Eigene Vorlage

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Dostarlimab

GlaxoSmithKline GmbH & Co. KG

Separater Anhang 4-G zu Modul 4A

Tabellen und Abbildungen

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Inhaltsverzeichnis

Characteristic	GARNET (n=129)		McMeekin OS/AE analyses (n=121)	
Mean age in years (standard deviation)	63,1	8,72	63,2	8,91
Min-Max	39-80		39-80	
Age group, n (%)				
<65 years	66	51,2%	61	50,4%
≥65 years	63	48,8%	60	49,6%
ECOG PS, n (%)				
0	55	42,6%	53	43,8%
1	74	57,4%	68	56,2%
Histology at diagnosis, n (%)				
Endometrioid carcinoma, type 1	85	65,9%	80	66,1%
Endometrial carcinoma, type 2	43	33,3%	40	33,1%
Serous carcinoma	5	3,9%	5	4,1%
Clear cell carcinoma	1	0,8%	1	0,8%
Squamous carcinoma	1	0,8%	1	0,8%
Undifferentiated carcinoma	5	3,9%	5	4,1%
Carcinosarcoma	0	0,0%	0	0,0%
Mixed carcinoma	7	5,4%	6	5,0%
Unspecified	17	13,2%	15	12,4%
Other[a]	7	5,4%	7	5,8%
Histology unknown at time of diagnosis	1	0,8%	1	0,8%
Most recent FIGO stage, n (%)				
I	13	10,1%	12	9,9%
II	4	3,1%	4	3,3%
III	24	18,6%	23	19,0%
IV	86	66,7%	80	66,1%
Unknown	2	1,6%	2	1,7%
Prior anticancer treatment, n (%)				
Any prior anti-cancer treatment	129	100,0%	121	100,0%
Surgery	116	89,9%	108	89,3%
Radiotherapy	94	72,9%	88	72,7%
Number of prior lines of therapy, n (%)				
1	82	63,6%	79	65,3%
2	32	24,8%	28	23,1%
3	11	8,5%	10	8,3%
≥4	4	3,1%	4	3,3%
BMI				
Mean BMI (standard deviation)	29,7	8,08	29,7	8,11
Min-Max	13.62-53.88		13.62-53.88	
Race, n (%)				
White	98	76,0%	91	75,2%
Black	3	2,3%	3	2,5%
Asian	5	3,9%	5	4,1%
American Indian or Alaska Native	3	2,3%	3	2,5%
Native Hawaiian or other Pacific Islander	0	0,0%	0	0,0%
Other	1	0,8%	1	0,8%
Unknown	19	14,7%	18	14,9%

Characteristic	McMeekin irORR analyses (n=106)		Makker (n=91)	
Mean age in years (standard deviation)	63,0	9,09	61,9	8,47
Min-Max	39-80		39-77	
Age group, n (%)				
<65 years	55	51,9%	53	58,2%
≥65 years	51	48,1%	38	41,8%
ECOG PS, n (%)				
0	45	42,5%	34	37,4%
1	61	57,5%	57	62,6%
Histology at diagnosis, n (%)				
Endometrioid carcinoma, type 1	73	68,9%	60	65,9%
Endometrial carcinoma, type 2	32	30,2%	31	34,1%
Serous carcinoma	4	3,8%	3	3,3%
Clear cell carcinoma	1	0,9%	1	1,1%
Squamous carcinoma	1	0,9%	1	1,1%
Undifferentiated carcinoma	5	4,7%	5	5,5%
Carcinosarcoma	0	0,0%	0	0,0%
Mixed carcinoma	3	2,8%	4	4,4%
Unspecified	12	11,3%	12	13,2%
Other[a]	6	5,7%	5	5,5%
Histology unknown at time of diagnosis	1	0,9%	0	0,0%
Most recent FIGO stage, n (%)				
I	12	11,3%	11	12,1%
II	4	3,8%	3	3,3%
III	18	17,0%	18	19,8%
IV	70	66,0%	57	62,6%
Unknown	2	1,9%	2	2,2%
Prior anticancer treatment, n (%)				
Any prior anti-cancer treatment	106	100,0%	91	100,0%
Surgery	95	89,6%	82	90,1%
Radiotherapy	76	71,7%	66	72,5%
Number of prior lines of therapy, n (%)				
1	67	63,2%	55	60,4%
2	27	25,5%	27	29,7%
3	8	7,5%	7	7,7%
≥4	4	3,8%	2	2,2%
BMI				
Mean BMI (standard deviation)	29,3	8,02	29,0	8,57
Min-Max	13.62-53.88		13.62-53.88	
Race, n (%)				
White	82	77,4%	88	96,7%
Black	3	2,8%	3	3,3%
Asian	4	3,8%	0	0,0%
American Indian or Alaska Native	3	2,8%	0	0,0%
Native Hawaiian or other Pacific Islander	0	0,0%	0	0,0%
Other	0	0,0%	0	0,0%
Unknown	14	13,2%	0	0,0%

Characteristic	Julius (n=129)		Rubinstein (n=128)	
Mean age in years (standard deviation)	63,1	8,72	63,3	8,49
Min-Max	39-80		41-80	
Age group, n (%)				
<65 years	66	51,2%	65	50,8%
≥65 years	12	9,3%	63	49,2%
ECOG PS, n (%)				
0	55	42,6%	55	43,0%
1	74	57,4%	73	57,0%
Histology at diagnosis, n (%)				
Endometrioid carcinoma, type 1	85	65,9%	85	66,4%
Endometrial carcinoma, type 2	43	33,3%	42	32,8%
Serous carcinoma	5	3,9%	5	3,9%
Clear cell carcinoma	1	0,8%	1	0,8%
Squamous carcinoma	1	0,8%	1	0,8%
Undifferentiated carcinoma	5	3,9%	5	3,9%
Carcinosarcoma	0	0,0%	0	0,0%
Mixed carcinoma	7	5,4%	6	4,7%
Unspecified	17	13,2%	17	13,3%
Other[a]	7	5,4%	7	5,5%
Histology unknown at time of diagnosis	1	0,8%	1	0,8%
Most recent FIGO stage, n (%)				
I	13	10,1%	13	10,2%
II	4	3,1%	4	3,1%
III	24	18,6%	24	18,8%
IV	86	66,7%	85	66,4%
Unknown	2	1,6%	2	1,6%
Prior anticancer treatment, n (%)				
Any prior anti-cancer treatment	129	100,0%	128	100,0%
Surgery	116	89,9%	116	90,6%
Radiotherapy	94	72,9%	93	72,7%
Number of prior lines of therapy, n (%)				
1	82	63,6%	82	64,1%
2	32	24,8%	31	24,2%
3	11	8,5%	11	8,6%
≥4	4	3,1%	4	3,1%
BMI				
Mean BMI (standard deviation)	29,7	8,08	29,7	8,11
Min-Max	13.62-53.88		13.62-53.88	
Race, n (%)				
White	98	76,0%	97	75,8%
Black	3	2,3%	3	2,3%
Asian	5	3,9%	5	3,9%
American Indian or Alaska Native	3	2,3%	3	2,3%
Native Hawaiian or other Pacific Islander	0	0,0%	0	0,0%
Other	1	0,8%	1	0,8%
Unknown	19	14,7%	19	14,8%

Characteristic	Mazgani (n=90)		Mazgani Endometroid (n=85)	
Mean age in years (standard deviation)	63,7	8,66	63,5	8,68
Min-Max	41-80		41-80	
Age group, n (%)				
<65 years	46	51,1%	44	51,8%
≥65 years	44	48,9%	41	48,2%
ECOG PS, n (%)				
0	38	42,2%	36	42,4%
1	52	57,8%	49	57,6%
Histology at diagnosis, n (%)				
Endometrioid carcinoma, type 1	85	94,4%	85	100,0%
Endometrial carcinoma, type 2	1	1,1%	0	0,0%
Serous carcinoma	1	1,1%	0	0,0%
Clear cell carcinoma	0	0,0%	0	0,0%
Squamous carcinoma	0	0,0%	0	0,0%
Undifferentiated carcinoma	0	0,0%	0	0,0%
Carcinosarcoma	0	0,0%	0	0,0%
Mixed carcinoma	0	0,0%	0	0,0%
Unspecified	0	0,0%	0	0,0%
Other[a]	0	0,0%	0	0,0%
Histology unknown at time of diagnosis	0	0,0%	0	0,0%
Most recent FIGO stage, n (%)				
I	13	14,4%	12	14,1%
II	4	4,4%	4	4,7%
III	14	15,6%	12	14,1%
IV	58	64,4%	56	65,9%
Unknown	1	1,1%	1	1,2%
Prior anticancer treatment, n (%)				
Any prior anti-cancer treatment	90	100,0%	82	96,5%
Surgery	83	92,2%	78	91,8%
Radiotherapy	68	75,6%	65	76,5%
Number of prior lines of therapy, n (%)				
1	57	63,3%	52	61,2%
2	22	24,4%	22	25,9%
3	8	8,9%	8	9,4%
≥4	3	3,3%		0,0%
BMI				
Mean BMI (standard deviation)	31,1	7,80	31,1	7,85
Min-Max	13.62-53.88		13.62-53.88	
Race, n (%)				
White	62	68,9%		0,0%
Black	2	2,2%		0,0%
Asian	3	3,3%		0,0%
American Indian or Alaska Native	1	1,1%		0,0%
Native Hawaiian or other Pacific Islander	0	0,0%		0,0%
Other	1	1,1%		0,0%
Unknown	16	17,8%		0,0%

Baseline characteristics of GARNET ITT and RWE cohort before and after matching (RWE cohort, base case)

	GARNET ITT before matching	RWE cohort (base case)	Scenario 1	Scenario 2	Scenario 3
Effective sample size (ESS)	**129**	**999**	**31**	**64**	**63**
Race/ethnicity					
Black	3 (2.3%)	57 (5.7%)	2.1%	2.8%	5.7%
Other Race	8 (6.2%)	78 (7.8%)	4.6%	6.2%	7.8%
White	98 (76.0%)	841 (84.2%)	77.2%	77.8%	84.2%
Unknown	20 (15.5%)	23 (2.3%)	16.1%	13.2%	2.3%
Age category					
<65 years	66 (51.2%)	428 (42.8%)	39.5%	47.4%	52.4%
≥65 years	63 (48.8%)	571 (57.2%)	60.5%	52.6%	47.6%
ECOG performance status at index					
0	55 (42.6%)	320 (32.0%)	47.8%	40.6%	40.7%
1	74 (57.4%)	181 (18.1%)	52.2%	59.4%	59.3%
Unknown	0 (0.0%)	498 (49.8%)	0.0%	0.0%	0.0%
Histology at initial diagnosis					
Endometrioid	90 (69.8%)	424 (42.4%)	42.4%	42.4%	42.4%
Non-endometrioid	31 (24.0%)	575 (57.6%)	57.6%	57.6%	57.6%
Unknown	8 (6.2%)	0 (0.0%)	0.0%	0.0%	0.0%
FIGO Stage at initial diagnosis					
Stage I/II	57 (44.2%)	221 (22.1%)	30.4%	39.7%	22.1%
Stage III/IV	72 (55.8%)	778 (77.9%)	69.6%	60.3%	77.9%
Disease grade at initial diagnosis					
Grade 1/2	87 (67.4%)	274 (27.4%)	27.5%	44.0%	43.7%
Grade 3/4	36 (27.9%)	389 (38.9%)	38.9%	49.3%	49.8%
Unknown	6 (4.7%)	336 (33.6%)	33.6%	6.7%	6.5%
Number of prior platinum-based therapies in the advanced/recurrent setting					
0	2 (1.6%)	0 (0%)	0.0%	0.0%	2.2%
1	110 (85.2%)	999 (100.0%)	100.0%	100.0%	81.4%
2+	17 (13.2%)	0 (0.0%)	0.0%	0.0%	16.4%
Surgery for advanced or recurrent endometrial cancer					
Yes	116 (89.9%)	815 (81.6%)	77.6%	88.8%	81.6%
No	13 (10.1%)	184 (18.4%)	22.4%	11.2%	18.4%

Scenario 1: Matching variables are histology, grade and number of prior platinum-based therapies
Scenario 2: Matching variables are histology and number of prior platinum-based therapies
Scenario 3: Matching variables are race, histology, stage at initial diagnosis and surgery

Baseline characteristics of GARNET ITT and RWE cohort before and after matching (RWE cohort, ECOG≤1)

	GARNET ITT before matching	RWE cohort (ECOG≤1)	Scenario 1	Scenario 2	Scenario 3
Effective sample size (ESS)	**129**	**501**	**35**	**64**	**51**
Race/ethnicity					
Black	3 (2.3%)	21 (4.2%)	2.2%	2.8%	4.2%
Other Race	8 (6.2%)	33 (6.6%)	4.8%	6.2%	6.6%
White	98 (76.0%)	439 (87.6%)	77.0%	77.7%	87.6%
Unknown	20 (15.5%)	8 (1.6%)	16.0%	13.2%	1.6%
Age category					
<65 years	66 (51.2%)	202 (40.3%)	40.4%	47.4%	43.9%
≥65 years	63 (48.8%)	299 (59.7%)	59.6%	52.6%	56.1%
ECOG performance status at index					
0	55 (42.6%)	320 (63.9%)	47.5%	40.6%	63.9%
1	74 (57.4%)	181 (36.1%)	52.5%	59.4%	36.1%
Unknown	0 (0.0%)	0 (0.0%)	0.0%	0.0%	0.0%
Histology at initial diagnosis					
Endometrioid	90 (69.8%)	213 (42.5%)	42.5%	42.5%	42.5%
Non-endometrioid	31 (24.0%)	288 (57.5%)	57.5%	57.5%	57.5%
Unknown	8 (6.2%)	0 (0.0%)	0.0%	0.0%	0.0%
FIGO Stage at initial diagnosis					
Stage I/II	57 (44.2%)	121 (24.2%)	31.2%	39.8%	24.2%
Stage III/IV	72 (55.8%)	380 (75.8%)	68.8%	60.2%	75.8%
Disease grade at initial diagnosis					
Grade 1/2	87 (67.4%)	141 (28.1%)	28.2%	44.0%	39.8%
Grade 3/4	36 (27.9%)	206 (41.1%)	41.1%	49.2%	53.3%
Unknown	6 (4.7%)	154 (30.7%)	30.7%	6.8%	6.9%
Number of prior platinum-based therapies in the advanced/recurrent setting					
0	2 (1.6%)	0 (0.0%)	0.0%	0.0%	1.4%
1	110 (85.2%)	501 (100.0%)	100.0%	100.0%	83.7%
2+	17 (13.2%)	0 (0.0%)	0.0%	0.0%	14.9%
Surgery for advanced or recurrent endometrial cancer					
Yes	116 (89.9%)	413 (82.4%)	78.8%	88.8%	82.4%
No	13 (10.1%)	88 (17.6%)	21.2%	11.2%	17.6%

Scenario 1: Matching variables are histology, grade and number of prior platinum-based therapies
Scenario 2: Matching variables are histology and number of prior platinum-based therapies
Scenario 3: Matching variables are race/ethnicity, ECOG, histology, stage at initial diagnosis and surgery

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Baseline	Actual	n	97
		Mean (std)	70.1 (20.02)
		Median	70.0
		Q1, Q3	60.0, 85.0
		Min, Max	0, 100
Week 3	Actual	n	83
		Mean (std)	69.1 (19.14)
		Median	70.0
		Q1, Q3	60.0, 85.0
		Min, Max	10, 95
	Change from BL	n	83
		Mean (std)	-0.5 (12.36)
		Median	0.0
		Q1, Q3	-5.0, 5.0
		Min, Max	-40, 30

BL: baseline; Std: standard deviation; VAS = visual analog scale.
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Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 6	Actual	n	80
		Mean (std)	72.0 (17.89)
		Median	75.0
		Q1, Q3	60.0, 85.0
		Min, Max	30, 100
	Change from BL	n	80
		Mean (std)	2.0 (14.78)
		Median	0.0
		Q1, Q3	-5.0, 10.0
		Min, Max	-50, 40
Week 9	Actual	n	75
		Mean (std)	74.9 (19.12)
		Median	80.0
		Q1, Q3	65.0, 90.0
		Min, Max	4, 100
	Change from BL	n	75
		Mean (std)	4.5 (16.61)
		Median	0.0
		Q1, Q3	-5.0, 10.0
		Min, Max	-51, 55

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 12	Actual	n	65
		Mean (std)	77.5 (17.09)
		Median	78.0
		Q1, Q3	70.0, 90.0
		Min, Max	30, 100
	Change from BL	n	65
		Mean (std)	5.2 (13.54)
		Median	5.0
		Q1, Q3	0.0, 10.0
		Min, Max	-30, 49
Week 18	Actual	n	48
		Mean (std)	77.5 (16.78)
		Median	80.0
		Q1, Q3	70.0, 90.0
		Min, Max	35, 100
	Change from BL	n	48
		Mean (std)	4.7 (15.46)
		Median	0.5
		Q1, Q3	-5.0, 10.0
		Min, Max	-25, 45

BL: baseline; Std: standard deviation; VAS = visual analog scale.
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Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 24	Actual	n	42
		Mean (std)	75.5 (16.75)
		Median	77.5
		Q1, Q3	65.0, 90.0
		Min, Max	40, 99
	Change from BL	n	42
		Mean (std)	3.0 (16.19)
		Median	0.0
		Q1, Q3	-5.0, 10.0
		Min, Max	-40, 40
Week 30	Actual	n	34
		Mean (std)	74.5 (17.07)
		Median	80.0
		Q1, Q3	70.0, 85.0
		Min, Max	20, 100
	Change from BL	n	34
		Mean (std)	0.9 (17.37)
		Median	0.0
		Q1, Q3	-5.0, 10.0
		Min, Max	-40, 35

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 36	Actual	n	33
		Mean (std)	77.2 (16.17)
		Median	80.0
		Q1, Q3	70.0, 90.0
		Min, Max	35, 99
	Change from BL	n	33
		Mean (std)	4.1 (15.31)
		Median	5.0
		Q1, Q3	-5.0, 15.0
		Min, Max	-25, 40
Week 42	Actual	n	24
		Mean (std)	77.8 (16.94)
		Median	80.0
		Q1, Q3	70.0, 90.0
		Min, Max	25, 98
	Change from BL	n	24
		Mean (std)	4.9 (16.40)
		Median	2.5
		Q1, Q3	-5.0, 12.5
		Min, Max	-35, 45

BL: baseline; Std: standard deviation; VAS = visual analog scale.
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Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 48	Actual	n	22
		Mean (std)	76.9 (15.78)
		Median	81.5
		Q1, Q3	70.0, 89.0
		Min, Max	45, 95
	Change from BL	n	22
		Mean (std)	4.5 (15.33)
		Median	1.5
		Q1, Q3	-10.0, 15.0
		Min, Max	-15, 45
Week 54	Actual	n	18
		Mean (std)	74.0 (15.77)
		Median	80.0
		Q1, Q3	60.0, 85.0
		Min, Max	40, 95
	Change from BL	n	18
		Mean (std)	1.2 (16.50)
		Median	0.0
		Q1, Q3	-10.0, 5.0
		Min, Max	-25, 45

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 60	Actual	n	13
		Mean (std)	82.5 (10.86)
		Median	85.0
		Q1, Q3	75.0, 90.0
		Min, Max	60, 98
	Change from BL	n	13
		Mean (std)	7.5 (16.99)
		Median	5.0
		Q1, Q3	-5.0, 15.0
		Min, Max	-15, 48
Week 66	Actual	n	11
		Mean (std)	81.6 (12.82)
		Median	80.0
		Q1, Q3	70.0, 95.0
		Min, Max	65, 100
	Change from BL	n	11
		Mean (std)	8.9 (20.93)
		Median	10.0
		Q1, Q3	0.0, 15.0
		Min, Max	-20, 48

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 72	Actual	n	9
		Mean (std)	84.2 (13.06)
		Median	90.0
		Q1, Q3	75.0, 95.0
		Min, Max	60, 98
	Change from BL	n	9
		Mean (std)	12.6 (20.19)
		Median	15.0
		Q1, Q3	-5.0, 20.0
		Min, Max	-15, 48
Week 78	Actual	n	7
		Mean (std)	80.0 (11.55)
		Median	80.0
		Q1, Q3	70.0, 90.0
		Min, Max	60, 90
	Change from BL	n	7
		Mean (std)	8.6 (16.00)
		Median	10.0
		Q1, Q3	-5.0, 20.0
		Min, Max	-15, 30

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 84	Actual	n	4
		Mean (std)	80.0 (13.54)
		Median	85.0
		Q1, Q3	72.5, 87.5
		Min, Max	60, 90
	Change from BL	n	4
		Mean (std)	3.8 (20.97)
		Median	7.5
		Q1, Q3	-10.0, 17.5
		Min, Max	-25, 25
Week 90	Actual	n	2
		Mean (std)	67.5 (3.54)
		Median	67.5
		Q1, Q3	65.0, 70.0
		Min, Max	65, 70
	Change from BL	n	2
		Mean (std)	-15.0 (7.07)
		Median	-15.0
		Q1, Q3	-20.0, -10.0
		Min, Max	-20, -10

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Week 96	Actual	n	1
		Mean (std)	65.0 ( )
		Median	65.0
		Q1, Q3	65.0, 65.0
		Min, Max	65, 65
	Change from BL	n	1
		Mean (std)	-20.0 ( )
		Median	-20.0
		Q1, Q3	-20.0, -20.0
		Min, Max	-20, -20
End of Treatment	Actual	n	30
		Mean (std)	59.0 (25.71)
		Median	62.5
		Q1, Q3	45.0, 80.0
		Min, Max	6, 100
	Change from BL	n	30
		Mean (std)	-5.0 (20.16)
		Median	-5.0
		Q1, Q3	-15.0, 5.0
		Min, Max	-44, 35

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Safety Follow-up	Actual	n	5
		Mean (std)	66.0 (10.84)
		Median	70.0
		Q1, Q3	60.0, 75.0
		Min, Max	50, 75
	Change from BL	n	5
		Mean (std)	0.0 (31.02)
		Median	-5.0
		Q1, Q3	-15.0, 20.0
		Min, Max	-40, 40
Survival Follow-up 1	Actual	n	6
		Mean (std)	63.7 (16.45)
		Median	67.5
		Q1, Q3	50.0, 75.0
		Min, Max	40, 82
	Change from BL	n	6
		Mean (std)	-0.5 (18.32)
		Median	-5.0
		Q1, Q3	-15.0, 15.0
		Min, Max	-20, 27

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Survival Follow-up 2	Actual	n	3
		Mean (std)	79.0 (7.94)
		Median	82.0
		Q1, Q3	70.0, 85.0
		Min, Max	70, 85
	Change from BL	n	3
		Mean (std)	12.3 (13.65)
		Median	10.0
		Q1, Q3	0.0, 27.0
		Min, Max	0, 27
Survival Follow-up 3	Actual	n	1
		Mean (std)	70.0 ( )
		Median	70.0
		Q1, Q3	70.0, 70.0
		Min, Max	70, 70
	Change from BL	n	1
		Mean (std)	15.0 ( )
		Median	15.0
		Q1, Q3	15.0, 15.0
		Min, Max	15, 15

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 11
Summary of EQ-5D-5L VAS Score by Visit – Cohort A1
(Safety Analysis Set)

Visit	Actual/ Change	Statistic	COHORT A1 (N=129)
Survival Follow-up 4	Actual	n	1
		Mean (std)	85.0 ( )
		Median	85.0
		Q1, Q3	85.0, 85.0
		Min, Max	85, 85
	Change from BL	n	1
		Mean (std)	30.0 ( )
		Median	30.0
		Q1, Q3	30.0, 30.0
		Min, Max	30, 30
Survival Follow-up 5	Actual	n	1
		Mean (std)	90.0 ( )
		Median	90.0
		Q1, Q3	90.0, 90.0
		Min, Max	90, 90
	Change from BL	n	1
		Mean (std)	35.0 ( )
		Median	35.0
		Q1, Q3	35.0, 35.0
		Min, Max	35, 35

BL: baseline; Std: standard deviation; VAS = visual analog scale.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-11-EQ-5D-5L
Rundate: 17NOV2020:11:33:13 Datacut date: 01MAR2020

Table 14
Summary of Frequency and Proportion of Responders in EQ-5D VAS (MCID = 15) - Cohort A1
(Safety Analysis Set)

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		84
	Responders	n (%)	10 (11.9)
	Non-Responders	n (%)	74 (88.1)
Week 6	N		80
	Responders	n (%)	16 (20.0)
	Non-Responders	n (%)	64 (80.0)
Week 9	N		75
	Responders	n (%)	18 (24.0)
	Non-Responders	n (%)	57 (76.0)
Week 12	N		65
	Responders	n (%)	12 (18.5)
	Non-Responders	n (%)	53 (81.5)
Week 18	N		48
	Responders	n (%)	11 (22.9)
	Non-Responders	n (%)	37 (77.1)
Week 24	N		42
	Responders	n (%)	9 (21.4)
	Non-Responders	n (%)	33 (78.6)
Week 30	N		34
	Responders	n (%)	7 (20.6)
	Non-Responders	n (%)	27 (79.4)

[1] Subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-14-EQ-5D-5L-RESP
Rundate: 30NOV2020:07:04:38 Datacut date: 01MAR2020

Table 14
Summary of Frequency and Proportion of Responders in EQ-5D VAS (MCID = 15) - Cohort A1
(Safety Analysis Set)

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 36	N		33
	Responders	n (%)	10 (30.3)
	Non-Responders	n (%)	23 (69.7)
Week 42	N		24
	Responders	n (%)	6 (25.0)
	Non-Responders	n (%)	18 (75.0)
Week 48	N		22
	Responders	n (%)	7 (31.8)
	Non-Responders	n (%)	15 (68.2)
Week 54	N		18
	Responders	n (%)	4 (22.2)
	Non-Responders	n (%)	14 (77.8)
Week 60	N		13
	Responders	n (%)	4 (30.8)
	Non-Responders	n (%)	9 (69.2)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	5 (55.6)
	Non-Responders	n (%)	4 (44.4)

[1] Subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-14-EQ-5D-5L-RESP
Rundate: 30NOV2020:07:04:38 Datacut date: 01MAR2020

Table 14
Summary of Frequency and Proportion of Responders in EQ-5D VAS (MCID = 15) - Cohort A1
(Safety Analysis Set)

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
End of Treatment	N		34
	Responders	n (%)	3 (8.8)
	Non-Responders	n (%)	31 (91.2)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		8
	Responders	n (%)	2 (25.0)
	Non-Responders	n (%)	6 (75.0)

[1] Subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-14-EQ-5D-5L-RESP
Rundate: 30NOV2020:07:04:38 Datacut date: 01MAR2020

Table 14
Summary of Frequency and Proportion of Responders in EQ-5D VAS (MCID = 15) - Cohort A1
(Safety Analysis Set)

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] Subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-14-EQ-5D-5L-RESP
Rundate: 30NOV2020:07:04:38 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	21 (25.6)
	Non-Responders	n (%)	61 (74.4)
Week 6	N		79
	Responders	n (%)	24 (30.4)
	Non-Responders	n (%)	55 (69.6)
Week 9	N		75
	Responders	n (%)	26 (34.7)
	Non-Responders	n (%)	49 (65.3)
Week 12	N		65
	Responders	n (%)	24 (36.9)
	Non-Responders	n (%)	41 (63.1)
Week 18	N		49
	Responders	n (%)	20 (40.8)
	Non-Responders	n (%)	29 (59.2)
Week 24	N		41
	Responders	n (%)	12 (29.3)
	Non-Responders	n (%)	29 (70.7)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	12 (35.3)
	Non-Responders	n (%)	22 (64.7)
Week 36	N		32
	Responders	n (%)	13 (40.6)
	Non-Responders	n (%)	19 (59.4)
Week 42	N		25
	Responders	n (%)	8 (32.0)
	Non-Responders	n (%)	17 (68.0)
Week 48	N		22
	Responders	n (%)	6 (27.3)
	Non-Responders	n (%)	16 (72.7)
Week 54	N		17
	Responders	n (%)	8 (47.1)
	Non-Responders	n (%)	9 (52.9)
Week 60	N		13
	Responders	n (%)	2 (15.4)
	Non-Responders	n (%)	11 (84.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	5 (45.5)
	Non-Responders	n (%)	6 (54.5)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	5 (16.7)
	Non-Responders	n (%)	25 (83.3)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	11 (13.4)
	Non-Responders	n (%)	71 (86.6)
Week 6	N		78
	Responders	n (%)	13 (16.7)
	Non-Responders	n (%)	65 (83.3)
Week 9	N		75
	Responders	n (%)	14 (18.7)
	Non-Responders	n (%)	61 (81.3)
Week 12	N		65
	Responders	n (%)	14 (21.5)
	Non-Responders	n (%)	51 (78.5)
Week 18	N		49
	Responders	n (%)	12 (24.5)
	Non-Responders	n (%)	37 (75.5)
Week 24	N		42
	Responders	n (%)	9 (21.4)
	Non-Responders	n (%)	33 (78.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	9 (26.5)
	Non-Responders	n (%)	25 (73.5)
Week 36	N		32
	Responders	n (%)	10 (31.3)
	Non-Responders	n (%)	22 (68.8)
Week 42	N		23
	Responders	n (%)	5 (21.7)
	Non-Responders	n (%)	18 (78.3)
Week 48	N		22
	Responders	n (%)	4 (18.2)
	Non-Responders	n (%)	18 (81.8)
Week 54	N		18
	Responders	n (%)	7 (38.9)
	Non-Responders	n (%)	11 (61.1)
Week 60	N		13
	Responders	n (%)	2 (15.4)
	Non-Responders	n (%)	11 (84.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	4 (36.4)
	Non-Responders	n (%)	7 (63.6)
Week 72	N		9
	Responders	n (%)	3 (33.3)
	Non-Responders	n (%)	6 (66.7)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	2 (6.7)
	Non-Responders	n (%)	28 (93.3)
Safety Follow-up	N		6
	Responders	n (%)	3 (50.0)
	Non-Responders	n (%)	3 (50.0)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		81
	Responders	n (%)	16 (19.8)
	Non-Responders	n (%)	65 (80.2)
Week 6	N		78
	Responders	n (%)	20 (25.6)
	Non-Responders	n (%)	58 (74.4)
Week 9	N		75
	Responders	n (%)	25 (33.3)
	Non-Responders	n (%)	50 (66.7)
Week 12	N		65
	Responders	n (%)	20 (30.8)
	Non-Responders	n (%)	45 (69.2)
Week 18	N		48
	Responders	n (%)	18 (37.5)
	Non-Responders	n (%)	30 (62.5)
Week 24	N		41
	Responders	n (%)	13 (31.7)
	Non-Responders	n (%)	28 (68.3)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	13 (38.2)
	Non-Responders	n (%)	21 (61.8)
Week 36	N		32
	Responders	n (%)	15 (46.9)
	Non-Responders	n (%)	17 (53.1)
Week 42	N		25
	Responders	n (%)	10 (40.0)
	Non-Responders	n (%)	15 (60.0)
Week 48	N		22
	Responders	n (%)	7 (31.8)
	Non-Responders	n (%)	15 (68.2)
Week 54	N		18
	Responders	n (%)	5 (27.8)
	Non-Responders	n (%)	13 (72.2)
Week 60	N		13
	Responders	n (%)	3 (23.1)
	Non-Responders	n (%)	10 (76.9)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	3 (33.3)
	Non-Responders	n (%)	6 (66.7)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	6 (20.0)
	Non-Responders	n (%)	24 (80.0)
Safety Follow-up	N		6
	Responders	n (%)	3 (50.0)
	Non-Responders	n (%)	3 (50.0)
Survival Follow-up 1	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	22 (26.8)
	Non-Responders	n (%)	60 (73.2)
Week 6	N		79
	Responders	n (%)	22 (27.8)
	Non-Responders	n (%)	57 (72.2)
Week 9	N		75
	Responders	n (%)	23 (30.7)
	Non-Responders	n (%)	52 (69.3)
Week 12	N		65
	Responders	n (%)	17 (26.2)
	Non-Responders	n (%)	48 (73.8)
Week 18	N		49
	Responders	n (%)	16 (32.7)
	Non-Responders	n (%)	33 (67.3)
Week 24	N		41
	Responders	n (%)	16 (39.0)
	Non-Responders	n (%)	25 (61.0)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	10 (29.4)
	Non-Responders	n (%)	24 (70.6)
Week 36	N		32
	Responders	n (%)	11 (34.4)
	Non-Responders	n (%)	21 (65.6)
Week 42	N		25
	Responders	n (%)	9 (36.0)
	Non-Responders	n (%)	16 (64.0)
Week 48	N		22
	Responders	n (%)	7 (31.8)
	Non-Responders	n (%)	15 (68.2)
Week 54	N		17
	Responders	n (%)	7 (41.2)
	Non-Responders	n (%)	10 (58.8)
Week 60	N		13
	Responders	n (%)	6 (46.2)
	Non-Responders	n (%)	7 (53.8)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	6 (54.5)
	Non-Responders	n (%)	5 (45.5)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	7 (23.3)
	Non-Responders	n (%)	23 (76.7)
Safety Follow-up	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	16 (19.5)
	Non-Responders	n (%)	66 (80.5)
Week 6	N		79
	Responders	n (%)	15 (19.0)
	Non-Responders	n (%)	64 (81.0)
Week 9	N		75
	Responders	n (%)	20 (26.7)
	Non-Responders	n (%)	55 (73.3)
Week 12	N		65
	Responders	n (%)	13 (20.0)
	Non-Responders	n (%)	52 (80.0)
Week 18	N		49
	Responders	n (%)	9 (18.4)
	Non-Responders	n (%)	40 (81.6)
Week 24	N		41
	Responders	n (%)	9 (22.0)
	Non-Responders	n (%)	32 (78.0)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	7 (20.6)
	Non-Responders	n (%)	27 (79.4)
Week 36	N		32
	Responders	n (%)	6 (18.8)
	Non-Responders	n (%)	26 (81.3)
Week 42	N		25
	Responders	n (%)	4 (16.0)
	Non-Responders	n (%)	21 (84.0)
Week 48	N		22
	Responders	n (%)	4 (18.2)
	Non-Responders	n (%)	18 (81.8)
Week 54	N		17
	Responders	n (%)	2 (11.8)
	Non-Responders	n (%)	15 (88.2)
Week 60	N		13
	Responders	n (%)	2 (15.4)
	Non-Responders	n (%)	11 (84.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	6 (20.0)
	Non-Responders	n (%)	24 (80.0)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	3 (100)
	Non-Responders	n (%)	0
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		81
	Responders	n (%)	24 (29.6)
	Non-Responders	n (%)	57 (70.4)
Week 6	N		79
	Responders	n (%)	29 (36.7)
	Non-Responders	n (%)	50 (63.3)
Week 9	N		74
	Responders	n (%)	29 (39.2)
	Non-Responders	n (%)	45 (60.8)
Week 12	N		64
	Responders	n (%)	23 (35.9)
	Non-Responders	n (%)	41 (64.1)
Week 18	N		48
	Responders	n (%)	21 (43.8)
	Non-Responders	n (%)	27 (56.3)
Week 24	N		41
	Responders	n (%)	18 (43.9)
	Non-Responders	n (%)	23 (56.1)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	16 (47.1)
	Non-Responders	n (%)	18 (52.9)
Week 36	N		31
	Responders	n (%)	15 (48.4)
	Non-Responders	n (%)	16 (51.6)
Week 42	N		25
	Responders	n (%)	11 (44.0)
	Non-Responders	n (%)	14 (56.0)
Week 48	N		22
	Responders	n (%)	10 (45.5)
	Non-Responders	n (%)	12 (54.5)
Week 54	N		16
	Responders	n (%)	6 (37.5)
	Non-Responders	n (%)	10 (62.5)
Week 60	N		13
	Responders	n (%)	5 (38.5)
	Non-Responders	n (%)	8 (61.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	4 (36.4)
	Non-Responders	n (%)	7 (63.6)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	8 (26.7)
	Non-Responders	n (%)	22 (73.3)
Safety Follow-up	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 1	N		6
	Responders	n (%)	3 (50.0)
	Non-Responders	n (%)	3 (50.0)
Survival Follow-up 2	N		3
	Responders	n (%)	3 (100)
	Non-Responders	n (%)	0
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	24 (29.3)
	Non-Responders	n (%)	58 (70.7)
Week 6	N		79
	Responders	n (%)	26 (32.9)
	Non-Responders	n (%)	53 (67.1)
Week 9	N		75
	Responders	n (%)	32 (42.7)
	Non-Responders	n (%)	43 (57.3)
Week 12	N		65
	Responders	n (%)	26 (40.0)
	Non-Responders	n (%)	39 (60.0)
Week 18	N		49
	Responders	n (%)	23 (46.9)
	Non-Responders	n (%)	26 (53.1)
Week 24	N		42
	Responders	n (%)	19 (45.2)
	Non-Responders	n (%)	23 (54.8)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	14 (41.2)
	Non-Responders	n (%)	20 (58.8)
Week 36	N		32
	Responders	n (%)	15 (46.9)
	Non-Responders	n (%)	17 (53.1)
Week 42	N		25
	Responders	n (%)	13 (52.0)
	Non-Responders	n (%)	12 (48.0)
Week 48	N		22
	Responders	n (%)	7 (31.8)
	Non-Responders	n (%)	15 (68.2)
Week 54	N		18
	Responders	n (%)	7 (38.9)
	Non-Responders	n (%)	11 (61.1)
Week 60	N		13
	Responders	n (%)	4 (30.8)
	Non-Responders	n (%)	9 (69.2)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	4 (36.4)
	Non-Responders	n (%)	7 (63.6)
Week 72	N		9
	Responders	n (%)	5 (55.6)
	Non-Responders	n (%)	4 (44.4)
Week 78	N		7
	Responders	n (%)	4 (57.1)
	Non-Responders	n (%)	3 (42.9)
Week 84	N		4
	Responders	n (%)	3 (75.0)
	Non-Responders	n (%)	1 (25.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	7 (23.3)
	Non-Responders	n (%)	23 (76.7)
Safety Follow-up	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	11 (13.4)
	Non-Responders	n (%)	71 (86.6)
Week 6	N		79
	Responders	n (%)	13 (16.5)
	Non-Responders	n (%)	66 (83.5)
Week 9	N		75
	Responders	n (%)	18 (24.0)
	Non-Responders	n (%)	57 (76.0)
Week 12	N		65
	Responders	n (%)	15 (23.1)
	Non-Responders	n (%)	50 (76.9)
Week 18	N		49
	Responders	n (%)	12 (24.5)
	Non-Responders	n (%)	37 (75.5)
Week 24	N		42
	Responders	n (%)	14 (33.3)
	Non-Responders	n (%)	28 (66.7)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	10 (29.4)
	Non-Responders	n (%)	24 (70.6)
Week 36	N		32
	Responders	n (%)	9 (28.1)
	Non-Responders	n (%)	23 (71.9)
Week 42	N		25
	Responders	n (%)	4 (16.0)
	Non-Responders	n (%)	21 (84.0)
Week 48	N		22
	Responders	n (%)	5 (22.7)
	Non-Responders	n (%)	17 (77.3)
Week 54	N		18
	Responders	n (%)	5 (27.8)
	Non-Responders	n (%)	13 (72.2)
Week 60	N		13
	Responders	n (%)	3 (23.1)
	Non-Responders	n (%)	10 (76.9)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	6 (20.0)
	Non-Responders	n (%)	24 (80.0)
Safety Follow-up	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	26 (31.7)
	Non-Responders	n (%)	56 (68.3)
Week 6	N		79
	Responders	n (%)	33 (41.8)
	Non-Responders	n (%)	46 (58.2)
Week 9	N		75
	Responders	n (%)	37 (49.3)
	Non-Responders	n (%)	38 (50.7)
Week 12	N		65
	Responders	n (%)	30 (46.2)
	Non-Responders	n (%)	35 (53.8)
Week 18	N		49
	Responders	n (%)	24 (49.0)
	Non-Responders	n (%)	25 (51.0)
Week 24	N		42
	Responders	n (%)	20 (47.6)
	Non-Responders	n (%)	22 (52.4)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	19 (55.9)
	Non-Responders	n (%)	15 (44.1)
Week 36	N		32
	Responders	n (%)	18 (56.3)
	Non-Responders	n (%)	14 (43.8)
Week 42	N		25
	Responders	n (%)	12 (48.0)
	Non-Responders	n (%)	13 (52.0)
Week 48	N		22
	Responders	n (%)	11 (50.0)
	Non-Responders	n (%)	11 (50.0)
Week 54	N		18
	Responders	n (%)	7 (38.9)
	Non-Responders	n (%)	11 (61.1)
Week 60	N		13
	Responders	n (%)	7 (53.8)
	Non-Responders	n (%)	6 (46.2)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	7 (63.6)
	Non-Responders	n (%)	4 (36.4)
Week 72	N		9
	Responders	n (%)	5 (55.6)
	Non-Responders	n (%)	4 (44.4)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	9 (30.0)
	Non-Responders	n (%)	21 (70.0)
Safety Follow-up	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 1	N		6
	Responders	n (%)	3 (50.0)
	Non-Responders	n (%)	3 (50.0)
Survival Follow-up 2	N		3
	Responders	n (%)	3 (100)
	Non-Responders	n (%)	0
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		80
	Responders	n (%)	6 (7.5)
	Non-Responders	n (%)	74 (92.5)
Week 6	N		78
	Responders	n (%)	8 (10.3)
	Non-Responders	n (%)	70 (89.7)
Week 9	N		73
	Responders	n (%)	9 (12.3)
	Non-Responders	n (%)	64 (87.7)
Week 12	N		63
	Responders	n (%)	8 (12.7)
	Non-Responders	n (%)	55 (87.3)
Week 18	N		48
	Responders	n (%)	6 (12.5)
	Non-Responders	n (%)	42 (87.5)
Week 24	N		41
	Responders	n (%)	8 (19.5)
	Non-Responders	n (%)	33 (80.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	5 (14.7)
	Non-Responders	n (%)	29 (85.3)
Week 36	N		32
	Responders	n (%)	5 (15.6)
	Non-Responders	n (%)	27 (84.4)
Week 42	N		25
	Responders	n (%)	3 (12.0)
	Non-Responders	n (%)	22 (88.0)
Week 48	N		22
	Responders	n (%)	2 (9.1)
	Non-Responders	n (%)	20 (90.9)
Week 54	N		18
	Responders	n (%)	2 (11.1)
	Non-Responders	n (%)	16 (88.9)
Week 60	N		13
	Responders	n (%)	1 (7.7)
	Non-Responders	n (%)	12 (92.3)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	1 (9.1)
	Non-Responders	n (%)	10 (90.9)
Week 72	N		9
	Responders	n (%)	0
	Non-Responders	n (%)	9 (100)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	0
	Non-Responders	n (%)	4 (100)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		29
	Responders	n (%)	4 (13.8)
	Non-Responders	n (%)	25 (86.2)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	0
	Non-Responders	n (%)	3 (100)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		81
	Responders	n (%)	22 (27.2)
	Non-Responders	n (%)	59 (72.8)
Week 6	N		79
	Responders	n (%)	21 (26.6)
	Non-Responders	n (%)	58 (73.4)
Week 9	N		73
	Responders	n (%)	26 (35.6)
	Non-Responders	n (%)	47 (64.4)
Week 12	N		65
	Responders	n (%)	25 (38.5)
	Non-Responders	n (%)	40 (61.5)
Week 18	N		48
	Responders	n (%)	11 (22.9)
	Non-Responders	n (%)	37 (77.1)
Week 24	N		41
	Responders	n (%)	12 (29.3)
	Non-Responders	n (%)	29 (70.7)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	8 (23.5)
	Non-Responders	n (%)	26 (76.5)
Week 36	N		32
	Responders	n (%)	13 (40.6)
	Non-Responders	n (%)	19 (59.4)
Week 42	N		25
	Responders	n (%)	7 (28.0)
	Non-Responders	n (%)	18 (72.0)
Week 48	N		22
	Responders	n (%)	9 (40.9)
	Non-Responders	n (%)	13 (59.1)
Week 54	N		18
	Responders	n (%)	7 (38.9)
	Non-Responders	n (%)	11 (61.1)
Week 60	N		13
	Responders	n (%)	5 (38.5)
	Non-Responders	n (%)	8 (61.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	7 (63.6)
	Non-Responders	n (%)	4 (36.4)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	9 (30.0)
	Non-Responders	n (%)	21 (70.0)
Safety Follow-up	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 1	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	13 (15.9)
	Non-Responders	n (%)	69 (84.1)
Week 6	N		79
	Responders	n (%)	17 (21.5)
	Non-Responders	n (%)	62 (78.5)
Week 9	N		75
	Responders	n (%)	22 (29.3)
	Non-Responders	n (%)	53 (70.7)
Week 12	N		65
	Responders	n (%)	21 (32.3)
	Non-Responders	n (%)	44 (67.7)
Week 18	N		49
	Responders	n (%)	20 (40.8)
	Non-Responders	n (%)	29 (59.2)
Week 24	N		42
	Responders	n (%)	12 (28.6)
	Non-Responders	n (%)	30 (71.4)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	11 (32.4)
	Non-Responders	n (%)	23 (67.6)
Week 36	N		32
	Responders	n (%)	11 (34.4)
	Non-Responders	n (%)	21 (65.6)
Week 42	N		25
	Responders	n (%)	9 (36.0)
	Non-Responders	n (%)	16 (64.0)
Week 48	N		22
	Responders	n (%)	7 (31.8)
	Non-Responders	n (%)	15 (68.2)
Week 54	N		18
	Responders	n (%)	8 (44.4)
	Non-Responders	n (%)	10 (55.6)
Week 60	N		13
	Responders	n (%)	4 (30.8)
	Non-Responders	n (%)	9 (69.2)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	4 (36.4)
	Non-Responders	n (%)	7 (63.6)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	7 (23.3)
	Non-Responders	n (%)	23 (76.7)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	12 (14.6)
	Non-Responders	n (%)	70 (85.4)
Week 6	N		79
	Responders	n (%)	16 (20.3)
	Non-Responders	n (%)	63 (79.7)
Week 9	N		75
	Responders	n (%)	19 (25.3)
	Non-Responders	n (%)	56 (74.7)
Week 12	N		65
	Responders	n (%)	11 (16.9)
	Non-Responders	n (%)	54 (83.1)
Week 18	N		48
	Responders	n (%)	9 (18.8)
	Non-Responders	n (%)	39 (81.3)
Week 24	N		41
	Responders	n (%)	7 (17.1)
	Non-Responders	n (%)	34 (82.9)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		33
	Responders	n (%)	6 (18.2)
	Non-Responders	n (%)	27 (81.8)
Week 36	N		32
	Responders	n (%)	7 (21.9)
	Non-Responders	n (%)	25 (78.1)
Week 42	N		25
	Responders	n (%)	4 (16.0)
	Non-Responders	n (%)	21 (84.0)
Week 48	N		22
	Responders	n (%)	5 (22.7)
	Non-Responders	n (%)	17 (77.3)
Week 54	N		18
	Responders	n (%)	5 (27.8)
	Non-Responders	n (%)	13 (72.2)
Week 60	N		13
	Responders	n (%)	5 (38.5)
	Non-Responders	n (%)	8 (61.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-15-EORTC-QLQ-C30-RESP
Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	4 (36.4)
	Non-Responders	n (%)	7 (63.6)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	8 (26.7)
	Non-Responders	n (%)	22 (73.3)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		81
	Responders	n (%)	16 (19.8)
	Non-Responders	n (%)	65 (80.2)
Week 6	N		78
	Responders	n (%)	17 (21.8)
	Non-Responders	n (%)	61 (78.2)
Week 9	N		74
	Responders	n (%)	18 (24.3)
	Non-Responders	n (%)	56 (75.7)
Week 12	N		64
	Responders	n (%)	15 (23.4)
	Non-Responders	n (%)	49 (76.6)
Week 18	N		49
	Responders	n (%)	9 (18.4)
	Non-Responders	n (%)	40 (81.6)
Week 24	N		41
	Responders	n (%)	9 (22.0)
	Non-Responders	n (%)	32 (78.0)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	7 (20.6)
	Non-Responders	n (%)	27 (79.4)
Week 36	N		32
	Responders	n (%)	7 (21.9)
	Non-Responders	n (%)	25 (78.1)
Week 42	N		25
	Responders	n (%)	4 (16.0)
	Non-Responders	n (%)	21 (84.0)
Week 48	N		22
	Responders	n (%)	3 (13.6)
	Non-Responders	n (%)	19 (86.4)
Week 54	N		17
	Responders	n (%)	2 (11.8)
	Non-Responders	n (%)	15 (88.2)
Week 60	N		12
	Responders	n (%)	2 (16.7)
	Non-Responders	n (%)	10 (83.3)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	2 (18.2)
	Non-Responders	n (%)	9 (81.8)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	9 (30.0)
	Non-Responders	n (%)	21 (70.0)
Safety Follow-up	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	9 (11.0)
	Non-Responders	n (%)	73 (89.0)
Week 6	N		79
	Responders	n (%)	8 (10.1)
	Non-Responders	n (%)	71 (89.9)
Week 9	N		74
	Responders	n (%)	14 (18.9)
	Non-Responders	n (%)	60 (81.1)
Week 12	N		62
	Responders	n (%)	8 (12.9)
	Non-Responders	n (%)	54 (87.1)
Week 18	N		48
	Responders	n (%)	9 (18.8)
	Non-Responders	n (%)	39 (81.3)
Week 24	N		40
	Responders	n (%)	6 (15.0)
	Non-Responders	n (%)	34 (85.0)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		32
	Responders	n (%)	5 (15.6)
	Non-Responders	n (%)	27 (84.4)
Week 36	N		31
	Responders	n (%)	4 (12.9)
	Non-Responders	n (%)	27 (87.1)
Week 42	N		25
	Responders	n (%)	3 (12.0)
	Non-Responders	n (%)	22 (88.0)
Week 48	N		22
	Responders	n (%)	4 (18.2)
	Non-Responders	n (%)	18 (81.8)
Week 54	N		16
	Responders	n (%)	2 (12.5)
	Non-Responders	n (%)	14 (87.5)
Week 60	N		13
	Responders	n (%)	2 (15.4)
	Non-Responders	n (%)	11 (84.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	2 (18.2)
	Non-Responders	n (%)	9 (81.8)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	0
	Non-Responders	n (%)	4 (100)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	1 (3.3)
	Non-Responders	n (%)	29 (96.7)
Safety Follow-up	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 1	N		6
	Responders	n (%)	0
	Non-Responders	n (%)	6 (100)
Survival Follow-up 2	N		3
	Responders	n (%)	0
	Non-Responders	n (%)	3 (100)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Table 15
Summary of Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-10) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 10 or as "Non-Responders" if change was < 10 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -10 or as "Non-Responders" if change was > -10 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:22:35 Datacut date: 01MAR2020

Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	21 (25.6)
	Non-Responders	n (%)	61 (74.4)
Week 6	N		79
	Responders	n (%)	24 (30.4)
	Non-Responders	n (%)	55 (69.6)
Week 9	N		75
	Responders	n (%)	26 (34.7)
	Non-Responders	n (%)	49 (65.3)
Week 12	N		65
	Responders	n (%)	24 (36.9)
	Non-Responders	n (%)	41 (63.1)
Week 18	N		49
	Responders	n (%)	20 (40.8)
	Non-Responders	n (%)	29 (59.2)
Week 24	N		41
	Responders	n (%)	12 (29.3)
	Non-Responders	n (%)	29 (70.7)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-16-EORTC-QLQ-C30-RESP
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	12 (35.3)
	Non-Responders	n (%)	22 (64.7)
Week 36	N		32
	Responders	n (%)	13 (40.6)
	Non-Responders	n (%)	19 (59.4)
Week 42	N		25
	Responders	n (%)	8 (32.0)
	Non-Responders	n (%)	17 (68.0)
Week 48	N		22
	Responders	n (%)	6 (27.3)
	Non-Responders	n (%)	16 (72.7)
Week 54	N		17
	Responders	n (%)	8 (47.1)
	Non-Responders	n (%)	9 (52.9)
Week 60	N		13
	Responders	n (%)	2 (15.4)
	Non-Responders	n (%)	11 (84.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	5 (45.5)
	Non-Responders	n (%)	6 (54.5)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Rundate: 01DEC2020:06:28:38 Datacut date: 01MAR2020

Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	5 (16.7)
	Non-Responders	n (%)	25 (83.3)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Global QOL Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-16-EORTC-QLQ-C30-RESP
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	7 (8.5)
	Non-Responders	n (%)	75 (91.5)
Week 6	N		78
	Responders	n (%)	7 (9.0)
	Non-Responders	n (%)	71 (91.0)
Week 9	N		75
	Responders	n (%)	12 (16.0)
	Non-Responders	n (%)	63 (84.0)
Week 12	N		65
	Responders	n (%)	9 (13.8)
	Non-Responders	n (%)	56 (86.2)
Week 18	N		49
	Responders	n (%)	8 (16.3)
	Non-Responders	n (%)	41 (83.7)
Week 24	N		42
	Responders	n (%)	7 (16.7)
	Non-Responders	n (%)	35 (83.3)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	5 (14.7)
	Non-Responders	n (%)	29 (85.3)
Week 36	N		32
	Responders	n (%)	7 (21.9)
	Non-Responders	n (%)	25 (78.1)
Week 42	N		23
	Responders	n (%)	2 (8.7)
	Non-Responders	n (%)	21 (91.3)
Week 48	N		22
	Responders	n (%)	4 (18.2)
	Non-Responders	n (%)	18 (81.8)
Week 54	N		18
	Responders	n (%)	4 (22.2)
	Non-Responders	n (%)	14 (77.8)
Week 60	N		13
	Responders	n (%)	2 (15.4)
	Non-Responders	n (%)	11 (84.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	2 (6.7)
	Non-Responders	n (%)	28 (93.3)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Physical Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		81
	Responders	n (%)	16 (19.8)
	Non-Responders	n (%)	65 (80.2)
Week 6	N		78
	Responders	n (%)	20 (25.6)
	Non-Responders	n (%)	58 (74.4)
Week 9	N		75
	Responders	n (%)	25 (33.3)
	Non-Responders	n (%)	50 (66.7)
Week 12	N		65
	Responders	n (%)	20 (30.8)
	Non-Responders	n (%)	45 (69.2)
Week 18	N		48
	Responders	n (%)	18 (37.5)
	Non-Responders	n (%)	30 (62.5)
Week 24	N		41
	Responders	n (%)	13 (31.7)
	Non-Responders	n (%)	28 (68.3)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	13 (38.2)
	Non-Responders	n (%)	21 (61.8)
Week 36	N		32
	Responders	n (%)	15 (46.9)
	Non-Responders	n (%)	17 (53.1)
Week 42	N		25
	Responders	n (%)	10 (40.0)
	Non-Responders	n (%)	15 (60.0)
Week 48	N		22
	Responders	n (%)	7 (31.8)
	Non-Responders	n (%)	15 (68.2)
Week 54	N		18
	Responders	n (%)	5 (27.8)
	Non-Responders	n (%)	13 (72.2)
Week 60	N		13
	Responders	n (%)	3 (23.1)
	Non-Responders	n (%)	10 (76.9)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	3 (33.3)
	Non-Responders	n (%)	6 (66.7)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	6 (20.0)
	Non-Responders	n (%)	24 (80.0)
Safety Follow-up	N		6
	Responders	n (%)	3 (50.0)
	Non-Responders	n (%)	3 (50.0)
Survival Follow-up 1	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Role Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	22 (26.8)
	Non-Responders	n (%)	60 (73.2)
Week 6	N		79
	Responders	n (%)	22 (27.8)
	Non-Responders	n (%)	57 (72.2)
Week 9	N		75
	Responders	n (%)	23 (30.7)
	Non-Responders	n (%)	52 (69.3)
Week 12	N		65
	Responders	n (%)	17 (26.2)
	Non-Responders	n (%)	48 (73.8)
Week 18	N		49
	Responders	n (%)	16 (32.7)
	Non-Responders	n (%)	33 (67.3)
Week 24	N		41
	Responders	n (%)	16 (39.0)
	Non-Responders	n (%)	25 (61.0)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	10 (29.4)
	Non-Responders	n (%)	24 (70.6)
Week 36	N		32
	Responders	n (%)	11 (34.4)
	Non-Responders	n (%)	21 (65.6)
Week 42	N		25
	Responders	n (%)	9 (36.0)
	Non-Responders	n (%)	16 (64.0)
Week 48	N		22
	Responders	n (%)	7 (31.8)
	Non-Responders	n (%)	15 (68.2)
Week 54	N		17
	Responders	n (%)	7 (41.2)
	Non-Responders	n (%)	10 (58.8)
Week 60	N		13
	Responders	n (%)	5 (38.5)
	Non-Responders	n (%)	8 (61.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	6 (54.5)
	Non-Responders	n (%)	5 (45.5)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	7 (23.3)
	Non-Responders	n (%)	23 (76.7)
Safety Follow-up	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Emotional Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	16 (19.5)
	Non-Responders	n (%)	66 (80.5)
Week 6	N		79
	Responders	n (%)	15 (19.0)
	Non-Responders	n (%)	64 (81.0)
Week 9	N		75
	Responders	n (%)	20 (26.7)
	Non-Responders	n (%)	55 (73.3)
Week 12	N		65
	Responders	n (%)	13 (20.0)
	Non-Responders	n (%)	52 (80.0)
Week 18	N		49
	Responders	n (%)	9 (18.4)
	Non-Responders	n (%)	40 (81.6)
Week 24	N		41
	Responders	n (%)	9 (22.0)
	Non-Responders	n (%)	32 (78.0)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	7 (20.6)
	Non-Responders	n (%)	27 (79.4)
Week 36	N		32
	Responders	n (%)	6 (18.8)
	Non-Responders	n (%)	26 (81.3)
Week 42	N		25
	Responders	n (%)	4 (16.0)
	Non-Responders	n (%)	21 (84.0)
Week 48	N		22
	Responders	n (%)	4 (18.2)
	Non-Responders	n (%)	18 (81.8)
Week 54	N		17
	Responders	n (%)	2 (11.8)
	Non-Responders	n (%)	15 (88.2)
Week 60	N		13
	Responders	n (%)	2 (15.4)
	Non-Responders	n (%)	11 (84.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-16-EORTC-QLQ-C30-RESP
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	6 (20.0)
	Non-Responders	n (%)	24 (80.0)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	3 (100)
	Non-Responders	n (%)	0
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Cognitive Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		81
	Responders	n (%)	24 (29.6)
	Non-Responders	n (%)	57 (70.4)
Week 6	N		79
	Responders	n (%)	29 (36.7)
	Non-Responders	n (%)	50 (63.3)
Week 9	N		74
	Responders	n (%)	29 (39.2)
	Non-Responders	n (%)	45 (60.8)
Week 12	N		64
	Responders	n (%)	23 (35.9)
	Non-Responders	n (%)	41 (64.1)
Week 18	N		48
	Responders	n (%)	21 (43.8)
	Non-Responders	n (%)	27 (56.3)
Week 24	N		41
	Responders	n (%)	18 (43.9)
	Non-Responders	n (%)	23 (56.1)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	16 (47.1)
	Non-Responders	n (%)	18 (52.9)
Week 36	N		31
	Responders	n (%)	15 (48.4)
	Non-Responders	n (%)	16 (51.6)
Week 42	N		25
	Responders	n (%)	11 (44.0)
	Non-Responders	n (%)	14 (56.0)
Week 48	N		22
	Responders	n (%)	10 (45.5)
	Non-Responders	n (%)	12 (54.5)
Week 54	N		16
	Responders	n (%)	6 (37.5)
	Non-Responders	n (%)	10 (62.5)
Week 60	N		13
	Responders	n (%)	5 (38.5)
	Non-Responders	n (%)	8 (61.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	4 (36.4)
	Non-Responders	n (%)	7 (63.6)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	8 (26.7)
	Non-Responders	n (%)	22 (73.3)
Safety Follow-up	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 1	N		6
	Responders	n (%)	3 (50.0)
	Non-Responders	n (%)	3 (50.0)
Survival Follow-up 2	N		3
	Responders	n (%)	3 (100)
	Non-Responders	n (%)	0
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Social Functioning Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	6 (7.3)
	Non-Responders	n (%)	76 (92.7)
Week 6	N		79
	Responders	n (%)	10 (12.7)
	Non-Responders	n (%)	69 (87.3)
Week 9	N		75
	Responders	n (%)	16 (21.3)
	Non-Responders	n (%)	59 (78.7)
Week 12	N		65
	Responders	n (%)	17 (26.2)
	Non-Responders	n (%)	48 (73.8)
Week 18	N		49
	Responders	n (%)	14 (28.6)
	Non-Responders	n (%)	35 (71.4)
Week 24	N		42
	Responders	n (%)	9 (21.4)
	Non-Responders	n (%)	33 (78.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	6 (17.6)
	Non-Responders	n (%)	28 (82.4)
Week 36	N		32
	Responders	n (%)	7 (21.9)
	Non-Responders	n (%)	25 (78.1)
Week 42	N		25
	Responders	n (%)	5 (20.0)
	Non-Responders	n (%)	20 (80.0)
Week 48	N		22
	Responders	n (%)	4 (18.2)
	Non-Responders	n (%)	18 (81.8)
Week 54	N		18
	Responders	n (%)	5 (27.8)
	Non-Responders	n (%)	13 (72.2)
Week 60	N		13
	Responders	n (%)	3 (23.1)
	Non-Responders	n (%)	10 (76.9)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	4 (13.3)
	Non-Responders	n (%)	26 (86.7)
Safety Follow-up	N		6
	Responders	n (%)	3 (50.0)
	Non-Responders	n (%)	3 (50.0)
Survival Follow-up 1	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Fatigue Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	11 (13.4)
	Non-Responders	n (%)	71 (86.6)
Week 6	N		79
	Responders	n (%)	13 (16.5)
	Non-Responders	n (%)	66 (83.5)
Week 9	N		75
	Responders	n (%)	18 (24.0)
	Non-Responders	n (%)	57 (76.0)
Week 12	N		65
	Responders	n (%)	15 (23.1)
	Non-Responders	n (%)	50 (76.9)
Week 18	N		49
	Responders	n (%)	12 (24.5)
	Non-Responders	n (%)	37 (75.5)
Week 24	N		42
	Responders	n (%)	14 (33.3)
	Non-Responders	n (%)	28 (66.7)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	10 (29.4)
	Non-Responders	n (%)	24 (70.6)
Week 36	N		32
	Responders	n (%)	9 (28.1)
	Non-Responders	n (%)	23 (71.9)
Week 42	N		25
	Responders	n (%)	4 (16.0)
	Non-Responders	n (%)	21 (84.0)
Week 48	N		22
	Responders	n (%)	5 (22.7)
	Non-Responders	n (%)	17 (77.3)
Week 54	N		18
	Responders	n (%)	5 (27.8)
	Non-Responders	n (%)	13 (72.2)
Week 60	N		13
	Responders	n (%)	3 (23.1)
	Non-Responders	n (%)	10 (76.9)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	3 (27.3)
	Non-Responders	n (%)	8 (72.7)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
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(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	6 (20.0)
	Non-Responders	n (%)	24 (80.0)
Safety Follow-up	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Nausea & Vomiting Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-16-EORTC-QLQ-C30-RESP
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	26 (31.7)
	Non-Responders	n (%)	56 (68.3)
Week 6	N		79
	Responders	n (%)	33 (41.8)
	Non-Responders	n (%)	46 (58.2)
Week 9	N		75
	Responders	n (%)	37 (49.3)
	Non-Responders	n (%)	38 (50.7)
Week 12	N		65
	Responders	n (%)	30 (46.2)
	Non-Responders	n (%)	35 (53.8)
Week 18	N		49
	Responders	n (%)	24 (49.0)
	Non-Responders	n (%)	25 (51.0)
Week 24	N		42
	Responders	n (%)	20 (47.6)
	Non-Responders	n (%)	22 (52.4)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	19 (55.9)
	Non-Responders	n (%)	15 (44.1)
Week 36	N		32
	Responders	n (%)	18 (56.3)
	Non-Responders	n (%)	14 (43.8)
Week 42	N		25
	Responders	n (%)	12 (48.0)
	Non-Responders	n (%)	13 (52.0)
Week 48	N		22
	Responders	n (%)	11 (50.0)
	Non-Responders	n (%)	11 (50.0)
Week 54	N		18
	Responders	n (%)	7 (38.9)
	Non-Responders	n (%)	11 (61.1)
Week 60	N		13
	Responders	n (%)	7 (53.8)
	Non-Responders	n (%)	6 (46.2)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	7 (63.6)
	Non-Responders	n (%)	4 (36.4)
Week 72	N		9
	Responders	n (%)	5 (55.6)
	Non-Responders	n (%)	4 (44.4)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	9 (30.0)
	Non-Responders	n (%)	21 (70.0)
Safety Follow-up	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 1	N		6
	Responders	n (%)	3 (50.0)
	Non-Responders	n (%)	3 (50.0)
Survival Follow-up 2	N		3
	Responders	n (%)	3 (100)
	Non-Responders	n (%)	0
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Pain Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-16-EORTC-QLQ-C30-RESP
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		80
	Responders	n (%)	6 (7.5)
	Non-Responders	n (%)	74 (92.5)
Week 6	N		78
	Responders	n (%)	8 (10.3)
	Non-Responders	n (%)	70 (89.7)
Week 9	N		73
	Responders	n (%)	9 (12.3)
	Non-Responders	n (%)	64 (87.7)
Week 12	N		63
	Responders	n (%)	8 (12.7)
	Non-Responders	n (%)	55 (87.3)
Week 18	N		48
	Responders	n (%)	6 (12.5)
	Non-Responders	n (%)	42 (87.5)
Week 24	N		41
	Responders	n (%)	8 (19.5)
	Non-Responders	n (%)	33 (80.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	5 (14.7)
	Non-Responders	n (%)	29 (85.3)
Week 36	N		32
	Responders	n (%)	5 (15.6)
	Non-Responders	n (%)	27 (84.4)
Week 42	N		25
	Responders	n (%)	3 (12.0)
	Non-Responders	n (%)	22 (88.0)
Week 48	N		22
	Responders	n (%)	2 (9.1)
	Non-Responders	n (%)	20 (90.9)
Week 54	N		18
	Responders	n (%)	2 (11.1)
	Non-Responders	n (%)	16 (88.9)
Week 60	N		13
	Responders	n (%)	1 (7.7)
	Non-Responders	n (%)	12 (92.3)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	1 (9.1)
	Non-Responders	n (%)	10 (90.9)
Week 72	N		9
	Responders	n (%)	0
	Non-Responders	n (%)	9 (100)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	0
	Non-Responders	n (%)	4 (100)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		29
	Responders	n (%)	4 (13.8)
	Non-Responders	n (%)	25 (86.2)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	0
	Non-Responders	n (%)	3 (100)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Dyspnea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		81
	Responders	n (%)	22 (27.2)
	Non-Responders	n (%)	59 (72.8)
Week 6	N		79
	Responders	n (%)	21 (26.6)
	Non-Responders	n (%)	58 (73.4)
Week 9	N		73
	Responders	n (%)	26 (35.6)
	Non-Responders	n (%)	47 (64.4)
Week 12	N		65
	Responders	n (%)	25 (38.5)
	Non-Responders	n (%)	40 (61.5)
Week 18	N		48
	Responders	n (%)	11 (22.9)
	Non-Responders	n (%)	37 (77.1)
Week 24	N		41
	Responders	n (%)	12 (29.3)
	Non-Responders	n (%)	29 (70.7)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	8 (23.5)
	Non-Responders	n (%)	26 (76.5)
Week 36	N		32
	Responders	n (%)	13 (40.6)
	Non-Responders	n (%)	19 (59.4)
Week 42	N		25
	Responders	n (%)	7 (28.0)
	Non-Responders	n (%)	18 (72.0)
Week 48	N		22
	Responders	n (%)	9 (40.9)
	Non-Responders	n (%)	13 (59.1)
Week 54	N		18
	Responders	n (%)	7 (38.9)
	Non-Responders	n (%)	11 (61.1)
Week 60	N		13
	Responders	n (%)	5 (38.5)
	Non-Responders	n (%)	8 (61.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	7 (63.6)
	Non-Responders	n (%)	4 (36.4)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	3 (42.9)
	Non-Responders	n (%)	4 (57.1)
Week 84	N		4
	Responders	n (%)	2 (50.0)
	Non-Responders	n (%)	2 (50.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	9 (30.0)
	Non-Responders	n (%)	21 (70.0)
Safety Follow-up	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 1	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Insomnia Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	13 (15.9)
	Non-Responders	n (%)	69 (84.1)
Week 6	N		79
	Responders	n (%)	17 (21.5)
	Non-Responders	n (%)	62 (78.5)
Week 9	N		75
	Responders	n (%)	22 (29.3)
	Non-Responders	n (%)	53 (70.7)
Week 12	N		65
	Responders	n (%)	21 (32.3)
	Non-Responders	n (%)	44 (67.7)
Week 18	N		49
	Responders	n (%)	20 (40.8)
	Non-Responders	n (%)	29 (59.2)
Week 24	N		42
	Responders	n (%)	12 (28.6)
	Non-Responders	n (%)	30 (71.4)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	11 (32.4)
	Non-Responders	n (%)	23 (67.6)
Week 36	N		32
	Responders	n (%)	11 (34.4)
	Non-Responders	n (%)	21 (65.6)
Week 42	N		25
	Responders	n (%)	9 (36.0)
	Non-Responders	n (%)	16 (64.0)
Week 48	N		22
	Responders	n (%)	7 (31.8)
	Non-Responders	n (%)	15 (68.2)
Week 54	N		18
	Responders	n (%)	8 (44.4)
	Non-Responders	n (%)	10 (55.6)
Week 60	N		13
	Responders	n (%)	4 (30.8)
	Non-Responders	n (%)	9 (69.2)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
Program: T:\Common\Clinical Operations\Programming\PD-1\4010-01-001-Part2B\GVD\Program\Tables\t-16-EORTC-QLQ-C30-RESP
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	4 (36.4)
	Non-Responders	n (%)	7 (63.6)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	7 (23.3)
	Non-Responders	n (%)	23 (76.7)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	4 (66.7)
	Non-Responders	n (%)	2 (33.3)
Survival Follow-up 2	N		3
	Responders	n (%)	2 (66.7)
	Non-Responders	n (%)	1 (33.3)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Appetite loss Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	12 (14.6)
	Non-Responders	n (%)	70 (85.4)
Week 6	N		79
	Responders	n (%)	16 (20.3)
	Non-Responders	n (%)	63 (79.7)
Week 9	N		75
	Responders	n (%)	19 (25.3)
	Non-Responders	n (%)	56 (74.7)
Week 12	N		65
	Responders	n (%)	11 (16.9)
	Non-Responders	n (%)	54 (83.1)
Week 18	N		48
	Responders	n (%)	9 (18.8)
	Non-Responders	n (%)	39 (81.3)
Week 24	N		41
	Responders	n (%)	7 (17.1)
	Non-Responders	n (%)	34 (82.9)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		33
	Responders	n (%)	6 (18.2)
	Non-Responders	n (%)	27 (81.8)
Week 36	N		32
	Responders	n (%)	7 (21.9)
	Non-Responders	n (%)	25 (78.1)
Week 42	N		25
	Responders	n (%)	4 (16.0)
	Non-Responders	n (%)	21 (84.0)
Week 48	N		22
	Responders	n (%)	5 (22.7)
	Non-Responders	n (%)	17 (77.3)
Week 54	N		18
	Responders	n (%)	5 (27.8)
	Non-Responders	n (%)	13 (72.2)
Week 60	N		13
	Responders	n (%)	5 (38.5)
	Non-Responders	n (%)	8 (61.5)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	4 (36.4)
	Non-Responders	n (%)	7 (63.6)
Week 72	N		9
	Responders	n (%)	4 (44.4)
	Non-Responders	n (%)	5 (55.6)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	8 (26.7)
	Non-Responders	n (%)	22 (73.3)
Safety Follow-up	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0
Survival Follow-up 4	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Constipation Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	1 (100)
	Non-Responders	n (%)	0

