Dokumentvorlage, Version vom 16.12.2021

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Pembrolizumab (KEYTRUDA®)

MSD Sharp & Dohme GmbH

Modul 4 B

Behandlung von Tumoren mit MSI-H oder mit einer dMMR bei Erwachsenen: Fortgeschrittenes oder rezidivierendes Endometriumkarzinom

Medizinischer Nutzen und medizinischer Zusatznutzen, Patientengruppen mit therapeutisch bedeutsamem Zusatznutzen

Stand: 18.07.2022

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

Im Folgenden werden ergänzend zu Abschnitt 4.3.2.3.3.2.1 die Rücklaufquoten des EORTC QLQ-C30 und die Rücklaufquoten des EQ-5D VAS dargestellt.

Alle Ergebnisse beziehen sich auf den Datenschnitt vom 05. Oktober 2020.

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

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

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EORTC QLQ-C30	N[b] = 84 n (%)
Baseline	Missing by Design	0 (0.0)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	0 (0.0)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	0 (0.0)
	Discontinued due to withdrawal by subject	0 (0.0)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	0 (0.0)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	84 (100.0)
	Not completed	8 (9.5)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	6 (7.1)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	0 (0.0)
	With visit, no record	2 (2.4)
	Completed	76 (90.5)
	Compliance (% in those expected to complete questionnaires)[d]	76 (90.5)
Week 3	Missing by Design	4 (4.8)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	0 (0.0)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	0 (0.0)
	Discontinued due to withdrawal by subject	0 (0.0)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	0 (0.0)
	Visit not scheduled	4 (4.8)
	Expected to Complete Questionnaires[c]	80 (95.2)
	Not completed	14 (16.7)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	2 (2.4)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	7 (8.3)
	With visit, no record	4 (4.8)
	Completed	66 (78.6)
	Compliance (% in those expected to complete questionnaires)[d]	66 (82.5)
Week 6	Missing by Design	7 (8.3)
	Discontinued due to adverse event	0 (0.0)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EORTC QLQ-C30	N[b] = 84 n (%)
	Discontinued due to clinical progression	1 (1.2)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	0 (0.0)
	Discontinued due to withdrawal by subject	1 (1.2)
	Completed study treatment	0 (0.0)
	Subject died	1 (1.2)
	Visit not reached	0 (0.0)
	Visit not scheduled	4 (4.8)
	Expected to Complete Questionnaires[c]	77 (91.7)
	Not completed	9 (10.7)
	Subject did not complete due to disease under study	1 (1.2)
	Not completed due to site staff error	0 (0.0)
	Subject in hospital or hospice	1 (1.2)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	2 (2.4)
	With visit, no record	4 (4.8)
	Completed	68 (81.0)
	Compliance (% in those expected to complete questionnaires)[d]	68 (88.3)
Week 9	Missing by Design	10 (11.9)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	3 (3.6)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	4 (4.8)
	Discontinued due to withdrawal by subject	1 (1.2)
	Completed study treatment	0 (0.0)
	Subject died	1 (1.2)
	Visit not reached	1 (1.2)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	74 (88.1)
	Not completed	6 (7.1)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	2 (2.4)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	2 (2.4)
	With visit, no record	2 (2.4)
	Completed	68 (81.0)
	Compliance (% in those expected to complete questionnaires)[d]	68 (91.9)
Week 18	Missing by Design	15 (17.9)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	4 (4.8)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	8 (9.5)
	Discontinued due to withdrawal by subject	1 (1.2)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	2 (2.4)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	69 (82.1)
	Not completed	14 (16.7)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	6 (7.1)
	Subject in hospital or hospice	0 (0.0)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EORTC QLQ-C30	N[b] = 84 n (%)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	3 (3.6)
	With visit, no record	5 (6.0)
	Completed	55 (65.5)
	Compliance (% in those expected to complete questionnaires)[d]	55 (79.7)
Week 27	Missing by Design	29 (34.5)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	4 (4.8)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	16 (19.0)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	6 (7.1)
	Visit not scheduled	1 (1.2)
	Expected to Complete Questionnaires[c]	55 (65.5)
	Not completed	12 (14.3)
