -4.94]	4.44	0.025	0.19	0.362
Placebo + CCRT[b]	230	22.32 (29.30)	140	5.00 (13.81)	242	-13.00 [-16.21; -9.79]	[0.56; 8.33]		[0.02; 0.36]	
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	20.83 (19.52)	25	6.67 (13.61)	40	-11.76 [-18.99; -4.53]	-5.69	0.167	-	
Placebo + CCRT[b]	40	15.00 (21.28)	26	6.41 (13.40)	41	-6.07 [-12.19; 0.04]	[-13.75; 2.38]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Symptomskala Verstopfung

Tabelle 4G-15: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Verstopfung aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Constipation	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	23.75 (30.49)	154	8.22 (18.79)	235	-15.00 [-18.40; -11.61]	-3.64	0.095	-	0.578
Placebo + CCRT[b]	223	24.51 (29.46)	141	10.64 (21.57)	234	-11.37 [-15.26; -7.47]	[-7.91; 0.63]			
≥ 65										
Pembrolizumab + CCRT[b]	35	20.95 (24.37)	23	13.04 (24.08)	37	-8.12 [-17.32; 1.09]	2.57	0.646	-	
Placebo + CCRT[b]	47	22.69 (30.38)	25	9.33 (18.05)	49	-10.69 [-18.84; -2.54]	[-8.40; 13.54]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	18.75 (26.82)	124	9.41 (19.74)	185	-9.77 [-13.30; -6.25]	-3.85	0.106	-	0.053
Placebo + CCRT[b]	194	21.48 (27.61)	121	12.40 (22.00)	203	-5.93 [-9.87; -1.98]	[-8.52; 0.82]			
1										
Pembrolizumab + CCRT[b]	85	32.94 (33.13)	53	7.55 (19.22)	87	-23.44 [-29.81; -17.08]	1.44	0.676	-	
Placebo + CCRT[b]	76	31.14 (33.26)	45	5.18 (17.34)	80	-24.88 [-31.42; -18.35]	[-5.33; 8.22]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	41.67 (35.18)	5	13.33 (29.82)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	40.00 (33.81)	5	13.33 (18.26)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	204	23.86 (29.17)	145	8.96 (18.94)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	206	24.11 (28.82)	133	11.53 (22.49)	213	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	45	16.30 (28.97)	27	7.41 (21.35)	52	- [-; -]	-	-	-	
Placebo + CCRT[b]	49	19.73 (30.37)	28	4.76 (11.88)	53	- [-; -]				

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Constipation	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	25.04 (30.09)	152	9.65 (20.53)	232	-14.89 [-18.49; -11.28]	-1.18	0.598	-	0.470
Placebo + CCRT[b]	230	25.22 (30.71)	140	9.29 (20.41)	242	-13.71 [-17.62; -9.79]	[-5.56; 3.20]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	14.17 (26.03)	25	4.00 (11.05)	40	-9.81 [-16.20; -3.42]	-10.10	0.023	-0.58	
Placebo + CCRT[b]	40	18.33 (21.28)	26	16.67 (23.57)	41	0.29 [-6.97; 7.54]	[-18.78; -1.42]		[-1.08; -0.08]	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	24.14 (29.41)	19	12.28 (25.36)	29	-10.73 [-22.24; 0.79]	-3.03	0.679	-	0.512
Placebo + CCRT[b]	28	26.19 (24.61)	19	17.54 (25.74)	28	-7.69 [-18.04; 2.66]	[-17.40; 11.34]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	23.28 (29.82)	158	8.44 (18.79)	243	-14.65 [-17.96; -11.33]	-2.63	0.203	-	
Placebo + CCRT[b]	242	23.97 (30.13)	147	9.52 (20.27)	255	-12.01 [-15.75; -8.27]	[-6.69; 1.42]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Symptomskala Diarrhö

Tabelle 4G-16: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Diarrhö aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Diarrhoea	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	5.75 (16.67)	154	10.61 (20.06)	235	4.93 [1.59; 8.27]	4.39	0.026	0.21	0.572
Placebo + CCRT[b]	223	6.73 (16.73)	141	6.15 (15.22)	234	0.54 [-2.18; 3.26]	[0.53; 8.25]		[0.03; 0.39]	
≥ 65										
Pembrolizumab + CCRT[b]	35	2.86 (9.47)	23	5.80 (12.92)	37	3.91 [-1.09; 8.92]	-0.69	0.859	-	
Placebo + CCRT[b]	47	4.96 (15.51)	25	8.00 (14.53)	49	4.60 [-1.84; 11.04]	[-8.34; 6.96]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	3.79 (12.27)	124	8.87 (18.09)	185	4.66 [1.27; 8.04]	2.21	0.292	-	0.061
Placebo + CCRT[b]	194	5.84 (16.63)	121	7.16 (15.64)	203	2.45 [-0.55; 5.45]	[-1.90; 6.32]			
1										
Pembrolizumab + CCRT[b]	85	8.63 (21.30)	53	12.58 (21.90)	87	5.05 [-1.14; 11.23]	7.33	0.032	0.32	
Placebo + CCRT[b]	76	7.89 (16.21)	45	4.44 (13.48)	80	-2.29 [-6.79; 2.22]	[0.65; 14.01]		[0.03; 0.61]	
Region										
North America										
Pembrolizumab + CCRT[b]	12	16.67 (33.33)	5	6.67 (14.91)	13	-18.43 [-40.85; 4.00]	-34.13	0.004	-1.30	0.130
Placebo + CCRT[b]	15	20.00 (32.85)	5	13.33 (18.26)	17	15.70 [4.73; 26.68]	[-56.99; -11.27]		[-2.17; -0.43]	
RoW										
Pembrolizumab + CCRT[b]	204	4.57 (13.27)	145	8.73 (16.21)	207	4.46 [1.67; 7.25]	3.43	0.054	-	
Placebo + CCRT[b]	206	5.66 (14.55)	133	5.26 (14.12)	213	1.03 [-1.65; 3.72]	[-0.05; 6.91]			
Western Europe										
Pembrolizumab + CCRT[b]	45	5.93 (19.19)	27	17.28 (31.17)	52	11.30 [0.15; 22.44]	8.17	0.177	-	
Placebo + CCRT[b]	49	5.44 (15.73)	28	10.71 (18.26)	53	3.13 [-2.45; 8.71]	[-3.69; 20.03]			

Study: KEYNOTE A18[a] EORTC QLQ-C30 Symptom Scales Diarrhoea	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	5.73 (15.81)	152	9.87 (19.87)	232	4.26 [0.94; 7.57]	4.38	0.023	0.21	0.585
Placebo + CCRT[b]	230	6.38 (16.71)	140	5.48 (14.20)	242	-0.13 [-2.74; 2.48]	[0.61; 8.16]		[0.03; 0.39]	
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	3.33 (16.54)	25	10.67 (15.87)	40	7.81 [1.34; 14.29]	-0.10	0.982	-	
Placebo + CCRT[b]	40	6.67 (15.47)	26	11.54 (18.72)	41	7.91 [1.02; 14.80]	[-8.85; 8.65]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	4.60 (19.36)	19	8.77 (15.08)	29	4.11 [-2.97; 11.19]	-5.65	0.278	-	0.703
Placebo + CCRT[b]	28	7.14 (16.62)	19	14.03 (20.23)	28	9.76 [1.25; 18.26]	[-15.86; 4.57]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	5.46 (15.47)	158	10.13 (19.80)	243	4.76 [1.52; 8.00]	4.62	0.014	0.22	
Placebo + CCRT[b]	242	6.34 (16.53)	147	5.44 (14.09)	255	0.14 [-2.39; 2.68]	[0.94; 8.29]		[0.05; 0.40]	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-CX24: Symptomskala Symptomerleben

Tabelle 4G-17: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Symptomerleben aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Symptom Experience	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	224	21.16 (14.86)	154	9.86 (12.12)	235	-11.29 [-13.06; -9.52]	0.26	0.819	-	0.092
Placebo + CCRT[b]	222	21.40 (15.47)	141	7.84 (10.84)	234	-11.55 [-13.45; -9.65]	[-1.98; 2.51]			
≥ 65										
Pembrolizumab + CCRT[b]	35	16.88 (13.44)	23	8.56 (10.03)	37	-8.64 [-13.21; -4.07]	-0.31	0.910	-	
Placebo + CCRT[b]	45	19.80 (17.04)	25	11.15 (11.29)	47	-8.33 [-13.03; -3.63]	[-5.61; 5.00]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	175	18.87 (13.76)	124	9.04 (11.81)	185	-10.35 [-12.40; -8.30]	-0.64	0.621	-	0.176
Placebo + CCRT[b]	192	20.55 (15.39)	121	8.76 (11.60)	202	-9.71 [-11.77; -7.65]	[-3.19; 1.90]			
1										
Pembrolizumab + CCRT[b]	84	24.13 (16.07)	53	11.21 (11.92)	87	-11.87 [-14.63; -9.11]	2.81	0.121	-	
Placebo + CCRT[b]	75	22.62 (16.55)	45	7.20 (8.93)	79	-14.68 [-18.09; -11.26]	[-0.74; 6.36]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	25.76 (10.92)	5	9.70 (9.44)	13	-14.27 [-22.54; -6.00]	0.33	0.950	-	0.329
Placebo + CCRT[b]	15	34.54 (22.44)	5	9.70 (7.23)	17	-14.60 [-24.46; -4.74]	[-10.12; 10.78]			
RoW										
Pembrolizumab + CCRT[b]	203	20.75 (14.92)	145	9.65 (11.66)	207	-10.86 [-12.75; -8.96]	-0.13	0.917	-	
Placebo + CCRT[b]	205	21.20 (15.25)	133	8.77 (11.44)	212	-10.73 [-12.74; -8.72]	[-2.51; 2.26]			
Western Europe										
Pembrolizumab + CCRT[b]	44	18.39 (14.59)	27	9.88 (13.54)	52	-9.89 [-13.29; -6.48]	0.82	0.698	-	

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Symptom Experience	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	47	16.57 (12.81)	28	6.06 (8.73)	52	-10.71 [-14.11; -7.31]	[-3.33; 4.97]			
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	219	20.57 (15.06)	152	10.31 (12.46)	232	-10.43 [-12.30; -8.56]	1.17	0.321	-	0.643
Placebo + CCRT[b]	227	21.50 (16.27)	140	8.07 (10.51)	240	-11.60 [-13.58; -9.62]	[-1.14; 3.48]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	20.60 (12.92)	25	5.94 (5.96)	40	-13.11 [-16.17; -10.06]	-4.55	0.030	-0.56	
Placebo + CCRT[b]	40	19.01 (12.06)	26	9.79 (13.15)	41	-8.57 [-11.90; -5.24]	[-8.66; -0.43]		[-1.07; -0.05]	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	22.15 (14.53)	19	8.45 (9.87)	29	-10.61 [-15.53; -5.70]	0.46	0.861	-	0.283
Placebo + CCRT[b]	28	17.10 (8.17)	19	6.54 (7.84)	28	-11.07 [-14.37; -7.78]	[-4.70; 5.62]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	230	20.38 (14.77)	158	9.84 (12.09)	243	-10.82 [-12.57; -9.07]	0.33	0.771	-	
Placebo + CCRT[b]	239	21.60 (16.32)	147	8.57 (11.27)	253	-11.15 [-13.10; -9.21]	[-1.91; 2.58]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-CX24: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire CX24; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-CX24: Symptomskala Lymphödeme