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		81
	Responders	n (%)	16 (19.8)
	Non-Responders	n (%)	65 (80.2)
Week 6	N		78
	Responders	n (%)	17 (21.8)
	Non-Responders	n (%)	61 (78.2)
Week 9	N		74
	Responders	n (%)	18 (24.3)
	Non-Responders	n (%)	56 (75.7)
Week 12	N		64
	Responders	n (%)	15 (23.4)
	Non-Responders	n (%)	49 (76.6)
Week 18	N		49
	Responders	n (%)	9 (18.4)
	Non-Responders	n (%)	40 (81.6)
Week 24	N		41
	Responders	n (%)	9 (22.0)
	Non-Responders	n (%)	32 (78.0)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		34
	Responders	n (%)	7 (20.6)
	Non-Responders	n (%)	27 (79.4)
Week 36	N		32
	Responders	n (%)	7 (21.9)
	Non-Responders	n (%)	25 (78.1)
Week 42	N		25
	Responders	n (%)	4 (16.0)
	Non-Responders	n (%)	21 (84.0)
Week 48	N		22
	Responders	n (%)	3 (13.6)
	Non-Responders	n (%)	19 (86.4)
Week 54	N		17
	Responders	n (%)	2 (11.8)
	Non-Responders	n (%)	15 (88.2)
Week 60	N		12
	Responders	n (%)	2 (16.7)
	Non-Responders	n (%)	10 (83.3)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	2 (18.2)
	Non-Responders	n (%)	9 (81.8)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	1 (14.3)
	Non-Responders	n (%)	6 (85.7)
Week 84	N		4
	Responders	n (%)	1 (25.0)
	Non-Responders	n (%)	3 (75.0)
Week 90	N		2
	Responders	n (%)	1 (50.0)
	Non-Responders	n (%)	1 (50.0)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	9 (30.0)
	Non-Responders	n (%)	21 (70.0)
Safety Follow-up	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 1	N		6
	Responders	n (%)	2 (33.3)
	Non-Responders	n (%)	4 (66.7)
Survival Follow-up 2	N		3
	Responders	n (%)	1 (33.3)
	Non-Responders	n (%)	2 (66.7)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Diarrhea Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 3	N		82
	Responders	n (%)	9 (11.0)
	Non-Responders	n (%)	73 (89.0)
Week 6	N		79
	Responders	n (%)	8 (10.1)
	Non-Responders	n (%)	71 (89.9)
Week 9	N		74
	Responders	n (%)	14 (18.9)
	Non-Responders	n (%)	60 (81.1)
Week 12	N		62
	Responders	n (%)	8 (12.9)
	Non-Responders	n (%)	54 (87.1)
Week 18	N		48
	Responders	n (%)	9 (18.8)
	Non-Responders	n (%)	39 (81.3)
Week 24	N		40
	Responders	n (%)	6 (15.0)
	Non-Responders	n (%)	34 (85.0)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 30	N		32
	Responders	n (%)	5 (15.6)
	Non-Responders	n (%)	27 (84.4)
Week 36	N		31
	Responders	n (%)	4 (12.9)
	Non-Responders	n (%)	27 (87.1)
Week 42	N		25
	Responders	n (%)	3 (12.0)
	Non-Responders	n (%)	22 (88.0)
Week 48	N		22
	Responders	n (%)	4 (18.2)
	Non-Responders	n (%)	18 (81.8)
Week 54	N		16
	Responders	n (%)	2 (12.5)
	Non-Responders	n (%)	14 (87.5)
Week 60	N		13
	Responders	n (%)	2 (15.4)
	Non-Responders	n (%)	11 (84.6)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Week 66	N		11
	Responders	n (%)	2 (18.2)
	Non-Responders	n (%)	9 (81.8)
Week 72	N		9
	Responders	n (%)	2 (22.2)
	Non-Responders	n (%)	7 (77.8)
Week 78	N		7
	Responders	n (%)	2 (28.6)
	Non-Responders	n (%)	5 (71.4)
Week 84	N		4
	Responders	n (%)	0
	Non-Responders	n (%)	4 (100)
Week 90	N		2
	Responders	n (%)	0
	Non-Responders	n (%)	2 (100)
Week 96	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
End of Treatment	N		30
	Responders	n (%)	1 (3.3)
	Non-Responders	n (%)	29 (96.7)
Safety Follow-up	N		6
	Responders	n (%)	1 (16.7)
	Non-Responders	n (%)	5 (83.3)
Survival Follow-up 1	N		6
	Responders	n (%)	0
	Non-Responders	n (%)	6 (100)
Survival Follow-up 2	N		3
	Responders	n (%)	0
	Non-Responders	n (%)	3 (100)
Survival Follow-up 3	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)
Survival Follow-up 4	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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Table 16
Summary and Frequency and Proportion of Responders in EORTC-QLQ-C30 (MCID = +/-15) - Cohort A1
(Safety Analysis Set)

EORTC: Financial difficulties Score

Visit	Category [1]	Statistic	COHORT A1 (N=129)
Survival Follow-up 5	N		1
	Responders	n (%)	0
	Non-Responders	n (%)	1 (100)

[1] For Global Health and Functional Scales, subjects were categorized as "Responders" if change from baseline was >= 15 or as "Non-Responders" if change was < 15 or if they were too ill to provide a response to the questionnaire. For Symptom scales and Single Items, subjects were categorized as "Responders" if change from baseline was <= -15 or as "Non-Responders" if change was > -15 or if they were too ill to provide a response to the questionnaire.
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Global Health Status/QOL Change from baseline at End of C3	n	161	163
	Mean	-2.2	-4.3
	SD	21.20	21.54
	Median	0.0	0.0
	Q1;Q3	-17;8	-17;8
	Range	-67;50	-100;67
Global Health Status/QOL Change from baseline at End of C6	n	104	99
	Mean	-2.1	-5.0
	SD	23.19	25.05
	Median	0.0	0.0
	Q1;Q3	-17;8	-17;8
	Range	-67;100	-67;58

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Global Health Status/QOL Change from baseline at End of therapy	n	138	138
	Mean	-9.6	-11.7
	SD	25.37	26.42
	Median	-8.3	-8.3
	Q1;Q3	-25;0	-33;8
	Range	-67;75	-83;67
Global Health Status/QOL Change from baseline at Follow-up 1 visit	n	49	43
	Mean	-1.2	-12.4
	SD	20.62	26.87
	Median	0.0	-8.3
	Q1;Q3	-8;8	-17;0
	Range	-58;58	-83;58
Global Health Status/QOL Change from baseline at Follow-up 2 visit	n	31	20
	Mean	-0.3	-7.1
	SD	22.62	30.38
	Median	0.0	-12.5
	Q1;Q3	-8;17	-25;13
	Range	-50;67	-67;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Global Health Status/QOL	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-6.7	-7.5
	SD	24.64	32.74
	Median	-8.3	-4.2
	Q1;Q3	-17;0	-17;0
	Range	-42;50	-58;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Physical Functioning Change from baseline at End of C3	n	162	164
	Mean	-6.5	-7.9
	SD	17.42	18.91
	Median	0.0	-6.7
	Q1;Q3	-13;0	-13;0
	Range	-80;33	-100;47
Physical Functioning Change from baseline at End of C6	n	103	99
	Mean	-8.3	-7.9
	SD	16.10	17.37
	Median	-6.7	-6.7
	Q1;Q3	-13;0	-20;5
	Range	-53;40	-60;27

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Physical Functioning	n	140	138
Change from baseline at End of therapy	Mean	-14.0	-15.3
	SD	20.37	21.98
	Median	-6.7	-13.3
	Q1;Q3	-20;0	-27;0
	Range	-87;33	-100;27
Physical Functioning	n	49	43
Change from baseline at Follow-up 1 visit	Mean	-4.4	-13.4
	SD	14.20	20.58
	Median	-6.7	-6.7
	Q1;Q3	-13;0	-20;0
	Range	-33;40	-80;20
Physical Functioning	n	31	20
Change from baseline at Follow-up 2 visit	Mean	-2.4	-12.9
	SD	13.17	24.25
	Median	0.0	-6.7
	Q1;Q3	-7;0	-36;0
	Range	-33;40	-60;27

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Physical Functioning	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-1.8	-6.2
	SD	14.58	15.15
	Median	0.0	-6.7
	Q1;Q3	-20;7	-13;7
	Range	-27;27	-28;20

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Role Functioning Change from baseline at End of C3	n	161	164
	Mean	-8.7	-11.1
	SD	28.99	26.96
	Median	0.0	0.0
	Q1;Q3	-33;0	-33;0
	Range	-100;67	-100;83
Role Functioning Change from baseline at End of C6	n	104	99
	Mean	-9.6	-8.2
	SD	28.03	27.91
	Median	0.0	0.0
	Q1;Q3	-25;0	-33;0
	Range	-100;67	-100;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Role Functioning Change from baseline at End of therapy	n	140	138
	Mean	-21.7	-22.5
	SD	31.34	30.91
	Median	-16.7	-16.7
	Q1;Q3	-33;0	-33;0
	Range	-100;67	-100;67
Role Functioning Change from baseline at Follow-up 1 visit	n	49	43
	Mean	-5.1	-19.0
	SD	20.19	30.12
	Median	0.0	-16.7
	Q1;Q3	-17;0	-33;0
	Range	-67;50	-100;33
Role Functioning Change from baseline at Follow-up 2 visit	n	31	20
	Mean	-2.7	-10.8
	SD	13.67	23.12
	Median	0.0	0.0
	Q1;Q3	-17;0	-25;0
	Range	-33;33	-67;17

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Role Functioning	n	15	9
Change from baseline at Follow-up 3 visit	Mean	-5.6	-11.1
	SD	15.00	25.00
	Median	0.0	-16.7
	Q1;Q3	-17;0	-33;17
	Range	-33;17	-50;17

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Emotional Functioning Change from baseline at End of C3	n	161	164
	Mean	1.0	1.6
	SD	18.56	21.75
	Median	0.0	0.0
	Q1;Q3	-8;8	-8;8
	Range	-67;50	-75;67
Emotional Functioning Change from baseline at End of C6	n	104	99
	Mean	1.3	2.9
	SD	20.36	21.64
	Median	0.0	0.0
	Q1;Q3	-8;8	-8;17
	Range	-67;58	-50;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Emotional Functioning	n	139	137
Change from baseline at End of therapy	Mean	-3.6	-2.1
	SD	22.15	24.51
	Median	0.0	0.0
	Q1;Q3	-17;8	-17;8
	Range	-67;50	-92;67
Emotional Functioning	n	49	43
Change from baseline at Follow-up 1 visit	Mean	4.6	-0.8
	SD	17.27	24.52
	Median	0.0	0.0
	Q1;Q3	0;17	-17;8
	Range	-33;50	-58;67
Emotional Functioning	n	31	20
Change from baseline at Follow-up 2 visit	Mean	5.6	2.5
	SD	16.72	21.81
	Median	0.0	0.0
	Q1;Q3	0;17	-17;13
	Range	-33;58	-25;50

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Emotional Functioning	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-1.3	4.2
	SD	29.69	29.20
	Median	8.3	0.0
	Q1;Q3	-25;17	-8;8
	Range	-78;33	-50;58

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Cognitive Functioning Change from baseline at End of C3	n	161	164
	Mean	-3.3	-3.6
	SD	20.98	21.51
	Median	0.0	0.0
	Q1;Q3	-17;0	-17;0
	Range	-67;67	-67;83
Cognitive Functioning Change from baseline at End of C6	n	104	99
	Mean	-4.2	-6.2
	SD	17.80	18.22
	Median	0.0	0.0
	Q1;Q3	-17;0	-17;0
	Range	-50;83	-67;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Cognitive Functioning Change from baseline at End of therapy	n	139	137
	Mean	-7.0	-8.6
	SD	22.51	22.79
	Median	0.0	0.0
	Q1;Q3	-17;0	-17;0
	Range	-83;50	-83;50
Cognitive Functioning Change from baseline at Follow-up 1 visit	n	49	43
	Mean	-3.7	-13.2
	SD	11.91	24.00
	Median	0.0	0.0
	Q1;Q3	0;0	-33;0
	Range	-33;33	-83;33
Cognitive Functioning Change from baseline at Follow-up 2 visit	n	31	20
	Mean	-5.9	-2.5
	SD	15.24	28.75
	Median	0.0	0.0
	Q1;Q3	-17;0	-17;17
	Range	-50;33	-83;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Cognitive Functioning	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-6.7	-11.7
	SD	16.43	22.29
	Median	0.0	-8.3
	Q1;Q3	-17;0	-33;0
	Range	-33;33	-33;33

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Social Functioning Change from baseline at End of C3	n	161	164
	Mean	-3.1	-9.8
	SD	23.95	26.04
	Median	0.0	0.0
	Q1;Q3	-17;0	-17;0
	Range	-100;67	-100;67
Social Functioning Change from baseline at End of C6	n	104	99
	Mean	-5.6	-7.9
	SD	22.23	30.52
	Median	0.0	0.0
	Q1;Q3	-17;0	-33;0
	Range	-67;67	-83;83

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Social Functioning Change from baseline at End of therapy	n	138	137
	Mean	-12.9	-15.2
	SD	28.48	31.54
	Median	0.0	0.0
	Q1;Q3	-33;0	-33;0
	Range	-100;67	-100;83
Social Functioning Change from baseline at Follow-up 1 visit	n	48	43
	Mean	-0.3	-11.2
	SD	25.61	29.93
	Median	0.0	0.0
	Q1;Q3	-17;0	-33;0
	Range	-67;67	-100;67
Social Functioning Change from baseline at Follow-up 2 visit	n	31	20
	Mean	-2.2	-4.2
	SD	11.97	27.51
	Median	0.0	0.0
	Q1;Q3	-17;0	-17;0
	Range	-33;17	-67;50

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Social Functioning	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-2.2	-15.0
	SD	21.70	27.72
	Median	0.0	-16.7
	Q1;Q3	0;0	-33;0
	Range	-67;33	-50;50

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Fatigue	n	162	164
Change from baseline at End of C3	Mean	10.5	12.1
	SD	23.80	25.60
	Median	11.1	11.1
	Q1;Q3	0;22	0;22
	Range	-56;67	-67;89
Fatigue	n	104	99
Change from baseline at End of C6	Mean	10.4	12.3
	SD	25.84	24.67
	Median	0.0	11.1
	Q1;Q3	0;22	0;33
	Range	-44;89	-56;78

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Fatigue Change from baseline at End of therapy	n	140	138
	Mean	17.3	19.6
	SD	25.31	27.85
	Median	11.1	11.1
	Q1;Q3	0;33	0;33
	Range	-44;100	-56;89
Fatigue Change from baseline at Follow-up 1 visit	n	49	43
	Mean	5.9	15.5
	SD	20.17	27.45
	Median	11.1	11.1
	Q1;Q3	0;11	0;33
	Range	-33;44	-44;78
Fatigue Change from baseline at Follow-up 2 visit	n	31	20
	Mean	6.8	22.2
	SD	20.62	28.61
	Median	0.0	27.8
	Q1;Q3	-11;22	0;44
	Range	-33;44	-44;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Fatigue	n	15	10
Change from baseline at Follow-up 3 visit	Mean	1.5	9.4
	SD	21.77	34.35
	Median	0.0	5.6
	Q1;Q3	-11;11	-11;33
	Range	-33;56	-44;78

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Nausea/Vomiting Change from baseline at End of C3	n	161	164
	Mean	9.2	7.3
	SD	24.64	23.15
	Median	0.0	0.0
	Q1;Q3	0;17	0;17
	Range	-67;100	-83;83
Nausea/Vomiting Change from baseline at End of C6	n	104	98
	Mean	6.1	10.5
	SD	22.64	22.11
	Median	0.0	0.0
	Q1;Q3	0;17	0;17
	Range	-83;83	-50;83

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Nausea/Vomiting	n	140	138
Change from baseline at End of therapy	Mean	11.2	9.2
	SD	27.08	22.97
	Median	0.0	0.0
	Q1;Q3	0;17	0;17
	Range	-67;100	-50;83
Nausea/Vomiting	n	49	43
Change from baseline at Follow-up 1 visit	Mean	-0.3	5.4
	SD	12.95	15.31
	Median	0.0	0.0
	Q1;Q3	0;0	0;17
	Range	-67;33	-17;50
Nausea/Vomiting	n	31	20
Change from baseline at Follow-up 2 visit	Mean	3.2	7.5
	SD	13.21	16.64
	Median	0.0	0.0
	Q1;Q3	0;0	0;8
	Range	-17;50	0;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Nausea/Vomiting	n	15	10
Change from baseline at Follow-up 3 visit	Mean	4.4	1.7
	SD	7.63	12.30
	Median	0.0	0.0
	Q1;Q3	0;17	0;17
	Range	0;17	-17;17

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain	n	162	164
Change from baseline at End of C3	Mean	-2.8	0.9
	SD	26.02	27.77
	Median	0.0	0.0
	Q1;Q3	-17;0	0;0
	Range	-100;50	-100;100
Pain	n	104	99
Change from baseline at End of C6	Mean	-1.0	0.0
	SD	25.32	24.51
	Median	0.0	0.0
	Q1;Q3	0;0	0;17
	Range	-100;83	-83;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain	n	140	138
Change from baseline at End of therapy	Mean	5.1	8.2
	SD	26.59	28.50
	Median	0.0	0.0
	Q1;Q3	0;17	0;17
	Range	-100;100	-83;83
Pain	n	49	43
Change from baseline at Follow-up 1 visit	Mean	3.7	8.1
	SD	17.10	28.49
	Median	0.0	0.0
	Q1;Q3	0;17	0;17
	Range	-33;50	-83;83
Pain	n	31	20
Change from baseline at Follow-up 2 visit	Mean	7.0	6.7
	SD	20.98	23.82
	Median	0.0	8.3
	Q1;Q3	0;17	-17;17
	Range	-33;67	-33;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-2.2	-5.0
	SD	18.76	20.86
	Median	0.0	0.0
	Q1;Q3	-17;17	-17;0
	Range	-33;33	-50;33

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Dyspnoea	n	162	164
Change from baseline at End of C3	Mean	1.9	6.5
	SD	25.81	26.34
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-100;100	-33;100
Dyspnoea	n	104	98
Change from baseline at End of C6	Mean	2.2	7.8
	SD	23.80	26.13
	Median	0.0	0.0
	Q1;Q3	0;0	0;33
	Range	-67;67	-33;100

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Dyspnoea Change from baseline at End of therapy	n	139	137
	Mean	7.2	14.1
	SD	23.66	29.35
	Median	0.0	0.0
	Q1;Q3	0;0	0;33
	Range	-33;100	-67;100
Dyspnoea Change from baseline at Follow-up 1 visit	n	49	43
	Mean	1.4	20.2
	SD	22.52	33.44
	Median	0.0	0.0
	Q1;Q3	0;0	0;33
	Range	-67;33	-67;100
Dyspnoea Change from baseline at Follow-up 2 visit	n	31	20
	Mean	1.1	8.3
	SD	21.92	26.21
	Median	0.0	0.0
	Q1;Q3	0;0	0;33
	Range	-33;33	-33;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Dyspnoea	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-4.4	3.3
	SD	17.21	18.92
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-33;33	-33;33

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Insomnia	n	161	164
Change from baseline at End of C3	Mean	-1.7	3.5
	SD	30.91	26.27
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-100;67	-67;100
Insomnia	n	103	98
Change from baseline at End of C6	Mean	-1.6	-0.3
	SD	28.92	27.28
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-67;100	-67;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Insomnia	n	137	138
Change from baseline at End of therapy	Mean	1.9	7.7
	SD	29.91	31.01
	Median	0.0	0.0
	Q1;Q3	0;33	0;33
	Range	-67;100	-67;100
Insomnia	n	49	43
Change from baseline at Follow-up 1 visit	Mean	0.7	10.1
	SD	28.46	32.15
	Median	0.0	0.0
	Q1;Q3	0;33	0;33
	Range	-67;67	-33;100
Insomnia	n	31	20
Change from baseline at Follow-up 2 visit	Mean	8.6	18.3
	SD	21.03	38.20
	Median	0.0	16.7
	Q1;Q3	0;33	0;33
	Range	-33;67	-33;100

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Insomnia	n	15	9
Change from baseline at Follow-up 3 visit	Mean	2.2	3.7
	SD	23.46	30.93
	Median	0.0	0.0
	Q1;Q3	0;0	0;33
	Range	-33;67	-67;33

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Appetite Loss Change from baseline at End of C3	n	162	163
	Mean	8.0	16.2
	SD	32.35	34.62
	Median	0.0	0.0
	Q1;Q3	0;33	0;33
	Range	-67;100	-100;100
Appetite Loss Change from baseline at End of C6	n	104	99
	Mean	16.3	13.8
	SD	35.07	28.97
	Median	0.0	0.0
	Q1;Q3	0;33	0;33
	Range	-67;100	-67;100

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Appetite Loss Change from baseline at End of therapy	n	139	138
	Mean	17.5	19.8
	SD	36.41	33.12
	Median	0.0	16.7
	Q1;Q3	0;33	0;33
	Range	-67;100	-67;100
Appetite Loss Change from baseline at Follow-up 1 visit	n	49	43
	Mean	2.7	27.9
	SD	27.08	33.28
	Median	0.0	33.3
	Q1;Q3	0;33	0;67
	Range	-67;67	-33;100
Appetite Loss Change from baseline at Follow-up 2 visit	n	31	20
	Mean	1.1	21.7
	SD	21.92	29.17
	Median	0.0	16.7
	Q1;Q3	0;0	0;33
	Range	-67;33	-33;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Appetite Loss	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.0	0.0
	SD	12.60	15.71
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-33;33	-33;33

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Constipation	n	159	163
Change from baseline at End of C3	Mean	5.2	4.3
	SD	26.66	31.89
	Median	0.0	0.0
	Q1;Q3	0;0	0;33
	Range	-100;100	-100;100
Constipation	n	104	98
Change from baseline at End of C6	Mean	4.2	7.8
	SD	33.07	30.20
	Median	0.0	0.0
	Q1;Q3	0;17	0;33
	Range	-100;100	-67;100

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Constipation	n	139	137
Change from baseline at End of therapy	Mean	7.2	6.8
	SD	34.46	31.35
	Median	0.0	0.0
	Q1;Q3	0;33	0;33
	Range	-100;100	-67;100
Constipation	n	49	43
Change from baseline at Follow-up 1 visit	Mean	1.4	8.5
	SD	26.32	37.86
	Median	0.0	0.0
	Q1;Q3	0;0	0;33
	Range	-67;67	-67;100
Constipation	n	31	20
Change from baseline at Follow-up 2 visit	Mean	-1.1	6.7
	SD	27.87	17.44
	Median	0.0	0.0
	Q1;Q3	-33;0	0;17
	Range	-67;67	-33;33

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Constipation	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.0	6.7
	SD	37.80	26.29
	Median	0.0	0.0
	Q1;Q3	-33;0	0;0
	Range	-67;100	-33;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Diarrhea	n	160	158
Change from baseline at End of C3	Mean	3.5	1.1
	SD	24.11	23.92
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-67;100	-100;100
Diarrhea	n	102	98
Change from baseline at End of C6	Mean	0.0	7.1
	SD	19.90	27.60
	Median	0.0	0.0
	Q1;Q3	0;0	0;33
	Range	-67;67	-67;100

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Diarrhea Change from baseline at End of therapy	n	137	136
	Mean	2.9	2.5
	SD	24.75	21.33
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-100;100	-100;100
Diarrhea Change from baseline at Follow-up 1 visit	n	48	43
	Mean	0.0	2.3
	SD	21.74	19.78
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-33;100	-33;67
Diarrhea Change from baseline at Follow-up 2 visit	n	31	20
	Mean	6.5	5.0
	SD	20.04	19.57
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-33;67	-33;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Diarrhea	n	15	10
Change from baseline at Follow-up 3 visit	Mean	8.9	3.3
	SD	29.46	10.54
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-33;100	0;33

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Financial difficulties	n	159	161
Change from baseline at End of C3	Mean	-0.2	-1.7
	SD	21.71	27.34
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-100;67	-100;100
Financial difficulties	n	104	97
Change from baseline at End of C6	Mean	4.8	-1.0
	SD	23.42	22.28
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-67;100	-100;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Financial difficulties	n	138	137
Change from baseline at End of therapy	Mean	4.6	2.2
	SD	24.56	29.76
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-67;100	-100;100
Financial difficulties	n	49	42
Change from baseline at Follow-up 1 visit	Mean	1.4	0.8
	SD	27.18	28.02
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-67;67	-67;67
Financial difficulties	n	31	20
Change from baseline at Follow-up 2 visit	Mean	6.5	-1.7
	SD	18.09	25.31
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-33;67	-67;67

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.1: QUALITY OF LIFE: C30 SCORES CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Financial difficulties	n	15	10
Change from baseline at Follow-up 3 visit	Mean	15.6	3.3
	SD	30.52	29.19
	Median	0.0	0.0
	Q1;Q3	0;33	0;33
	Range	-33;100	-67;33

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Doing Strenuous Activities Change from baseline at End of C3	n	162	162
	Mean	0.2	0.3
	SD	0.79	0.82
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;2	-2;3
Trouble Doing Strenuous Activities Change from baseline at End of C6	n	104	99
	Mean	0.2	0.2
	SD	0.84	0.68
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Doing Strenuous Activities Change from baseline at End of therapy	n	140	136
	Mean	0.4	0.5
	SD	0.82	0.93
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-1;3
Trouble Doing Strenuous Activities Change from baseline at Follow-up 1 visit	n	49	43
	Mean	0.0	0.4
	SD	0.79	0.85
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;2	-1;3
Trouble Doing Strenuous Activities Change from baseline at Follow-up 2 visit	n	31	20
	Mean	-0.1	0.3
	SD	0.75	0.98
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;2	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Doing Strenuous Activities	n	15	9
Change from baseline at Follow-up 3 visit	Mean	0.0	0.1
	SD	0.76	1.05
	Median	0.0	0.0
	Q1;Q3	-1;1	0;1
	Range	-1;1	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Taking a Long Walk Change from baseline at End of C3	n	162	163
	Mean	0.3	0.3
	SD	0.80	0.85
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Trouble Taking a Long Walk Change from baseline at End of C6	n	104	98
	Mean	0.4	0.2
	SD	0.87	0.84
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;2	-1;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Taking a Long Walk	n	139	138
Change from baseline at End of therapy	Mean	0.5	0.5
	SD	0.85	0.97
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-1;3
Trouble Taking a Long Walk	n	49	43
Change from baseline at Follow-up 1 visit	Mean	0.3	0.3
	SD	0.84	0.80
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;2	-1;2
Trouble Taking a Long Walk	n	31	20
Change from baseline at Follow-up 2 visit	Mean	0.2	0.5
	SD	0.79	1.15
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;1	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Taking a Long Walk	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.2	0.2
	SD	1.01	1.03
	Median	0.0	0.0
	Q1;Q3	0;1	-1;1
	Range	-2;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Taking a Short Walk Change from baseline at End of C3	n	161	164
	Mean	0.2	0.3
	SD	0.78	0.83
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Trouble Taking a Short Walk Change from baseline at End of C6	n	103	98
	Mean	0.3	0.3
	SD	0.72	0.84
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;2	-1;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Taking a Short Walk	n	138	138
Change from baseline at End of therapy	Mean	0.6	0.5
	SD	0.86	0.85
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;3	-1;3
Trouble Taking a Short Walk	n	49	43
Change from baseline at Follow-up 1 visit	Mean	0.3	0.3
	SD	0.68	0.87
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;2	-1;3
Trouble Taking a Short Walk	n	31	20
Change from baseline at Follow-up 2 visit	Mean	0.2	0.4
	SD	0.65	1.05
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;2	-1;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Taking a Short Walk	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.2	0.3
	SD	0.56	0.82
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;1	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need To Stay in Bed or a Chair Change from baseline at End of C3	n	162	163
	Mean	0.2	0.3
	SD	0.83	0.85
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Need To Stay in Bed or a Chair Change from baseline at End of C6	n	103	99
	Mean	0.3	0.3
	SD	0.87	0.81
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need To Stay in Bed or a Chair Change from baseline at End of therapy	n	140	138
	Mean	0.4	0.5
	SD	0.98	0.95
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-1;3
Need To Stay in Bed or a Chair Change from baseline at Follow-up 1 visit	n	49	43
	Mean	0.0	0.7
	SD	0.43	1.02
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-1;3
Need To Stay in Bed or a Chair Change from baseline at Follow-up 2 visit	n	31	19
	Mean	0.0	0.6
	SD	0.48	0.77
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;2	0;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need To Stay in Bed or a Chair Change from baseline at Follow-up 3 visit	n	15	10
	Mean	-0.1	0.3
	SD	0.52	0.48
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	0;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need Help With Eating Dressing Change from baseline at End of C3	n	162	164
	Mean	0.0	0.1
	SD	0.42	0.58
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;3	-1;3
Need Help With Eating Dressing Change from baseline at End of C6	n	103	99
	Mean	-0.0	0.1
	SD	0.43	0.50
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;2	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need Help With Eating Dressing Change from baseline at End of therapy	n	140	137
	Mean	0.2	0.3
	SD	0.70	0.72
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;3	-1;3
Need Help With Eating Dressing Change from baseline at Follow-up 1 visit	n	48	42
	Mean	0.0	0.3
	SD	0.35	0.60
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;2	-1;2
Need Help With Eating Dressing Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.0	0.2
	SD	0.18	0.49
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	0;1	0;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need Help With Eating Dressing	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.0	0.0
	SD	0.00	0.00
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	0;0	0;0

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Limited in Doing Your Work Change from baseline at End of C3	n	160	162
	Mean	0.3	0.3
	SD	0.89	0.83
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Limited in Doing Your Work Change from baseline at End of C6	n	104	98
	Mean	0.2	0.3
	SD	0.95	0.91
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Limited in Doing Your Work Change from baseline at End of therapy	n	139	137
	Mean	0.7	0.7
	SD	1.05	0.98
	Median	0.0	1.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Limited in Doing Your Work Change from baseline at Follow-up 1 visit	n	49	42
	Mean	0.1	0.6
	SD	0.76	0.89
	Median	0.0	0.5
	Q1;Q3	0;1	0;1
	Range	-1;2	-1;3
Limited in Doing Your Work Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.1	0.3
	SD	0.54	0.86
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Limited in Doing Your Work	n	15	9
Change from baseline at Follow-up 3 visit	Mean	0.1	0.1
	SD	0.59	0.93
	Median	0.0	0.0
	Q1;Q3	0;0	-1;1
	Range	-1;1	-1;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Limited in Pursuing Your Hobbies Change from baseline at End of C3	n	156	160
	Mean	0.3	0.4
	SD	0.94	0.93
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-3;3
Limited in Pursuing Your Hobbies Change from baseline at End of C6	n	102	98
	Mean	0.3	0.2
	SD	0.94	0.88
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Limited in Pursuing Your Hobbies	n	135	138
Change from baseline at End of therapy	Mean	0.6	0.7
	SD	0.96	1.01
	Median	0.0	1.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Limited in Pursuing Your Hobbies	n	47	43
Change from baseline at Follow-up 1 visit	Mean	0.1	0.6
	SD	0.72	1.03
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;2	-1;3
Limited in Pursuing Your Hobbies	n	30	20
Change from baseline at Follow-up 2 visit	Mean	0.1	0.4
	SD	0.52	0.67
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Limited in Pursuing Your Hobbies	n	15	9
Change from baseline at Follow-up 3 visit	Mean	0.3	0.6
	SD	0.46	0.73
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	0;1	0;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Short of Breath Change from baseline at End of C3	n	162	164
	Mean	0.1	0.2
	SD	0.77	0.79
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;3	-1;3
Short of Breath Change from baseline at End of C6	n	104	98
	Mean	0.1	0.2
	SD	0.71	0.78
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;2	-1;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Short of Breath Change from baseline at End of therapy	n	139	137
	Mean	0.2	0.4
	SD	0.71	0.88
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;3	-2;3
Short of Breath Change from baseline at Follow-up 1 visit	n	49	43
	Mean	0.0	0.6
	SD	0.68	1.00
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;1	-2;3
Short of Breath Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.0	0.3
	SD	0.66	0.79
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Short of Breath	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-0.1	0.1
	SD	0.52	0.57
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;1	-1;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain	n	162	163
Change from baseline at End of C3	Mean	-0.1	0.0
	SD	0.89	0.96
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;2	-3;3
Pain	n	104	97
Change from baseline at End of C6	Mean	-0.0	-0.0
	SD	0.90	0.83
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;2	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain	n	138	134
Change from baseline at End of therapy	Mean	0.1	0.1
	SD	0.85	0.93
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-3;3	-3;2
Pain	n	49	43
Change from baseline at Follow-up 1 visit	Mean	0.2	0.3
	SD	0.74	0.85
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;2	-2;2
Pain	n	31	20
Change from baseline at Follow-up 2 visit	Mean	0.2	0.2
	SD	0.79	0.88
	Median	0.0	0.0
	Q1;Q3	0;1	-1;1
	Range	-1;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-0.1	-0.1
	SD	0.80	0.57
	Median	0.0	0.0
	Q1;Q3	-1;1	0;0
	Range	-1;1	-1;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need to Rest Change from baseline at End of C3	n	160	161
	Mean	0.3	0.3
	SD	0.78	0.86
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;2
Need to Rest Change from baseline at End of C6	n	104	98
	Mean	0.3	0.3
	SD	0.88	0.92
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;2	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need to Rest Change from baseline at End of therapy	n	138	138
	Mean	0.4	0.6
	SD	0.86	0.99
	Median	0.0	1.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Need to Rest Change from baseline at Follow-up 1 visit	n	49	43
	Mean	0.2	0.3
	SD	0.75	0.98
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;2	-2;2
Need to Rest Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.3	0.5
	SD	0.73	0.95
	Median	0.0	1.0
	Q1;Q3	0;1	0;1
	Range	-1;2	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Need to Rest	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.1	0.4
	SD	0.80	1.17
	Median	0.0	0.5
	Q1;Q3	0;0	-1;1
	Range	-1;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Sleeping Change from baseline at End of C3	n	161	164
	Mean	-0.0	0.1
	SD	0.93	0.79
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;2	-2;3
Trouble Sleeping Change from baseline at End of C6	n	103	98
	Mean	-0.0	-0.0
	SD	0.87	0.82
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;3	-2;2

SAS Program Name: T_QOL_summary.sas
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Sleeping	n	137	138
Change from baseline at End of therapy	Mean	0.1	0.2
	SD	0.90	0.93
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Trouble Sleeping	n	49	43
Change from baseline at Follow-up 1 visit	Mean	0.0	0.3
	SD	0.85	0.96
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;2	-1;3
Trouble Sleeping	n	31	20
Change from baseline at Follow-up 2 visit	Mean	0.3	0.6
	SD	0.63	1.15
	Median	0.0	0.5
	Q1;Q3	0;1	0;1
	Range	-1;2	-1;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Trouble Sleeping	n	15	9
Change from baseline at Follow-up 3 visit	Mean	0.1	0.1
	SD	0.70	0.93
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;2	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Felt Weak	n	162	164
Change from baseline at End of C3	Mean	0.3	0.4
	SD	0.92	0.96
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Felt Weak	n	104	99
Change from baseline at End of C6	Mean	0.3	0.4
	SD	0.90	0.91
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;3	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Felt Weak	n	139	138
Change from baseline at End of therapy	Mean	0.6	0.6
	SD	0.91	1.08
	Median	1.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-3;3
Felt Weak	n	49	43
Change from baseline at Follow-up 1 visit	Mean	0.2	0.6
	SD	0.81	1.02
	Median	0.0	1.0
	Q1;Q3	0;1	0;1
	Range	-1;2	-2;3
Felt Weak	n	31	20
Change from baseline at Follow-up 2 visit	Mean	0.2	0.8
	SD	0.75	1.02
	Median	0.0	1.0
	Q1;Q3	0;1	0;2
	Range	-1;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Felt Weak	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.0	0.2
	SD	0.53	1.48
	Median	0.0	0.5
	Q1;Q3	0;0	-1;1
	Range	-1;1	-2;3

SAS Program Name: T_QOL_summary.sas
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Lacked Appetite Change from baseline at End of C3	n	162	163
	Mean	0.2	0.5
	SD	0.97	1.04
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-3;3
Lacked Appetite Change from baseline at End of C6	n	104	99
	Mean	0.5	0.4
	SD	1.05	0.87
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3

SAS Program Name: T_QOL_summary.sas
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Lacked Appetite Change from baseline at End of therapy	n	139	138
	Mean	0.5	0.6
	SD	1.09	0.99
	Median	0.0	0.5
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Lacked Appetite Change from baseline at Follow-up 1 visit	n	49	43
	Mean	0.1	0.8
	SD	0.81	1.00
	Median	0.0	1.0
	Q1;Q3	0;1	0;2
	Range	-2;2	-1;3
Lacked Appetite Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.0	0.7
	SD	0.66	0.88
	Median	0.0	0.5
	Q1;Q3	0;0	0;1
	Range	-2;1	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Lacked Appetite	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.0	0.0
	SD	0.38	0.47
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;1	-1;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Felt Nauseated	n	161	164
Change from baseline at End of C3	Mean	0.4	0.3
	SD	0.96	0.89
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;3	-3;3
Felt Nauseated	n	103	98
Change from baseline at End of C6	Mean	0.3	0.5
	SD	0.89	0.83
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;3	-1;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Felt Nauseated	n	138	138
Change from baseline at End of therapy	Mean	0.4	0.4
	SD	0.99	0.88
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;3	-2;3
Felt Nauseated	n	49	43
Change from baseline at Follow-up 1 visit	Mean	-0.0	0.2
	SD	0.63	0.75
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-3;1	-1;2
Felt Nauseated	n	31	19
Change from baseline at Follow-up 2 visit	Mean	0.1	0.3
	SD	0.62	0.58
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;2	0;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Felt Nauseated	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.3	0.0
	SD	0.46	0.67
	Median	0.0	0.0
	Q1;Q3	0;1	0;0
	Range	0;1	-1;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Vomited	n	161	163
Change from baseline at End of C3	Mean	0.2	0.1
	SD	0.71	0.66
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;3	-2;3
Vomited	n	104	98
Change from baseline at End of C6	Mean	0.1	0.2
	SD	0.62	0.67
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;3	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Vomited	n	140	137
Change from baseline at End of therapy	Mean	0.3	0.1
	SD	0.79	0.67
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;3	-2;3
Vomited	n	49	43
Change from baseline at Follow-up 1 visit	Mean	0.0	0.1
	SD	0.20	0.29
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;1	0;1
Vomited	n	31	20
Change from baseline at Follow-up 2 visit	Mean	0.1	0.2
	SD	0.25	0.49
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	0;1	0;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Vomited	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.0	0.1
	SD	0.00	0.32
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	0;0	0;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Constipated	n	159	163
Change from baseline at End of C3	Mean	0.2	0.1
	SD	0.80	0.96
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-3;3	-3;3
Constipated	n	104	98
Change from baseline at End of C6	Mean	0.1	0.2
	SD	0.99	0.91
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;3	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Constipated	n	139	137
Change from baseline at End of therapy	Mean	0.2	0.2
	SD	1.03	0.94
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;3	-2;3
Constipated	n	49	43
Change from baseline at Follow-up 1 visit	Mean	0.0	0.3
	SD	0.79	1.14
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;2	-2;3
Constipated	n	31	20
Change from baseline at Follow-up 2 visit	Mean	-0.0	0.2
	SD	0.84	0.52
	Median	0.0	0.0
	Q1;Q3	-1;0	0;1
	Range	-2;2	-1;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Constipated	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.0	0.2
	SD	1.13	0.79
	Median	0.0	0.0
	Q1;Q3	-1;0	0;0
	Range	-2;3	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Diarrhea	n	160	158
Change from baseline at End of C3	Mean	0.1	0.0
	SD	0.72	0.72
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;3	-3;3
Diarrhea	n	102	98
Change from baseline at End of C6	Mean	0.0	0.2
	SD	0.60	0.83
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;2	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Diarrhea	n	137	136
Change from baseline at End of therapy	Mean	0.1	0.1
	SD	0.74	0.64
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;3	-3;3
Diarrhea	n	48	43
Change from baseline at Follow-up 1 visit	Mean	0.0	0.1
	SD	0.65	0.59
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;3	-1;2
Diarrhea	n	31	20
Change from baseline at Follow-up 2 visit	Mean	0.2	0.2
	SD	0.60	0.59
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Diarrhea	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.3	0.1
	SD	0.88	0.32
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;3	0;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Tired	n	160	161
Change from baseline at End of C3	Mean	0.3	0.4
	SD	0.85	0.88
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;2	-2;3
Tired	n	100	98
Change from baseline at End of C6	Mean	0.4	0.4
	SD	0.93	0.86
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;3	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Tired	n	138	137
Change from baseline at End of therapy	Mean	0.5	0.6
	SD	0.85	0.96
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Tired	n	47	43
Change from baseline at Follow-up 1 visit	Mean	0.1	0.5
	SD	0.74	0.77
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;2	-1;2
Tired	n	31	19
Change from baseline at Follow-up 2 visit	Mean	0.2	0.8
	SD	0.78	0.98
	Median	0.0	1.0
	Q1;Q3	0;1	0;2
	Range	-1;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Tired	n	15	9
Change from baseline at Follow-up 3 visit	Mean	0.1	0.2
	SD	0.88	0.97
	Median	0.0	0.0
	Q1;Q3	-1;1	0;1
	Range	-1;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain Interfered With Activites Change from baseline at End of C3	n	160	162
	Mean	-0.1	0.0
	SD	0.81	0.84
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;2	-3;3
Pain Interfered With Activites Change from baseline at End of C6	n	103	99
	Mean	-0.0	0.0
	SD	0.79	0.80
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;3	-3;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain Interfered With Activites Change from baseline at End of therapy	n	139	136
	Mean	0.2	0.3
	SD	0.87	0.98
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;3	-3;3
Pain Interfered With Activites Change from baseline at Follow-up 1 visit	n	49	43
	Mean	0.0	0.2
	SD	0.48	1.04
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-3;3
Pain Interfered With Activites Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.2	0.3
	SD	0.67	0.91
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;2	-1;2

SAS Program Name: T_QOL_summary.sas
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Pain Interfered With Activites Change from baseline at Follow-up 3 visit	n	15	10
	Mean	-0.1	-0.2
	SD	0.59	0.79
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;1	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Difficulty in Concentrating Change from baseline at End of C3	n	160	164
	Mean	0.1	0.1
	SD	0.80	0.83
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;3	-2;3
Difficulty in Concentrating Change from baseline at End of C6	n	104	99
	Mean	0.1	0.1
	SD	0.69	0.81
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-3;2	-3;3

SAS Program Name: T_QOL_summary.sas
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Difficulty in Concentrating Change from baseline at End of therapy	n	138	137
	Mean	0.2	0.4
	SD	0.85	0.92
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Difficulty in Concentrating Change from baseline at Follow-up 1 visit	n	49	43
	Mean	0.0	0.5
	SD	0.41	0.96
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-1;3
Difficulty in Concentrating Change from baseline at Follow-up 2 visit	n	31	19
	Mean	0.1	0.1
	SD	0.56	0.78
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;1	-2;2

SAS Program Name: T_QOL_summary.sas
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Difficulty in Concentrating	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.1	0.4
	SD	0.64	0.84
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;1	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Tense	n	161	164
Change from baseline at End of C3	Mean	-0.1	-0.1
	SD	0.80	0.79
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;3	-2;2
Feel Tense	n	104	99
Change from baseline at End of C6	Mean	-0.1	-0.1
	SD	0.71	0.90
	Median	0.0	0.0
	Q1;Q3	0;0	-1;0
	Range	-2;2	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Tense	n	139	136
Change from baseline at End of therapy	Mean	0.1	0.0
	SD	0.86	0.94
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;2	-2;3
Feel Tense	n	49	43
Change from baseline at Follow-up 1 visit	Mean	-0.2	0.0
	SD	0.66	1.09
	Median	0.0	0.0
	Q1;Q3	-1;0	-1;1
	Range	-1;1	-2;3
Feel Tense	n	31	20
Change from baseline at Follow-up 2 visit	Mean	-0.1	-0.1
	SD	0.65	1.00
	Median	0.0	0.0
	Q1;Q3	0;0	-1;1
	Range	-2;1	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Tense	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.1	-0.1
	SD	1.10	0.99
	Median	0.0	0.0
	Q1;Q3	-1;1	0;0
	Range	-1;3	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Worry	n	160	164
Change from baseline at End of C3	Mean	-0.1	-0.1
	SD	0.74	0.81
	Median	0.0	0.0
	Q1;Q3	0;0	-1;0
	Range	-2;2	-2;3
Worry	n	101	99
Change from baseline at End of C6	Mean	-0.2	-0.1
	SD	0.85	0.86
	Median	0.0	0.0
	Q1;Q3	-1;0	-1;0
	Range	-3;2	-3;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Worry	n	138	137
Change from baseline at End of therapy	Mean	0.0	0.0
	SD	0.87	0.92
	Median	0.0	0.0
	Q1;Q3	0;1	-1;1
	Range	-3;2	-2;3
Worry	n	49	43
Change from baseline at Follow-up 1 visit	Mean	-0.2	-0.0
	SD	0.85	0.91
	Median	0.0	0.0
	Q1;Q3	-1;0	-1;0
	Range	-2;2	-2;2
Worry	n	31	19
Change from baseline at Follow-up 2 visit	Mean	-0.3	-0.1
	SD	0.65	0.94
	Median	0.0	0.0
	Q1;Q3	-1;0	-1;1
	Range	-2;1	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Worry	n	14	10
Change from baseline at Follow-up 3 visit	Mean	-0.4	-0.3
	SD	1.02	0.82
	Median	-0.5	0.0
	Q1;Q3	-1;0	-1;0
	Range	-2;1	-2;1

SAS Program Name: T_QOL_summary.sas
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TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Irritable Change from baseline at End of C3	n	161	163
	Mean	-0.0	0.0
	SD	0.78	0.80
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;3	-3;2
Feel Irritable Change from baseline at End of C6	n	104	98
	Mean	0.0	0.0
	SD	0.85	0.81
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Irritable	n	139	136
Change from baseline at End of therapy	Mean	0.1	0.2
	SD	0.88	0.88
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Feel Irritable	n	49	42
Change from baseline at Follow-up 1 visit	Mean	-0.1	0.0
	SD	0.67	0.82
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;1	-2;1
Feel Irritable	n	31	19
Change from baseline at Follow-up 2 visit	Mean	-0.1	-0.1
	SD	0.56	0.78
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;1	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Irritable	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.1	0.1
	SD	0.64	0.99
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;1	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Depressed	n	158	162
Change from baseline at End of C3	Mean	0.1	-0.0
	SD	0.70	0.89
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;2	-3;3
Feel Depressed	n	104	97
Change from baseline at End of C6	Mean	-0.0	-0.2
	SD	0.72	0.84
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;2	-3;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Depressed	n	138	131
Change from baseline at End of therapy	Mean	0.2	0.1
	SD	0.84	0.87
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-3;3
Feel Depressed	n	49	42
Change from baseline at Follow-up 1 visit	Mean	-0.0	0.0
	SD	0.68	0.72
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;1	-2;1
Feel Depressed	n	31	20
Change from baseline at Follow-up 2 visit	Mean	-0.1	-0.1
	SD	0.67	0.51
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;1	-1;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Feel Depressed	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.2	-0.2
	SD	1.01	1.03
	Median	0.0	0.0
	Q1;Q3	0;1	-1;0
	Range	-1;3	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Difficulty Remembering Change from baseline at End of C3	n	161	163
	Mean	0.1	0.1
	SD	0.72	0.71
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;3	-3;3
Difficulty Remembering Change from baseline at End of C6	n	103	97
	Mean	0.2	0.2
	SD	0.67	0.67
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Difficulty Remembering Change from baseline at End of therapy	n	138	136
	Mean	0.2	0.1
	SD	0.73	0.75
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Difficulty Remembering Change from baseline at Follow-up 1 visit	n	49	42
	Mean	0.2	0.3
	SD	0.53	0.73
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-1;2
Difficulty Remembering Change from baseline at Follow-up 2 visit	n	31	19
	Mean	0.2	0.1
	SD	0.56	1.10
	Median	0.0	0.0
	Q1;Q3	0;0	-1;1
	Range	-1;2	-2;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Difficulty Remembering	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.3	0.3
	SD	0.59	0.67
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;1	-1;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Interfered With Family Life Change from baseline at End of C3	n	160	163
	Mean	0.0	0.3
	SD	0.81	0.83
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;3	-2;3
Interfered With Family Life Change from baseline at End of C6	n	104	96
	Mean	0.1	0.2
	SD	0.73	0.91
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;2	-3;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Interfered With Family Life Change from baseline at End of therapy	n	138	135
	Mean	0.3	0.4
	SD	0.92	0.99
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-3;3	-2;3
Interfered With Family Life Change from baseline at Follow-up 1 visit	n	47	42
	Mean	0.0	0.2
	SD	0.86	0.92
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;2	-2;3
Interfered With Family Life Change from baseline at Follow-up 2 visit	n	30	20
	Mean	0.1	0.2
	SD	0.51	0.93
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Interfered With Family Life	n	14	10
Change from baseline at Follow-up 3 visit	Mean	0.0	0.5
	SD	0.55	0.97
	Median	0.0	1.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Interfered With Social Life Change from baseline at End of C3	n	156	163
	Mean	0.2	0.3
	SD	0.81	0.88
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-2;3
Interfered With Social Life Change from baseline at End of C6	n	102	98
	Mean	0.3	0.3
	SD	0.78	1.01
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;2	-3;3

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Interfered With Social Life Change from baseline at End of therapy	n	136	137
	Mean	0.5	0.5
	SD	0.92	1.04
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-2;3	-3;3
Interfered With Social Life Change from baseline at Follow-up 1 visit	n	47	43
	Mean	0.1	0.4
	SD	0.84	1.01
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-2;2	-2;3
Interfered With Social Life Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.0	0.1
	SD	0.52	0.85
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;2	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Interfered With Social Life	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-0.1	0.4
	SD	0.46	0.84
	Median	0.0	0.0
	Q1;Q3	0;0	0;1
	Range	-1;1	-1;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Caused Financial Difficulties Change from baseline at End of C3	n	159	161
	Mean	-0.0	-0.0
	SD	0.65	0.82
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-3;2	-3;3
Caused Financial Difficulties Change from baseline at End of C6	n	104	97
	Mean	0.1	-0.0
	SD	0.70	0.67
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;3	-3;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Caused Financial Difficulties Change from baseline at End of therapy	n	138	137
	Mean	0.1	0.1
	SD	0.74	0.89
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;3	-3;3
Caused Financial Difficulties Change from baseline at Follow-up 1 visit	n	49	42
	Mean	0.0	0.0
	SD	0.82	0.84
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-2;2	-2;2
Caused Financial Difficulties Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.2	-0.1
	SD	0.54	0.76
	Median	0.0	0.0
	Q1;Q3	0;0	0;0
	Range	-1;2	-2;2

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Caused Financial Difficulties	n	15	10
Change from baseline at Follow-up 3 visit	Mean	0.5	0.1
	SD	0.92	0.88
	Median	0.0	0.0
	Q1;Q3	0;1	0;1
	Range	-1;3	-2;1

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Overall Health Rate Change from baseline at End of C3	n	161	163
	Mean	-0.0	-0.3
	SD	1.32	1.30
	Median	0.0	0.0
	Q1;Q3	-1;1	-1;1
	Range	-4;3	-6;4
Overall Health Rate Change from baseline at End of C6	n	104	99
	Mean	-0.0	-0.3
	SD	1.40	1.51
	Median	0.0	0.0
	Q1;Q3	-1;1	-1;1
	Range	-3;6	-4;4

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Overall Health Rate	n	137	137
Change from baseline at End of therapy	Mean	-0.5	-0.7
	SD	1.57	1.58
	Median	0.0	-1.0
	Q1;Q3	-1;0	-2;0
	Range	-4;4	-5;4
Overall Health Rate	n	49	43
Change from baseline at Follow-up 1 visit	Mean	-0.0	-0.7
	SD	1.32	1.69
	Median	0.0	-1.0
	Q1;Q3	-1;1	-1;0
	Range	-3;3	-5;4
Overall Health Rate	n	31	20
Change from baseline at Follow-up 2 visit	Mean	-0.1	-0.5
	SD	1.49	1.96
	Median	0.0	-1.0
	Q1;Q3	-1;1	-2;1
	Range	-3;4	-4;4

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Overall Health Rate	n	15	10
Change from baseline at Follow-up 3 visit	Mean	-0.6	-0.3
	SD	1.72	1.89
	Median	-1.0	-0.5
	Q1;Q3	-1;0	-1;0
	Range	-4;3	-3;4

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Overall Quality of Life Rate Change from baseline at End of C3	n	161	163
	Mean	-0.2	-0.3
	SD	1.43	1.44
	Median	0.0	0.0
	Q1;Q3	-1;1	-1;1
	Range	-5;3	-6;4
Overall Quality of Life Rate Change from baseline at End of C6	n	104	98
	Mean	-0.2	-0.3
	SD	1.59	1.58
	Median	0.0	0.0
	Q1;Q3	-1;1	-1;1
	Range	-5;6	-4;5

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Overall Quality of Life Rate Change from baseline at End of therapy	n	138	138
	Mean	-0.7	-0.7
	SD	1.62	1.73
	Median	0.0	-1.0
	Q1;Q3	-2;0	-2;0
	Range	-5;5	-5;5
Overall Quality of Life Rate Change from baseline at Follow-up 1 visit	n	49	43
	Mean	-0.1	-0.8
	SD	1.33	1.67
	Median	0.0	-1.0
	Q1;Q3	-1;1	-1;0
	Range	-4;4	-5;3
Overall Quality of Life Rate Change from baseline at Follow-up 2 visit	n	31	20
	Mean	0.1	-0.4
	SD	1.36	1.79
	Median	0.0	0.0
	Q1;Q3	-1;1	-2;1
	Range	-3;4	-4;4

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

TABLE 14.2.19.3: QUALITY OF LIFE: INDIVIDUAL QUESTIONS C30 CHANGE FROM BASELINE SUMMARIES

Study: AEZS-108-050
Study Population: Intent-to-Treat

Number of patients		AEZS-108 N=256	Doxorubicin N=255
Overall Quality of Life Rate Change from baseline at Follow-up 3 visit	n	15	10
	Mean	-0.2	-0.6
	SD	1.37	2.12
	Median	0.0	-0.5
	Q1;Q3	-1;0	-1;0
	Range	-2;3	-4;4

SAS Program Name: T_QOL_summary.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 25 April 2017

Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Any Adverse Events	120 (95.2)	3 (100)	123 (95.3)
Gastrointestinal disorders	79 (62.7)	2 (66.7)	81 (62.8)
Nausea	40 (31.7)	2 (66.7)	42 (32.6)
Diarrhoea	35 (27.8)	1 (33.3)	36 (27.9)
Vomiting	24 (19.0)	0	24 (18.6)
Constipation	25 (19.8)	0	25 (19.4)
Abdominal pain	21 (16.7)	0	21 (16.3)
Abdominal distension	9 (7.1)	0	9 (7.0)
Dry mouth	3 (2.4)	1 (33.3)	4 (3.1)
Ascites	2 (1.6)	0	2 (1.6)
Dyspepsia	6 (4.8)	0	6 (4.7)
Haemorrhoids	3 (2.4)	0	3 (2.3)
Intestinal obstruction	2 (1.6)	0	2 (1.6)
Stomatitis	6 (4.8)	0	6 (4.7)
Gastrooesophageal reflux disease	4 (3.2)	0	4 (3.1)
Abdominal pain upper	4 (3.2)	0	4 (3.1)
Colitis	3 (2.4)	0	3 (2.3)
Abdominal pain lower	3 (2.4)	0	3 (2.3)
Rectal haemorrhage	2 (1.6)	0	2 (1.6)
Mouth ulceration	3 (2.4)	0	3 (2.3)
Proctalgia	2 (1.6)	0	2 (1.6)
Small intestinal obstruction	0	0	0
Abdominal discomfort	0	0	0
Anorectal discomfort	2 (1.6)	0	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_teae_socpt.sas, Output: t_14_3_1_2a_teae_socpt.rtf,
Generated on: 26AUG2020 03:08 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Ileus	0	0	0
Large intestinal obstruction	0	0	0
Anal incontinence	2 (1.6)	0	2 (1.6)
Cheilitis	1 (0.8)	0	1 (0.8)
Dysphagia	0	0	0
Flatulence	1 (0.8)	0	1 (0.8)
Gastric ulcer	1 (0.8)	0	1 (0.8)
Gastritis	2 (1.6)	0	2 (1.6)
Haematochezia	1 (0.8)	0	1 (0.8)
Lip swelling	1 (0.8)	0	1 (0.8)
Toothache	0	0	0
Abdominal tenderness	0	0	0
Anal haemorrhage	1 (0.8)	0	1 (0.8)
Bile acid malabsorption	0	1 (33.3)	1 (0.8)
Chronic gastritis	1 (0.8)	0	1 (0.8)
Colonic fistula	1 (0.8)	0	1 (0.8)
Dumping syndrome	1 (0.8)	0	1 (0.8)
Enterocolitis haemorrhagic	1 (0.8)	0	1 (0.8)
Eructation	0	0	0
Faeces soft	0	0	0
Gastric haemorrhage	0	0	0
Gastric ulcer perforation	1 (0.8)	0	1 (0.8)
Gastrointestinal haemorrhage	0	0	0
Gingival pain	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Haematemesis	1 (0.8)	0	1 (0.8)
Haemorrhoidal haemorrhage	0	0	0
Large intestine polyp	1 (0.8)	0	1 (0.8)
Lip dry	0	0	0
Melaena	1 (0.8)	0	1 (0.8)
Noninfective sialoadenitis	0	0	0
Odynophagia	1 (0.8)	0	1 (0.8)
Oesophagitis	0	0	0
Oral dysaesthesia	0	0	0
Oral pain	1 (0.8)	0	1 (0.8)
Pancreatitis	1 (0.8)	0	1 (0.8)
Pancreatitis acute	1 (0.8)	0	1 (0.8)
Paraesthesia oral	0	0	0
Post-tussive vomiting	0	0	0
Salivary gland calculus	0	0	0
Tongue dry	0	0	0
General disorders and administration site conditions	81 (64.3)	2 (66.7)	83 (64.3)
Fatigue	31 (24.6)	1 (33.3)	32 (24.8)
Asthenia	28 (22.2)	0	28 (21.7)
Pyrexia	13 (10.3)	1 (33.3)	14 (10.9)
Oedema peripheral	11 (8.7)	2 (66.7)	13 (10.1)
Chills	6 (4.8)	0	6 (4.7)
Pain	4 (3.2)	0	4 (3.1)
Peripheral swelling	3 (2.4)	0	3 (2.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
General disorders and administration site conditions			
Non-cardiac chest pain	2 (1.6)	0	2 (1.6)
Influenza like illness	2 (1.6)	0	2 (1.6)
Oedema	3 (2.4)	0	3 (2.3)
Chest pain	0	0	0
General physical health deterioration	2 (1.6)	0	2 (1.6)
Catheter site pain	0	0	0
Chest discomfort	2 (1.6)	0	2 (1.6)
Complication associated with device	1 (0.8)	0	1 (0.8)
Malaise	1 (0.8)	0	1 (0.8)
Mucosal inflammation	1 (0.8)	0	1 (0.8)
Catheter site bruise	0	0	0
Catheter site erythema	1 (0.8)	0	1 (0.8)
Catheter site pruritus	1 (0.8)	0	1 (0.8)
Catheter site swelling	0	0	0
Early satiety	1 (0.8)	0	1 (0.8)
Fat tissue decreased	0	0	0
Feeling cold	0	0	0
Feeling hot	0	0	0
Gait disturbance	0	0	0
Generalised oedema	0	0	0
Hernia pain	1 (0.8)	0	1 (0.8)
Hyperthermia	1 (0.8)	0	1 (0.8)
Localised oedema	1 (0.8)	0	1 (0.8)
Physical deconditioning	0	0	0

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
General disorders and administration site conditions			
Swelling face	0	0	0
Temperature intolerance	0	0	0
Thirst	0	0	0
Musculoskeletal and connective tissue disorders	55 (43.7)	2 (66.7)	57 (44.2)
Arthralgia	18 (14.3)	2 (66.7)	20 (15.5)
Back pain	19 (15.1)	0	19 (14.7)
Muscular weakness	9 (7.1)	0	9 (7.0)
Myalgia	13 (10.3)	1 (33.3)	14 (10.9)
Pain in extremity	8 (6.3)	0	8 (6.2)
Musculoskeletal pain	4 (3.2)	1 (33.3)	5 (3.9)
Muscle spasms	5 (4.0)	0	5 (3.9)
Joint swelling	1 (0.8)	0	1 (0.8)
Flank pain	2 (1.6)	0	2 (1.6)
Neck pain	1 (0.8)	0	1 (0.8)
Osteoarthritis	2 (1.6)	0	2 (1.6)
Osteoporosis	1 (0.8)	0	1 (0.8)
Arthritis	2 (1.6)	0	2 (1.6)
Groin pain	0	0	0
Joint range of motion decreased	1 (0.8)	0	1 (0.8)
Bone pain	0	0	0
Musculoskeletal chest pain	0	0	0
Musculoskeletal discomfort	0	0	0
Musculoskeletal stiffness	2 (1.6)	0	2 (1.6)
Spinal osteoarthritis	2 (1.6)	0	2 (1.6)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Musculoskeletal and connective tissue disorders			
Tendon pain	2 (1.6)	0	2 (1.6)
Coccydynia	1 (0.8)	0	1 (0.8)
Foot deformity	0	0	0
Gouty tophus	0	0	0
Hypercreatinaemia	0	0	0
Intervertebral disc degeneration	0	0	0
Joint stiffness	0	0	0
Ligamentum flavum hypertrophy	0	0	0
Limb discomfort	1 (0.8)	0	1 (0.8)
Lumbar spinal stenosis	0	0	0
Mobility decreased	0	0	0
Muscle atrophy	0	0	0
Muscle discomfort	1 (0.8)	0	1 (0.8)
Muscle tightness	1 (0.8)	0	1 (0.8)
Osteopenia	1 (0.8)	0	1 (0.8)
Pain in jaw	1 (0.8)	0	1 (0.8)
Plantar fasciitis	0	0	0
Rheumatoid arthritis	1 (0.8)	0	1 (0.8)
Scoliosis	1 (0.8)	0	1 (0.8)
Spinal deformity	0	0	0
Spinal pain	0	0	0
Spinal stenosis	1 (0.8)	0	1 (0.8)
Spondylolisthesis	0	0	0
Synovial cyst	0	1 (33.3)	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Musculoskeletal and connective tissue disorders			
Tendonitis	0	1 (33.3)	1 (0.8)
Vertebral foraminal stenosis	0	0	0
Infections and infestations	53 (42.1)	2 (66.7)	55 (42.6)
Urinary tract infection	19 (15.1)	1 (33.3)	20 (15.5)
Upper respiratory tract infection	9 (7.1)	1 (33.3)	10 (7.8)
Pneumonia	6 (4.8)	0	6 (4.7)
Nasopharyngitis	6 (4.8)	0	6 (4.7)
Bronchitis	6 (4.8)	0	6 (4.7)
Oral candidiasis	2 (1.6)	0	2 (1.6)
Sepsis	4 (3.2)	0	4 (3.1)
Cellulitis	2 (1.6)	0	2 (1.6)
Vaginal infection	2 (1.6)	0	2 (1.6)
Candida infection	0	1 (33.3)	1 (0.8)
Cystitis	2 (1.6)	0	2 (1.6)
Gastroenteritis	2 (1.6)	0	2 (1.6)
Infection	0	0	0
Lower respiratory tract infection	1 (0.8)	0	1 (0.8)
Pharyngitis	2 (1.6)	0	2 (1.6)
Pyelonephritis	2 (1.6)	0	2 (1.6)
Rhinitis	2 (1.6)	0	2 (1.6)
Sinusitis	1 (0.8)	1 (33.3)	2 (1.6)
Viral infection	0	1 (33.3)	1 (0.8)
Abdominal infection	1 (0.8)	0	1 (0.8)
Ear infection	1 (0.8)	0	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Infections and infestations			
Oral herpes	1 (0.8)	0	1 (0.8)
Abscess oral	0	0	0
Acute sinusitis	0	0	0
Bacteraemia	1 (0.8)	0	1 (0.8)
Clostridium difficile infection	0	0	0
Conjunctivitis	1 (0.8)	0	1 (0.8)
Demodicidosis	1 (0.8)	0	1 (0.8)
Diverticulitis	0	0	0
Erysipelas	0	0	0
Eye infection	0	0	0
Fungal infection	0	0	0
Fungal skin infection	0	1 (33.3)	1 (0.8)
Gastroenteritis viral	1 (0.8)	0	1 (0.8)
Gastrointestinal viral infection	1 (0.8)	0	1 (0.8)
Genital infection	1 (0.8)	0	1 (0.8)
Herpes virus infection	1 (0.8)	0	1 (0.8)
Herpes zoster	0	0	0
Hordeolum	0	0	0
Infected lymphocele	1 (0.8)	0	1 (0.8)
Influenza	0	0	0
Klebsiella infection	0	0	0
Lip infection	0	0	0
Nail infection	0	0	0
Oral fungal infection	0	0	0

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Infections and infestations			
Pharyngitis streptococcal	0	0	0
Pyelonephritis acute	0	0	0
Root canal infection	0	0	0
Sialoadenitis	0	0	0
Skin infection	0	0	0
Tooth abscess	0	0	0
Vulvovaginal candidiasis	1 (0.8)	0	1 (0.8)
Wound infection	1 (0.8)	0	1 (0.8)
Respiratory, thoracic and mediastinal disorders	42 (33.3)	2 (66.7)	44 (34.1)
Cough	19 (15.1)	2 (66.7)	21 (16.3)
Dyspnoea	8 (6.3)	1 (33.3)	9 (7.0)
Productive cough	9 (7.1)	0	9 (7.0)
Pulmonary embolism	4 (3.2)	0	4 (3.1)
Pleural effusion	1 (0.8)	0	1 (0.8)
Oropharyngeal pain	2 (1.6)	0	2 (1.6)
Nasal congestion	3 (2.4)	0	3 (2.3)
Rhinorrhoea	3 (2.4)	0	3 (2.3)
Wheezing	1 (0.8)	0	1 (0.8)
Dysphonia	2 (1.6)	0	2 (1.6)
Dyspnoea exertional	1 (0.8)	0	1 (0.8)
Epistaxis	1 (0.8)	0	1 (0.8)
Haemoptysis	0	0	0
Respiratory failure	0	0	0
Hypoxia	1 (0.8)	0	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Pneumonitis	2 (1.6)	0	2 (1.6)
Rhinitis allergic	0	0	0
Sneezing	2 (1.6)	0	2 (1.6)
Throat irritation	2 (1.6)	0	2 (1.6)
Aspiration	1 (0.8)	0	1 (0.8)
Atelectasis	0	0	0
Catarrh	0	0	0
Choking	0	0	0
Choking sensation	1 (0.8)	0	1 (0.8)
Hiccups	1 (0.8)	0	1 (0.8)
Hypoventilation	0	0	0
Increased bronchial secretion	1 (0.8)	0	1 (0.8)
Increased upper airway secretion	1 (0.8)	0	1 (0.8)
Interstitial lung disease	1 (0.8)	0	1 (0.8)
Nasal dryness	0	0	0
Oropharyngeal discomfort	0	0	0
Painful respiration	0	0	0
Pharyngeal erythema	0	0	0
Pleuritic pain	0	0	0
Pulmonary haemorrhage	0	0	0
Pulmonary infarction	1 (0.8)	0	1 (0.8)
Rales	0	0	0
Respiratory symptom	0	0	0
Rhinalgia	0	0	0

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Sputum retention	1 (0.8)	0	1 (0.8)
Upper-airway cough syndrome	0	0	0
Metabolism and nutrition disorders	41 (32.5)	2 (66.7)	43 (33.3)
Decreased appetite	16 (12.7)	0	16 (12.4)
Hypomagnesaemia	10 (7.9)	0	10 (7.8)
Hyponatraemia	6 (4.8)	1 (33.3)	7 (5.4)
Hypokalaemia	8 (6.3)	0	8 (6.2)
Dehydration	5 (4.0)	0	5 (3.9)
Hypoalbuminaemia	3 (2.4)	0	3 (2.3)
Hyperglycaemia	3 (2.4)	0	3 (2.3)
Hypercalcaemia	2 (1.6)	0	2 (1.6)
Hyperkalaemia	3 (2.4)	0	3 (2.3)
Hypocalcaemia	1 (0.8)	0	1 (0.8)
Hypermagnesaemia	0	0	0
Hypernatraemia	0	0	0
Hypophosphataemia	1 (0.8)	0	1 (0.8)
Hypoglycaemia	0	0	0
Malnutrition	1 (0.8)	0	1 (0.8)
Type 1 diabetes mellitus	0	0	0
Cachexia	0	0	0
Diabetic ketoacidosis	0	0	0
Folate deficiency	1 (0.8)	0	1 (0.8)
Gout	0	1 (33.3)	1 (0.8)
Hyperammonaemia	0	1 (33.3)	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Metabolism and nutrition disorders			
Hyperamylasaemia	1 (0.8)	0	1 (0.8)
Hypercholesterolaemia	0	0	0
Hyperglycaemic hyperosmolar nonketotic syndrome	1 (0.8)	0	1 (0.8)
Hypophagia	0	1 (33.3)	1 (0.8)
Increased appetite	1 (0.8)	0	1 (0.8)
Iron deficiency	1 (0.8)	0	1 (0.8)
Metabolic syndrome	1 (0.8)	0	1 (0.8)
Vitamin B12 deficiency	0	0	0
Vitamin D deficiency	0	0	0
Investigations	48 (38.1)	1 (33.3)	49 (38.0)
Aspartate aminotransferase increased	9 (7.1)	0	9 (7.0)
Blood creatinine increased	9 (7.1)	0	9 (7.0)
Alanine aminotransferase increased	9 (7.1)	0	9 (7.0)
Weight decreased	9 (7.1)	0	9 (7.0)
Amylase increased	6 (4.8)	0	6 (4.7)
Blood alkaline phosphatase increased	3 (2.4)	0	3 (2.3)
Lymphocyte count decreased	2 (1.6)	0	2 (1.6)
Gamma-glutamyltransferase increased	4 (3.2)	0	4 (3.1)
Lipase increased	4 (3.2)	0	4 (3.1)
Weight increased	5 (4.0)	0	5 (3.9)
Blood lactate dehydrogenase increased	2 (1.6)	0	2 (1.6)
Transaminases increased	3 (2.4)	0	3 (2.3)
Activated partial thromboplastin time prolonged	1 (0.8)	0	1 (0.8)
Blood bilirubin increased	1 (0.8)	0	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Neutrophil count decreased	1 (0.8)	0	1 (0.8)
White blood cell count decreased	1 (0.8)	0	1 (0.8)
Blood cholesterol increased	0	0	0
Blood thyroid stimulating hormone increased	1 (0.8)	0	1 (0.8)
International normalised ratio increased	0	0	0
Neutrophil count increased	1 (0.8)	0	1 (0.8)
White blood cell count increased	1 (0.8)	0	1 (0.8)
Blood magnesium decreased	0	0	0
Blood potassium increased	0	0	0
Blood thyroid stimulating hormone decreased	1 (0.8)	0	1 (0.8)
Blood urea increased	1 (0.8)	0	1 (0.8)
Platelet count decreased	0	0	0
Serum ferritin decreased	1 (0.8)	1 (33.3)	2 (1.6)
Thyroxine free increased	0	0	0
Tri-iodothyronine decreased	0	0	0
Troponin increased	0	0	0
Aspartate aminotransferase	0	0	0
Bilirubin conjugated increased	0	0	0
Bleeding time prolonged	0	0	0
Blood albumin decreased	0	0	0
Blood corticotrophin decreased	1 (0.8)	0	1 (0.8)
Blood creatine phosphokinase increased	0	0	0
Blood iron decreased	1 (0.8)	0	1 (0.8)
Blood potassium decreased	1 (0.8)	0	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Blood prolactin abnormal	0	0	0
Blood sodium decreased	0	0	0
Blood urine present	1 (0.8)	0	1 (0.8)
Electrocardiogram QT prolonged	1 (0.8)	0	1 (0.8)
Haemoglobin decreased	1 (0.8)	0	1 (0.8)
Mean platelet volume decreased	1 (0.8)	0	1 (0.8)
Nitrite urine present	1 (0.8)	0	1 (0.8)
Thyroxine increased	1 (0.8)	0	1 (0.8)
Tri-iodothyronine free decreased	0	0	0
White blood cells urine positive	0	0	0
Skin and subcutaneous tissue disorders	40 (31.7)	1 (33.3)	41 (31.8)
Rash	13 (10.3)	0	13 (10.1)
Pruritus	18 (14.3)	0	18 (14.0)
Dry skin	4 (3.2)	1 (33.3)	5 (3.9)
Skin lesion	3 (2.4)	0	3 (2.3)
Erythema	2 (1.6)	0	2 (1.6)
Urticaria	3 (2.4)	1 (33.3)	4 (3.1)
Hyperhidrosis	1 (0.8)	0	1 (0.8)
Rash maculo-papular	1 (0.8)	0	1 (0.8)
Rash pruritic	0	0	0
Alopecia	2 (1.6)	0	2 (1.6)
Dermatitis contact	1 (0.8)	0	1 (0.8)
Eczema	2 (1.6)	0	2 (1.6)
Night sweats	0	1 (33.3)	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Skin and subcutaneous tissue disorders			
Rash macular	0	0	0
Blister	0	0	0
Dermatitis acneiform	0	0	0
Dermatitis allergic	0	0	0
Drug eruption	1 (0.8)	0	1 (0.8)
Onychoclasis	1 (0.8)	0	1 (0.8)
Dermatitis	0	0	0
Dermatitis psoriasiform	0	0	0
Exfoliative rash	0	0	0
Hypertrichosis	1 (0.8)	0	1 (0.8)
Nail discolouration	1 (0.8)	0	1 (0.8)
Nail disorder	0	0	0
Onychalgia	0	0	0
Onychomadesis	1 (0.8)	0	1 (0.8)
Pain of skin	0	1 (33.3)	1 (0.8)
Papule	1 (0.8)	0	1 (0.8)
Pemphigoid	1 (0.8)	0	1 (0.8)
Petechiae	0	0	0
Prurigo	1 (0.8)	0	1 (0.8)
Psoriasis	0	0	0
Skin burning sensation	1 (0.8)	0	1 (0.8)
Skin disorder	0	0	0
Skin haemorrhage	0	0	0
Skin mass	0	0	0