	Subject did not complete due to disease under study	1 (1.2)
	Not completed due to site staff error	3 (3.6)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	5 (6.0)
	With visit, no record	2 (2.4)
	Completed	43 (51.2)
	Compliance (% in those expected to complete questionnaires)[d]	43 (78.2)
Week 39	Missing by Design	33 (39.3)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	4 (4.8)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	20 (23.8)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	1 (1.2)
	Visit not reached	6 (7.1)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	51 (60.7)
	Not completed	18 (21.4)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	5 (6.0)
	Subject in hospital or hospice	1 (1.2)
	Subject was physically unable to complete	1 (1.2)
	Subject refused for other reasons	0 (0.0)
	Other	3 (3.6)
	With visit, no record	8 (9.5)
	Completed	33 (39.3)
	Compliance (% in those expected to complete questionnaires)[d]	33 (64.7)
Week 51	Missing by Design	49 (58.3)
	Discontinued due to adverse event	2 (2.4)
	Discontinued due to clinical progression	4 (4.8)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	23 (27.4)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EORTC QLQ-C30	N[b] = 84 n (%)
	Subject died	1 (1.2)
	Visit not reached	14 (16.7)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	35 (41.7)
	Not completed	8 (9.5)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	5 (6.0)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	2 (2.4)
	With visit, no record	0 (0.0)
	Completed	27 (32.1)
	Compliance (% in those expected to complete questionnaires)[d]	27 (77.1)
Week 63	Missing by Design	50 (59.5)
	Discontinued due to adverse event	2 (2.4)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	23 (27.4)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	14 (16.7)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	34 (40.5)
	Not completed	16 (19.0)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	4 (4.8)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	3 (3.6)
	Other	3 (3.6)
	With visit, no record	6 (7.1)
	Completed	18 (21.4)
	Compliance (% in those expected to complete questionnaires)[d]	18 (52.9)
Week 75	Missing by Design	55 (65.5)
	Discontinued due to adverse event	2 (2.4)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	26 (31.0)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	16 (19.0)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	29 (34.5)
	Not completed	9 (10.7)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	4 (4.8)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	1 (1.2)
	With visit, no record	3 (3.6)
	Completed	20 (23.8)
	Compliance (% in those expected to complete questionnaires)[d]	20 (69.0)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EORTC QLQ-C30	N[b] = 84 n (%)
Week 87	Missing by Design	59 (70.2)
	Discontinued due to adverse event	3 (3.6)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	28 (33.3)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	17 (20.2)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	25 (29.8)
	Not completed	12 (14.3)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	3 (3.6)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	5 (6.0)
	With visit, no record	4 (4.8)
	Completed	13 (15.5)
	Compliance (% in those expected to complete questionnaires)[d]	13 (52.0)
Week 99	Missing by Design	61 (72.6)
	Discontinued due to adverse event	5 (6.0)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	28 (33.3)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	17 (20.2)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	23 (27.4)
	Not completed	5 (6.0)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	1 (1.2)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	2 (2.4)
	Other	1 (1.2)
	With visit, no record	1 (1.2)
	Completed	18 (21.4)
	Compliance (% in those expected to complete questionnaires)[d]	18 (78.3)
Week 111	Missing by Design	64 (76.2)
	Discontinued due to adverse event	5 (6.0)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	28 (33.3)
	Discontinued due to withdrawal by subject	4 (4.8)
	Completed study treatment	1 (1.2)
	Subject died	0 (0.0)
	Visit not reached	17 (20.2)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	20 (23.8)
	Not completed	9 (10.7)
	Subject did not complete due to disease under study	0 (0.0)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EORTC QLQ-C30	N[b] = 84 n (%)
	Not completed due to site staff error	2 (2.4)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	3 (3.6)
	Other	2 (2.4)
	With visit, no record	2 (2.4)
	Completed	11 (13.1)
	Compliance (% in those expected to complete questionnaires)[d]	11 (55.0)