Tabelle 4G-18: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala Lymphödeme aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Lymphoedema	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	224	4.02 (12.58)	154	7.58 (19.25)	235	2.44 [-0.54; 5.43]	0.49	0.783	-	0.515
Placebo + CCRT[b]	222	5.86 (16.50)	141	6.15 (12.97)	234	1.95 [-0.44; 4.34]	[-3.01; 4.00]			
≥ 65										
Pembrolizumab + CCRT[b]	35	3.81 (10.76)	23	4.35 (11.48)	37	-0.70 [-6.48; 5.08]	-1.95	0.596	-	
Placebo + CCRT[b]	45	11.11 (22.47)	25	9.33 (18.05)	47	1.25 [-4.71; 7.20]	[-9.15; 5.26]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	175	3.05 (10.28)	124	6.72 (18.02)	185	1.51 [-1.86; 4.87]	-0.58	0.766	-	0.196
Placebo + CCRT[b]	192	6.94 (18.32)	121	6.89 (13.55)	202	2.09 [-0.51; 4.70]	[-4.42; 3.25]			
1										
Pembrolizumab + CCRT[b]	84	5.95 (15.66)	53	8.18 (19.51)	87	1.80 [-2.90; 6.50]	2.31	0.465	-	
Placebo + CCRT[b]	75	6.22 (16.16)	45	5.93 (14.72)	79	-0.52 [-5.52; 4.48]	[-3.90; 8.53]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	2.78 (9.62)	5	0.00 (0.00)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	13.33 (27.60)	5	6.67 (14.91)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	203	3.28 (10.50)	145	7.13 (17.65)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	205	6.50 (15.86)	133	7.02 (14.24)	212	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	44	7.58 (18.83)	27	8.64 (23.74)	52	- [-; -]	-	-	-	

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Lymphoedema	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	47	5.67 (21.22)	28	4.76 (11.88)	52	- [-; -]				
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	219	4.41 (13.00)	152	7.24 (18.76)	232	1.33 [-1.61; 4.27]	-0.75	0.677	-	0.825
Placebo + CCRT[b]	227	6.75 (18.11)	140	6.90 (14.13)	240	2.08 [-0.45; 4.60]	[-4.26; 2.77]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	1.67 (7.36)	25	6.67 (16.67)	40	4.70 [-2.26; 11.66]	3.93	0.325	-	
Placebo + CCRT[b]	40	6.67 (15.47)	26	5.13 (12.26)	41	0.77 [-3.65; 5.18]	[-3.91; 11.76]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	4.60 (11.70)	19	8.77 (15.08)	29	4.67 [-2.97; 12.31]	7.06	0.104	-	0.552
Placebo + CCRT[b]	28	8.33 (19.51)	19	3.51 (10.51)	28	-2.39 [-8.55; 3.78]	[-1.46; 15.57]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	230	3.91 (12.43)	158	6.96 (18.83)	243	1.60 [-1.28; 4.49]	-0.79	0.653	-	
Placebo + CCRT[b]	239	6.55 (17.52)	147	7.03 (14.19)	253	2.39 [0.02; 4.77]	[-4.22; 2.64]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-CX24: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire CX24; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-CX24: Symptomskala periphere Neuropathie

Tabelle 4G-19: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala periphere Neuropathie aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Peripheral Neuropathy	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	224	10.12 (17.48)	154	18.61 (25.56)	235	8.44 [4.60; 12.29]	5.39	0.030	0.25	0.567
Placebo + CCRT[b]	222	9.91 (19.34)	141	13.00 (20.23)	234	3.06 [-0.56; 6.68]	[0.52; 10.26]		[0.02; 0.47]	
≥ 65										
Pembrolizumab + CCRT[b]	35	7.62 (21.52)	23	10.14 (15.68)	37	3.14 [-4.33; 10.61]	-6.91	0.226	-	
Placebo + CCRT[b]	45	15.56 (27.16)	25	26.67 (30.43)	47	10.05 [0.10; 20.01]	[-18.11; 4.28]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	2.78 (9.62)	5	13.33 (18.26)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	20.00 (27.60)	5	20.00 (29.82)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	203	10.84 (18.25)	145	17.70 (23.91)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	205	12.03 (21.55)	133	15.04 (21.11)	212	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	44	6.82 (18.44)	27	17.28 (29.77)	52	- [-; -]	-	-	-	
Placebo + CCRT[b]	47	2.84 (11.69)	28	14.29 (27.86)	52	- [-; -]				
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	219	9.89 (18.30)	152	17.54 (24.85)	232	7.15 [3.32; 10.98]	3.32	0.180	-	0.690
Placebo + CCRT[b]	227	11.60 (20.98)	140	14.76 (20.88)	240	3.83 [0.16; 7.50]	[-1.53; 8.18]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	9.17 (16.86)	25	17.33 (23.80)	40	9.37 [0.95; 17.79]	2.06	0.738	-	

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Peripheral Neuropathy	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	40	6.67 (20.25)	26	16.67 (30.19)	41	7.31 [-2.03; 16.66]	[-10.03; 14.15]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	10.34 (18.05)	19	21.05 (27.69)	29	10.30 [-1.15; 21.74]	7.42	0.303	-	0.896
Placebo + CCRT[b]	28	8.33 (23.35)	19	12.28 (22.80)	28	2.88 [-7.50; 13.25]	[-6.71; 21.55]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	230	9.71 (18.09)	158	17.09 (24.31)	243	7.17 [3.53; 10.80]	2.35	0.338	-	
Placebo + CCRT[b]	239	11.16 (20.64)	147	15.42 (22.50)	253	4.82 [1.13; 8.51]	[-2.45; 7.15]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment and study visit as covariates, and treatment-by-study visit interaction

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; EORTC QLQ-CX24: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire CX24; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-CX24: Symptomskala menopausale Symptome

Tabelle 4G-20: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Symptomskala menopausale Symptome aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Menopausal Symptoms	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	224	16.96 (25.05)	154	18.61 (27.48)	235	2.39 [-2.00; 6.78]	-0.91	0.749	-	0.228
Placebo + CCRT[b]	222	17.57 (25.10)	141	19.15 (25.58)	234	3.30 [-0.99; 7.59]	[-6.49; 4.67]			
≥ 65										
Pembrolizumab + CCRT[b]	35	16.19 (23.39)	23	14.49 (24.26)	37	-0.18 [-10.61; 10.25]	7.48	0.173	-	
Placebo + CCRT[b]	45	14.07 (23.02)	25	6.67 (13.61)	47	-7.66 [-14.90; -0.42]	[-3.28; 18.23]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	175	12.57 (19.75)	124	16.67 (26.37)	185	3.12 [-1.70; 7.94]	-0.19	0.948	-	0.178
Placebo + CCRT[b]	192	16.84 (25.06)	121	17.08 (22.82)	202	3.32 [-0.78; 7.41]	[-5.96; 5.57]			
1										
Pembrolizumab + CCRT[b]	84	25.79 (31.20)	53	21.38 (28.57)	87	0.36 [-7.14; 7.86]	2.87	0.582	-	
Placebo + CCRT[b]	75	17.33 (24.11)	45	17.78 (28.96)	79	-2.51 [-11.16; 6.14]	[-7.35; 13.09]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	25.00 (35.18)	5	0.00 (0.00)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	17.78 (35.34)	5	20.00 (18.26)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	203	16.75 (23.54)	145	19.08 (27.14)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	205	17.23 (24.16)	133	16.54 (24.14)	212	- [-; -]				

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Menopausal Symptoms	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Western Europe										
Pembrolizumab + CCRT[b]	44	15.15 (27.33)	27	16.05 (28.30)	52	- [-; -]	-	-	-	
Placebo + CCRT[b]	47	15.60 (23.93)	28	20.24 (27.72)	52	- [-; -]				
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	219	15.98 (24.59)	152	19.30 (28.07)	232	3.51 [-1.03; 8.04]	1.71	0.552	-	0.573
Placebo + CCRT[b]	227	17.62 (25.91)	140	17.62 (25.11)	240	1.80 [-2.48; 6.08]	[-3.93; 7.35]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	21.67 (25.65)	25	10.67 (18.56)	40	-5.56 [-13.26; 2.14]	-5.35	0.292	-	
Placebo + CCRT[b]	40	13.33 (16.54)	26	15.38 (21.56)	41	-0.20 [-8.19; 7.79]	[-15.33; 4.62]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	20.69 (25.84)	19	15.79 (28.04)	29	-1.74 [-15.15; 11.68]	6.50	0.336	-	0.831
Placebo + CCRT[b]	28	14.28 (16.80)	19	7.02 (13.96)	28	-8.23 [-14.58; -1.88]	[-6.76; 19.76]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	230	16.38 (24.67)	158	18.35 (27.01)	243	2.66 [-1.59; 6.91]	-0.14	0.960	-	
Placebo + CCRT[b]	239	17.29 (25.53)	147	18.59 (25.32)	253	2.80 [-1.40; 7.00]	[-5.54; 5.26]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-CX24: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire CX24; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

PGI-C

Tabelle 4G-21: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Fragebogen PGI-C aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
PGI-C Improvement at Week 54	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Risk Ratio/ Peto-Odds Ratio[d] [95 %-CI]**	**p-Value[e]**	**p-Value for Interaction[f] Test**
Age							
< 65	146	135 (92.5)	132	123 (93.2)	0.99 [0.93; 1.06]	0.818	0.773
≥ 65	23	20 (87.0)	26	22 (84.6)	1.03 [0.82; 1.29]	0.817	
ECOG Performance Status							
0	116	108 (93.1)	113	104 (92.0)	1.01 [0.94; 1.09]	0.758	0.619
1	53	47 (88.7)	45	41 (91.1)	0.97 [0.85; 1.11]	0.693	
Region							
Western Europe	27	22 (81.5)	26	23 (88.5)	0.92 [0.73; 1.16]	0.482	0.455
North America	5	4 (80.0)	6	3 (50.0)	1.60 [0.64; 3.98]	0.326	
RoW	137	129 (94.2)	126	119 (94.4)	1.00 [0.94; 1.06]	0.921	
Planned Type of EBRT							
IMRT or VMAT	145	136 (93.8)	134	123 (91.8)	1.02 [0.96; 1.09]	0.518	0.170
Non-IMRT and Non-VMAT	24	19 (79.2)	24	22 (91.7)	0.86 [0.68; 1.10]	0.225	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	18	14 (77.8)	14	10 (71.4)	1.09 [0.72; 1.65]	0.685	0.671
≥ 70 Gy	151	141 (93.4)	144	135 (93.8)	1.00 [0.94; 1.06]	0.897	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: full-analysis-set population with FIGO III to IVA and non-missing PGI-C assessment at week 54

d: Based on Mantel Haenszel method with treatment as covariate

e: Two-sided p-value using Wald test

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

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; PGI-C: Patient Global Impression Change; RoW: Rest of the World; VMAT: Volumetric Modulated Arc Therapy

PGI-S

Tabelle 4G-22: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Fragebogen PGI-S aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] PGI-Severity	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	224	1.67 (0.95)	154	0.44 (0.60)	235	-1.19 [-1.31; -1.08]	0.01	0.909	-	0.631
Placebo + CCRT[b]	222	1.63 (0.87)	140	0.37 (0.55)	234	-1.20 [-1.31; -1.08]	[-0.12; 0.13]			
≥ 65										
Pembrolizumab + CCRT[b]	35	1.46 (0.92)	23	0.43 (0.66)	37	-0.99 [-1.31; -0.67]	-0.03	0.863	-	
Placebo + CCRT[b]	45	1.44 (0.94)	25	0.44 (0.82)	47	-0.96 [-1.33; -0.59]	[-0.43; 0.36]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	175	1.52 (0.95)	124	0.35 (0.54)	185	-1.15 [-1.28; -1.02]	-0.07	0.370	-	0.939
Placebo + CCRT[b]	192	1.53 (0.86)	120	0.37 (0.63)	202	-1.09 [-1.22; -0.95]	[-0.21; 0.08]			
1										
Pembrolizumab + CCRT[b]	84	1.90 (0.91)	53	0.64 (0.71)	87	-1.18 [-1.38; -0.99]	0.19	0.097	-	
Placebo + CCRT[b]	75	1.77 (0.92)	45	0.42 (0.50)	79	-1.37 [-1.58; -1.16]	[-0.03; 0.41]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	2.00 (0.74)	5	0.60 (0.89)	13	-1.24 [-1.78; -0.69]	-0.37	0.286	-	0.545
Placebo + CCRT[b]	15	1.60 (1.12)	5	0.60 (0.55)	17	-0.87 [-1.43; -0.30]	[-1.05; 0.31]			
RoW										
Pembrolizumab + CCRT[b]	203	1.67 (0.94)	145	0.38 (0.55)	207	-1.24 [-1.36; -1.13]	-0.04	0.579	-	
Placebo + CCRT[b]	205	1.62 (0.89)	133	0.38 (0.61)	212	-1.21 [-1.34; -1.08]	[-0.17; 0.09]			
Western Europe										
Pembrolizumab + CCRT[b]	44	1.43 (1.02)	27	0.70 (0.78)	52	-0.74 [-1.04; -0.44]	0.31	0.069	-	
Placebo + CCRT[b]	47	1.47 (0.80)	27	0.37 (0.56)	52	-1.05 [-1.32; -0.78]	[-0.02; 0.64]			
Planned Type of EBRT										