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Skin and subcutaneous tissue disorders			
Skin reaction	0	1 (33.3)	1 (0.8)
Skin ulcer	1 (0.8)	0	1 (0.8)
Skin warm	1 (0.8)	0	1 (0.8)
Blood and lymphatic system disorders	40 (31.7)	0	40 (31.0)
Anaemia	35 (27.8)	0	35 (27.1)
Neutropenia	6 (4.8)	0	6 (4.7)
Leukocytosis	2 (1.6)	0	2 (1.6)
Thrombocytopenia	0	0	0
Leukopenia	2 (1.6)	0	2 (1.6)
Autoimmune haemolytic anaemia	0	0	0
Iron deficiency anaemia	1 (0.8)	0	1 (0.8)
Lymphopenia	1 (0.8)	0	1 (0.8)
Nervous system disorders	32 (25.4)	3 (100)	35 (27.1)
Headache	12 (9.5)	0	12 (9.3)
Dizziness	9 (7.1)	0	9 (7.0)
Neuropathy peripheral	4 (3.2)	0	4 (3.1)
Dysgeusia	3 (2.4)	0	3 (2.3)
Peripheral sensory neuropathy	0	0	0
Restless legs syndrome	0	0	0
Cognitive disorder	2 (1.6)	0	2 (1.6)
Neuralgia	2 (1.6)	1 (33.3)	3 (2.3)
Carpal tunnel syndrome	2 (1.6)	0	2 (1.6)
Dysarthria	1 (0.8)	0	1 (0.8)
Epilepsy	0	1 (33.3)	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Nervous system disorders			
Memory impairment	0	0	0
Syncope	1 (0.8)	0	1 (0.8)
Tremor	1 (0.8)	0	1 (0.8)
Apraxia	1 (0.8)	0	1 (0.8)
Autonomic seizure	0	0	0
Balance disorder	0	0	0
Burning sensation	0	0	0
Dizziness postural	0	0	0
Dysaesthesia	1 (0.8)	0	1 (0.8)
Encephalopathy	1 (0.8)	0	1 (0.8)
Facial paresis	1 (0.8)	0	1 (0.8)
Formication	1 (0.8)	0	1 (0.8)
Hypoaesthesia	0	0	0
Hypogeusia	0	0	0
Ischaemic stroke	0	0	0
Lethargy	0	1 (33.3)	1 (0.8)
Leukoencephalopathy	1 (0.8)	0	1 (0.8)
Neurotoxicity	0	0	0
Paraesthesia	1 (0.8)	0	1 (0.8)
Parkinson's disease	1 (0.8)	0	1 (0.8)
Presyncope	0	0	0
Seizure like phenomena	0	0	0
Somnolence	1 (0.8)	0	1 (0.8)
Tension headache	0	0	0

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Psychiatric disorders	21 (16.7)	1 (33.3)	22 (17.1)
Insomnia	8 (6.3)	0	8 (6.2)
Anxiety	5 (4.0)	0	5 (3.9)
Depression	4 (3.2)	0	4 (3.1)
Confusional state	2 (1.6)	0	2 (1.6)
Depressed mood	2 (1.6)	0	2 (1.6)
Agitation	1 (0.8)	0	1 (0.8)
Alcoholism	1 (0.8)	0	1 (0.8)
Behaviour disorder	0	0	0
Bradyphrenia	1 (0.8)	0	1 (0.8)
Delirium	0	0	0
Disorientation	0	0	0
Hallucination	0	0	0
Mood altered	0	1 (33.3)	1 (0.8)
Nervousness	1 (0.8)	0	1 (0.8)
Renal and urinary disorders	25 (19.8)	0	25 (19.4)
Urinary incontinence	4 (3.2)	0	4 (3.1)
Haematuria	3 (2.4)	0	3 (2.3)
Micturition urgency	3 (2.4)	0	3 (2.3)
Acute kidney injury	4 (3.2)	0	4 (3.1)
Dysuria	3 (2.4)	0	3 (2.3)
Hydronephrosis	3 (2.4)	0	3 (2.3)
Pollakiuria	0	0	0
Urinary tract obstruction	1 (0.8)	0	1 (0.8)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Renal and urinary disorders			
Proteinuria	1 (0.8)	0	1 (0.8)
Chromaturia	2 (1.6)	0	2 (1.6)
Nephritis	1 (0.8)	0	1 (0.8)
Renal colic	2 (1.6)	0	2 (1.6)
Renal failure	1 (0.8)	0	1 (0.8)
Urinary tract pain	1 (0.8)	0	1 (0.8)
Urogenital fistula	2 (1.6)	0	2 (1.6)
Glycosuria	0	0	0
Hydroureter	0	0	0
Incontinence	0	0	0
Renal impairment	0	0	0
Tubulointerstitial nephritis	1 (0.8)	0	1 (0.8)
Ureteric stenosis	0	0	0
Urge incontinence	0	0	0
Urinary retention	0	0	0
Urine abnormality	1 (0.8)	0	1 (0.8)
Urine odour abnormal	1 (0.8)	0	1 (0.8)
Vascular disorders	23 (18.3)	2 (66.7)	25 (19.4)
Hypertension	5 (4.0)	2 (66.7)	7 (5.4)
Deep vein thrombosis	5 (4.0)	0	5 (3.9)
Hot flush	5 (4.0)	0	5 (3.9)
Embolism	1 (0.8)	0	1 (0.8)
Flushing	3 (2.4)	0	3 (2.3)
Hypotension	2 (1.6)	0	2 (1.6)

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Vascular disorders			
Lymphoedema	2 (1.6)	0	2 (1.6)
Thrombophlebitis superficial	2 (1.6)	0	2 (1.6)
Vena cava thrombosis	0	0	0
Pallor	0	0	0
Pelvic venous thrombosis	0	0	0
Peripheral embolism	0	0	0
Peripheral venous disease	1 (0.8)	0	1 (0.8)
Shock	1 (0.8)	0	1 (0.8)
Varicose vein	1 (0.8)	0	1 (0.8)
Reproductive system and breast disorders	22 (17.5)	1 (33.3)	23 (17.8)
Pelvic pain	7 (5.6)	0	7 (5.4)
Vaginal haemorrhage	5 (4.0)	0	5 (3.9)
Vaginal discharge	5 (4.0)	0	5 (3.9)
Vulvovaginal pruritus	0	0	0
Breast pain	0	0	0
Female genital tract fistula	2 (1.6)	0	2 (1.6)
Metrorrhagia	2 (1.6)	0	2 (1.6)
Vulvovaginal dryness	1 (0.8)	1 (33.3)	2 (1.6)
Vulvovaginal pain	1 (0.8)	0	1 (0.8)
Breast haematoma	1 (0.8)	0	1 (0.8)
Nipple pain	0	0	0
Pelvic floor muscle weakness	0	0	0
Perineal pain	1 (0.8)	0	1 (0.8)
Vaginal lesion	0	0	0

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Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Reproductive system and breast disorders			
Vulval disorder	1 (0.8)	0	1 (0.8)
Vulvovaginal discomfort	0	0	0
Injury, poisoning and procedural complications	17 (13.5)	1 (33.3)	18 (14.0)
Fall	1 (0.8)	0	1 (0.8)
Contusion	2 (1.6)	0	2 (1.6)
Infusion related reaction	0	0	0
Procedural pain	1 (0.8)	0	1 (0.8)
Femur fracture	0	0	0
Gastroenteritis radiation	2 (1.6)	0	2 (1.6)
Incision site pain	0	0	0
Ligament sprain	1 (0.8)	1 (33.3)	2 (1.6)
Skin laceration	1 (0.8)	0	1 (0.8)
Spinal compression fracture	1 (0.8)	0	1 (0.8)
Wound	2 (1.6)	0	2 (1.6)
Accidental overdose	0	0	0
Acetabulum fracture	0	0	0
Compression fracture	1 (0.8)	0	1 (0.8)
Eye contusion	0	0	0
Fractured sacrum	0	0	0
Gastrointestinal stoma complication	0	0	0
Medication error	0	0	0
Post procedural haemorrhage	0	0	0
Skin abrasion	1 (0.8)	0	1 (0.8)
Stoma site pain	1 (0.8)	0	1 (0.8)

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System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Injury, poisoning and procedural complications			
Stress fracture	1 (0.8)	0	1 (0.8)
Tendon rupture	1 (0.8)	0	1 (0.8)
Thermal burn	1 (0.8)	0	1 (0.8)
Thoracic vertebral fracture	0	0	0
Toxicity to various agents	1 (0.8)	0	1 (0.8)
Vascular access complication	0	0	0
Wound complication	1 (0.8)	0	1 (0.8)
Wound dehiscence	1 (0.8)	0	1 (0.8)
Endocrine disorders	11 (8.7)	1 (33.3)	12 (9.3)
Hypothyroidism	9 (7.1)	1 (33.3)	10 (7.8)
Hyperthyroidism	4 (3.2)	0	4 (3.1)
Adrenal insufficiency	1 (0.8)	0	1 (0.8)
Thyroiditis	0	0	0
Glucocorticoid deficiency	1 (0.8)	0	1 (0.8)
Hypophysitis	1 (0.8)	0	1 (0.8)
Eye disorders	13 (10.3)	0	13 (10.1)
Dry eye	4 (3.2)	0	4 (3.1)
Vision blurred	3 (2.4)	0	3 (2.3)
Cataract	2 (1.6)	0	2 (1.6)
Visual impairment	0	0	0
Vitreous floaters	1 (0.8)	0	1 (0.8)
Blindness	0	0	0
Conjunctival haemorrhage	0	0	0
Conjunctival hyperaemia	0	0	0

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System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Eye disorders			
Diplopia	1 (0.8)	0	1 (0.8)
Eye irritation	1 (0.8)	0	1 (0.8)
Eye pain	0	0	0
Eye pruritus	0	0	0
Iridocyclitis	1 (0.8)	0	1 (0.8)
Lacrimation increased	1 (0.8)	0	1 (0.8)
Ocular discomfort	1 (0.8)	0	1 (0.8)
Ocular hypertension	0	0	0
Uveitis	1 (0.8)	0	1 (0.8)
Cardiac disorders	6 (4.8)	1 (33.3)	7 (5.4)
Tachycardia	1 (0.8)	1 (33.3)	2 (1.6)
Atrial fibrillation	2 (1.6)	0	2 (1.6)
Angina pectoris	1 (0.8)	0	1 (0.8)
Bradycardia	1 (0.8)	0	1 (0.8)
Palpitations	0	0	0
Pericardial effusion	1 (0.8)	0	1 (0.8)
Sinus bradycardia	0	0	0
Sinus tachycardia	1 (0.8)	0	1 (0.8)
Atrial flutter	0	0	0
Bundle branch block right	0	0	0
Myocardial infarction	1 (0.8)	0	1 (0.8)
Supraventricular extrasystoles	1 (0.8)	0	1 (0.8)
Ventricular extrasystoles	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	6 (4.8)	0	6 (4.7)

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System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain	2 (1.6)	0	2 (1.6)
Acrochordon	0	0	0
Acute promyelocytic leukaemia	0	0	0
Cancer pain	1 (0.8)	0	1 (0.8)
Colon adenoma	1 (0.8)	0	1 (0.8)
Malignant ascites	0	0	0
Malignant melanoma	1 (0.8)	0	1 (0.8)
Melanocytic naevus	0	0	0
Metastases to central nervous system	0	0	0
Parathyroid tumour benign	0	0	0
Seborrhoeic keratosis	1 (0.8)	0	1 (0.8)
Tumour haemorrhage	0	0	0
Tumour invasion	0	0	0
Tumour necrosis	0	0	0
Ear and labyrinth disorders	5 (4.0)	0	5 (3.9)
Tinnitus	2 (1.6)	0	2 (1.6)
Vertigo	2 (1.6)	0	2 (1.6)
Cerumen impaction	1 (0.8)	0	1 (0.8)
Deafness	0	0	0
Ear discomfort	0	0	0
Ear pain	0	0	0
Hypoacusis	1 (0.8)	0	1 (0.8)
Hepatobiliary disorders	2 (1.6)	0	2 (1.6)
Bile duct stenosis	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_teae_socpt.sas, Output: t_14_3_1_2a_teae_socpt.rtf,
Generated on: 26AUG2020 03:08 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.2a Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Hepatobiliary disorders			
Cholecystitis	1 (0.8)	0	1 (0.8)
Gallbladder disorder	0	0	0
Hepatic function abnormal	1 (0.8)	0	1 (0.8)
Hepatitis	0	0	0
Hyperbilirubinaemia	0	0	0
Hypertransaminasaemia	1 (0.8)	0	1 (0.8)
Jaundice	0	0	0
Immune system disorders	0	0	0
Seasonal allergy	0	0	0
Contrast media allergy	0	0	0
Drug hypersensitivity	0	0	0
Iodine allergy	0	0	0
Product issues	0	0	0
Device occlusion	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Any Grade >=3 TEAE	61 (48.4)	1 (33.3)	62 (48.1)
Gastrointestinal disorders	18 (14.3)	0	18 (14.0)
Abdominal pain	7 (5.6)	0	7 (5.4)
Grade 3	7 (5.6)	0	7 (5.4)
Grade 4	0	0	0
Grade 5	0	0	0
Intestinal obstruction	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Nausea	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Ascites	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Diarrhoea	3 (2.4)	0	3 (2.3)
Grade 3	3 (2.4)	0	3 (2.3)
Grade 4	0	0	0
Grade 5	0	0	0
Small intestinal obstruction	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Vomiting	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Colitis	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Constipation	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Large intestinal obstruction	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Ileus	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Abdominal distension	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Abdominal pain lower	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Abdominal pain upper	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Anal haemorrhage	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Colonic fistula	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Gastric ulcer perforation	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Gastrointestinal haemorrhage	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Noninfective sialoadenitis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Oesophagitis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Pancreatitis	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Pancreatitis acute	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Stomatitis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Blood and lymphatic system disorders	20 (15.9)	0	20 (15.5)
Anaemia	19 (15.1)	0	19 (14.7)
Grade 3	19 (15.1)	0	19 (14.7)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Blood and lymphatic system disorders			
Leukopenia	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Neutropenia	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Autoimmune haemolytic anaemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Leukocytosis	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Blood and lymphatic system disorders			
Thrombocytopenia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Investigations	14 (11.1)	0	14 (10.9)
Alanine aminotransferase increased	3 (2.4)	0	3 (2.3)
Grade 3	3 (2.4)	0	3 (2.3)
Grade 4	0	0	0
Grade 5	0	0	0
Amylase increased	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Aspartate aminotransferase increased	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Lymphocyte count decreased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Lipase increased	3 (2.4)	0	3 (2.3)
Grade 3	3 (2.4)	0	3 (2.3)
Grade 4	0	0	0
Grade 5	0	0	0
Gamma-glutamyltransferase increased	2 (1.6)	0	2 (1.6)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	1 (0.8)	0	1 (0.8)
Grade 5	0	0	0
Blood alkaline phosphatase increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Blood creatinine increased	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Transaminases increased	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
White blood cell count increased	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Activated partial thromboplastin time prolonged	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Blood bilirubin increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Blood cholesterol increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Blood potassium decreased	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Blood sodium decreased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Haemoglobin decreased	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
International normalised ratio increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Neutrophil count decreased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Troponin increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)	
Investigations				
Weight increased	1 (0.8)	0	1 (0.8)	
Grade 3	1 (0.8)	0	1 (0.8)	
Grade 4	0	0	0	
Grade 5	0	0	0	
White blood cell count decreased	0	0	0	
Grade 3	0	0	0	
Grade 4	0	0	0	
Grade 5	0	0	0	
Metabolism and nutrition disorders	9 (7.1)	1 (33.3)	10 (7.8)	18 (12.4)
Hyponatraemia	4 (3.2)	1 (33.3)	5 (3.9)	
Grade 3	3 (2.4)	1 (33.3)	4 (3.1)	
Grade 4	1 (0.8)	0	1 (0.8)	
Grade 5	0	0	0	
Hypoalbuminaemia	1 (0.8)	0	1 (0.8)	
Grade 3	1 (0.8)	0	1 (0.8)	
Grade 4	0	0	0	
Grade 5	0	0	0	

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Metabolism and nutrition disorders			
Dehydration	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Hyperglycaemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Decreased appetite	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Hypercalcaemia	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Generated on: 26AUG2020 03:08 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Metabolism and nutrition disorders			
Hyperglycaemic hyperosmolar nonketotic syndrome	1 (0.8)	0	1 (0.8)
Grade 3	0	0	0
Grade 4	1 (0.8)	0	1 (0.8)
Grade 5	0	0	0
Hyperkalaemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Hypermagnesaemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Hypokalaemia	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

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For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Metabolism and nutrition disorders			
Hypophagia	0	1 (33.3)	1 (0.8)
Grade 3	0	1 (33.3)	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Malnutrition	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Respiratory, thoracic and mediastinal disorders	8 (6.3)	0	8 (6.2)
Dyspnoea	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Pulmonary embolism	4 (3.2)	0	4 (3.1)
Grade 3	3 (2.4)	0	3 (2.3)
Grade 4	1 (0.8)	0	1 (0.8)
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Pleural effusion	1 (0.8)	0	1 (0.8)
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	1 (0.8)	0	1 (0.8)
Respiratory failure	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Aspiration	1 (0.8)	0	1 (0.8)
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	1 (0.8)	0	1 (0.8)
Atelectasis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Cough	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Hypoxia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Increased bronchial secretion	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Pulmonary infarction	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Infections and infestations	12 (9.5)	0	12 (9.3)
Pneumonia	3 (2.4)	0	3 (2.3)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	1 (0.8)	0	1 (0.8)
Sepsis	4 (3.2)	0	4 (3.1)
Grade 3	0	0	0
Grade 4	3 (2.4)	0	3 (2.3)
Grade 5	1 (0.8)	0	1 (0.8)
Urinary tract infection	3 (2.4)	0	3 (2.3)
Grade 3	3 (2.4)	0	3 (2.3)
Grade 4	0	0	0
Grade 5	0	0	0
Bronchitis	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0

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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Infections and infestations			
Pyelonephritis	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Abdominal infection	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Abscess oral	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Bacteraemia	1 (0.8)	0	1 (0.8)
Grade 3	0	0	0
Grade 4	1 (0.8)	0	1 (0.8)
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Infections and infestations			
Clostridium difficile infection	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Diverticulitis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Infection	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Pyelonephritis acute	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Infections and infestations			
Upper respiratory tract infection	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Viral infection	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
General disorders and administration site conditions	8 (6.3)	0	8 (6.2)
Fatigue	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Asthenia	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
General disorders and administration site conditions			
General physical health deterioration	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Oedema	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Pain	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Peripheral swelling	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
General disorders and administration site conditions			
Non-cardiac chest pain	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Pyrexia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Musculoskeletal and connective tissue disorders	9 (7.1)	0	9 (7.0)
Back pain	4 (3.2)	0	4 (3.1)
Grade 3	4 (3.2)	0	4 (3.1)
Grade 4	0	0	0
Grade 5	0	0	0
Arthralgia	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Musculoskeletal and connective tissue disorders			
Pain in extremity	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Flank pain	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Muscular weakness	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Groin pain	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
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System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Musculoskeletal and connective tissue disorders			
Ligamentum flavum hypertrophy	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Lumbar spinal stenosis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Mobility decreased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Osteoarthritis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Renal and urinary disorders	7 (5.6)	0	7 (5.4)
Acute kidney injury	4 (3.2)	0	4 (3.1)
Grade 3	4 (3.2)	0	4 (3.1)
Grade 4	0	0	0
Grade 5	0	0	0
Urinary tract obstruction	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Hydronephrosis	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Renal failure	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Renal and urinary disorders			
Urogenital fistula	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Vascular disorders	4 (3.2)	0	4 (3.1)
Hypertension	3 (2.4)	0	3 (2.3)
Grade 3	3 (2.4)	0	3 (2.3)
Grade 4	0	0	0
Grade 5	0	0	0
Hypotension	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Embolism	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Vascular disorders			
Deep vein thrombosis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Shock	1 (0.8)	0	1 (0.8)
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	1 (0.8)	0	1 (0.8)
Nervous system disorders	6 (4.8)	1 (33.3)	7 (5.4)
Epilepsy	0	1 (33.3)	1 (0.8)
Grade 3	0	1 (33.3)	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Neuralgia	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_teae_ctcae3.sas, Output: t_14_3_1_5a_teae_ctcae3.rtf,
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Nervous system disorders			
Syncope	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Apraxia	1 (0.8)	0	1 (0.8)
Grade 3	0	0	0
Grade 4	1 (0.8)	0	1 (0.8)
Grade 5	0	0	0
Autonomic seizure	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Encephalopathy	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Nervous system disorders			
Facial paresis	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Neuropathy peripheral	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Seizure like phenomena	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Injury, poisoning and procedural complications	2 (1.6)	0	2 (1.6)
Wound	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Injury, poisoning and procedural complications			
Accidental overdose	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Femur fracture	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Gastrointestinal stoma complication	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Infusion related reaction	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	2 (1.6)	0	2 (1.6)
Tumour pain	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Acute promyelocytic leukaemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Malignant ascites	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Metastases to central nervous system	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Reproductive system and breast disorders	1 (0.8)	0	1 (0.8)
Pelvic pain	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Hepatobiliary disorders	1 (0.8)	0	1 (0.8)
Cholecystitis	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Hepatitis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Hyperbilirubinaemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Skin and subcutaneous tissue disorders	1 (0.8)	0	1 (0.8)
Drug eruption	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Pruritus	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Rash	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Rash maculo-papular	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Cardiac disorders	1 (0.8)	0	1 (0.8)
Atrial fibrillation	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Tachycardia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Psychiatric disorders	1 (0.8)	0	1 (0.8)
Confusional state	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Hallucination	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.5a CTCAE Grade 3 or Greater Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Endocrine disorders	0	0	0
Adrenal insufficiency	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Eye disorders	1 (0.8)	0	1 (0.8)
Cataract	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Any Treatment-Related Adverse Event	80 (63.5)	2 (66.7)	82 (63.6)
General disorders and administration site conditions	44 (34.9)	0	44 (34.1)
Fatigue	17 (13.5)	0	17 (13.2)
Asthenia	18 (14.3)	0	18 (14.0)
Chills	4 (3.2)	0	4 (3.1)
Pyrexia	4 (3.2)	0	4 (3.1)
Pain	0	0	0
Oedema	1 (0.8)	0	1 (0.8)
Oedema peripheral	2 (1.6)	0	2 (1.6)
Peripheral swelling	1 (0.8)	0	1 (0.8)
Chest pain	0	0	0
Feeling cold	0	0	0
Hyperthermia	1 (0.8)	0	1 (0.8)
Influenza like illness	0	0	0
Mucosal inflammation	0	0	0
Swelling face	0	0	0
Thirst	0	0	0
Gastrointestinal disorders	37 (29.4)	1 (33.3)	38 (29.5)
Diarrhoea	20 (15.9)	1 (33.3)	21 (16.3)
Nausea	16 (12.7)	0	16 (12.4)

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Vomiting	5 (4.0)	0	5 (3.9)
Constipation	5 (4.0)	0	5 (3.9)
Abdominal pain	3 (2.4)	0	3 (2.3)
Colitis	3 (2.4)	0	3 (2.3)
Stomatitis	2 (1.6)	0	2 (1.6)
Dyspepsia	1 (0.8)	0	1 (0.8)
Abdominal pain upper	1 (0.8)	0	1 (0.8)
Dry mouth	1 (0.8)	0	1 (0.8)
Abdominal discomfort	0	0	0
Abdominal distension	0	0	0
Gastrooesophageal reflux disease	1 (0.8)	0	1 (0.8)
Dysphagia	0	0	0
Enterocolitis haemorrhagic	1 (0.8)	0	1 (0.8)
Eructation	0	0	0
Gingival pain	0	0	0
Haematochezia	1 (0.8)	0	1 (0.8)
Haemorrhoids	0	0	0
Intestinal obstruction	0	0	0
Oesophagitis	0	0	0
Pancreatitis	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Pancreatitis acute	1 (0.8)	0	1 (0.8)
Paraesthesia oral	0	0	0
Rectal haemorrhage	1 (0.8)	0	1 (0.8)
Tongue dry	0	0	0
Skin and subcutaneous tissue disorders	22 (17.5)	1 (33.3)	23 (17.8)
Rash	7 (5.6)	0	7 (5.4)
Pruritus	11 (8.7)	0	11 (8.5)
Dry skin	2 (1.6)	0	2 (1.6)
Rash pruritic	0	0	0
Alopecia	2 (1.6)	0	2 (1.6)
Erythema	1 (0.8)	0	1 (0.8)
Rash macular	0	0	0
Onychoclasis	1 (0.8)	0	1 (0.8)
Rash maculo-papular	1 (0.8)	0	1 (0.8)
Skin lesion	2 (1.6)	0	2 (1.6)
Dermatitis acneiform	0	0	0
Dermatitis allergic	0	0	0
Dermatitis psoriasiform	0	0	0
Eczema	1 (0.8)	0	1 (0.8)
Exfoliative rash	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Skin and subcutaneous tissue disorders			
Hyperhidrosis	0	0	0
Nail discolouration	1 (0.8)	0	1 (0.8)
Nail disorder	0	0	0
Night sweats	0	0	0
Onychalgia	0	0	0
Pain of skin	0	1 (33.3)	1 (0.8)
Papule	1 (0.8)	0	1 (0.8)
Pemphigoid	1 (0.8)	0	1 (0.8)
Prurigo	1 (0.8)	0	1 (0.8)
Psoriasis	0	0	0
Skin reaction	0	1 (33.3)	1 (0.8)
Urticaria	1 (0.8)	0	1 (0.8)
Investigations	20 (15.9)	0	20 (15.5)
Aspartate aminotransferase increased	4 (3.2)	0	4 (3.1)
Alanine aminotransferase increased	5 (4.0)	0	5 (3.9)
Amylase increased	5 (4.0)	0	5 (3.9)
Blood creatinine increased	4 (3.2)	0	4 (3.1)
Lymphocyte count decreased	2 (1.6)	0	2 (1.6)
Blood alkaline phosphatase increased	1 (0.8)	0	1 (0.8)
Lipase increased	4 (3.2)	0	4 (3.1)

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Weight decreased	1 (0.8)	0	1 (0.8)
Blood bilirubin increased	1 (0.8)	0	1 (0.8)
Blood thyroid stimulating hormone decreased	1 (0.8)	0	1 (0.8)
Blood thyroid stimulating hormone increased	1 (0.8)	0	1 (0.8)
Gamma-glutamyltransferase increased	1 (0.8)	0	1 (0.8)
Neutrophil count decreased	1 (0.8)	0	1 (0.8)
Platelet count decreased	0	0	0
Thyroxine free increased	0	0	0
Transaminases increased	2 (1.6)	0	2 (1.6)
Tri-iodothyronine decreased	0	0	0
White blood cell count decreased	1 (0.8)	0	1 (0.8)
Activated partial thromboplastin time prolonged	1 (0.8)	0	1 (0.8)
Aspartate aminotransferase	0	0	0
Blood lactate dehydrogenase increased	0	0	0
Blood prolactin abnormal	0	0	0
Blood urea increased	1 (0.8)	0	1 (0.8)
Thyroxine increased	1 (0.8)	0	1 (0.8)
Tri-iodothyronine free decreased	0	0	0
Troponin increased	0	0	0
Weight increased	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Musculoskeletal and connective tissue disorders	25 (19.8)	1 (33.3)	26 (20.2)
Arthralgia	11 (8.7)	0	11 (8.5)
Myalgia	6 (4.8)	0	6 (4.7)
Muscular weakness	5 (4.0)	0	5 (3.9)
Musculoskeletal pain	3 (2.4)	0	3 (2.3)
Muscle spasms	2 (1.6)	0	2 (1.6)
Pain in extremity	0	0	0
Arthritis	1 (0.8)	0	1 (0.8)
Groin pain	0	0	0
Muscle discomfort	1 (0.8)	0	1 (0.8)
Rheumatoid arthritis	1 (0.8)	0	1 (0.8)
Tendon pain	1 (0.8)	0	1 (0.8)
Tendonitis	0	1 (33.3)	1 (0.8)
Metabolism and nutrition disorders	11 (8.7)	0	11 (8.5)
Decreased appetite	5 (4.0)	0	5 (3.9)
Hypomagnesaemia	4 (3.2)	0	4 (3.1)
Hyperglycaemia	0	0	0
Hypokalaemia	1 (0.8)	0	1 (0.8)
Hyponatraemia	2 (1.6)	0	2 (1.6)
Hypocalcaemia	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Metabolism and nutrition disorders			
Type 1 diabetes mellitus	0	0	0
Dehydration	0	0	0
Diabetic ketoacidosis	0	0	0
Hypercalcaemia	0	0	0
Hypermagnesaemia	0	0	0
Hypernatraemia	0	0	0
Hypoalbuminaemia	0	0	0
Endocrine disorders	10 (7.9)	1 (33.3)	11 (8.5)
Hypothyroidism	8 (6.3)	1 (33.3)	9 (7.0)
Hyperthyroidism	3 (2.4)	0	3 (2.3)
Adrenal insufficiency	1 (0.8)	0	1 (0.8)
Hypophysitis	1 (0.8)	0	1 (0.8)
Thyroiditis	0	0	0
Blood and lymphatic system disorders	11 (8.7)	0	11 (8.5)
Anaemia	9 (7.1)	0	9 (7.0)
Neutropenia	3 (2.4)	0	3 (2.3)
Thrombocytopenia	0	0	0
Autoimmune haemolytic anaemia	0	0	0
Leukopenia	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Respiratory, thoracic and mediastinal disorders	11 (8.7)	0	11 (8.5)
Cough	4 (3.2)	0	4 (3.1)
Dyspnoea	2 (1.6)	0	2 (1.6)
Nasal congestion	0	0	0
Pulmonary embolism	1 (0.8)	0	1 (0.8)
Choking sensation	1 (0.8)	0	1 (0.8)
Dysphonia	1 (0.8)	0	1 (0.8)
Increased upper airway secretion	1 (0.8)	0	1 (0.8)
Interstitial lung disease	1 (0.8)	0	1 (0.8)
Oropharyngeal pain	0	0	0
Painful respiration	0	0	0
Pneumonitis	1 (0.8)	0	1 (0.8)
Rhinitis allergic	0	0	0
Sputum retention	1 (0.8)	0	1 (0.8)
Nervous system disorders	8 (6.3)	0	8 (6.2)
Dizziness	2 (1.6)	0	2 (1.6)
Headache	3 (2.4)	0	3 (2.3)
Dysgeusia	1 (0.8)	0	1 (0.8)
Autonomic seizure	0	0	0
Burning sensation	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Nervous system disorders			
Formication	1 (0.8)	0	1 (0.8)
Hypogeusia	0	0	0
Memory impairment	0	0	0
Neuropathy peripheral	1 (0.8)	0	1 (0.8)
Paraesthesia	1 (0.8)	0	1 (0.8)
Peripheral sensory neuropathy	0	0	0
Restless legs syndrome	0	0	0
Eye disorders	7 (5.6)	0	7 (5.4)
Dry eye	3 (2.4)	0	3 (2.3)
Vision blurred	1 (0.8)	0	1 (0.8)
Blindness	0	0	0
Eye irritation	1 (0.8)	0	1 (0.8)
Eye pain	0	0	0
Eye pruritus	0	0	0
Iridocyclitis	1 (0.8)	0	1 (0.8)
Lacrimation increased	1 (0.8)	0	1 (0.8)
Uveitis	1 (0.8)	0	1 (0.8)
Vitreous floaters	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Vascular disorders	3 (2.4)	0	3 (2.3)
Flushing	1 (0.8)	0	1 (0.8)
Hypertension	1 (0.8)	0	1 (0.8)
Hot flush	1 (0.8)	0	1 (0.8)
Hypotension	0	0	0
Lymphoedema	0	0	0
Renal and urinary disorders	3 (2.4)	0	3 (2.3)
Nephritis	1 (0.8)	0	1 (0.8)
Acute kidney injury	0	0	0
Incontinence	0	0	0
Proteinuria	1 (0.8)	0	1 (0.8)
Tubulointerstitial nephritis	1 (0.8)	0	1 (0.8)
Infections and infestations	1 (0.8)	0	1 (0.8)
Bronchitis	1 (0.8)	0	1 (0.8)
Nail infection	0	0	0
Oral candidiasis	0	0	0
Pneumonia	0	0	0
Rhinitis	0	0	0
Viral infection	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Injury, poisoning and procedural complications	1 (0.8)	0	1 (0.8)
Infusion related reaction	0	0	0
Gastroenteritis radiation	1 (0.8)	0	1 (0.8)
Psychiatric disorders	1 (0.8)	0	1 (0.8)
Insomnia	1 (0.8)	0	1 (0.8)
Agitation	0	0	0
Anxiety	0	0	0
Confusional state	0	0	0
Delirium	0	0	0
Cardiac disorders	0	0	0
Bradycardia	0	0	0
Palpitations	0	0	0
Sinus bradycardia	0	0	0
Hepatobiliary disorders	0	0	0
Hepatitis	0	0	0
Jaundice	0	0	0
Ear and labyrinth disorders	1 (0.8)	0	1 (0.8)
Tinnitus	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.6a Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Reproductive system and breast disorders	0	0	0
Nipple pain	0	0	0
Vulvovaginal pruritus	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Only treatment-emergent adverse events are summarized.
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class and preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing).
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Any Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events	17 (13.5)	0	17 (13.2)
Investigations	7 (5.6)	0	7 (5.4)
Alanine aminotransferase increased	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Amylase increased	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Lipase increased	3 (2.4)	0	3 (2.3)
Grade 3	3 (2.4)	0	3 (2.3)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Aspartate aminotransferase increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Transaminases increased	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Blood alkaline phosphatase increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Blood bilirubin increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Gamma-glutamyltransferase increased	1 (0.8)	0	1 (0.8)
Grade 3	0	0	0
Grade 4	1 (0.8)	0	1 (0.8)
Grade 5	0	0	0
Lymphocyte count decreased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Troponin increased	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Gastrointestinal disorders	6 (4.8)	0	6 (4.7)
Diarrhoea	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0
Colitis	2 (1.6)	0	2 (1.6)
Grade 3	2 (1.6)	0	2 (1.6)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Constipation	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Nausea	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Abdominal pain upper	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Intestinal obstruction	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Oesophagitis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Pancreatitis	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Pancreatitis acute	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Stomatitis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Vomiting	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Blood and lymphatic system disorders	6 (4.8)	0	6 (4.7)
Anaemia	5 (4.0)	0	5 (3.9)
Grade 3	5 (4.0)	0	5 (3.9)
Grade 4	0	0	0
Grade 5	0	0	0
Autoimmune haemolytic anaemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Leukopenia	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Blood and lymphatic system disorders			
Neutropenia	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
General disorders and administration site conditions	1 (0.8)	0	1 (0.8)
Fatigue	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Asthenia	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
General disorders and administration site conditions			
Pyrexia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Metabolism and nutrition disorders	0	0	0
Hyperglycaemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Hyponatraemia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Respiratory, thoracic and mediastinal disorders	1 (0.8)	0	1 (0.8)
Pulmonary embolism	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Cough	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Dyspnoea	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Vascular disorders	1 (0.8)	0	1 (0.8)
Hypertension	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0
Hypotension	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Skin and subcutaneous tissue disorders	0	0	0
Rash	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Skin and subcutaneous tissue disorders			
Rash maculo-papular	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Endocrine disorders	0	0	0
Adrenal insufficiency	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Hepatobiliary disorders	0	0	0
Hepatitis	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Infections and infestations	0	0	0
Pneumonia	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Injury, poisoning and procedural complications	0	0	0
Infusion related reaction	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0
Musculoskeletal and connective tissue disorders	1 (0.8)	0	1 (0.8)
Arthralgia	1 (0.8)	0	1 (0.8)
Grade 3	1 (0.8)	0	1 (0.8)
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.9a CTCAE Grade 3 or Greater Treatment-Related Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Nervous system disorders	0	0	0
Autonomic seizure	0	0	0
Grade 3	0	0	0
Grade 4	0	0	0
Grade 5	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. Adverse event severity coded using NCI CTCAE v4.03
For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing). Events are summarized according to the maximum CTC grade experienced by the subject for that event.
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Table 14.3.1.11a Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Any serious TEAE	43 (34.1)	1 (33.3)	44 (34.1)
Gastrointestinal disorders	13 (10.3)	0	13 (10.1)
Abdominal pain	4 (3.2)	0	4 (3.1)
Intestinal obstruction	2 (1.6)	0	2 (1.6)
Ascites	0	0	0
Vomiting	0	0	0
Nausea	0	0	0
Ileus	0	0	0
Large intestinal obstruction	0	0	0
Small intestinal obstruction	0	0	0
Colitis	2 (1.6)	0	2 (1.6)
Abdominal distension	0	0	0
Anal haemorrhage	1 (0.8)	0	1 (0.8)
Constipation	1 (0.8)	0	1 (0.8)
Diarrhoea	0	0	0
Gastric ulcer perforation	1 (0.8)	0	1 (0.8)
Gastrointestinal haemorrhage	0	0	0
Oesophagitis	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier). SAE's between first dose date and 90 days after EOT visit date are summarized.
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Table 14.3.1.11a Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Gastrointestinal disorders			
Pancreatitis	1 (0.8)	0	1 (0.8)
Pancreatitis acute	1 (0.8)	0	1 (0.8)
Stomatitis	0	0	0
Infections and infestations	12 (9.5)	0	12 (9.3)
Sepsis	4 (3.2)	0	4 (3.1)
Pneumonia	2 (1.6)	0	2 (1.6)
Urinary tract infection	3 (2.4)	0	3 (2.3)
Pyelonephritis	2 (1.6)	0	2 (1.6)
Bronchitis	2 (1.6)	0	2 (1.6)
Abdominal infection	0	0	0
Abscess oral	0	0	0
Bacteraemia	1 (0.8)	0	1 (0.8)
Diverticulitis	0	0	0
Infection	0	0	0
Pyelonephritis acute	0	0	0
Upper respiratory tract infection	1 (0.8)	0	1 (0.8)
Viral infection	0	0	0
Respiratory, thoracic and mediastinal disorders	8 (6.3)	0	8 (6.2)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier). SAE's between first dose date and 90 days after EOT visit date are summarized.
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Table 14.3.1.11a Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Dyspnoea	1 (0.8)	0	1 (0.8)
Pulmonary embolism	3 (2.4)	0	3 (2.3)
Pleural effusion	1 (0.8)	0	1 (0.8)
Respiratory failure	0	0	0
Hypoxia	1 (0.8)	0	1 (0.8)
Aspiration	1 (0.8)	0	1 (0.8)
Pneumonitis	1 (0.8)	0	1 (0.8)
Pulmonary haemorrhage	0	0	0
General disorders and administration site conditions	9 (7.1)	0	9 (7.0)
Pyrexia	3 (2.4)	0	3 (2.3)
General physical health deterioration	2 (1.6)	0	2 (1.6)
Asthenia	1 (0.8)	0	1 (0.8)
Fatigue	0	0	0
Pain	2 (1.6)	0	2 (1.6)
Oedema	1 (0.8)	0	1 (0.8)
Peripheral swelling	0	0	0
Renal and urinary disorders	6 (4.8)	0	6 (4.7)
Acute kidney injury	4 (3.2)	0	4 (3.1)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier). SAE's between first dose date and 90 days after EOT visit date are summarized.
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Table 14.3.1.11a Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Renal and urinary disorders			
Renal failure	1 (0.8)	0	1 (0.8)
Urinary tract obstruction	1 (0.8)	0	1 (0.8)
Haematuria	0	0	0
Tubulointerstitial nephritis	1 (0.8)	0	1 (0.8)
Metabolism and nutrition disorders	2 (1.6)	1 (33.3)	3 (2.3)
Dehydration	1 (0.8)	0	1 (0.8)
Hyponatraemia	0	0	0
Diabetic ketoacidosis	0	0	0
Hypercalcaemia	0	0	0
Hyperglycaemic hyperosmolar nonketotic syndrome	1 (0.8)	0	1 (0.8)
Hypophagia	0	1 (33.3)	1 (0.8)
Nervous system disorders	3 (2.4)	1 (33.3)	4 (3.1)
Epilepsy	0	1 (33.3)	1 (0.8)
Apraxia	1 (0.8)	0	1 (0.8)
Autonomic seizure	0	0	0
Encephalopathy	1 (0.8)	0	1 (0.8)
Facial paresis	1 (0.8)	0	1 (0.8)
Seizure like phenomena	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier). SAE's between first dose date and 90 days after EOT visit date are summarized.
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Table 14.3.1.11a Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Nervous system disorders			
Syncope	0	0	0
Musculoskeletal and connective tissue disorders	3 (2.4)	0	3 (2.3)
Back pain	1 (0.8)	0	1 (0.8)
Arthralgia	0	0	0
Muscular weakness	1 (0.8)	0	1 (0.8)
Myalgia	1 (0.8)	0	1 (0.8)
Pain in extremity	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	3 (2.4)	0	3 (2.3)
Tumour pain	2 (1.6)	0	2 (1.6)
Acute promyelocytic leukaemia	0	0	0
Malignant ascites	0	0	0
Malignant melanoma	1 (0.8)	0	1 (0.8)
Metastases to central nervous system	0	0	0
Vascular disorders	1 (0.8)	0	1 (0.8)
Deep vein thrombosis	0	0	0
Embolism	0	0	0
Hypotension	0	0	0
Shock	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier). SAE's between first dose date and 90 days after EOT visit date are summarized.
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Table 14.3.1.11a Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Vascular disorders			
Vena cava thrombosis	0	0	0
Blood and lymphatic system disorders	0	0	0
Anaemia	0	0	0
Autoimmune haemolytic anaemia	0	0	0
Injury, poisoning and procedural complications	0	0	0
Femur fracture	0	0	0
Accidental overdose	0	0	0
Gastrointestinal stoma complication	0	0	0
Medication error	0	0	0
Cardiac disorders	1 (0.8)	0	1 (0.8)
Angina pectoris	0	0	0
Atrial flutter	0	0	0
Bundle branch block right	0	0	0
Myocardial infarction	1 (0.8)	0	1 (0.8)
Tachycardia	0	0	0
Investigations	2 (1.6)	0	2 (1.6)
Troponin increased	0	0	0
Aspartate aminotransferase increased	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier). SAE's between first dose date and 90 days after EOT visit date are summarized.
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Table 14.3.1.11a Serious Treatment-Emergent Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Investigations			
Transaminases increased	1 (0.8)	0	1 (0.8)
Skin and subcutaneous tissue disorders	2 (1.6)	0	2 (1.6)
Drug eruption	1 (0.8)	0	1 (0.8)
Pemphigoid	1 (0.8)	0	1 (0.8)
Rash maculo-papular	0	0	0
Hepatobiliary disorders	1 (0.8)	0	1 (0.8)
Cholecystitis	1 (0.8)	0	1 (0.8)
Hepatitis	0	0	0
Endocrine disorders	0	0	0
Adrenal insufficiency	0	0	0
Eye disorders	1 (0.8)	0	1 (0.8)
Iridocyclitis	1 (0.8)	0	1 (0.8)
Reproductive system and breast disorders	0	0	0
Pelvic pain	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier). SAE's between first dose date and 90 days after EOT visit date are summarized.
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_sae_socpt.sas, Output: t_14_3_1_11a_sae_socpt.rtf,
Generated on: 26AUG2020 03:08 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.13a Treatment-Related Serious Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Any treatment-related serious adverse events	12 (9.5)	0	12 (9.3)
Gastrointestinal disorders	5 (4.0)	0	5 (3.9)
Colitis	2 (1.6)	0	2 (1.6)
Constipation	1 (0.8)	0	1 (0.8)
Intestinal obstruction	0	0	0
Nausea	0	0	0
Oesophagitis	0	0	0
Pancreatitis	1 (0.8)	0	1 (0.8)
Pancreatitis acute	1 (0.8)	0	1 (0.8)
Stomatitis	0	0	0
Vomiting	0	0	0
General disorders and administration site conditions	2 (1.6)	0	2 (1.6)
Pyrexia	1 (0.8)	0	1 (0.8)
Asthenia	1 (0.8)	0	1 (0.8)
Fatigue	0	0	0
Respiratory, thoracic and mediastinal disorders	2 (1.6)	0	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing)
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_trel_sae.sas, Output: t_14_3_1_13a_trel_sae.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.3.1.13a Treatment-Related Serious Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Pulmonary embolism	1 (0.8)	0	1 (0.8)
Dyspnoea	0	0	0
Pneumonitis	1 (0.8)	0	1 (0.8)
Investigations	1 (0.8)	0	1 (0.8)
Transaminases increased	1 (0.8)	0	1 (0.8)
Troponin increased	0	0	0
Skin and subcutaneous tissue disorders	1 (0.8)	0	1 (0.8)
Pemphigoid	1 (0.8)	0	1 (0.8)
Rash maculo-papular	0	0	0
Blood and lymphatic system disorders	0	0	0
Autoimmune haemolytic anaemia	0	0	0
Endocrine disorders	0	0	0
Adrenal insufficiency	0	0	0
Eye disorders	1 (0.8)	0	1 (0.8)
Iridocyclitis	1 (0.8)	0	1 (0.8)
Hepatobiliary disorders	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing)
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_trel_sae.sas, Output: t_14_3_1_13a_trel_sae.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.3.1.13a Treatment-Related Serious Adverse Events by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Hepatobiliary disorders			
Hepatitis	0	0	0
Metabolism and nutrition disorders	0	0	0
Diabetic ketoacidosis	0	0	0
Musculoskeletal and connective tissue disorders	1 (0.8)	0	1 (0.8)
Myalgia	1 (0.8)	0	1 (0.8)
Nervous system disorders	0	0	0
Autonomic seizure	0	0	0
Renal and urinary disorders	1 (0.8)	0	1 (0.8)
Tubulointerstitial nephritis	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing)
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_trel_sae.sas, Output: t_14_3_1_13a_trel_sae.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.3.1.14a Treatment-Emergent Adverse Events Leading to Withdrawal of Study Treatment by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Any Adverse Events Leading to Withdrawal	15 (11.9)	0	15 (11.6)
Investigations	4 (3.2)	0	4 (3.1)
Alanine aminotransferase increased	2 (1.6)	0	2 (1.6)
Aspartate aminotransferase increased	1 (0.8)	0	1 (0.8)
Transaminases increased	2 (1.6)	0	2 (1.6)
Amylase increased	0	0	0
Blood creatinine increased	0	0	0
Gamma-glutamyltransferase increased	1 (0.8)	0	1 (0.8)
Gastrointestinal disorders	2 (1.6)	0	2 (1.6)
Ascites	0	0	0
Diarrhoea	0	0	0
Intestinal obstruction	1 (0.8)	0	1 (0.8)
Large intestinal obstruction	0	0	0
Oesophagitis	0	0	0
Pancreatitis	1 (0.8)	0	1 (0.8)
Stomatitis	0	0	0
Vomiting	0	0	0
Renal and urinary disorders	2 (1.6)	0	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_teae_wthdrw.sas, Output: t_14_3_1_14a_teae_wthdrw.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.14a Treatment-Emergent Adverse Events Leading to Withdrawal of Study Treatment by System Organ Class and Preferred Term
(Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Renal and urinary disorders			
Acute kidney injury	1 (0.8)	0	1 (0.8)
Renal failure	0	0	0
Tubulointerstitial nephritis	1 (0.8)	0	1 (0.8)
Respiratory, thoracic and mediastinal disorders	3 (2.4)	0	3 (2.3)
Aspiration	1 (0.8)	0	1 (0.8)
Pleural effusion	1 (0.8)	0	1 (0.8)
Pneumonitis	1 (0.8)	0	1 (0.8)
Infections and infestations	2 (1.6)	0	2 (1.6)
Bronchitis	1 (0.8)	0	1 (0.8)
Pneumonia	1 (0.8)	0	1 (0.8)
Sepsis	1 (0.8)	0	1 (0.8)
Nervous system disorders	1 (0.8)	0	1 (0.8)
Apraxia	1 (0.8)	0	1 (0.8)
Autonomic seizure	0	0	0
Blood and lymphatic system disorders	0	0	0
Autoimmune haemolytic anaemia	0	0	0
Endocrine disorders	0	0	0
Adrenal insufficiency	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_teae_wthdrw.sas, Output: t_14_3_1_14a_teae_wthdrw.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.14a Treatment-Emergent Adverse Events Leading to Withdrawal of Study Treatment by System Organ Class and Preferred Term
(Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
General disorders and administration site conditions	0	0	0
Pyrexia	0	0	0
Injury, poisoning and procedural complications	0	0	0
Infusion related reaction	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	0	0
Acute promyelocytic leukaemia	0	0	0
Vascular disorders	1 (0.8)	0	1 (0.8)
Shock	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_teae_wthdrw.sas, Output: t_14_3_1_14a_teae_wthdrw.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.16a Treatment-Related Adverse Events Leading to Withdrawal of Study Treatment by System Organ Class and Preferred Term (Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
Any Treatment-Related Adverse Events Leading to Withdrawal	5 (4.0)	0	5 (3.9)
Investigations	3 (2.4)	0	3 (2.3)
Alanine aminotransferase increased	1 (0.8)	0	1 (0.8)
Aspartate aminotransferase increased	1 (0.8)	0	1 (0.8)
Transaminases increased	2 (1.6)	0	2 (1.6)
Amylase increased	0	0	0
Gamma-glutamyltransferase increased	1 (0.8)	0	1 (0.8)
Gastrointestinal disorders	1 (0.8)	0	1 (0.8)
Diarrhoea	0	0	0
Oesophagitis	0	0	0
Pancreatitis	1 (0.8)	0	1 (0.8)
Stomatitis	0	0	0
Vomiting	0	0	0
Blood and lymphatic system disorders	0	0	0
Autoimmune haemolytic anaemia	0	0	0
Endocrine disorders	0	0	0
Adrenal insufficiency	0	0	0

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing)
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_trel_wthdrw.sas, Output: t_14_3_1_16a_trel_wthdrw.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.16a Treatment-Related Adverse Events Leading to Withdrawal of Study Treatment by System Organ Class and Preferred Term
(Safety Analysis Set)

System Organ Class Preferred Term [n (%)]	dMMR or (MMR-unk & MSI-H) EC dMMR (N=126)	 MMR-unk/MSI-H (N=3)	 Total (N=129)
General disorders and administration site conditions	0	0	0
Pyrexia	0	0	0
Injury, poisoning and procedural complications	0	0	0
Infusion related reaction	0	0	0
Nervous system disorders	0	0	0
Autonomic seizure	0	0	0
Renal and urinary disorders	1 (0.8)	0	1 (0.8)
Tubulointerstitial nephritis	1 (0.8)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment (EOT) visit (or until the start of alternate anticancer therapy, whichever occurs earlier).
Note: Treatment related Adverse events refer to any TEAE assessed by the Investigator as related to study treatment (‘Related’, ‘Possibly Related’, or missing)
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_trel_wthdrw.sas, Output: t_14_3_1_16a_trel_wthdrw.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Gastrointestinal disorders			
Total Pts with at Least one TEAE*	181 (71.8%)	191 (76.7%)	372 (74.3%)
Nausea	135 (53.6%)	143 (57.4%)	278 (55.5%)
Vomiting	74 (29.4%)	65 (26.1%)	139 (27.7%)
Constipation	64 (25.4%)	59 (23.7%)	123 (24.6%)
Diarrhoea	52 (20.6%)	42 (16.9%)	94 (18.8%)
Abdominal pain	41 (16.3%)	42 (16.9%)	83 (16.6%)
Stomatitis	31 (12.3%)	31 (12.4%)	62 (12.4%)
Dyspepsia	15 (6.0%)	22 (8.8%)	37 (7.4%)
Abdominal pain upper	19 (7.5%)	11 (4.4%)	30 (6.0%)
Dry mouth	9 (3.6%)	11 (4.4%)	20 (4.0%)
Ascites	11 (4.4%)	8 (3.2%)	19 (3.8%)
Gastrooesophageal reflux disease	11 (4.4%)	8 (3.2%)	19 (3.8%)
Abdominal distension	9 (3.6%)	9 (3.6%)	18 (3.6%)
Haemorrhoids	6 (2.4%)	7 (2.8%)	13 (2.6%)
Oral pain	6 (2.4%)	7 (2.8%)	13 (2.6%)
Dysphagia	6 (2.4%)	5 (2.0%)	11 (2.2%)
Intestinal obstruction	6 (2.4%)	3 (1.2%)	9 (1.8%)
Small intestinal obstruction	5 (2.0%)	4 (1.6%)	9 (1.8%)
Flatulence	5 (2.0%)	3 (1.2%)	8 (1.6%)
Abdominal pain lower	5 (2.0%)	2 (0.8%)	7 (1.4%)
Gastritis	3 (1.2%)	3 (1.2%)	6 (1.2%)
Abdominal discomfort	3 (1.2%)	1 (0.4%)	4 (0.8%)
Gingival bleeding	3 (1.2%)	1 (0.4%)	4 (0.8%)
Mouth ulceration	3 (1.2%)	1 (0.4%)	4 (0.8%)

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Oesophagitis	2 (0.8%)	2 (0.8%)	4 (0.8%)
Rectal haemorrhage	4 (1.6%)	0	4 (0.8%)
Aphthous stomatitis	2 (0.8%)	1 (0.4%)	3 (0.6%)
Gingival pain	2 (0.8%)	1 (0.4%)	3 (0.6%)
Ileus	2 (0.8%)	1 (0.4%)	3 (0.6%)
Proctalgia	1 (0.4%)	2 (0.8%)	3 (0.6%)
Toothache	2 (0.8%)	1 (0.4%)	3 (0.6%)
Anal fissure	0	2 (0.8%)	2 (0.4%)
Faecal incontinence	1 (0.4%)	1 (0.4%)	2 (0.4%)
Gastrointestinal hypomotility	2 (0.8%)	0	2 (0.4%)
Proctitis	2 (0.8%)	0	2 (0.4%)
Abdominal mass	0	1 (0.4%)	1 (0.2%)
Abdominal wall haematoma	0	1 (0.4%)	1 (0.2%)
Acute abdomen	1 (0.4%)	0	1 (0.2%)
Anal ulcer	0	1 (0.4%)	1 (0.2%)
Anorectal disorder	0	1 (0.4%)	1 (0.2%)
Cheilitis	0	1 (0.4%)	1 (0.2%)
Colitis	1 (0.4%)	0	1 (0.2%)
Colonic obstruction	1 (0.4%)	0	1 (0.2%)
Dental discomfort	0	1 (0.4%)	1 (0.2%)
Enterocutaneous fistula	0	1 (0.4%)	1 (0.2%)
Gastritis erosive	0	1 (0.4%)	1 (0.2%)
Gastrointestinal pain	0	1 (0.4%)	1 (0.2%)
Glossodynia	1 (0.4%)	0	1 (0.2%)
Haematemesis	0	1 (0.4%)	1 (0.2%)

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Haematochezia	0	1 (0.4%)	1 (0.2%)
Ileal stenosis	0	1 (0.4%)	1 (0.2%)
Ileus paralytic	0	1 (0.4%)	1 (0.2%)
Intestinal perforation	1 (0.4%)	0	1 (0.2%)
Lip oedema	1 (0.4%)	0	1 (0.2%)
Lip pain	0	1 (0.4%)	1 (0.2%)
Lip ulceration	0	1 (0.4%)	1 (0.2%)
Odynophagia	0	1 (0.4%)	1 (0.2%)
Oral disorder	1 (0.4%)	0	1 (0.2%)
Periodontal disease	0	1 (0.4%)	1 (0.2%)
Peritoneal adhesions	0	1 (0.4%)	1 (0.2%)
Subileus	0	1 (0.4%)	1 (0.2%)
Tongue pigmentation	1 (0.4%)	0	1 (0.2%)
Tooth loss	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	761	736	1497
Blood and lymphatic system disorders			
Total Pts with at Least one TEAE*	187 (74.2%)	181 (72.7%)	368 (73.5%)
Neutropenia	134 (53.2%)	128 (51.4%)	262 (52.3%)
Anaemia	121 (48.0%)	111 (44.6%)	232 (46.3%)
Leukopenia	76 (30.2%)	70 (28.1%)	146 (29.1%)
Thrombocytopenia	32 (12.7%)	29 (11.6%)	61 (12.2%)
Febrile neutropenia	23 (9.1%)	10 (4.0%)	33 (6.6%)
Lymphopenia	10 (4.0%)	13 (5.2%)	23 (4.6%)
Leukocytosis	5 (2.0%)	3 (1.2%)	8 (1.6%)

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Thrombocytosis	2 (0.8%)	3 (1.2%)	5 (1.0%)
Pancytopenia	3 (1.2%)	1 (0.4%)	4 (0.8%)
Coagulopathy	1 (0.4%)	0	1 (0.2%)
Eosinophilia	0	1 (0.4%)	1 (0.2%)
Lymphocytosis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	722	608	1330
General disorders and administration site conditions			
Total Pts with at Least one TEAE*	168 (66.7%)	160 (64.3%)	328 (65.5%)
Fatigue	109 (43.3%)	107 (43.0%)	216 (43.1%)
Asthenia	38 (15.1%)	26 (10.4%)	64 (12.8%)
Pyrexia	29 (11.5%)	32 (12.9%)	61 (12.2%)
Mucosal inflammation	27 (10.7%)	21 (8.4%)	48 (9.6%)
Oedema peripheral	20 (7.9%)	25 (10.0%)	45 (9.0%)
Pain	16 (6.3%)	8 (3.2%)	24 (4.8%)
Chest pain	7 (2.8%)	5 (2.0%)	12 (2.4%)
Malaise	7 (2.8%)	5 (2.0%)	12 (2.4%)
Chills	5 (2.0%)	4 (1.6%)	9 (1.8%)
Oedema	0	6 (2.4%)	6 (1.2%)
General physical health deterioration	4 (1.6%)	1 (0.4%)	5 (1.0%)
Performance status decreased	4 (1.6%)	1 (0.4%)	5 (1.0%)
Condition aggravated	2 (0.8%)	1 (0.4%)	3 (0.6%)
Face oedema	1 (0.4%)	2 (0.8%)	3 (0.6%)
Chest discomfort	1 (0.4%)	1 (0.4%)	2 (0.4%)
Extravasation	1 (0.4%)	1 (0.4%)	2 (0.4%)

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Influenza like illness	1 (0.4%)	1 (0.4%)	2 (0.4%)
Localised oedema	1 (0.4%)	1 (0.4%)	2 (0.4%)
Administration site reaction	1 (0.4%)	0	1 (0.2%)
Catheter site inflammation	1 (0.4%)	0	1 (0.2%)
Catheter site pain	0	1 (0.4%)	1 (0.2%)
Device malfunction	1 (0.4%)	0	1 (0.2%)
Drug intolerance	0	1 (0.4%)	1 (0.2%)
Facial pain	1 (0.4%)	0	1 (0.2%)
Feeling cold	1 (0.4%)	0	1 (0.2%)
Gait disturbance	0	1 (0.4%)	1 (0.2%)
Generalised oedema	0	1 (0.4%)	1 (0.2%)
Hyperpyrexia	1 (0.4%)	0	1 (0.2%)
Infusion site extravasation	1 (0.4%)	0	1 (0.2%)
Infusion site inflammation	0	1 (0.4%)	1 (0.2%)
Infusion site irritation	1 (0.4%)	0	1 (0.2%)
Infusion site reaction	1 (0.4%)	0	1 (0.2%)
Injection site bruising	0	1 (0.4%)	1 (0.2%)
Irritability	1 (0.4%)	0	1 (0.2%)
Mucosal dryness	0	1 (0.4%)	1 (0.2%)
Non-cardiac chest pain	1 (0.4%)	0	1 (0.2%)
Sense of oppression	1 (0.4%)	0	1 (0.2%)
Systemic inflammatory response syndrome	0	1 (0.4%)	1 (0.2%)
Thrombosis in device	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	365	346	711

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Metabolism and nutrition disorders			
Total Pts with at Least one TEAE*	114 (45.2%)	112 (45.0%)	226 (45.1%)
Decreased appetite	72 (28.6%)	67 (26.9%)	139 (27.7%)
Hypokalaemia	31 (12.3%)	32 (12.9%)	63 (12.6%)
Dehydration	18 (7.1%)	17 (6.8%)	35 (7.0%)
Hyponatraemia	19 (7.5%)	12 (4.8%)	31 (6.2%)
Hypomagnesaemia	16 (6.3%)	9 (3.6%)	25 (5.0%)
Hyperglycaemia	7 (2.8%)	5 (2.0%)	12 (2.4%)
Hypocalcaemia	3 (1.2%)	7 (2.8%)	10 (2.0%)
Hyperkalaemia	3 (1.2%)	5 (2.0%)	8 (1.6%)
Hypophosphataemia	4 (1.6%)	4 (1.6%)	8 (1.6%)
Hypoalbuminaemia	4 (1.6%)	3 (1.2%)	7 (1.4%)
Hyperuricaemia	2 (0.8%)	2 (0.8%)	4 (0.8%)
Hypoproteinaemia	1 (0.4%)	2 (0.8%)	3 (0.6%)
Hypercalcaemia	0	2 (0.8%)	2 (0.4%)
Hypoglycaemia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Appetite disorder	1 (0.4%)	0	1 (0.2%)
Cachexia	1 (0.4%)	0	1 (0.2%)
Fluid overload	0	1 (0.4%)	1 (0.2%)
Fluid retention	0	1 (0.4%)	1 (0.2%)
Folate deficiency	0	1 (0.4%)	1 (0.2%)
Hypercholesterolaemia	1 (0.4%)	0	1 (0.2%)
Hypercreatininaemia	1 (0.4%)	0	1 (0.2%)
Hypermagnesaemia	1 (0.4%)	0	1 (0.2%)
Malnutrition	0	1 (0.4%)	1 (0.2%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Metabolic acidosis	1 (0.4%)	0	1 (0.2%)
Tetany	0	1 (0.4%)	1 (0.2%)
Vitamin D deficiency	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	230	219	449
Skin and subcutaneous tissue disorders			
Total Pts with at Least one TEAE*	105 (41.7%)	105 (42.2%)	210 (41.9%)
Alopecia	89 (35.3%)	90 (36.1%)	179 (35.7%)
Rash	10 (4.0%)	7 (2.8%)	17 (3.4%)
Nail discolouration	6 (2.4%)	5 (2.0%)	11 (2.2%)
Pruritus	7 (2.8%)	3 (1.2%)	10 (2.0%)
Dry skin	5 (2.0%)	4 (1.6%)	9 (1.8%)
Palmar-plantar erythrodysaesthesia syndrome	7 (2.8%)	1 (0.4%)	8 (1.6%)
Onychomadesis	2 (0.8%)	5 (2.0%)	7 (1.4%)
Pain of skin	4 (1.6%)	3 (1.2%)	7 (1.4%)
Skin hyperpigmentation	4 (1.6%)	1 (0.4%)	5 (1.0%)
Blister	2 (0.8%)	2 (0.8%)	4 (0.8%)
Nail pigmentation	0	4 (1.6%)	4 (0.8%)
Erythema	1 (0.4%)	2 (0.8%)	3 (0.6%)
Nail disorder	3 (1.2%)	0	3 (0.6%)
Decubitus ulcer	0	2 (0.8%)	2 (0.4%)
Nail bed disorder	1 (0.4%)	1 (0.4%)	2 (0.4%)
Photosensitivity reaction	0	2 (0.8%)	2 (0.4%)
Rash papular	1 (0.4%)	1 (0.4%)	2 (0.4%)
Skin discolouration	1 (0.4%)	1 (0.4%)	2 (0.4%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Skin lesion	0	2 (0.8%)	2 (0.4%)
Acne	0	1 (0.4%)	1 (0.2%)
Dermatitis	0	1 (0.4%)	1 (0.2%)
Dermatitis contact	1 (0.4%)	0	1 (0.2%)
Hyperhidrosis	0	1 (0.4%)	1 (0.2%)
Nail dystrophy	1 (0.4%)	0	1 (0.2%)
Nail ridging	0	1 (0.4%)	1 (0.2%)
Pigmentation disorder	1 (0.4%)	0	1 (0.2%)
Pruritus generalised	1 (0.4%)	0	1 (0.2%)
Purpura	1 (0.4%)	0	1 (0.2%)
Rash erythematous	0	1 (0.4%)	1 (0.2%)
Rash macular	1 (0.4%)	0	1 (0.2%)
Rash maculo-papular	0	1 (0.4%)	1 (0.2%)
Scar pain	1 (0.4%)	0	1 (0.2%)
Skin ulcer	1 (0.4%)	0	1 (0.2%)
Swelling face	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	158	148	306
Investigations			
Total Pts with at Least one TEAE*	99 (39.3%)	107 (43.0%)	206 (41.1%)
White blood cell count decreased	26 (10.3%)	34 (13.7%)	60 (12.0%)
Neutrophil count decreased	26 (10.3%)	28 (11.2%)	54 (10.8%)
Ejection fraction decreased	14 (5.6%)	15 (6.0%)	29 (5.8%)
Weight decreased	14 (5.6%)	15 (6.0%)	29 (5.8%)
Blood creatinine increased	10 (4.0%)	16 (6.4%)	26 (5.2%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Aspartate aminotransferase increased	14 (5.6%)	10 (4.0%)	24 (4.8%)
Alanine aminotransferase increased	10 (4.0%)	11 (4.4%)	21 (4.2%)
Gamma-glutamyltransferase increased	8 (3.2%)	13 (5.2%)	21 (4.2%)
Lymphocyte count decreased	7 (2.8%)	12 (4.8%)	19 (3.8%)
Platelet count decreased	9 (3.6%)	8 (3.2%)	17 (3.4%)
Blood alkaline phosphatase increased	9 (3.6%)	7 (2.8%)	16 (3.2%)
Eastern Cooperative Oncology Group performance status worsened	5 (2.0%)	5 (2.0%)	10 (2.0%)
Blood lactate dehydrogenase increased	2 (0.8%)	5 (2.0%)	7 (1.4%)
Blood urea increased	3 (1.2%)	3 (1.2%)	6 (1.2%)
Electrocardiogram QT prolonged	4 (1.6%)	2 (0.8%)	6 (1.2%)
Platelet count increased	3 (1.2%)	3 (1.2%)	6 (1.2%)
Protein total decreased	2 (0.8%)	4 (1.6%)	6 (1.2%)
Blood albumin decreased	2 (0.8%)	3 (1.2%)	5 (1.0%)
Blood uric acid increased	0	4 (1.6%)	4 (0.8%)
Neutrophil count increased	2 (0.8%)	2 (0.8%)	4 (0.8%)
Blood chloride decreased	0	3 (1.2%)	3 (0.6%)
Blood magnesium decreased	1 (0.4%)	2 (0.8%)	3 (0.6%)
Albumin urine present	2 (0.8%)	0	2 (0.4%)
Blood alkaline phosphatase	0	2 (0.8%)	2 (0.4%)
C-reactive protein increased	2 (0.8%)	0	2 (0.4%)
International normalised ratio increased	1 (0.4%)	1 (0.4%)	2 (0.4%)
Protein urine	1 (0.4%)	1 (0.4%)	2 (0.4%)
Red blood cell count decreased	1 (0.4%)	1 (0.4%)	2 (0.4%)
Weight increased	2 (0.8%)	0	2 (0.4%)
White blood cell count increased	1 (0.4%)	1 (0.4%)	2 (0.4%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Activated partial thromboplastin time prolonged	0	1 (0.4%)	1 (0.2%)
Blood albumin	0	1 (0.4%)	1 (0.2%)
Blood bilirubin increased	0	1 (0.4%)	1 (0.2%)
Blood calcium decreased	0	1 (0.4%)	1 (0.2%)
Blood calcium increased	1 (0.4%)	0	1 (0.2%)
Blood creatine increased	0	1 (0.4%)	1 (0.2%)
Blood creatinine decreased	0	1 (0.4%)	1 (0.2%)
Blood glucose increased	1 (0.4%)	0	1 (0.2%)
Blood phosphorus decreased	1 (0.4%)	0	1 (0.2%)
Blood potassium decreased	0	1 (0.4%)	1 (0.2%)
Blood pressure decreased	1 (0.4%)	0	1 (0.2%)
Blood pressure systolic increased	1 (0.4%)	0	1 (0.2%)
Blood sodium decreased	1 (0.4%)	0	1 (0.2%)
Blood uric acid decreased	0	1 (0.4%)	1 (0.2%)
Body temperature increased	1 (0.4%)	0	1 (0.2%)
Ejection fraction	0	1 (0.4%)	1 (0.2%)
Electrocardiogram repolarisation abnormality	1 (0.4%)	0	1 (0.2%)
Eosinophil count decreased	1 (0.4%)	0	1 (0.2%)
Glomerular filtration rate decreased	0	1 (0.4%)	1 (0.2%)
Haemoglobin decreased	0	1 (0.4%)	1 (0.2%)
Heart rate increased	1 (0.4%)	0	1 (0.2%)
Hypophonesis	0	1 (0.4%)	1 (0.2%)
Lymphocyte count increased	1 (0.4%)	0	1 (0.2%)
Monocyte count decreased	0	1 (0.4%)	1 (0.2%)
Thyroid function test normal	1 (0.4%)	0	1 (0.2%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Transaminases	1 (0.4%)	0	1 (0.2%)
Transaminases increased	1 (0.4%)	0	1 (0.2%)
Troponin increased	1 (0.4%)	0	1 (0.2%)
Urine analysis abnormal	0	1 (0.4%)	1 (0.2%)
Vitamin D abnormal	0	1 (0.4%)	1 (0.2%)
White blood cell count	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	241	293	534
Infections and infestations			
Total Pts with at Least one TEAE*	89 (35.3%)	85 (34.1%)	174 (34.7%)
Urinary tract infection	31 (12.3%)	38 (15.3%)	69 (13.8%)
Nasopharyngitis	7 (2.8%)	5 (2.0%)	12 (2.4%)
Pneumonia	6 (2.4%)	6 (2.4%)	12 (2.4%)
Upper respiratory tract infection	6 (2.4%)	5 (2.0%)	11 (2.2%)
Oral candidiasis	5 (2.0%)	4 (1.6%)	9 (1.8%)
Bronchitis	4 (1.6%)	4 (1.6%)	8 (1.6%)
Sepsis	5 (2.0%)	3 (1.2%)	8 (1.6%)
Cystitis	3 (1.2%)	3 (1.2%)	6 (1.2%)
Herpes zoster	2 (0.8%)	4 (1.6%)	6 (1.2%)
Influenza	4 (1.6%)	2 (0.8%)	6 (1.2%)
Gingivitis	1 (0.4%)	4 (1.6%)	5 (1.0%)
Sinusitis	2 (0.8%)	3 (1.2%)	5 (1.0%)
Cellulitis	4 (1.6%)	0	4 (0.8%)
Infection	1 (0.4%)	2 (0.8%)	3 (0.6%)
Pharyngitis	1 (0.4%)	2 (0.8%)	3 (0.6%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Respiratory tract infection	2 (0.8%)	1 (0.4%)	3 (0.6%)
Rhinitis	3 (1.2%)	0	3 (0.6%)
Staphylococcal infection	1 (0.4%)	2 (0.8%)	3 (0.6%)
Tooth infection	1 (0.4%)	2 (0.8%)	3 (0.6%)
Vaginal infection	1 (0.4%)	2 (0.8%)	3 (0.6%)
Candidiasis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Clostridium difficile infection	2 (0.8%)	0	2 (0.4%)
Device related infection	2 (0.8%)	0	2 (0.4%)
Enterococcal infection	2 (0.8%)	0	2 (0.4%)
Fungal infection	2 (0.8%)	0	2 (0.4%)
Fungal skin infection	1 (0.4%)	1 (0.4%)	2 (0.4%)
Lower respiratory tract infection	2 (0.8%)	0	2 (0.4%)
Neutropenic sepsis	0	2 (0.8%)	2 (0.4%)
Oesophageal candidiasis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Oral fungal infection	1 (0.4%)	1 (0.4%)	2 (0.4%)
Otitis media	0	2 (0.8%)	2 (0.4%)
Skin infection	0	2 (0.8%)	2 (0.4%)
Urosepsis	2 (0.8%)	0	2 (0.4%)
Abdominal infection	1 (0.4%)	0	1 (0.2%)
Anal infection	0	1 (0.4%)	1 (0.2%)
Bacteraemia	1 (0.4%)	0	1 (0.2%)
Bacterial infection	0	1 (0.4%)	1 (0.2%)
Bacteriuria	1 (0.4%)	0	1 (0.2%)
Beta haemolytic streptococcal infection	1 (0.4%)	0	1 (0.2%)
Ear infection	0	1 (0.4%)	1 (0.2%)

