14.2.1 Primary efficacy analysis

14.2.1.1 Primary efficacy analysis by cohort

Table 14.2.1.1.1 Overall response rate based on the investigator's assessment according to RECIST criteria - EEP set (N = 47)

			Cohort II Murlentamab + Trifluridine/tipiracil		
		Cohort I Murlentamab N = 13	Cohort II N = 13	Cohort II expansion N = 21	Total N = 34
Overall response rate (ORR)	N	13	13	21	34
	Missing values	0	0	0	0
	No	13 (100.0%) [100.00 ; 100.00]	13 (100.0%) [100.00 ; 100.00]	20 (95.2%) [86.13 ; 100.00]	33 (97.1%) [91.38 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (4.8%) [0.00 ; 13.87]	1 (2.9%) [0.00 ; 8.62]
Progression-Free Survival (PFS) at 6 months	N	13	13	21	34
	Missing values	0	0	0	0
	No	13 (100.0%) [100.00 ; 100.00]	9 (69.2%) [44.14 ; 94.32]	16 (76.2%) [57.97 ; 94.41]	25 (73.5%) [58.70 ; 88.36]
	Yes	0 (0.0%) [- ; -]	4 (30.8%) [5.68 ; 55.86]	5 (23.8%) [5.59 ; 42.03]	9 (26.5%) [11.64 ; 41.30]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.1.2 Overall response rate based on the IRC-assessed response according to RECIST criteria - EEP set (N = 47)

			Cohort II Murlentamab + Trifluridine/tipiracil		
		Cohort I Murlentamab N = 13	Cohort II N = 13	Cohort II expansion N = 21	Total N = 34
Overall response rate (ORR)	N	13	13	21	34
	Missing values	0	0	0	0
	No	13 (100.0%) [100.00 ; 100.00]	13 (100.0%) [100.00 ; 100.00]	20 (95.2%) [86.13 ; 100.00]	33 (97.1%) [91.38 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (4.8%) [0.00 ; 13.87]	1 (2.9%) [0.00 ; 8.62]
Progression-Free Survival (PFS) at 6 months	N	13	13	21	34
	Missing values	0	0	0	0
	No	13 (100.0%) [100.00 ; 100.00]	10 (76.9%) [54.02 ; 99.83]	14 (66.7%) [46.50 ; 86.83]	24 (70.6%) [55.27 ; 85.90]
	Yes	0 (0.0%) [- ; -]	3 (23.1%) [0.17 ; 45.98]	7 (33.3%) [13.17 ; 53.50]	10 (29.4%) [14.10 ; 44.73]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.1.3 Overall response rate based on the investigator's assessment according to RECIST criteria - mITT set (N = 65)

		Cohort I Murlentamab N = 21	Cohort II Murlentamab + Trifluridine/tipiracil		
			Cohort II N = 18	Cohort II expansion N = 26	Total N = 44
Overall response rate (ORR)	N	21	18	26	44
	Missing values	0	0	0	0
	No	21 (100.0%) [100.00 ; 100.00]	18 (100.0%) [100.00 ; 100.00]	25 (96.2%) [88.76 ; 100.00]	43 (97.7%) [93.32 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (3.8%) [0.00 ; 11.24]	1 (2.3%) [0.00 ; 6.68]
Progression-Free Survival (PFS) at 6 months	N	21	18	26	44
	Missing values	0	0	0	0
	No	21 (100.0%) [100.00 ; 100.00]	13 (72.2%) [51.53 ; 92.91]	21 (80.8%) [65.62 ; 95.92]	34 (77.3%) [64.89 ; 89.66]
	Yes	0 (0.0%) [- ; -]	5 (27.8%) [7.09 ; 48.47]	5 (19.2%) [4.08 ; 34.38]	10 (22.7%) [10.34 ; 35.11]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.1.4 Overall response rate based on the IRC-assessed response according to RECIST criteria - mITT set (N = 65)

			Cohort II Murlentamab + Trifluridine/tipiracil		
		Cohort I Murlentamab N = 21	Cohort II N = 18	Cohort II expansion N = 26	Total N = 44
Overall response rate (ORR)	N	21	18	26	44
	Missing values	0	0	0	0
	No	21 (100.0%) [100.00 ; 100.00]	18 (100.0%) [100.00 ; 100.00]	25 (96.2%) [88.76 ; 100.00]	43 (97.7%) [93.32 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (3.8%) [0.00 ; 11.24]	1 (2.3%) [0.00 ; 6.68]
Progression-Free Survival (PFS) at 6 months	N	21	18	26	44
	Missing values	0	0	0	0
	No	21 (100.0%) [100.00 ; 100.00]	15 (83.3%) [66.12 ; 100.00]	19 (73.1%) [56.03 ; 90.13]	34 (77.3%) [64.89 ; 89.66]
	Yes	0 (0.0%) [- ; -]	3 (16.7%) [0.00 ; 33.88]	7 (26.9%) [9.87 ; 43.97]	10 (22.7%) [10.34 ; 35.11]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.1.5 Overall response rate based on the investigator's assessment according to RECIST criteria - PP set (N = 37)