Study: KEYNOTE A18[a] PGI-Severity	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
IMRT or VMAT										
Pembrolizumab + CCRT[b]	219	1.65 (0.97)	152	0.44 (0.62)	232	-1.15 [-1.27; -1.04]	0.05	0.485	-	0.245
Placebo + CCRT[b]	227	1.60 (0.87)	139	0.36 (0.54)	240	-1.20 [-1.32; -1.08]	[-0.08; 0.17]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	1.63 (0.87)	25	0.40 (0.58)	40	-1.21 [-1.44; -0.97]	-0.19	0.284	-	
Placebo + CCRT[b]	40	1.55 (0.96)	26	0.50 (0.86)	41	-1.02 [-1.36; -0.68]	[-0.54; 0.16]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	1.72 (0.96)	19	0.32 (0.58)	29	-1.33 [-1.63; -1.02]	-0.08	0.706	-	0.385
Placebo + CCRT[b]	28	1.57 (1.00)	19	0.32 (0.75)	28	-1.25 [-1.63; -0.87]	[-0.47; 0.32]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	230	1.63 (0.95)	158	0.45 (0.61)	243	-1.14 [-1.26; -1.03]	0.02	0.762	-	
Placebo + CCRT[b]	239	1.60 (0.87)	146	0.39 (0.58)	253	-1.16 [-1.28; -1.04]	[-0.11; 0.15]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment and study visit as covariates, and treatment-by-study visit interaction

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; PGI: Patient Global Impression; PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EQ-5D VAS

Tabelle 4G-23: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Fragebogen EQ-5D VAS aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EQ-5D VAS EQ-5D VAS Score	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	223	71.72 (21.75)	154	83.77 (14.56)	235	10.82 [8.42; 13.22]	1.63	0.286	-	0.223
Placebo + CCRT[b]	222	70.12 (20.69)	140	83.37 (14.57)	234	9.19 [6.57; 11.80]	[-1.37; 4.64]			
≥ 65										
Pembrolizumab + CCRT[b]	35	73.57 (18.34)	23	75.48 (18.30)	37	2.61 [-4.48; 9.70]	-2.66	0.560	-	
Placebo + CCRT[b]	44	70.45 (17.33)	25	77.08 (18.52)	47	5.27 [-0.99; 11.54]	[-11.62; 6.29]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	175	75.32 (19.32)	124	83.98 (13.68)	185	8.44 [5.96; 10.93]	1.78	0.284	-	0.448
Placebo + CCRT[b]	191	70.77 (19.47)	120	82.38 (14.90)	202	6.67 [3.87; 9.47]	[-1.47; 5.02]			
1										
Pembrolizumab + CCRT[b]	83	64.92 (23.55)	53	79.70 (18.32)	87	12.65 [7.67; 17.64]	-0.61	0.840	-	
Placebo + CCRT[b]	75	68.67 (21.83)	45	82.51 (16.63)	79	13.27 [8.56; 17.98]	[-6.57; 5.34]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	73.42 (15.44)	5	80.80 (17.73)	13	2.59 [-7.63; 12.81]	-5.60	0.468	-	0.617
Placebo + CCRT[b]	14	60.64 (30.27)	5	90.60 (9.32)	17	8.20 [-4.88; 21.27]	[-20.79; 9.59]			
RoW										
Pembrolizumab + CCRT[b]	202	73.25 (21.55)	145	84.54 (14.05)	207	10.21 [7.66; 12.76]	1.74	0.271	-	
Placebo + CCRT[b]	205	72.73 (19.23)	133	83.68 (14.48)	212	8.47 [5.79; 11.15]	[-1.36; 4.83]			
Western Europe										
Pembrolizumab + CCRT[b]	44	65.70 (20.72)	27	73.15 (18.09)	52	7.70 [2.03; 13.38]	-0.66	0.871	-	
Placebo + CCRT[b]	47	61.87 (17.65)	27	74.67 (17.96)	52	8.36 [1.95; 14.77]	[-8.61; 7.29]			

Study: KEYNOTE A18[a] EQ-5D VAS EQ-5D VAS Score	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	70.55 (17.31)	19	82.63 (12.37)	29	10.03 [3.52; 16.55]	4.53	0.261	-	0.274
Placebo + CCRT[b]	28	73.18 (18.92)	19	82.11 (13.71)	28	5.50 [-0.49; 11.49]	[-3.38; 12.45]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	229	72.15 (21.77)	158	82.70 (15.64)	243	9.88 [7.42; 12.33]	0.99	0.530	-	
Placebo + CCRT[b]	238	69.82 (20.29)	146	82.46 (15.58)	253	8.89 [6.28; 11.49]	[-2.10; 4.09]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment and study visit as covariates, and treatment-by-study visit interaction

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; EQ-5D: European Quality of Life 5 Dimensions; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VAS: Visual Analog Scale

Anhang 4-G2.3: Gesundheitsbezogene Lebensqualität

EORTC QLQ-C30: Globaler Gesundheitsstatus

Tabelle 4G-24: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den globalen Gesundheitsstatus aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Global Health Status/QoL Global Health Status	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	64.27 (23.65)	154	76.35 (16.98)	235	10.99 [8.14; 13.85]	0.60	0.751	-	0.197
Placebo + CCRT[b]	223	64.39 (22.65)	141	77.54 (17.90)	234	10.40 [7.16; 13.64]	[-3.08; 4.28]			
≥ 65										
Pembrolizumab + CCRT[b]	35	65.71 (24.15)	23	71.01 (20.24)	37	4.92 [-3.82; 13.66]	0.76	0.896	-	
Placebo + CCRT[b]	47	62.94 (18.29)	25	68.00 (23.28)	49	4.16 [-4.48; 12.80]	[-10.61; 12.13]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	68.75 (22.01)	124	77.02 (15.15)	185	8.41 [5.39; 11.42]	1.31	0.523	-	0.526
Placebo + CCRT[b]	194	65.08 (21.41)	121	75.69 (19.29)	203	7.10 [3.59; 10.61]	[-2.71; 5.33]			
1										
Pembrolizumab + CCRT[b]	85	55.59 (24.65)	53	72.48 (21.78)	87	14.02 [8.32; 19.73]	-1.59	0.665	-	
Placebo + CCRT[b]	76	61.73 (23.18)	45	77.22 (18.50)	80	15.62 [9.66; 21.58]	[-8.80; 5.62]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	63.19 (22.03)	5	75.00 (16.67)	13	10.36 [-1.52; 22.23]	4.33	0.622	-	0.111
Placebo + CCRT[b]	15	53.89 (24.57)	5	81.67 (12.36)	17	6.02 [-10.39; 22.43]	[-12.98; 21.65]			
RoW										
Pembrolizumab + CCRT[b]	204	66.30 (24.08)	145	77.13 (16.60)	207	9.96 [6.85; 13.07]	0.40	0.834	-	
Placebo + CCRT[b]	206	65.98 (21.98)	133	77.57 (17.65)	213	9.55 [6.29; 12.81]	[-3.38; 4.19]			
Western Europe										

Study: KEYNOTE A18[a] EORTC QLQ-C30 Global Health Status/QoL Global Health Status	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Pembrolizumab + CCRT[b]	45	56.48 (20.86)	27	67.90 (20.50)	52	10.84 [4.49; 17.20]	3.23	0.532	-	
Placebo + CCRT[b]	49	59.52 (19.69)	28	68.15 (24.22)	53	7.62 [-1.13; 16.37]	[-6.90; 13.35]			
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	65.35 (24.23)	152	75.82 (18.27)	232	9.74 [6.73; 12.76]	-0.59	0.765	-	0.869
Placebo + CCRT[b]	230	63.91 (22.18)	140	77.20 (18.90)	242	10.33 [7.03; 13.64]	[-4.49; 3.30]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	59.58 (19.93)	25	74.67 (11.65)	40	12.18 [6.09; 18.27]	7.18	0.084	-	
Placebo + CCRT[b]	40	65.42 (20.63)	26	70.19 (19.03)	41	5.00 [-2.43; 12.42]	[-0.97; 15.32]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	55.75 (19.43)	19	72.81 (17.09)	29	12.82 [3.18; 22.46]	3.55	0.532	-	0.986
Placebo + CCRT[b]	28	63.10 (18.62)	19	71.93 (18.68)	28	9.27 [0.79; 17.75]	[-7.59; 14.68]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	65.55 (23.97)	158	76.00 (17.53)	243	9.71 [6.89; 12.53]	0.11	0.953	-	
Placebo + CCRT[b]	242	64.26 (22.31)	147	76.64 (19.08)	255	9.60 [6.34; 12.86]	[-3.63; 3.85]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; PRO: Patient Reported Outcome; QoL: Quality of Life; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Funktionsskala Körperliche Funktion

Tabelle 4G-25: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Körperliche Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Physical Functioning	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	83.57 (18.78)	154	91.95 (12.54)	235	6.48 [4.41; 8.55]	0.33	0.803	-	0.700
Placebo + CCRT[b]	223	83.92 (18.01)	141	93.05 (11.38)	234	6.15 [3.92; 8.38]	[-2.29; 2.96]			
≥ 65										
Pembrolizumab + CCRT[b]	35	85.14 (14.38)	23	81.45 (16.32)	37	-4.06 [-10.05; 1.93]	-7.60	0.103	-	
Placebo + CCRT[b]	47	80.99 (18.12)	25	87.47 (17.88)	49	3.54 [-4.05; 11.13]	[-16.75; 1.54]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	87.31 (14.63)	124	91.34 (13.63)	185	3.62 [1.41; 5.82]	-0.71	0.638	-	0.858
Placebo + CCRT[b]	194	85.64 (16.52)	121	92.73 (12.26)	203	4.33 [1.89; 6.77]	[-3.67; 2.25]			
1										
Pembrolizumab + CCRT[b]	85	76.47 (22.43)	53	88.81 (13.19)	87	8.56 [4.39; 12.73]	-1.17	0.675	-	
Placebo + CCRT[b]	76	77.72 (20.44)	45	90.81 (13.73)	80	9.73 [5.01; 14.45]	[-6.62; 4.29]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	80.00 (21.08)	5	92.00 (8.69)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	72.89 (32.12)	5	92.00 (14.45)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	204	84.22 (17.90)	145	90.80 (13.31)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	206	84.69 (16.78)	133	93.18 (11.59)	213	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	45	82.81 (19.25)	27	89.14 (15.49)	52	- [-; -]	-	-	-	

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Physical Functioning	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	49	81.22 (16.48)	28	87.62 (16.30)	53	- [-; -]				
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	84.16 (18.42)	152	90.53 (13.86)	232	4.97 [2.67; 7.28]	-1.19	0.432	-	0.063
Placebo + CCRT[b]	230	83.13 (18.33)	140	92.10 (12.63)	242	6.16 [3.68; 8.65]	[-4.16; 1.78]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	81.67 (17.26)	25	90.93 (11.37)	40	5.16 [1.64; 8.68]	3.19	0.197	-	
Placebo + CCRT[b]	40	85.00 (16.31)	26	92.82 (13.05)	41	1.97 [-1.64; 5.58]	[-1.66; 8.05]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	85.29 (16.27)	19	90.53 (15.45)	29	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	28	87.14 (15.81)	19	96.84 (7.82)	28	- [-; -]				
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	83.59 (18.49)	158	90.59 (13.31)	243	- [-; -]	-	-	-	
Placebo + CCRT[b]	242	82.97 (18.25)	147	91.61 (13.06)	255	- [-; -]				