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Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Furuncle	0	1 (0.4%)	1 (0.2%)
Gastroenteritis	0	1 (0.4%)	1 (0.2%)
Genital herpes	0	1 (0.4%)	1 (0.2%)
Genital infection fungal	1 (0.4%)	0	1 (0.2%)
Hordeolum	1 (0.4%)	0	1 (0.2%)
Klebsiella infection	1 (0.4%)	0	1 (0.2%)
Lung infection	1 (0.4%)	0	1 (0.2%)
Lymphangitis	0	1 (0.4%)	1 (0.2%)
Oropharyngeal candidiasis	0	1 (0.4%)	1 (0.2%)
Pelvic infection	0	1 (0.4%)	1 (0.2%)
Periodontitis	1 (0.4%)	0	1 (0.2%)
Pneumocystis jiroveci pneumonia	0	1 (0.4%)	1 (0.2%)
Postoperative wound infection	0	1 (0.4%)	1 (0.2%)
Respiratory tract infection viral	0	1 (0.4%)	1 (0.2%)
Septic shock	0	1 (0.4%)	1 (0.2%)
Skin candida	1 (0.4%)	0	1 (0.2%)
Staphylococcal sepsis	1 (0.4%)	0	1 (0.2%)
Streptococcal infection	1 (0.4%)	0	1 (0.2%)
Tinea pedis	1 (0.4%)	0	1 (0.2%)
Tooth abscess	0	1 (0.4%)	1 (0.2%)
Tracheobronchitis	1 (0.4%)	0	1 (0.2%)
Urethritis	1 (0.4%)	0	1 (0.2%)
Urinary tract infection enterococcal	1 (0.4%)	0	1 (0.2%)
Viral infection	1 (0.4%)	0	1 (0.2%)
Vulvitis	1 (0.4%)	0	1 (0.2%)

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Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Vulvovaginal mycotic infection	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	133	135	268
Respiratory, thoracic and mediastinal disorders			
Total Pts with at Least one TEAE*	81 (32.1%)	72 (28.9%)	153 (30.5%)
Dyspnoea	29 (11.5%)	34 (13.7%)	63 (12.6%)
Cough	30 (11.9%)	21 (8.4%)	51 (10.2%)
Pulmonary embolism	9 (3.6%)	9 (3.6%)	18 (3.6%)
Oropharyngeal pain	9 (3.6%)	7 (2.8%)	16 (3.2%)
Pleural effusion	10 (4.0%)	5 (2.0%)	15 (3.0%)
Nasal congestion	5 (2.0%)	4 (1.6%)	9 (1.8%)
Productive cough	3 (1.2%)	5 (2.0%)	8 (1.6%)
Dyspnoea exertional	5 (2.0%)	1 (0.4%)	6 (1.2%)
Epistaxis	4 (1.6%)	2 (0.8%)	6 (1.2%)
Sinus congestion	0	5 (2.0%)	5 (1.0%)
Rhinitis allergic	2 (0.8%)	2 (0.8%)	4 (0.8%)
Dysphonia	1 (0.4%)	2 (0.8%)	3 (0.6%)
Upper-airway cough syndrome	0	3 (1.2%)	3 (0.6%)
Acute respiratory failure	2 (0.8%)	0	2 (0.4%)
Pneumonitis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Respiratory disorder	1 (0.4%)	1 (0.4%)	2 (0.4%)
Respiratory failure	2 (0.8%)	0	2 (0.4%)
Rhinorrhoea	1 (0.4%)	1 (0.4%)	2 (0.4%)
Acute pulmonary oedema	1 (0.4%)	0	1 (0.2%)
Asthma	0	1 (0.4%)	1 (0.2%)

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Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Chronic obstructive pulmonary disease	1 (0.4%)	0	1 (0.2%)
Dry throat	1 (0.4%)	0	1 (0.2%)
Haemoptysis	0	1 (0.4%)	1 (0.2%)
Hiccups	1 (0.4%)	0	1 (0.2%)
Hyperventilation	0	1 (0.4%)	1 (0.2%)
Hypoxia	1 (0.4%)	0	1 (0.2%)
Increased upper airway secretion	1 (0.4%)	0	1 (0.2%)
Laryngeal granuloma	0	1 (0.4%)	1 (0.2%)
Laryngeal pain	1 (0.4%)	0	1 (0.2%)
Nasal discomfort	1 (0.4%)	0	1 (0.2%)
Orthopnoea	0	1 (0.4%)	1 (0.2%)
Paranasal sinus hypersecretion	0	1 (0.4%)	1 (0.2%)
Pharyngeal inflammation	1 (0.4%)	0	1 (0.2%)
Pharyngeal oedema	1 (0.4%)	0	1 (0.2%)
Pneumothorax	1 (0.4%)	0	1 (0.2%)
Sinus disorder	0	1 (0.4%)	1 (0.2%)
Sneezing	0	1 (0.4%)	1 (0.2%)
Throat irritation	1 (0.4%)	0	1 (0.2%)
Wheezing	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	139	127	266
Nervous system disorders			
Total Pts with at Least one TEAE*	70 (27.8%)	79 (31.7%)	149 (29.7%)
Dysgeusia	28 (11.1%)	21 (8.4%)	49 (9.8%)
Dizziness	18 (7.1%)	26 (10.4%)	44 (8.8%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Headache	17 (6.7%)	25 (10.0%)	42 (8.4%)
Peripheral sensory neuropathy	9 (3.6%)	10 (4.0%)	19 (3.8%)
Neuropathy peripheral	7 (2.8%)	6 (2.4%)	13 (2.6%)
Paraesthesia	5 (2.0%)	6 (2.4%)	11 (2.2%)
Hypoaesthesia	6 (2.4%)	3 (1.2%)	9 (1.8%)
Lethargy	3 (1.2%)	5 (2.0%)	8 (1.6%)
Amnesia	1 (0.4%)	4 (1.6%)	5 (1.0%)
Neuralgia	3 (1.2%)	2 (0.8%)	5 (1.0%)
Syncope	2 (0.8%)	2 (0.8%)	4 (0.8%)
Presyncope	2 (0.8%)	1 (0.4%)	3 (0.6%)
Sinus headache	1 (0.4%)	2 (0.8%)	3 (0.6%)
Somnolence	1 (0.4%)	2 (0.8%)	3 (0.6%)
Tremor	2 (0.8%)	1 (0.4%)	3 (0.6%)
Cognitive disorder	1 (0.4%)	1 (0.4%)	2 (0.4%)
Disturbance in attention	0	2 (0.8%)	2 (0.4%)
Memory impairment	0	2 (0.8%)	2 (0.4%)
Restless legs syndrome	0	2 (0.8%)	2 (0.4%)
Ageusia	0	1 (0.4%)	1 (0.2%)
Aphonia	1 (0.4%)	0	1 (0.2%)
Aura	1 (0.4%)	0	1 (0.2%)
Balance disorder	0	1 (0.4%)	1 (0.2%)
Cerebrovascular accident	1 (0.4%)	0	1 (0.2%)
Dizziness postural	0	1 (0.4%)	1 (0.2%)
Drooling	1 (0.4%)	0	1 (0.2%)
Dysarthria	1 (0.4%)	0	1 (0.2%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Encephalopathy	0	1 (0.4%)	1 (0.2%)
Epilepsy	0	1 (0.4%)	1 (0.2%)
Head discomfort	1 (0.4%)	0	1 (0.2%)
Myoclonus	1 (0.4%)	0	1 (0.2%)
Paresis	0	1 (0.4%)	1 (0.2%)
Polyneuropathy	0	1 (0.4%)	1 (0.2%)
Transient ischaemic attack	0	1 (0.4%)	1 (0.2%)
VIIth nerve paralysis	0	1 (0.4%)	1 (0.2%)
Vascular encephalopathy	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	127	149	276
Musculoskeletal and connective tissue disorders			
Total Pts with at Least one TEAE*	70 (27.8%)	67 (26.9%)	137 (27.3%)
Back pain	26 (10.3%)	25 (10.0%)	51 (10.2%)
Pain in extremity	13 (5.2%)	15 (6.0%)	28 (5.6%)
Arthralgia	12 (4.8%)	14 (5.6%)	26 (5.2%)
Myalgia	8 (3.2%)	9 (3.6%)	17 (3.4%)
Musculoskeletal pain	9 (3.6%)	4 (1.6%)	13 (2.6%)
Bone pain	3 (1.2%)	9 (3.6%)	12 (2.4%)
Muscular weakness	6 (2.4%)	3 (1.2%)	9 (1.8%)
Neck pain	4 (1.6%)	4 (1.6%)	8 (1.6%)
Muscle spasms	4 (1.6%)	3 (1.2%)	7 (1.4%)
Flank pain	3 (1.2%)	3 (1.2%)	6 (1.2%)
Musculoskeletal chest pain	2 (0.8%)	3 (1.2%)	5 (1.0%)
Joint swelling	1 (0.4%)	3 (1.2%)	4 (0.8%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Groin pain	2 (0.8%)	1 (0.4%)	3 (0.6%)
Pain in jaw	2 (0.8%)	1 (0.4%)	3 (0.6%)
Osteoporosis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Intervertebral disc protrusion	0	1 (0.4%)	1 (0.2%)
Joint stiffness	0	1 (0.4%)	1 (0.2%)
Rhabdomyolysis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	110	113	223
Renal and urinary disorders			
Total Pts with at Least one TEAE*	43 (17.1%)	37 (14.9%)	80 (16.0%)
Proteinuria	12 (4.8%)	7 (2.8%)	19 (3.8%)
Dysuria	7 (2.8%)	6 (2.4%)	13 (2.6%)
Haematuria	7 (2.8%)	4 (1.6%)	11 (2.2%)
Pollakiuria	6 (2.4%)	4 (1.6%)	10 (2.0%)
Hydronephrosis	4 (1.6%)	5 (2.0%)	9 (1.8%)
Renal failure acute	5 (2.0%)	4 (1.6%)	9 (1.8%)
Renal failure	3 (1.2%)	2 (0.8%)	5 (1.0%)
Urinary incontinence	4 (1.6%)	1 (0.4%)	5 (1.0%)
Urinary tract pain	1 (0.4%)	3 (1.2%)	4 (0.8%)
Urinary retention	2 (0.8%)	1 (0.4%)	3 (0.6%)
Chromaturia	0	2 (0.8%)	2 (0.4%)
Glycosuria	1 (0.4%)	1 (0.4%)	2 (0.4%)
Leukocyturia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Microalbuminuria	1 (0.4%)	1 (0.4%)	2 (0.4%)
Micturition urgency	0	2 (0.8%)	2 (0.4%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Nocturia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Urinary tract obstruction	1 (0.4%)	1 (0.4%)	2 (0.4%)
Incontinence	0	1 (0.4%)	1 (0.2%)
Nephrolithiasis	0	1 (0.4%)	1 (0.2%)
Renal colic	1 (0.4%)	0	1 (0.2%)
Renal impairment	0	1 (0.4%)	1 (0.2%)
Urethritis noninfective	1 (0.4%)	0	1 (0.2%)
Urogenital fistula	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	63	55	118
Vascular disorders			
Total Pts with at Least one TEAE*	42 (16.7%)	33 (13.3%)	75 (15.0%)
Deep vein thrombosis	9 (3.6%)	8 (3.2%)	17 (3.4%)
Hot flush	8 (3.2%)	6 (2.4%)	14 (2.8%)
Hypotension	6 (2.4%)	5 (2.0%)	11 (2.2%)
Embolism	3 (1.2%)	4 (1.6%)	7 (1.4%)
Hypertension	5 (2.0%)	1 (0.4%)	6 (1.2%)
Phlebitis	3 (1.2%)	2 (0.8%)	5 (1.0%)
Thrombophlebitis	2 (0.8%)	2 (0.8%)	4 (0.8%)
Thrombosis	2 (0.8%)	2 (0.8%)	4 (0.8%)
Circulatory collapse	2 (0.8%)	1 (0.4%)	3 (0.6%)
Flushing	2 (0.8%)	1 (0.4%)	3 (0.6%)
Haematoma	2 (0.8%)	0	2 (0.4%)
Lymphoedema	0	2 (0.8%)	2 (0.4%)
Superior vena cava syndrome	0	2 (0.8%)	2 (0.4%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Arteriosclerosis	0	1 (0.4%)	1 (0.2%)
Haemorrhage	1 (0.4%)	0	1 (0.2%)
Hypertensive crisis	0	1 (0.4%)	1 (0.2%)
Intermittent claudication	0	1 (0.4%)	1 (0.2%)
Jugular vein thrombosis	1 (0.4%)	0	1 (0.2%)
Pallor	1 (0.4%)	0	1 (0.2%)
Thrombophlebitis superficial	0	1 (0.4%)	1 (0.2%)
Vascular fragility	1 (0.4%)	0	1 (0.2%)
Venous thrombosis limb	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	51	41	92
Cardiac disorders			
Total Pts with at Least one TEAE*	27 (10.7%)	41 (16.5%)	68 (13.6%)
Tachycardia	7 (2.8%)	11 (4.4%)	18 (3.6%)
Sinus tachycardia	3 (1.2%)	9 (3.6%)	12 (2.4%)
Palpitations	6 (2.4%)	3 (1.2%)	9 (1.8%)
Atrial fibrillation	4 (1.6%)	3 (1.2%)	7 (1.4%)
Mitral valve incompetence	1 (0.4%)	3 (1.2%)	4 (0.8%)
Cardiac arrest	2 (0.8%)	1 (0.4%)	3 (0.6%)
Cardiotoxicity	1 (0.4%)	2 (0.8%)	3 (0.6%)
Atrial flutter	0	2 (0.8%)	2 (0.4%)
Cardiac failure	1 (0.4%)	1 (0.4%)	2 (0.4%)
Left ventricular dysfunction	0	2 (0.8%)	2 (0.4%)
Mitral valve disease	1 (0.4%)	1 (0.4%)	2 (0.4%)
Myocardial infarction	1 (0.4%)	1 (0.4%)	2 (0.4%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Supraventricular tachycardia	0	2 (0.8%)	2 (0.4%)
Tricuspid valve disease	0	2 (0.8%)	2 (0.4%)
Acute coronary syndrome	1 (0.4%)	0	1 (0.2%)
Atrioventricular block	0	1 (0.4%)	1 (0.2%)
Bundle branch block right	0	1 (0.4%)	1 (0.2%)
Cardiac aneurysm	0	1 (0.4%)	1 (0.2%)
Cardio-respiratory arrest	0	1 (0.4%)	1 (0.2%)
Extrasystoles	0	1 (0.4%)	1 (0.2%)
Hypertensive heart disease	0	1 (0.4%)	1 (0.2%)
Intracardiac thrombus	0	1 (0.4%)	1 (0.2%)
Papillary muscle haemorrhage	0	1 (0.4%)	1 (0.2%)
Tachyarrhythmia	0	1 (0.4%)	1 (0.2%)
Ventricular extrasystoles	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	31	59	90
Psychiatric disorders			
Total Pts with at Least one TEAE*	39 (15.5%)	29 (11.6%)	68 (13.6%)
Anxiety	11 (4.4%)	14 (5.6%)	25 (5.0%)
Insomnia	12 (4.8%)	13 (5.2%)	25 (5.0%)
Depression	11 (4.4%)	9 (3.6%)	20 (4.0%)
Confusional state	2 (0.8%)	0	2 (0.4%)
Depressed mood	2 (0.8%)	0	2 (0.4%)
Food aversion	1 (0.4%)	1 (0.4%)	2 (0.4%)
Mental status changes	2 (0.8%)	0	2 (0.4%)
Mood swings	0	2 (0.8%)	2 (0.4%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Agitation	1 (0.4%)	0	1 (0.2%)
Eating disorder	0	1 (0.4%)	1 (0.2%)
Initial insomnia	0	1 (0.4%)	1 (0.2%)
Sleep disorder	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	46	43	89
Reproductive system and breast disorders			
Total Pts with at Least one TEAE*	22 (8.7%)	19 (7.6%)	41 (8.2%)
Vaginal haemorrhage	7 (2.8%)	6 (2.4%)	13 (2.6%)
Pelvic pain	4 (1.6%)	4 (1.6%)	8 (1.6%)
Vaginal discharge	4 (1.6%)	2 (0.8%)	6 (1.2%)
Vulvovaginal pain	2 (0.8%)	1 (0.4%)	3 (0.6%)
Female genital tract fistula	0	2 (0.8%)	2 (0.4%)
Metrorrhagia	0	2 (0.8%)	2 (0.4%)
Vulvovaginal pruritus	0	2 (0.8%)	2 (0.4%)
Dyspareunia	1 (0.4%)	0	1 (0.2%)
Genital haemorrhage	0	1 (0.4%)	1 (0.2%)
Genital rash	1 (0.4%)	0	1 (0.2%)
Uterine haemorrhage	1 (0.4%)	0	1 (0.2%)
Vaginal erosion	1 (0.4%)	0	1 (0.2%)
Vaginal inflammation	0	1 (0.4%)	1 (0.2%)
Vulvovaginal burning sensation	0	1 (0.4%)	1 (0.2%)
Vulvovaginal discomfort	1 (0.4%)	0	1 (0.2%)
Vulvovaginal dryness	1 (0.4%)	0	1 (0.2%)
Vulvovaginal rash	0	1 (0.4%)	1 (0.2%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Total Number of TEAEs	26	24	50
Eye disorders			
Total Pts with at Least one TEAE*	22 (8.7%)	18 (7.2%)	40 (8.0%)
Vision blurred	6 (2.4%)	4 (1.6%)	10 (2.0%)
Conjunctivitis	6 (2.4%)	1 (0.4%)	7 (1.4%)
Lacrimation increased	3 (1.2%)	4 (1.6%)	7 (1.4%)
Dry eye	3 (1.2%)	2 (0.8%)	5 (1.0%)
Eye irritation	2 (0.8%)	0	2 (0.4%)
Visual acuity reduced	2 (0.8%)	0	2 (0.4%)
Visual impairment	1 (0.4%)	1 (0.4%)	2 (0.4%)
Asthenopia	1 (0.4%)	0	1 (0.2%)
Blepharitis	0	1 (0.4%)	1 (0.2%)
Blindness	0	1 (0.4%)	1 (0.2%)
Cataract	1 (0.4%)	0	1 (0.2%)
Conjunctival hyperaemia	0	1 (0.4%)	1 (0.2%)
Diplopia	0	1 (0.4%)	1 (0.2%)
Eye discharge	0	1 (0.4%)	1 (0.2%)
Ocular hyperaemia	1 (0.4%)	0	1 (0.2%)
Photopsia	0	1 (0.4%)	1 (0.2%)
Vitreous haemorrhage	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	26	19	45
Injury, poisoning and procedural complications			
Total Pts with at Least one TEAE*	15 (6.0%)	14 (5.6%)	29 (5.8%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Contusion	3 (1.2%)	4 (1.6%)	7 (1.4%)
Fall	1 (0.4%)	5 (2.0%)	6 (1.2%)
Infusion related reaction	2 (0.8%)	0	2 (0.4%)
Limb injury	2 (0.8%)	0	2 (0.4%)
Vascular access complication	1 (0.4%)	1 (0.4%)	2 (0.4%)
Eschar	1 (0.4%)	0	1 (0.2%)
Face injury	1 (0.4%)	0	1 (0.2%)
Femur fracture	1 (0.4%)	0	1 (0.2%)
Hand fracture	0	1 (0.4%)	1 (0.2%)
Head injury	0	1 (0.4%)	1 (0.2%)
Hip fracture	0	1 (0.4%)	1 (0.2%)
Incision site complication	0	1 (0.4%)	1 (0.2%)
Joint dislocation	0	1 (0.4%)	1 (0.2%)
Ligament sprain	0	1 (0.4%)	1 (0.2%)
Post procedural urine leak	1 (0.4%)	0	1 (0.2%)
Procedural pain	0	1 (0.4%)	1 (0.2%)
Radiation associated pain	1 (0.4%)	0	1 (0.2%)
Radius fracture	0	1 (0.4%)	1 (0.2%)
Scapula fracture	1 (0.4%)	0	1 (0.2%)
Skeletal injury	1 (0.4%)	0	1 (0.2%)
Soft tissue injury	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	20	20	40
Immune system disorders			
Total Pts with at Least one TEAE*	15 (6.0%)	4 (1.6%)	19 (3.8%)

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Hypersensitivity	13 (5.2%)	3 (1.2%)	16 (3.2%)
Seasonal allergy	1 (0.4%)	1 (0.4%)	2 (0.4%)
Drug hypersensitivity	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	15	4	19
Ear and labyrinth disorders			
Total Pts with at Least one TEAE*	6 (2.4%)	8 (3.2%)	14 (2.8%)
Tinnitus	4 (1.6%)	6 (2.4%)	10 (2.0%)
Ear pain	1 (0.4%)	2 (0.8%)	3 (0.6%)
Vertigo	2 (0.8%)	1 (0.4%)	3 (0.6%)
Hearing impaired	1 (0.4%)	1 (0.4%)	2 (0.4%)
Deafness	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	9	13	22
Hepatobiliary disorders			
Total Pts with at Least one TEAE*	7 (2.8%)	3 (1.2%)	10 (2.0%)
Hepatic pain	3 (1.2%)	0	3 (0.6%)
Hyperbilirubinaemia	2 (0.8%)	0	2 (0.4%)
Cholecystitis acute	0	1 (0.4%)	1 (0.2%)
Cholestasis	1 (0.4%)	0	1 (0.2%)
Hepatic failure	1 (0.4%)	0	1 (0.2%)
Hepatic function abnormal	0	1 (0.4%)	1 (0.2%)
Hypertransaminasaemia	1 (0.4%)	0	1 (0.2%)
Liver disorder	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	8	3	11

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TABLE 14.3.1.2: TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Total Pts with at Least one TEAE*	2 (0.8%)	6 (2.4%)	8 (1.6%)
Tumour pain	2 (0.8%)	1 (0.4%)	3 (0.6%)
Leukaemia	0	1 (0.4%)	1 (0.2%)
Malignant neoplasm progression	0	1 (0.4%)	1 (0.2%)
Metastases to central nervous system	0	1 (0.4%)	1 (0.2%)
Metastatic uterine cancer	0	1 (0.4%)	1 (0.2%)
Tumour haemorrhage	0	1 (0.4%)	1 (0.2%)
Tumour necrosis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	2	7	9
Surgical and medical procedures			
Total Pts with at Least one TEAE*	1 (0.4%)	1 (0.4%)	2 (0.4%)
Prophylaxis of nausea and vomiting	1 (0.4%)	0	1 (0.2%)
Sinus operation	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	1	1	2
Endocrine disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	0	1 (0.2%)
Autoimmune thyroiditis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	0	1

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Blood and lymphatic system disorders			
Total Pts with at Least one TEAE*	179 (71.0%)	177 (71.1%)	356 (71.1%)
Neutropenia	132 (52.4%)	126 (50.6%)	258 (51.5%)
Anaemia	107 (42.5%)	101 (40.6%)	208 (41.5%)
Leukopenia	74 (29.4%)	68 (27.3%)	142 (28.3%)
Thrombocytopenia	31 (12.3%)	29 (11.6%)	60 (12.0%)
Febrile neutropenia	23 (9.1%)	10 (4.0%)	33 (6.6%)
Lymphopenia	10 (4.0%)	12 (4.8%)	22 (4.4%)
Pancytopenia	2 (0.8%)	1 (0.4%)	3 (0.6%)
Leukocytosis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Thrombocytosis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Lymphocytosis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	678	568	1246
Gastrointestinal disorders			
Total Pts with at Least one TEAE*	152 (60.3%)	161 (64.7%)	313 (62.5%)
Nausea	120 (47.6%)	125 (50.2%)	245 (48.9%)
Vomiting	63 (25.0%)	48 (19.3%)	111 (22.2%)
Diarrhoea	36 (14.3%)	33 (13.3%)	69 (13.8%)
Constipation	33 (13.1%)	28 (11.2%)	61 (12.2%)
Stomatitis	30 (11.9%)	29 (11.6%)	59 (11.8%)
Dyspepsia	10 (4.0%)	13 (5.2%)	23 (4.6%)
Abdominal pain	6 (2.4%)	9 (3.6%)	15 (3.0%)
Dry mouth	8 (3.2%)	7 (2.8%)	15 (3.0%)
Oral pain	5 (2.0%)	7 (2.8%)	12 (2.4%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Gastrooesophageal reflux disease	6 (2.4%)	4 (1.6%)	10 (2.0%)
Abdominal pain upper	5 (2.0%)	2 (0.8%)	7 (1.4%)
Dysphagia	4 (1.6%)	3 (1.2%)	7 (1.4%)
Gastritis	3 (1.2%)	1 (0.4%)	4 (0.8%)
Gingival bleeding	3 (1.2%)	1 (0.4%)	4 (0.8%)
Mouth ulceration	3 (1.2%)	1 (0.4%)	4 (0.8%)
Aphthous stomatitis	2 (0.8%)	1 (0.4%)	3 (0.6%)
Flatulence	3 (1.2%)	0	3 (0.6%)
Abdominal discomfort	1 (0.4%)	1 (0.4%)	2 (0.4%)
Abdominal distension	1 (0.4%)	1 (0.4%)	2 (0.4%)
Gingival pain	2 (0.8%)	0	2 (0.4%)
Abdominal pain lower	0	1 (0.4%)	1 (0.2%)
Ascites	0	1 (0.4%)	1 (0.2%)
Cheilitis	0	1 (0.4%)	1 (0.2%)
Colitis	1 (0.4%)	0	1 (0.2%)
Gastrointestinal pain	0	1 (0.4%)	1 (0.2%)
Glossodynia	1 (0.4%)	0	1 (0.2%)
Haemorrhoids	0	1 (0.4%)	1 (0.2%)
Lip pain	0	1 (0.4%)	1 (0.2%)
Lip ulceration	0	1 (0.4%)	1 (0.2%)
Oesophagitis	0	1 (0.4%)	1 (0.2%)
Oral disorder	1 (0.4%)	0	1 (0.2%)
Periodontal disease	0	1 (0.4%)	1 (0.2%)
Small intestinal obstruction	0	1 (0.4%)	1 (0.2%)
Tongue pigmentation	1 (0.4%)	0	1 (0.2%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Total Number of TEAEs	498	491	989
General disorders and administration site conditions			
Total Pts with at Least one TEAE*	134 (53.2%)	128 (51.4%)	262 (52.3%)
Fatigue	100 (39.7%)	99 (39.8%)	199 (39.7%)
Asthenia	28 (11.1%)	19 (7.6%)	47 (9.4%)
Mucosal inflammation	23 (9.1%)	21 (8.4%)	44 (8.8%)
Pyrexia	10 (4.0%)	10 (4.0%)	20 (4.0%)
Oedema peripheral	5 (2.0%)	8 (3.2%)	13 (2.6%)
Malaise	7 (2.8%)	3 (1.2%)	10 (2.0%)
Chills	0	3 (1.2%)	3 (0.6%)
Chest pain	1 (0.4%)	1 (0.4%)	2 (0.4%)
General physical health deterioration	2 (0.8%)	0	2 (0.4%)
Oedema	0	2 (0.8%)	2 (0.4%)
Administration site reaction	1 (0.4%)	0	1 (0.2%)
Chest discomfort	0	1 (0.4%)	1 (0.2%)
Condition aggravated	1 (0.4%)	0	1 (0.2%)
Drug intolerance	0	1 (0.4%)	1 (0.2%)
Face oedema	0	1 (0.4%)	1 (0.2%)
Facial pain	1 (0.4%)	0	1 (0.2%)
Feeling cold	1 (0.4%)	0	1 (0.2%)
Influenza like illness	1 (0.4%)	0	1 (0.2%)
Infusion site inflammation	0	1 (0.4%)	1 (0.2%)
Infusion site reaction	1 (0.4%)	0	1 (0.2%)
Injection site bruising	0	1 (0.4%)	1 (0.2%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Irritability	1 (0.4%)	0	1 (0.2%)
Pain	0	1 (0.4%)	1 (0.2%)
Sense of oppression	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	243	246	489
Skin and subcutaneous tissue disorders			
Total Pts with at Least one TEAE*	98 (38.9%)	96 (38.6%)	194 (38.7%)
Alopecia	87 (34.5%)	87 (34.9%)	174 (34.7%)
Rash	9 (3.6%)	5 (2.0%)	14 (2.8%)
Nail discolouration	6 (2.4%)	5 (2.0%)	11 (2.2%)
Palmar-plantar erythrodysaesthesia syndrome	6 (2.4%)	1 (0.4%)	7 (1.4%)
Pruritus	5 (2.0%)	2 (0.8%)	7 (1.4%)
Dry skin	2 (0.8%)	3 (1.2%)	5 (1.0%)
Onychomadesis	1 (0.4%)	4 (1.6%)	5 (1.0%)
Nail pigmentation	0	4 (1.6%)	4 (0.8%)
Skin hyperpigmentation	3 (1.2%)	1 (0.4%)	4 (0.8%)
Pain of skin	3 (1.2%)	0	3 (0.6%)
Erythema	1 (0.4%)	1 (0.4%)	2 (0.4%)
Nail bed disorder	1 (0.4%)	1 (0.4%)	2 (0.4%)
Nail disorder	2 (0.8%)	0	2 (0.4%)
Skin discolouration	1 (0.4%)	1 (0.4%)	2 (0.4%)
Acne	0	1 (0.4%)	1 (0.2%)
Dermatitis contact	1 (0.4%)	0	1 (0.2%)
Hyperhidrosis	0	1 (0.4%)	1 (0.2%)
Nail ridging	0	1 (0.4%)	1 (0.2%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Photosensitivity reaction	0	1 (0.4%)	1 (0.2%)
Pigmentation disorder	1 (0.4%)	0	1 (0.2%)
Pruritus generalised	1 (0.4%)	0	1 (0.2%)
Rash erythematous	0	1 (0.4%)	1 (0.2%)
Rash macular	1 (0.4%)	0	1 (0.2%)
Rash maculo-papular	0	1 (0.4%)	1 (0.2%)
Rash papular	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	137	125	262
Investigations			
Total Pts with at Least one TEAE*	74 (29.4%)	88 (35.3%)	162 (32.3%)
White blood cell count decreased	26 (10.3%)	34 (13.7%)	60 (12.0%)
Neutrophil count decreased	26 (10.3%)	28 (11.2%)	54 (10.8%)
Ejection fraction decreased	14 (5.6%)	14 (5.6%)	28 (5.6%)
Aspartate aminotransferase increased	11 (4.4%)	10 (4.0%)	21 (4.2%)
Alanine aminotransferase increased	8 (3.2%)	9 (3.6%)	17 (3.4%)
Weight decreased	7 (2.8%)	10 (4.0%)	17 (3.4%)
Lymphocyte count decreased	5 (2.0%)	10 (4.0%)	15 (3.0%)
Platelet count decreased	6 (2.4%)	6 (2.4%)	12 (2.4%)
Blood alkaline phosphatase increased	5 (2.0%)	4 (1.6%)	9 (1.8%)
Blood creatinine increased	5 (2.0%)	4 (1.6%)	9 (1.8%)
Gamma-glutamyltransferase increased	3 (1.2%)	6 (2.4%)	9 (1.8%)
Blood lactate dehydrogenase increased	2 (0.8%)	5 (2.0%)	7 (1.4%)
Eastern Cooperative Oncology Group performance status worsened	2 (0.8%)	3 (1.2%)	5 (1.0%)
Electrocardiogram QT prolonged	3 (1.2%)	2 (0.8%)	5 (1.0%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Blood albumin decreased	2 (0.8%)	1 (0.4%)	3 (0.6%)
Blood magnesium decreased	1 (0.4%)	2 (0.8%)	3 (0.6%)
Albumin urine present	2 (0.8%)	0	2 (0.4%)
Blood chloride decreased	0	2 (0.8%)	2 (0.4%)
Platelet count increased	1 (0.4%)	1 (0.4%)	2 (0.4%)
Protein urine	1 (0.4%)	1 (0.4%)	2 (0.4%)
Red blood cell count decreased	1 (0.4%)	1 (0.4%)	2 (0.4%)
Blood uric acid increased	0	1 (0.4%)	1 (0.2%)
Body temperature increased	1 (0.4%)	0	1 (0.2%)
Ejection fraction	0	1 (0.4%)	1 (0.2%)
Electrocardiogram repolarisation abnormality	1 (0.4%)	0	1 (0.2%)
Glomerular filtration rate decreased	0	1 (0.4%)	1 (0.2%)
Haemoglobin decreased	0	1 (0.4%)	1 (0.2%)
Monocyte count decreased	0	1 (0.4%)	1 (0.2%)
Neutrophil count increased	0	1 (0.4%)	1 (0.2%)
Protein total decreased	0	1 (0.4%)	1 (0.2%)
Transaminases	1 (0.4%)	0	1 (0.2%)
Urine analysis abnormal	0	1 (0.4%)	1 (0.2%)
White blood cell count	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	166	211	377
Metabolism and nutrition disorders			
Total Pts with at Least one TEAE*	80 (31.7%)	72 (28.9%)	152 (30.3%)
Decreased appetite	57 (22.6%)	53 (21.3%)	110 (22.0%)
Hypokalaemia	12 (4.8%)	15 (6.0%)	27 (5.4%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Dehydration	11 (4.4%)	4 (1.6%)	15 (3.0%)
Hyponatraemia	10 (4.0%)	4 (1.6%)	14 (2.8%)
Hypomagnesaemia	7 (2.8%)	6 (2.4%)	13 (2.6%)
Hyperglycaemia	2 (0.8%)	2 (0.8%)	4 (0.8%)
Hyperkalaemia	1 (0.4%)	3 (1.2%)	4 (0.8%)
Hypophosphataemia	2 (0.8%)	2 (0.8%)	4 (0.8%)
Hypoalbuminaemia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Hypocalcaemia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Appetite disorder	1 (0.4%)	0	1 (0.2%)
Fluid overload	0	1 (0.4%)	1 (0.2%)
Fluid retention	0	1 (0.4%)	1 (0.2%)
Hypercholesterolaemia	1 (0.4%)	0	1 (0.2%)
Tetany	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	122	109	231
Nervous system disorders			
Total Pts with at Least one TEAE*	50 (19.8%)	56 (22.5%)	106 (21.2%)
Dysgeusia	28 (11.1%)	20 (8.0%)	48 (9.6%)
Dizziness	14 (5.6%)	10 (4.0%)	24 (4.8%)
Headache	7 (2.8%)	11 (4.4%)	18 (3.6%)
Peripheral sensory neuropathy	7 (2.8%)	9 (3.6%)	16 (3.2%)
Lethargy	3 (1.2%)	5 (2.0%)	8 (1.6%)
Paraesthesia	3 (1.2%)	5 (2.0%)	8 (1.6%)
Neuropathy peripheral	3 (1.2%)	3 (1.2%)	6 (1.2%)
Hypoaesthesia	3 (1.2%)	2 (0.8%)	5 (1.0%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Amnesia	1 (0.4%)	2 (0.8%)	3 (0.6%)
Neuralgia	2 (0.8%)	1 (0.4%)	3 (0.6%)
Disturbance in attention	0	2 (0.8%)	2 (0.4%)
Somnolence	0	2 (0.8%)	2 (0.4%)
Syncope	1 (0.4%)	1 (0.4%)	2 (0.4%)
Tremor	1 (0.4%)	1 (0.4%)	2 (0.4%)
Ageusia	0	1 (0.4%)	1 (0.2%)
Aura	1 (0.4%)	0	1 (0.2%)
Cognitive disorder	1 (0.4%)	0	1 (0.2%)
Dizziness postural	0	1 (0.4%)	1 (0.2%)
Presyncope	0	1 (0.4%)	1 (0.2%)
Sinus headache	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	82	85	167
Infections and infestations			
Total Pts with at Least one TEAE*	22 (8.7%)	25 (10.0%)	47 (9.4%)
Urinary tract infection	5 (2.0%)	11 (4.4%)	16 (3.2%)
Oral candidiasis	3 (1.2%)	3 (1.2%)	6 (1.2%)
Gingivitis	1 (0.4%)	2 (0.8%)	3 (0.6%)
Pneumonia	2 (0.8%)	1 (0.4%)	3 (0.6%)
Sepsis	3 (1.2%)	0	3 (0.6%)
Bronchitis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Candidiasis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Herpes zoster	1 (0.4%)	1 (0.4%)	2 (0.4%)
Nasopharyngitis	1 (0.4%)	1 (0.4%)	2 (0.4%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Neutropenic sepsis	0	2 (0.8%)	2 (0.4%)
Oral fungal infection	1 (0.4%)	1 (0.4%)	2 (0.4%)
Vaginal infection	0	2 (0.8%)	2 (0.4%)
Bacterial infection	0	1 (0.4%)	1 (0.2%)
Cystitis	0	1 (0.4%)	1 (0.2%)
Fungal infection	1 (0.4%)	0	1 (0.2%)
Infection	1 (0.4%)	0	1 (0.2%)
Lower respiratory tract infection	1 (0.4%)	0	1 (0.2%)
Lung infection	1 (0.4%)	0	1 (0.2%)
Oesophageal candidiasis	1 (0.4%)	0	1 (0.2%)
Oropharyngeal candidiasis	0	1 (0.4%)	1 (0.2%)
Otitis media	0	1 (0.4%)	1 (0.2%)
Pharyngitis	0	1 (0.4%)	1 (0.2%)
Septic shock	0	1 (0.4%)	1 (0.2%)
Sinusitis	1 (0.4%)	0	1 (0.2%)
Skin candida	1 (0.4%)	0	1 (0.2%)
Streptococcal infection	1 (0.4%)	0	1 (0.2%)
Upper respiratory tract infection	1 (0.4%)	0	1 (0.2%)
Urethritis	1 (0.4%)	0	1 (0.2%)
Urosepsis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	32	34	66
Respiratory, thoracic and mediastinal disorders			
Total Pts with at Least one TEAE*	24 (9.5%)	20 (8.0%)	44 (8.8%)
Dyspnoea	7 (2.8%)	11 (4.4%)	18 (3.6%)

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TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Cough	4 (1.6%)	3 (1.2%)	7 (1.4%)
Dyspnoea exertional	3 (1.2%)	1 (0.4%)	4 (0.8%)
Oropharyngeal pain	3 (1.2%)	1 (0.4%)	4 (0.8%)
Epistaxis	3 (1.2%)	0	3 (0.6%)
Pneumonitis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Pulmonary embolism	1 (0.4%)	1 (0.4%)	2 (0.4%)
Sinus congestion	0	2 (0.8%)	2 (0.4%)
Acute pulmonary oedema	1 (0.4%)	0	1 (0.2%)
Acute respiratory failure	1 (0.4%)	0	1 (0.2%)
Asthma	0	1 (0.4%)	1 (0.2%)
Chronic obstructive pulmonary disease	1 (0.4%)	0	1 (0.2%)
Dry throat	1 (0.4%)	0	1 (0.2%)
Dysphonia	1 (0.4%)	0	1 (0.2%)
Nasal congestion	1 (0.4%)	0	1 (0.2%)
Nasal discomfort	1 (0.4%)	0	1 (0.2%)
Orthopnoea	0	1 (0.4%)	1 (0.2%)
Paranasal sinus hypersecretion	0	1 (0.4%)	1 (0.2%)
Productive cough	1 (0.4%)	0	1 (0.2%)
Rhinorrhoea	1 (0.4%)	0	1 (0.2%)
Throat irritation	1 (0.4%)	0	1 (0.2%)
Upper-airway cough syndrome	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	33	28	61
Musculoskeletal and connective tissue disorders			
Total Pts with at Least one TEAE*	13 (5.2%)	22 (8.8%)	35 (7.0%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Arthralgia	5 (2.0%)	5 (2.0%)	10 (2.0%)
Myalgia	3 (1.2%)	7 (2.8%)	10 (2.0%)
Pain in extremity	1 (0.4%)	6 (2.4%)	7 (1.4%)
Back pain	0	5 (2.0%)	5 (1.0%)
Bone pain	0	4 (1.6%)	4 (0.8%)
Muscular weakness	4 (1.6%)	0	4 (0.8%)
Joint stiffness	0	1 (0.4%)	1 (0.2%)
Musculoskeletal pain	0	1 (0.4%)	1 (0.2%)
Pain in jaw	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	16	31	47
Cardiac disorders			
Total Pts with at Least one TEAE*	14 (5.6%)	19 (7.6%)	33 (6.6%)
Tachycardia	3 (1.2%)	4 (1.6%)	7 (1.4%)
Palpitations	4 (1.6%)	1 (0.4%)	5 (1.0%)
Sinus tachycardia	1 (0.4%)	4 (1.6%)	5 (1.0%)
Atrial fibrillation	3 (1.2%)	1 (0.4%)	4 (0.8%)
Cardiotoxicity	1 (0.4%)	2 (0.8%)	3 (0.6%)
Mitral valve incompetence	1 (0.4%)	2 (0.8%)	3 (0.6%)
Cardiac failure	1 (0.4%)	1 (0.4%)	2 (0.4%)
Left ventricular dysfunction	0	2 (0.8%)	2 (0.4%)
Mitral valve disease	1 (0.4%)	1 (0.4%)	2 (0.4%)
Tricuspid valve disease	0	2 (0.8%)	2 (0.4%)
Acute coronary syndrome	1 (0.4%)	0	1 (0.2%)
Atrial flutter	0	1 (0.4%)	1 (0.2%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Atrioventricular block	0	1 (0.4%)	1 (0.2%)
Extrasystoles	0	1 (0.4%)	1 (0.2%)
Intracardiac thrombus	0	1 (0.4%)	1 (0.2%)
Myocardial infarction	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	17	28	45
Renal and urinary disorders			
Total Pts with at Least one TEAE*	9 (3.6%)	15 (6.0%)	24 (4.8%)
Proteinuria	7 (2.8%)	4 (1.6%)	11 (2.2%)
Pollakiuria	1 (0.4%)	3 (1.2%)	4 (0.8%)
Dysuria	0	3 (1.2%)	3 (0.6%)
Chromaturia	0	2 (0.8%)	2 (0.4%)
Haematuria	0	2 (0.8%)	2 (0.4%)
Nocturia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Renal failure	1 (0.4%)	1 (0.4%)	2 (0.4%)
Microalbuminuria	0	1 (0.4%)	1 (0.2%)
Renal failure acute	1 (0.4%)	0	1 (0.2%)
Renal impairment	0	1 (0.4%)	1 (0.2%)
Urinary tract pain	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	12	19	31
Eye disorders			
Total Pts with at Least one TEAE*	12 (4.8%)	8 (3.2%)	20 (4.0%)
Vision blurred	4 (1.6%)	2 (0.8%)	6 (1.2%)
Dry eye	2 (0.8%)	2 (0.8%)	4 (0.8%)

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Conjunctivitis	2 (0.8%)	1 (0.4%)	3 (0.6%)
Lacrimation increased	1 (0.4%)	2 (0.8%)	3 (0.6%)
Eye irritation	2 (0.8%)	0	2 (0.4%)
Asthenopia	1 (0.4%)	0	1 (0.2%)
Diplopia	0	1 (0.4%)	1 (0.2%)
Visual impairment	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	13	8	21
Vascular disorders			
Total Pts with at Least one TEAE*	12 (4.8%)	8 (3.2%)	20 (4.0%)
Hypotension	3 (1.2%)	3 (1.2%)	6 (1.2%)
Hot flush	3 (1.2%)	2 (0.8%)	5 (1.0%)
Phlebitis	2 (0.8%)	1 (0.4%)	3 (0.6%)
Flushing	2 (0.8%)	0	2 (0.4%)
Deep vein thrombosis	1 (0.4%)	0	1 (0.2%)
Hypertensive crisis	0	1 (0.4%)	1 (0.2%)
Intermittent claudication	0	1 (0.4%)	1 (0.2%)
Pallor	1 (0.4%)	0	1 (0.2%)
Vascular fragility	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	13	8	21
Immune system disorders			
Total Pts with at Least one TEAE*	13 (5.2%)	0	13 (2.6%)
Hypersensitivity	13 (5.2%)	0	13 (2.6%)
Total Number of TEAEs	13	0	13

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Psychiatric disorders			
Total Pts with at Least one TEAE*	4 (1.6%)	7 (2.8%)	11 (2.2%)
Insomnia	1 (0.4%)	4 (1.6%)	5 (1.0%)
Anxiety	0	3 (1.2%)	3 (0.6%)
Depression	1 (0.4%)	1 (0.4%)	2 (0.4%)
Food aversion	1 (0.4%)	1 (0.4%)	2 (0.4%)
Depressed mood	1 (0.4%)	0	1 (0.2%)
Eating disorder	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	5	12	17
Ear and labyrinth disorders			
Total Pts with at Least one TEAE*	4 (1.6%)	4 (1.6%)	8 (1.6%)
Tinnitus	3 (1.2%)	3 (1.2%)	6 (1.2%)
Hearing impaired	1 (0.4%)	1 (0.4%)	2 (0.4%)
Vertigo	1 (0.4%)	1 (0.4%)	2 (0.4%)
Ear pain	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	6	7	13
Reproductive system and breast disorders			
Total Pts with at Least one TEAE*	4 (1.6%)	3 (1.2%)	7 (1.4%)
Genital haemorrhage	0	1 (0.4%)	1 (0.2%)
Genital rash	1 (0.4%)	0	1 (0.2%)
Pelvic pain	1 (0.4%)	0	1 (0.2%)
Uterine haemorrhage	1 (0.4%)	0	1 (0.2%)

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Vaginal discharge	0	1 (0.4%)	1 (0.2%)
Vaginal inflammation	0	1 (0.4%)	1 (0.2%)
Vulvovaginal burning sensation	0	1 (0.4%)	1 (0.2%)
Vulvovaginal dryness	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	7	4	11
Injury, poisoning and procedural complications			
Total Pts with at Least one TEAE*	3 (1.2%)	1 (0.4%)	4 (0.8%)
Contusion	1 (0.4%)	1 (0.4%)	2 (0.4%)
Infusion related reaction	2 (0.8%)	0	2 (0.4%)
Total Number of TEAEs	4	1	5
Hepatobiliary disorders			
Total Pts with at Least one TEAE*	2 (0.8%)	1 (0.4%)	3 (0.6%)
Hyperbilirubinaemia	2 (0.8%)	0	2 (0.4%)
Liver disorder	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	2	1	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Total Pts with at Least one TEAE*	0	1 (0.4%)	1 (0.2%)
Tumour necrosis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	1	1
Surgical and medical procedures			
Total Pts with at Least one TEAE*	1 (0.4%)	0	1 (0.2%)

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Participants are only counted once for each preferred term.
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SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.5: RELATED TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Prophylaxis of nausea and vomiting	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	0	1

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Blood and lymphatic system disorders			
Total Pts with at Least one TEAE*	46 (18.3%)	30 (12.0%)	76 (15.2%)
Neutropenia	21 (8.3%)	15 (6.0%)	36 (7.2%)
Anaemia	16 (6.3%)	9 (3.6%)	25 (5.0%)
Febrile neutropenia	17 (6.7%)	8 (3.2%)	25 (5.0%)
Thrombocytopenia	8 (3.2%)	3 (1.2%)	11 (2.2%)
Leukopenia	4 (1.6%)	6 (2.4%)	10 (2.0%)
Pancytopenia	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	79	47	126
Gastrointestinal disorders			
Total Pts with at Least one TEAE*	32 (12.7%)	20 (8.0%)	52 (10.4%)
Nausea	11 (4.4%)	8 (3.2%)	19 (3.8%)
Vomiting	7 (2.8%)	9 (3.6%)	16 (3.2%)
Abdominal pain	5 (2.0%)	3 (1.2%)	8 (1.6%)
Intestinal obstruction	6 (2.4%)	2 (0.8%)	8 (1.6%)
Small intestinal obstruction	3 (1.2%)	4 (1.6%)	7 (1.4%)
Stomatitis	5 (2.0%)	0	5 (1.0%)
Ascites	2 (0.8%)	2 (0.8%)	4 (0.8%)
Diarrhoea	2 (0.8%)	2 (0.8%)	4 (0.8%)
Ileus	2 (0.8%)	1 (0.4%)	3 (0.6%)
Gastrointestinal hypomotility	2 (0.8%)	0	2 (0.4%)
Abdominal pain upper	1 (0.4%)	0	1 (0.2%)
Acute abdomen	1 (0.4%)	0	1 (0.2%)
Colonic obstruction	1 (0.4%)	0	1 (0.2%)

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Enterocutaneous fistula	0	1 (0.4%)	1 (0.2%)
Gastritis	0	1 (0.4%)	1 (0.2%)
Haematemesis	0	1 (0.4%)	1 (0.2%)
Ileal stenosis	0	1 (0.4%)	1 (0.2%)
Intestinal perforation	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	55	45	100
Infections and infestations			
Total Pts with at Least one TEAE*	21 (8.3%)	15 (6.0%)	36 (7.2%)
Sepsis	5 (2.0%)	3 (1.2%)	8 (1.6%)
Urinary tract infection	3 (1.2%)	3 (1.2%)	6 (1.2%)
Pneumonia	3 (1.2%)	2 (0.8%)	5 (1.0%)
Herpes zoster	1 (0.4%)	1 (0.4%)	2 (0.4%)
Lower respiratory tract infection	2 (0.8%)	0	2 (0.4%)
Neutropenic sepsis	0	2 (0.8%)	2 (0.4%)
Oral candidiasis	1 (0.4%)	1 (0.4%)	2 (0.4%)
Urosepsis	2 (0.8%)	0	2 (0.4%)
Abdominal infection	1 (0.4%)	0	1 (0.2%)
Bacteraemia	1 (0.4%)	0	1 (0.2%)
Bronchitis	1 (0.4%)	0	1 (0.2%)
Cellulitis	1 (0.4%)	0	1 (0.2%)
Device related infection	1 (0.4%)	0	1 (0.2%)
Infection	1 (0.4%)	0	1 (0.2%)
Influenza	1 (0.4%)	0	1 (0.2%)
Oesophageal candidiasis	1 (0.4%)	0	1 (0.2%)

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SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Oral fungal infection	1 (0.4%)	0	1 (0.2%)
Periodontitis	1 (0.4%)	0	1 (0.2%)
Pneumocystis jiroveci pneumonia	0	1 (0.4%)	1 (0.2%)
Postoperative wound infection	0	1 (0.4%)	1 (0.2%)
Septic shock	0	1 (0.4%)	1 (0.2%)
Staphylococcal infection	0	1 (0.4%)	1 (0.2%)
Tooth abscess	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	27	17	44
General disorders and administration site conditions			
Total Pts with at Least one TEAE*	15 (6.0%)	9 (3.6%)	24 (4.8%)
Pyrexia	4 (1.6%)	3 (1.2%)	7 (1.4%)
Fatigue	3 (1.2%)	0	3 (0.6%)
General physical health deterioration	3 (1.2%)	0	3 (0.6%)
Asthenia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Condition aggravated	1 (0.4%)	1 (0.4%)	2 (0.4%)
Oedema	0	2 (0.8%)	2 (0.4%)
Chest pain	1 (0.4%)	0	1 (0.2%)
Hyperpyrexia	1 (0.4%)	0	1 (0.2%)
Malaise	0	1 (0.4%)	1 (0.2%)
Mucosal inflammation	1 (0.4%)	0	1 (0.2%)
Pain	0	1 (0.4%)	1 (0.2%)
Performance status decreased	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	18	10	28

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Respiratory, thoracic and mediastinal disorders			
Total Pts with at Least one TEAE*	17 (6.7%)	6 (2.4%)	23 (4.6%)
Pulmonary embolism	7 (2.8%)	5 (2.0%)	12 (2.4%)
Dyspnoea	6 (2.4%)	1 (0.4%)	7 (1.4%)
Pleural effusion	3 (1.2%)	3 (1.2%)	6 (1.2%)
Respiratory failure	2 (0.8%)	0	2 (0.4%)
Acute pulmonary oedema	1 (0.4%)	0	1 (0.2%)
Acute respiratory failure	1 (0.4%)	0	1 (0.2%)
Chronic obstructive pulmonary disease	1 (0.4%)	0	1 (0.2%)
Cough	1 (0.4%)	0	1 (0.2%)
Dyspnoea exertional	1 (0.4%)	0	1 (0.2%)
Pneumothorax	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	24	10	34
Metabolism and nutrition disorders			
Total Pts with at Least one TEAE*	14 (5.6%)	8 (3.2%)	22 (4.4%)
Dehydration	8 (3.2%)	2 (0.8%)	10 (2.0%)
Hypokalaemia	3 (1.2%)	2 (0.8%)	5 (1.0%)
Hyponatraemia	3 (1.2%)	1 (0.4%)	4 (0.8%)
Hyperkalaemia	1 (0.4%)	2 (0.8%)	3 (0.6%)
Decreased appetite	1 (0.4%)	1 (0.4%)	2 (0.4%)
Hypophosphataemia	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	17	9	26

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
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Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Cardiac disorders			
Total Pts with at Least one TEAE*	7 (2.8%)	8 (3.2%)	15 (3.0%)
Atrial fibrillation	2 (0.8%)	2 (0.8%)	4 (0.8%)
Cardiac arrest	1 (0.4%)	1 (0.4%)	2 (0.4%)
Tachycardia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Acute coronary syndrome	1 (0.4%)	0	1 (0.2%)
Atrial flutter	0	1 (0.4%)	1 (0.2%)
Cardiac failure	1 (0.4%)	0	1 (0.2%)
Cardio-respiratory arrest	0	1 (0.4%)	1 (0.2%)
Cardiotoxicity	1 (0.4%)	0	1 (0.2%)
Intracardiac thrombus	0	1 (0.4%)	1 (0.2%)
Left ventricular dysfunction	0	1 (0.4%)	1 (0.2%)
Supraventricular tachycardia	0	1 (0.4%)	1 (0.2%)
Tachyarrhythmia	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	7	10	17
Investigations			
Total Pts with at Least one TEAE*	6 (2.4%)	6 (2.4%)	12 (2.4%)
Neutrophil count decreased	2 (0.8%)	2 (0.8%)	4 (0.8%)
Ejection fraction decreased	2 (0.8%)	1 (0.4%)	3 (0.6%)
Aspartate aminotransferase increased	1 (0.4%)	1 (0.4%)	2 (0.4%)
Blood creatinine increased	1 (0.4%)	1 (0.4%)	2 (0.4%)
White blood cell count decreased	1 (0.4%)	1 (0.4%)	2 (0.4%)
Alanine aminotransferase increased	1 (0.4%)	0	1 (0.2%)

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Blood alkaline phosphatase increased	0	1 (0.4%)	1 (0.2%)
Blood lactate dehydrogenase increased	0	1 (0.4%)	1 (0.2%)
Eastern Cooperative Oncology Group performance status worsened	0	1 (0.4%)	1 (0.2%)
Gamma-glutamyltransferase increased	0	1 (0.4%)	1 (0.2%)
International normalised ratio increased	1 (0.4%)	0	1 (0.2%)
Platelet count decreased	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	10	10	20
Renal and urinary disorders			
Total Pts with at Least one TEAE*	7 (2.8%)	5 (2.0%)	12 (2.4%)
Renal failure acute	4 (1.6%)	1 (0.4%)	5 (1.0%)
Hydronephrosis	0	2 (0.8%)	2 (0.4%)
Haematuria	1 (0.4%)	0	1 (0.2%)
Renal colic	1 (0.4%)	0	1 (0.2%)
Renal failure	0	1 (0.4%)	1 (0.2%)
Urinary incontinence	1 (0.4%)	0	1 (0.2%)
Urinary tract obstruction	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	7	5	12
Vascular disorders			
Total Pts with at Least one TEAE*	5 (2.0%)	7 (2.8%)	12 (2.4%)
Embolism	2 (0.8%)	2 (0.8%)	4 (0.8%)
Deep vein thrombosis	2 (0.8%)	1 (0.4%)	3 (0.6%)
Superior vena cava syndrome	0	2 (0.8%)	2 (0.4%)
Hypertensive crisis	0	1 (0.4%)	1 (0.2%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Hypotension	0	1 (0.4%)	1 (0.2%)
Thrombophlebitis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	5	7	12
Nervous system disorders			
Total Pts with at Least one TEAE*	3 (1.2%)	5 (2.0%)	8 (1.6%)
Dizziness	0	2 (0.8%)	2 (0.4%)
Cerebrovascular accident	1 (0.4%)	0	1 (0.2%)
Epilepsy	0	1 (0.4%)	1 (0.2%)
Headache	0	1 (0.4%)	1 (0.2%)
Paresis	0	1 (0.4%)	1 (0.2%)
Syncope	1 (0.4%)	0	1 (0.2%)
Transient ischaemic attack	0	1 (0.4%)	1 (0.2%)
Tremor	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	3	6	9
Musculoskeletal and connective tissue disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	5 (2.0%)	6 (1.2%)
Back pain	0	2 (0.8%)	2 (0.4%)
Flank pain	0	1 (0.4%)	1 (0.2%)
Muscular weakness	1 (0.4%)	0	1 (0.2%)
Musculoskeletal pain	0	1 (0.4%)	1 (0.2%)
Rhabdomyolysis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	1	5	6

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Injury, poisoning and procedural complications			
Total Pts with at Least one TEAE*	2 (0.8%)	1 (0.4%)	3 (0.6%)
Hip fracture	0	1 (0.4%)	1 (0.2%)
Post procedural urine leak	1 (0.4%)	0	1 (0.2%)
Scapula fracture	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	2	1	3
Reproductive system and breast disorders			
Total Pts with at Least one TEAE*	3 (1.2%)	0	3 (0.6%)
Vaginal haemorrhage	2 (0.8%)	0	2 (0.4%)
Genital rash	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	3	0	3
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Total Pts with at Least one TEAE*	0	2 (0.8%)	2 (0.4%)
Malignant neoplasm progression	0	1 (0.4%)	1 (0.2%)
Metastatic uterine cancer	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	2	2
Hepatobiliary disorders			
Total Pts with at Least one TEAE*	0	1 (0.4%)	1 (0.2%)
Cholecystitis acute	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	1	1

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.9: SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Immune system disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	0	1 (0.2%)
Drug hypersensitivity	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	0	1
Psychiatric disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	0	1 (0.2%)
Confusional state	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	0	1

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.12: RELATED SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Blood and lymphatic system disorders			
Total Pts with at Least one TEAE*	45 (17.9%)	29 (11.6%)	74 (14.8%)
Neutropenia	21 (8.3%)	15 (6.0%)	36 (7.2%)
Febrile neutropenia	17 (6.7%)	8 (3.2%)	25 (5.0%)
Anaemia	15 (6.0%)	8 (3.2%)	23 (4.6%)
Thrombocytopenia	8 (3.2%)	2 (0.8%)	10 (2.0%)
Leukopenia	3 (1.2%)	6 (2.4%)	9 (1.8%)
Pancytopenia	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	77	44	121
Gastrointestinal disorders			
Total Pts with at Least one TEAE*	10 (4.0%)	8 (3.2%)	18 (3.6%)
Nausea	6 (2.4%)	5 (2.0%)	11 (2.2%)
Vomiting	3 (1.2%)	6 (2.4%)	9 (1.8%)
Stomatitis	5 (2.0%)	0	5 (1.0%)
Diarrhoea	0	2 (0.8%)	2 (0.4%)
Ascites	0	1 (0.4%)	1 (0.2%)
Gastritis	0	1 (0.4%)	1 (0.2%)
Small intestinal obstruction	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	18	21	39
Infections and infestations			
Total Pts with at Least one TEAE*	11 (4.4%)	4 (1.6%)	15 (3.0%)
Sepsis	3 (1.2%)	0	3 (0.6%)
Neutropenic sepsis	0	2 (0.8%)	2 (0.4%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.12: RELATED SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Bronchitis	1 (0.4%)	0	1 (0.2%)
Herpes zoster	1 (0.4%)	0	1 (0.2%)
Infection	1 (0.4%)	0	1 (0.2%)
Lower respiratory tract infection	1 (0.4%)	0	1 (0.2%)
Oesophageal candidiasis	1 (0.4%)	0	1 (0.2%)
Oral candidiasis	0	1 (0.4%)	1 (0.2%)
Oral fungal infection	1 (0.4%)	0	1 (0.2%)
Pneumonia	1 (0.4%)	0	1 (0.2%)
Septic shock	0	1 (0.4%)	1 (0.2%)
Urinary tract infection	1 (0.4%)	0	1 (0.2%)
Urosepsis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	12	4	16
General disorders and administration site conditions			
Total Pts with at Least one TEAE*	9 (3.6%)	2 (0.8%)	11 (2.2%)
Fatigue	3 (1.2%)	0	3 (0.6%)
Asthenia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Pyrexia	2 (0.8%)	0	2 (0.4%)
Condition aggravated	1 (0.4%)	0	1 (0.2%)
General physical health deterioration	1 (0.4%)	0	1 (0.2%)
Mucosal inflammation	1 (0.4%)	0	1 (0.2%)
Oedema	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	10	2	12

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.12: RELATED SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Metabolism and nutrition disorders			
Total Pts with at Least one TEAE*	7 (2.8%)	3 (1.2%)	10 (2.0%)
Dehydration	4 (1.6%)	0	4 (0.8%)
Hyponatraemia	2 (0.8%)	1 (0.4%)	3 (0.6%)
Decreased appetite	0	1 (0.4%)	1 (0.2%)
Hyperkalaemia	0	1 (0.4%)	1 (0.2%)
Hypokalaemia	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	7	3	10
Cardiac disorders			
Total Pts with at Least one TEAE*	6 (2.4%)	3 (1.2%)	9 (1.8%)
Atrial fibrillation	2 (0.8%)	1 (0.4%)	3 (0.6%)
Tachycardia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Acute coronary syndrome	1 (0.4%)	0	1 (0.2%)
Cardiac failure	1 (0.4%)	0	1 (0.2%)
Cardiotoxicity	1 (0.4%)	0	1 (0.2%)
Intracardiac thrombus	0	1 (0.4%)	1 (0.2%)
Left ventricular dysfunction	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	6	4	10
Investigations			
Total Pts with at Least one TEAE*	5 (2.0%)	4 (1.6%)	9 (1.8%)
Neutrophil count decreased	2 (0.8%)	2 (0.8%)	4 (0.8%)
Ejection fraction decreased	2 (0.8%)	1 (0.4%)	3 (0.6%)

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SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.12: RELATED SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Aspartate aminotransferase increased	1 (0.4%)	1 (0.4%)	2 (0.4%)
White blood cell count decreased	1 (0.4%)	1 (0.4%)	2 (0.4%)
Alanine aminotransferase increased	1 (0.4%)	0	1 (0.2%)
Blood alkaline phosphatase increased	0	1 (0.4%)	1 (0.2%)
Blood creatinine increased	1 (0.4%)	0	1 (0.2%)
Blood lactate dehydrogenase increased	0	1 (0.4%)	1 (0.2%)
Gamma-glutamyltransferase increased	0	1 (0.4%)	1 (0.2%)
Platelet count decreased	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	9	8	17
Respiratory, thoracic and mediastinal disorders			
Total Pts with at Least one TEAE*	4 (1.6%)	1 (0.4%)	5 (1.0%)
Pulmonary embolism	1 (0.4%)	1 (0.4%)	2 (0.4%)
Acute pulmonary oedema	1 (0.4%)	0	1 (0.2%)
Acute respiratory failure	1 (0.4%)	0	1 (0.2%)
Chronic obstructive pulmonary disease	1 (0.4%)	0	1 (0.2%)
Dyspnoea	1 (0.4%)	0	1 (0.2%)
Dyspnoea exertional	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	6	1	7
Renal and urinary disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	1 (0.4%)	2 (0.4%)
Renal failure	0	1 (0.4%)	1 (0.2%)
Renal failure acute	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	1	2

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SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.12: RELATED SERIOUS TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Vascular disorders			
Total Pts with at Least one TEAE*	0	2 (0.8%)	2 (0.4%)
Hypertensive crisis	0	1 (0.4%)	1 (0.2%)
Hypotension	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	2	2
Musculoskeletal and connective tissue disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	0	1 (0.2%)
Muscular weakness	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	0	1
Nervous system disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	0	1 (0.2%)
Syncope	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	0	1
Reproductive system and breast disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	0	1 (0.2%)
Genital rash	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	0	1

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Blood and lymphatic system disorders			
Total Pts with at Least one TEAE*	153 (60.7%)	144 (57.8%)	297 (59.3%)
Neutropenia	119 (47.2%)	112 (45.0%)	231 (46.1%)
Leukopenia	53 (21.0%)	45 (18.1%)	98 (19.6%)
Anaemia	52 (20.6%)	38 (15.3%)	90 (18.0%)
Febrile neutropenia	23 (9.1%)	9 (3.6%)	32 (6.4%)
Thrombocytopenia	9 (3.6%)	6 (2.4%)	15 (3.0%)
Lymphopenia	4 (1.6%)	3 (1.2%)	7 (1.4%)
Leukocytosis	2 (0.8%)	1 (0.4%)	3 (0.6%)
Pancytopenia	2 (0.8%)	0	2 (0.4%)
Total Number of TEAEs	354	295	649
Investigations			
Total Pts with at Least one TEAE*	40 (15.9%)	56 (22.5%)	96 (19.2%)
Neutrophil count decreased	21 (8.3%)	25 (10.0%)	46 (9.2%)
White blood cell count decreased	20 (7.9%)	20 (8.0%)	40 (8.0%)
Lymphocyte count decreased	4 (1.6%)	10 (4.0%)	14 (2.8%)
Ejection fraction decreased	4 (1.6%)	5 (2.0%)	9 (1.8%)
Gamma-glutamyltransferase increased	2 (0.8%)	5 (2.0%)	7 (1.4%)
Platelet count decreased	4 (1.6%)	3 (1.2%)	7 (1.4%)
Albumin urine present	2 (0.8%)	0	2 (0.4%)
Blood creatinine increased	0	2 (0.8%)	2 (0.4%)
Eastern Cooperative Oncology Group performance status worsened	1 (0.4%)	1 (0.4%)	2 (0.4%)
Activated partial thromboplastin time prolonged	0	1 (0.4%)	1 (0.2%)
Aspartate aminotransferase increased	0	1 (0.4%)	1 (0.2%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Blood calcium decreased	0	1 (0.4%)	1 (0.2%)
Blood lactate dehydrogenase increased	0	1 (0.4%)	1 (0.2%)
Blood magnesium decreased	0	1 (0.4%)	1 (0.2%)
Blood uric acid increased	0	1 (0.4%)	1 (0.2%)
C-reactive protein increased	1 (0.4%)	0	1 (0.2%)
Ejection fraction	0	1 (0.4%)	1 (0.2%)
Heart rate increased	1 (0.4%)	0	1 (0.2%)
Red blood cell count decreased	1 (0.4%)	0	1 (0.2%)
Weight decreased	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	72	89	161
Gastrointestinal disorders			
Total Pts with at Least one TEAE*	43 (17.1%)	32 (12.9%)	75 (15.0%)
Nausea	12 (4.8%)	13 (5.2%)	25 (5.0%)
Vomiting	11 (4.4%)	13 (5.2%)	24 (4.8%)
Abdominal pain	8 (3.2%)	4 (1.6%)	12 (2.4%)
Small intestinal obstruction	5 (2.0%)	4 (1.6%)	9 (1.8%)
Stomatitis	5 (2.0%)	3 (1.2%)	8 (1.6%)
Ascites	5 (2.0%)	2 (0.8%)	7 (1.4%)
Intestinal obstruction	6 (2.4%)	1 (0.4%)	7 (1.4%)
Diarrhoea	2 (0.8%)	4 (1.6%)	6 (1.2%)
Abdominal pain upper	4 (1.6%)	1 (0.4%)	5 (1.0%)
Abdominal pain lower	1 (0.4%)	2 (0.8%)	3 (0.6%)
Constipation	3 (1.2%)	0	3 (0.6%)
Ileus	2 (0.8%)	1 (0.4%)	3 (0.6%)

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Acute abdomen	1 (0.4%)	0	1 (0.2%)
Colitis	1 (0.4%)	0	1 (0.2%)
Colonic obstruction	1 (0.4%)	0	1 (0.2%)
Enterocutaneous fistula	0	1 (0.4%)	1 (0.2%)
Haematemesis	0	1 (0.4%)	1 (0.2%)
Ileal stenosis	0	1 (0.4%)	1 (0.2%)
Ileus paralytic	0	1 (0.4%)	1 (0.2%)
Intestinal perforation	1 (0.4%)	0	1 (0.2%)
Oral pain	1 (0.4%)	0	1 (0.2%)
Tooth loss	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	78	72	150
General disorders and administration site conditions			
Total Pts with at Least one TEAE*	32 (12.7%)	25 (10.0%)	57 (11.4%)
Fatigue	13 (5.2%)	14 (5.6%)	27 (5.4%)
Asthenia	6 (2.4%)	6 (2.4%)	12 (2.4%)
Pyrexia	2 (0.8%)	2 (0.8%)	4 (0.8%)
Mucosal inflammation	3 (1.2%)	0	3 (0.6%)
Oedema peripheral	3 (1.2%)	0	3 (0.6%)
Pain	1 (0.4%)	2 (0.8%)	3 (0.6%)
Chest pain	2 (0.8%)	0	2 (0.4%)
Condition aggravated	1 (0.4%)	1 (0.4%)	2 (0.4%)
General physical health deterioration	1 (0.4%)	1 (0.4%)	2 (0.4%)
Oedema	0	2 (0.8%)	2 (0.4%)
Performance status decreased	2 (0.8%)	0	2 (0.4%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
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TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Catheter site pain	0	1 (0.4%)	1 (0.2%)
Hyperpyrexia	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	39	31	70
Metabolism and nutrition disorders			
Total Pts with at Least one TEAE*	32 (12.7%)	21 (8.4%)	53 (10.6%)
Hypokalaemia	13 (5.2%)	10 (4.0%)	23 (4.6%)
Dehydration	10 (4.0%)	3 (1.2%)	13 (2.6%)
Hyponatraemia	6 (2.4%)	4 (1.6%)	10 (2.0%)
Hypophosphataemia	3 (1.2%)	3 (1.2%)	6 (1.2%)
Decreased appetite	3 (1.2%)	1 (0.4%)	4 (0.8%)
Hypocalcaemia	1 (0.4%)	3 (1.2%)	4 (0.8%)
Hypomagnesaemia	3 (1.2%)	1 (0.4%)	4 (0.8%)
Hyperglycaemia	2 (0.8%)	1 (0.4%)	3 (0.6%)
Hyperkalaemia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Hypoalbuminaemia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Cachexia	1 (0.4%)	0	1 (0.2%)
Metabolic acidosis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	53	32	85
Infections and infestations			
Total Pts with at Least one TEAE*	19 (7.5%)	18 (7.2%)	37 (7.4%)
Sepsis	5 (2.0%)	3 (1.2%)	8 (1.6%)
Pneumonia	2 (0.8%)	2 (0.8%)	4 (0.8%)
Urinary tract infection	1 (0.4%)	3 (1.2%)	4 (0.8%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Cellulitis	2 (0.8%)	0	2 (0.4%)
Herpes zoster	1 (0.4%)	1 (0.4%)	2 (0.4%)
Urosepsis	2 (0.8%)	0	2 (0.4%)
Abdominal infection	1 (0.4%)	0	1 (0.2%)
Bacteraemia	1 (0.4%)	0	1 (0.2%)
Bronchitis	1 (0.4%)	0	1 (0.2%)
Clostridium difficile infection	1 (0.4%)	0	1 (0.2%)
Device related infection	1 (0.4%)	0	1 (0.2%)
Enterococcal infection	1 (0.4%)	0	1 (0.2%)
Infection	0	1 (0.4%)	1 (0.2%)
Influenza	1 (0.4%)	0	1 (0.2%)
Lower respiratory tract infection	1 (0.4%)	0	1 (0.2%)
Nasopharyngitis	0	1 (0.4%)	1 (0.2%)
Neutropenic sepsis	0	1 (0.4%)	1 (0.2%)
Oral candidiasis	1 (0.4%)	0	1 (0.2%)
Oral fungal infection	1 (0.4%)	0	1 (0.2%)
Periodontitis	1 (0.4%)	0	1 (0.2%)
Pneumocystis jiroveci pneumonia	0	1 (0.4%)	1 (0.2%)
Postoperative wound infection	0	1 (0.4%)	1 (0.2%)
Septic shock	0	1 (0.4%)	1 (0.2%)
Skin infection	0	1 (0.4%)	1 (0.2%)
Staphylococcal infection	0	1 (0.4%)	1 (0.2%)
Staphylococcal sepsis	1 (0.4%)	0	1 (0.2%)
Tooth abscess	0	1 (0.4%)	1 (0.2%)
Tooth infection	0	1 (0.4%)	1 (0.2%)