			Cohort II Murlentamab + Trifluridine/tipiracil		
		Cohort I Murlentamab N = 9	Cohort II N = 11	Cohort II expansion N = 17	Total N = 28
Overall response rate (ORR)	N	9	11	17	28
	Missing values	0	0	0	0
	No	9 (100.0%) [100.00 ; 100.00]	11 (100.0%) [100.00 ; 100.00]	16 (94.1%) [82.93 ; 100.00]	27 (96.4%) [89.55 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (5.9%) [0.00 ; 17.07]	1 (3.6%) [0.00 ; 10.45]
Progression-Free Survival (PFS) at 6 months	N	9	11	17	28
	Missing values	0	0	0	0
	No	9 (100.0%) [100.00 ; 100.00]	7 (63.6%) [35.21 ; 92.06]	14 (82.4%) [64.23 ; 100.00]	21 (75.0%) [58.96 ; 91.04]
	Yes	0 (0.0%) [- ; -]	4 (36.4%) [7.94 ; 64.79]	3 (17.6%) [0.00 ; 35.77]	7 (25.0%) [8.96 ; 41.04]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.1.6 Overall response rate based on the IRC-assessed response according to RECIST criteria - PP set (N = 37)

			Cohort II Murlentamab + Trifluridine/tipiracil		
		Cohort I Murlentamab N = 9	Cohort II N = 11	Cohort II expansion N = 17	Total N = 28
Overall response rate (ORR)	N	9	11	17	28
	Missing values	0	0	0	0
	No	9 (100.0%) [100.00 ; 100.00]	11 (100.0%) [100.00 ; 100.00]	16 (94.1%) [82.93 ; 100.00]	27 (96.4%) [89.55 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (5.9%) [0.00 ; 17.07]	1 (3.6%) [0.00 ; 10.45]
Progression-Free Survival (PFS) at 6 months	N	9	11	17	28
	Missing values	0	0	0	0
	No	9 (100.0%) [100.00 ; 100.00]	8 (72.7%) [46.41 ; 99.05]	12 (70.6%) [48.93 ; 92.25]	20 (71.4%) [54.70 ; 88.16]
	Yes	0 (0.0%) [- ; -]	3 (27.3%) [0.95 ; 53.59]	5 (29.4%) [7.75 ; 51.07]	8 (28.6%) [11.84 ; 45.30]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

14.2.1.2 Primary efficacy analysis according to the AMHRII membrane expression

Table 14.2.1.2.1 Overall response rate based on the investigator's assessment according to RECIST criteria - EEP set (N = 47)

		Cohort I Murlentamab		Cohort II Murlentamab + Trifluridine/tipiracil	
		AMHRII membrane expression < 20% N = 6	**AMHRII membrane expression ≥ 20% N = 3**	**AMHRII membrane expression < 20% N = 17**	**AMHRII membrane expression ≥ 20% N = 13**
Overall response rate (ORR)	N	6	3	17	13
	Missing values	0	0	0	0
	No	6 (100.0%) [100.00 ; 100.00]	3 (100.0%) [100.00 ; 100.00]	17 (100.0%) [100.00 ; 100.00]	12 (92.3%) [77.82 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (7.7%) [0.00 ; 22.18]
Progression-Free Survival (PFS) at 6 months	N	6	3	17	13
	Missing values	0	0	0	0
	No	6 (100.0%) [100.00 ; 100.00]	3 (100.0%) [100.00 ; 100.00]	14 (82.4%) [64.23 ; 100.00]	8 (61.5%) [35.09 ; 87.99]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	3 (17.6%) [0.00 ; 35.77]	5 (38.5%) [12.01 ; 64.91]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.2.2 Overall response rate based on the IRC-assessed response according to RECIST criteria - EEP set (N = 47)

		Cohort I Murlentamab		Cohort II Murlentamab + Trifluridine/tipiracil	
		AMHRII membrane expression < 20% N = 6	**AMHRII membrane expression ≥ 20% N = 3**	**AMHRII membrane expression < 20% N = 17**	**AMHRII membrane expression ≥ 20% N = 13**
Overall response rate (ORR)	N	6	3	17	13
	Missing values	0	0	0	0
	No	6 (100.0%) [100.00 ; 100.00]	3 (100.0%) [100.00 ; 100.00]	17 (100.0%) [100.00 ; 100.00]	12 (92.3%) [77.82 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (7.7%) [0.00 ; 22.18]
Progression-Free Survival (PFS) at 6 months	N	6	3	17	13
	Missing values	0	0	0	0
	No	6 (100.0%) [100.00 ; 100.00]	3 (100.0%) [100.00 ; 100.00]	14 (82.4%) [64.23 ; 100.00]	7 (53.8%) [26.75 ; 80.95]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	3 (17.6%) [0.00 ; 35.77]	6 (46.2%) [19.05 ; 73.25]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.2.3 Overall response rate based on the investigator's assessment according to RECIST criteria - mITT set (N = 65)