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Funktionsskala Rollenfunktion

Tabelle 4G-26: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Rollenfunktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Role Functioning	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	77.88 (27.97)	154	88.64 (20.85)	235	7.71 [4.54; 10.88]	0.17	0.933	-	0.617
Placebo + CCRT[b]	223	79.22 (26.17)	141	90.54 (18.07)	234	7.54 [4.10; 10.98]	[-3.91; 4.26]			
≥ 65										
Pembrolizumab + CCRT[b]	35	84.29 (21.37)	23	78.99 (25.73)	37	-4.85 [-14.73; 5.03]	-8.76	0.175	-	
Placebo + CCRT[b]	47	78.72 (25.70)	25	86.00 (23.90)	49	3.91 [-5.23; 13.05]	[-21.44; 3.91]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	81.82 (24.12)	124	87.37 (21.71)	185	4.12 [0.51; 7.74]	-1.91	0.420	-	0.482
Placebo + CCRT[b]	194	81.62 (23.38)	121	90.91 (19.00)	203	6.04 [2.33; 9.74]	[-6.56; 2.74]			
1										
Pembrolizumab + CCRT[b]	85	72.35 (31.97)	53	87.42 (21.90)	87	11.05 [5.34; 16.76]	1.21	0.747	-	
Placebo + CCRT[b]	76	72.81 (31.13)	45	87.04 (19.10)	80	9.84 [3.43; 16.25]	[-6.15; 8.57]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	70.83 (22.61)	5	86.67 (13.94)	13	18.71 [1.07; 36.36]	-10.08	0.321	-	0.632
Placebo + CCRT[b]	15	58.89 (33.85)	5	93.33 (14.91)	17	28.79 [9.84; 47.75]	[-30.06; 9.91]			
RoW										
Pembrolizumab + CCRT[b]	204	81.13 (26.09)	145	89.31 (19.90)	207	5.42 [2.16; 8.68]	-0.89	0.670	-	
Placebo + CCRT[b]	206	82.20 (24.39)	133	91.48 (17.36)	213	6.31 [2.91; 9.71]	[-5.01; 3.22]			
Western Europe										
Pembrolizumab + CCRT[b]	45	70.00 (31.50)	27	77.16 (28.92)	52	6.88 [-2.92; 16.68]	-2.00	0.743	-	

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Role Functioning	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	49	72.45 (26.69)	28	81.55 (24.99)	53	8.88 [-0.16; 17.92]	[-13.98; 9.98]			
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	78.96 (27.82)	152	87.17 (22.65)	232	6.03 [2.53; 9.52]	-1.73	0.442	-	0.163
Placebo + CCRT[b]	230	78.48 (26.51)	140	89.76 (18.92)	242	7.75 [4.16; 11.34]	[-6.13; 2.68]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	77.50 (24.03)	25	88.67 (15.00)	40	7.23 [1.63; 12.83]	4.95	0.222	-	
Placebo + CCRT[b]	40	82.92 (23.11)	26	90.39 (20.09)	41	2.28 [-4.21; 8.77]	[-3.00; 12.89]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	75.86 (26.94)	19	85.09 (24.15)	29	4.71 [-7.30; 16.73]	-7.36	0.225	-	0.456
Placebo + CCRT[b]	28	80.36 (24.87)	19	94.74 (12.49)	28	12.07 [3.65; 20.50]	[-19.25; 4.53]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	79.09 (27.30)	158	87.66 (21.46)	243	6.13 [3.05; 9.21]	-0.39	0.855	-	
Placebo + CCRT[b]	242	78.99 (26.22)	147	89.23 (19.68)	255	6.52 [3.02; 10.02]	[-4.53; 3.76]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Funktionsskala Emotionale Funktion

Tabelle 4G-27: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Emotionale Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Emotional Functioning	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	72.75 (22.28)	154	84.36 (19.67)	235	10.48 [7.74; 13.22]	4.33	0.027	0.23	0.459
Placebo + CCRT[b]	223	72.68 (21.91)	141	82.09 (21.15)	234	6.15 [3.06; 9.24]	[0.48; 8.17]		[0.03; 0.44]	
≥ 65										
Pembrolizumab + CCRT[b]	35	77.62 (19.36)	23	86.59 (15.43)	37	10.31 [3.11; 17.50]	3.32	0.508	-	
Placebo + CCRT[b]	47	73.05 (21.99)	25	81.00 (21.32)	49	6.99 [-1.71; 15.70]	[-6.51; 13.14]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	75.76 (19.03)	124	85.62 (18.57)	185	9.66 [6.67; 12.65]	5.14	0.019	0.29	0.505
Placebo + CCRT[b]	194	74.18 (20.46)	121	81.96 (21.17)	203	4.51 [1.08; 7.94]	[0.85; 9.43]		[0.05; 0.52]	
1										
Pembrolizumab + CCRT[b]	85	68.53 (26.46)	53	82.39 (20.46)	87	11.28 [6.29; 16.27]	0.34	0.921	-	
Placebo + CCRT[b]	76	69.08 (24.94)	45	81.85 (21.19)	80	10.94 [5.26; 16.63]	[-6.37; 7.04]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	66.67 (19.46)	5	90.00 (10.87)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	56.67 (26.20)	5	81.67 (16.03)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	204	75.29 (22.02)	145	85.81 (18.35)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	206	74.47 (21.90)	133	83.77 (20.95)	213	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	45	66.67 (20.95)	27	77.47 (23.09)	52	- [-; -]	-	-	-	

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Emotional Functioning	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	49	70.41 (18.33)	28	73.21 (21.08)	53	- [-; -]				
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	73.08 (22.27)	152	84.27 (19.60)	232	10.79 [7.90; 13.69]	4.33	0.038	0.22	0.102
Placebo + CCRT[b]	230	71.01 (22.46)	140	80.89 (21.75)	242	6.47 [3.13; 9.80]	[0.25; 8.41]		[0.01; 0.43]	
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	75.21 (20.19)	25	87.00 (16.33)	40	7.74 [3.15; 12.32]	3.39	0.350	-	
Placebo + CCRT[b]	40	82.71 (14.91)	26	87.50 (16.54)	41	4.34 [-1.68; 10.37]	[-3.73; 10.52]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	71.55 (21.99)	19	83.33 (19.24)	29	8.12 [0.90; 15.34]	-6.87	0.113	-	0.069
Placebo + CCRT[b]	28	76.19 (18.10)	19	91.23 (12.87)	28	14.99 [8.62; 21.35]	[-15.37; 1.63]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	73.63 (21.97)	158	84.81 (19.20)	243	10.44 [7.69; 13.18]	5.32	0.008	0.28	
Placebo + CCRT[b]	242	72.35 (22.28)	147	80.73 (21.70)	255	5.12 [1.92; 8.31]	[1.41; 9.23]		[0.07; 0.48]	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Funktionsskala Kognitive Funktion

Tabelle 4G-28: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Kognitive Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Cognitive Functioning	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	84.59 (20.72)	154	86.15 (19.13)	235	-0.66 [-3.48; 2.16]	0.87	0.637	-	0.432
Placebo + CCRT[b]	223	89.09 (17.34)	141	88.42 (17.01)	234	-1.53 [-4.38; 1.33]	[-2.74; 4.48]			
≥ 65										
Pembrolizumab + CCRT[b]	35	82.86 (21.95)	23	87.68 (14.40)	37	3.19 [-3.24; 9.63]	6.37	0.240	-	
Placebo + CCRT[b]	47	79.43 (22.84)	25	76.00 (27.25)	49	-3.18 [-12.86; 6.51]	[-4.27; 17.01]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	88.26 (16.46)	124	87.23 (17.92)	185	-1.89 [-4.84; 1.06]	2.09	0.332	-	0.486
Placebo + CCRT[b]	194	88.75 (18.29)	121	86.50 (20.33)	203	-3.98 [-7.39; -0.57]	[-2.14; 6.32]			
1										
Pembrolizumab + CCRT[b]	85	76.27 (26.15)	53	84.28 (19.99)	87	4.27 [-0.89; 9.43]	0.61	0.842	-	
Placebo + CCRT[b]	76	83.99 (19.52)	45	86.67 (16.51)	80	3.67 [-1.26; 8.60]	[-5.37; 6.58]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	77.78 (23.92)	5	90.00 (14.91)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	77.78 (21.52)	5	83.33 (16.67)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	204	84.56 (20.66)	145	87.47 (16.73)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	206	87.14 (19.07)	133	86.59 (19.62)	213	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	45	85.18 (21.09)	27	79.63 (26.28)	52	- [-; -]	-	-	-	

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Cognitive Functioning	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	49	91.50 (15.26)	28	86.91 (18.90)	53	- [-; -]				
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	84.39 (21.29)	152	85.75 (19.32)	232	-0.58 [-3.49; 2.34]	1.39	0.482	-	0.302
Placebo + CCRT[b]	230	87.68 (18.11)	140	86.31 (19.31)	242	-1.97 [-5.11; 1.18]	[-2.49; 5.27]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	84.17 (18.47)	25	90.00 (12.73)	40	3.85 [-1.28; 8.98]	4.23	0.269	-	
Placebo + CCRT[b]	40	85.83 (22.18)	26	87.82 (19.75)	41	-0.39 [-6.85; 6.08]	[-3.27; 11.74]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	85.06 (20.09)	19	85.09 (17.48)	29	-0.78 [-7.57; 6.02]	-4.19	0.360	-	0.135
Placebo + CCRT[b]	28	83.93 (22.90)	19	89.47 (15.92)	28	3.41 [-4.01; 10.83]	[-13.16; 4.78]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	84.27 (20.99)	158	86.50 (18.73)	243	0.08 [-2.73; 2.89]	2.42	0.206	-	
Placebo + CCRT[b]	242	87.81 (18.20)	147	86.17 (19.74)	255	-2.34 [-5.40; 0.71]	[-1.34; 6.18]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-C30: Funktionsskala Soziale Funktion

Tabelle 4G-29: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Soziale Funktion aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Social Functioning	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	226	79.57 (24.18)	154	87.01 (20.10)	235	6.68 [3.72; 9.64]	-0.57	0.772	-	0.397
Placebo + CCRT[b]	223	77.50 (24.47)	141	88.06 (19.45)	234	7.25 [4.09; 10.41]	[-4.41; 3.27]			
≥ 65										
Pembrolizumab + CCRT[b]	35	88.09 (19.20)	23	90.58 (14.93)	37	7.26 [-0.56; 15.09]	7.38	0.149	-	
Placebo + CCRT[b]	47	80.14 (23.73)	25	85.33 (21.69)	49	-0.12 [-9.79; 9.56]	[-2.65; 17.41]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	176	84.28 (19.41)	124	88.84 (17.87)	185	4.75 [1.71; 7.78]	0.67	0.754	-	0.866
Placebo + CCRT[b]	194	81.10 (22.01)	121	88.15 (20.00)	203	4.08 [0.61; 7.55]	[-3.52; 4.86]			
1										
Pembrolizumab + CCRT[b]	85	73.33 (29.57)	53	84.28 (22.74)	87	9.59 [3.81; 15.38]	-1.87	0.620	-	
Placebo + CCRT[b]	76	69.96 (28.02)	45	86.30 (19.23)	80	11.47 [4.96; 17.97]	[-9.27; 5.53]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	73.61 (24.06)	5	86.67 (13.94)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	64.44 (37.20)	5	86.67 (13.94)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	204	82.27 (23.17)	145	88.97 (17.92)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	206	79.45 (23.71)	133	88.85 (19.97)	213	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	45	75.56 (25.52)	27	79.63 (26.28)	52	- [-; -]	-	-	-	