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Total Number of TEAEs	25	19	44
Respiratory, thoracic and mediastinal disorders			
Total Pts with at Least one TEAE*	14 (5.6%)	11 (4.4%)	25 (5.0%)
Pulmonary embolism	8 (3.2%)	6 (2.4%)	14 (2.8%)
Pleural effusion	5 (2.0%)	4 (1.6%)	9 (1.8%)
Dyspnoea	3 (1.2%)	4 (1.6%)	7 (1.4%)
Respiratory failure	2 (0.8%)	0	2 (0.4%)
Acute pulmonary oedema	1 (0.4%)	0	1 (0.2%)
Acute respiratory failure	1 (0.4%)	0	1 (0.2%)
Chronic obstructive pulmonary disease	1 (0.4%)	0	1 (0.2%)
Hypoxia	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	22	16	38
Renal and urinary disorders			
Total Pts with at Least one TEAE*	12 (4.8%)	6 (2.4%)	18 (3.6%)
Renal failure acute	4 (1.6%)	2 (0.8%)	6 (1.2%)
Hydronephrosis	2 (0.8%)	3 (1.2%)	5 (1.0%)
Renal failure	1 (0.4%)	1 (0.4%)	2 (0.4%)
Urinary tract obstruction	1 (0.4%)	1 (0.4%)	2 (0.4%)
Haematuria	1 (0.4%)	0	1 (0.2%)
Proteinuria	1 (0.4%)	0	1 (0.2%)
Renal colic	1 (0.4%)	0	1 (0.2%)
Urinary retention	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	13	7	20

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SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Cardiac disorders			
Total Pts with at Least one TEAE*	8 (3.2%)	9 (3.6%)	17 (3.4%)
Atrial fibrillation	3 (1.2%)	1 (0.4%)	4 (0.8%)
Cardiac arrest	2 (0.8%)	1 (0.4%)	3 (0.6%)
Left ventricular dysfunction	0	2 (0.8%)	2 (0.4%)
Acute coronary syndrome	1 (0.4%)	0	1 (0.2%)
Atrial flutter	0	1 (0.4%)	1 (0.2%)
Cardiac failure	1 (0.4%)	0	1 (0.2%)
Cardio-respiratory arrest	0	1 (0.4%)	1 (0.2%)
Cardiotoxicity	1 (0.4%)	0	1 (0.2%)
Intracardiac thrombus	0	1 (0.4%)	1 (0.2%)
Mitral valve incompetence	0	1 (0.4%)	1 (0.2%)
Supraventricular tachycardia	0	1 (0.4%)	1 (0.2%)
Tachyarrhythmia	0	1 (0.4%)	1 (0.2%)
Tachycardia	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	9	11	20
Nervous system disorders			
Total Pts with at Least one TEAE*	7 (2.8%)	10 (4.0%)	17 (3.4%)
Headache	2 (0.8%)	2 (0.8%)	4 (0.8%)
Syncope	2 (0.8%)	2 (0.8%)	4 (0.8%)
Dizziness	0	3 (1.2%)	3 (0.6%)
Lethargy	0	2 (0.8%)	2 (0.4%)
Balance disorder	0	1 (0.4%)	1 (0.2%)

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Date of Table Generation: 20 April 2017

TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Cerebrovascular accident	1 (0.4%)	0	1 (0.2%)
Dysgeusia	0	1 (0.4%)	1 (0.2%)
Neuralgia	1 (0.4%)	0	1 (0.2%)
Paresis	0	1 (0.4%)	1 (0.2%)
Presyncope	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	7	12	19
Vascular disorders			
Total Pts with at Least one TEAE*	7 (2.8%)	7 (2.8%)	14 (2.8%)
Deep vein thrombosis	4 (1.6%)	1 (0.4%)	5 (1.0%)
Embolism	0	3 (1.2%)	3 (0.6%)
Hypertension	3 (1.2%)	0	3 (0.6%)
Hypertensive crisis	0	1 (0.4%)	1 (0.2%)
Hypotension	0	1 (0.4%)	1 (0.2%)
Phlebitis	0	1 (0.4%)	1 (0.2%)
Superior vena cava syndrome	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	7	8	15
Musculoskeletal and connective tissue disorders			
Total Pts with at Least one TEAE*	5 (2.0%)	6 (2.4%)	11 (2.2%)
Back pain	0	4 (1.6%)	4 (0.8%)
Arthralgia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Bone pain	1 (0.4%)	0	1 (0.2%)
Flank pain	1 (0.4%)	0	1 (0.2%)
Groin pain	1 (0.4%)	0	1 (0.2%)

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TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Joint swelling	0	1 (0.4%)	1 (0.2%)
Muscular weakness	1 (0.4%)	0	1 (0.2%)
Rhabdomyolysis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	5	7	12
Skin and subcutaneous tissue disorders			
Total Pts with at Least one TEAE*	6 (2.4%)	2 (0.8%)	8 (1.6%)
Alopecia	5 (2.0%)	2 (0.8%)	7 (1.4%)
Pruritus	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	6	2	8
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Total Pts with at Least one TEAE*	1 (0.4%)	5 (2.0%)	6 (1.2%)
Tumour pain	1 (0.4%)	1 (0.4%)	2 (0.4%)
Leukaemia	0	1 (0.4%)	1 (0.2%)
Malignant neoplasm progression	0	1 (0.4%)	1 (0.2%)
Metastatic uterine cancer	0	1 (0.4%)	1 (0.2%)
Tumour necrosis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	1	5	6
Reproductive system and breast disorders			
Total Pts with at Least one TEAE*	2 (0.8%)	4 (1.6%)	6 (1.2%)
Female genital tract fistula	0	2 (0.8%)	2 (0.4%)
Genital rash	1 (0.4%)	0	1 (0.2%)
Pelvic pain	0	1 (0.4%)	1 (0.2%)

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TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Uterine haemorrhage	1 (0.4%)	0	1 (0.2%)
Vulvovaginal burning sensation	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	2	4	6
Injury, poisoning and procedural complications			
Total Pts with at Least one TEAE*	2 (0.8%)	1 (0.4%)	3 (0.6%)
Femur fracture	1 (0.4%)	0	1 (0.2%)
Hip fracture	0	1 (0.4%)	1 (0.2%)
Radiation associated pain	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	2	1	3
Psychiatric disorders			
Total Pts with at Least one TEAE*	2 (0.8%)	1 (0.4%)	3 (0.6%)
Anxiety	1 (0.4%)	1 (0.4%)	2 (0.4%)
Confusional state	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	2	1	3
Hepatobiliary disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	1 (0.4%)	2 (0.4%)
Cholecystitis acute	0	1 (0.4%)	1 (0.2%)
Hepatic pain	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	1	2
Eye disorders			
Total Pts with at Least one TEAE*	0	1 (0.4%)	1 (0.2%)

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TABLE 14.3.1.16: GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Vision blurred	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	1	1

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AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.18: RELATED GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Blood and lymphatic system disorders			
Total Pts with at Least one TEAE*	148 (58.7%)	141 (56.6%)	289 (57.7%)
Neutropenia	118 (46.8%)	111 (44.6%)	229 (45.7%)
Leukopenia	52 (20.6%)	44 (17.7%)	96 (19.2%)
Anaemia	42 (16.7%)	36 (14.5%)	78 (15.6%)
Febrile neutropenia	23 (9.1%)	9 (3.6%)	32 (6.4%)
Thrombocytopenia	9 (3.6%)	5 (2.0%)	14 (2.8%)
Lymphopenia	4 (1.6%)	3 (1.2%)	7 (1.4%)
Pancytopenia	2 (0.8%)	0	2 (0.4%)
Total Number of TEAEs	338	285	623
Investigations			
Total Pts with at Least one TEAE*	36 (14.3%)	49 (19.7%)	85 (17.0%)
Neutrophil count decreased	21 (8.3%)	25 (10.0%)	46 (9.2%)
White blood cell count decreased	20 (7.9%)	20 (8.0%)	40 (8.0%)
Lymphocyte count decreased	3 (1.2%)	8 (3.2%)	11 (2.2%)
Ejection fraction decreased	4 (1.6%)	4 (1.6%)	8 (1.6%)
Gamma-glutamyltransferase increased	2 (0.8%)	3 (1.2%)	5 (1.0%)
Platelet count decreased	2 (0.8%)	3 (1.2%)	5 (1.0%)
Albumin urine present	2 (0.8%)	0	2 (0.4%)
Aspartate aminotransferase increased	0	1 (0.4%)	1 (0.2%)
Blood lactate dehydrogenase increased	0	1 (0.4%)	1 (0.2%)
Blood magnesium decreased	0	1 (0.4%)	1 (0.2%)
Ejection fraction	0	1 (0.4%)	1 (0.2%)
Red blood cell count decreased	1 (0.4%)	0	1 (0.2%)

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TABLE 14.3.1.18: RELATED GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Total Number of TEAEs	65	78	143
General disorders and administration site conditions			
Total Pts with at Least one TEAE*	20 (7.9%)	13 (5.2%)	33 (6.6%)
Fatigue	10 (4.0%)	11 (4.4%)	21 (4.2%)
Asthenia	3 (1.2%)	4 (1.6%)	7 (1.4%)
Mucosal inflammation	3 (1.2%)	0	3 (0.6%)
Pyrexia	2 (0.8%)	0	2 (0.4%)
Condition aggravated	1 (0.4%)	0	1 (0.2%)
Oedema peripheral	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	23	16	39
Gastrointestinal disorders			
Total Pts with at Least one TEAE*	17 (6.7%)	15 (6.0%)	32 (6.4%)
Nausea	7 (2.8%)	8 (3.2%)	15 (3.0%)
Vomiting	5 (2.0%)	7 (2.8%)	12 (2.4%)
Stomatitis	5 (2.0%)	3 (1.2%)	8 (1.6%)
Diarrhoea	1 (0.4%)	3 (1.2%)	4 (0.8%)
Abdominal pain lower	0	1 (0.4%)	1 (0.2%)
Abdominal pain upper	1 (0.4%)	0	1 (0.2%)
Ascites	0	1 (0.4%)	1 (0.2%)
Colitis	1 (0.4%)	0	1 (0.2%)
Small intestinal obstruction	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	26	34	60

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AEs are coded using MedDRA (Version 16.0)

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TABLE 14.3.1.18: RELATED GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Metabolism and nutrition disorders			
Total Pts with at Least one TEAE*	15 (6.0%)	8 (3.2%)	23 (4.6%)
Hypokalaemia	5 (2.0%)	3 (1.2%)	8 (1.6%)
Dehydration	5 (2.0%)	1 (0.4%)	6 (1.2%)
Hyponatraemia	3 (1.2%)	1 (0.4%)	4 (0.8%)
Decreased appetite	2 (0.8%)	1 (0.4%)	3 (0.6%)
Hypophosphataemia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Hyperglycaemia	0	1 (0.4%)	1 (0.2%)
Hyperkalaemia	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	18	9	27
Infections and infestations			
Total Pts with at Least one TEAE*	9 (3.6%)	2 (0.8%)	11 (2.2%)
Sepsis	3 (1.2%)	0	3 (0.6%)
Bronchitis	1 (0.4%)	0	1 (0.2%)
Herpes zoster	1 (0.4%)	0	1 (0.2%)
Lower respiratory tract infection	1 (0.4%)	0	1 (0.2%)
Neutropenic sepsis	0	1 (0.4%)	1 (0.2%)
Oral fungal infection	1 (0.4%)	0	1 (0.2%)
Pneumonia	1 (0.4%)	0	1 (0.2%)
Septic shock	0	1 (0.4%)	1 (0.2%)
Urinary tract infection	1 (0.4%)	0	1 (0.2%)
Urosepsis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	10	2	12

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TABLE 14.3.1.18: RELATED GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Cardiac disorders			
Total Pts with at Least one TEAE*	5 (2.0%)	3 (1.2%)	8 (1.6%)
Atrial fibrillation	2 (0.8%)	0	2 (0.4%)
Left ventricular dysfunction	0	2 (0.8%)	2 (0.4%)
Acute coronary syndrome	1 (0.4%)	0	1 (0.2%)
Cardiac failure	1 (0.4%)	0	1 (0.2%)
Cardiotoxicity	1 (0.4%)	0	1 (0.2%)
Intracardiac thrombus	0	1 (0.4%)	1 (0.2%)
Tachycardia	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	6	4	10
Nervous system disorders			
Total Pts with at Least one TEAE*	2 (0.8%)	4 (1.6%)	6 (1.2%)
Lethargy	0	2 (0.8%)	2 (0.4%)
Syncope	1 (0.4%)	1 (0.4%)	2 (0.4%)
Dysgeusia	0	1 (0.4%)	1 (0.2%)
Neuralgia	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	2	4	6
Skin and subcutaneous tissue disorders			
Total Pts with at Least one TEAE*	5 (2.0%)	1 (0.4%)	6 (1.2%)
Alopecia	5 (2.0%)	1 (0.4%)	6 (1.2%)
Total Number of TEAEs	5	1	6

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TABLE 14.3.1.18: RELATED GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Respiratory, thoracic and mediastinal disorders			
Total Pts with at Least one TEAE*	2 (0.8%)	2 (0.8%)	4 (0.8%)
Pulmonary embolism	1 (0.4%)	1 (0.4%)	2 (0.4%)
Acute pulmonary oedema	1 (0.4%)	0	1 (0.2%)
Acute respiratory failure	1 (0.4%)	0	1 (0.2%)
Chronic obstructive pulmonary disease	1 (0.4%)	0	1 (0.2%)
Dyspnoea	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	4	2	6
Renal and urinary disorders			
Total Pts with at Least one TEAE*	2 (0.8%)	1 (0.4%)	3 (0.6%)
Proteinuria	1 (0.4%)	0	1 (0.2%)
Renal failure	0	1 (0.4%)	1 (0.2%)
Renal failure acute	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	2	1	3
Reproductive system and breast disorders			
Total Pts with at Least one TEAE*	2 (0.8%)	1 (0.4%)	3 (0.6%)
Genital rash	1 (0.4%)	0	1 (0.2%)
Uterine haemorrhage	1 (0.4%)	0	1 (0.2%)
Vulvovaginal burning sensation	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	2	1	3

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Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.18: RELATED GRADE 3 OR HIGHER TREATMENT EMERGENT ADVERSE EVENTS – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Vascular disorders			
Total Pts with at Least one TEAE*	0	2 (0.8%)	2 (0.4%)
Hypertensive crisis	0	1 (0.4%)	1 (0.2%)
Hypotension	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	2	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Total Pts with at Least one TEAE*	0	1 (0.4%)	1 (0.2%)
Tumour necrosis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	1	1

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.20: TREATMENT EMERGENT ADVERSE EVENTS RESULTING IN DISCONTINUATION OF STUDY TREATMENT – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Investigations			
Total Pts with at Least one TEAE*	9 (3.6%)	14 (5.6%)	23 (4.6%)
Ejection fraction decreased	8 (3.2%)	12 (4.8%)	20 (4.0%)
Blood creatinine increased	0	1 (0.4%)	1 (0.2%)
Blood lactate dehydrogenase increased	0	1 (0.4%)	1 (0.2%)
Electrocardiogram QT prolonged	0	1 (0.4%)	1 (0.2%)
Lymphocyte count increased	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	9	15	24
General disorders and administration site conditions			
Total Pts with at Least one TEAE*	5 (2.0%)	7 (2.8%)	12 (2.4%)
Fatigue	1 (0.4%)	3 (1.2%)	4 (0.8%)
Asthenia	1 (0.4%)	0	1 (0.2%)
Drug intolerance	0	1 (0.4%)	1 (0.2%)
General physical health deterioration	1 (0.4%)	0	1 (0.2%)
Mucosal inflammation	1 (0.4%)	0	1 (0.2%)
Oedema	0	1 (0.4%)	1 (0.2%)
Oedema peripheral	0	1 (0.4%)	1 (0.2%)
Pain	0	1 (0.4%)	1 (0.2%)
Performance status decreased	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	5	7	12
Infections and infestations			
Total Pts with at Least one TEAE*	5 (2.0%)	6 (2.4%)	11 (2.2%)
Sepsis	1 (0.4%)	2 (0.8%)	3 (0.6%)

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.20: TREATMENT EMERGENT ADVERSE EVENTS RESULTING IN DISCONTINUATION OF STUDY TREATMENT – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Bacteraemia	1 (0.4%)	0	1 (0.2%)
Bronchitis	1 (0.4%)	0	1 (0.2%)
Candidiasis	0	1 (0.4%)	1 (0.2%)
Cellulitis	1 (0.4%)	0	1 (0.2%)
Lymphangitis	0	1 (0.4%)	1 (0.2%)
Oral candidiasis	0	1 (0.4%)	1 (0.2%)
Postoperative wound infection	0	1 (0.4%)	1 (0.2%)
Septic shock	0	1 (0.4%)	1 (0.2%)
Urethritis	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	5	7	12
Respiratory, thoracic and mediastinal disorders			
Total Pts with at Least one TEAE*	4 (1.6%)	4 (1.6%)	8 (1.6%)
Pulmonary embolism	1 (0.4%)	2 (0.8%)	3 (0.6%)
Dyspnoea	0	2 (0.8%)	2 (0.4%)
Pleural effusion	0	2 (0.8%)	2 (0.4%)
Acute pulmonary oedema	1 (0.4%)	0	1 (0.2%)
Acute respiratory failure	1 (0.4%)	0	1 (0.2%)
Chronic obstructive pulmonary disease	1 (0.4%)	0	1 (0.2%)
Pneumonitis	1 (0.4%)	0	1 (0.2%)
Respiratory failure	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	6	6	12
Blood and lymphatic system disorders			
Total Pts with at Least one TEAE*	3 (1.2%)	3 (1.2%)	6 (1.2%)

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Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.20: TREATMENT EMERGENT ADVERSE EVENTS RESULTING IN DISCONTINUATION OF STUDY TREATMENT – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Anaemia	2 (0.8%)	1 (0.4%)	3 (0.6%)
Neutropenia	1 (0.4%)	1 (0.4%)	2 (0.4%)
Febrile neutropenia	0	1 (0.4%)	1 (0.2%)
Thrombocytopenia	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	3	4	7
Cardiac disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	4 (1.6%)	5 (1.0%)
Cardiotoxicity	0	2 (0.8%)	2 (0.4%)
Acute coronary syndrome	1 (0.4%)	0	1 (0.2%)
Atrial flutter	0	1 (0.4%)	1 (0.2%)
Tachyarrhythmia	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	1	4	5
Gastrointestinal disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	4 (1.6%)	5 (1.0%)
Stomatitis	1 (0.4%)	2 (0.8%)	3 (0.6%)
Ascites	0	1 (0.4%)	1 (0.2%)
Haematemesis	0	1 (0.4%)	1 (0.2%)
Nausea	0	1 (0.4%)	1 (0.2%)
Vomiting	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	1	6	7
Musculoskeletal and connective tissue disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	2 (0.8%)	3 (0.6%)

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

TABLE 14.3.1.20: TREATMENT EMERGENT ADVERSE EVENTS RESULTING IN DISCONTINUATION OF STUDY TREATMENT – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Pain in extremity	0	1 (0.4%)	1 (0.2%)
Pain in jaw	1 (0.4%)	0	1 (0.2%)
Rhabdomyolysis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	1	2	3
Metabolism and nutrition disorders			
Total Pts with at Least one TEAE*	2 (0.8%)	0	2 (0.4%)
Decreased appetite	1 (0.4%)	0	1 (0.2%)
Hyponatraemia	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	2	0	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Total Pts with at Least one TEAE*	0	2 (0.8%)	2 (0.4%)
Leukaemia	0	1 (0.4%)	1 (0.2%)
Tumour necrosis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	2	2
Nervous system disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	1 (0.4%)	2 (0.4%)
Dizziness	0	1 (0.4%)	1 (0.2%)
Neuropathy peripheral	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	1	2
Renal and urinary disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	1 (0.4%)	2 (0.4%)

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

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Date of Table Generation: 20 April 2017

TABLE 14.3.1.20: TREATMENT EMERGENT ADVERSE EVENTS RESULTING IN DISCONTINUATION OF STUDY TREATMENT – BY SOC AND PT

Study: AEZS-108-050
Study Population: Safety Population

Number of participants	AEZS-108 N=252	Doxorubicin N=249	All N=501
Hydronephrosis	0	1 (0.4%)	1 (0.2%)
Renal failure acute	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	1	2
Hepatobiliary disorders			
Total Pts with at Least one TEAE*	0	1 (0.4%)	1 (0.2%)
Cholecystitis acute	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	1	1
Reproductive system and breast disorders			
Total Pts with at Least one TEAE*	1 (0.4%)	0	1 (0.2%)
Uterine haemorrhage	1 (0.4%)	0	1 (0.2%)
Total Number of TEAEs	1	0	1
Skin and subcutaneous tissue disorders			
Total Pts with at Least one TEAE*	0	1 (0.4%)	1 (0.2%)
Dermatitis	0	1 (0.4%)	1 (0.2%)
Total Number of TEAEs	0	1	1

*Treatment emergent AE is adverse event that occurs after randomization and through the end of the study or up to 30 days after the last dose of study treatment. AE that is considered treatment-related regardless of the start date of the event or AE that is present before randomization but worsens in intensity or the investigator subsequently considers treatment-related.
Participants are only counted once for each preferred term.
AEs are coded using MedDRA (Version 16.0)

SAS Program Name: T_teae1.sas
Date of Data Extraction: 05 April 2017
Date of Table Generation: 20 April 2017

Subgruppenanalyse zu EORTC QLQ-C30 (TTD) (GARNET vs. ZoptEC)

Subgroup analysis of TTD on modified ASM analysis

Table 1: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD

Race group		White		Non-White	
		Dostarlimab (N=49)	Doxorubicin (N=176)	Dostarlimab (N=13)	Doxorubicin (N=12)
	Event	21	91	6	9
	Censored	28	85	7	3
	Median (95% CI)	8.444 (2.300, NR)	4.567 (4.140, 5.750)	NA (1.905, NR)	2.530 (0.854, 4.600)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	13	54	14	46
	Censored	20	49	15	39
	Median (95% CI)	NA (2.103, NR)	4.600 (4.140, 6.899)	4.140 (2.168, NR)	4.140 (2.563, 4.994)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	9	61	18	39
	Censored	19	40	16	48
	Median (95% CI)	NA (2.103, NR)	4.074 (2.563, 4.501)	4.140 (2.103, NR)	5.651 (4.369, NA)
NR=Not Reached					

Table 2: Results of Subgroup analysis with stabilized-IPTW on TTD: Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.601	0.419, 0.861	0.184	0.0056
	non-White	25	0.266	0.106, 0.665	0.468	0.0046
Age group	<65	136	0.572	0.360, 0.911	0.237	0.0185
	>=65	114	0.559	0.361, 0.865	0.223	0.0090
Baseline ECOG performance	0	129	0.390	0.245, 0.622	0.237	<.0001
	1	121	0.924	0.561, 1.523	0.255	0.7579

Subgroup analysis of TTD (EORTC Cognitive Functioning Score) on Main analysis

Table 3: Quartiles Information - Subgroup data with stabilized-IPTW on TTD (EORTC Cognitive Functioning Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=176)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	22	82	6	6
	Censored	27	94	7	6
	Median (95% CI)	NR (2.300, NR)	4.600 (4.205, 7.228)	NR (1.938, NA)	5.651 (2.300, NR)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	16	52	12	36
	Censored	17	51	17	49
	Median (95% CI)	4.862 (2.070, NR)	4.370 (4.172, 7.228)	NR (2.103, NR)	5.684 (4.205, 8.575)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	11	46	17	42
	Censored	17	55	17	45
	Median (95% CI)	NR (2.103, NR)	5.421 (4.172, 7.326)	4.107 (2.103, NR)	4.600 (4.205, 9.528)
NR=Not Reached					

Table 4: Results of Subgroup analysis with stabilized-IPTW on TTD (EORTC Cognitive Functioning Score): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.598	0.414, 0.864	0.187	0.0061
	non-White	25	0.733	0.267, 2.013	0.516	0.5464
Age group	<65	136	0.615	0.406, 0.929	0.211	0.0210
	>=65	114	0.721	0.430, 1.208	0.263	0.2139
Baseline ECOG performance	0	129	0.610	0.375, 0.994	0.249	0.0474
	1	121	0.737	0.464, 1.170	0.236	0.1954

Subgroup analysis of TTD (EORTC Emotional Functioning Score) on Main analysis

Table 5: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (EORTC Cognitive Functioning Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	Doxorubicin (N=176)	Dostarlimab (N=13)	Doxorubicin (N=12)
	Event	21	63	5	5
	Censored	28	113	8	7
	Median (95% CI)	NR (4.107, NR)	9.528 (6.407, NR)	NR (2.037, NR)	6.965 (2.300, NR)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	15	38	11	30
	Censored	18	65	18	55
	Median (95% CI)	6.407 (2.103, NR)	9.528 (4.600, NR)	NR (2.103, NR)	8.575 (5.651, NR)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	11	31	15	37
	Censored	17	70	19	50
	Median (95% CI)	6.407 (2.103, NR)	12.715 (6.965, NR)	8.444 (2.168, NR)	7.556 (4.304, 9.528)
NR=Not Reached					

Table 6: Results of Subgroup analysis with stabilized-IPTW on TTD (EORTC Emotional Functioning Score): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.846	0.542, 1.320	0.227	0.4613
	non-White	25	0.599	0.205, 1.753	0.548	0.3495
Age group	<65	136	1.045	0.625, 1.748	0.262	0.8661
	>=65	114	0.839	0.461, 1.526	0.305	0.5647
Baseline ECOG performance	0	129	1.116	0.604, 2.061	0.313	0.7256
	1	121	0.734	0.453, 1.190	0.247	0.2099

Subgroup analysis of TTD (EORTC Physical Functioning Score) on Main analysis

Table 7: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (EORTC Physical Functioning Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=176)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	27	105	5	9
	Censored	22	71	8	3
	Median (95% CI)	4.435 (2.103, NR)	4.271 (2.694, 5.421)	NR (2.037, NR)	2.530 (2.103, 5.224)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	15	61	17	53
	Censored	18	42	12	32
	Median (95% CI)	NR (2.201, NR)	4.304 (2.530, 5.421)	2.168 (2.070, 5.585)	4.140 (2.497, 4.468)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	13	61	19	53
	Censored	15	40	15	34
	Median (95% CI)	6.407 (2.103, NR)	4.140 (2.530, 4.567)	2.858 (2.070, NR)	4.600 (2.595, 6.867)
NR=Not Reached					

Table 8: Results of Subgroup analysis with stabilized-IPTW on TTD (EORTC Physical Functioning Score): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.808	0.578, 1.130	0.171	0.2134
	non-White	25	0.257	0.116, 0.566	0.404	0.0008
Age group	<65	136	0.590	0.375, 0.929	0.232	0.0228
	>=65	114	0.854	0.567, 1.286	0.209	0.4506
Baseline ECOG performance	0	129	0.689	0.450, 1.056	0.218	0.0875
	1	121	0.762	0.488, 1.190	0.227	0.2324

Subgroup analysis of TTD (EORTC Role Functioning Score) on Main analysis

Table 9: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (EORTC Role Functioning Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	Doxorubicin (N=176)	Dostarlimab (N=13)	Doxorubicin (N=12)
	Event	33	103	5	11
	Censored	16	73	8	1
	Median (95% CI)	2.136 (2.103, 4.862)	4.172 (2.793, 4.567)	NR (2.004, NR)	2.497 (0.854, 4.140)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	19	62	19	52
	Censored	14	41	10	33
	Median (95% CI)	4.862 (2.103, NR)	4.172 (2.530, 4.830)	2.103 (2.070, 4.435)	3.121 (2.530, 4.370)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	15	66	23	48
	Censored	13	35	11	39
	Median (95% CI)	2.103 (2.070, NR)	2.694 (2.497, 4.140)	2.201 (2.103, 5.520)	4.501 (3.023, 7.064)
NR=Not Reached					

Table 10: Results of Subgroup analysis with stabilized-IPTW on TTD (EORTC Role Functioning Score) : Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.965	0.713, 1.308	0.155	0.8198
	non-White	25	0.218	0.103, 0.463	0.383	<.0001
Age group	<65	136	0.762	0.519, 1.119	0.196	0.1658
	>=65	114	1.021	0.698, 1.491	0.194	0.9162
Baseline ECOG performance	0	129	0.790	0.513, 1.218	0.221	0.2861
	1	121	0.959	0.672, 1.369	0.181	0.8197

Subgroup analysis of TTD (EORTC Social Functioning Score) on Main analysis

Table 11: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (EORTC Social Functioning Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	Doxorubicin (N=176)	Dostarlimab (N=13)	Doxorubicin (N=12)
	Event	20	97	4	6
	Censored	29	79	9	6
	Median (95% CI)	NR (2.497, NR)	4.172 (3.121, 4.830)	NR (1.938, NR)	4.140 (2.300, NR)
Age group		< 65		>=65	
		Dostarlimab (N=33)	Doxorubicin (N=103)	Dostarlimab (N=29)	Doxorubicin (N=85)
	Event	12	53	12	50
	Censored	21	50	17	35
	Median (95% CI)	NR (4.895, NR)	4.600 (3.220, 7.228)	NR (2.070, NR)	4.140 (2.694, 4.468)
Baseline ECOG performance		0		1	
		Dostarlimab (N=28)	Doxorubicin (N=101)	Dostarlimab (N=34)	Doxorubicin (N=87)
	Event	8	51	16	52
	Censored	20	50	18	35
	Median (95% CI)	NR (4.895, NR)	4.468 (3.121, 6.899)	8.049 (2.103, NR)	4.172 (2.694, 6.209)
NR=Not Reached					

Table 12: Results of Subgroup analysis with stabilized-IPTW on TTD (EORTC Social Functioning Score): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.447	0.310, 0.646	0.188	<.0001
	non-White	25	0.241	0.091, 0.638	0.497	0.0042
Age group	<65	136	0.415	0.260, 0.662	0.239	0.0002
	>=65	114	0.502	0.321, 0.785	0.228	0.0025
Baseline ECOG performance	0	129	0.323	0.185, 0.564	0.285	<.0001
	1	121	0.599	0.398, 0.901	0.208	0.0139

Subgroup analysis of TTD (EORTC Fatigue Score) on Main analysis

Table 13: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (EORTC Fatigue Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	Doxorubicin (N=176)	Dostarlimab (N=13)	Doxorubicin (N=12)
	Event	35	127	5	10
	Censored	14	49	8	2
	Median (95% CI)	2.103 (2.070, 2.990)	2.661 (2.464, 2.793)	NR (2.070, NR)	2.530 (2.070, 4.369)
Age group		< 65		>=65	
		Dostarlimab (N=33)	Doxorubicin (N=103)	Dostarlimab (N=29)	Doxorubicin (N=85)
	Event	19	73	21	64
	Censored	14	30	8	21
	Median (95% CI)	4.107 (2.070, 7.129)	2.662 (2.431, 4.172)	2.103 (2.070, 2.497)	2.595 (2.300, 2.793)
Baseline ECOG performance		0		1	
		Dostarlimab (N=28)	Doxorubicin (N=101)	Dostarlimab (N=34)	Doxorubicin (N=87)
	Event	18	76	22	61
	Censored	10	25	12	26
	Median (95% CI)	2.103 (2.070, 4.172)	2.530 (2.366, 2.760)	2.365 (2.070, 6.308)	2.694 (2.464, 4.172)
NR=Not Reached					

Table 14: Results of Subgroup analysis with stabilized-IPTW on TTD (EORTC Fatigue Score): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.837	0.643, 1.089	0.134	0.1855
	non-White	25	0.241	0.132, 0.439	0.307	<.0001
Age group	<65	136	0.630	0.448, 0.886	0.174	0.0080
	>=65	114	1.124	0.829, 1.524	0.155	0.4529
Baseline ECOG performance	0	129	0.921	0.660, 1.285	0.170	0.6283
	1	121	0.672	0.478, 0.944	0.174	0.0220

Subgroup analysis of TTD (EORTC Nausea & Vomiting Score) on Main analysis

Table 15: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (EORTC Nausea & Vomiting Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	Doxorubicin (N=176)	Dostarlimab (N=13)	Doxorubicin (N=12)
	Event	23	95	6	7
	Censored	26	81	7	5
	Median (95% CI)	8.444 (2.497, NR)	4.370 (3.450, 4.830)	NR (1.906, NR)	3.023 (2.070, NR)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	14	58	15	44
	Censored	19	45	14	41
	Median (95% CI)	9.495 (4.140, NR)	4.172 (2.694, 4.830)	8.444 (2.103, NR)	4.370 (2.825, 6.439)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	12	56	17	46
	Censored	16	45	17	41
	Median (95% CI)	5.618 (2.136, NR)	4.140 (2.661, 4.862)	7.129 (2.366, NR)	4.600 (3.023, 6.439)
NR=Not Reached					

Table 16: Results of Subgroup analysis with stabilized-IPTW on TTD (EORTC Nausea & Vomiting Score): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.668	0.462, 0.966	0.188	0.0321
	non-White	25	0.504	0.188, 1.351	0.504	0.1732
Age group	<65	136	0.558	0.345, 0.902	0.245	0.0173
	>=65	114	0.756	0.477, 1.199	0.235	0.2346
Baseline ECOG performance	0	129	0.625	0.366, 1.065	0.272	0.0840
	1	121	0.717	0.471, 1.090	0.214	0.1196

Subgroup analysis of TTD (EORTC Pain Score) on Main analysis

Table 17: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (EORTC Pain Functioning Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=176)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	28	84	6	9
	Censored	21	92	7	3
	Median (95% CI)	4.107 (2.103, 9.495)	6.275 (4.567, 6.899)	2.103 (1.906, NR)	4.600 (0.854, 6.669)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	23	53	11	40
	Censored	10	50	18	45
	Median (95% CI)	2.103 (2.070, 4.107)	5.191 (4.567, 6.834)	NR (2.168, NR)	5.684 (4.140, 7.557)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	14	50	20	43
	Censored	14	51	14	44
	Median (95% CI)	4.140 (2.070, NR)	6.407 (4.830, 7.589)	2.365 (2.070, NR)	4.600 (4.172, 6.637)
NR=Not Reached					

Table 18: Results of Subgroup analysis with stabilized-IPTW on TTD (EORTC Pain Score): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	1.017	0.741, 1.395	0.162	0.9184
	non-White	25	0.532	0.212, 1.331	0.468	0.1774
Age group	<65	136	1.352	0.955, 1.912	0.177	0.0889
	>=65	114	0.665	0.411, 1.077	0.246	0.0975
Baseline ECOG performance	0	129	1.137	0.765, 1.688	0.202	0.5255
	1	121	0.824	0.547, 1.242	0.209	0.3550

Subgroup analysis of TTD (Dyspnea) on Main analysis

Table 19: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (Dyspnoea)

Race group		White		Non-White	
		Dostarlimab (N=48)	**Doxorubicin (N=175)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	18	70	2	7
	Censored	30	105	11	5
	Median (95% CI)	14.982 (4.074, NR)	6.702 (4.731, 9.528)	NR (4.074, NR)	5.224 (2.070, 7.064)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=102)**	**Dostarlimab (N=28)**	**Doxorubicin (N=85)**
	Event	10	41	10	36
	Censored	23	61	18	49
	Median (95% CI)	NR (2.103, NR)	6.702 (4.468, 10.053)	14.982 (2.070, NR)	5.815 (4.370, 9.265)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=33)**	**Doxorubicin (N=86)**
	Event	9	43	11	34
	Censored	19	58	22	52
	Median (95% CI)	14.982 (2.103, NR)	4.830 (4.140, 12.715)	NR (4.074, NR)	7.064 (5.224, 9.265)
Note: 2 patients are missing. NR=Not Reached					

Table 20: Results of Subgroup analysis with stabilized-IPTW on TTD (Dyspnoea): Main data

Group	Class	N (=250*)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	223	0.724	0.495, 1.060	0.194	0.0969
	non-White	25	0.253	0.114, 0.562	0.407	0.0007
Age group	<65	135	0.571	0.340, 0.959	0.265	0.0342
	>=65	113	0.821	0.521, 1.296	0.233	0.3974
Baseline ECOG performance	0	129	0.597	0.357, 0.997	0.262	0.0488
	1	119	0.669	0.418, 1.071	0.240	0.0941

Subgroup analysis of TTD (Insomnia) on Main analysis

Table 21: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (Insomnia Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=176)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	22	74	4	8
	Censored	27	102	9	4
	Median (95% CI)	NR (2.103, NR)	7.228 (5.749, 7.786)	NR (2.004, NR)	7.064 (0.854, 9.101)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	15	52	11	30
	Censored	18	51	18	55
	Median (95% CI)	NR (2.070, NR)	5.060 (4.370, 7.261)	NR (2.070, NR)	7.359 (6.407, 12.715)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	11	42	15	40
	Censored	17	59	19	47
	Median (95% CI)	NR (2.070, NR)	6.702 (4.534, 12.255)	NR (2.070, NR)	7.064 (4.665, 7.359)
NR=Not Reached					

Table 22: Results of Subgroup analysis with stabilized-IPTW on TTD (Insomnia): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	223	0.852	0.584, 1.243	0.193	0.4049
	non-White	25	0.265	0.087, 0.809	0.570	0.0197
Age group	<65	135	0.619	0.397, 0.965	0.226	0.0344
	>=65	113	1.256	0.738, 2.137	0.271	0.4003
Baseline ECOG performance	0	129	0.739	0.439, 1.246	0.266	0.2565
	1	119	0.766	0.484, 1.213	0.235	0.2557

Subgroup analysis of TTD (Appetite Loss) on Main analysis

Table 23: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (Appetite Loss Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=176)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	16	97	5	10
	Censored	33	79	8	2
	Median (95% CI)	NR (NR, NR)	4.501 (3.680, 5.421)	NR (1.938, NR)	3.023 (0.854, 4.567)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	12	58	9	49
	Censored	21	45	20	36
	Median (95% CI)	NR (5.520, NR)	4.501 (3.023, 4.698)	NR (2.497, NR)	4.172 (2.694, 5.815)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	6	56	15	51
	Censored	22	45	19	36
	Median (95% CI)	NR (5.520, NR)	4.370 (3.121, 5.421)	NR (2.300, NR)	4.172 (2.497, 4.632)
NR=Not Reached					

Table 24: Results of Subgroup analysis with stabilized-IPTW on TTD (Appetite Loss): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	223	0.307	0.200, 0.470	0.218	<.0001
	non-White	25	0.191	0.088, 0.418	0.399	<.0001
Age group	<65	135	0.348	0.216, 0.560	0.243	<.0001
	>=65	113	0.295	0.168, 0.521	0.289	<.0001
Baseline ECOG performance	0	129	0.269	0.147, 0.495	0.310	<.0001
	1	119	0.372	0.238, 0.583	0.229	<.0001

Subgroup analysis of TTD (Constipation) on Main analysis

Table 25: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (Constipation)

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=176)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	23	74	5	5
	Censored	26	102	8	7
	Median (95% CI)	4.140 (2.103, NR)	4.961 (4.370, 9.528)	NR (1.938, NR)	5.191 (2.300, NR)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	13	44	15	35
	Censored	20	59	14	50
	Median (95% CI)	NR (3.515, NR)	4.961 (4.501, 9.528)	2.497 (2.070, NR)	4.567 (4.140, 10.809)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	10	52	18	27
	Censored	18	49	16	60
	Median (95% CI)	NR (2.103, NR)	4.172 (2.825, 6.867)	3.515 (2.070, NR)	7.261 (4.600, 10.809)
NR=Not Reached					

Table 26: Results of Subgroup analysis with stabilized-IPTW on TTD (Constipation): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	223	0.818	0.558, 1.200	0.195	0.3046
	non-White	25	0.437	0.133, 1.434	0.606	0.1724
Age group	<65	135	0.551	0.319, 0.953	0.279	0.0330
	>=65	113	0.976	0.612, 1.557	0.238	0.9192
Baseline ECOG performance	0	129	0.460	0.250, 0.847	0.312	0.0127
	1	119	1.119	0.679, 1.845	0.255	0.6595

Subgroup analysis of TTD (Diarrhea) on Main analysis

Table 27: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (Diarrhea)

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=173)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	16	48	5	3
	Censored	33	125	8	
	Median (95% CI)	NR (8.312, NR)	11.532 (6.899, NR)	NR (1.938, NR)	NR (2.530, NR)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=102)**	**Dostarlimab (N=29)**	**Doxorubicin (N=83)**
	Event	11	27	10	24
	Censored	22	75	19	59
	Median (95% CI)	NR (9.232, NR)	NR (6.702, NR)	NR (4.074, NR)	11.532 (5.815, NR)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=100)**	**Dostarlimab (N=34)**	**Doxorubicin (N=85)**
	Event	10	32	11	19
	Censored	18	68	23	66
	Median (95% CI)	NR (4.140, NR)	8.082 (4.600, NR)	NR (7.129, NR)	NR (7.359, NR)
NR=Not Reached					

Table 28: Results of Subgroup analysis with stabilized-IPTW on TTD (Diarrhea): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	222	0.664	0.431, 1.024	0.221	0.0638
	non-White	25	1.163	0.255, 5.297	0.774	0.8457
Age group	<65	135	0.626	0.366, 1.071	0.274	0.0873
	>=65	112	0.713	0.388, 1.309	0.310	0.2750
Baseline ECOG performance	0	128	0.644	0.368, 1.125	0.285	0.1222
	1	119	0.719	0.390, 1.325	0.312	0.2896

Subgroup analysis of TTD (Financial difficulties) on Main analysis

Table 29: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on TTD (Financial difficulties

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=174)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	16	44	3	5
	Censored	33	130	10	7
	Median (95% CI)	NR (14.259, NR)	NR (9.528, NR)	NR (2.070, NR)	6.965 (2.530, 6.965)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=102)**	**Dostarlimab (N=29)**	**Doxorubicin (N=84)**
	Event	14	26	5	23
	Censored	19	76	24	61
	Median (95% CI)	NR (3.515, NR)	9.528 (7.261, NR)	NR (14.259, NR)	NR (5.749, NR)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=100)**	**Dostarlimab (N=34)**	**Doxorubicin (N=86)**
	Event	1	25	18	24
	Censored	27	75	16	62
	Median (95% CI)	NR (NR, NR)	NR (6.965, NR)	4.370 (2.103, NR)	9.528 (4.600, NR)
NR=Not Reached					

Table 30: Results of Subgroup analysis with stabilized-IPTW on TTD (Financial difficulties): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	223	0.710	0.412, 1.223	0.278	0.2169
	non-White	25	0.310	0.131, 0.737	0.441	0.0080
Age group	<65	135	0.824	0.456, 1.490	0.302	0.5229
	>=65	113	0.478	0.213, 1.074	0.413	0.0738
Baseline ECOG performance	0	128	0.094	0.014, 0.653	0.989	0.0168
	1	120	1.154	0.706, 1.886	0.250	0.5668

SENSITIVITÄTSANALYSEN FÜR GESAMTÜBERLEBEN MIT DER VOLLEN SAFETY-POPULATION (GARNET VS. ZoptEC)

Sensitivity analysis on OS

A sensitivity analysis was conducted on the Safety Analysis Data Set to assess whether this would affect the OS results.

Statistical analysis using the Safety Analysis on OS

The Safety Analysis Data Set includes all patients who received at least one dose of each study treatment, N=129 for GARNET and N=249 for ZoptEC. Note that one patient (US01-0005-doxorubicin) is missing in the analysis because this patient did not have baseline ECOG performance score. So, stabilized-IPTW cannot be used on this patient. The results of this sensitivity analysis are presented in Table 10.

Table 1: Results for the safety analysis data set on OS with adjusting stabilized-IPTW

	N (=377*)	Hazard ratio (dostarlimab/doxorubicin)	95% CI	StdErr	p_value
Cox PH model	377	0.403	0.280, 0.581	0.186	<.0001
Assumption check	377	1.352	0.913, 2.002	0.200	0.1317
*Dostarlimab = 129, doxorubicin = 248 for this sensitivity analysis.					

The sensitivity analysis reveals that the results from the Main Analysis Data Set (n=325) and the Safety Analysis Data Set (n=377) are not significantly different from one another in terms of HR estimates (0.409 and 0.403), 95% CIs ([0.277, 0.605] and [0.280, 0.581]), and p-values (<.0001 and <.0001). This sensitivity analysis provides further validation that treatment with dostarlimab is expected to result in approximately a 59.0% reduction in the risk of death compared to doxorubicin.

Objective Response Rate

Table 1: Original unadjusted ORR results

	Dostarlimab (N=92)	Doxorubicin (N=233)
No of ORR	40	32
No of non-ORR	52	201
Proportion (95% CI)	0.435 (0.332, 0.542)	0.137 (0.096, 0.188)

Table 2: Unadjusted ORR results

Odds Ratio/Relative Risk/Risk Difference – Overall Response Rate With non- stabilized-IPTW				
Outcome scale	**Estimation (N=325)** dostarlimab (N1=92) doxorubicin(N2=233)	**95% CI**	**StdErr**	**p_value**
Odds ratio (Doxorubicin / Dostarlimab)	**0.207**	**0.119, 0.361**	**0.2836**	**<.0001**
Relative risk (Doxorubicin / Dostarlimab)	**0.316**	**0.212, 0.470**	**0.2027**	**<.0001**
	Estimation	**95% CI**	**StdErr**	**p_value**
Risk difference (Doxorubicin - Dostarlimab)	**-0.297**	**-0.408, -0.187**	**0.0564**	**<.0001**

Safety – SAE

Table 3: Original unadjusted SAE Results

	Dostarlimab (N=129)	Doxorubicin (N=249)
No of SAE	44	75
No of non-SAE	85	174
Proportion of SAE (95% CI)	0.341 (0.260, 0.430)	0.301 (0.245, 0.362)

Table 4: Matched unadjusted SAE results

	Dostarlimab (N=92)	Doxorubicin (N=233)
No of SAE	31	67
No of non-SAE	61	166

Proportion of SAE (95% CI)	0.337 (0.242, 0.443)	0.288 (0.230, 0.350)

Table 5: Unadjusted matched SAE results

Odds Ratio/Relative Risk/Risk Difference – Serious Adverse Event with non-stabilized-IPTW				
Outcome scale	**Estimation (N=325)** dostarlimab (N1=92) doxorubicin(N2=233)	**95% CI**	**StdErr**	**p_value**
Odds ratio (Dostarlimab/Doxorubicin)	**1.2591**	**0.751, 2.112**	**0.2638**	**0.3825**
Relative risk (Dostarlimab/Doxorubicin)	**1.1718**	**0.825, 1.664**	**0.1789**	**0.3756**
	Estimation	**95% CI**	**StdErr**	**p_value**
Risk difference (Dostarlimab/Doxorubicin)	**0.0494**	**-.063, 0.162**	**0.0509**	**0.4330**

Safety – TEAE

For the following dataset as originally reported:

Table 6: Original unadjusted TEAE results

	Dostarlimab (N=129)	Doxorubicin (N=249)
No of TEAE	15	38
No of non-TEAE	114	211
Proportion of TEAE (95% CI)	0.116 (0.067, 0.185)	0.153 (0.110, 0.203)

Table 7: Matched unadjusted TEAE results

	Dostarlimab (N=92)	Doxorubicin (N=233)
No of TEAE	8	32
No of non-TEAE	84	201
Proportion of TEAE (95% CI)	0.087 (0.038, 0.164)	0.137 (0.096, 0.188)

Table 8: Unadjusted matched TEAE results

Odds Ratio/Relative Risk/Risk Difference – Discontinuation due to TEAE with non-stabilized-IPTW				
Outcome scale	**Estimation (N=325)** dostarlimab (N1=92) doxorubicin(N2=233)	**95% CI**	**StdErr**	**p_value**
Odds ratio (Dostarlimab/Doxorubicin)	0.5982	0.265, 1.352	0.4161	0.2169
Relative risk (Dostarlimab/Doxorubicin)	0.6332	0.303, 1.322	0.3756	0.2237
	Estimation	**95% CI**	**StdErr**	**p_value**
Risk difference (Dostarlimab/Doxorubicin)	-0.0504	-.123, 0.022	0.0370	0.1737

Safety – CTCAE grade 3 or higher

Table 9: Original unadjusted unmatched CTCAE grade > 3 results

	Dostarlimab (N=129)	Doxorubicin (N=249)
No of CTCAE Grade ≥ 3	62	195
Proportion of CTCAE Grade ≥ 3 (95% CI)	0.481 (0.392, 0.570)	0.783 (0.727, 0.833)

Table 10: Unadjusted matched CTCAE > 3 results

	Dostarlimab (N=92)	Doxorubicin (N=233)
No of CTCAE Grade ≥ 3	45	180
Proportion of CTCAE Grade ≥ 3 (95% CI)	0.489 (0.383, 0.596)	0.773 (0.713, 0.825)

Table 11: Matched unadjusted CTCAE > 3 results

Odds Ratio/Relative Risk/Risk Difference – CTCAE with non-stabilized-IPTW				
Outcome scale	**Estimation (N=325)** dostarlimab (N1=92) doxorubicin(N2=233)	**95% CI**	**StdErr**	**p_value**
Odds ratio (Dostarlimab/Doxorubicin)	0.2819	0.169, 0.470	0.2606	<.0001

Odds Ratio/Relative Risk/Risk Difference – CTCAE with non-stabilized-IPTW				
Outcome scale	**Estimation (N=325)** dostarlimab (N1=92) doxorubicin(N2=233)	**95% CI**	**StdErr**	**p_value**
Relative risk (Dostarlimab/Doxorubicin)	0.6332	0.508, 0.789	0.1123	<.0001
	Estimation	**95% CI**	**StdErr**	**p_value**
Risk difference (Dostarlimab/Doxorubicin)	-0.2834	-.399, -.168	0.0589	<.0001

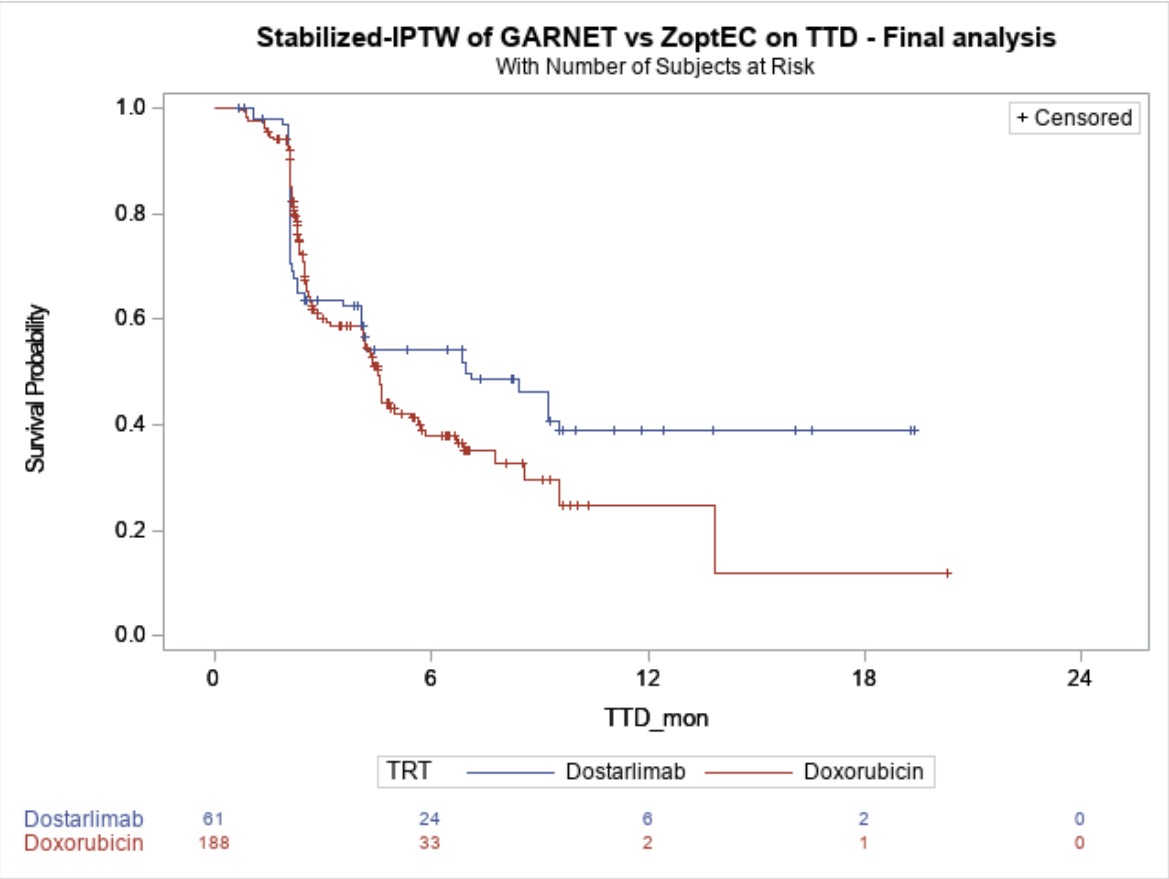
EORTC QLQ-C30 - Zeit bis zur Verschlechterung - Sensitivitätsanalysen ohne Zensierungen (TTD) (GARNET vs. ZoptEC)

Sensitivity analysis of Time to Deterioration (TTD) with IPTW – Assessment Scheduled Matching (ASM)

Table 1: Results of Sensitivity analysis on TTD adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	8.375	0.0038		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.628	0.462, 0.856	0.157	0.0032

Figure 1: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 2: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
Status of TTD		
Event	**31**	**100**
Censored	**31**	**88**
TTD (in Months)		
Median (95% CI)	**6.932 (2.497, NR)**	**4.534 (4.074, 5.421)**

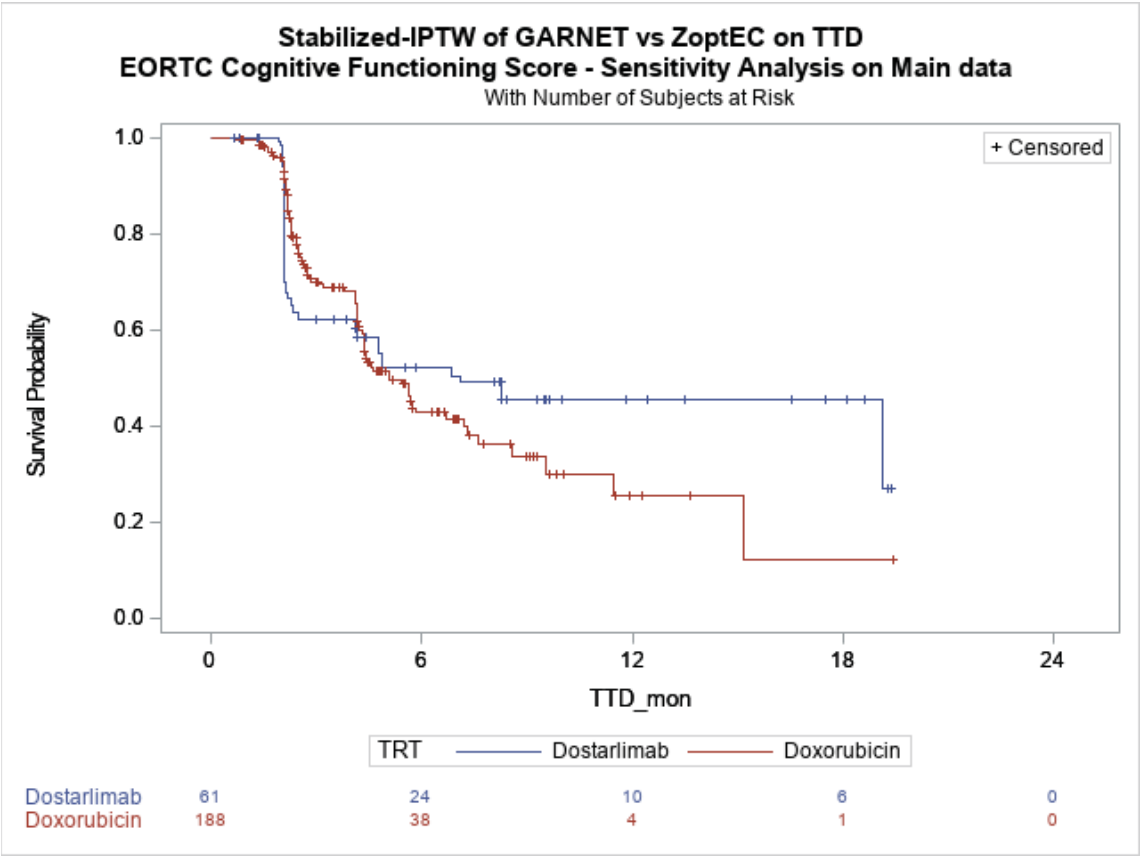
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - (EORTC Cognitive Functioning Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 3: Results of Sensitivity analysis on TTD (EORTC Cognitive Functioning Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	12.33	0.0004		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/Doxorubicin)	250	0.658	0.479, 0.902	0.161	0.0094

Figure 2: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (EORTC Cognitive Functioning Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number
of risk is 61/188.

Table 4: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (EORTC Cognitive Functioning Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	Doxorubicin (N=188/188*[2])
Status of TTD		
Event	31	88
Censored	31	100
TTD (in Months)		
Median (95% CI)	7.129 (2.366, NR)	5.060 (4.370, 7.228)

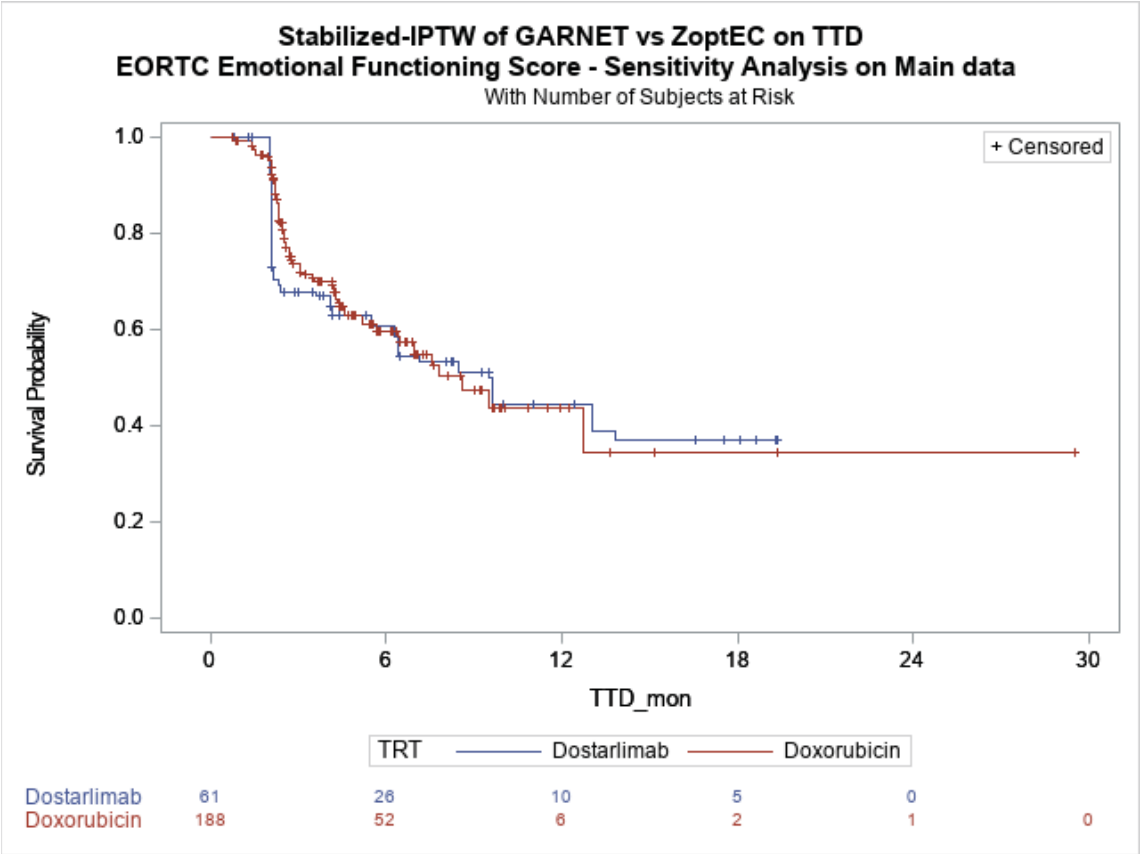
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - (EORTC Emotional Functioning Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 5: Results of Sensitivity analysis on TTD (EORTC Emotional Functioning Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	4.512	0.0337		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/Doxorubicin)	250	0.876	0.604, 1.270	0.190	0.4838

Figure 3: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (EORTC Emotional Functioning Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 6: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (EORTC Emotional Functioning Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
Status of TTD		
Event	**30**	**68**
Censored	**32**	**120**
TTD (in Months)		
Median (95% CI)	**9.528 (4.172, NR)**	**8.575 (6.407, NR)**

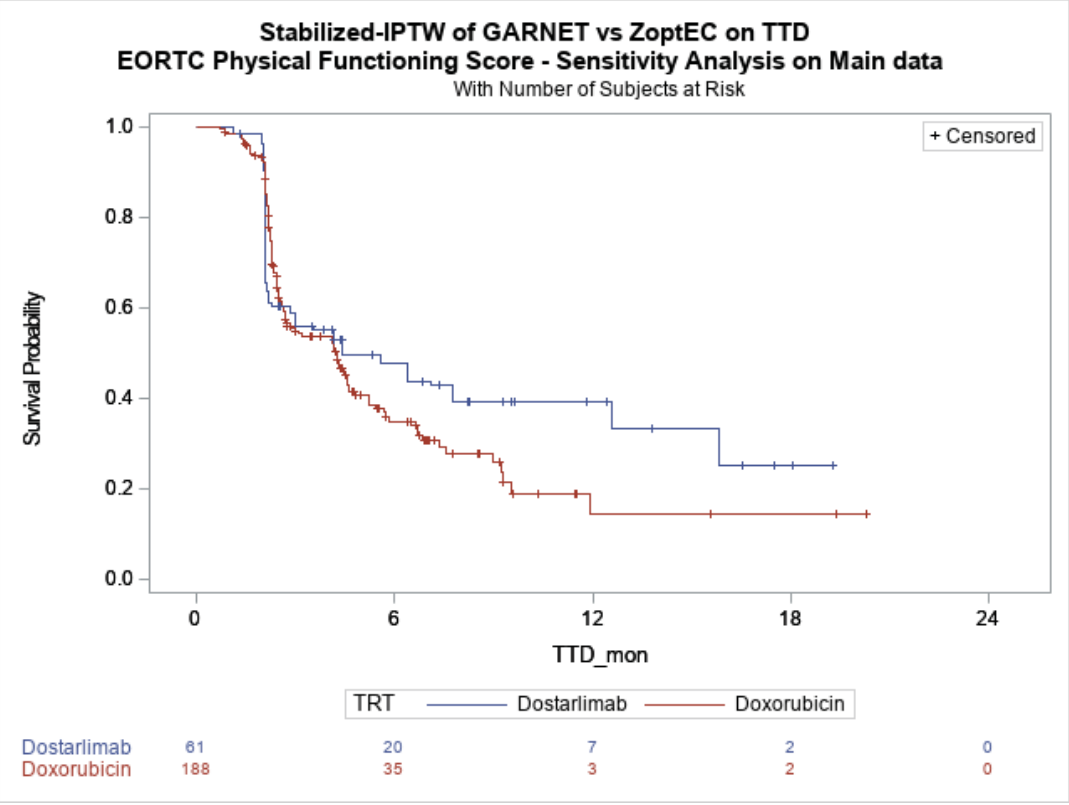
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - (EORTC Physical Functioning Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 7: Results of Sensitivity analysis on TTD (EORTC Physical Functioning Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	8.856	0.0029		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.706	0.526, 0.946	0.150	0.0199

Figure 4: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (EORTC Physical Functioning Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 8: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (EORTC Physical Functioning Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	Doxorubicin (N=188/188*[2])
Status of TTD		
Event	35	114
Censored	27	74
TTD (in Months)		
Median (95% CI)	4.435 (2.136, 12.583)	4.271 (2.694, 4.600)

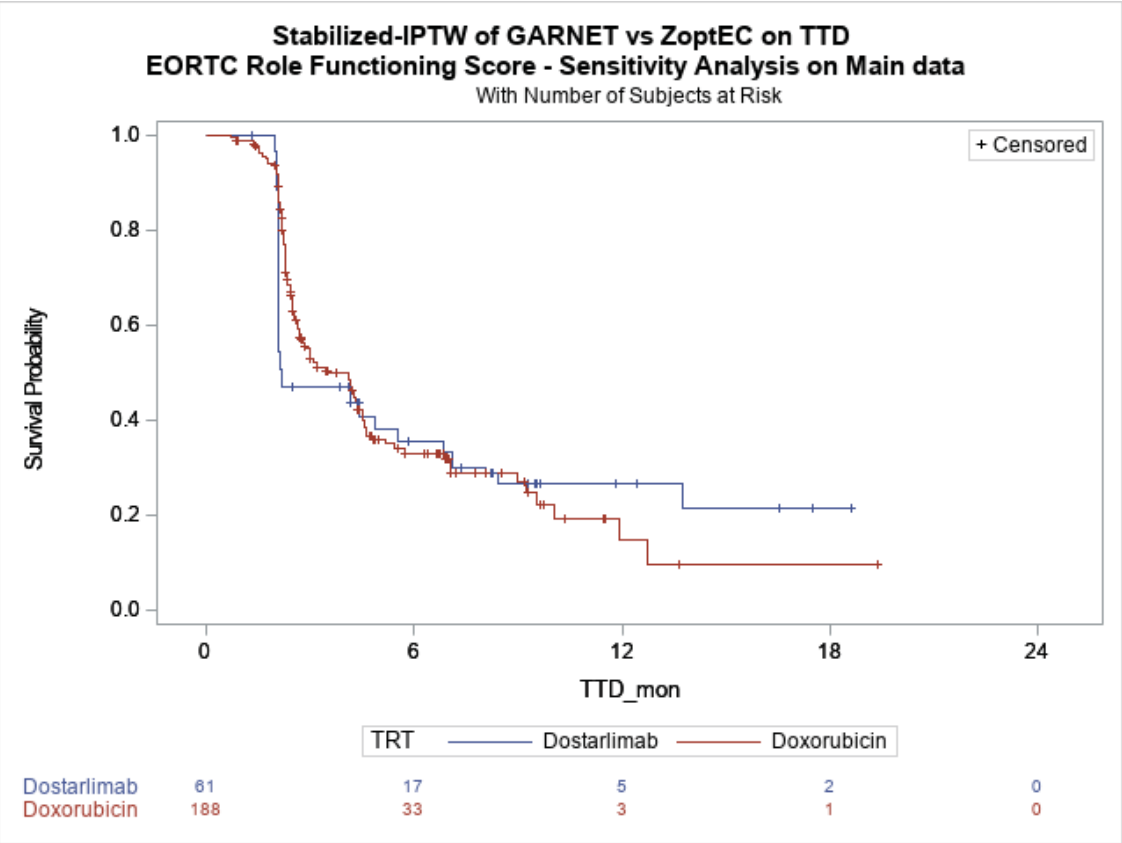
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - (EORTC Role Functioning Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 9: Results of Sensitivity analysis on TTD (EORTC Role Functioning Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	14.71	0.0001		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/Doxorubicin)	250	0.844	0.644, 1.104	0.137	0.2159

Figure 5: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (EORTC Role Functioning Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 10: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (EORTC Role Functioning Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
Status of TTD		
Event	**41**	**114**
Censored	**21**	**74**
TTD (in Months)		
Median (95% CI)	**2.168 (2.103, 5.520)**	**3.515 (2.694, 4.501)**

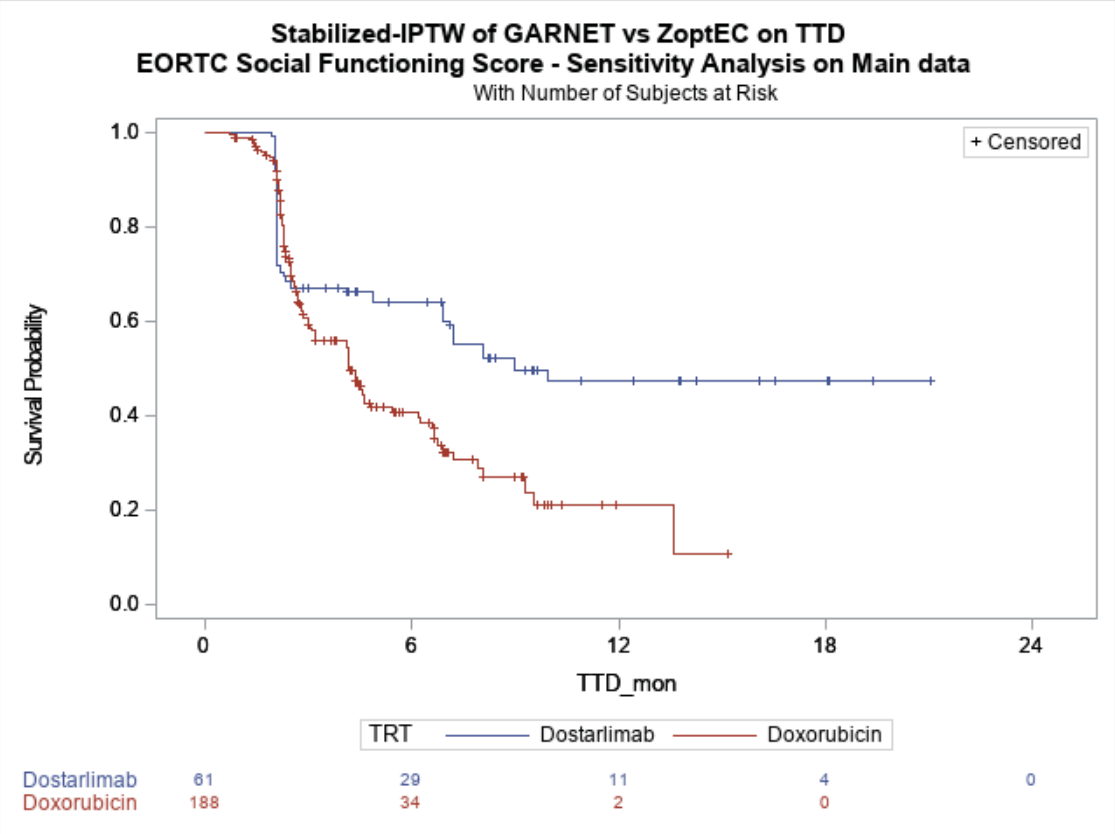
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - (EORTC Social Functioning Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 11: Results of Sensitivity analysis on TTD (EORTC Social Functioning Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	14.43	0.0001		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/Doxorubicin)	250	0.480	0.352, 0.654	0.158	<.0001

Figure 6: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (EORTC Social Functioning Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 12: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (EORTC Social Functioning Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	Doxorubicin (N=188/188*[2])
Status of TTD		
Event	28	103
Censored	34	85
TTD (in Months)		
Median (95% CI)	9.002 (4.895, NR)	4.172 (3.121, 5.421)

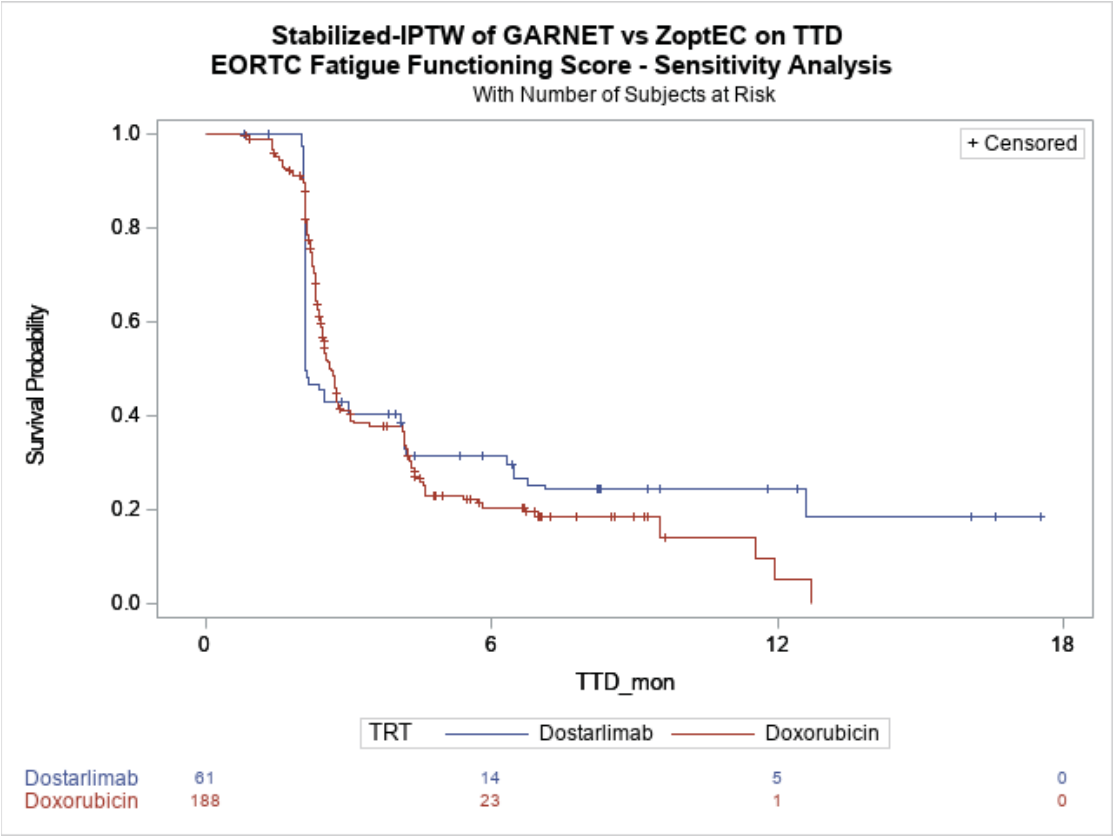
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - (EORTC Fatigue Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 13: Results of Sensitivity analysis on TTD (EORTC Fatigue Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	15.19	<0.0001		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.731	0.577, 0.926	0.121	0.0093