a: Database Cutoff Date: 05OCT2020
b: Number of participants: full-analysis-set-population with MSI-H endometrial carcinoma, at least one line of prior therapy
c: Expected to complete questionnaire includes all participants who do not have missing data due to a missing by design reason
d: Compliance is the proportion of participants who completed the PRO questionnaire among those who are expected to complete the questionnaire at each time point, excluding those missing by design. All the other percentages are defined as the proportion of participants in the analysis population (N)
EORTC QLQ-C30: European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Core 30 items; MSI-H: Microsatellite Instability-High; PRO: Patient Reported Outcome

Anhang 4-G1.2: Rücklaufquoten des EQ-5D VAS

Tabelle 4G-2: Gründe für das Fehlen von Werten im EQ-5D VAS

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EQ-5D-3L	N[b] = 84 n (%)
Baseline	Missing by Design	0 (0.0)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	0 (0.0)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	0 (0.0)
	Discontinued due to withdrawal by subject	0 (0.0)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	0 (0.0)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	84 (100.0)
	Not completed	5 (6.0)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	4 (4.8)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	0 (0.0)
	With visit, no record	1 (1.2)
	Completed	79 (94.0)
	Compliance (% in those expected to complete questionnaires)[d]	79 (94.0)
Week 3	Missing by Design	4 (4.8)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	0 (0.0)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	0 (0.0)
	Discontinued due to withdrawal by subject	0 (0.0)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	0 (0.0)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EQ-5D-3L	N[b] = 84 n (%)
	Visit not scheduled	4 (4.8)
	Expected to Complete Questionnaires[c]	80 (95.2)
	Not completed	12 (14.3)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	2 (2.4)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	5 (6.0)
	With visit, no record	4 (4.8)
	Completed	68 (81.0)
	Compliance (% in those expected to complete questionnaires)[d]	68 (85.0)
Week 6	Missing by Design	7 (8.3)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	1 (1.2)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	0 (0.0)
	Discontinued due to withdrawal by subject	1 (1.2)
	Completed study treatment	0 (0.0)
	Subject died	1 (1.2)
	Visit not reached	0 (0.0)
	Visit not scheduled	4 (4.8)
	Expected to Complete Questionnaires[c]	77 (91.7)
	Not completed	9 (10.7)
	Subject did not complete due to disease under study	1 (1.2)
	Not completed due to site staff error	0 (0.0)
	Subject in hospital or hospice	1 (1.2)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	2 (2.4)
	With visit, no record	4 (4.8)
	Completed	68 (81.0)
	Compliance (% in those expected to complete questionnaires)[d]	68 (88.3)
Week 9	Missing by Design	10 (11.9)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	3 (3.6)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	4 (4.8)
	Discontinued due to withdrawal by subject	1 (1.2)
	Completed study treatment	0 (0.0)
	Subject died	1 (1.2)
	Visit not reached	1 (1.2)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	74 (88.1)
	Not completed	5 (6.0)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	2 (2.4)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	1 (1.2)
	With visit, no record	2 (2.4)
	Completed	69 (82.1)
	Compliance (% in those expected to complete questionnaires)[d]	69 (93.2)
Week 18	Missing by Design	15 (17.9)
	Discontinued due to adverse event	0 (0.0)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EQ-5D-3L	N[b] = 84 n (%)
	Discontinued due to clinical progression	4 (4.8)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	8 (9.5)
	Discontinued due to withdrawal by subject	1 (1.2)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	2 (2.4)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	69 (82.1)
	Not completed	14 (16.7)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	6 (7.1)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	3 (3.6)
	With visit, no record	5 (6.0)
	Completed	55 (65.5)
	Compliance (% in those expected to complete questionnaires)[d]	55 (79.7)
Week 27	Missing by Design	29 (34.5)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	4 (4.8)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	16 (19.0)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	6 (7.1)
	Visit not scheduled	1 (1.2)
	Expected to Complete Questionnaires[c]	55 (65.5)
	Not completed	10 (11.9)
	Subject did not complete due to disease under study	1 (1.2)
	Not completed due to site staff error	2 (2.4)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	4 (4.8)
	With visit, no record	2 (2.4)
	Completed	45 (53.6)
	Compliance (% in those expected to complete questionnaires)[d]	45 (81.8)
Week 39	Missing by Design	33 (39.3)
	Discontinued due to adverse event	0 (0.0)
	Discontinued due to clinical progression	4 (4.8)
	Discontinued due to complete response	0 (0.0)
	Discontinued due to physician decision	0 (0.0)
	Discontinued due to progressive disease	20 (23.8)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	1 (1.2)
	Visit not reached	6 (7.1)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	51 (60.7)
	Not completed	18 (21.4)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	5 (6.0)
	Subject in hospital or hospice	1 (1.2)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EQ-5D-3L	N[b] = 84 n (%)
	Subject was physically unable to complete	1 (1.2)
	Subject refused for other reasons	0 (0.0)
	Other	3 (3.6)
	With visit, no record	8 (9.5)
	Completed	33 (39.3)
	Compliance (% in those expected to complete questionnaires)[d]	33 (64.7)
Week 51	Missing by Design	49 (58.3)
	Discontinued due to adverse event	2 (2.4)
	Discontinued due to clinical progression	4 (4.8)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	23 (27.4)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	1 (1.2)
	Visit not reached	14 (16.7)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	35 (41.7)
	Not completed	7 (8.3)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	5 (6.0)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	2 (2.4)
	With visit, no record	0 (0.0)
	Completed	28 (33.3)
	Compliance (% in those expected to complete questionnaires)[d]	28 (80.0)
Week 63	Missing by Design	50 (59.5)
	Discontinued due to adverse event	2 (2.4)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	23 (27.4)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	14 (16.7)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	34 (40.5)
	Not completed	15 (17.9)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	3 (3.6)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	3 (3.6)
	Other	3 (3.6)
	With visit, no record	6 (7.1)
	Completed	19 (22.6)
	Compliance (% in those expected to complete questionnaires)[d]	19 (55.9)
Week 75	Missing by Design	55 (65.5)
	Discontinued due to adverse event	2 (2.4)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	26 (31.0)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EQ-5D-3L	N[b] = 84 n (%)
	Subject died	0 (0.0)
	Visit not reached	16 (19.0)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	29 (34.5)
	Not completed	8 (9.5)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	3 (3.6)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	1 (1.2)
	Other	1 (1.2)
	With visit, no record	3 (3.6)
	Completed	21 (25.0)
	Compliance (% in those expected to complete questionnaires)[d]	21 (72.4)
Week 87	Missing by Design	59 (70.2)
	Discontinued due to adverse event	3 (3.6)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	28 (33.3)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	17 (20.2)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	25 (29.8)
	Not completed	12 (14.3)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	3 (3.6)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	0 (0.0)
	Other	5 (6.0)
	With visit, no record	4 (4.8)
	Completed	13 (15.5)
	Compliance (% in those expected to complete questionnaires)[d]	13 (52.0)
Week 99	Missing by Design	61 (72.6)
	Discontinued due to adverse event	5 (6.0)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	28 (33.3)
	Discontinued due to withdrawal by subject	2 (2.4)
	Completed study treatment	0 (0.0)
	Subject died	0 (0.0)
	Visit not reached	17 (20.2)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	23 (27.4)
	Not completed	5 (6.0)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	1 (1.2)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	2 (2.4)
	Other	1 (1.2)
	With visit, no record	1 (1.2)
	Completed	18 (21.4)
	Compliance (% in those expected to complete questionnaires)[d]	18 (78.3)