Study: KEYNOTE A18[a] EORTC QLQ-C30 Functional Scales Social Functioning	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	49	75.85 (20.99)	28	82.14 (19.21)	53	- [-; -]				
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	221	80.77 (24.07)	152	86.95 (19.93)	232	6.26 [3.13; 9.39]	-0.49	0.813	-	0.636
Placebo + CCRT[b]	230	76.81 (24.89)	140	87.02 (20.00)	242	6.76 [3.30; 10.21]	[-4.58; 3.59]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	80.42 (21.97)	25	90.67 (16.72)	40	7.80 [2.93; 12.68]	5.37	0.173	-	
Placebo + CCRT[b]	40	84.58 (19.75)	26	91.03 (18.40)	41	2.44 [-4.30; 9.17]	[-2.35; 13.08]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	79.31 (25.84)	19	89.47 (17.75)	29	10.22 [4.23; 16.21]	-0.76	0.846	-	0.612
Placebo + CCRT[b]	28	82.74 (17.85)	19	94.74 (12.49)	28	10.98 [4.21; 17.75]	[-8.41; 6.89]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	232	80.89 (23.49)	158	87.24 (19.74)	243	6.19 [3.18; 9.19]	0.50	0.805	-	
Placebo + CCRT[b]	242	77.41 (24.93)	147	86.73 (20.36)	255	5.69 [2.31; 9.06]	[-3.49; 4.49]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire - Core 30 items; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-CX24: Funktionsskala sexuelle Aktivität

Tabelle 4G-30: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für ddie Funktionsskala Sexuelle Aktivität aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Functional Scales Sexual Activity	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	223	95.22 (14.04)	151	93.16 (14.05)	235	-2.28 [-4.77; 0.22]	1.61	0.377	-	0.281
Placebo + CCRT[b]	214	93.15 (16.93)	139	89.69 (19.60)	231	-3.88 [-6.86; -0.91]	[-1.96; 5.18]			
≥ 65										
Pembrolizumab + CCRT[b]	32	96.88 (13.01)	23	100.00 (0.00)	36	1.75 [-0.30; 3.81]	0.35	0.393	-	
Placebo + CCRT[b]	44	99.24 (5.02)	25	100.00 (0.00)	47	1.40 [-0.85; 3.65]	[-0.45; 1.14]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	172	95.35 (14.57)	121	93.39 (14.02)	185	-2.06 [-4.80; 0.68]	2.43	0.222	-	0.207
Placebo + CCRT[b]	185	94.05 (14.56)	120	89.17 (20.34)	201	-4.49 [-7.71; -1.27]	[-1.47; 6.34]			
1										
Pembrolizumab + CCRT[b]	83	95.58 (12.51)	53	95.60 (11.39)	86	-1.26 [-4.86; 2.34]	-1.47	0.523	-	
Placebo + CCRT[b]	73	94.52 (18.44)	44	96.97 (9.69)	77	0.21 [-3.34; 3.76]	[-5.99; 3.04]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	100.00 (0.00)	5	86.67 (18.26)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	97.78 (8.61)	5	100.00 (0.00)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	199	96.48 (12.71)	142	94.60 (12.95)	206	- [-; -]	-	-	-	
Placebo + CCRT[b]	198	94.11 (15.17)	131	92.11 (17.46)	209	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	44	89.39 (18.71)	27	92.59 (14.12)	52	- [-; -]	-	-	-	

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Functional Scales Sexual Activity	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	45	93.33 (19.59)	28	85.71 (23.00)	52	- [-; -]				
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	215	94.88 (14.76)	149	93.51 (13.80)	231	-1.54 [-4.02; 0.94]	1.78	0.321	-	0.953
Placebo + CCRT[b]	218	93.73 (15.89)	138	90.34 (19.40)	237	-3.32 [-6.25; -0.39]	[-1.73; 5.29]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	98.33 (7.36)	25	97.33 (9.23)	40	-3.08 [-7.48; 1.31]	-0.55	0.850	-	
Placebo + CCRT[b]	40	96.67 (14.72)	26	96.15 (10.86)	41	-2.53 [-6.64; 1.58]	[-6.32; 5.21]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	97.70 (8.60)	19	98.25 (7.65)	29	-0.03 [-1.82; 1.75]	0.56	0.797	-	0.834
Placebo + CCRT[b]	28	98.81 (6.30)	19	98.25 (7.65)	28	-0.59 [-4.70; 3.51]	[-3.70; 4.82]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	226	95.13 (14.43)	155	93.55 (13.75)	242	-1.99 [-4.45; 0.48]	1.35	0.442	-	
Placebo + CCRT[b]	230	93.62 (16.42)	145	90.35 (19.21)	250	-3.34 [-6.19; -0.49]	[-2.09; 4.79]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-CX24: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire CX24; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-CX24: Funktionsskala Sorge vor schmerzhaftem Geschlechtsverkehr, sexuelle Aktivität und sexuellem Erleben

Tabelle 4G-31: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Sorge vor schmerzhaftem Geschlechtsverkehr, sexuelle Aktivität und sexuellem Erleben aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Sexual Worry	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	221	21.57 (31.66)	150	21.11 (32.86)	235	-0.59 [-5.28; 4.10]	4.39	0.140	-	0.774
Placebo + CCRT[b]	213	22.69 (34.44)	139	14.15 (25.69)	231	-4.97 [-9.47; -0.48]	[-1.44; 10.22]			
≥ 65										
Pembrolizumab + CCRT[b]	32	6.25 (21.48)	22	4.55 (11.71)	36	0.41 [-4.87; 5.69]	-2.98	0.567	-	
Placebo + CCRT[b]	44	1.52 (7.02)	25	8.00 (27.69)	47	3.39 [-5.92; 12.70]	[-13.19; 7.24]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	170	18.82 (28.99)	120	20.28 (30.65)	185	1.77 [-3.21; 6.75]	3.46	0.281	-	0.256
Placebo + CCRT[b]	184	18.12 (30.54)	120	13.89 (26.84)	201	-1.69 [-6.41; 3.04]	[-2.83; 9.74]			
1										
Pembrolizumab + CCRT[b]	83	21.28 (34.76)	52	16.03 (33.33)	86	-5.54 [-13.16; 2.07]	4.20	0.395	-	
Placebo + CCRT[b]	73	21.46 (37.01)	44	11.36 (23.78)	77	-9.74 [-17.53; -1.95]	[-5.47; 13.86]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	30.56 (38.82)	5	20.00 (18.26)	13	-12.32 [-30.51; 5.87]	-24.36	0.113	-	0.311
Placebo + CCRT[b]	15	33.33 (45.43)	5	20.00 (44.72)	17	12.04 [-14.61; 38.70]	[-54.58; 5.85]			
RoW										
Pembrolizumab + CCRT[b]	199	18.09 (30.09)	141	17.49 (31.26)	206	-0.08 [-4.67; 4.52]	3.86	0.172	-	
Placebo + CCRT[b]	196	17.01 (30.47)	131	11.96 (24.48)	209	-3.94 [-7.98; 0.10]	[-1.68; 9.41]			
Western Europe										
Pembrolizumab + CCRT[b]	42	23.81 (32.33)	26	26.92 (34.02)	52	0.47 [-10.44; 11.39]	4.18	0.577	-	

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Symptom Scales Sexual Worry	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Placebo + CCRT[b]	46	23.19 (35.04)	28	17.86 (29.37)	52	-3.71 [-16.05; 8.64]	[-10.51; 18.86]			
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	213	20.50 (31.76)	147	21.09 (32.89)	231	0.44 [-4.27; 5.15]	3.79	0.218	-	0.260
Placebo + CCRT[b]	217	20.89 (33.70)	138	14.73 (27.32)	237	-3.35 [-8.03; 1.32]	[-2.24; 9.83]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	15.00 (26.09)	25	6.67 (16.67)	40	-2.72 [-8.59; 3.14]	1.01	0.792	-	
Placebo + CCRT[b]	40	9.17 (22.63)	26	5.13 (15.47)	41	-3.73 [-9.91; 2.45]	[-6.49; 8.51]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	8.05 (21.18)	19	3.51 (10.51)	29	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	28	5.95 (15.85)	19	7.02 (23.78)	28	- [-; -]				
≥ 70 Gy										
Pembrolizumab + CCRT[b]	224	21.13 (31.72)	153	20.91 (32.64)	242	- [-; -]	-	-	-	
Placebo + CCRT[b]	229	20.67 (33.62)	145	14.02 (26.26)	250	- [-; -]				

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-CX24: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire CX24; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

EORTC QLQ-CX24: Funktionsskala Körperbild

Tabelle 4G-32: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für die Funktionsskala Körperbild aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Functional Scales Body Image	**Baseline**		**Week 60**		**Change from Baseline to Week 60**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**			**p-Value for Interaction Test[g]**
							Mean Difference at Week 60		**Standardized Mean Difference at Week 60**	
	N[c]	**Mean (SD)**	**N[c]**	**Mean (SD)**	**N[d]**	**Mean [95 %-CI][e]**	**[95 %-CI][e]**	**p-Value**	**[95 %-CI][f]**	
Age										
< 65										
Pembrolizumab + CCRT[b]	224	82.29 (22.98)	154	87.81 (20.28)	235	4.68 [1.46; 7.90]	2.44	0.250	-	0.646
Placebo + CCRT[b]	222	79.53 (23.93)	141	85.97 (20.77)	234	2.24 [-0.92; 5.40]	[-1.72; 6.59]			
≥ 65										
Pembrolizumab + CCRT[b]	35	85.72 (22.15)	23	90.34 (15.09)	37	5.43 [-0.54; 11.40]	2.71	0.543	-	
Placebo + CCRT[b]	45	81.98 (22.38)	25	84.45 (18.43)	47	2.72 [-5.75; 11.19]	[-6.03; 11.46]			
ECOG Performance Status										
0										
Pembrolizumab + CCRT[b]	175	85.72 (20.70)	124	87.64 (19.74)	185	1.76 [-1.81; 5.33]	0.68	0.766	-	0.200
Placebo + CCRT[b]	192	81.42 (22.69)	121	85.68 (20.96)	202	1.09 [-2.09; 4.26]	[-3.78; 5.13]			
1										
Pembrolizumab + CCRT[b]	84	76.59 (25.87)	53	89.31 (19.61)	87	11.42 [6.70; 16.15]	5.28	0.148	-	
Placebo + CCRT[b]	75	76.15 (25.75)	45	85.93 (19.01)	79	6.14 [-0.48; 12.77]	[-1.87; 12.43]			
Region										
North America										
Pembrolizumab + CCRT[b]	12	82.41 (25.72)	5	80.00 (29.82)	13	- [-; -]	-	-	-	n.a.
Placebo + CCRT[b]	15	72.59 (26.18)	5	66.67 (23.57)	17	- [-; -]				
RoW										
Pembrolizumab + CCRT[b]	203	82.32 (22.56)	145	88.51 (20.05)	207	- [-; -]	-	-	-	
Placebo + CCRT[b]	205	80.60 (23.61)	133	87.64 (19.28)	212	- [-; -]				
Western Europe										
Pembrolizumab + CCRT[b]	44	84.85 (23.85)	27	87.66 (15.51)	52	- [-; -]	-	-	-	
Placebo + CCRT[b]	47	79.43 (23.17)	28	80.16 (22.90)	52	- [-; -]				