Figure 7: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (EORTC Fatigue Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 14: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (EORTC Fatigue Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
TTD (in Months)		
Event	**42**	**137**
Censored	**20**	**51**
TTD (in Months)		
Median (95% CI)	**2.103 (2.103, 4.140)**	**2.628 (2.464, 2.793)**

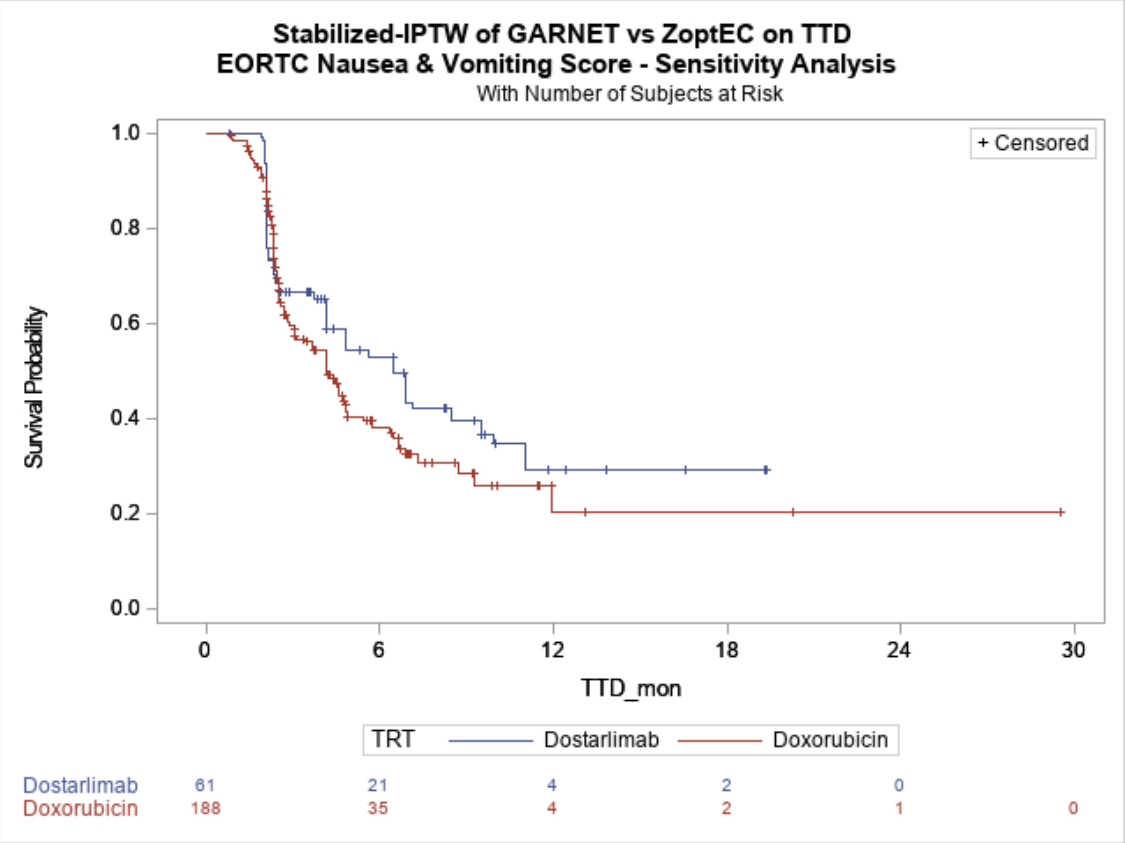
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - (EORTC Nausea & Vomiting Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 15: Results of Sensitivity analysis on TTD (EORTC Nausea & Vomiting Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	4.581	0.0323		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.726	0.532, 0.991	0.159	0.0439

Figure 8: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (EORTC Nausea & Vomiting Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 16: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (EORTC Nausea & Vomiting Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	Doxorubicin (N=188/188*[2])
Status of TTD		
Event	34	102
Censored	28	86
TTD (in Months)		
Median (95% CI)	6.472 (4.139, 11.006)	4.173 (3.023, 4.830)

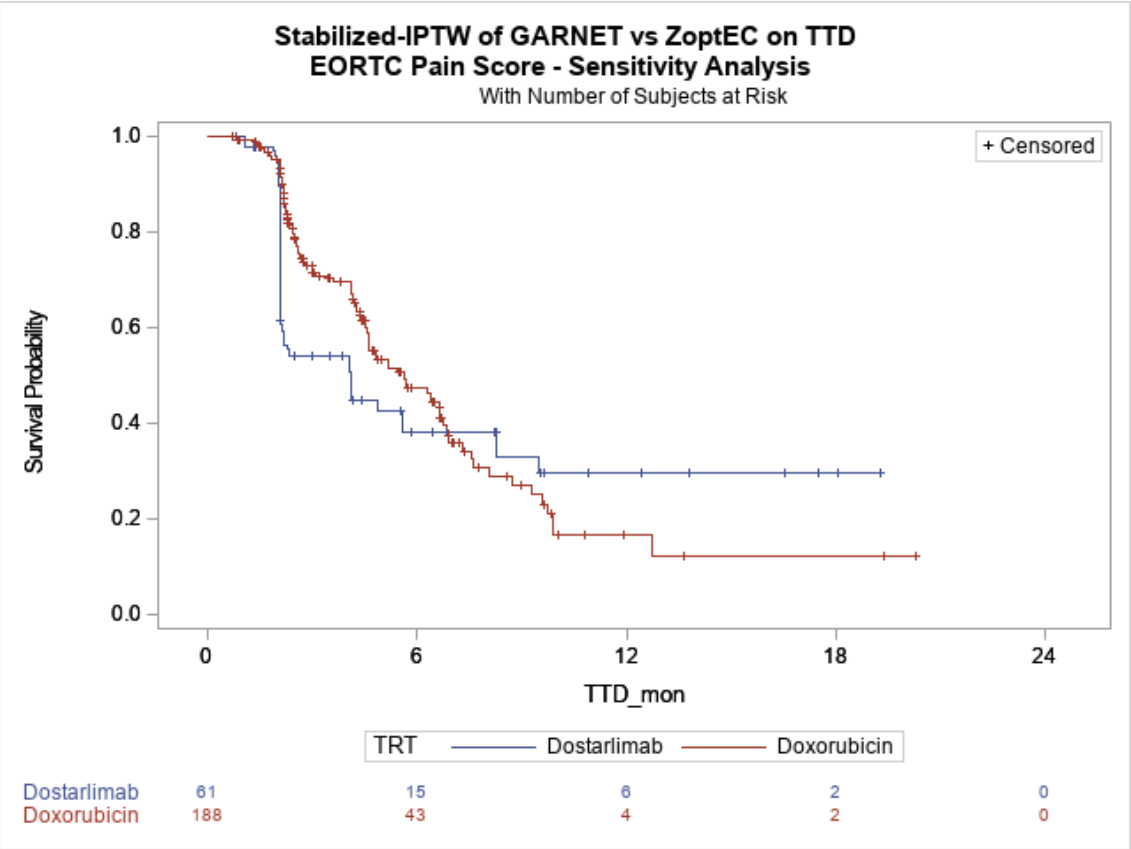
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - (EORTC Pain Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 17: Results of Sensitivity analysis on TTD (EORTC Pain Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	24.73	<0.0001		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/Doxorubicin)	250	0.950	0.717, 1.259	0.144	0.7202

Figure 9: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (EORTC Pain Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 18: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (EORTC Pain Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
Status of TTD		
Event	**35**	**93**
Censored	**27**	**95**
TTD (in Months)		
Median (95% CI)	**4.107 (2.103, 8.279)**	**5.651 (4.600, 6.735)**

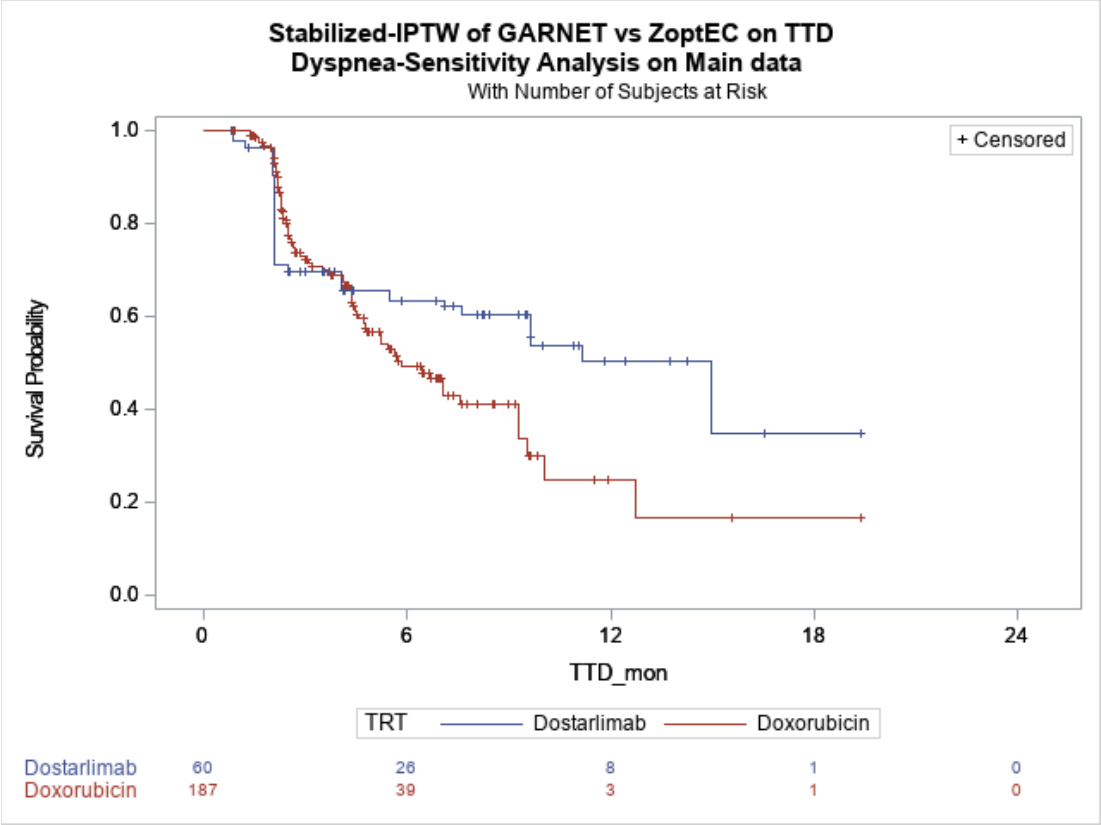
Note: *1 = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*2 = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - Dyspnea- with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 19: Results of Sensitivity analysis on TTD (Dyspnoea) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	248*	14.12	0.0002		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	248*	0.661	0.477, 0.915	0.166	0.0126
Note: *= 2 patients are missing.					

Figure 10: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (Dyspnoea)



Note: Number of subjects are 61/187 but after applying to stabilized-IPTW, starting number of risk is 60/187.

Table 20: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (Dyspnoea)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=61/60*[1])	Doxorubicin (N=187/187*[2])
Status of TTD		
Event	24	77
Censored	37	110
TTD (in Months)		
Median (95% CI)	14.982 (5.487, NR)	5.815 (4.731, 9.265)

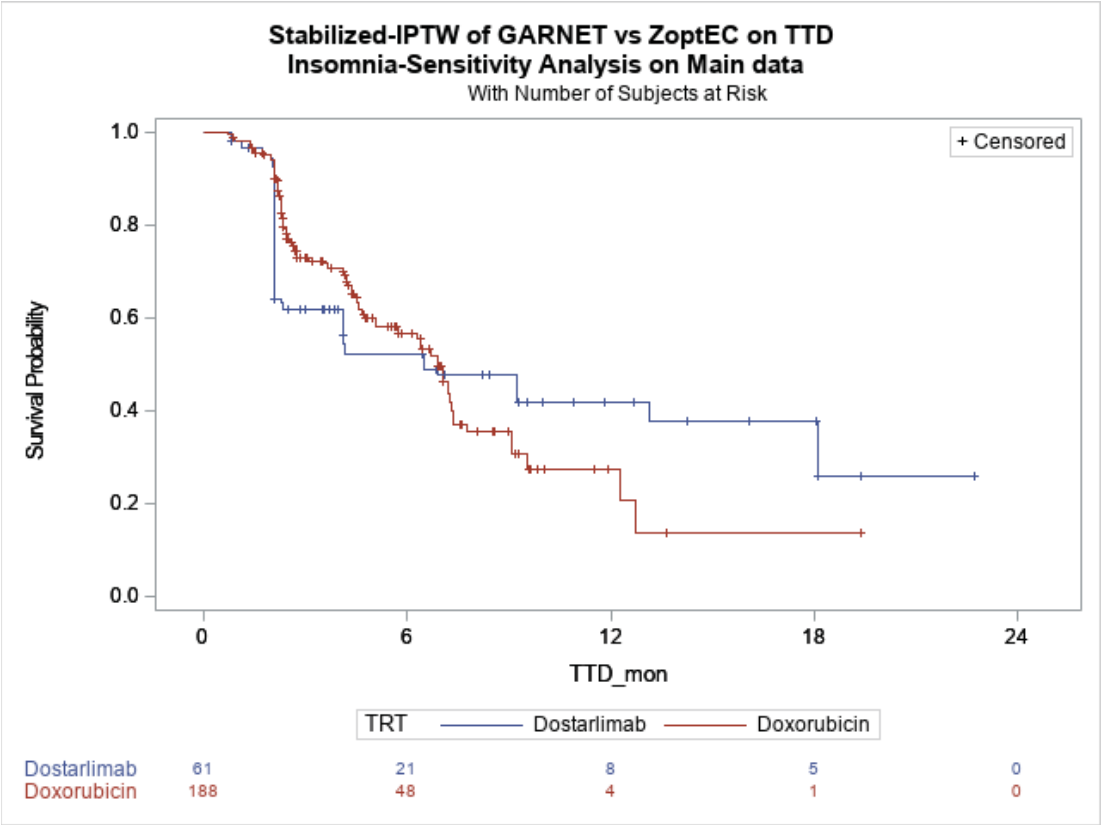
Note: *[1] = Number of subjects are 61 but after applying to weight under IPTW, starting number of risks are 60.
*[2] = Number of subjects are 187 but after applying to weight under IPTW, starting number of risks are 187.
NR=Not Reached
2 patients are missing.

Sensitivity analysis of Time to Deterioration (TTD) - Insomnia- with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 21: Results of Sensitivity analysis on TTD (Insomnia) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	14.01	0.0002		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.821	0.599, 1.125	0.161	0.2199

Figure 11: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on TTD (Insomnia)



Note: Number of subjects are 61/187 but after applying to stabilized-IPTW, starting number of risk is 60/187.

Table 22: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on TTD (Insomnia)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
Status of TTD		
Event	**31**	**82**
Censored	**31**	**106**
TTD (in Months)		
Median (95% CI)	**6.472 (2.103, 18.103)**	**6.899 (5.060, 7.359)**

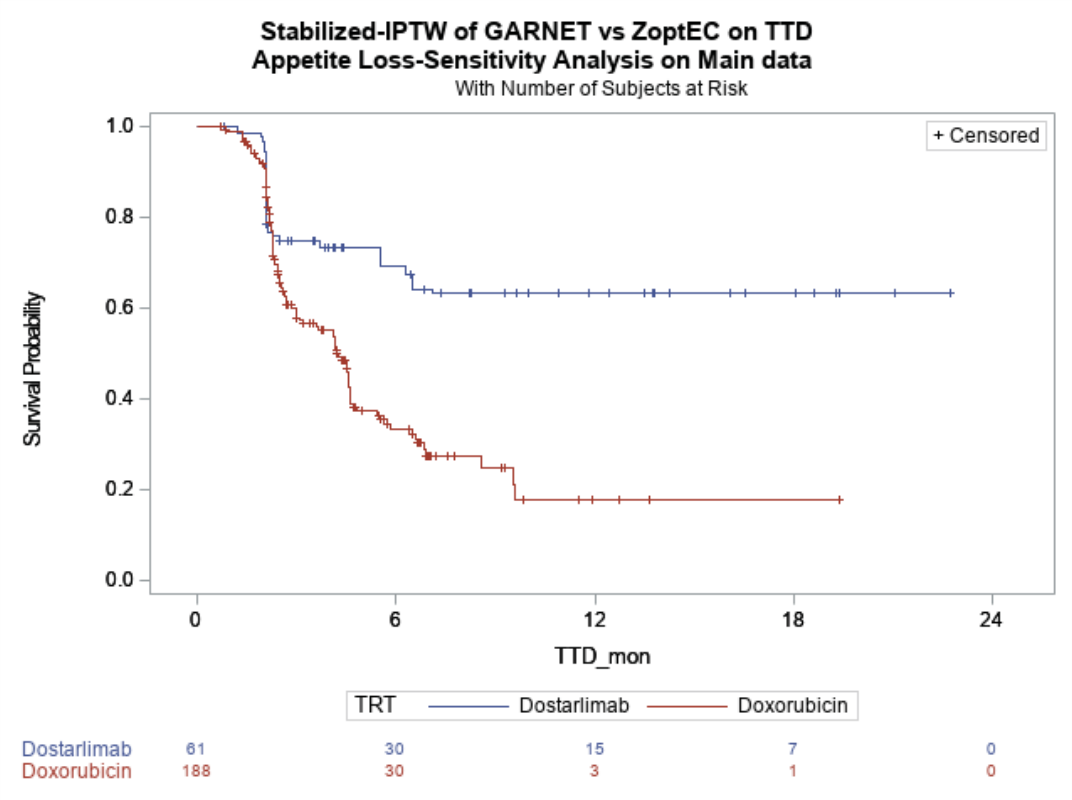
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - Appetite Loss- with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 23: Results of Main analysis on TTD (Appetite Loss) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	10.88	0.0010		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Main analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.315	0.219, 0.453	0.185	<0.0001

Figure 12: Kaplan-Meier curves with stabilized-IPTW of Main data on TTD (Appetite Loss)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 24: Summary of the number of censored and uncensored values and Quartiles Information - Main data with stabilized-IPTW on TTD (Appetite Loss)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	Doxorubicin (N=188/188*[2])
Status of TTD		
Event	22	107
Censored	40	81
TTD (in Months)		
Median (95% CI)	NR (6.472, NR)	4.238 (3.023, 4.600)

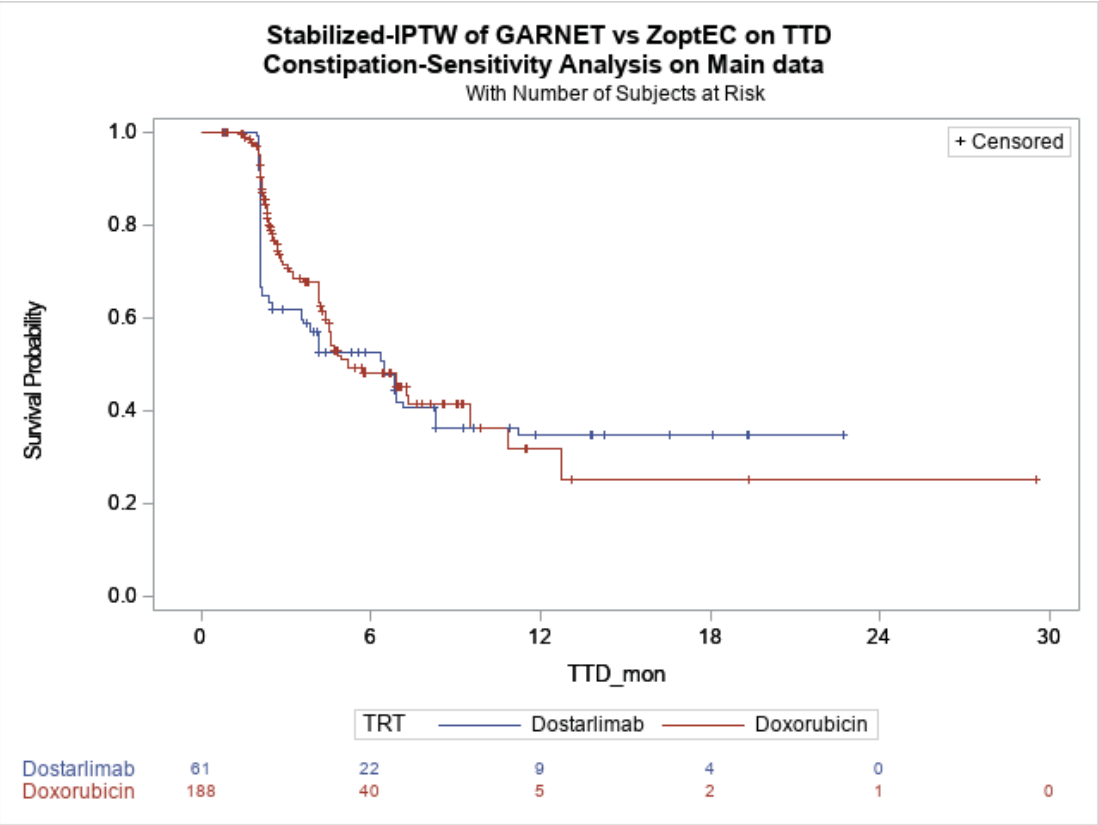
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - Constipation - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 25: Results of Main analysis on TTD (Constipation) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	7.985	0.0047		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Main analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.882	0.633, 1.229	0.169	0.4575

Figure 13: Kaplan-Meier curves with stabilized-IPTW of Main data on TTD (Constipation)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 26: Summary of the number of censored and uncensored values and Quartiles Information - Main data with stabilized-IPTW on TTD (Constipation)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
Status of TTD		
Event	**33**	**78**
Censored	**29**	**110**
TTD (in Months)		
Median (95% CI)	**6.472 (2.366, 11.203)**	**5.191 (4.501, 9.528)**

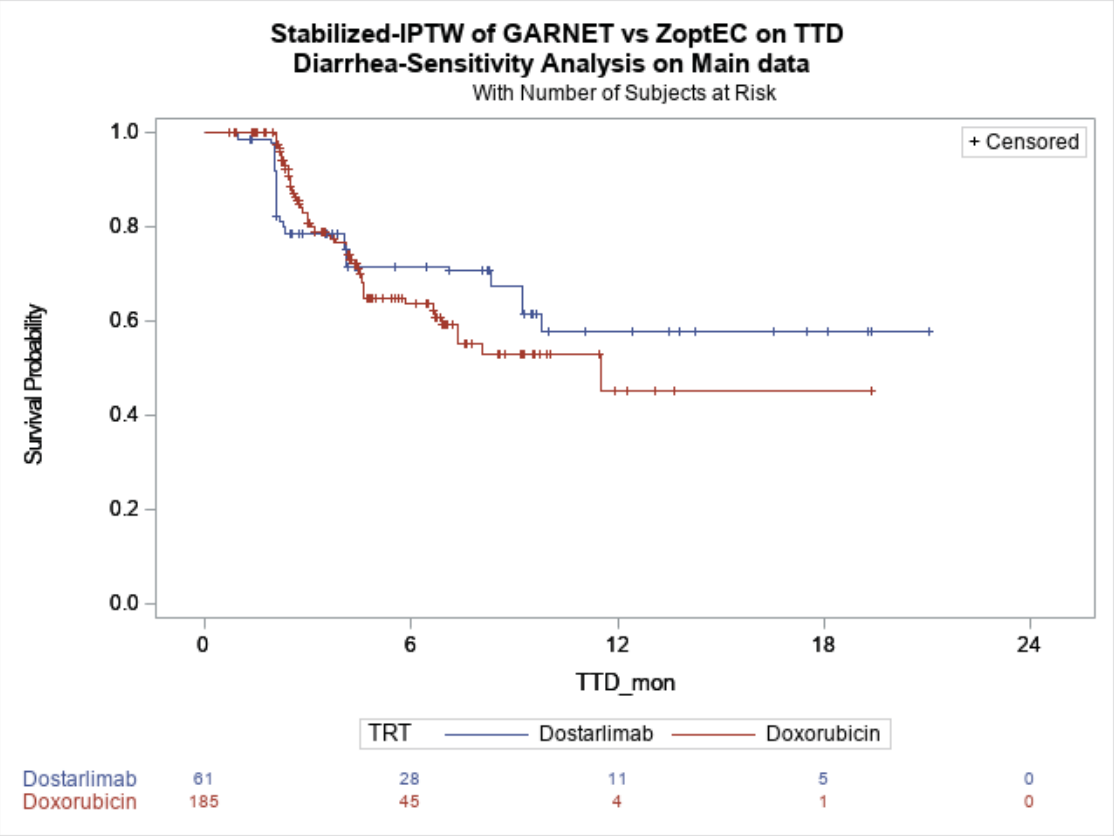
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - Diarrhea - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 27: Results of Main analysis on TTD (Diarrhea) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	247	8.666	0.0032		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Main analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	247	0.689	0.461, 1.030	0.205	0.0695

Figure 14: Kaplan-Meier curves with stabilized-IPTW of Main data on TTD (Diarrhea)



Note: Number of subjects are 62/185 but after applying to stabilized-IPTW, starting number of risk is 61/185.

Table 28: Summary of the number of censored and uncensored values and Quartiles Information - Main data with stabilized-IPTW on TTD (Diarrhea)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	Doxorubicin (N=185/185*[2])
Status of TTD		
Event	21	51
Censored	41	134
TTD (in Months)		
Median (95% CI)	NA (9.232, NA)	11.532 (6.899, NA)

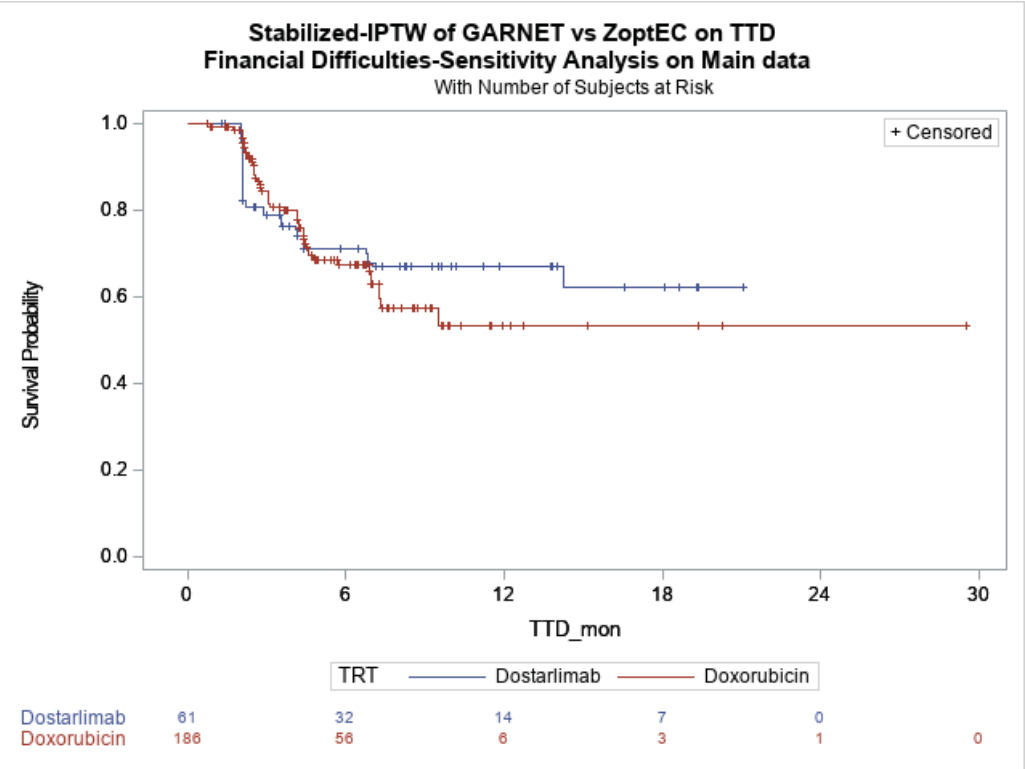
Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 185 but after applying to weight under IPTW, starting number of risks are 185.
NR=Not Reached

Sensitivity analysis of Time to Deterioration (TTD) - Financial difficulties- with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 29: Results of Main analysis on TTD (Financial difficulties) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	248	8.702	0.0032		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Main analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/Doxorubicin)	248	0.699	0.444, 1.102	0.232	0.1228

Figure 15: Kaplan-Meier curves with stabilized-IPTW of Main data on TTD (Financial difficulties)



Note: Number of subjects are 62/186 but after applying to stabilized-IPTW, starting number of risk is 61/186.

Table 30: Summary of the number of censored and uncensored values and Quartiles Information - Main data with stabilized-IPTW on TTD (Financial difficulties)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=186/186*[2])**
Status of TTD		
Event	**21**	**49**
Censored	**41**	**137**
TTD (in Months)		
Median (95% CI)	**NR (14.259, NR)**	**NR (7.261, NR)**

Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 186 but after applying to weight under IPTW, starting number of risks are 186.
NR=Not Reached

Sensitivitätsanalysen mit der ungewichteten Safety-Population der GARNET (GARNET vs. englisches Register)

Survival outcomes of GARNET ITT and RWE cohort before and after matching (RWE cohort, base case)

	RWE cohort (base case)	GARNET ITT before matching
Effective sample size (ESS)	**999**	**129**
Overall survival		
Median OS, months (95% CI)	10.3 (9.2; 11.1)	NE (18.4; NE)
OS rate at 6 months (95% CI)	0.70 (0.67; 0.73)	0.83 (0.75; 0.89)
OS rate at 12 months (95% CI)	0.44 (0.40; 0.47)	0.72 (0.62; 0.80)
OS rate at 18 months (95% CI)	0.29 (0.26; 0.32)	0.63 (0.51; 0.72)
Hazard ratio for OS (95% CI) [dostarlimab vs. usual care]		0.39 (0.28; 0.54)
P-value for hazard ratio		<0.0001

CI: Confidence interval

Survival outcomes of GARNET ITT and RWE cohort before and after matching (RWE cohort, ECOG≤1)

	RWE cohort (ECOG≤1)	GARNET ITT before matching
Effective sample size (ESS)	**501**	**129**
Overall survival		
Median OS, months (95% CI)	10.3 (9.0; 11.1)	NE (18.4; NE)
OS rate at 6 months (95% CI)	0.72 (0.68; 0.76)	0.83 (0.75; 0.89)
OS rate at 12 months (95% CI)	0.43 (0.38; 0.47)	0.72 (0.62; 0.80)
OS rate at 18 months (95% CI)	0.27 (0.23; 0.32)	0.63 (0.51; 0.72)
Hazard ratio for OS (95% CI) [dostarlimab vs. usual care]		0.38 (0.27; 0.54)
P-value for hazard ratio		<0.0001

CI: Confidence interval

Kaplan-Meier Curves

In addition to summarizing survival outcomes in Table 3.5 and Table 3.6, Kaplan-Meier (KM) plots of OS, PFS, and TTD of GARNET ITT and RWE cohorts (base case and ECOG≤1, respectively) before and after matching, under three different matching scenarios, were generated. The KM plots for OS are shown in Figure 3.1 and

Figure 3.2 for the comparison vs. the RWE base case, and the RWE ECOG≤1 cohort respectively. In general, patients in the GARNET ITT cohort had larger overall survival probability than patients in the RWE cohorts in the unadjusted analysis and all three scenarios. The numbers at risk at given time points in the unadjusted analysis can be found in Figures A1 and A17 in Appendix A.

KM curves for the secondary endpoints are shown in Figures A.5 to A.16, and A.21 to A32 in Appendix A.

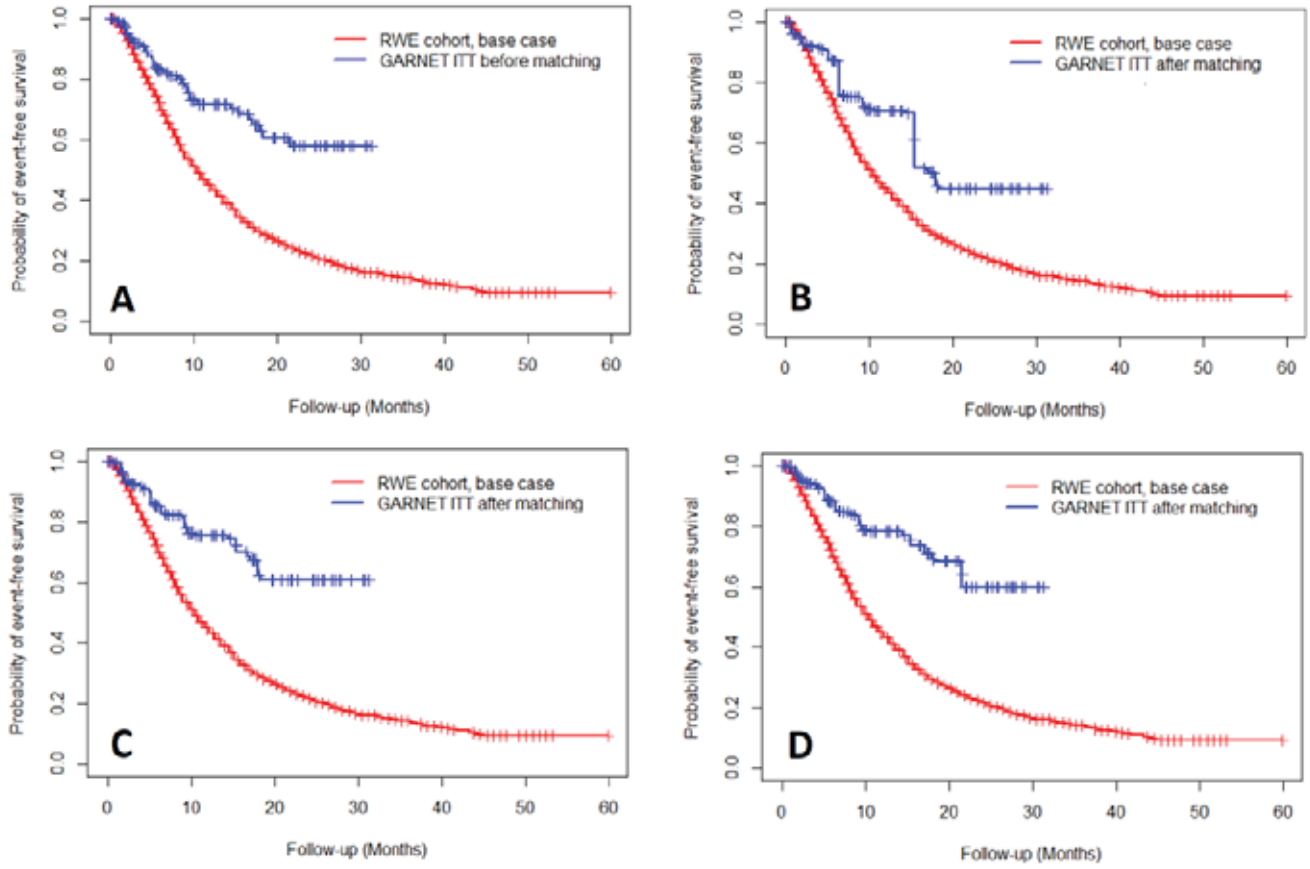


Figure 3.1. Kaplan Meier curves for overall survival – dostarlimab (GARNET ITT cohort) vs. current treatment paradigm (RWE cohort, base case); A: unadjusted, B: matching scenario 1 [matching variables: histology, grade and number of prior platinum-based therapies], C: matching scenario 2 [matching variables: histology and number of prior platinum-based therapies], D: matching scenario 3 [matching variables: race/ethnicity, histology, stage at initial diagnosis and surgery]

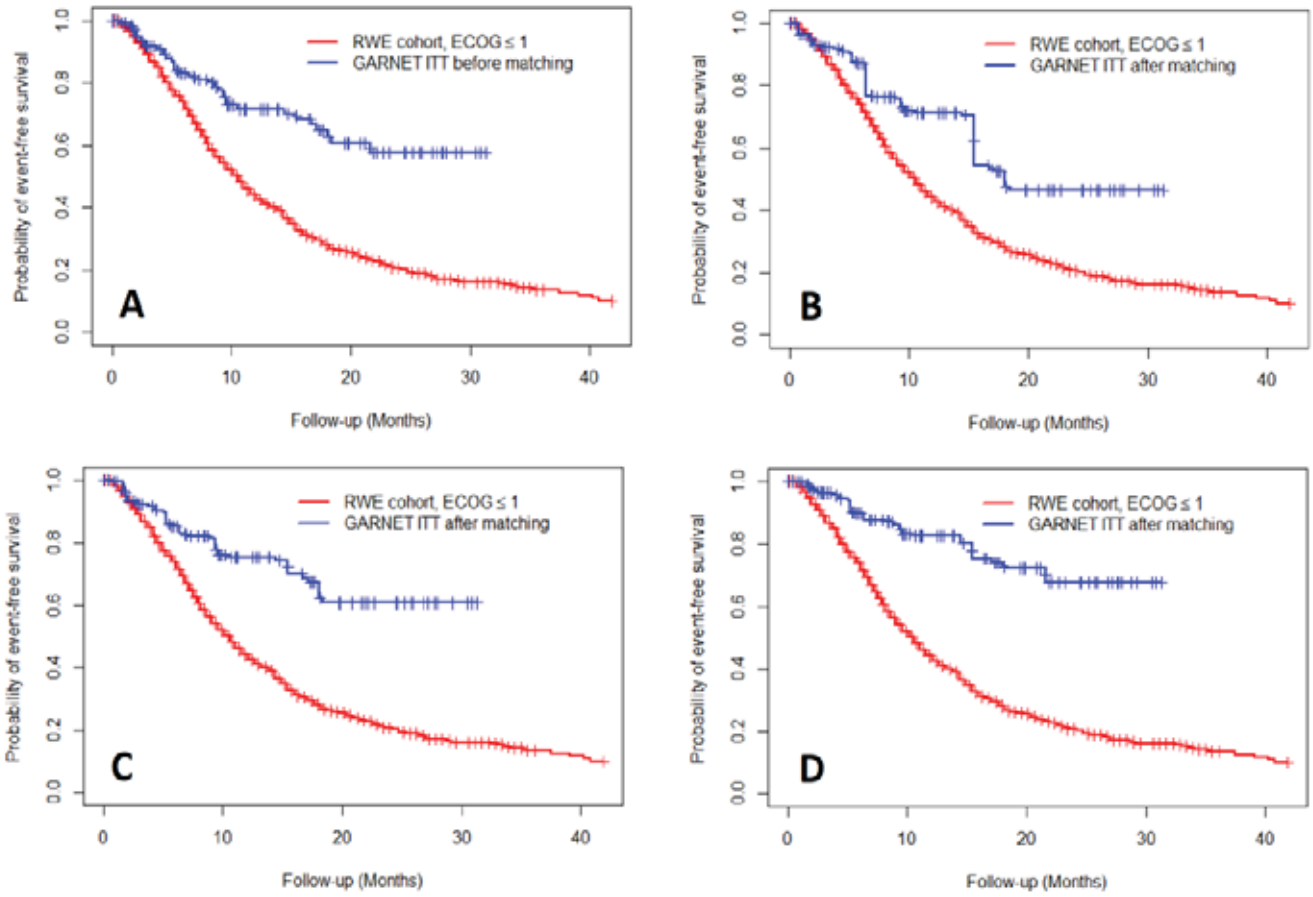


Figure 3.2: Kaplan Meier curves for overall survival – dostarlimab (GARNET ITT cohort) vs. current treatment paradigm (RWE ECOG≤1 cohort); A: unadjusted, B: matching scenario 1 [matching variables: histology, grade and number of prior platinum-based therapies], C: matching scenario 2 [matching variables: histology and number of prior platinum-based therapies], D: matching scenario 3 [matching variables: race/ethnicity, ECOG, histology, stage at initial diagnosis and surgery]

Ergebnisse für EORTC QLQ-C30 mit Schwellenwert 15 inklusive Sensitivitäts- und Subgruppenanalyse (TTD) (GARNET vs. ZoptEC)

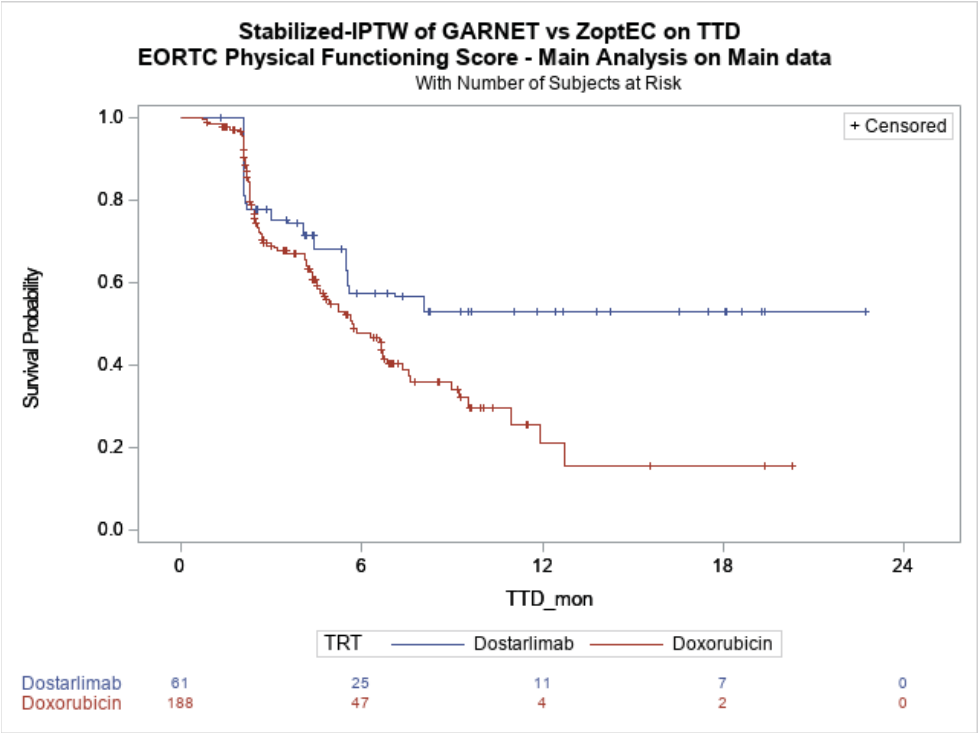
1. Time to Deterioration (TTD) – 15-point scale EORTC Physical Functioning Score

1.1. Main analysis of 15pt TTD – EORTC Physical Functioning Score - with IPTW by modified Assessment-Scheduled Matching (ASM)

Table 1: Results of Main analysis on 15pt TTD (EORTC Physical Functioning Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	**Chi-square**	**p-value**		
Assumption check	**250**	**6.426**	**0.0112**		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Main analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	**Hazard ratio (Dostarlimab/Doxorubicin)**	**95% CI**	**StdErr**	**p_value**
AFT model (Dostarlimab/ Doxorubicin)	**250**	**0.535**	**0.380, 0.752**	**0.174**	**0.0003**

Figure 1: Kaplan-Meier curves with stabilized-IPTW of Main data on 15pt TTD (EORTC Physical Functioning Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 2: Summary of the number of censored and uncensored values and Quartiles Information - Main data with stabilized-IPTW on 15pt TTD (EORTC Physical Functioning Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
Status of TTD		
Event	**23**	**91**
Censored	**39**	**97**
TTD (in Months)		
Median (95% CI)	**NR (5.487, NR)**	**5.684 (4.534, 6.687)**

Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

1.2. Subgroup analysis of 15pt TTD (EORTC Physical Functioning Score) on Main analysis

Table 3: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on 15pt TTD (EORTC Physical Functioning Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	Doxorubicin (N=176)	Dostarlimab (N=13)	Doxorubicin (N=12)
	Event	21	83	2	8
	Censored	28	93	11	4
	Median (95% CI)	8.049 (4.435, NR)	6.308 (4.731, 7.589)	NR (3.581, NR)	4.304 (2.300, 6.669)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	11	49	12	42
	Censored	22	54	17	43
	Median (95% CI)	NR (5.520, NR)	6.604 (4.534, 9.528)	4.435 (2.103, NR)	5.684 (4.140, 7.556)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	9	47	14	44
	Censored	19	54	20	43
	Median (95% CI)	NR (4.435, NR)	5.815 (4.370, 9.002)	8.049 (5.487, NR)	5.749 (4.370, 7.556)
NR=Not Reached					

Table 4: Results of Subgroup analysis with stabilized-IPTW on 15pt TTD (EORTC Physical Functioning Score): Main data

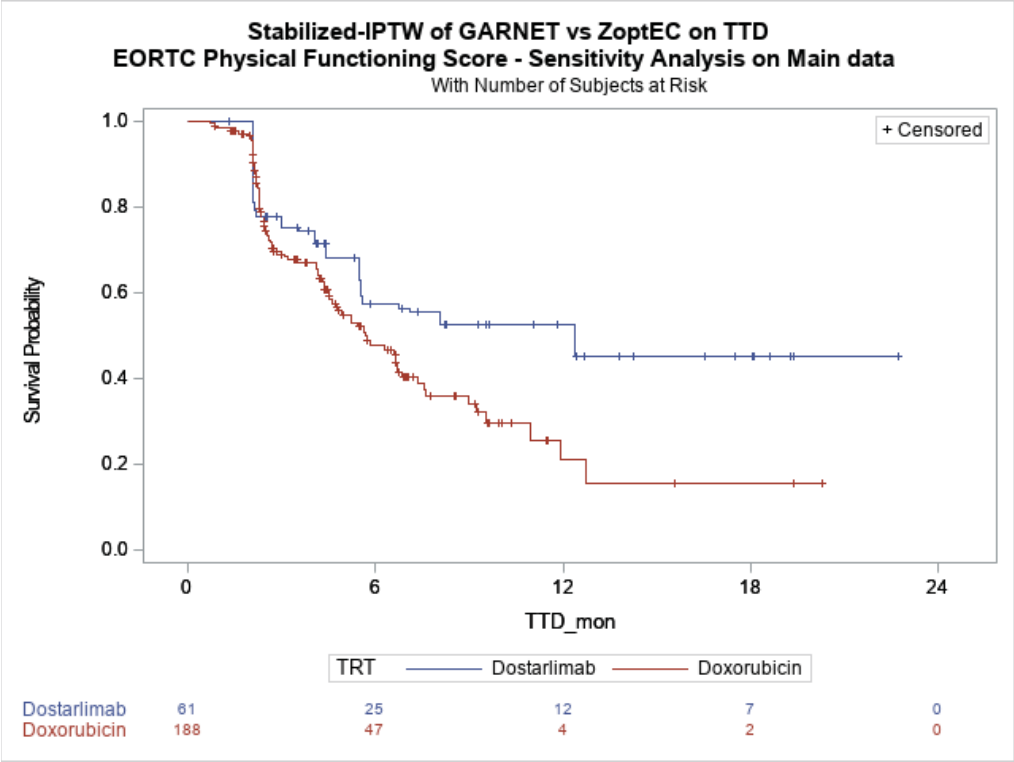
Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.633	0.437, 0.917	0.189	0.0157
	non-White	25	0.206	0.085, 0.500	0.453	0.0005
Age group	<65	136	0.437	0.265, 0.723	0.256	0.0013
	>=65	114	0.751	0.472, 1.195	0.237	0.2267
Baseline ECOG performance	0	129	0.496	0.298, 0.826	0.260	0.0070
	1	121	0.565	0.348, 0.916	0.247	0.0207

1.3. Sensitivity analysis of 15pt TTD - (EORTC Physical Functioning Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 5: Results of Sensitivity analysis on 15pt TTD (EORTC Physical Functioning Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	4.594	0.0321		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.558	0.402, 0.774	0.167	0.0005

Figure 2: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on 15pt TTD (EORTC Physical Functioning Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 6: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on 15pt TTD (EORTC Physical Functioning Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	Doxorubicin (N=188/188*[2])
Status of TTD		
Event	25	91
Censored	37	97
TTD (in Months)		
Median (95% CI)	12.353 (5.487, NR)	5.684 (4.534, 6.867)

Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

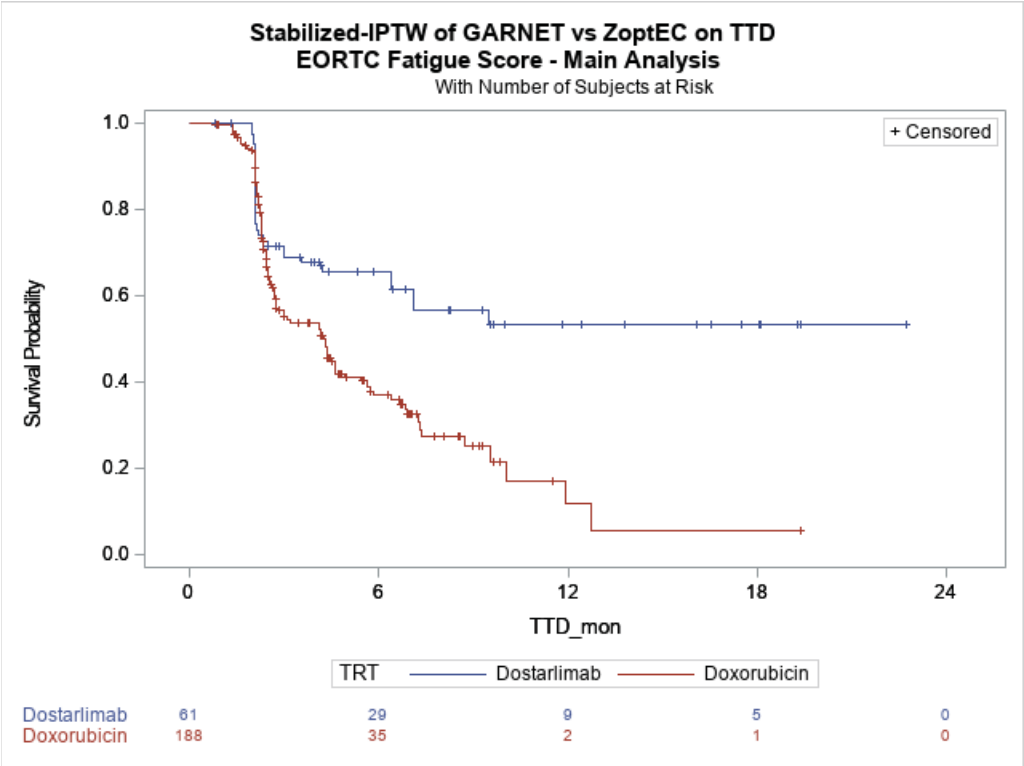
2. Time to Deterioration (TTD) – 15-point scale EORTC Fatigue Score

2.1. Main analysis of 15pt TTD – EORTC Fatigue Score - with IPTW by modified Assessment-Scheduled Matching (ASM)

Table 7: Results of Main analysis on 15pt TTD (EORTC Fatigue Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	250	12.45	0.0004		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Main analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.428	0.309, 0.594	0.167	<.0001

Figure 3: Kaplan-Meier curves with stabilized-IPTW of Main data on 15pt TTD (EORTC Fatigue Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 8: Summary of the number of censored and uncensored values and Quartiles Information - Main data with stabilized-IPTW on 15pt TTD (EORTC Fatigue Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab (N=62/61*[1])	**Doxorubicin (N=188/188*[2])**
Status of TTD		
Event	**23**	**106**
Censored	**39**	**82**
TTD (in Months)		
Median (95% CI)	**NR (6.407, NR)**	**4.304 (2.760, 4.928)**

Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

2.2. Subgroup analysis of 15pt TTD (EORTC Fatigue Score) on Main analysis

Table 9: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on 15pt TTD (EORTC Fatigue Score)

Race group		White		Non-White	
		Dostarlimab (N=49)	**Doxorubicin (N=176)**	**Dostarlimab (N=13)**	**Doxorubicin (N=12)**
	Event	20	96	3	10
	Censored	29	80	10	2
	Median (95% CI)	NR (2.990, NR)	4.370 (2.760, 6.407)	NR (3.581, NR)	3.023 (2.300, 4.304)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=33)	**Doxorubicin (N=103)**	**Dostarlimab (N=29)**	**Doxorubicin (N=85)**
	Event	11	61	12	45
	Censored	22	42	17	40
	Median (95% CI)	NR (6.407, NR)	4.370 (2.694, 6.702)	NR (2.168, NR)	4.140 (2.694, 5.815)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=28)	**Doxorubicin (N=101)**	**Dostarlimab (N=34)**	**Doxorubicin (N=87)**
	Event	9	59	14	47
	Censored	19	42	20	40
	Median (95% CI)	NR (2.103, NR)	2.760 (2.497, 4.370)	9.495 (2.497, NR)	4.600 (3.220, 6.867)
NR=Not Reached					

Table 10: Results of Subgroup analysis with stabilized-IPTW on 15pt TTD (EORTC Fatigue Score): Main data

Group	Class	N (=250)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	White	225	0.492	0.341, 0.710	0.187	0.0001
	non-White	25	0.198	0.116, 0.337	0.272	<.0001
Age group	<65	136	0.405	0.259, 0.633	0.228	<.0001
	>=65	114	0.570	0.364, 0.894	0.229	0.0143
Baseline ECOG performance	0	129	0.449	0.274, 0.733	0.251	0.0014
	1	121	0.456	0.299, 0.694	0.215	0.0003

2.3. Sensitivity analysis of 15pt TTD – (EORTC Fatigue Score) - with IPTW – Assessment-Scheduled Matching (ASM) by article

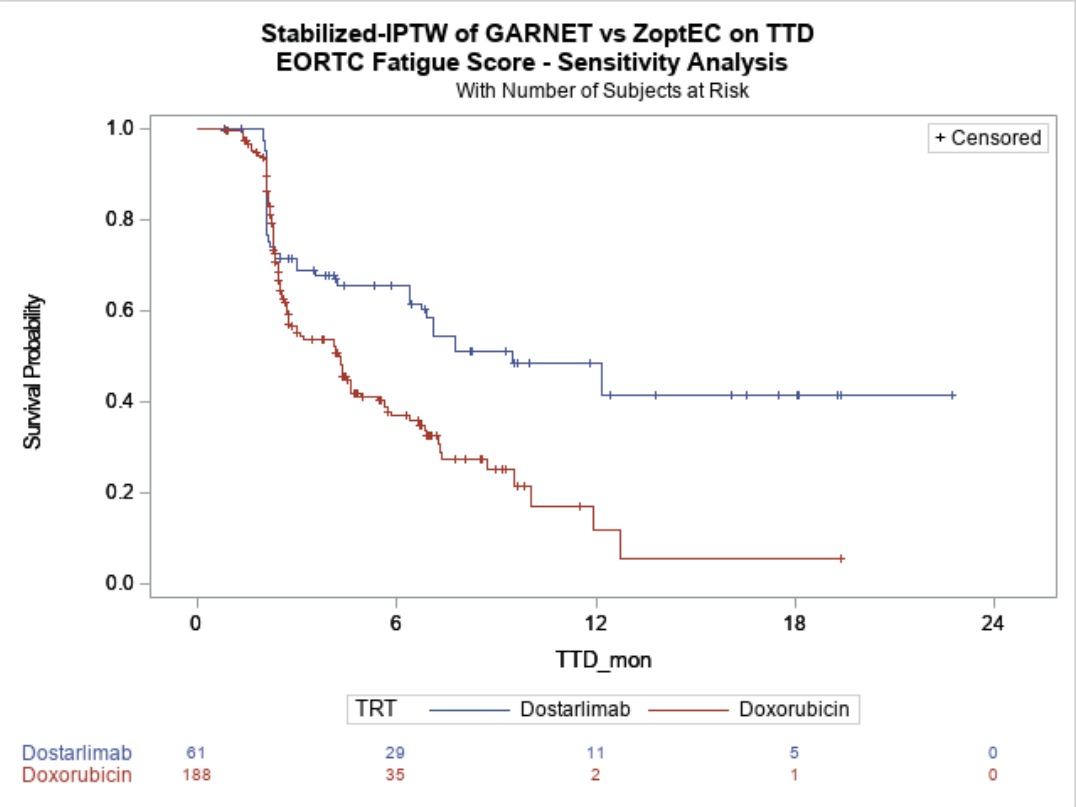
Table 11: Results of Sensitivity analysis on 15pt TTD (EORTC Fatigue Score) adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios			
	N	**Chi-square**	**p-value**

Assumption check of proportional hazard ratios			
Assumption check	250	12.45	0.0004
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.			

Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	250	0.468	0.345, 0.634	0.155	<.0001

Figure 4: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on 15pt TTD (EORTC Fatigue Score)



Note: Number of subjects are 62/188 but after applying to stabilized-IPTW, starting number of risk is 61/188.

Table 12: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on 15pt TTD (EORTC Fatigue Score)

Kaplan-Meier Analysis: Time to Deterioration		
	Dostarlimab	Doxorubicin

	(N=62/61*[1])	(N=188/188*[2])
Status of TTD		
Event	**27**	**106**
Censored	**35**	**82**
TTD (in Months)		
Median (95% CI)	**9.495 (6.407, NR)**	**4.304 (2.760, 4.928)**

Note: *[1] = Number of subjects are 62 but after applying to weight under IPTW, starting number of risks are 61.
*[2] = Number of subjects are 188 but after applying to weight under IPTW, starting number of risks are 188.
NR=Not Reached

Subgroup analysis of PFS on Main analysis

Table 1: Summary of the number of censored and uncensored values and Quartile Information - Subgroup data with stabilized-IPTW on PFS

Race group		White		Non-White	
		Dostarlimab (N=73)	**Doxorubicin (N=218)**	**Dostarlimab (N=19)**	**Doxorubicin (N=15)**
	Event	37	132	8	6
	Censored	36	86	11	9
	Median (95% CI)	12.222 (3.220, NR)	4.632 (4.074, 6.604)	NR (2.595, NR)	6.275 (1.873, 10.579)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=47)	**Doxorubicin (N=124)**	**Dostarlimab (N=45)**	**Doxorubicin (N=109)**
	Event	22	71	23	67
	Censored	25	53	22	42
	Median (95% CI)	NR (3.285, NR)	6.242 (4.435, 7.589)	5.158 (2.070, NR)	3.975 (2.366, 5.191)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=38)	**Doxorubicin (N=119)**	**Dostarlimab (N=54)**	**Doxorubicin (N=114)**
	Event	12	73	33	65
	Censored	26	46	21	49
	Median (95% CI)	NR (NR, NR)	4.665 (3.154, 6.899)	4.140 (2.628, 12.222)	6.045 (3.975, 6.899)
NR=Not Reached					

Table 2: Results of Subgroup analysis with stabilized-IPTW on PFS: Main data

Group	Class	N (=325)	Hazard ratio (Dostarlimab/ Doxorubicin)	95% CI	StdErr	p_value
Race group	**White**	291	0.372	0.270, 0.512	0.163	<.0001
	non-White	34	0.257	0.092, 0.720	0.525	0.0097
Age group	**<65**	171	0.375	0.250, 0.561	0.206	<.0001
	>=65	154	0.343	0.223, 0.527	0.220	<.0001
Baseline ECOG performance	**0**	157	0.203	0.119, 0.346	0.272	<.0001
	1	168	0.576	0.393, 0.844	0.195	0.0047

Sensitivity analysis of Progression Free Survival (PFS) with IPTW – Assessment-Scheduled Matching (ASM) by article

Table 3: Results of Sensitivity analysis on PFS adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	325	54.22	<0.0001		
Note that Cox PH model cannot be performed because proportional hazard assumption is violated (p-value is less than 0.05). Therefore, we use Accelerated Failure Time (AFT) model with Weibull distribution.					
Sensitivity analysis Accelerated Failure Time (AFT) model with Weibull distribution.					
	N	Hazard ratio (Dostarlimab/Doxorubicin)	95% CI	StdErr	p_value
AFT model (Dostarlimab/ Doxorubicin)	325	0.415	0.312, 0.552	0.145	<0.0001

Figure 1: Sensitivity Analysis on PFS with adjusting stabilized-IPTW Schoenfeld Residual Plot

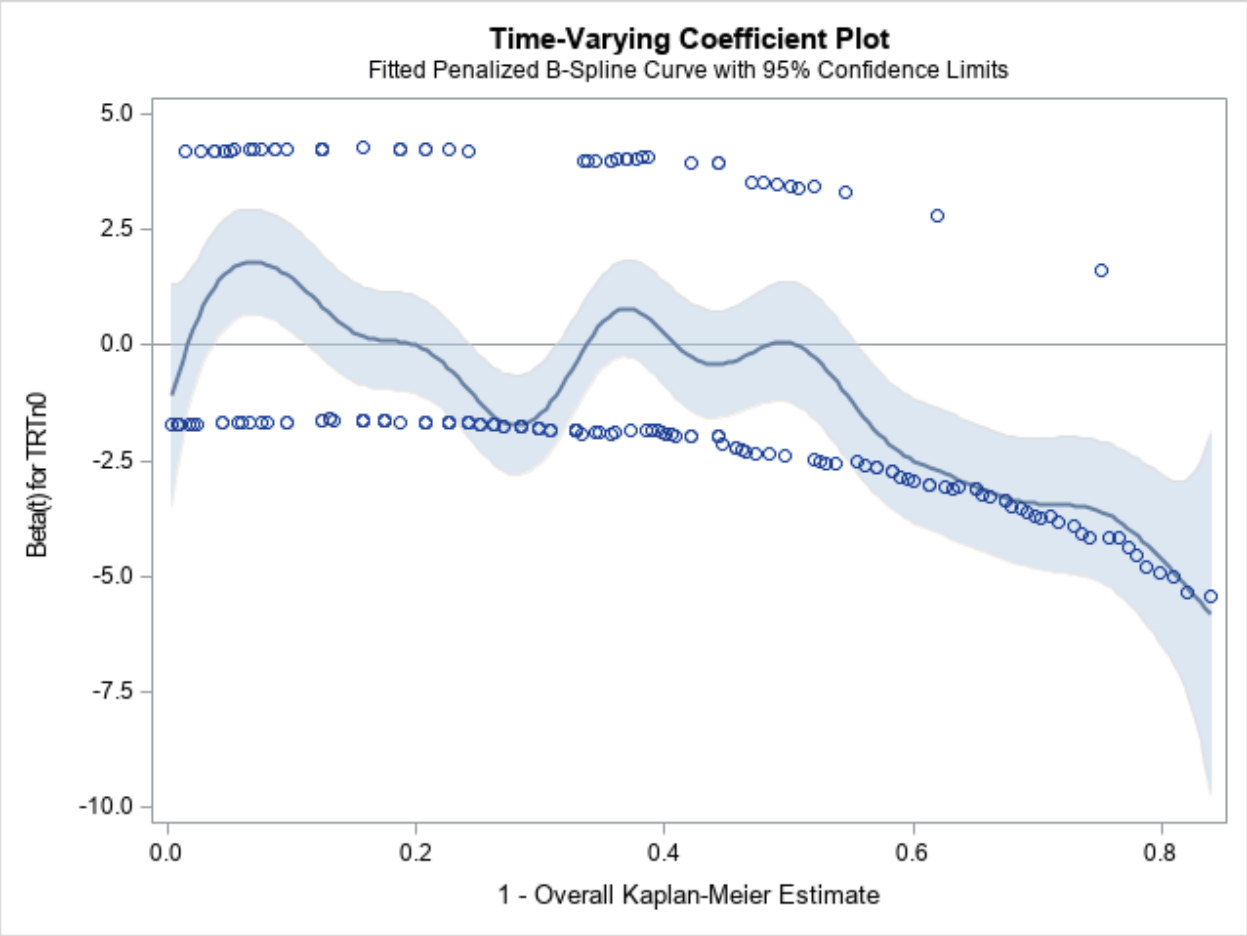
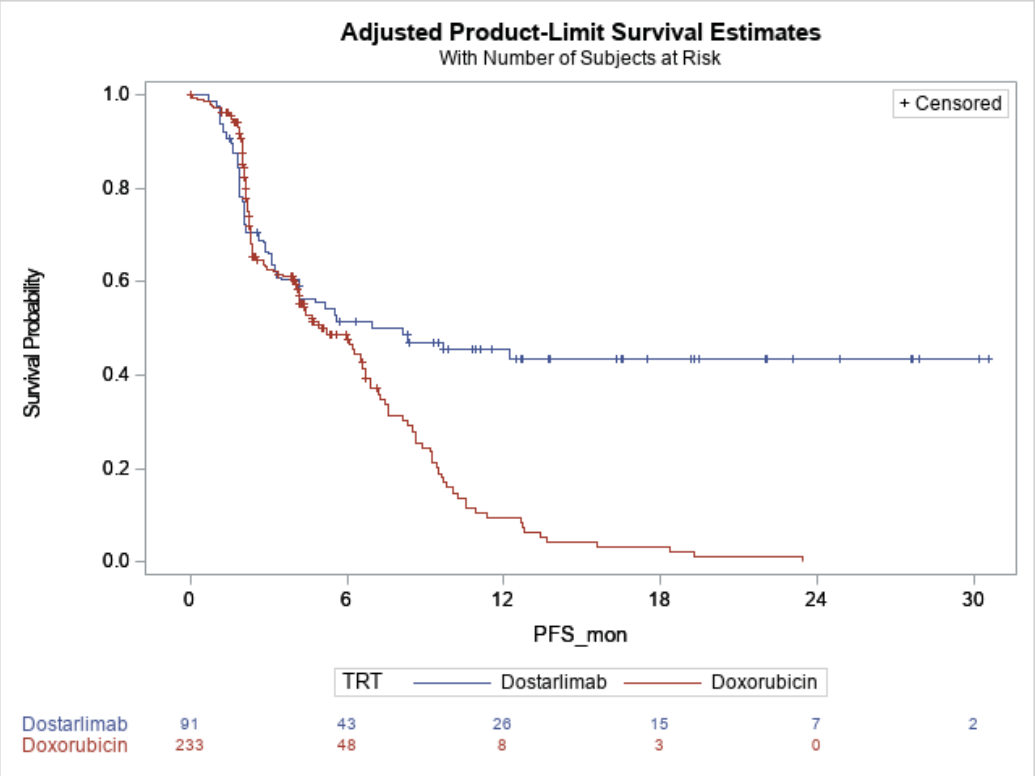


Figure 2: Kaplan-Meier curves with stabilized-IPTW of Sensitivity analysis on PFS



Note: Number of subjects are 92/233 but after applying to stabilized-IPTW, starting number of risk is 91/233.

Table 4: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity analysis with stabilized-IPTW on PFS

Kaplan-Meier Analysis: Progression Free Survival		
	Dostarlimab (N=92/91*[1])	**Doxorubicin (N=233/233*[2])**
Status of PFS		
Event	**49**	**138**
Censored	**43**	**95**
PFS (in Months)		
Median (95% CI)	**7.195 (3.285, NR)**	**4.928 (4.140, 6.604)**

Note: *[1] = Number of subjects are 92 but after applying to weight under IPTW, starting number of risks are 91.
*[2] = Number of subjects are 233 but after applying to weight under IPTW, starting number of risks are 233.
NR=Not Reached

Subgroup analysis of DOR on Main analysis

Table 1: Summary of the number of censored and uncensored values and Quartiles Information - Subgroup data with stabilized-IPTW on DOR

Race group		White		Non-White	
		Dostarlimab (N=30)	**Doxorubicin (N=30)**	**Dostarlimab (N=10)**	**Doxorubicin (N=2)**
	Event	2	18	0	1
	Censored	28	12	10	1
	Median (95% CI)	NR (NR, NR)	6.243 (4.863, 9.463)	NR (NR, NR)	8.379 (8.379, NR)
Age group		**< 65**		**>=65**	
		Dostarlimab (N=21)	**Doxorubicin (N=22)**	**Dostarlimab (N=19)**	**Doxorubicin (N=10)**
	Event	1	12	1	7
	Censored	20	10	18	3
	Median (95% CI)	NR (NR, NR)	8.970 (4.731, NR)	NR (NR, NR)	6.243 (4.666, 9.463)
Baseline ECOG performance		**0**		**1**	
		Dostarlimab (N=24)	**Doxorubicin (N=19)**	**Dostarlimab (N=16)**	**Doxorubicin (N=13)**
	Event	2	10	0	9
	Censored	22	9	16	4
	Median (95% CI)	NR (13.865, NR)	6.243 (3.450, NR)	NR (NR, NR)	8.378 (3.976, 10.974)
NR=Not Reached					

Table 2: Results of Subgroup analysis with stabilized-IPTW on DOR: Main data

Group	Class	N (=72)	Hazard ratio (Doxorubicin/ Dostarlimab)	95% CI	StdErr	p_value
Race group	**White**	60	0.040	0.008, 0.205	0.839	0.0001
	non-White	12	Model failed because there is none of event for Dostarlimab and only 2 subjects for Doxorubicin.			
Age group	**<65**	43	0.061	0.008, 0.444	1.010	0.0057
	>=65	29	0.032	0.003, 0.323	1.183	0.0035
Baseline ECOG performance	**0**	43	0.087	0.019, 0.395	0.771	0.0015
	1	29	0.000	0.000, 0.000	3267	0.9953

Main analysis of Duration of Response (DOR) with IPTW by Assessment-Scheduled Matching (ASM)

Table 3: Results of Main sensitivity analysis on DOR adjusting with stabilized-IPTW

Assumption check of proportional hazard ratios					
	N	Chi-square	p-value		
Assumption check	72	0.663	0.4155		
Main analysis Cox PH model					
	N	Hazard ratio (Doxorubicin/ Dostarlimab)	95% CI	StdErr	p_value
Cox PH model (Doxorubicin/ Dostarlimab)	72	0.131	0.050, 0.341	0.489	<.0001

Figure 1: Results of Main sensitivity analysis on DOR adjusting with stabilized-IPTW – Schoenfeld Residual Plot

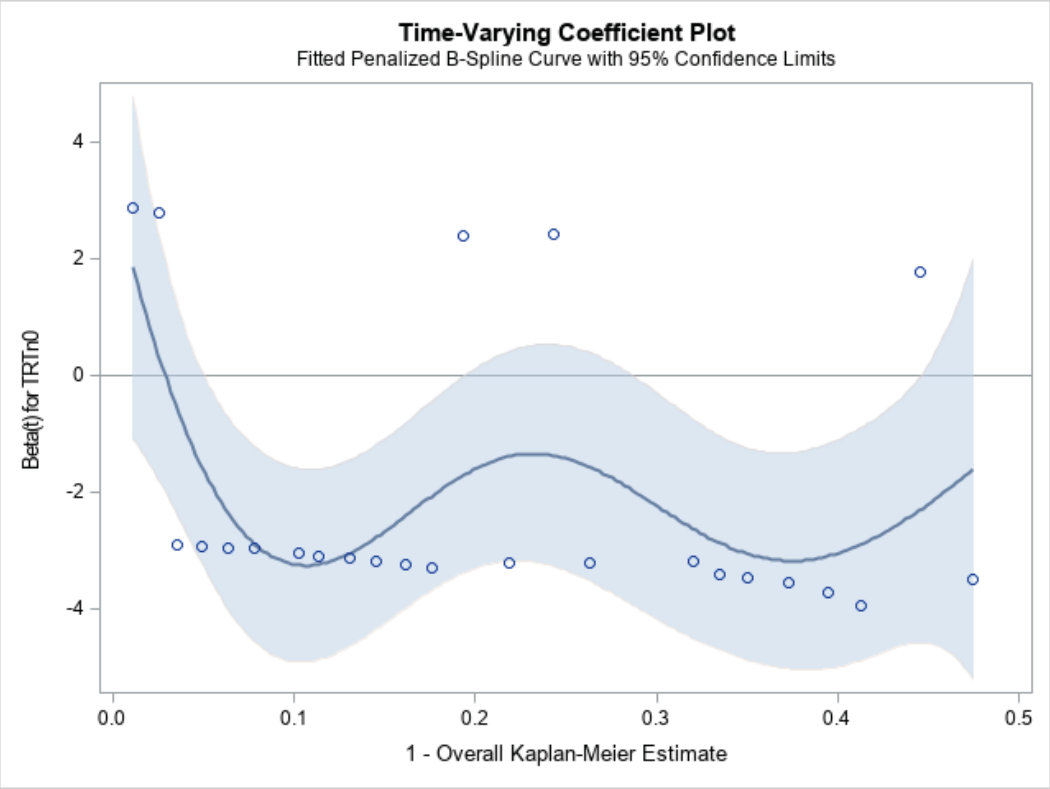
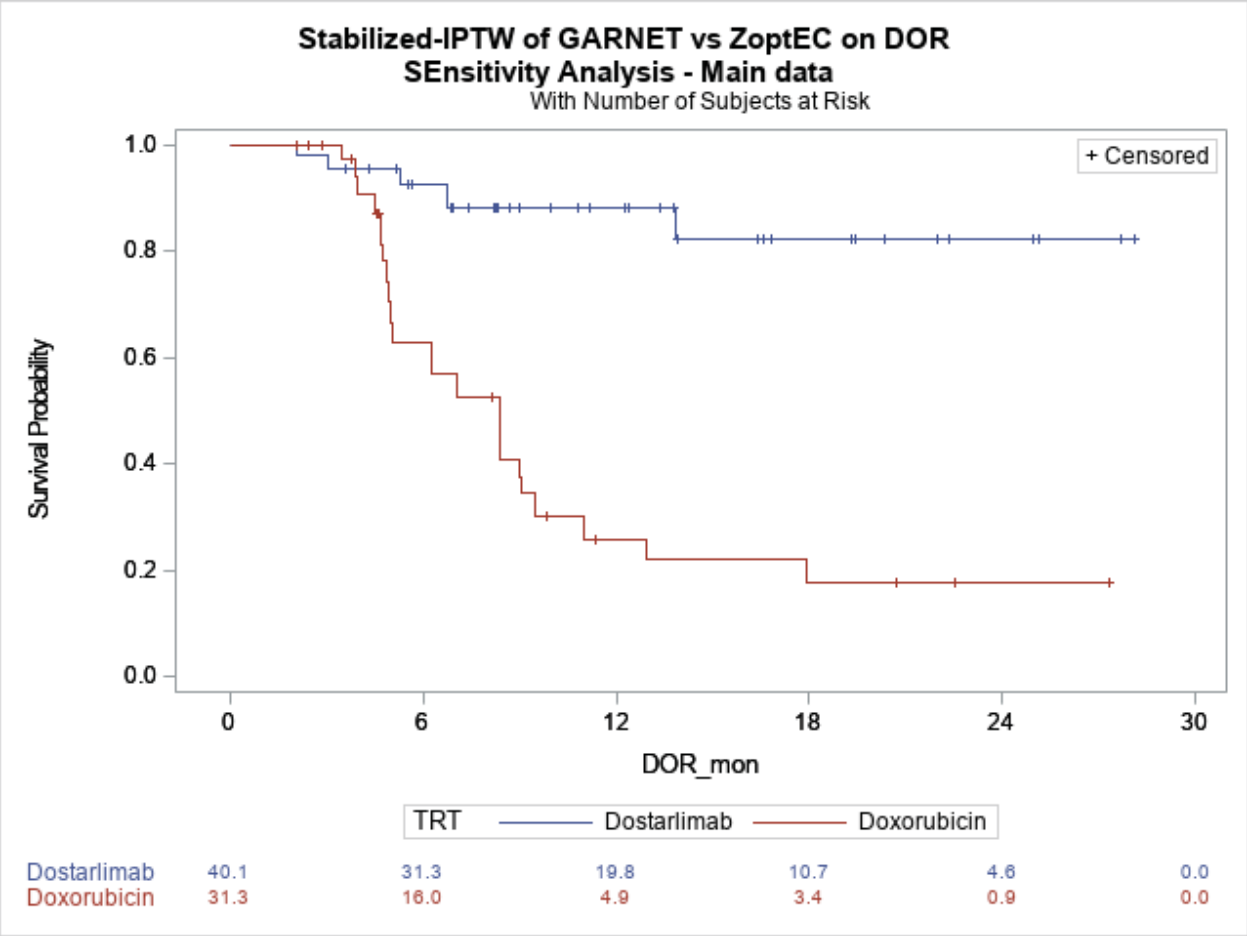


Figure 2: Kaplan-Meier curves with stabilized-IPTW of Sensitivity data on DOR



Note: Number of subjects are 40/31 but after applying to stabilized-IPTW, starting number of risk is 40/31.