Study: KEYNOTE 158[a]		Pembrolizumab
Visit	EQ-5D-3L	N[b] = 84 n (%)
Week 111	Missing by Design	64 (76.2)
	Discontinued due to adverse event	5 (6.0)
	Discontinued due to clinical progression	6 (7.1)
	Discontinued due to complete response	1 (1.2)
	Discontinued due to physician decision	2 (2.4)
	Discontinued due to progressive disease	28 (33.3)
	Discontinued due to withdrawal by subject	4 (4.8)
	Completed study treatment	1 (1.2)
	Subject died	0 (0.0)
	Visit not reached	17 (20.2)
	Visit not scheduled	0 (0.0)
	Expected to Complete Questionnaires[c]	20 (23.8)
	Not completed	9 (10.7)
	Subject did not complete due to disease under study	0 (0.0)
	Not completed due to site staff error	2 (2.4)
	Subject in hospital or hospice	0 (0.0)
	Subject was physically unable to complete	0 (0.0)
	Subject refused for other reasons	3 (3.6)
	Other	2 (2.4)
	With visit, no record	2 (2.4)
	Completed	11 (13.1)
	Compliance (% in those expected to complete questionnaires)[d]	11 (55.0)

a: Database Cutoff Date: 05OCT2020

b: Number of participants: full-analysis-set-population with MSI-H endometrial carcinoma, at least one line of prior therapy

c: Expected to complete questionnaire includes all participants who do not have missing data due to a missing by design reason

d: Compliance is the proportion of participants who completed the PRO questionnaire among those who are expected to complete the questionnaire at each time point, excluding those missing by design. All the other percentages are defined as the proportion of participants in the analysis population (N)

EQ-5D-3L: 3-level version of the EuroQol-5 Dimension of health questionnaire; MSI-H: Microsatellite Instability-High; PRO: Patient Reported Outcome

Anhang 4-G2: Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) anhand der zugeordneten PT

Die Definition der Immunvermittelten unerwünschten Ereignisse (AEOSI) anhand der zugeordneten PT in der Studie KEYNOTE 158 sind Anhang 4G des Moduls 4C (Magenkarzinom) zu entnehmen.