Study: KEYNOTE A18[a] EORTC QLQ-CX24 Functional Scales Body Image	Baseline		Week 60		Change from Baseline to Week 60		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]			p-Value for Interaction Test[g]
							Mean Difference at Week 60		Standardized Mean Difference at Week 60	
	N[c]	Mean (SD)	N[c]	Mean (SD)	N[d]	Mean [95 %-CI][e]	[95 %-CI][e]	p-Value	[95 %-CI][f]	
Planned Type of EBRT										
IMRT or VMAT										
Pembrolizumab + CCRT[b]	219	83.16 (22.18)	152	88.09 (19.14)	232	5.66 [2.52; 8.80]	2.71	0.197	-	0.281
Placebo + CCRT[b]	227	78.41 (24.61)	140	85.16 (21.01)	240	2.95 [-0.38; 6.28]	[-1.41; 6.83]			
non-IMRT and non-VMAT										
Pembrolizumab + CCRT[b]	40	80.56 (26.48)	25	88.45 (23.01)	40	0.58 [-6.62; 7.79]	1.65	0.718	-	
Placebo + CCRT[b]	40	88.61 (14.78)	26	88.89 (16.63)	41	-1.07 [-6.89; 4.76]	[-7.29; 10.59]			
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)										
< 70 Gy										
Pembrolizumab + CCRT[b]	29	77.40 (26.31)	19	84.80 (25.45)	29	0.92 [-7.84; 9.69]	0.00	> 0.999	-	0.787
Placebo + CCRT[b]	28	84.92 (17.69)	19	87.14 (15.83)	28	0.92 [-7.47; 9.31]	[-11.53; 11.53]			
≥ 70 Gy										
Pembrolizumab + CCRT[b]	230	83.43 (22.36)	158	88.54 (18.91)	243	5.45 [2.37; 8.52]	3.15	0.123	-	
Placebo + CCRT[b]	239	79.36 (24.22)	147	85.56 (20.95)	253	2.30 [-0.87; 5.47]	[-0.85; 7.14]			

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants in full-analysis-set population with FIGO III to IVA with data available at respective timepoint

d: Number of participants in full-analysis-set population with FIGO III to IVA with data available for analysis

e: Based on constrained longitudinal data analysis model with the PRO scores as the response variable, and treatment by study visit interaction as covariates

f: Standardized mean difference (Hedges's g) is only calculated if confidence interval for mean difference does not include zero

g: Based on constrained longitudinal data analysis model with change as the response variable, baseline, treatment, subgroup, study visit, treatment by subgroup interaction, treatment by study visit interaction, subgroup by study visit interaction and treatment by study visit and by subgroup interaction as covariates

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative of Gynecology and Obstetrics; EORTC QLQ-CX24: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire CX24; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); PRO: Patient Reported Outcome; RoW: Rest of the World; SD: Standard Deviation; VMAT: Volumetric Modulated Arc Therapy

Anhang 4-G2.4: Nebenwirkungen

Unerwünschte Ereignisse Gesamtraten

Unerwünschte Ereignisse gesamt

Tabelle 4G-33: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0{,}05$) für den Endpunkt Unerwünschte Ereignisse gesamt aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
Adverse Events	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
Age							
< 65	253	253 (100.0)	247	245 (99.2)	1.01 [1.00; 1.02]	0.152	n.a.
≥ 65	42	42 (100.0)	57	57 (100.0)	n.a. [n.a.; n.a.]	n.a.	
ECOG Performance Status							
0	194	194 (100.0)	211	209 (99.1)	1.01 [1.00; 1.02]	0.175	n.a.
1	101	101 (100.0)	93	93 (100.0)	n.a. [n.a.; n.a.]	n.a.	
Region							
Western Europe	52	52 (100.0)	55	54 (98.2)	1.02 [0.98; 1.06]	0.331	n.a.
North America	14	14 (100.0)	17	17 (100.0)	n.a. [n.a.; n.a.]	n.a.	
RoW	229	229 (100.0)	232	231 (99.6)	1.00 [1.00; 1.01]	0.320	
Planned Type of EBRT							
IMRT or VMAT	255	255 (100.0)	263	261 (99.2)	1.01 [1.00; 1.02]	0.163	n.a.
Non-IMRT and Non-VMAT	40	40 (100.0)	41	41 (100.0)	n.a. [n.a.; n.a.]	n.a.	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	31 (100.0)	29	29 (100.0)	n.a. [n.a.; n.a.]	n.a.	n.a.
≥ 70 Gy	264	264 (100.0)	275	273 (99.3)	1.01 [1.00; 1.02]	0.165	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report ‘n.a.’). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report ‘n.a.’

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Schwerwiegende unerwünschte Ereignisse

Tabelle 4G-34: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwerwiegende unerwünschte Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
Serious Adverse Events	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
Age							
< 65	253	87 (34.4)	247	76 (30.8)	1.12 [0.87; 1.44]	0.389	0.219
≥ 65	42	13 (31.0)	57	23 (40.4)	0.77 [0.44; 1.33]	0.339	
ECOG Performance Status							
0	194	61 (31.4)	211	62 (29.4)	1.07 [0.80; 1.44]	0.653	0.688
1	101	39 (38.6)	93	37 (39.8)	0.97 [0.68; 1.38]	0.868	
Region							
Western Europe	52	19 (36.5)	55	24 (43.6)	0.84 [0.52; 1.34]	0.456	0.174
North America	14	5 (35.7)	17	10 (58.8)	0.61 [0.27; 1.36]	0.208	
RoW	229	76 (33.2)	232	65 (28.0)	1.18 [0.90; 1.56]	0.229	
Planned Type of EBRT							
IMRT or VMAT	255	86 (33.7)	263	92 (35.0)	0.96 [0.76; 1.22]	0.764	0.067
Non-IMRT and Non-VMAT	40	14 (35.0)	41	7 (17.1)	2.05 [0.92; 4.54]	0.067	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	12 (38.7)	29	7 (24.1)	1.60 [0.73; 3.51]	0.229	0.245
≥ 70 Gy	264	88 (33.3)	275	92 (33.5)	1.00 [0.78; 1.26]	0.976	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report ‘n.a.’). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report ‘n.a.’

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5)

Tabelle 4G-35: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
Severe Adverse Events (CTCAE-Grade 3-5)	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
Age							
< 65	253	201 (79.4)	247	171 (69.2)	1.15 [1.03; 1.27]	0.009	0.290
≥ 65	42	31 (73.8)	57	42 (73.7)	1.00 [0.79; 1.27]	0.989	
ECOG Performance Status							
0	194	146 (75.3)	211	143 (67.8)	1.11 [0.98; 1.26]	0.096	0.539
1	101	86 (85.1)	93	70 (75.3)	1.13 [0.98; 1.30]	0.084	
Region							
Western Europe	52	39 (75.0)	55	30 (54.5)	1.38 [1.03; 1.83]	0.028	0.446
North America	14	11 (78.6)	17	13 (76.5)	1.03 [0.70; 1.50]	0.891	
RoW	229	182 (79.5)	232	170 (73.3)	1.08 [0.98; 1.20]	0.118	
Planned Type of EBRT							
IMRT or VMAT	255	196 (76.9)	263	180 (68.4)	1.12 [1.01; 1.25]	0.032	0.606
Non-IMRT and Non-VMAT	40	36 (90.0)	41	33 (80.5)	1.12 [0.93; 1.34]	0.231	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	27 (87.1)	29	20 (69.0)	1.26 [0.96; 1.67]	0.091	0.297
≥ 70 Gy	264	205 (77.7)	275	193 (70.2)	1.11 [1.00; 1.22]	0.049	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report ‘n.a.’). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report ‘n.a.’

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Therapieabbruch wegen unerwünschter Ereignisse

Tabelle 4G-36: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Therapieabbruch wegen unerwünschter Ereignisse aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
Adverse Events Leading to Treatment Discontinuation	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
Age							
< 65	253	52 (20.6)	247	34 (13.8)	1.49 [1.01; 2.22]	0.045	0.550
≥ 65	42	10 (23.8)	57	12 (21.1)	1.13 [0.54; 2.37]	0.746	
ECOG Performance Status							
0	194	37 (19.1)	211	27 (12.8)	1.49 [0.94; 2.35]	0.084	0.609
1	101	25 (24.8)	93	19 (20.4)	1.21 [0.72; 2.05]	0.474	
Region							
Western Europe	52	11 (21.2)	55	5 (9.1)	2.33 [0.87; 6.24]	0.082	0.456
North America	14	2 (14.3)	17	3 (17.6)	0.81 [0.16; 4.19]	0.803	
RoW	229	49 (21.4)	232	38 (16.4)	1.31 [0.89; 1.91]	0.169	
Planned Type of EBRT							
IMRT or VMAT	255	52 (20.4)	263	37 (14.1)	1.45 [0.99; 2.13]	0.057	0.629
Non-IMRT and Non-VMAT	40	10 (25.0)	41	9 (22.0)	1.14 [0.52; 2.50]	0.748	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	9 (29.0)	29	2 (6.9)	4.21 [0.99; 17.88]	0.028	0.083
≥ 70 Gy	264	53 (20.1)	275	44 (16.0)	1.25 [0.87; 1.80]	0.219	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report ‘n.a.’). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report ‘n.a.’

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Unerwünschte Ereignisse (gegliedert nach SOC und PT)

Unerwünschte Ereignisse gesamt (SOC und PT)

Tabelle 4G-37: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0{,}05$) für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für SOC aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18a	**Pembrolizumab + CCRTb**		**Placebo + CCRTb**		**Pembrolizumab + CCRTb vs. Placebo + CCRTb**		
Adverse Events	**Nc**	**Participants with Event n (%)**	**Nc**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Valuee**	**p-Value for Interaction Testf**
SOC[g]: Endocrine disorders							
Age							
< 65	253	81 (32.02)	247	28 (11.34)	2.82 [1.91; 4.18]	<0.001	0.957
≥ 65	42	14 (33.33)	57	7 (12.28)	2.71 [1.20; 6.13]	0.012	
ECOG Performance Status							
0	194	60 (30.93)	211	22 (10.43)	2.97 [1.90; 4.64]	<0.001	0.718
1	101	35 (34.65)	93	13 (13.98)	2.48 [1.40; 4.39]	0.001	
Region							
Western Europe	52	12 (23.08)	55	8 (14.55)	1.59 [0.71; 3.57]	0.260	0.263
North America	14	4 (28.57)	17	2 (11.76)	2.43 [0.52; 11.36]	0.246	
RoW	229	79 (34.50)	232	25 (10.78)	3.20 [2.12; 4.83]	<0.001	
Planned Type of EBRT							
IMRT or VMAT	255	86 (33.73)	263	34 (12.93)	2.61 [1.82; 3.73]	<0.001	0.246
Non-IMRT and Non-VMAT	40	9 (22.50)	41	1 (2.44)	9.23 [1.22; 69.51]	0.006	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	7 (22.58)	29	1 (3.45)	6.55 [0.86; 50.02]	0.031	0.449
≥ 70 Gy	264	88 (33.33)	275	34 (12.36)	2.70 [1.88; 3.86]	<0.001	
SOC[g]: Injury, poisoning and procedural complications							
Age							
< 65	253	74 (29.25)	247	64 (25.91)	1.13 [0.85; 1.50]	0.404	0.914
≥ 65	42	12 (28.57)	57	15 (26.32)	1.09 [0.57; 2.07]	0.804	
ECOG Performance Status							
0	194	56 (28.87)	211	49 (23.22)	1.24 [0.89; 1.73]	0.196	0.283
1	101	30 (29.70)	93	30 (32.26)	0.92 [0.60; 1.40]	0.701	
Region							
Western Europe	52	7 (13.46)	55	7 (12.73)	1.06 [0.40; 2.81]	0.911	0.208
North America	14	9 (64.29)	17	5 (29.41)	2.19 [0.95; 5.03]	0.056	
RoW	229	70 (30.57)	232	67 (28.88)	1.06 [0.80; 1.40]	0.692	
Planned Type of EBRT							
IMRT or VMAT	255	74 (29.02)	263	72 (27.38)	1.06 [0.81; 1.40]	0.678	0.253
Non-IMRT and Non-VMAT	40	12 (30.00)	41	7 (17.07)	1.76 [0.77; 4.01]	0.172	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	9 (29.03)	29	7 (24.14)	1.20 [0.52; 2.81]	0.671	0.869
≥ 70 Gy	264	77 (29.17)	275	72 (26.18)	1.11 [0.85; 1.46]	0.439	
SOC[g]: Investigations							
Age							
< 65	253	194 (76.68)	247	188 (76.11)	1.01 [0.91; 1.11]	0.882	0.639
≥ 65	42	30 (71.43)	57	43 (75.44)	0.95 [0.74; 1.21]	0.656	