Table 4: Summary of the number of censored and uncensored values and Quartiles Information - Sensitivity data with stabilized-IPTW on DOR

Kaplan-Meier Analysis: Duration of Response		
	Dostarlimab (N=40/40*[1])	**Doxorubicin (N=31/32*[2])**
Status of DOR		
Event	**5**	**19**
Censored	**35**	**13**
DOR (in Months)		
Median (95% CI)	**NR (NR, NR)**	**8.378 (4.862, 10.973)**

Note: *[1] = Number of subjects are 40 but after applying to weight under IPTW, starting number of risks are 40.
*[2] = Number of subjects are 31 but after applying to weight under IPTW, starting number of risks are 31.
NR=Not Reached

Table 14.2.3a Tumor response summary by MSI Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR

Variable	MSI-H (N=70)	MSS (N=26)	Unknown/Missing (N=7)	Total (N=103)
Best Overall Response by RECIST 1.1 [n(%)][a]				
CR	9 (12.9)	1 (3.8)	1 (14.3)	11 (10.7)
PR	21 (30.0)	10 (38.5)	4 (57.1)	35 (34.0)
SD	8 (11.4)	5 (19.2)	0	13 (12.6)
PD	28 (40.0)	9 (34.6)	2 (28.6)	39 (37.9)
Not Evaluable	2 (2.9)	1 (3.8)	0	3 (2.9)
Not Done	2 (2.9)	0	0	2 (1.9)
Confirmed Objective Response Rate (ORR)				
n(%)	30 (42.9)	11 (42.3)	5 (71.4)	46 (44.7)
95% CI[b]	(31.1, 55.3)	(23.4, 63.1)	(29.0, 96.3)	(34.9, 54.8)
Response Ongoing[c]	28 (93.3)	8 (72.7)	5 (100)	41 (89.1)
Disease Control Rate (DCR)				
n(%)	38 (54.3)	16 (61.5)	5 (71.4)	59 (57.3)
95% CI[b]	(41.9, 66.3)	(40.6, 79.8)	(29.0, 96.3)	(47.2, 67.0)

MSI status as defined by Foundation medicine. MSI-H = microsatellite instability-high, MSS = microsatellite stable.
Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders.
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_3a_recist.rtf,
Generated on: 26AUG2020 03:07 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.2.3a Tumor response summary by MSI Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: MMR-unk/MSI-H

Variable	MSI-H (N=2)	MSS (N=0)	Unknown/Missing (N=0)	Total (N=2)
Best Overall Response by RECIST 1.1 [n(%)][a]				
CR	0	0	0	0
PR	1 (50.0)	0	0	1 (50.0)
SD	0	0	0	0
PD	0	0	0	0
Not Evaluable	0	0	0	0
Not Done	1 (50.0)	0	0	1 (50.0)
Confirmed Objective Response Rate (ORR)				
n(%)	1 (50.0)	0	0	1 (50.0)
95% CI[b]	(1.3, 98.7)	-	-	(1.3, 98.7)
Response Ongoing[c]	1 (100)	0	0	1 (100)
Disease Control Rate (DCR)				
n(%)	1 (50.0)	0	0	1 (50.0)
95% CI[b]	(1.3, 98.7)	-	-	(1.3, 98.7)

MSI status as defined by Foundation medicine. MSI-H = microsatellite instability-high, MSS = microsatellite stable.
Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders.
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_3a_recist.rtf,
Generated on: 26AUG2020 03:07 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.2.3a Tumor response summary by MSI Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR or MMR-unk/MSI-H

Variable	MSI-H (N=72)	MSS (N=26)	Unknown/Missing (N=7)	Total (N=105)
Best Overall Response by RECIST 1.1 [n(%)][a]				
CR	9 (12.5)	1 (3.8)	1 (14.3)	11 (10.5)
PR	22 (30.6)	10 (38.5)	4 (57.1)	36 (34.3)
SD	8 (11.1)	5 (19.2)	0	13 (12.4)
PD	28 (38.9)	9 (34.6)	2 (28.6)	39 (37.1)
Not Evaluable	2 (2.8)	1 (3.8)	0	3 (2.9)
Not Done	3 (4.2)	0	0	3 (2.9)
Confirmed Objective Response Rate (ORR)				
n(%)	31 (43.1)	11 (42.3)	5 (71.4)	47 (44.8)
95% CI[b]	(31.4, 55.3)	(23.4, 63.1)	(29.0, 96.3)	(35.0, 54.8)
Response Ongoing[c]	29 (93.5)	8 (72.7)	5 (100)	42 (89.4)
Disease Control Rate (DCR)				
n(%)	39 (54.2)	16 (61.5)	5 (71.4)	60 (57.1)
95% CI[b]	(42.0, 66.0)	(40.6, 79.8)	(29.0, 96.3)	(47.1, 66.8)

MSI status as defined by Foundation medicine. MSI-H = microsatellite instability-high, MSS = microsatellite stable.
Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders.
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_3a_recist.rtf,
Generated on: 26AUG2020 03:07 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.2.4a Tumor response summary by number of prior therapies - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR

Variable	1 Prior Therapy (N=65)	>=2 Prior Therapies (N=38)	Total (N=103)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	6 (9.2)	5 (13.2)	11 (10.7)
PR	26 (40.0)	9 (23.7)	35 (34.0)
SD	9 (13.8)	4 (10.5)	13 (12.6)
PD	19 (29.2)	20 (52.6)	39 (37.9)
Not Evaluable	3 (4.6)	0	3 (2.9)
Not Done	2 (3.1)	0	2 (1.9)
Confirmed Objective Response Rate (ORR)			
n(%)	32 (49.2)	14 (36.8)	46 (44.7)
95% CI[b]	(36.6, 61.9)	(21.8, 54.0)	(34.9, 54.8)
Response Ongoing[c]	28 (87.5)	13 (92.9)	41 (89.1)
Disease Control Rate (DCR)			
n(%)	41 (63.1)	18 (47.4)	59 (57.3)
95% CI[b]	(50.2, 74.7)	(31.0, 64.2)	(47.2, 67.0)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_4a_recist.rtf,
Generated on: 26AUG2020 03:07 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.2.4a Tumor response summary by number of prior therapies - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: MMR-unk/MSI-H

Variable	1 Prior Therapy (N=1)	>=2 Prior Therapies (N=1)	Total (N=2)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	0	0	0
PR	1 (100)	0	1 (50.0)
SD	0	0	0
PD	0	0	0
Not Evaluable	0	0	0
Not Done	0	1 (100)	1 (50.0)
Confirmed Objective Response Rate (ORR)			
n(%)	1 (100)	0	1 (50.0)
95% CI[b]	(2.5, 100.0)	(0.0, 97.5)	(1.3, 98.7)
Response Ongoing[c]	1 (100)	0	1 (100)
Disease Control Rate (DCR)			
n(%)	1 (100)	0	1 (50.0)
95% CI[b]	(2.5, 100.0)	(0.0, 97.5)	(1.3, 98.7)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_4a_recist.rtf,
Generated on: 26AUG2020 03:07 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.2.4a Tumor response summary by number of prior therapies - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR or MMR-unk/MSI-H

Variable	1 Prior Therapy (N=66)	>=2 Prior Therapies (N=39)	Total (N=105)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	6 (9.1)	5 (12.8)	11 (10.5)
PR	27 (40.9)	9 (23.1)	36 (34.3)
SD	9 (13.6)	4 (10.3)	13 (12.4)
PD	19 (28.8)	20 (51.3)	39 (37.1)
Not Evaluable	3 (4.5)	0	3 (2.9)
Not Done	2 (3.0)	1 (2.6)	3 (2.9)
Confirmed Objective Response Rate (ORR)			
n(%)	33 (50.0)	14 (35.9)	47 (44.8)
95% CI[b]	(37.4, 62.6)	(21.2, 52.8)	(35.0, 54.8)
Response Ongoing[c]	29 (87.9)	13 (92.9)	42 (89.4)
Disease Control Rate (DCR)			
n(%)	42 (63.6)	18 (46.2)	60 (57.1)
95% CI[b]	(50.9, 75.1)	(30.1, 62.8)	(47.1, 66.8)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_4a_recist.rtf,
Generated on: 26AUG2020 03:07 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.2.5a Tumor response summary by Prior Radiation Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR

Variable	Prior Radiation (N=73)	No Prior Radiation (N=30)	Total (N=103)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	8 (11.0)	3 (10.0)	11 (10.7)
PR	26 (35.6)	9 (30.0)	35 (34.0)
SD	11 (15.1)	2 (6.7)	13 (12.6)
PD	25 (34.2)	14 (46.7)	39 (37.9)
Not Evaluable	3 (4.1)	0	3 (2.9)
Not Done	0	2 (6.7)	2 (1.9)
Confirmed Objective Response Rate (ORR)			
n(%)	34 (46.6)	12 (40.0)	46 (44.7)
95% CI[b]	(34.8, 58.6)	(22.7, 59.4)	(34.9, 54.8)
Response Ongoing[c]	30 (88.2)	11 (91.7)	41 (89.1)
Disease Control Rate (DCR)			
n(%)	45 (61.6)	14 (46.7)	59 (57.3)
95% CI[b]	(49.5, 72.8)	(28.3, 65.7)	(47.2, 67.0)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_5a_recist.rtf,
Generated on: 26AUG2020 03:07 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.2.5a Tumor response summary by Prior Radiation Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: MMR-unk/MSI-H

Variable	Prior Radiation (N=1)	No Prior Radiation (N=1)	Total (N=2)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	0	0	0
PR	1 (100)	0	1 (50.0)
SD	0	0	0
PD	0	0	0
Not Evaluable	0	0	0
Not Done	0	1 (100)	1 (50.0)
Confirmed Objective Response Rate (ORR)			
n(%)	1 (100)	0	1 (50.0)
95% CI[b]	(2.5, 100.0)	(0.0, 97.5)	(1.3, 98.7)
Response Ongoing[c]	1 (100)	0	1 (100)
Disease Control Rate (DCR)			
n(%)	1 (100)	0	1 (50.0)
95% CI[b]	(2.5, 100.0)	(0.0, 97.5)	(1.3, 98.7)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_5a_recist.rtf,
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Table 14.2.5a Tumor response summary by Prior Radiation Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR or MMR-unk/MSI-H

Variable	Prior Radiation (N=74)	No Prior Radiation (N=31)	Total (N=105)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	8 (10.8)	3 (9.7)	11 (10.5)
PR	27 (36.5)	9 (29.0)	36 (34.3)
SD	11 (14.9)	2 (6.5)	13 (12.4)
PD	25 (33.8)	14 (45.2)	39 (37.1)
Not Evaluable	3 (4.1)	0	3 (2.9)
Not Done	0	3 (9.7)	3 (2.9)
Confirmed Objective Response Rate (ORR)			
n(%)	35 (47.3)	12 (38.7)	47 (44.8)
95% CI[b]	(35.6, 59.3)	(21.8, 57.8)	(35.0, 54.8)
Response Ongoing[c]	31 (88.6)	11 (91.7)	42 (89.4)
Disease Control Rate (DCR)			
n(%)	46 (62.2)	14 (45.2)	60 (57.1)
95% CI[b]	(50.1, 73.2)	(27.3, 64.0)	(47.1, 66.8)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_5a_recist.rtf,
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Table 14.2.6a Tumor response summary by Best overall response from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR

Variable	CR/PR (N=43)	SD (N=20)	PD (N=14)	Missing (N=26)	Total (N=103)
Best Overall Response by RECIST 1.1 [n(%)][a]					
CR	3 (7.0)	4 (20.0)	1 (7.1)	3 (11.5)	11 (10.7)
PR	17 (39.5)	9 (45.0)	2 (14.3)	7 (26.9)	35 (34.0)
SD	6 (14.0)	2 (10.0)	0	5 (19.2)	13 (12.6)
PD	15 (34.9)	4 (20.0)	9 (64.3)	11 (42.3)	39 (37.9)
Not Evaluable	2 (4.7)	0	1 (7.1)	0	3 (2.9)
Not Done	0	1 (5.0)	1 (7.1)	0	2 (1.9)
Confirmed Objective Response Rate (ORR)					
n(%)	20 (46.5)	13 (65.0)	3 (21.4)	10 (38.5)	46 (44.7)
95% CI[b]	(31.2, 62.3)	(40.8, 84.6)	(4.7, 50.8)	(20.2, 59.4)	(34.9, 54.8)
Response Ongoing[c]	17 (85.0)	12 (92.3)	2 (66.7)	10 (100)	41 (89.1)
Disease Control Rate (DCR)					
n(%)	26 (60.5)	15 (75.0)	3 (21.4)	15 (57.7)	59 (57.3)
95% CI[b]	(44.4, 75.0)	(50.9, 91.3)	(4.7, 50.8)	(36.9, 76.6)	(47.2, 67.0)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_6a_recist.rtf,
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Table 14.2.6a Tumor response summary by Best overall response from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: MMR-unk/MSI-H

Variable	CR/PR (N=1)	SD (N=0)	PD (N=1)	Missing (N=0)	Total (N=2)
Best Overall Response by RECIST 1.1 [n(%)][a]					
CR	0	0	0	0	0
PR	1 (100)	0	0	0	1 (50.0)
SD	0	0	0	0	0
PD	0	0	0	0	0
Not Evaluable	0	0	0	0	0
Not Done	0	0	1 (100)	0	1 (50.0)
Confirmed Objective Response Rate (ORR)					
n(%)	1 (100)	0	0	0	1 (50.0)
95% CI[b]	(2.5, 100.0)	-	(0.0, 97.5)	-	(1.3, 98.7)
Response Ongoing[c]	1 (100)	0	0	0	1 (100)
Disease Control Rate (DCR)					
n(%)	1 (100)	0	0	0	1 (50.0)
95% CI[b]	(2.5, 100.0)	-	(0.0, 97.5)	-	(1.3, 98.7)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_6a_recist.rtf,
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Table 14.2.6a Tumor response summary by Best overall response from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR or MMR-unk/MSI-H

Variable	CR/PR (N=44)	SD (N=20)	PD (N=15)	Missing (N=26)	Total (N=105)
Best Overall Response by RECIST 1.1 [n(%)][a]					
CR	3 (6.8)	4 (20.0)	1 (6.7)	3 (11.5)	11 (10.5)
PR	18 (40.9)	9 (45.0)	2 (13.3)	7 (26.9)	36 (34.3)
SD	6 (13.6)	2 (10.0)	0	5 (19.2)	13 (12.4)
PD	15 (34.1)	4 (20.0)	9 (60.0)	11 (42.3)	39 (37.1)
Not Evaluable	2 (4.5)	0	1 (6.7)	0	3 (2.9)
Not Done	0	1 (5.0)	2 (13.3)	0	3 (2.9)
Confirmed Objective Response Rate (ORR)					
n(%)	21 (47.7)	13 (65.0)	3 (20.0)	10 (38.5)	47 (44.8)
95% CI[b]	(32.5, 63.3)	(40.8, 84.6)	(4.3, 48.1)	(20.2, 59.4)	(35.0, 54.8)
Response Ongoing[c]	18 (85.7)	12 (92.3)	2 (66.7)	10 (100)	42 (89.4)
Disease Control Rate (DCR)					
n(%)	27 (61.4)	15 (75.0)	3 (20.0)	15 (57.7)	60 (57.1)
95% CI[b]	(45.5, 75.6)	(50.9, 91.3)	(4.3, 48.1)	(36.9, 76.6)	(47.1, 66.8)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_6a_recist.rtf,
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Table 14.2.7a Tumor response summary by Progression free interval from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: MMR-unk/MSI-H

Variable	<6 months (N=1)	>=6 months (N=1)	Missing (N=0)	Total (N=2)
Best Overall Response by RECIST 1.1 [n(%)][a]				
CR	0	0	0	0
PR	0	1 (100)	0	1 (50.0)
SD	0	0	0	0
PD	0	0	0	0
Not Evaluable	0	0	0	0
Not Done	1 (100)	0	0	1 (50.0)
Confirmed Objective Response Rate (ORR)				
n(%)	0	1 (100)	0	1 (50.0)
95% CI[b]	(0.0, 97.5)	(2.5, 100.0)	-	(1.3, 98.7)
Response Ongoing[c]	0	1 (100)	0	1 (100)
Disease Control Rate (DCR)				
n(%)	0	1 (100)	0	1 (50.0)
95% CI[b]	(0.0, 97.5)	(2.5, 100.0)	-	(1.3, 98.7)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_7a_recist.rtf,
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Table 14.2.7a Tumor response summary by Progression free interval from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR or MMR-unk/MSI-H

Variable	<6 months (N=39)	>=6 months (N=64)	Missing (N=2)	Total (N=105)
Best Overall Response by RECIST 1.1 [n(%)][a]				
CR	5 (12.8)	6 (9.4)	0	11 (10.5)
PR	10 (25.6)	24 (37.5)	2 (100)	36 (34.3)
SD	3 (7.7)	10 (15.6)	0	13 (12.4)
PD	18 (46.2)	21 (32.8)	0	39 (37.1)
Not Evaluable	1 (2.6)	2 (3.1)	0	3 (2.9)
Not Done	2 (5.1)	1 (1.6)	0	3 (2.9)
Confirmed Objective Response Rate (ORR)				
n(%)	15 (38.5)	30 (46.9)	2 (100)	47 (44.8)
95% CI[b]	(23.4, 55.4)	(34.3, 59.8)	(15.8, 100.0)	(35.0, 54.8)
Response Ongoing[c]	13 (86.7)	27 (90.0)	2 (100)	42 (89.4)
Disease Control Rate (DCR)				
n(%)	18 (46.2)	40 (62.5)	2 (100)	60 (57.1)
95% CI[b]	(30.1, 62.8)	(49.5, 74.3)	(15.8, 100.0)	(47.1, 66.8)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_7a_recist.rtf,
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Table 14.2.8a Tumor response summary by Prior Bevacizumab Use - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR

Variable	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=98)	Total (N=103)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	0	11 (11.2)	11 (10.7)
PR	1 (20.0)	34 (34.7)	35 (34.0)
SD	2 (40.0)	11 (11.2)	13 (12.6)
PD	2 (40.0)	37 (37.8)	39 (37.9)
Not Evaluable	0	3 (3.1)	3 (2.9)
Not Done	0	2 (2.0)	2 (1.9)
Confirmed Objective Response Rate (ORR)			
n(%)	1 (20.0)	45 (45.9)	46 (44.7)
95% CI[b]	(0.5, 71.6)	(35.8, 56.3)	(34.9, 54.8)
Response Ongoing[c]	1 (100)	40 (88.9)	41 (89.1)
Disease Control Rate (DCR)			
n(%)	3 (60.0)	56 (57.1)	59 (57.3)
95% CI[b]	(14.7, 94.7)	(46.7, 67.1)	(47.2, 67.0)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_8a_recist.rtf,
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Table 14.2.8a Tumor response summary by Prior Bevacizumab Use - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: MMR-unk/MSI-H

Variable	Prior Bevacizumab Use (N=0)	No Prior Bevacizumab Use (N=2)	Total (N=2)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	0	0	0
PR	0	1 (50.0)	1 (50.0)
SD	0	0	0
PD	0	0	0
Not Evaluable	0	0	0
Not Done	0	1 (50.0)	1 (50.0)
Confirmed Objective Response Rate (ORR)			
n(%)	0	1 (50.0)	1 (50.0)
95% CI[b]	-	(1.3, 98.7)	(1.3, 98.7)
Response Ongoing[c]	0	1 (100)	1 (100)
Disease Control Rate (DCR)			
n(%)	0	1 (50.0)	1 (50.0)
95% CI[b]	-	(1.3, 98.7)	(1.3, 98.7)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_8a_recist.rtf,
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Table 14.2.8a Tumor response summary by Prior Bevacizumab Use - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set)

EC: dMMR or MMR-unk/MSI-H

Variable	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=100)	Total (N=105)
Best Overall Response by RECIST 1.1 [n(%)][a]			
CR	0	11 (11.0)	11 (10.5)
PR	1 (20.0)	35 (35.0)	36 (34.3)
SD	2 (40.0)	11 (11.0)	13 (12.4)
PD	2 (40.0)	37 (37.0)	39 (37.1)
Not Evaluable	0	3 (3.0)	3 (2.9)
Not Done	0	3 (3.0)	3 (2.9)
Confirmed Objective Response Rate (ORR)			
n(%)	1 (20.0)	46 (46.0)	47 (44.8)
95% CI[b]	(0.5, 71.6)	(36.0, 56.3)	(35.0, 54.8)
Response Ongoing[c]	1 (100)	41 (89.1)	42 (89.4)
Disease Control Rate (DCR)			
n(%)	3 (60.0)	57 (57.0)	60 (57.1)
95% CI[b]	(14.7, 94.7)	(46.7, 66.9)	(47.1, 66.8)

Note: ORR is defined as the percentage of patients with a RECIST v1.1 confirmed CR or PR. DCR is defined as the percentage of patients with a RECIST v1.1 confirmed PR, confirmed CR, SD. Response assessments are based on blinded independent central review (BICR).
a CR=Complete Response, PR=Partial Response, SD=Stable Disease, PD=Progressive Disease.
b Exact 2 sided 95% Confidence interval for the binomial proportion.
c All responders who have not yet died or progressed (including clinical progression), denominator for percentage is number of responders
Source: Listing 16.1.15a, Dataset: ADRS, Program: t_recist.sas, Output: t_14_2_8a_recist.rtf,
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Table 14.2.14a Kaplan Meier Analysis of Duration of Response by MSI-H status - RECIST v1.1 based on BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR

Variable	MSI-H (N=30)	MSS (N=11)	Unknown/Missing (N=5)	Total (N=46)
DOR				
Status [n (%)]				
Events observed	2 (6.7)	3 (27.3)	0 (0.0)	5 (10.9)
Censored	28 (93.3)	8 (72.7)	5 (100.0)	41 (89.1)
DOR (months)				
Min, Max	2.63, 28.09+	2.79+, 22.34+	4.34+, 27.66+	2.63, 28.09+
Quartile (95% CI)[a]				
25%	NR (9.7, NR)	13.9 (9.8, NR)	NR (NR, NR)	NR (9.8, NR)
50%	NR (NR, NR)	15.2 (9.8, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (13.9, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	26 (86.7)	8 (72.7)	2 (40.0)	36 (78.3)
DOR Distribution Function (95% CI)				
Month 6	96.7 (78.6, 99.5)	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)	97.8 (85.6, 99.7)
Month 12	91.6 (69.4, 97.9)	83.3 (27.3, 97.5)	100.0 (100.0, 100.0)	90.6 (72.9, 97.0)
Month 18	91.6 (69.4, 97.9)	41.7 (5.6, 76.7)	100.0 (100.0, 100.0)	79.2 (54.9, 91.3)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_14a_dor_recist_or.rtf,
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Table 14.2.14a Kaplan Meier Analysis of Duration of Response by MSI-H status - RECIST v1.1 based on BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: MMR-unk/MSI-H

Variable	MSI-H (N=1)	MSS (N=0)	Unknown/Missing (N=0)	Total (N=1)
DOR				
Status [n (%)]				
Events observed	0 (0.0)			0 (0.0)
Censored	1 (100.0)			1 (100.0)
DOR (months)				
Min, Max	19.32+, 19.32+			19.32+, 19.32+
Quartile (95% CI)[a]				
25%	NR (NR, NR)			NR (NR, NR)
50%	NR (NR, NR)			NR (NR, NR)
75%	NR (NR, NR)			NR (NR, NR)
Duration ≥6 months [n (%)]	1 (100.0)			1 (100.0)
DOR Distribution Function (95% CI)				
Month 6	100.0 (100.0, 100.0)			100.0 (100.0, 100.0)
Month 12	100.0 (100.0, 100.0)			100.0 (100.0, 100.0)
Month 18	100.0 (100.0, 100.0)			100.0 (100.0, 100.0)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_14a_dor_recist_or.rtf,
Generated on: 26AUG2020 03:08 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.2.14a Kaplan Meier Analysis of Duration of Response by MSI-H status - RECIST v1.1 based on BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR or MMR-unk/MSI-H

Variable	MSI-H (N=31)	MSS (N=11)	Unknown/Missing (N=5)	Total (N=47)
DOR				
Status [n (%)]				
Events observed	2 (6.5)	3 (27.3)	0 (0.0)	5 (10.6)
Censored	29 (93.5)	8 (72.7)	5 (100.0)	42 (89.4)
DOR (months)				
Min, Max	2.63, 28.09+	2.79+, 22.34+	4.34+, 27.66+	2.63, 28.09+
Quartile (95% CI)[a]				
25%	NR (9.7, NR)	13.9 (9.8, NR)	NR (NR, NR)	NR (9.8, NR)
50%	NR (NR, NR)	15.2 (9.8, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (13.9, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	27 (87.1)	8 (72.7)	2 (40.0)	37 (78.7)
DOR Distribution Function (95% CI)				
Month 6	96.8 (79.2, 99.5)	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)	97.9 (85.8, 99.7)
Month 12	91.9 (70.6, 98.0)	83.3 (27.3, 97.5)	100.0 (100.0, 100.0)	90.9 (73.7, 97.1)
Month 18	91.9 (70.6, 98.0)	41.7 (5.6, 76.7)	100.0 (100.0, 100.0)	80.1 (56.8, 91.7)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_14a_dor_recist_or.rtf,
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Table 14.2.15a Kaplan Meier Analysis of Duration of Response by number of prior therapies - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR

Variable	1 Prior Therapy (N=32)	>=2 Prior Therapies (N=14)	Total (N=46)
DOR			
Status [n (%)]			
Events observed	4 (12.5)	1 (7.1)	5 (10.9)
Censored	28 (87.5)	13 (92.9)	41 (89.1)
DOR (months)			
Min, Max	2.63, 27.66+	2.79+, 28.09+	2.63, 28.09+
Quartile (95% CI)[a]			
25%	15.2 (9.8, NR)	NR (9.7, NR)	NR (9.8, NR)
50%	NR (15.2, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	24 (75.0)	12 (85.7)	36 (78.3)
DOR Distribution Function (95% CI)			
Month 6	96.9 (79.8, 99.6)	100.0 (100.0, 100.0)	97.8 (85.6, 99.7)
Month 12	90.4 (64.3, 97.7)	91.7 (53.9, 98.8)	90.6 (72.9, 97.0)
Month 18	73.1 (40.5, 89.7)	91.7 (53.9, 98.8)	79.2 (54.9, 91.3)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_15a_dor_recist_or.rtf,
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Table 14.2.15a Kaplan Meier Analysis of Duration of Response by number of prior therapies - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: MMR-unk/MSI-H

Variable	1 Prior Therapy (N=1)	>=2 Prior Therapies (N=0)	Total (N=1)
DOR			
Status [n (%)]			
Events observed	0 (0.0)		0 (0.0)
Censored	1 (100.0)		1 (100.0)
DOR (months)			
Min, Max	19.32+, 19.32+		19.32+, 19.32+
Quartile (95% CI)[a]			
25%	NR (NR, NR)		NR (NR, NR)
50%	NR (NR, NR)		NR (NR, NR)
75%	NR (NR, NR)		NR (NR, NR)
Duration ≥6 months [n (%)]	1 (100.0)		1 (100.0)
DOR Distribution Function (95% CI)			
Month 6	100.0 (100.0, 100.0)		100.0 (100.0, 100.0)
Month 12	100.0 (100.0, 100.0)		100.0 (100.0, 100.0)
Month 18	100.0 (100.0, 100.0)		100.0 (100.0, 100.0)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_15a_dor_recist_or.rtf,
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Table 14.2.15a Kaplan Meier Analysis of Duration of Response by number of prior therapies - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR or MMR-unk/MSI-H

Variable	1 Prior Therapy (N=33)	>=2 Prior Therapies (N=14)	Total (N=47)
DOR			
Status [n (%)]			
Events observed	4 (12.1)	1 (7.1)	5 (10.6)
Censored	29 (87.9)	13 (92.9)	42 (89.4)
DOR (months)			
Min, Max	2.63, 27.66+	2.79+, 28.09+	2.63, 28.09+
Quartile (95% CI)[a]			
25%	NR (9.8, NR)	NR (9.7, NR)	NR (9.8, NR)
50%	NR (15.2, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	25 (75.8)	12 (85.7)	37 (78.7)
DOR Distribution Function (95% CI)			
Month 6	97.0 (80.4, 99.6)	100.0 (100.0, 100.0)	97.9 (85.8, 99.7)
Month 12	90.9 (66.1, 97.8)	91.7 (53.9, 98.8)	90.9 (73.7, 97.1)
Month 18	75.0 (43.9, 90.4)	91.7 (53.9, 98.8)	80.1 (56.8, 91.7)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_15a_dor_recist_or.rtf,
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Table 14.2.16a Kaplan Meier Analysis of Duration of Response by Prior Radiation Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR

Variable	Prior Radiation (N=34)	No Prior Radiation (N=12)	Total (N=46)
DOR			
Status [n (%)]			
Events observed	4 (11.8)	1 (8.3)	5 (10.9)
Censored	30 (88.2)	11 (91.7)	41 (89.1)
DOR (months)			
Min, Max	2.63, 28.09+	2.79+, 27.66+	2.63, 28.09+
Quartile (95% CI)[a]			
25%	NR (9.8, NR)	NR (9.7, NR)	NR (9.8, NR)
50%	NR (15.2, NR)	NR (9.7, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	28 (82.4)	8 (66.7)	36 (78.3)
DOR Distribution Function (95% CI)			
Month 6	97.1 (80.9, 99.6)	100.0 (100.0, 100.0)	97.8 (85.6, 99.7)
Month 12	92.4 (72.1, 98.1)	83.3 (27.3, 97.5)	90.6 (72.9, 97.0)
Month 18	76.8 (46.3, 91.3)	83.3 (27.3, 97.5)	79.2 (54.9, 91.3)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_16a_dor_recist_or.rtf,
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Table 14.2.16a Kaplan Meier Analysis of Duration of Response by Prior Radiation Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: MMR-unk/MSI-H

Variable	Prior Radiation (N=1)	No Prior Radiation (N=0)	Total (N=1)
DOR			
Status [n (%)]			
Events observed	0 (0.0)		0 (0.0)
Censored	1 (100.0)		1 (100.0)
DOR (months)			
Min, Max	19.32+, 19.32+		19.32+, 19.32+
Quartile (95% CI)[a]			
25%	NR (NR, NR)		NR (NR, NR)
50%	NR (NR, NR)		NR (NR, NR)
75%	NR (NR, NR)		NR (NR, NR)
Duration ≥6 months [n (%)]	1 (100.0)		1 (100.0)
DOR Distribution Function (95% CI)			
Month 6	100.0 (100.0, 100.0)		100.0 (100.0, 100.0)
Month 12	100.0 (100.0, 100.0)		100.0 (100.0, 100.0)
Month 18	100.0 (100.0, 100.0)		100.0 (100.0, 100.0)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_16a_dor_recist_or.rtf,
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Table 14.2.16a Kaplan Meier Analysis of Duration of Response by Prior Radiation Status - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR or MMR-unk/MSI-H

Variable	Prior Radiation (N=35)	No Prior Radiation (N=12)	Total (N=47)
DOR			
Status [n (%)]			
Events observed	4 (11.4)	1 (8.3)	5 (10.6)
Censored	31 (88.6)	11 (91.7)	42 (89.4)
DOR (months)			
Min, Max	2.63, 28.09+	2.79+, 27.66+	2.63, 28.09+
Quartile (95% CI)[a]			
25%	NR (9.8, NR)	NR (9.7, NR)	NR (9.8, NR)
50%	NR (15.2, NR)	NR (9.7, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	29 (82.9)	8 (66.7)	37 (78.7)
DOR Distribution Function (95% CI)			
Month 6	97.1 (81.4, 99.6)	100.0 (100.0, 100.0)	97.9 (85.8, 99.7)
Month 12	92.7 (73.1, 98.2)	83.3 (27.3, 97.5)	90.9 (73.7, 97.1)
Month 18	78.3 (49.3, 91.9)	83.3 (27.3, 97.5)	80.1 (56.8, 91.7)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_16a_dor_recist_or.rtf,
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Table 14.2.17a Kaplan Meier Analysis of Duration of Response by best overall response from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR

Variable	CR/PR (N=20)	SD (N=13)	PD (N=3)	Missing (N=10)	Total (N=46)
DOR					
Status [n (%)]					
Events observed	3 (15.0)	1 (7.7)	1 (33.3)	0 (0.0)	5 (10.9)
Censored	17 (85.0)	12 (92.3)	2 (66.7)	10 (100.0)	41 (89.1)
DOR (months)					
Min, Max	3.09+, 28.09+	2.63, 27.66+	8.28+, 14.06+	2.79+, 24.97+	2.63, 28.09+
Quartile (95% CI)[a]					
25%	15.2 (9.7, NR)	NR (2.6, NR)	9.8 (9.8, NR)	NR (NR, NR)	NR (9.8, NR)
50%	NR (13.9, NR)	NR (NR, NR)	NR (9.8, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (9.8, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	16 (80.0)	9 (69.2)	3 (100.0)	8 (80.0)	36 (78.3)
DOR Distribution Function (95% CI)					
Month 6	100.0 (100.0, 100.0)	92.3 (56.6, 98.9)	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)	97.8 (85.6, 99.7)
Month 12	92.3 (56.6, 98.9)	92.3 (56.6, 98.9)	50.0 (0.6, 91.0)	100.0 (100.0, 100.0)	90.6 (72.9, 97.0)
Month 18	69.2 (30.6, 89.2)	92.3 (56.6, 98.9)	NR (NR, NR)	100.0 (100.0, 100.0)	79.2 (54.9, 91.3)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_17a_dor_recist_or.rtf,
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Table 14.2.17a Kaplan Meier Analysis of Duration of Response by best overall response from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: MMR-unk/MSI-H

Variable	CR/PR (N=1)	SD (N=0)	PD (N=0)	Missing (N=0)	Total (N=1)
DOR					
Status [n (%)]					
Events observed	0 (0.0)				0 (0.0)
Censored	1 (100.0)				1 (100.0)
DOR (months)					
Min, Max	19.32+, 19.32+				19.32+, 19.32+
Quartile (95% CI)[a]					
25%	NR (NR, NR)				NR (NR, NR)
50%	NR (NR, NR)				NR (NR, NR)
75%	NR (NR, NR)				NR (NR, NR)
Duration ≥6 months [n (%)]	1 (100.0)				1 (100.0)
DOR Distribution Function (95% CI)					
Month 6	100.0 (100.0, 100.0)				100.0 (100.0, 100.0)
Month 12	100.0 (100.0, 100.0)				100.0 (100.0, 100.0)
Month 18	100.0 (100.0, 100.0)				100.0 (100.0, 100.0)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_17a_dor_recist_or.rtf,
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Table 14.2.17a Kaplan Meier Analysis of Duration of Response by best overall response from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR or MMR-unk/MSI-H

Variable	CR/PR (N=21)	SD (N=13)	PD (N=3)	Missing (N=10)	Total (N=47)
DOR					
Status [n (%)]					
Events observed	3 (14.3)	1 (7.7)	1 (33.3)	0 (0.0)	5 (10.6)
Censored	18 (85.7)	12 (92.3)	2 (66.7)	10 (100.0)	42 (89.4)
DOR (months)					
Min, Max	3.09+, 28.09+	2.63, 27.66+	8.28+, 14.06+	2.79+, 24.97+	2.63, 28.09+
Quartile (95% CI)[a]					
25%	15.2 (9.7, NR)	NR (2.6, NR)	9.8 (9.8, NR)	NR (NR, NR)	NR (9.8, NR)
50%	NR (13.9, NR)	NR (NR, NR)	NR (9.8, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (9.8, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	17 (81.0)	9 (69.2)	3 (100.0)	8 (80.0)	37 (78.7)
DOR Distribution Function (95% CI)					
Month 6	100.0 (100.0, 100.0)	92.3 (56.6, 98.9)	100.0 (100.0, 100.0)	100.0 (100.0, 100.0)	97.9 (85.8, 99.7)
Month 12	92.9 (59.1, 99.0)	92.3 (56.6, 98.9)	50.0 (0.6, 91.0)	100.0 (100.0, 100.0)	90.9 (73.7, 97.1)
Month 18	72.2 (35.3, 90.3)	92.3 (56.6, 98.9)	NR (NR, NR)	100.0 (100.0, 100.0)	80.1 (56.8, 91.7)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_17a_dor_recist_or.rtf,
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Table 14.2.18a Kaplan Meier Analysis of Duration of Response by progression free interval from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR

Variable	< 6 months (N=15)	>= 6 months (N=29)	Missing (N=2)	Total (N=46)
DOR				
Status [n (%)]				
Events observed	2 (13.3)	3 (10.3)	0 (0.0)	5 (10.9)
Censored	13 (86.7)	26 (89.7)	2 (100.0)	41 (89.1)
DOR (months)				
Min, Max	2.79+, 28.09+	2.63, 27.66+	7.06+, 7.39+	2.63, 28.09+
Quartile (95% CI)[a]				
25%	NR (9.8, NR)	NR (9.7, NR)	NR (NR, NR)	NR (9.8, NR)
50%	NR (9.8, NR)	NR (13.9, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	12 (80.0)	22 (75.9)	2 (100.0)	36 (78.3)
DOR Distribution Function (95% CI)				
Month 6	100.0 (100.0, 100.0)	96.6 (77.9, 99.5)	100.0 (100.0, 100.0)	97.8 (85.6, 99.7)
Month 12	90.0 (47.3, 98.5)	90.9 (66.9, 97.7)	NR (NR, NR)	90.6 (72.9, 97.0)
Month 18	77.1 (34.5, 93.9)	80.8 (47.2, 94.1)	NR (NR, NR)	79.2 (54.9, 91.3)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_18a_dor_recist_or.rtf,
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Table 14.2.18a Kaplan Meier Analysis of Duration of Response by progression free interval from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: MMR-unk/MSI-H

Variable	< 6 months (N=0)	>= 6 months (N=1)	Missing (N=0)	Total (N=1)
DOR				
Status [n (%)]				
Events observed		0 (0.0)		0 (0.0)
Censored		1 (100.0)		1 (100.0)
DOR (months)				
Min, Max		19.32+, 19.32+		19.32+, 19.32+
Quartile (95% CI)[a]				
25%		NR (NR, NR)		NR (NR, NR)
50%		NR (NR, NR)		NR (NR, NR)
75%		NR (NR, NR)		NR (NR, NR)
Duration ≥6 months [n (%)]		1 (100.0)		1 (100.0)
DOR Distribution Function (95% CI)				
Month 6		100.0 (100.0, 100.0)		100.0 (100.0, 100.0)
Month 12		100.0 (100.0, 100.0)		100.0 (100.0, 100.0)
Month 18		100.0 (100.0, 100.0)		100.0 (100.0, 100.0)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject’s response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_18a_dor_recist_or.rtf,
Generated on: 26AUG2020 03:08 Data extraction: 23JUL2020 Data cutoff: 01MAR2020
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Table 14.2.18a Kaplan Meier Analysis of Duration of Response by progression free interval from last platinum-containing prior anti-cancer therapy - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR or MMR-unk/MSI-H

Variable	< 6 months (N=15)	>= 6 months (N=30)	Missing (N=2)	Total (N=47)
DOR				
Status [n (%)]				
Events observed	2 (13.3)	3 (10.0)	0 (0.0)	5 (10.6)
Censored	13 (86.7)	27 (90.0)	2 (100.0)	42 (89.4)
DOR (months)				
Min, Max	2.79+, 28.09+	2.63, 27.66+	7.06+, 7.39+	2.63, 28.09+
Quartile (95% CI)[a]				
25%	NR (9.8, NR)	NR (9.7, NR)	NR (NR, NR)	NR (9.8, NR)
50%	NR (9.8, NR)	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	12 (80.0)	23 (76.7)	2 (100.0)	37 (78.7)
DOR Distribution Function (95% CI)				
Month 6	100.0 (100.0, 100.0)	96.7 (78.6, 99.5)	100.0 (100.0, 100.0)	97.9 (85.8, 99.7)
Month 12	90.0 (47.3, 98.5)	91.3 (68.3, 97.8)	NR (NR, NR)	90.9 (73.7, 97.1)
Month 18	77.1 (34.5, 93.9)	82.2 (50.6, 94.5)	NR (NR, NR)	80.1 (56.8, 91.7)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_18a_dor_recist_or.rtf,
Generated on: 26AUG2020 03:08 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.2.19a Kaplan Meier Analysis of Duration of Response by Prior Bevacizumab Use - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR

Variable	Prior Bevacizumab Use (N=1)	No Prior Bevacizumab Use (N=45)	Total (N=46)
DOR			
Status [n (%)]			
Events observed	0 (0.0)	5 (11.1)	5 (10.9)
Censored	1 (100.0)	40 (88.9)	41 (89.1)
DOR (months)			
Min, Max	3.09+, 3.09+	2.63, 28.09+	2.63, 28.09+
Quartile (95% CI)[a]			
25%	NR (NR, NR)	NR (9.8, NR)	NR (9.8, NR)
50%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	0 (0.0)	36 (80.0)	36 (78.3)
DOR Distribution Function (95% CI)			
Month 6	NR (NR, NR)	97.8 (85.3, 99.7)	97.8 (85.6, 99.7)
Month 12	NR (NR, NR)	90.5 (72.8, 96.9)	90.6 (72.9, 97.0)
Month 18	NR (NR, NR)	79.1 (54.9, 91.3)	79.2 (54.9, 91.3)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_19a_dor_recist_or.rtf,
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Table 14.2.19a Kaplan Meier Analysis of Duration of Response by Prior Bevacizumab Use - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: MMR-unk/MSI-H

Variable	Prior Bevacizumab Use (N=0)	No Prior Bevacizumab Use (N=1)	Total (N=1)
DOR			
Status [n (%)]			
Events observed		0 (0.0)	0 (0.0)
Censored		1 (100.0)	1 (100.0)
DOR (months)			
Min, Max		19.32+, 19.32+	19.32+, 19.32+
Quartile (95% CI)[a]			
25%		NR (NR, NR)	NR (NR, NR)
50%		NR (NR, NR)	NR (NR, NR)
75%		NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]		1 (100.0)	1 (100.0)
DOR Distribution Function (95% CI)			
Month 6		100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
Month 12		100.0 (100.0, 100.0)	100.0 (100.0, 100.0)
Month 18		100.0 (100.0, 100.0)	100.0 (100.0, 100.0)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_19a_dor_recist_or.rtf,
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Table 14.2.19a Kaplan Meier Analysis of Duration of Response by Prior Bevacizumab Use - RECIST v1.1 assessed by BICR (Primary Efficacy Analysis Set - Patients with Objective Response)

EC: dMMR or MMR-unk/MSI-H

Variable	Prior Bevacizumab Use (N=1)	No Prior Bevacizumab Use (N=46)	Total (N=47)
DOR			
Status [n (%)]			
Events observed	0 (0.0)	5 (10.9)	5 (10.6)
Censored	1 (100.0)	41 (89.1)	42 (89.4)
DOR (months)			
Min, Max	3.09+, 3.09+	2.63, 28.09+	2.63, 28.09+
Quartile (95% CI)[a]			
25%	NR (NR, NR)	NR (9.8, NR)	NR (9.8, NR)
50%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
75%	NR (NR, NR)	NR (NR, NR)	NR (NR, NR)
Duration ≥6 months [n (%)]	0 (0.0)	37 (80.4)	37 (78.7)
DOR Distribution Function (95% CI)			
Month 6	NR (NR, NR)	97.8 (85.6, 99.7)	97.9 (85.8, 99.7)
Month 12	NR (NR, NR)	90.8 (73.6, 97.0)	90.9 (73.7, 97.1)
Month 18	NR (NR, NR)	80.1 (56.7, 91.7)	80.1 (56.8, 91.7)

Note: DOR: Duration of Response per RECIST v1.1 based on blinded independent central review (BICR).
a 95% Confidence intervals generated using the method of Brookmeyer and Crowley (1982).
+ indicates subject's response is ongoing
NR=Not Reachable.
Source: Listing 16.1.15a, Dataset: ADTTE, Program: t_dor_recist_or.sas, Output: t_14_2_19a_dor_recist_or.rtf,
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Any Adverse Events	76 (93.8)	44 (97.8)	120 (95.2)
General disorders and administration site conditions	50 (61.7)	31 (68.9)	81 (64.3)
Fatigue	14 (17.3)	17 (37.8)	31 (24.6)
Asthenia	20 (24.7)	8 (17.8)	28 (22.2)
Pyrexia	7 (8.6)	6 (13.3)	13 (10.3)
Oedema peripheral	6 (7.4)	5 (11.1)	11 (8.7)
Chills	3 (3.7)	3 (6.7)	6 (4.8)
Pain	2 (2.5)	2 (4.4)	4 (3.2)
Oedema	3 (3.7)	0	3 (2.4)
Peripheral swelling	1 (1.2)	2 (4.4)	3 (2.4)
Chest discomfort	1 (1.2)	1 (2.2)	2 (1.6)
General physical health deterioration	1 (1.2)	1 (2.2)	2 (1.6)
Influenza like illness	2 (2.5)	0	2 (1.6)
Non-cardiac chest pain	1 (1.2)	1 (2.2)	2 (1.6)
Catheter site erythema	0	1 (2.2)	1 (0.8)
Catheter site pruritus	1 (1.2)	0	1 (0.8)
Complication associated with device	1 (1.2)	0	1 (0.8)
Early satiety	1 (1.2)	0	1 (0.8)
Hernia pain	0	1 (2.2)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_sub_teae.sas, Output: t_14_3_1_22a_sub_teae.rtf,
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
General disorders and administration site conditions			
Hyperthermia	1 (1.2)	0	1 (0.8)
Localised oedema	0	1 (2.2)	1 (0.8)
Malaise	0	1 (2.2)	1 (0.8)
Mucosal inflammation	1 (1.2)	0	1 (0.8)
Gastrointestinal disorders	50 (61.7)	29 (64.4)	79 (62.7)
Nausea	26 (32.1)	14 (31.1)	40 (31.7)
Diarrhoea	22 (27.2)	13 (28.9)	35 (27.8)
Constipation	10 (12.3)	15 (33.3)	25 (19.8)
Vomiting	14 (17.3)	10 (22.2)	24 (19.0)
Abdominal pain	11 (13.6)	10 (22.2)	21 (16.7)
Abdominal distension	6 (7.4)	3 (6.7)	9 (7.1)
Dyspepsia	3 (3.7)	3 (6.7)	6 (4.8)
Stomatitis	3 (3.7)	3 (6.7)	6 (4.8)
Abdominal pain upper	3 (3.7)	1 (2.2)	4 (3.2)
Gastrooesophageal reflux disease	0	4 (8.9)	4 (3.2)
Abdominal pain lower	2 (2.5)	1 (2.2)	3 (2.4)
Colitis	1 (1.2)	2 (4.4)	3 (2.4)
Dry mouth	0	3 (6.7)	3 (2.4)
Haemorrhoids	2 (2.5)	1 (2.2)	3 (2.4)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_sub_teae.sas, Output: t_14_3_1_22a_sub_teae.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Gastrointestinal disorders			
Mouth ulceration	2 (2.5)	1 (2.2)	3 (2.4)
Anal incontinence	2 (2.5)	0	2 (1.6)
Anorectal discomfort	0	2 (4.4)	2 (1.6)
Ascites	2 (2.5)	0	2 (1.6)
Gastritis	0	2 (4.4)	2 (1.6)
Intestinal obstruction	2 (2.5)	0	2 (1.6)
Proctalgia	0	2 (4.4)	2 (1.6)
Rectal haemorrhage	1 (1.2)	1 (2.2)	2 (1.6)
Anal haemorrhage	0	1 (2.2)	1 (0.8)
Cheilitis	0	1 (2.2)	1 (0.8)
Chronic gastritis	0	1 (2.2)	1 (0.8)
Colonic fistula	0	1 (2.2)	1 (0.8)
Dumping syndrome	0	1 (2.2)	1 (0.8)
Enterocolitis haemorrhagic	1 (1.2)	0	1 (0.8)
Flatulence	1 (1.2)	0	1 (0.8)
Gastric ulcer	0	1 (2.2)	1 (0.8)
Gastric ulcer perforation	0	1 (2.2)	1 (0.8)
Haematemesis	0	1 (2.2)	1 (0.8)
Haematochezia	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Gastrointestinal disorders			
Large intestine polyp	1 (1.2)	0	1 (0.8)
Lip swelling	0	1 (2.2)	1 (0.8)
Melaena	0	1 (2.2)	1 (0.8)
Odynophagia	0	1 (2.2)	1 (0.8)
Oral pain	0	1 (2.2)	1 (0.8)
Pancreatitis	0	1 (2.2)	1 (0.8)
Pancreatitis acute	1 (1.2)	0	1 (0.8)
Musculoskeletal and connective tissue disorders	32 (39.5)	23 (51.1)	55 (43.7)
Back pain	10 (12.3)	9 (20.0)	19 (15.1)
Arthralgia	10 (12.3)	8 (17.8)	18 (14.3)
Myalgia	6 (7.4)	7 (15.6)	13 (10.3)
Muscular weakness	4 (4.9)	5 (11.1)	9 (7.1)
Pain in extremity	4 (4.9)	4 (8.9)	8 (6.3)
Muscle spasms	2 (2.5)	3 (6.7)	5 (4.0)
Musculoskeletal pain	1 (1.2)	3 (6.7)	4 (3.2)
Arthritis	1 (1.2)	1 (2.2)	2 (1.6)
Flank pain	1 (1.2)	1 (2.2)	2 (1.6)
Musculoskeletal stiffness	2 (2.5)	0	2 (1.6)
Osteoarthritis	1 (1.2)	1 (2.2)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_sub_teae.sas, Output: t_14_3_1_22a_sub_teae.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis	1 (1.2)	1 (2.2)	2 (1.6)
Tendon pain	1 (1.2)	1 (2.2)	2 (1.6)
Coccydynia	1 (1.2)	0	1 (0.8)
Joint range of motion decreased	0	1 (2.2)	1 (0.8)
Joint swelling	0	1 (2.2)	1 (0.8)
Limb discomfort	0	1 (2.2)	1 (0.8)
Muscle discomfort	1 (1.2)	0	1 (0.8)
Muscle tightness	1 (1.2)	0	1 (0.8)
Neck pain	1 (1.2)	0	1 (0.8)
Osteopenia	0	1 (2.2)	1 (0.8)
Osteoporosis	0	1 (2.2)	1 (0.8)
Pain in jaw	0	1 (2.2)	1 (0.8)
Rheumatoid arthritis	0	1 (2.2)	1 (0.8)
Scoliosis	0	1 (2.2)	1 (0.8)
Spinal stenosis	0	1 (2.2)	1 (0.8)
Infections and infestations	33 (40.7)	20 (44.4)	53 (42.1)
Urinary tract infection	10 (12.3)	9 (20.0)	19 (15.1)
Upper respiratory tract infection	7 (8.6)	2 (4.4)	9 (7.1)
Bronchitis	3 (3.7)	3 (6.7)	6 (4.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Infections and infestations			
Nasopharyngitis	4 (4.9)	2 (4.4)	6 (4.8)
Pneumonia	2 (2.5)	4 (8.9)	6 (4.8)
Sepsis	4 (4.9)	0	4 (3.2)
Cellulitis	2 (2.5)	0	2 (1.6)
Cystitis	1 (1.2)	1 (2.2)	2 (1.6)
Gastroenteritis	1 (1.2)	1 (2.2)	2 (1.6)
Oral candidiasis	1 (1.2)	1 (2.2)	2 (1.6)
Pharyngitis	1 (1.2)	1 (2.2)	2 (1.6)
Pyelonephritis	2 (2.5)	0	2 (1.6)
Rhinitis	2 (2.5)	0	2 (1.6)
Vaginal infection	2 (2.5)	0	2 (1.6)
Abdominal infection	0	1 (2.2)	1 (0.8)
Bacteraemia	0	1 (2.2)	1 (0.8)
Conjunctivitis	1 (1.2)	0	1 (0.8)
Demodicidosis	1 (1.2)	0	1 (0.8)
Ear infection	1 (1.2)	0	1 (0.8)
Gastroenteritis viral	0	1 (2.2)	1 (0.8)
Gastrointestinal viral infection	0	1 (2.2)	1 (0.8)
Genital infection	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_sub_teae.sas, Output: t_14_3_1_22a_sub_teae.rtf,
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Infections and infestations			
Herpes virus infection	0	1 (2.2)	1 (0.8)
Infected lymphocele	1 (1.2)	0	1 (0.8)
Lower respiratory tract infection	1 (1.2)	0	1 (0.8)
Oral herpes	0	1 (2.2)	1 (0.8)
Sinusitis	0	1 (2.2)	1 (0.8)
Vulvovaginal candidiasis	0	1 (2.2)	1 (0.8)
Wound infection	0	1 (2.2)	1 (0.8)
Investigations	24 (29.6)	24 (53.3)	48 (38.1)
Alanine aminotransferase increased	5 (6.2)	4 (8.9)	9 (7.1)
Aspartate aminotransferase increased	6 (7.4)	3 (6.7)	9 (7.1)
Blood creatinine increased	4 (4.9)	5 (11.1)	9 (7.1)
Weight decreased	6 (7.4)	3 (6.7)	9 (7.1)
Amylase increased	3 (3.7)	3 (6.7)	6 (4.8)
Weight increased	1 (1.2)	4 (8.9)	5 (4.0)
Gamma-glutamyltransferase increased	1 (1.2)	3 (6.7)	4 (3.2)
Lipase increased	1 (1.2)	3 (6.7)	4 (3.2)
Blood alkaline phosphatase increased	1 (1.2)	2 (4.4)	3 (2.4)
Transaminases increased	1 (1.2)	2 (4.4)	3 (2.4)
Blood lactate dehydrogenase increased	1 (1.2)	1 (2.2)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Investigations			
Lymphocyte count decreased	1 (1.2)	1 (2.2)	2 (1.6)
Activated partial thromboplastin time prolonged	1 (1.2)	0	1 (0.8)
Blood bilirubin increased	0	1 (2.2)	1 (0.8)
Blood corticotrophin decreased	1 (1.2)	0	1 (0.8)
Blood iron decreased	1 (1.2)	0	1 (0.8)
Blood potassium decreased	1 (1.2)	0	1 (0.8)
Blood thyroid stimulating hormone decreased	0	1 (2.2)	1 (0.8)
Blood thyroid stimulating hormone increased	1 (1.2)	0	1 (0.8)
Blood urea increased	1 (1.2)	0	1 (0.8)
Blood urine present	0	1 (2.2)	1 (0.8)
Electrocardiogram QT prolonged	1 (1.2)	0	1 (0.8)
Haemoglobin decreased	1 (1.2)	0	1 (0.8)
Mean platelet volume decreased	1 (1.2)	0	1 (0.8)
Neutrophil count decreased	0	1 (2.2)	1 (0.8)
Neutrophil count increased	0	1 (2.2)	1 (0.8)
Nitrite urine present	0	1 (2.2)	1 (0.8)
Serum ferritin decreased	0	1 (2.2)	1 (0.8)
Thyroxine increased	0	1 (2.2)	1 (0.8)
White blood cell count decreased	0	1 (2.2)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Investigations			
White blood cell count increased	0	1 (2.2)	1 (0.8)
Respiratory, thoracic and mediastinal disorders	26 (32.1)	16 (35.6)	42 (33.3)
Cough	11 (13.6)	8 (17.8)	19 (15.1)
Productive cough	5 (6.2)	4 (8.9)	9 (7.1)
Dyspnoea	6 (7.4)	2 (4.4)	8 (6.3)
Pulmonary embolism	1 (1.2)	3 (6.7)	4 (3.2)
Nasal congestion	2 (2.5)	1 (2.2)	3 (2.4)
Rhinorrhoea	2 (2.5)	1 (2.2)	3 (2.4)
Dysphonia	1 (1.2)	1 (2.2)	2 (1.6)
Oropharyngeal pain	0	2 (4.4)	2 (1.6)
Pneumonitis	1 (1.2)	1 (2.2)	2 (1.6)
Sneezing	1 (1.2)	1 (2.2)	2 (1.6)
Throat irritation	0	2 (4.4)	2 (1.6)
Aspiration	1 (1.2)	0	1 (0.8)
Choking sensation	0	1 (2.2)	1 (0.8)
Dyspnoea exertional	0	1 (2.2)	1 (0.8)
Epistaxis	0	1 (2.2)	1 (0.8)
Hiccups	0	1 (2.2)	1 (0.8)
Hypoxia	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Respiratory, thoracic and mediastinal disorders			
Increased bronchial secretion	1 (1.2)	0	1 (0.8)
Increased upper airway secretion	0	1 (2.2)	1 (0.8)
Interstitial lung disease	1 (1.2)	0	1 (0.8)
Pleural effusion	0	1 (2.2)	1 (0.8)
Pulmonary infarction	0	1 (2.2)	1 (0.8)
Sputum retention	0	1 (2.2)	1 (0.8)
Wheezing	1 (1.2)	0	1 (0.8)
Metabolism and nutrition disorders	24 (29.6)	17 (37.8)	41 (32.5)
Decreased appetite	9 (11.1)	7 (15.6)	16 (12.7)
Hypomagnesaemia	6 (7.4)	4 (8.9)	10 (7.9)
Hypokalaemia	3 (3.7)	5 (11.1)	8 (6.3)
Hyponatraemia	3 (3.7)	3 (6.7)	6 (4.8)
Dehydration	3 (3.7)	2 (4.4)	5 (4.0)
Hyperglycaemia	3 (3.7)	0	3 (2.4)
Hyperkalaemia	3 (3.7)	0	3 (2.4)
Hypoalbuminaemia	2 (2.5)	1 (2.2)	3 (2.4)
Hypercalcaemia	1 (1.2)	1 (2.2)	2 (1.6)
Folate deficiency	0	1 (2.2)	1 (0.8)
Hyperamylasaemia	0	1 (2.2)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Metabolism and nutrition disorders			
Hyperglycaemic hyperosmolar nonketotic syndrome	0	1 (2.2)	1 (0.8)
Hypocalcaemia	1 (1.2)	0	1 (0.8)
Hypophosphataemia	0	1 (2.2)	1 (0.8)
Increased appetite	1 (1.2)	0	1 (0.8)
Iron deficiency	0	1 (2.2)	1 (0.8)
Malnutrition	0	1 (2.2)	1 (0.8)
Metabolic syndrome	0	1 (2.2)	1 (0.8)
Blood and lymphatic system disorders	20 (24.7)	20 (44.4)	40 (31.7)
Anaemia	18 (22.2)	17 (37.8)	35 (27.8)
Neutropenia	2 (2.5)	4 (8.9)	6 (4.8)
Leukocytosis	2 (2.5)	0	2 (1.6)
Leukopenia	0	2 (4.4)	2 (1.6)
Iron deficiency anaemia	0	1 (2.2)	1 (0.8)
Lymphopenia	0	1 (2.2)	1 (0.8)
Skin and subcutaneous tissue disorders	25 (30.9)	15 (33.3)	40 (31.7)
Pruritus	10 (12.3)	8 (17.8)	18 (14.3)
Rash	7 (8.6)	6 (13.3)	13 (10.3)
Dry skin	4 (4.9)	0	4 (3.2)
Skin lesion	3 (3.7)	0	3 (2.4)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Skin and subcutaneous tissue disorders			
Urticaria	1 (1.2)	2 (4.4)	3 (2.4)
Alopecia	0	2 (4.4)	2 (1.6)
Eczema	2 (2.5)	0	2 (1.6)
Erythema	1 (1.2)	1 (2.2)	2 (1.6)
Dermatitis contact	1 (1.2)	0	1 (0.8)
Drug eruption	1 (1.2)	0	1 (0.8)
Hyperhidrosis	1 (1.2)	0	1 (0.8)
Hypertrichosis	0	1 (2.2)	1 (0.8)
Nail discolouration	0	1 (2.2)	1 (0.8)
Onychoclasis	0	1 (2.2)	1 (0.8)
Onychomadesis	1 (1.2)	0	1 (0.8)
Papule	1 (1.2)	0	1 (0.8)
Pemphigoid	0	1 (2.2)	1 (0.8)
Prurigo	1 (1.2)	0	1 (0.8)
Rash maculo-papular	1 (1.2)	0	1 (0.8)
Skin burning sensation	1 (1.2)	0	1 (0.8)
Skin ulcer	0	1 (2.2)	1 (0.8)
Skin warm	0	1 (2.2)	1 (0.8)
Nervous system disorders	15 (18.5)	17 (37.8)	32 (25.4)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Nervous system disorders			
Headache	6 (7.4)	6 (13.3)	12 (9.5)
Dizziness	3 (3.7)	6 (13.3)	9 (7.1)
Neuropathy peripheral	3 (3.7)	1 (2.2)	4 (3.2)
Dysgeusia	2 (2.5)	1 (2.2)	3 (2.4)
Carpal tunnel syndrome	2 (2.5)	0	2 (1.6)
Cognitive disorder	0	2 (4.4)	2 (1.6)
Neuralgia	1 (1.2)	1 (2.2)	2 (1.6)
Apraxia	1 (1.2)	0	1 (0.8)
Dysaesthesia	0	1 (2.2)	1 (0.8)
Dysarthria	1 (1.2)	0	1 (0.8)
Encephalopathy	0	1 (2.2)	1 (0.8)
Facial paresis	1 (1.2)	0	1 (0.8)
Formication	0	1 (2.2)	1 (0.8)
Leukoencephalopathy	0	1 (2.2)	1 (0.8)
Paraesthesia	0	1 (2.2)	1 (0.8)
Parkinson's disease	1 (1.2)	0	1 (0.8)
Somnolence	0	1 (2.2)	1 (0.8)
Syncope	1 (1.2)	0	1 (0.8)
Tremor	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Renal and urinary disorders	17 (21.0)	8 (17.8)	25 (19.8)
Acute kidney injury	3 (3.7)	1 (2.2)	4 (3.2)
Urinary incontinence	1 (1.2)	3 (6.7)	4 (3.2)
Dysuria	1 (1.2)	2 (4.4)	3 (2.4)
Haematuria	1 (1.2)	2 (4.4)	3 (2.4)
Hydronephrosis	3 (3.7)	0	3 (2.4)
Micturition urgency	1 (1.2)	2 (4.4)	3 (2.4)
Chromaturia	1 (1.2)	1 (2.2)	2 (1.6)
Renal colic	2 (2.5)	0	2 (1.6)
Urogenital fistula	2 (2.5)	0	2 (1.6)
Nephritis	0	1 (2.2)	1 (0.8)
Proteinuria	1 (1.2)	0	1 (0.8)
Renal failure	1 (1.2)	0	1 (0.8)
Tubulointerstitial nephritis	1 (1.2)	0	1 (0.8)
Urinary tract obstruction	1 (1.2)	0	1 (0.8)
Urinary tract pain	0	1 (2.2)	1 (0.8)
Urine abnormality	0	1 (2.2)	1 (0.8)
Urine odour abnormal	0	1 (2.2)	1 (0.8)
Vascular disorders	11 (13.6)	12 (26.7)	23 (18.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Vascular disorders			
Deep vein thrombosis	1 (1.2)	4 (8.9)	5 (4.0)
Hot flush	2 (2.5)	3 (6.7)	5 (4.0)
Hypertension	2 (2.5)	3 (6.7)	5 (4.0)
Flushing	2 (2.5)	1 (2.2)	3 (2.4)
Hypotension	2 (2.5)	0	2 (1.6)
Lymphoedema	1 (1.2)	1 (2.2)	2 (1.6)
Thrombophlebitis superficial	1 (1.2)	1 (2.2)	2 (1.6)
Embolism	1 (1.2)	0	1 (0.8)
Peripheral venous disease	1 (1.2)	0	1 (0.8)
Shock	1 (1.2)	0	1 (0.8)
Varicose vein	0	1 (2.2)	1 (0.8)
Reproductive system and breast disorders	13 (16.0)	9 (20.0)	22 (17.5)
Pelvic pain	3 (3.7)	4 (8.9)	7 (5.6)
Vaginal discharge	3 (3.7)	2 (4.4)	5 (4.0)
Vaginal haemorrhage	3 (3.7)	2 (4.4)	5 (4.0)
Female genital tract fistula	2 (2.5)	0	2 (1.6)
Metrorrhagia	2 (2.5)	0	2 (1.6)
Breast haematoma	0	1 (2.2)	1 (0.8)
Perineal pain	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Reproductive system and breast disorders			
Vulval disorder	1 (1.2)	0	1 (0.8)
Vulvovaginal dryness	0	1 (2.2)	1 (0.8)
Vulvovaginal pain	0	1 (2.2)	1 (0.8)
Psychiatric disorders	13 (16.0)	8 (17.8)	21 (16.7)
Insomnia	4 (4.9)	4 (8.9)	8 (6.3)
Anxiety	4 (4.9)	1 (2.2)	5 (4.0)
Depression	4 (4.9)	0	4 (3.2)
Confusional state	1 (1.2)	1 (2.2)	2 (1.6)
Depressed mood	1 (1.2)	1 (2.2)	2 (1.6)
Agitation	0	1 (2.2)	1 (0.8)
Alcoholism	1 (1.2)	0	1 (0.8)
Bradyphrenia	0	1 (2.2)	1 (0.8)
Nervousness	1 (1.2)	0	1 (0.8)
Injury, poisoning and procedural complications	10 (12.3)	7 (15.6)	17 (13.5)
Contusion	1 (1.2)	1 (2.2)	2 (1.6)
Gastroenteritis radiation	0	2 (4.4)	2 (1.6)
Wound	1 (1.2)	1 (2.2)	2 (1.6)
Compression fracture	0	1 (2.2)	1 (0.8)
Fall	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Injury, poisoning and procedural complications			
Ligament sprain	1 (1.2)	0	1 (0.8)
Procedural pain	0	1 (2.2)	1 (0.8)
Skin abrasion	1 (1.2)	0	1 (0.8)
Skin laceration	0	1 (2.2)	1 (0.8)
Spinal compression fracture	1 (1.2)	0	1 (0.8)
Stoma site pain	1 (1.2)	0	1 (0.8)
Stress fracture	1 (1.2)	0	1 (0.8)
Tendon rupture	1 (1.2)	0	1 (0.8)
Thermal burn	0	1 (2.2)	1 (0.8)
Toxicity to various agents	1 (1.2)	0	1 (0.8)
Wound complication	0	1 (2.2)	1 (0.8)
Wound dehiscence	1 (1.2)	0	1 (0.8)
Eye disorders	7 (8.6)	6 (13.3)	13 (10.3)
Dry eye	3 (3.7)	1 (2.2)	4 (3.2)
Vision blurred	0	3 (6.7)	3 (2.4)
Cataract	1 (1.2)	1 (2.2)	2 (1.6)
Diplopia	0	1 (2.2)	1 (0.8)
Eye irritation	1 (1.2)	0	1 (0.8)
Iridocyclitis	0	1 (2.2)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Eye disorders			
Lacrimation increased	1 (1.2)	0	1 (0.8)
Ocular discomfort	1 (1.2)	0	1 (0.8)
Uveitis	1 (1.2)	0	1 (0.8)
Vitreous floaters	1 (1.2)	0	1 (0.8)
Endocrine disorders	6 (7.4)	5 (11.1)	11 (8.7)
Hypothyroidism	4 (4.9)	5 (11.1)	9 (7.1)
Hyperthyroidism	3 (3.7)	1 (2.2)	4 (3.2)
Adrenal insufficiency	0	1 (2.2)	1 (0.8)
Glucocorticoid deficiency	1 (1.2)	0	1 (0.8)
Hypophysitis	1 (1.2)	0	1 (0.8)
Cardiac disorders	4 (4.9)	2 (4.4)	6 (4.8)
Atrial fibrillation	2 (2.5)	0	2 (1.6)
Angina pectoris	0	1 (2.2)	1 (0.8)
Bradycardia	0	1 (2.2)	1 (0.8)
Myocardial infarction	0	1 (2.2)	1 (0.8)
Pericardial effusion	1 (1.2)	0	1 (0.8)
Sinus tachycardia	1 (1.2)	0	1 (0.8)
Supraventricular extrasystoles	0	1 (2.2)	1 (0.8)
Tachycardia	0	1 (2.2)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=81)	≥2 Prior Therapies (N=45)	Total (N=126)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5 (6.2)	1 (2.2)	6 (4.8)
Tumour pain	1 (1.2)	1 (2.2)	2 (1.6)
Cancer pain	1 (1.2)	0	1 (0.8)
Colon adenoma	1 (1.2)	0	1 (0.8)
Malignant melanoma	1 (1.2)	0	1 (0.8)
Seborrhoeic keratosis	1 (1.2)	0	1 (0.8)
Ear and labyrinth disorders	1 (1.2)	4 (8.9)	5 (4.0)
Tinnitus	0	2 (4.4)	2 (1.6)
Vertigo	0	2 (4.4)	2 (1.6)
Cerumen impaction	1 (1.2)	0	1 (0.8)
Hypoacusis	1 (1.2)	0	1 (0.8)
Hepatobiliary disorders	0	2 (4.4)	2 (1.6)
Cholecystitis	0	1 (2.2)	1 (0.8)
Hepatic function abnormal	0	1 (2.2)	1 (0.8)
Hypertransaminasaemia	0	1 (2.2)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=1)	≥2 Prior Therapies (N=2)	Total (N=3)
Any Adverse Events	1 (100)	2 (100)	3 (100)
Nervous system disorders	1 (100)	2 (100)	3 (100)
Epilepsy	0	1 (50.0)	1 (33.3)
Lethargy	0	1 (50.0)	1 (33.3)
Neuralgia	1 (100)	0	1 (33.3)
Gastrointestinal disorders	1 (100)	1 (50.0)	2 (66.7)
Nausea	1 (100)	1 (50.0)	2 (66.7)
Bile acid malabsorption	0	1 (50.0)	1 (33.3)
Diarrhoea	0	1 (50.0)	1 (33.3)
Dry mouth	0	1 (50.0)	1 (33.3)
General disorders and administration site conditions	1 (100)	1 (50.0)	2 (66.7)
Oedema peripheral	1 (100)	1 (50.0)	2 (66.7)
Fatigue	1 (100)	0	1 (33.3)
Pyrexia	1 (100)	0	1 (33.3)
Infections and infestations	1 (100)	1 (50.0)	2 (66.7)
Candida infection	0	1 (50.0)	1 (33.3)
Fungal skin infection	1 (100)	0	1 (33.3)
Sinusitis	1 (100)	0	1 (33.3)
Upper respiratory tract infection	1 (100)	0	1 (33.3)