		Cohort I Murlentamab		Cohort II Murlentamab + Trifluridine/tipiracil	
		AMHRII membrane expression < 20% N = 12	**AMHRII membrane expression ≥ 20% N = 4**	**AMHRII membrane expression < 20% N = 24**	**AMHRII membrane expression ≥ 20% N = 16**
Overall response rate (ORR)	N	12	4	24	16
	Missing values	0	0	0	0
	No	12 (100.0%) [100.00 ; 100.00]	4 (100.0%) [100.00 ; 100.00]	24 (100.0%) [100.00 ; 100.00]	15 (93.8%) [81.89 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (6.3%) [0.00 ; 18.11]
Progression-Free Survival (PFS) at 6 months	N	12	4	24	16
	Missing values	0	0	0	0
	No	12 (100.0%) [100.00 ; 100.00]	4 (100.0%) [100.00 ; 100.00]	20 (83.3%) [68.42 ; 98.24]	11 (68.8%) [46.04 ; 91.46]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	4 (16.7%) [1.76 ; 31.58]	5 (31.3%) [8.54 ; 53.96]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.2.4 Overall response rate based on the IRC-assessed response according to RECIST criteria - mITT set (N = 65)

		Cohort I Murlentamab		Cohort II Murlentamab + Trifluridine/tipiracil	
		AMHRII membrane expression < 20% N = 12	**AMHRII membrane expression ≥ 20% N = 4**	**AMHRII membrane expression < 20% N = 24**	**AMHRII membrane expression ≥ 20% N = 16**
Overall response rate (ORR)	N	12	4	24	16
	Missing values	0	0	0	0
	No	12 (100.0%) [100.00 ; 100.00]	4 (100.0%) [100.00 ; 100.00]	24 (100.0%) [100.00 ; 100.00]	15 (93.8%) [81.89 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (6.3%) [0.00 ; 18.11]
Progression-Free Survival (PFS) at 6 months	N	12	4	24	16
	Missing values	0	0	0	0
	No	12 (100.0%) [100.00 ; 100.00]	4 (100.0%) [100.00 ; 100.00]	21 (87.5%) [74.27 ; 100.00]	10 (62.5%) [38.78 ; 86.22]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	3 (12.5%) [0.00 ; 25.73]	6 (37.5%) [13.78 ; 61.22]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.2.5 Overall response rate based on the investigator's assessment according to RECIST criteria - PP set (N = 37)

		Cohort I Murlentamab		Cohort II Murlentamab + Trifluridine/tipiracil	
		AMHRII membrane expression < 20% N = 4	**AMHRII membrane expression ≥ 20% N = 2**	**AMHRII membrane expression < 20% N = 14**	**AMHRII membrane expression ≥ 20% N = 12**
Overall response rate (ORR)	N	4	2	14	12
	Missing values	0	0	0	0
	No	4 (100.0%) [100.00 ; 100.00]	2 (100.0%) [100.00 ; 100.00]	14 (100.0%) [100.00 ; 100.00]	11 (91.7%) [76.03 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (8.3%) [0.00 ; 23.97]
Progression-Free Survival (PFS) at 6 months	N	4	2	14	12
	Missing values	0	0	0	0
	No	4 (100.0%) [100.00 ; 100.00]	2 (100.0%) [100.00 ; 100.00]	12 (85.7%) [67.38 ; 100.00]	7 (58.3%) [30.44 ; 86.23]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	2 (14.3%) [0.00 ; 32.62]	5 (41.7%) [13.77 ; 69.56]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals

Table 14.2.1.2.6 Overall response rate based on the IRC-assessed response according to RECIST criteria - PP set (N = 37)

		Cohort I Murlentamab		Cohort II Murlentamab + Trifluridine/tipiracil	
		AMHRII membrane expression < 20% N = 4	**AMHRII membrane expression ≥ 20% N = 2**	**AMHRII membrane expression < 20% N = 14**	**AMHRII membrane expression ≥ 20% N = 12**
Overall response rate (ORR)	N	4	2	14	12
	Missing values	0	0	0	0
	No	4 (100.0%) [100.00 ; 100.00]	2 (100.0%) [100.00 ; 100.00]	14 (100.0%) [100.00 ; 100.00]	11 (91.7%) [76.03 ; 100.00]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	1 (8.3%) [0.00 ; 23.97]
Progression-Free Survival (PFS) at 6 months	N	4	2	14	12
	Missing values	0	0	0	0
	No	4 (100.0%) [100.00 ; 100.00]	2 (100.0%) [100.00 ; 100.00]	12 (85.7%) [67.38 ; 100.00]	6 (50.0%) [21.71 ; 78.29]
	Yes	0 (0.0%) [- ; -]	0 (0.0%) [- ; -]	2 (14.3%) [0.00 ; 32.62]	6 (50.0%) [21.71 ; 78.29]

ORR : proportion of patients who achieve partial or complete response (PR or CR) using RECIST criteria from the end of cycle 2 (i.e. 8 weeks) and subsequently confirmed 4 weeks later. The patient who achieved a treatment response was confirmed 8 weeks later.
PFS at 6 months = patients progression-free and alive at 6 months
Note: Confidence intervals are 95% two-sided exact binomial Clopper-Pearson confidence intervals