Study: KEYNOTE A18a	Pembrolizumab + CCRTb		Placebo + CCRTb		Pembrolizumab + CCRTb vs. Placebo + CCRTb		
Adverse Events	**Nc**	**Participants with Event n (%)**	**Nc**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Valuee**	**p-Value for Interaction Testf**
ECOG Performance Status							
0	194	137 (70.62)	211	148 (70.14)	1.01 [0.89; 1.14]	0.917	0.525
1	101	87 (86.14)	93	83 (89.25)	0.97 [0.87; 1.07]	0.512	
Region							
Western Europe	52	30 (57.69)	55	32 (58.18)	0.99 [0.72; 1.37]	0.959	0.759
North America	14	10 (71.43)	17	14 (82.35)	0.87 [0.58; 1.29]	0.476	
RoW	229	184 (80.35)	232	185 (79.74)	1.01 [0.92; 1.10]	0.870	
Planned Type of EBRT							
IMRT or VMAT	255	192 (75.29)	263	197 (74.90)	1.01 [0.91; 1.11]	0.919	0.724
Non-IMRT and Non-VMAT	40	32 (80.00)	41	34 (82.93)	0.96 [0.78; 1.19]	0.736	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	25 (80.65)	29	23 (79.31)	1.02 [0.79; 1.31]	0.898	0.886
≥ 70 Gy	264	199 (75.38)	275	208 (75.64)	1.00 [0.91; 1.10]	0.945	
SOC[g]: Skin and subcutaneous tissue disorders							
Age							
< 65	253	66 (26.09)	247	40 (16.19)	1.61 [1.13; 2.29]	0.007	0.526
≥ 65	42	9 (21.43)	57	10 (17.54)	1.22 [0.54; 2.74]	0.629	
ECOG Performance Status							
0	194	51 (26.29)	211	36 (17.06)	1.54 [1.05; 2.25]	0.024	0.974
1	101	24 (23.76)	93	14 (15.05)	1.58 [0.87; 2.86]	0.128	
Region							
Western Europe	52	12 (23.08)	55	8 (14.55)	1.59 [0.71; 3.57]	0.260	0.377
North America	14	7 (50.00)	17	10 (58.82)	0.85 [0.44; 1.64]	0.629	
RoW	229	56 (24.45)	232	32 (13.79)	1.77 [1.20; 2.63]	0.004	
Planned Type of EBRT							
IMRT or VMAT	255	59 (23.14)	263	38 (14.45)	1.60 [1.11; 2.32]	0.011	0.847
Non-IMRT and Non-VMAT	40	16 (40.00)	41	12 (29.27)	1.37 [0.74; 2.51]	0.313	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	14 (45.16)	29	11 (37.93)	1.19 [0.65; 2.18]	0.573	0.601
≥ 70 Gy	264	61 (23.11)	275	39 (14.18)	1.63 [1.13; 2.35]	0.008	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report 'n.a.'). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report 'n.a.'

g: 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 treament 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

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Tabelle 4G-38: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Unerwünschte Ereignisse gesamt (SOC und PT) für PT aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
Adverse Events	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
SOC: Endocrine disorders PT[g]: Hyperthyroidism							
Age							
< 65	253	34 (13.44)	247	8 (3.24)	4.15 [1.96; 8.78]	<0.001	0.434
≥ 65	42	3 (7.14)	57	2 (3.51)	2.04 [0.36; 11.65]	0.417	
ECOG Performance Status							
0	194	21 (10.82)	211	5 (2.37)	4.57 [1.76; 11.88]	0.001	0.576
1	101	16 (15.84)	93	5 (5.38)	2.95 [1.12; 7.73]	0.019	
Region							
Western Europe	52	6 (11.54)	55	2 (3.64)	3.17 [0.67; 15.02]	0.122	0.834
North America	14	1 (7.14)	17	0	n.a. [n.a.; n.a.]	n.a.	
RoW	229	30 (13.10)	232	8 (3.45)	3.80 [1.78; 8.11]	<0.001	
Planned Type of EBRT							
IMRT or VMAT	255	34 (13.33)	263	10 (3.80)	3.51 [1.77; 6.95]	<0.001	0.361
Non-IMRT and Non-VMAT	40	3 (7.50)	41	0	n.a. [n.a.; n.a.]	n.a.	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	2 (6.45)	29	0	n.a. [n.a.; n.a.]	n.a.	0.485
≥ 70 Gy	264	35 (13.26)	275	10 (3.64)	3.65 [1.84; 7.21]	<0.001	
SOC: Endocrine disorders PT[g]: Hypothyroidism							
Age							
< 65	253	55 (21.74)	247	20 (8.10)	2.68 [1.66; 4.34]	<0.001	0.666
≥ 65	42	12 (28.57)	57	5 (8.77)	3.26 [1.24; 8.54]	0.010	
ECOG Performance Status							
0	194	45 (23.20)	211	16 (7.58)	3.06 [1.79; 5.23]	<0.001	0.509
1	101	22 (21.78)	93	9 (9.68)	2.25 [1.09; 4.64]	0.022	
Region							
Western Europe	52	8 (15.38)	55	6 (10.91)	1.41 [0.52; 3.79]	0.495	0.175
North America	14	2 (14.29)	17	2 (11.76)	1.21 [0.20; 7.55]	0.838	
RoW	229	57 (24.89)	232	17 (7.33)	3.40 [2.04; 5.66]	<0.001	
Planned Type of EBRT							
IMRT or VMAT	255	62 (24.31)	263	24 (9.13)	2.66 [1.72; 4.13]	<0.001	0.610
Non-IMRT and Non-VMAT	40	5 (12.50)	41	1 (2.44)	5.13 [0.63; 41.95]	0.086	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	4 (12.90)	29	1 (3.45)	3.74 [0.44; 31.55]	0.189	0.841
≥ 70 Gy	264	63 (23.86)	275	24 (8.73)	2.73 [1.76; 4.24]	<0.001	
SOC: Injury, poisoning and procedural complications PT[g]: Gastroenteritis radiation							
Age							
< 65	253	11 (4.35)	247	2 (0.81)	5.37 [1.20; 23.98]	0.013	0.363
≥ 65	42	1 (2.38)	57	1 (1.75)	1.36 [0.09; 21.08]	0.828	
ECOG Performance Status							
0	194	4 (2.06)	211	1 (0.47)	4.35 [0.49; 38.59]	0.149	0.930
1	101	8 (7.92)	93	2 (2.15)	3.68 [0.80; 16.90]	0.070	

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]		Placebo + CCRT[b]		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Adverse Events	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
Region							
Western Europe	52	2 (3.85)	55	1 (1.82)	2.12 [0.20; 22.64]	0.527	0.537
North America	14	0	17	0	n.a. [n.a.; n.a.]	n.a.	
RoW	229	10 (4.37)	232	2 (0.86)	5.07 [1.12; 22.87]	0.018	
Planned Type of EBRT							
IMRT or VMAT	255	10 (3.92)	263	3 (1.14)	3.44 [0.96; 12.35]	0.043	0.445
Non-IMRT and Non-VMAT	40	2 (5.00)	41	0	n.a. [n.a.; n.a.]	n.a.	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	1 (3.23)	29	0	n.a. [n.a.; n.a.]	n.a.	0.623
≥ 70 Gy	264	11 (4.17)	275	3 (1.09)	3.82 [1.08; 13.54]	0.025	
SOC: Investigations PT[g]: Alanine aminotransferase increased							
Age							
< 65	253	57 (22.53)	247	38 (15.38)	1.46 [1.01; 2.12]	0.042	0.254
≥ 65	42	1 (2.38)	57	3 (5.26)	0.45 [0.05; 4.20]	0.474	
ECOG Performance Status							
0	194	32 (16.49)	211	26 (12.32)	1.34 [0.83; 2.16]	0.232	0.589
1	101	26 (25.74)	93	15 (16.13)	1.60 [0.90; 2.82]	0.102	
Region							
Western Europe	52	3 (5.77)	55	2 (3.64)	1.59 [0.28; 9.12]	0.603	0.913
North America	14	2 (14.29)	17	1 (5.88)	2.43 [0.24; 24.07]	0.438	
RoW	229	53 (23.14)	232	38 (16.38)	1.41 [0.97; 2.05]	0.068	
Planned Type of EBRT							
IMRT or VMAT	255	51 (20.00)	263	31 (11.79)	1.70 [1.12; 2.56]	0.011	0.080
Non-IMRT and Non-VMAT	40	7 (17.50)	41	10 (24.39)	0.72 [0.30; 1.70]	0.449	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	7 (22.58)	29	4 (13.79)	1.64 [0.53; 5.01]	0.383	0.817
≥ 70 Gy	264	51 (19.32)	275	37 (13.45)	1.44 [0.97; 2.12]	0.066	
SOC: Skin and subcutaneous tissue disorders PT[g]: Rash							
Age							
< 65	253	18 (7.11)	247	6 (2.43)	2.93 [1.18; 7.26]	0.014	0.405
≥ 65	42	3 (7.14)	57	3 (5.26)	1.36 [0.29; 6.39]	0.700	
ECOG Performance Status							
0	194	15 (7.73)	211	5 (2.37)	3.26 [1.21; 8.81]	0.013	0.283
1	101	6 (5.94)	93	4 (4.30)	1.38 [0.40; 4.74]	0.607	
Planned Type of EBRT							
IMRT or VMAT	255	16 (6.27)	263	8 (3.04)	2.06 [0.90; 4.74]	0.080	0.402
Non-IMRT and Non-VMAT	40	5 (12.50)	41	1 (2.44)	5.13 [0.63; 41.95]	0.086	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	4 (12.90)	29	1 (3.45)	3.74 [0.44; 31.55]	0.189	0.628
≥ 70 Gy	264	17 (6.44)	275	8 (2.91)	2.21 [0.97; 5.04]	0.052	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]		Placebo + CCRT[b]		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Adverse Events	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**

in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report 'n.a.'). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report 'n.a.'

g: 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 treament 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

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Schwerwiegende unerwünschte Ereignisse (SOC und PT)

Tabelle 4G-39: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0{,}05$) für den Endpunkt schwerwiegende unerwünschte Ereignisse (SOC und PT) für SOC aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
Serious Adverse Events	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
SOC[g]: Blood and lymphatic system disorders							
Age							
< 65	253	13 (5.14)	247	6 (2.43)	2.12 [0.82; 5.48]	0.114	0.850
≥ 65	42	2 (4.76)	57	1 (1.75)	2.71 [0.25; 28.95]	0.391	
ECOG Performance Status							
0	194	10 (5.15)	211	6 (2.84)	1.81 [0.67; 4.89]	0.234	0.428
1	101	5 (4.95)	93	1 (1.08)	4.60 [0.55; 38.68]	0.120	
Region							
Western Europe	52	3 (5.77)	55	2 (3.64)	1.59 [0.28; 9.12]	0.603	0.312
North America	14	0	17	1 (5.88)	n.a. [n.a.; n.a.]	n.a.	
RoW	229	12 (5.24)	232	4 (1.72)	3.04 [0.99; 9.28]	0.039	
Planned Type of EBRT							
IMRT or VMAT	255	15 (5.88)	263	7 (2.66)	2.21 [0.92; 5.33]	0.069	n.a.
Non-IMRT and Non-VMAT	40	0	41	0	n.a. [n.a.; n.a.]	n.a.	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	0	29	0	n.a. [n.a.; n.a.]	n.a.	n.a.
≥ 70 Gy	264	15 (5.68)	275	7 (2.55)	2.23 [0.92; 5.39]	0.066	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report 'n.a.'). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report 'n.a.'

g: A system organ class appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treament 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

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Tabelle 4G-40: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt schwerwiegende unerwünschte Ereignisse (SOC und PT) für PT aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
Serious Adverse Events	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
SOC: Blood and lymphatic system disorders PT[g]: Anaemia							
Age							
< 65	253	12 (4.74)	247	3 (1.21)	3.91 [1.12; 13.67]	0.021	0.564
≥ 65	42	1 (2.38)	57	0	n.a. [n.a.; n.a.]	n.a.	
ECOG Performance Status							
0	194	10 (5.15)	211	2 (0.95)	5.44 [1.21; 24.51]	0.013	0.613
1	101	3 (2.97)	93	1 (1.08)	2.76 [0.29; 26.09]	0.355	
Region							
Western Europe	52	2 (3.85)	55	1 (1.82)	2.12 [0.20; 22.64]	0.527	0.083
North America	14	0	17	1 (5.88)	n.a. [n.a.; n.a.]	n.a.	
RoW	229	11 (4.80)	232	1 (0.43)	11.14 [1.45; 85.62]	0.003	
Planned Type of EBRT							
IMRT or VMAT	255	13 (5.10)	263	3 (1.14)	4.47 [1.29; 15.50]	0.009	n.a.
Non-IMRT and Non-VMAT	40	0	41	0	n.a. [n.a.; n.a.]	n.a.	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	0	29	0	n.a. [n.a.; n.a.]	n.a.	n.a.
≥ 70 Gy	264	13 (4.92)	275	3 (1.09)	4.51 [1.30; 15.66]	0.009	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report ‘n.a.’). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report ‘n.a.’

g: 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 treament 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

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT)

Tabelle 4G-41: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0,05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) für SOC aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	**Pembrolizumab + CCRT[b]**		**Placebo + CCRT[b]**		**Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]**		
Severe Adverse Events (CTCAE-Grade 3-5)	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
SOC[g]: Blood and lymphatic system disorders							
Age							
< 65	253	107 (42.29)	247	82 (33.20)	1.27 [1.01; 1.60]	0.036	0.894
≥ 65	42	18 (42.86)	57	20 (35.09)	1.22 [0.74; 2.01]	0.434	
ECOG Performance Status							
0	194	79 (40.72)	211	68 (32.23)	1.26 [0.98; 1.64]	0.076	0.990
1	101	46 (45.54)	93	34 (36.56)	1.25 [0.88; 1.75]	0.205	
Region							
Western Europe	52	19 (36.54)	55	16 (29.09)	1.26 [0.73; 2.17]	0.414	0.725
North America	14	6 (42.86)	17	8 (47.06)	0.91 [0.41; 2.00]	0.818	
RoW	229	100 (43.67)	232	78 (33.62)	1.30 [1.03; 1.64]	0.027	
Planned Type of EBRT							
IMRT or VMAT	255	111 (43.53)	263	91 (34.60)	1.26 [1.01; 1.56]	0.037	0.988
Non-IMRT and Non-VMAT	40	14 (35.00)	41	11 (26.83)	1.30 [0.68; 2.52]	0.429	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	14 (45.16)	29	8 (27.59)	1.64 [0.81; 3.32]	0.162	0.449
≥ 70 Gy	264	111 (42.05)	275	94 (34.18)	1.23 [0.99; 1.53]	0.060	
SOC[g]: Metabolism and nutrition disorders							
Age							
< 65	253	27 (10.67)	247	20 (8.10)	1.32 [0.76; 2.29]	0.324	0.252
≥ 65	42	5 (11.90)	57	10 (17.54)	0.68 [0.25; 1.84]	0.442	
ECOG Performance Status							
0	194	19 (9.79)	211	17 (8.06)	1.22 [0.65; 2.27]	0.540	0.572
1	101	13 (12.87)	93	13 (13.98)	0.92 [0.45; 1.88]	0.822	
Region							
Western Europe	52	5 (9.62)	55	1 (1.82)	5.29 [0.64; 43.76]	0.081	0.233
North America	14	3 (21.43)	17	4 (23.53)	0.91 [0.24; 3.41]	0.891	
RoW	229	24 (10.48)	232	25 (10.78)	0.97 [0.57; 1.65]	0.918	
Planned Type of EBRT							
IMRT or VMAT	255	26 (10.20)	263	26 (9.89)	1.03 [0.62; 1.73]	0.907	0.541
Non-IMRT and Non-VMAT	40	6 (15.00)	41	4 (9.76)	1.54 [0.47; 5.04]	0.476	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	3 (9.68)	29	3 (10.34)	0.94 [0.20; 4.27]	0.932	0.826
≥ 70 Gy	264	29 (10.98)	275	27 (9.82)	1.12 [0.68; 1.84]	0.658	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]		Placebo + CCRT[b]		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Severe Adverse Events (CTCAE-Grade 3-5)	N[c]	Participants with Event n (%)	N[c]	Participants with Event n (%)	Relative Risk [95 %-CI][d]	p-Value[e]	p-Value for Interaction Test[f]
in both treatment groups, report 'n.a.'							
f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report 'n.a.'). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report 'n.a.'							
g: A system organ class appears on this report only if its incidence ≥5% or (incidence ≥1% and in at least 10 participants) in one or more treament 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							
CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy							

Tabelle 4G-42: Subgruppenanalysen der Teilpopulation FIGO 2014 Stadium III bis IVA mit nicht signifikantem Interaktionstest ($p \geq 0{,}05$) für den Endpunkt Schwere unerwünschte Ereignisse (CTCAE-Grad 3-5) (SOC und PT) für PT aus RCT mit dem zu bewertenden Arzneimittel

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]		Placebo + CCRT[b]		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Severe Adverse Events (CTCAE-Grade 3-5)	N[c]	Participants with Event n (%)	N[c]	Participants with Event n (%)	Relative Risk [95 %-CI][d]	p-Value[e]	p-Value for Interaction Test[f]
SOC: Blood and lymphatic system disorders PT[g]: Anaemia							
Age							
< 65	253	75 (29.64)	247	55 (22.27)	1.33 [0.99; 1.80]	0.060	0.815
≥ 65	42	11 (26.19)	57	10 (17.54)	1.49 [0.70; 3.19]	0.301	
ECOG Performance Status							
0	194	53 (27.32)	211	42 (19.91)	1.37 [0.96; 1.96]	0.079	0.952
1	101	33 (32.67)	93	23 (24.73)	1.32 [0.84; 2.08]	0.224	
Region							
Western Europe	52	12 (23.08)	55	9 (16.36)	1.41 [0.65; 3.07]	0.384	0.409
North America	14	4 (28.57)	17	7 (41.18)	0.69 [0.25; 1.89]	0.473	
RoW	229	70 (30.57)	232	49 (21.12)	1.45 [1.06; 1.99]	0.021	
Planned Type of EBRT							
IMRT or VMAT	255	74 (29.02)	263	58 (22.05)	1.32 [0.98; 1.77]	0.069	0.526
Non-IMRT and Non-VMAT	40	12 (30.00)	41	7 (17.07)	1.76 [0.77; 4.01]	0.172	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	11 (35.48)	29	4 (13.79)	2.57 [0.92; 7.18]	0.055	0.182
≥ 70 Gy	264	75 (28.41)	275	61 (22.18)	1.28 [0.96; 1.72]	0.096	
SOC: Metabolism and nutrition disorders PT[g]: Hypokalaemia							
Age							
< 65	253	20 (7.91)	247	8 (3.24)	2.44 [1.10; 5.44]	0.023	0.570
≥ 65	42	2 (4.76)	57	2 (3.51)	1.36 [0.20; 9.25]	0.756	
ECOG Performance Status							
0	194	15 (7.73)	211	7 (3.32)	2.33 [0.97; 5.59]	0.051	0.916
1	101	7 (6.93)	93	3 (3.23)	2.15 [0.57; 8.07]	0.245	
Region							
Western Europe	52	3 (5.77)	55	0	n.a. [n.a.; n.a.]	n.a.	0.408
North America	14	2 (14.29)	17	2 (11.76)	1.21 [0.20; 7.55]	0.838	

Study: KEYNOTE A18[a]	Pembrolizumab + CCRT[b]		Placebo + CCRT[b]		Pembrolizumab + CCRT[b] vs. Placebo + CCRT[b]		
Severe Adverse Events (CTCAE-Grade 3-5)	**N[c]**	**Participants with Event n (%)**	**N[c]**	**Participants with Event n (%)**	**Relative Risk [95 %-CI][d]**	**p-Value[e]**	**p-Value for Interaction Test[f]**
RoW	229	17 (7.42)	232	8 (3.45)	2.15 [0.95; 4.89]	0.060	
Planned Type of EBRT							
IMRT or VMAT	255	18 (7.06)	263	8 (3.04)	2.32 [1.03; 5.24]	0.036	0.911
Non-IMRT and Non-VMAT	40	4 (10.00)	41	2 (4.88)	2.05 [0.40; 10.57]	0.382	
Planned Total Radiotherapy Dose (EBRT + brachytherapy dose)							
< 70 Gy	31	3 (9.68)	29	1 (3.45)	2.81 [0.31; 25.48]	0.338	0.830
≥ 70 Gy	264	19 (7.20)	275	9 (3.27)	2.20 [1.01; 4.77]	0.040	

a: Database Cutoff Date: 08JAN2024

b: CCRT is Chemoradiotherapy [Treatment with cisplatin and radiotherapy (EBRT followed by brachytherapy)]

c: Number of participants: all-participants-as-treated population with FIGO III to IVA

d: Based on 2x2 contingency table, using Wald confidence interval. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

e: Based on Mantel-Haenszel Chi-Squared test. In case of no participant with event in at least one treatment group or all participants with event in both treatment groups, report 'n.a.'

f: Based on Breslow-Day test with subgroup as stratification factor. In case no participant or all participants with event in both treatment groups for a subgroup category, it is excluded from interaction test (if only one subgroup category remaining, report 'n.a.'). In case no participant or all participants with event in at least one treatment group across all subgroup categories, report 'n.a.'

g: 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 treament 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

CCRT: Concurrent Chemoradiotherapy; CI: Confidence Interval; CTCAE: Common Terminology Criteria for Adverse Events; EBRT: External Beam Radiotherapy; ECOG: Eastern Cooperative Oncology Group; FIGO: International Federation of Gynecology and Obstetrics; Gy: Gray; IMRT: Intensity-Modulated Radiation Therapy; n.a.: not applicable (when estimation not possible); RoW: Rest of World; VMAT: Volumetric Modulated Arc Therapy

Anhang 4-G3: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) anhand der zugeordneten PT

Tabelle 4G-43: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) anhand der zugeordneten PT in der Studie KEYNOTE A18

AEOSI	Preferred Terms	Immune-mediated (Yes/No)
Pneumonitis	Acute interstitial pneumonitis, Autoimmune lung disease, Interstitial lung disease, Pneumonitis, Idiopathic pneumonia syndrome, Organising pneumonia, Immune-mediated 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

AEOSI	Preferred Terms	Immune-mediated (Yes/No)
Adrenal Insufficiency	Adrenal insufficiency, Adrenocortical insufficiency acute, Secondary adrenocortical insufficiency, Primary adrenal insufficiency, Addison's disease, Immune-mediated adrenal insufficiency	Yes
Hypophysitis	Hypophysitis, Hypopituitarism, Lymphocytic hypophysitis, Immune-mediated hypophysitis	Yes
Hyperthyroidism	Hyperthyroidism, Basedow's disease, Thyrotoxic crisis, Immune-mediated hyperthyroidism	Yes
Hypothyroidism	Hypothyroidism, Hypothyroidic goitre, Myxoedema, Myxoedema coma, Primary hypothyroidism, Autoimmune hypothyroidism, Immune-mediated hypothyroidism	Yes
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

AEOSI	Preferred Terms	Immune-mediated (Yes/No)
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, Immune-mediated myositis, Rhabdomyolysis, Myopathy, Dermatomyositis, Autoimmune myositis	Yes

AEOSI	Preferred Terms	Immune-mediated (Yes/No)
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, Immune-mediated encephalitis	Yes
Sarcoidosis	Sarcoidosis, Cutaneous sarcoidosis, Ocular sarcoidosis, Pulmonary sarcoidosis, Sarcoidosis of lymph node	Yes
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

AEOSI	Preferred Terms	Immune-mediated (Yes/No)
Myelitis	Myelitis, Myelitis transverse, Acute necrotising 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	Yes