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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=1)	≥2 Prior Therapies (N=2)	Total (N=3)
Infections and infestations			
Urinary tract infection	0	1 (50.0)	1 (33.3)
Viral infection	1 (100)	0	1 (33.3)
Metabolism and nutrition disorders	1 (100)	1 (50.0)	2 (66.7)
Gout	1 (100)	0	1 (33.3)
Hyperammonaemia	0	1 (50.0)	1 (33.3)
Hyponatraemia	0	1 (50.0)	1 (33.3)
Hypophagia	0	1 (50.0)	1 (33.3)
Musculoskeletal and connective tissue disorders	1 (100)	1 (50.0)	2 (66.7)
Arthralgia	1 (100)	1 (50.0)	2 (66.7)
Musculoskeletal pain	1 (100)	0	1 (33.3)
Myalgia	1 (100)	0	1 (33.3)
Synovial cyst	1 (100)	0	1 (33.3)
Tendonitis	1 (100)	0	1 (33.3)
Respiratory, thoracic and mediastinal disorders	1 (100)	1 (50.0)	2 (66.7)
Cough	1 (100)	1 (50.0)	2 (66.7)
Dyspnoea	1 (100)	0	1 (33.3)
Vascular disorders	0	2 (100)	2 (66.7)
Hypertension	0	2 (100)	2 (66.7)
Cardiac disorders	1 (100)	0	1 (33.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=1)	≥2 Prior Therapies (N=2)	Total (N=3)
Cardiac disorders			
Tachycardia	1 (100)	0	1 (33.3)
Endocrine disorders	1 (100)	0	1 (33.3)
Hypothyroidism	1 (100)	0	1 (33.3)
Injury, poisoning and procedural complications	1 (100)	0	1 (33.3)
Ligament sprain	1 (100)	0	1 (33.3)
Investigations	1 (100)	0	1 (33.3)
Serum ferritin decreased	1 (100)	0	1 (33.3)
Psychiatric disorders	1 (100)	0	1 (33.3)
Mood altered	1 (100)	0	1 (33.3)
Reproductive system and breast disorders	0	1 (50.0)	1 (33.3)
Vulvovaginal dryness	0	1 (50.0)	1 (33.3)
Skin and subcutaneous tissue disorders	1 (100)	0	1 (33.3)
Dry skin	1 (100)	0	1 (33.3)
Night sweats	1 (100)	0	1 (33.3)
Pain of skin	1 (100)	0	1 (33.3)
Skin reaction	1 (100)	0	1 (33.3)
Urticaria	1 (100)	0	1 (33.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Any Adverse Events	77 (93.9)	46 (97.9)	123 (95.3)
General disorders and administration site conditions	51 (62.2)	32 (68.1)	83 (64.3)
Fatigue	15 (18.3)	17 (36.2)	32 (24.8)
Asthenia	20 (24.4)	8 (17.0)	28 (21.7)
Pyrexia	8 (9.8)	6 (12.8)	14 (10.9)
Oedema peripheral	7 (8.5)	6 (12.8)	13 (10.1)
Chills	3 (3.7)	3 (6.4)	6 (4.7)
Pain	2 (2.4)	2 (4.3)	4 (3.1)
Oedema	3 (3.7)	0	3 (2.3)
Peripheral swelling	1 (1.2)	2 (4.3)	3 (2.3)
Chest discomfort	1 (1.2)	1 (2.1)	2 (1.6)
General physical health deterioration	1 (1.2)	1 (2.1)	2 (1.6)
Influenza like illness	2 (2.4)	0	2 (1.6)
Non-cardiac chest pain	1 (1.2)	1 (2.1)	2 (1.6)
Catheter site erythema	0	1 (2.1)	1 (0.8)
Catheter site pruritus	1 (1.2)	0	1 (0.8)
Complication associated with device	1 (1.2)	0	1 (0.8)
Early satiety	1 (1.2)	0	1 (0.8)
Hernia pain	0	1 (2.1)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
General disorders and administration site conditions			
Hyperthermia	1 (1.2)	0	1 (0.8)
Localised oedema	0	1 (2.1)	1 (0.8)
Malaise	0	1 (2.1)	1 (0.8)
Mucosal inflammation	1 (1.2)	0	1 (0.8)
Gastrointestinal disorders	51 (62.2)	30 (63.8)	81 (62.8)
Nausea	27 (32.9)	15 (31.9)	42 (32.6)
Diarrhoea	22 (26.8)	14 (29.8)	36 (27.9)
Constipation	10 (12.2)	15 (31.9)	25 (19.4)
Vomiting	14 (17.1)	10 (21.3)	24 (18.6)
Abdominal pain	11 (13.4)	10 (21.3)	21 (16.3)
Abdominal distension	6 (7.3)	3 (6.4)	9 (7.0)
Dyspepsia	3 (3.7)	3 (6.4)	6 (4.7)
Stomatitis	3 (3.7)	3 (6.4)	6 (4.7)
Abdominal pain upper	3 (3.7)	1 (2.1)	4 (3.1)
Dry mouth	0	4 (8.5)	4 (3.1)
Gastrooesophageal reflux disease	0	4 (8.5)	4 (3.1)
Abdominal pain lower	2 (2.4)	1 (2.1)	3 (2.3)
Colitis	1 (1.2)	2 (4.3)	3 (2.3)
Haemorrhoids	2 (2.4)	1 (2.1)	3 (2.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Gastrointestinal disorders			
Mouth ulceration	2 (2.4)	1 (2.1)	3 (2.3)
Anal incontinence	2 (2.4)	0	2 (1.6)
Anorectal discomfort	0	2 (4.3)	2 (1.6)
Ascites	2 (2.4)	0	2 (1.6)
Gastritis	0	2 (4.3)	2 (1.6)
Intestinal obstruction	2 (2.4)	0	2 (1.6)
Proctalgia	0	2 (4.3)	2 (1.6)
Rectal haemorrhage	1 (1.2)	1 (2.1)	2 (1.6)
Anal haemorrhage	0	1 (2.1)	1 (0.8)
Bile acid malabsorption	0	1 (2.1)	1 (0.8)
Cheilitis	0	1 (2.1)	1 (0.8)
Chronic gastritis	0	1 (2.1)	1 (0.8)
Colonic fistula	0	1 (2.1)	1 (0.8)
Dumping syndrome	0	1 (2.1)	1 (0.8)
Enterocolitis haemorrhagic	1 (1.2)	0	1 (0.8)
Flatulence	1 (1.2)	0	1 (0.8)
Gastric ulcer	0	1 (2.1)	1 (0.8)
Gastric ulcer perforation	0	1 (2.1)	1 (0.8)
Haematemesis	0	1 (2.1)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Gastrointestinal disorders			
Haematochezia	1 (1.2)	0	1 (0.8)
Large intestine polyp	1 (1.2)	0	1 (0.8)
Lip swelling	0	1 (2.1)	1 (0.8)
Melaena	0	1 (2.1)	1 (0.8)
Odynophagia	0	1 (2.1)	1 (0.8)
Oral pain	0	1 (2.1)	1 (0.8)
Pancreatitis	0	1 (2.1)	1 (0.8)
Pancreatitis acute	1 (1.2)	0	1 (0.8)
Musculoskeletal and connective tissue disorders	33 (40.2)	24 (51.1)	57 (44.2)
Arthralgia	11 (13.4)	9 (19.1)	20 (15.5)
Back pain	10 (12.2)	9 (19.1)	19 (14.7)
Myalgia	7 (8.5)	7 (14.9)	14 (10.9)
Muscular weakness	4 (4.9)	5 (10.6)	9 (7.0)
Pain in extremity	4 (4.9)	4 (8.5)	8 (6.2)
Muscle spasms	2 (2.4)	3 (6.4)	5 (3.9)
Musculoskeletal pain	2 (2.4)	3 (6.4)	5 (3.9)
Arthritis	1 (1.2)	1 (2.1)	2 (1.6)
Flank pain	1 (1.2)	1 (2.1)	2 (1.6)
Musculoskeletal stiffness	2 (2.4)	0	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Musculoskeletal and connective tissue disorders			
Osteoarthritis	1 (1.2)	1 (2.1)	2 (1.6)
Spinal osteoarthritis	1 (1.2)	1 (2.1)	2 (1.6)
Tendon pain	1 (1.2)	1 (2.1)	2 (1.6)
Coccydynia	1 (1.2)	0	1 (0.8)
Joint range of motion decreased	0	1 (2.1)	1 (0.8)
Joint swelling	0	1 (2.1)	1 (0.8)
Limb discomfort	0	1 (2.1)	1 (0.8)
Muscle discomfort	1 (1.2)	0	1 (0.8)
Muscle tightness	1 (1.2)	0	1 (0.8)
Neck pain	1 (1.2)	0	1 (0.8)
Osteopenia	0	1 (2.1)	1 (0.8)
Osteoporosis	0	1 (2.1)	1 (0.8)
Pain in jaw	0	1 (2.1)	1 (0.8)
Rheumatoid arthritis	0	1 (2.1)	1 (0.8)
Scoliosis	0	1 (2.1)	1 (0.8)
Spinal stenosis	0	1 (2.1)	1 (0.8)
Synovial cyst	1 (1.2)	0	1 (0.8)
Tendonitis	1 (1.2)	0	1 (0.8)
Infections and infestations	34 (41.5)	21 (44.7)	55 (42.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Infections and infestations			
Urinary tract infection	10 (12.2)	10 (21.3)	20 (15.5)
Upper respiratory tract infection	8 (9.8)	2 (4.3)	10 (7.8)
Bronchitis	3 (3.7)	3 (6.4)	6 (4.7)
Nasopharyngitis	4 (4.9)	2 (4.3)	6 (4.7)
Pneumonia	2 (2.4)	4 (8.5)	6 (4.7)
Sepsis	4 (4.9)	0	4 (3.1)
Cellulitis	2 (2.4)	0	2 (1.6)
Cystitis	1 (1.2)	1 (2.1)	2 (1.6)
Gastroenteritis	1 (1.2)	1 (2.1)	2 (1.6)
Oral candidiasis	1 (1.2)	1 (2.1)	2 (1.6)
Pharyngitis	1 (1.2)	1 (2.1)	2 (1.6)
Pyelonephritis	2 (2.4)	0	2 (1.6)
Rhinitis	2 (2.4)	0	2 (1.6)
Sinusitis	1 (1.2)	1 (2.1)	2 (1.6)
Vaginal infection	2 (2.4)	0	2 (1.6)
Abdominal infection	0	1 (2.1)	1 (0.8)
Bacteraemia	0	1 (2.1)	1 (0.8)
Candida infection	0	1 (2.1)	1 (0.8)
Conjunctivitis	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Infections and infestations			
Demodicidosis	1 (1.2)	0	1 (0.8)
Ear infection	1 (1.2)	0	1 (0.8)
Fungal skin infection	1 (1.2)	0	1 (0.8)
Gastroenteritis viral	0	1 (2.1)	1 (0.8)
Gastrointestinal viral infection	0	1 (2.1)	1 (0.8)
Genital infection	1 (1.2)	0	1 (0.8)
Herpes virus infection	0	1 (2.1)	1 (0.8)
Infected lymphocele	1 (1.2)	0	1 (0.8)
Lower respiratory tract infection	1 (1.2)	0	1 (0.8)
Oral herpes	0	1 (2.1)	1 (0.8)
Viral infection	1 (1.2)	0	1 (0.8)
Vulvovaginal candidiasis	0	1 (2.1)	1 (0.8)
Wound infection	0	1 (2.1)	1 (0.8)
Investigations	25 (30.5)	24 (51.1)	49 (38.0)
Alanine aminotransferase increased	5 (6.1)	4 (8.5)	9 (7.0)
Aspartate aminotransferase increased	6 (7.3)	3 (6.4)	9 (7.0)
Blood creatinine increased	4 (4.9)	5 (10.6)	9 (7.0)
Weight decreased	6 (7.3)	3 (6.4)	9 (7.0)
Amylase increased	3 (3.7)	3 (6.4)	6 (4.7)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Investigations			
Weight increased	1 (1.2)	4 (8.5)	5 (3.9)
Gamma-glutamyltransferase increased	1 (1.2)	3 (6.4)	4 (3.1)
Lipase increased	1 (1.2)	3 (6.4)	4 (3.1)
Blood alkaline phosphatase increased	1 (1.2)	2 (4.3)	3 (2.3)
Transaminases increased	1 (1.2)	2 (4.3)	3 (2.3)
Blood lactate dehydrogenase increased	1 (1.2)	1 (2.1)	2 (1.6)
Lymphocyte count decreased	1 (1.2)	1 (2.1)	2 (1.6)
Serum ferritin decreased	1 (1.2)	1 (2.1)	2 (1.6)
Activated partial thromboplastin time prolonged	1 (1.2)	0	1 (0.8)
Blood bilirubin increased	0	1 (2.1)	1 (0.8)
Blood corticotrophin decreased	1 (1.2)	0	1 (0.8)
Blood iron decreased	1 (1.2)	0	1 (0.8)
Blood potassium decreased	1 (1.2)	0	1 (0.8)
Blood thyroid stimulating hormone decreased	0	1 (2.1)	1 (0.8)
Blood thyroid stimulating hormone increased	1 (1.2)	0	1 (0.8)
Blood urea increased	1 (1.2)	0	1 (0.8)
Blood urine present	0	1 (2.1)	1 (0.8)
Electrocardiogram QT prolonged	1 (1.2)	0	1 (0.8)
Haemoglobin decreased	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Investigations			
Mean platelet volume decreased	1 (1.2)	0	1 (0.8)
Neutrophil count decreased	0	1 (2.1)	1 (0.8)
Neutrophil count increased	0	1 (2.1)	1 (0.8)
Nitrite urine present	0	1 (2.1)	1 (0.8)
Thyroxine increased	0	1 (2.1)	1 (0.8)
White blood cell count decreased	0	1 (2.1)	1 (0.8)
White blood cell count increased	0	1 (2.1)	1 (0.8)
Respiratory, thoracic and mediastinal disorders	27 (32.9)	17 (36.2)	44 (34.1)
Cough	12 (14.6)	9 (19.1)	21 (16.3)
Dyspnoea	7 (8.5)	2 (4.3)	9 (7.0)
Productive cough	5 (6.1)	4 (8.5)	9 (7.0)
Pulmonary embolism	1 (1.2)	3 (6.4)	4 (3.1)
Nasal congestion	2 (2.4)	1 (2.1)	3 (2.3)
Rhinorrhoea	2 (2.4)	1 (2.1)	3 (2.3)
Dysphonia	1 (1.2)	1 (2.1)	2 (1.6)
Oropharyngeal pain	0	2 (4.3)	2 (1.6)
Pneumonitis	1 (1.2)	1 (2.1)	2 (1.6)
Sneezing	1 (1.2)	1 (2.1)	2 (1.6)
Throat irritation	0	2 (4.3)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Aspiration	1 (1.2)	0	1 (0.8)
Choking sensation	0	1 (2.1)	1 (0.8)
Dyspnoea exertional	0	1 (2.1)	1 (0.8)
Epistaxis	0	1 (2.1)	1 (0.8)
Hiccups	0	1 (2.1)	1 (0.8)
Hypoxia	1 (1.2)	0	1 (0.8)
Increased bronchial secretion	1 (1.2)	0	1 (0.8)
Increased upper airway secretion	0	1 (2.1)	1 (0.8)
Interstitial lung disease	1 (1.2)	0	1 (0.8)
Pleural effusion	0	1 (2.1)	1 (0.8)
Pulmonary infarction	0	1 (2.1)	1 (0.8)
Sputum retention	0	1 (2.1)	1 (0.8)
Wheezing	1 (1.2)	0	1 (0.8)
Metabolism and nutrition disorders	25 (30.5)	18 (38.3)	43 (33.3)
Decreased appetite	9 (11.0)	7 (14.9)	16 (12.4)
Hypomagnesaemia	6 (7.3)	4 (8.5)	10 (7.8)
Hypokalaemia	3 (3.7)	5 (10.6)	8 (6.2)
Hyponatraemia	3 (3.7)	4 (8.5)	7 (5.4)
Dehydration	3 (3.7)	2 (4.3)	5 (3.9)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Metabolism and nutrition disorders			
Hyperglycaemia	3 (3.7)	0	3 (2.3)
Hyperkalaemia	3 (3.7)	0	3 (2.3)
Hypoalbuminaemia	2 (2.4)	1 (2.1)	3 (2.3)
Hypercalcaemia	1 (1.2)	1 (2.1)	2 (1.6)
Folate deficiency	0	1 (2.1)	1 (0.8)
Gout	1 (1.2)	0	1 (0.8)
Hyperammonaemia	0	1 (2.1)	1 (0.8)
Hyperamylasaemia	0	1 (2.1)	1 (0.8)
Hyperglycaemic hyperosmolar nonketotic syndrome	0	1 (2.1)	1 (0.8)
Hypocalcaemia	1 (1.2)	0	1 (0.8)
Hypophagia	0	1 (2.1)	1 (0.8)
Hypophosphataemia	0	1 (2.1)	1 (0.8)
Increased appetite	1 (1.2)	0	1 (0.8)
Iron deficiency	0	1 (2.1)	1 (0.8)
Malnutrition	0	1 (2.1)	1 (0.8)
Metabolic syndrome	0	1 (2.1)	1 (0.8)
Skin and subcutaneous tissue disorders	26 (31.7)	15 (31.9)	41 (31.8)
Pruritus	10 (12.2)	8 (17.0)	18 (14.0)
Rash	7 (8.5)	6 (12.8)	13 (10.1)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Skin and subcutaneous tissue disorders			
Dry skin	5 (6.1)	0	5 (3.9)
Urticaria	2 (2.4)	2 (4.3)	4 (3.1)
Skin lesion	3 (3.7)	0	3 (2.3)
Alopecia	0	2 (4.3)	2 (1.6)
Eczema	2 (2.4)	0	2 (1.6)
Erythema	1 (1.2)	1 (2.1)	2 (1.6)
Dermatitis contact	1 (1.2)	0	1 (0.8)
Drug eruption	1 (1.2)	0	1 (0.8)
Hyperhidrosis	1 (1.2)	0	1 (0.8)
Hypertrichosis	0	1 (2.1)	1 (0.8)
Nail discolouration	0	1 (2.1)	1 (0.8)
Night sweats	1 (1.2)	0	1 (0.8)
Onychoclasis	0	1 (2.1)	1 (0.8)
Onychomadesis	1 (1.2)	0	1 (0.8)
Pain of skin	1 (1.2)	0	1 (0.8)
Papule	1 (1.2)	0	1 (0.8)
Pemphigoid	0	1 (2.1)	1 (0.8)
Prurigo	1 (1.2)	0	1 (0.8)
Rash maculo-papular	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Skin and subcutaneous tissue disorders			
Skin burning sensation	1 (1.2)	0	1 (0.8)
Skin reaction	1 (1.2)	0	1 (0.8)
Skin ulcer	0	1 (2.1)	1 (0.8)
Skin warm	0	1 (2.1)	1 (0.8)
Blood and lymphatic system disorders	20 (24.4)	20 (42.6)	40 (31.0)
Anaemia	18 (22.0)	17 (36.2)	35 (27.1)
Neutropenia	2 (2.4)	4 (8.5)	6 (4.7)
Leukocytosis	2 (2.4)	0	2 (1.6)
Leukopenia	0	2 (4.3)	2 (1.6)
Iron deficiency anaemia	0	1 (2.1)	1 (0.8)
Lymphopenia	0	1 (2.1)	1 (0.8)
Nervous system disorders	16 (19.5)	19 (40.4)	35 (27.1)
Headache	6 (7.3)	6 (12.8)	12 (9.3)
Dizziness	3 (3.7)	6 (12.8)	9 (7.0)
Neuropathy peripheral	3 (3.7)	1 (2.1)	4 (3.1)
Dysgeusia	2 (2.4)	1 (2.1)	3 (2.3)
Neuralgia	2 (2.4)	1 (2.1)	3 (2.3)
Carpal tunnel syndrome	2 (2.4)	0	2 (1.6)
Cognitive disorder	0	2 (4.3)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Nervous system disorders			
Apraxia	1 (1.2)	0	1 (0.8)
Dysaesthesia	0	1 (2.1)	1 (0.8)
Dysarthria	1 (1.2)	0	1 (0.8)
Encephalopathy	0	1 (2.1)	1 (0.8)
Epilepsy	0	1 (2.1)	1 (0.8)
Facial paresis	1 (1.2)	0	1 (0.8)
Formication	0	1 (2.1)	1 (0.8)
Lethargy	0	1 (2.1)	1 (0.8)
Leukoencephalopathy	0	1 (2.1)	1 (0.8)
Paraesthesia	0	1 (2.1)	1 (0.8)
Parkinson's disease	1 (1.2)	0	1 (0.8)
Somnolence	0	1 (2.1)	1 (0.8)
Syncope	1 (1.2)	0	1 (0.8)
Tremor	1 (1.2)	0	1 (0.8)
Renal and urinary disorders	17 (20.7)	8 (17.0)	25 (19.4)
Acute kidney injury	3 (3.7)	1 (2.1)	4 (3.1)
Urinary incontinence	1 (1.2)	3 (6.4)	4 (3.1)
Dysuria	1 (1.2)	2 (4.3)	3 (2.3)
Haematuria	1 (1.2)	2 (4.3)	3 (2.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Renal and urinary disorders			
Hydronephrosis	3 (3.7)	0	3 (2.3)
Micturition urgency	1 (1.2)	2 (4.3)	3 (2.3)
Chromaturia	1 (1.2)	1 (2.1)	2 (1.6)
Renal colic	2 (2.4)	0	2 (1.6)
Urogenital fistula	2 (2.4)	0	2 (1.6)
Nephritis	0	1 (2.1)	1 (0.8)
Proteinuria	1 (1.2)	0	1 (0.8)
Renal failure	1 (1.2)	0	1 (0.8)
Tubulointerstitial nephritis	1 (1.2)	0	1 (0.8)
Urinary tract obstruction	1 (1.2)	0	1 (0.8)
Urinary tract pain	0	1 (2.1)	1 (0.8)
Urine abnormality	0	1 (2.1)	1 (0.8)
Urine odour abnormal	0	1 (2.1)	1 (0.8)
Vascular disorders	11 (13.4)	14 (29.8)	25 (19.4)
Hypertension	2 (2.4)	5 (10.6)	7 (5.4)
Deep vein thrombosis	1 (1.2)	4 (8.5)	5 (3.9)
Hot flush	2 (2.4)	3 (6.4)	5 (3.9)
Flushing	2 (2.4)	1 (2.1)	3 (2.3)
Hypotension	2 (2.4)	0	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Vascular disorders			
Lymphoedema	1 (1.2)	1 (2.1)	2 (1.6)
Thrombophlebitis superficial	1 (1.2)	1 (2.1)	2 (1.6)
Embolism	1 (1.2)	0	1 (0.8)
Peripheral venous disease	1 (1.2)	0	1 (0.8)
Shock	1 (1.2)	0	1 (0.8)
Varicose vein	0	1 (2.1)	1 (0.8)
Reproductive system and breast disorders	13 (15.9)	10 (21.3)	23 (17.8)
Pelvic pain	3 (3.7)	4 (8.5)	7 (5.4)
Vaginal discharge	3 (3.7)	2 (4.3)	5 (3.9)
Vaginal haemorrhage	3 (3.7)	2 (4.3)	5 (3.9)
Female genital tract fistula	2 (2.4)	0	2 (1.6)
Metrorrhagia	2 (2.4)	0	2 (1.6)
Vulvovaginal dryness	0	2 (4.3)	2 (1.6)
Breast haematoma	0	1 (2.1)	1 (0.8)
Perineal pain	1 (1.2)	0	1 (0.8)
Vulval disorder	1 (1.2)	0	1 (0.8)
Vulvovaginal pain	0	1 (2.1)	1 (0.8)
Psychiatric disorders	14 (17.1)	8 (17.0)	22 (17.1)
Insomnia	4 (4.9)	4 (8.5)	8 (6.2)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Psychiatric disorders			
Anxiety	4 (4.9)	1 (2.1)	5 (3.9)
Depression	4 (4.9)	0	4 (3.1)
Confusional state	1 (1.2)	1 (2.1)	2 (1.6)
Depressed mood	1 (1.2)	1 (2.1)	2 (1.6)
Agitation	0	1 (2.1)	1 (0.8)
Alcoholism	1 (1.2)	0	1 (0.8)
Bradyphrenia	0	1 (2.1)	1 (0.8)
Mood altered	1 (1.2)	0	1 (0.8)
Nervousness	1 (1.2)	0	1 (0.8)
Injury, poisoning and procedural complications	11 (13.4)	7 (14.9)	18 (14.0)
Contusion	1 (1.2)	1 (2.1)	2 (1.6)
Gastroenteritis radiation	0	2 (4.3)	2 (1.6)
Ligament sprain	2 (2.4)	0	2 (1.6)
Wound	1 (1.2)	1 (2.1)	2 (1.6)
Compression fracture	0	1 (2.1)	1 (0.8)
Fall	1 (1.2)	0	1 (0.8)
Procedural pain	0	1 (2.1)	1 (0.8)
Skin abrasion	1 (1.2)	0	1 (0.8)
Skin laceration	0	1 (2.1)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Injury, poisoning and procedural complications			
Spinal compression fracture	1 (1.2)	0	1 (0.8)
Stoma site pain	1 (1.2)	0	1 (0.8)
Stress fracture	1 (1.2)	0	1 (0.8)
Tendon rupture	1 (1.2)	0	1 (0.8)
Thermal burn	0	1 (2.1)	1 (0.8)
Toxicity to various agents	1 (1.2)	0	1 (0.8)
Wound complication	0	1 (2.1)	1 (0.8)
Wound dehiscence	1 (1.2)	0	1 (0.8)
Eye disorders	7 (8.5)	6 (12.8)	13 (10.1)
Dry eye	3 (3.7)	1 (2.1)	4 (3.1)
Vision blurred	0	3 (6.4)	3 (2.3)
Cataract	1 (1.2)	1 (2.1)	2 (1.6)
Diplopia	0	1 (2.1)	1 (0.8)
Eye irritation	1 (1.2)	0	1 (0.8)
Iridocyclitis	0	1 (2.1)	1 (0.8)
Lacrimation increased	1 (1.2)	0	1 (0.8)
Ocular discomfort	1 (1.2)	0	1 (0.8)
Uveitis	1 (1.2)	0	1 (0.8)
Vitreous floaters	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Endocrine disorders	7 (8.5)	5 (10.6)	12 (9.3)
Hypothyroidism	5 (6.1)	5 (10.6)	10 (7.8)
Hyperthyroidism	3 (3.7)	1 (2.1)	4 (3.1)
Adrenal insufficiency	0	1 (2.1)	1 (0.8)
Glucocorticoid deficiency	1 (1.2)	0	1 (0.8)
Hypophysitis	1 (1.2)	0	1 (0.8)
Cardiac disorders	5 (6.1)	2 (4.3)	7 (5.4)
Atrial fibrillation	2 (2.4)	0	2 (1.6)
Tachycardia	1 (1.2)	1 (2.1)	2 (1.6)
Angina pectoris	0	1 (2.1)	1 (0.8)
Bradycardia	0	1 (2.1)	1 (0.8)
Myocardial infarction	0	1 (2.1)	1 (0.8)
Pericardial effusion	1 (1.2)	0	1 (0.8)
Sinus tachycardia	1 (1.2)	0	1 (0.8)
Supraventricular extrasystoles	0	1 (2.1)	1 (0.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5 (6.1)	1 (2.1)	6 (4.7)
Tumour pain	1 (1.2)	1 (2.1)	2 (1.6)
Cancer pain	1 (1.2)	0	1 (0.8)
Colon adenoma	1 (1.2)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.22a Subgroup Analysis of Treatment-Emergent Adverse Events by number of Prior Therapies by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	1 Prior Therapy (N=82)	≥2 Prior Therapies (N=47)	Total (N=129)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma	1 (1.2)	0	1 (0.8)
Seborrhoeic keratosis	1 (1.2)	0	1 (0.8)
Ear and labyrinth disorders	1 (1.2)	4 (8.5)	5 (3.9)
Tinnitus	0	2 (4.3)	2 (1.6)
Vertigo	0	2 (4.3)	2 (1.6)
Cerumen impaction	1 (1.2)	0	1 (0.8)
Hypoacusis	1 (1.2)	0	1 (0.8)
Hepatobiliary disorders	0	2 (4.3)	2 (1.6)
Cholecystitis	0	1 (2.1)	1 (0.8)
Hepatic function abnormal	0	1 (2.1)	1 (0.8)
Hypertransaminasaemia	0	1 (2.1)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Any Adverse Events	87 (94.6)	33 (97.1)	120 (95.2)
General disorders and administration site conditions	58 (63.0)	23 (67.6)	81 (64.3)
Fatigue	24 (26.1)	7 (20.6)	31 (24.6)
Asthenia	17 (18.5)	11 (32.4)	28 (22.2)
Pyrexia	8 (8.7)	5 (14.7)	13 (10.3)
Oedema peripheral	10 (10.9)	1 (2.9)	11 (8.7)
Chills	5 (5.4)	1 (2.9)	6 (4.8)
Pain	3 (3.3)	1 (2.9)	4 (3.2)
Oedema	1 (1.1)	2 (5.9)	3 (2.4)
Peripheral swelling	3 (3.3)	0	3 (2.4)
Chest discomfort	1 (1.1)	1 (2.9)	2 (1.6)
General physical health deterioration	1 (1.1)	1 (2.9)	2 (1.6)
Influenza like illness	0	2 (5.9)	2 (1.6)
Non-cardiac chest pain	2 (2.2)	0	2 (1.6)
Catheter site erythema	1 (1.1)	0	1 (0.8)
Catheter site pruritus	1 (1.1)	0	1 (0.8)
Complication associated with device	0	1 (2.9)	1 (0.8)
Early satiety	0	1 (2.9)	1 (0.8)
Hernia pain	0	1 (2.9)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
General disorders and administration site conditions			
Hyperthermia	1 (1.1)	0	1 (0.8)
Localised oedema	1 (1.1)	0	1 (0.8)
Malaise	1 (1.1)	0	1 (0.8)
Mucosal inflammation	1 (1.1)	0	1 (0.8)
Gastrointestinal disorders	56 (60.9)	23 (67.6)	79 (62.7)
Nausea	30 (32.6)	10 (29.4)	40 (31.7)
Diarrhoea	28 (30.4)	7 (20.6)	35 (27.8)
Constipation	18 (19.6)	7 (20.6)	25 (19.8)
Vomiting	15 (16.3)	9 (26.5)	24 (19.0)
Abdominal pain	12 (13.0)	9 (26.5)	21 (16.7)
Abdominal distension	6 (6.5)	3 (8.8)	9 (7.1)
Dyspepsia	3 (3.3)	3 (8.8)	6 (4.8)
Stomatitis	4 (4.3)	2 (5.9)	6 (4.8)
Abdominal pain upper	3 (3.3)	1 (2.9)	4 (3.2)
Gastrooesophageal reflux disease	4 (4.3)	0	4 (3.2)
Abdominal pain lower	3 (3.3)	0	3 (2.4)
Colitis	3 (3.3)	0	3 (2.4)
Dry mouth	3 (3.3)	0	3 (2.4)
Haemorrhoids	3 (3.3)	0	3 (2.4)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Gastrointestinal disorders			
Mouth ulceration	2 (2.2)	1 (2.9)	3 (2.4)
Anal incontinence	1 (1.1)	1 (2.9)	2 (1.6)
Anorectal discomfort	2 (2.2)	0	2 (1.6)
Ascites	1 (1.1)	1 (2.9)	2 (1.6)
Gastritis	2 (2.2)	0	2 (1.6)
Intestinal obstruction	2 (2.2)	0	2 (1.6)
Proctalgia	2 (2.2)	0	2 (1.6)
Rectal haemorrhage	2 (2.2)	0	2 (1.6)
Anal haemorrhage	0	1 (2.9)	1 (0.8)
Cheilitis	1 (1.1)	0	1 (0.8)
Chronic gastritis	1 (1.1)	0	1 (0.8)
Colonic fistula	1 (1.1)	0	1 (0.8)
Dumping syndrome	0	1 (2.9)	1 (0.8)
Enterocolitis haemorrhagic	1 (1.1)	0	1 (0.8)
Flatulence	1 (1.1)	0	1 (0.8)
Gastric ulcer	1 (1.1)	0	1 (0.8)
Gastric ulcer perforation	1 (1.1)	0	1 (0.8)
Haematemesis	1 (1.1)	0	1 (0.8)
Haematochezia	1 (1.1)	0	1 (0.8)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Gastrointestinal disorders			
Large intestine polyp	1 (1.1)	0	1 (0.8)
Lip swelling	1 (1.1)	0	1 (0.8)
Melaena	1 (1.1)	0	1 (0.8)
Odynophagia	1 (1.1)	0	1 (0.8)
Oral pain	1 (1.1)	0	1 (0.8)
Pancreatitis	1 (1.1)	0	1 (0.8)
Pancreatitis acute	0	1 (2.9)	1 (0.8)
Musculoskeletal and connective tissue disorders	43 (46.7)	12 (35.3)	55 (43.7)
Back pain	12 (13.0)	7 (20.6)	19 (15.1)
Arthralgia	17 (18.5)	1 (2.9)	18 (14.3)
Myalgia	11 (12.0)	2 (5.9)	13 (10.3)
Muscular weakness	8 (8.7)	1 (2.9)	9 (7.1)
Pain in extremity	6 (6.5)	2 (5.9)	8 (6.3)
Muscle spasms	3 (3.3)	2 (5.9)	5 (4.0)
Musculoskeletal pain	2 (2.2)	2 (5.9)	4 (3.2)
Arthritis	2 (2.2)	0	2 (1.6)
Flank pain	2 (2.2)	0	2 (1.6)
Musculoskeletal stiffness	2 (2.2)	0	2 (1.6)
Osteoarthritis	1 (1.1)	1 (2.9)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis	1 (1.1)	1 (2.9)	2 (1.6)
Tendon pain	1 (1.1)	1 (2.9)	2 (1.6)
Coccydynia	1 (1.1)	0	1 (0.8)
Joint range of motion decreased	1 (1.1)	0	1 (0.8)
Joint swelling	1 (1.1)	0	1 (0.8)
Limb discomfort	1 (1.1)	0	1 (0.8)
Muscle discomfort	1 (1.1)	0	1 (0.8)
Muscle tightness	1 (1.1)	0	1 (0.8)
Neck pain	1 (1.1)	0	1 (0.8)
Osteopenia	1 (1.1)	0	1 (0.8)
Osteoporosis	1 (1.1)	0	1 (0.8)
Pain in jaw	1 (1.1)	0	1 (0.8)
Rheumatoid arthritis	1 (1.1)	0	1 (0.8)
Scoliosis	1 (1.1)	0	1 (0.8)
Spinal stenosis	1 (1.1)	0	1 (0.8)
Infections and infestations	42 (45.7)	11 (32.4)	53 (42.1)
Urinary tract infection	17 (18.5)	2 (5.9)	19 (15.1)
Upper respiratory tract infection	7 (7.6)	2 (5.9)	9 (7.1)
Bronchitis	4 (4.3)	2 (5.9)	6 (4.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Infections and infestations			
Nasopharyngitis	6 (6.5)	0	6 (4.8)
Pneumonia	6 (6.5)	0	6 (4.8)
Sepsis	2 (2.2)	2 (5.9)	4 (3.2)
Cellulitis	1 (1.1)	1 (2.9)	2 (1.6)
Cystitis	2 (2.2)	0	2 (1.6)
Gastroenteritis	2 (2.2)	0	2 (1.6)
Oral candidiasis	1 (1.1)	1 (2.9)	2 (1.6)
Pharyngitis	2 (2.2)	0	2 (1.6)
Pyelonephritis	1 (1.1)	1 (2.9)	2 (1.6)
Rhinitis	2 (2.2)	0	2 (1.6)
Vaginal infection	2 (2.2)	0	2 (1.6)
Abdominal infection	1 (1.1)	0	1 (0.8)
Bacteraemia	1 (1.1)	0	1 (0.8)
Conjunctivitis	1 (1.1)	0	1 (0.8)
Demodicidosis	1 (1.1)	0	1 (0.8)
Ear infection	1 (1.1)	0	1 (0.8)
Gastroenteritis viral	1 (1.1)	0	1 (0.8)
Gastrointestinal viral infection	0	1 (2.9)	1 (0.8)
Genital infection	0	1 (2.9)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Infections and infestations			
Herpes virus infection	1 (1.1)	0	1 (0.8)
Infected lymphocele	1 (1.1)	0	1 (0.8)
Lower respiratory tract infection	1 (1.1)	0	1 (0.8)
Oral herpes	1 (1.1)	0	1 (0.8)
Sinusitis	1 (1.1)	0	1 (0.8)
Vulvovaginal candidiasis	1 (1.1)	0	1 (0.8)
Wound infection	1 (1.1)	0	1 (0.8)
Investigations	37 (40.2)	11 (32.4)	48 (38.1)
Alanine aminotransferase increased	6 (6.5)	3 (8.8)	9 (7.1)
Aspartate aminotransferase increased	6 (6.5)	3 (8.8)	9 (7.1)
Blood creatinine increased	7 (7.6)	2 (5.9)	9 (7.1)
Weight decreased	7 (7.6)	2 (5.9)	9 (7.1)
Amylase increased	6 (6.5)	0	6 (4.8)
Weight increased	5 (5.4)	0	5 (4.0)
Gamma-glutamyltransferase increased	4 (4.3)	0	4 (3.2)
Lipase increased	3 (3.3)	1 (2.9)	4 (3.2)
Blood alkaline phosphatase increased	3 (3.3)	0	3 (2.4)
Transaminases increased	2 (2.2)	1 (2.9)	3 (2.4)
Blood lactate dehydrogenase increased	1 (1.1)	1 (2.9)	2 (1.6)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Investigations			
Lymphocyte count decreased	2 (2.2)	0	2 (1.6)
Activated partial thromboplastin time prolonged	1 (1.1)	0	1 (0.8)
Blood bilirubin increased	1 (1.1)	0	1 (0.8)
Blood corticotrophin decreased	0	1 (2.9)	1 (0.8)
Blood iron decreased	0	1 (2.9)	1 (0.8)
Blood potassium decreased	1 (1.1)	0	1 (0.8)
Blood thyroid stimulating hormone decreased	1 (1.1)	0	1 (0.8)
Blood thyroid stimulating hormone increased	1 (1.1)	0	1 (0.8)
Blood urea increased	1 (1.1)	0	1 (0.8)
Blood urine present	1 (1.1)	0	1 (0.8)
Electrocardiogram QT prolonged	1 (1.1)	0	1 (0.8)
Haemoglobin decreased	1 (1.1)	0	1 (0.8)
Mean platelet volume decreased	0	1 (2.9)	1 (0.8)
Neutrophil count decreased	1 (1.1)	0	1 (0.8)
Neutrophil count increased	1 (1.1)	0	1 (0.8)
Nitrite urine present	1 (1.1)	0	1 (0.8)
Serum ferritin decreased	1 (1.1)	0	1 (0.8)
Thyroxine increased	1 (1.1)	0	1 (0.8)
White blood cell count decreased	1 (1.1)	0	1 (0.8)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Investigations			
White blood cell count increased	1 (1.1)	0	1 (0.8)
Respiratory, thoracic and mediastinal disorders	32 (34.8)	10 (29.4)	42 (33.3)
Cough	17 (18.5)	2 (5.9)	19 (15.1)
Productive cough	8 (8.7)	1 (2.9)	9 (7.1)
Dyspnoea	4 (4.3)	4 (11.8)	8 (6.3)
Pulmonary embolism	3 (3.3)	1 (2.9)	4 (3.2)
Nasal congestion	3 (3.3)	0	3 (2.4)
Rhinorrhoea	3 (3.3)	0	3 (2.4)
Dysphonia	2 (2.2)	0	2 (1.6)
Oropharyngeal pain	2 (2.2)	0	2 (1.6)
Pneumonitis	2 (2.2)	0	2 (1.6)
Sneezing	1 (1.1)	1 (2.9)	2 (1.6)
Throat irritation	1 (1.1)	1 (2.9)	2 (1.6)
Aspiration	1 (1.1)	0	1 (0.8)
Choking sensation	1 (1.1)	0	1 (0.8)
Dyspnoea exertional	1 (1.1)	0	1 (0.8)
Epistaxis	1 (1.1)	0	1 (0.8)
Hiccups	1 (1.1)	0	1 (0.8)
Hypoxia	1 (1.1)	0	1 (0.8)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Respiratory, thoracic and mediastinal disorders			
Increased bronchial secretion	1 (1.1)	0	1 (0.8)
Increased upper airway secretion	1 (1.1)	0	1 (0.8)
Interstitial lung disease	0	1 (2.9)	1 (0.8)
Pleural effusion	1 (1.1)	0	1 (0.8)
Pulmonary infarction	1 (1.1)	0	1 (0.8)
Sputum retention	1 (1.1)	0	1 (0.8)
Wheezing	0	1 (2.9)	1 (0.8)
Metabolism and nutrition disorders	26 (28.3)	15 (44.1)	41 (32.5)
Decreased appetite	10 (10.9)	6 (17.6)	16 (12.7)
Hypomagnesaemia	7 (7.6)	3 (8.8)	10 (7.9)
Hypokalaemia	6 (6.5)	2 (5.9)	8 (6.3)
Hyponatraemia	4 (4.3)	2 (5.9)	6 (4.8)
Dehydration	2 (2.2)	3 (8.8)	5 (4.0)
Hyperglycaemia	2 (2.2)	1 (2.9)	3 (2.4)
Hyperkalaemia	1 (1.1)	2 (5.9)	3 (2.4)
Hypoalbuminaemia	1 (1.1)	2 (5.9)	3 (2.4)
Hypercalcaemia	1 (1.1)	1 (2.9)	2 (1.6)
Folate deficiency	1 (1.1)	0	1 (0.8)
Hyperamylasaemia	1 (1.1)	0	1 (0.8)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Metabolism and nutrition disorders			
Hyperglycaemic hyperosmolar nonketotic syndrome	1 (1.1)	0	1 (0.8)
Hypocalcaemia	1 (1.1)	0	1 (0.8)
Hypophosphataemia	1 (1.1)	0	1 (0.8)
Increased appetite	0	1 (2.9)	1 (0.8)
Iron deficiency	1 (1.1)	0	1 (0.8)
Malnutrition	1 (1.1)	0	1 (0.8)
Metabolic syndrome	1 (1.1)	0	1 (0.8)
Blood and lymphatic system disorders	26 (28.3)	14 (41.2)	40 (31.7)
Anaemia	23 (25.0)	12 (35.3)	35 (27.8)
Neutropenia	4 (4.3)	2 (5.9)	6 (4.8)
Leukocytosis	0	2 (5.9)	2 (1.6)
Leukopenia	2 (2.2)	0	2 (1.6)
Iron deficiency anaemia	1 (1.1)	0	1 (0.8)
Lymphopenia	1 (1.1)	0	1 (0.8)
Skin and subcutaneous tissue disorders	27 (29.3)	13 (38.2)	40 (31.7)
Pruritus	13 (14.1)	5 (14.7)	18 (14.3)
Rash	10 (10.9)	3 (8.8)	13 (10.3)
Dry skin	1 (1.1)	3 (8.8)	4 (3.2)
Skin lesion	3 (3.3)	0	3 (2.4)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Skin and subcutaneous tissue disorders			
Urticaria	3 (3.3)	0	3 (2.4)
Alopecia	2 (2.2)	0	2 (1.6)
Eczema	1 (1.1)	1 (2.9)	2 (1.6)
Erythema	1 (1.1)	1 (2.9)	2 (1.6)
Dermatitis contact	0	1 (2.9)	1 (0.8)
Drug eruption	0	1 (2.9)	1 (0.8)
Hyperhidrosis	1 (1.1)	0	1 (0.8)
Hypertrichosis	1 (1.1)	0	1 (0.8)
Nail discolouration	1 (1.1)	0	1 (0.8)
Onychoclasis	1 (1.1)	0	1 (0.8)
Onychomadesis	0	1 (2.9)	1 (0.8)
Papule	0	1 (2.9)	1 (0.8)
Pemphigoid	1 (1.1)	0	1 (0.8)
Prurigo	0	1 (2.9)	1 (0.8)
Rash maculo-papular	1 (1.1)	0	1 (0.8)
Skin burning sensation	1 (1.1)	0	1 (0.8)
Skin ulcer	1 (1.1)	0	1 (0.8)
Skin warm	1 (1.1)	0	1 (0.8)
Nervous system disorders	26 (28.3)	6 (17.6)	32 (25.4)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Nervous system disorders			
Headache	10 (10.9)	2 (5.9)	12 (9.5)
Dizziness	7 (7.6)	2 (5.9)	9 (7.1)
Neuropathy peripheral	2 (2.2)	2 (5.9)	4 (3.2)
Dysgeusia	3 (3.3)	0	3 (2.4)
Carpal tunnel syndrome	1 (1.1)	1 (2.9)	2 (1.6)
Cognitive disorder	2 (2.2)	0	2 (1.6)
Neuralgia	1 (1.1)	1 (2.9)	2 (1.6)
Apraxia	1 (1.1)	0	1 (0.8)
Dysaesthesia	1 (1.1)	0	1 (0.8)
Dysarthria	0	1 (2.9)	1 (0.8)
Encephalopathy	1 (1.1)	0	1 (0.8)
Facial paresis	0	1 (2.9)	1 (0.8)
Formication	1 (1.1)	0	1 (0.8)
Leukoencephalopathy	1 (1.1)	0	1 (0.8)
Paraesthesia	1 (1.1)	0	1 (0.8)
Parkinson's disease	1 (1.1)	0	1 (0.8)
Somnolence	1 (1.1)	0	1 (0.8)
Syncope	1 (1.1)	0	1 (0.8)
Tremor	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Renal and urinary disorders	21 (22.8)	4 (11.8)	25 (19.8)
Acute kidney injury	4 (4.3)	0	4 (3.2)
Urinary incontinence	4 (4.3)	0	4 (3.2)
Dysuria	3 (3.3)	0	3 (2.4)
Haematuria	3 (3.3)	0	3 (2.4)
Hydronephrosis	1 (1.1)	2 (5.9)	3 (2.4)
Micturition urgency	3 (3.3)	0	3 (2.4)
Chromaturia	2 (2.2)	0	2 (1.6)
Renal colic	1 (1.1)	1 (2.9)	2 (1.6)
Urogenital fistula	2 (2.2)	0	2 (1.6)
Nephritis	1 (1.1)	0	1 (0.8)
Proteinuria	0	1 (2.9)	1 (0.8)
Renal failure	1 (1.1)	0	1 (0.8)
Tubulointerstitial nephritis	1 (1.1)	0	1 (0.8)
Urinary tract obstruction	1 (1.1)	0	1 (0.8)
Urinary tract pain	1 (1.1)	0	1 (0.8)
Urine abnormality	1 (1.1)	0	1 (0.8)
Urine odour abnormal	1 (1.1)	0	1 (0.8)
Vascular disorders	16 (17.4)	7 (20.6)	23 (18.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Vascular disorders			
Deep vein thrombosis	3 (3.3)	2 (5.9)	5 (4.0)
Hot flush	3 (3.3)	2 (5.9)	5 (4.0)
Hypertension	5 (5.4)	0	5 (4.0)
Flushing	1 (1.1)	2 (5.9)	3 (2.4)
Hypotension	2 (2.2)	0	2 (1.6)
Lymphoedema	1 (1.1)	1 (2.9)	2 (1.6)
Thrombophlebitis superficial	1 (1.1)	1 (2.9)	2 (1.6)
Embolism	1 (1.1)	0	1 (0.8)
Peripheral venous disease	1 (1.1)	0	1 (0.8)
Shock	1 (1.1)	0	1 (0.8)
Varicose vein	1 (1.1)	0	1 (0.8)
Reproductive system and breast disorders	17 (18.5)	5 (14.7)	22 (17.5)
Pelvic pain	6 (6.5)	1 (2.9)	7 (5.6)
Vaginal discharge	4 (4.3)	1 (2.9)	5 (4.0)
Vaginal haemorrhage	4 (4.3)	1 (2.9)	5 (4.0)
Female genital tract fistula	2 (2.2)	0	2 (1.6)
Metrorrhagia	1 (1.1)	1 (2.9)	2 (1.6)
Breast haematoma	1 (1.1)	0	1 (0.8)
Perineal pain	0	1 (2.9)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Reproductive system and breast disorders			
Vulval disorder	0	1 (2.9)	1 (0.8)
Vulvovaginal dryness	1 (1.1)	0	1 (0.8)
Vulvovaginal pain	1 (1.1)	0	1 (0.8)
Psychiatric disorders	13 (14.1)	8 (23.5)	21 (16.7)
Insomnia	7 (7.6)	1 (2.9)	8 (6.3)
Anxiety	0	5 (14.7)	5 (4.0)
Depression	2 (2.2)	2 (5.9)	4 (3.2)
Confusional state	1 (1.1)	1 (2.9)	2 (1.6)
Depressed mood	2 (2.2)	0	2 (1.6)
Agitation	1 (1.1)	0	1 (0.8)
Alcoholism	1 (1.1)	0	1 (0.8)
Bradyphrenia	1 (1.1)	0	1 (0.8)
Nervousness	0	1 (2.9)	1 (0.8)
Injury, poisoning and procedural complications	15 (16.3)	2 (5.9)	17 (13.5)
Contusion	2 (2.2)	0	2 (1.6)
Gastroenteritis radiation	2 (2.2)	0	2 (1.6)
Wound	2 (2.2)	0	2 (1.6)
Compression fracture	1 (1.1)	0	1 (0.8)
Fall	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Injury, poisoning and procedural complications			
Ligament sprain	1 (1.1)	0	1 (0.8)
Procedural pain	1 (1.1)	0	1 (0.8)
Skin abrasion	0	1 (2.9)	1 (0.8)
Skin laceration	1 (1.1)	0	1 (0.8)
Spinal compression fracture	1 (1.1)	0	1 (0.8)
Stoma site pain	1 (1.1)	0	1 (0.8)
Stress fracture	1 (1.1)	0	1 (0.8)
Tendon rupture	1 (1.1)	0	1 (0.8)
Thermal burn	0	1 (2.9)	1 (0.8)
Toxicity to various agents	1 (1.1)	0	1 (0.8)
Wound complication	1 (1.1)	0	1 (0.8)
Wound dehiscence	1 (1.1)	0	1 (0.8)
Eye disorders	9 (9.8)	4 (11.8)	13 (10.3)
Dry eye	1 (1.1)	3 (8.8)	4 (3.2)
Vision blurred	2 (2.2)	1 (2.9)	3 (2.4)
Cataract	2 (2.2)	0	2 (1.6)
Diplopia	1 (1.1)	0	1 (0.8)
Eye irritation	1 (1.1)	0	1 (0.8)
Iridocyclitis	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Eye disorders			
Lacrimation increased	1 (1.1)	0	1 (0.8)
Ocular discomfort	1 (1.1)	0	1 (0.8)
Uveitis	1 (1.1)	0	1 (0.8)
Vitreous floaters	1 (1.1)	0	1 (0.8)
Endocrine disorders	8 (8.7)	3 (8.8)	11 (8.7)
Hypothyroidism	8 (8.7)	1 (2.9)	9 (7.1)
Hyperthyroidism	3 (3.3)	1 (2.9)	4 (3.2)
Adrenal insufficiency	1 (1.1)	0	1 (0.8)
Glucocorticoid deficiency	0	1 (2.9)	1 (0.8)
Hypophysitis	0	1 (2.9)	1 (0.8)
Cardiac disorders	2 (2.2)	4 (11.8)	6 (4.8)
Atrial fibrillation	1 (1.1)	1 (2.9)	2 (1.6)
Angina pectoris	1 (1.1)	0	1 (0.8)
Bradycardia	0	1 (2.9)	1 (0.8)
Myocardial infarction	1 (1.1)	0	1 (0.8)
Pericardial effusion	0	1 (2.9)	1 (0.8)
Sinus tachycardia	0	1 (2.9)	1 (0.8)
Supraventricular extrasystoles	1 (1.1)	0	1 (0.8)
Tachycardia	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=92)	No Prior Radiation (N=34)	Total (N=126)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	4 (4.3)	2 (5.9)	6 (4.8)
Tumour pain	1 (1.1)	1 (2.9)	2 (1.6)
Cancer pain	0	1 (2.9)	1 (0.8)
Colon adenoma	1 (1.1)	0	1 (0.8)
Malignant melanoma	1 (1.1)	0	1 (0.8)
Seborrhoeic keratosis	1 (1.1)	0	1 (0.8)
Ear and labyrinth disorders	5 (5.4)	0	5 (4.0)
Tinnitus	2 (2.2)	0	2 (1.6)
Vertigo	2 (2.2)	0	2 (1.6)
Cerumen impaction	1 (1.1)	0	1 (0.8)
Hypoacusis	1 (1.1)	0	1 (0.8)
Hepatobiliary disorders	1 (1.1)	1 (2.9)	2 (1.6)
Cholecystitis	1 (1.1)	0	1 (0.8)
Hepatic function abnormal	0	1 (2.9)	1 (0.8)
Hypertransaminasaemia	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=2)	No Prior Radiation (N=1)	Total (N=3)
Any Adverse Events	2 (100)	1 (100)	3 (100)
Nervous system disorders	2 (100)	1 (100)	3 (100)
Epilepsy	0	1 (100)	1 (33.3)
Lethargy	1 (50.0)	0	1 (33.3)
Neuralgia	1 (50.0)	0	1 (33.3)
Gastrointestinal disorders	2 (100)	0	2 (66.7)
Nausea	2 (100)	0	2 (66.7)
Bile acid malabsorption	1 (50.0)	0	1 (33.3)
Diarrhoea	1 (50.0)	0	1 (33.3)
Dry mouth	1 (50.0)	0	1 (33.3)
General disorders and administration site conditions	2 (100)	0	2 (66.7)
Oedema peripheral	2 (100)	0	2 (66.7)
Fatigue	1 (50.0)	0	1 (33.3)
Pyrexia	1 (50.0)	0	1 (33.3)
Infections and infestations	2 (100)	0	2 (66.7)
Candida infection	1 (50.0)	0	1 (33.3)
Fungal skin infection	1 (50.0)	0	1 (33.3)
Sinusitis	1 (50.0)	0	1 (33.3)
Upper respiratory tract infection	1 (50.0)	0	1 (33.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=2)	No Prior Radiation (N=1)	Total (N=3)
Infections and infestations			
Urinary tract infection	1 (50.0)	0	1 (33.3)
Viral infection	1 (50.0)	0	1 (33.3)
Metabolism and nutrition disorders	1 (50.0)	1 (100)	2 (66.7)
Gout	1 (50.0)	0	1 (33.3)
Hyperammonaemia	0	1 (100)	1 (33.3)
Hyponatraemia	0	1 (100)	1 (33.3)
Hypophagia	0	1 (100)	1 (33.3)
Musculoskeletal and connective tissue disorders	2 (100)	0	2 (66.7)
Arthralgia	2 (100)	0	2 (66.7)
Musculoskeletal pain	1 (50.0)	0	1 (33.3)
Myalgia	1 (50.0)	0	1 (33.3)
Synovial cyst	1 (50.0)	0	1 (33.3)
Tendonitis	1 (50.0)	0	1 (33.3)
Respiratory, thoracic and mediastinal disorders	2 (100)	0	2 (66.7)
Cough	2 (100)	0	2 (66.7)
Dyspnoea	1 (50.0)	0	1 (33.3)
Vascular disorders	1 (50.0)	1 (100)	2 (66.7)
Hypertension	1 (50.0)	1 (100)	2 (66.7)
Cardiac disorders	1 (50.0)	0	1 (33.3)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=2)	No Prior Radiation (N=1)	Total (N=3)
Cardiac disorders			
Tachycardia	1 (50.0)	0	1 (33.3)
Endocrine disorders	1 (50.0)	0	1 (33.3)
Hypothyroidism	1 (50.0)	0	1 (33.3)
Injury, poisoning and procedural complications	1 (50.0)	0	1 (33.3)
Ligament sprain	1 (50.0)	0	1 (33.3)
Investigations	1 (50.0)	0	1 (33.3)
Serum ferritin decreased	1 (50.0)	0	1 (33.3)
Psychiatric disorders	1 (50.0)	0	1 (33.3)
Mood altered	1 (50.0)	0	1 (33.3)
Reproductive system and breast disorders	1 (50.0)	0	1 (33.3)
Vulvovaginal dryness	1 (50.0)	0	1 (33.3)
Skin and subcutaneous tissue disorders	1 (50.0)	0	1 (33.3)
Dry skin	1 (50.0)	0	1 (33.3)
Night sweats	1 (50.0)	0	1 (33.3)
Pain of skin	1 (50.0)	0	1 (33.3)
Skin reaction	1 (50.0)	0	1 (33.3)
Urticaria	1 (50.0)	0	1 (33.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Any Adverse Events	89 (94.7)	34 (97.1)	123 (95.3)
General disorders and administration site conditions	60 (63.8)	23 (65.7)	83 (64.3)
Fatigue	25 (26.6)	7 (20.0)	32 (24.8)
Asthenia	17 (18.1)	11 (31.4)	28 (21.7)
Pyrexia	9 (9.6)	5 (14.3)	14 (10.9)
Oedema peripheral	12 (12.8)	1 (2.9)	13 (10.1)
Chills	5 (5.3)	1 (2.9)	6 (4.7)
Pain	3 (3.2)	1 (2.9)	4 (3.1)
Oedema	1 (1.1)	2 (5.7)	3 (2.3)
Peripheral swelling	3 (3.2)	0	3 (2.3)
Chest discomfort	1 (1.1)	1 (2.9)	2 (1.6)
General physical health deterioration	1 (1.1)	1 (2.9)	2 (1.6)
Influenza like illness	0	2 (5.7)	2 (1.6)
Non-cardiac chest pain	2 (2.1)	0	2 (1.6)
Catheter site erythema	1 (1.1)	0	1 (0.8)
Catheter site pruritus	1 (1.1)	0	1 (0.8)
Complication associated with device	0	1 (2.9)	1 (0.8)
Early satiety	0	1 (2.9)	1 (0.8)
Hernia pain	0	1 (2.9)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
General disorders and administration site conditions			
Hyperthermia	1 (1.1)	0	1 (0.8)
Localised oedema	1 (1.1)	0	1 (0.8)
Malaise	1 (1.1)	0	1 (0.8)
Mucosal inflammation	1 (1.1)	0	1 (0.8)
Gastrointestinal disorders	58 (61.7)	23 (65.7)	81 (62.8)
Nausea	32 (34.0)	10 (28.6)	42 (32.6)
Diarrhoea	29 (30.9)	7 (20.0)	36 (27.9)
Constipation	18 (19.1)	7 (20.0)	25 (19.4)
Vomiting	15 (16.0)	9 (25.7)	24 (18.6)
Abdominal pain	12 (12.8)	9 (25.7)	21 (16.3)
Abdominal distension	6 (6.4)	3 (8.6)	9 (7.0)
Dyspepsia	3 (3.2)	3 (8.6)	6 (4.7)
Stomatitis	4 (4.3)	2 (5.7)	6 (4.7)
Abdominal pain upper	3 (3.2)	1 (2.9)	4 (3.1)
Dry mouth	4 (4.3)	0	4 (3.1)
Gastrooesophageal reflux disease	4 (4.3)	0	4 (3.1)
Abdominal pain lower	3 (3.2)	0	3 (2.3)
Colitis	3 (3.2)	0	3 (2.3)
Haemorrhoids	3 (3.2)	0	3 (2.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Gastrointestinal disorders			
Mouth ulceration	2 (2.1)	1 (2.9)	3 (2.3)
Anal incontinence	1 (1.1)	1 (2.9)	2 (1.6)
Anorectal discomfort	2 (2.1)	0	2 (1.6)
Ascites	1 (1.1)	1 (2.9)	2 (1.6)
Gastritis	2 (2.1)	0	2 (1.6)
Intestinal obstruction	2 (2.1)	0	2 (1.6)
Proctalgia	2 (2.1)	0	2 (1.6)
Rectal haemorrhage	2 (2.1)	0	2 (1.6)
Anal haemorrhage	0	1 (2.9)	1 (0.8)
Bile acid malabsorption	1 (1.1)	0	1 (0.8)
Cheilitis	1 (1.1)	0	1 (0.8)
Chronic gastritis	1 (1.1)	0	1 (0.8)
Colonic fistula	1 (1.1)	0	1 (0.8)
Dumping syndrome	0	1 (2.9)	1 (0.8)
Enterocolitis haemorrhagic	1 (1.1)	0	1 (0.8)
Flatulence	1 (1.1)	0	1 (0.8)
Gastric ulcer	1 (1.1)	0	1 (0.8)
Gastric ulcer perforation	1 (1.1)	0	1 (0.8)
Haematemesis	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Gastrointestinal disorders			
Haematochezia	1 (1.1)	0	1 (0.8)
Large intestine polyp	1 (1.1)	0	1 (0.8)
Lip swelling	1 (1.1)	0	1 (0.8)
Melaena	1 (1.1)	0	1 (0.8)
Odynophagia	1 (1.1)	0	1 (0.8)
Oral pain	1 (1.1)	0	1 (0.8)
Pancreatitis	1 (1.1)	0	1 (0.8)
Pancreatitis acute	0	1 (2.9)	1 (0.8)
Musculoskeletal and connective tissue disorders	45 (47.9)	12 (34.3)	57 (44.2)
Arthralgia	19 (20.2)	1 (2.9)	20 (15.5)
Back pain	12 (12.8)	7 (20.0)	19 (14.7)
Myalgia	12 (12.8)	2 (5.7)	14 (10.9)
Muscular weakness	8 (8.5)	1 (2.9)	9 (7.0)
Pain in extremity	6 (6.4)	2 (5.7)	8 (6.2)
Muscle spasms	3 (3.2)	2 (5.7)	5 (3.9)
Musculoskeletal pain	3 (3.2)	2 (5.7)	5 (3.9)
Arthritis	2 (2.1)	0	2 (1.6)
Flank pain	2 (2.1)	0	2 (1.6)
Musculoskeletal stiffness	2 (2.1)	0	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Musculoskeletal and connective tissue disorders			
Osteoarthritis	1 (1.1)	1 (2.9)	2 (1.6)
Spinal osteoarthritis	1 (1.1)	1 (2.9)	2 (1.6)
Tendon pain	1 (1.1)	1 (2.9)	2 (1.6)
Coccydynia	1 (1.1)	0	1 (0.8)
Joint range of motion decreased	1 (1.1)	0	1 (0.8)
Joint swelling	1 (1.1)	0	1 (0.8)
Limb discomfort	1 (1.1)	0	1 (0.8)
Muscle discomfort	1 (1.1)	0	1 (0.8)
Muscle tightness	1 (1.1)	0	1 (0.8)
Neck pain	1 (1.1)	0	1 (0.8)
Osteopenia	1 (1.1)	0	1 (0.8)
Osteoporosis	1 (1.1)	0	1 (0.8)
Pain in jaw	1 (1.1)	0	1 (0.8)
Rheumatoid arthritis	1 (1.1)	0	1 (0.8)
Scoliosis	1 (1.1)	0	1 (0.8)
Spinal stenosis	1 (1.1)	0	1 (0.8)
Synovial cyst	1 (1.1)	0	1 (0.8)
Tendonitis	1 (1.1)	0	1 (0.8)
Infections and infestations	44 (46.8)	11 (31.4)	55 (42.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Infections and infestations			
Urinary tract infection	18 (19.1)	2 (5.7)	20 (15.5)
Upper respiratory tract infection	8 (8.5)	2 (5.7)	10 (7.8)
Bronchitis	4 (4.3)	2 (5.7)	6 (4.7)
Nasopharyngitis	6 (6.4)	0	6 (4.7)
Pneumonia	6 (6.4)	0	6 (4.7)
Sepsis	2 (2.1)	2 (5.7)	4 (3.1)
Cellulitis	1 (1.1)	1 (2.9)	2 (1.6)
Cystitis	2 (2.1)	0	2 (1.6)
Gastroenteritis	2 (2.1)	0	2 (1.6)
Oral candidiasis	1 (1.1)	1 (2.9)	2 (1.6)
Pharyngitis	2 (2.1)	0	2 (1.6)
Pyelonephritis	1 (1.1)	1 (2.9)	2 (1.6)
Rhinitis	2 (2.1)	0	2 (1.6)
Sinusitis	2 (2.1)	0	2 (1.6)
Vaginal infection	2 (2.1)	0	2 (1.6)
Abdominal infection	1 (1.1)	0	1 (0.8)
Bacteraemia	1 (1.1)	0	1 (0.8)
Candida infection	1 (1.1)	0	1 (0.8)
Conjunctivitis	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Infections and infestations			
Demodicidosis	1 (1.1)	0	1 (0.8)
Ear infection	1 (1.1)	0	1 (0.8)
Fungal skin infection	1 (1.1)	0	1 (0.8)
Gastroenteritis viral	1 (1.1)	0	1 (0.8)
Gastrointestinal viral infection	0	1 (2.9)	1 (0.8)
Genital infection	0	1 (2.9)	1 (0.8)
Herpes virus infection	1 (1.1)	0	1 (0.8)
Infected lymphocele	1 (1.1)	0	1 (0.8)
Lower respiratory tract infection	1 (1.1)	0	1 (0.8)
Oral herpes	1 (1.1)	0	1 (0.8)
Viral infection	1 (1.1)	0	1 (0.8)
Vulvovaginal candidiasis	1 (1.1)	0	1 (0.8)
Wound infection	1 (1.1)	0	1 (0.8)
Investigations	38 (40.4)	11 (31.4)	49 (38.0)
Alanine aminotransferase increased	6 (6.4)	3 (8.6)	9 (7.0)
Aspartate aminotransferase increased	6 (6.4)	3 (8.6)	9 (7.0)
Blood creatinine increased	7 (7.4)	2 (5.7)	9 (7.0)
Weight decreased	7 (7.4)	2 (5.7)	9 (7.0)
Amylase increased	6 (6.4)	0	6 (4.7)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Investigations			
Weight increased	5 (5.3)	0	5 (3.9)
Gamma-glutamyltransferase increased	4 (4.3)	0	4 (3.1)
Lipase increased	3 (3.2)	1 (2.9)	4 (3.1)
Blood alkaline phosphatase increased	3 (3.2)	0	3 (2.3)
Transaminases increased	2 (2.1)	1 (2.9)	3 (2.3)
Blood lactate dehydrogenase increased	1 (1.1)	1 (2.9)	2 (1.6)
Lymphocyte count decreased	2 (2.1)	0	2 (1.6)
Serum ferritin decreased	2 (2.1)	0	2 (1.6)
Activated partial thromboplastin time prolonged	1 (1.1)	0	1 (0.8)
Blood bilirubin increased	1 (1.1)	0	1 (0.8)
Blood corticotrophin decreased	0	1 (2.9)	1 (0.8)
Blood iron decreased	0	1 (2.9)	1 (0.8)
Blood potassium decreased	1 (1.1)	0	1 (0.8)
Blood thyroid stimulating hormone decreased	1 (1.1)	0	1 (0.8)
Blood thyroid stimulating hormone increased	1 (1.1)	0	1 (0.8)
Blood urea increased	1 (1.1)	0	1 (0.8)
Blood urine present	1 (1.1)	0	1 (0.8)
Electrocardiogram QT prolonged	1 (1.1)	0	1 (0.8)
Haemoglobin decreased	1 (1.1)	0	1 (0.8)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Investigations			
Mean platelet volume decreased	0	1 (2.9)	1 (0.8)
Neutrophil count decreased	1 (1.1)	0	1 (0.8)
Neutrophil count increased	1 (1.1)	0	1 (0.8)
Nitrite urine present	1 (1.1)	0	1 (0.8)
Thyroxine increased	1 (1.1)	0	1 (0.8)
White blood cell count decreased	1 (1.1)	0	1 (0.8)
White blood cell count increased	1 (1.1)	0	1 (0.8)
Respiratory, thoracic and mediastinal disorders	34 (36.2)	10 (28.6)	44 (34.1)
Cough	19 (20.2)	2 (5.7)	21 (16.3)
Dyspnoea	5 (5.3)	4 (11.4)	9 (7.0)
Productive cough	8 (8.5)	1 (2.9)	9 (7.0)
Pulmonary embolism	3 (3.2)	1 (2.9)	4 (3.1)
Nasal congestion	3 (3.2)	0	3 (2.3)
Rhinorrhoea	3 (3.2)	0	3 (2.3)
Dysphonia	2 (2.1)	0	2 (1.6)
Oropharyngeal pain	2 (2.1)	0	2 (1.6)
Pneumonitis	2 (2.1)	0	2 (1.6)
Sneezing	1 (1.1)	1 (2.9)	2 (1.6)
Throat irritation	1 (1.1)	1 (2.9)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Aspiration	1 (1.1)	0	1 (0.8)
Choking sensation	1 (1.1)	0	1 (0.8)
Dyspnoea exertional	1 (1.1)	0	1 (0.8)
Epistaxis	1 (1.1)	0	1 (0.8)
Hiccups	1 (1.1)	0	1 (0.8)
Hypoxia	1 (1.1)	0	1 (0.8)
Increased bronchial secretion	1 (1.1)	0	1 (0.8)
Increased upper airway secretion	1 (1.1)	0	1 (0.8)
Interstitial lung disease	0	1 (2.9)	1 (0.8)
Pleural effusion	1 (1.1)	0	1 (0.8)
Pulmonary infarction	1 (1.1)	0	1 (0.8)
Sputum retention	1 (1.1)	0	1 (0.8)
Wheezing	0	1 (2.9)	1 (0.8)
Metabolism and nutrition disorders	27 (28.7)	16 (45.7)	43 (33.3)
Decreased appetite	10 (10.6)	6 (17.1)	16 (12.4)
Hypomagnesaemia	7 (7.4)	3 (8.6)	10 (7.8)
Hypokalaemia	6 (6.4)	2 (5.7)	8 (6.2)
Hyponatraemia	4 (4.3)	3 (8.6)	7 (5.4)
Dehydration	2 (2.1)	3 (8.6)	5 (3.9)

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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Metabolism and nutrition disorders			
Hyperglycaemia	2 (2.1)	1 (2.9)	3 (2.3)
Hyperkalaemia	1 (1.1)	2 (5.7)	3 (2.3)
Hypoalbuminaemia	1 (1.1)	2 (5.7)	3 (2.3)
Hypercalcaemia	1 (1.1)	1 (2.9)	2 (1.6)
Folate deficiency	1 (1.1)	0	1 (0.8)
Gout	1 (1.1)	0	1 (0.8)
Hyperammonaemia	0	1 (2.9)	1 (0.8)
Hyperamylasaemia	1 (1.1)	0	1 (0.8)
Hyperglycaemic hyperosmolar nonketotic syndrome	1 (1.1)	0	1 (0.8)
Hypocalcaemia	1 (1.1)	0	1 (0.8)
Hypophagia	0	1 (2.9)	1 (0.8)
Hypophosphataemia	1 (1.1)	0	1 (0.8)
Increased appetite	0	1 (2.9)	1 (0.8)
Iron deficiency	1 (1.1)	0	1 (0.8)
Malnutrition	1 (1.1)	0	1 (0.8)
Metabolic syndrome	1 (1.1)	0	1 (0.8)
Skin and subcutaneous tissue disorders	28 (29.8)	13 (37.1)	41 (31.8)
Pruritus	13 (13.8)	5 (14.3)	18 (14.0)
Rash	10 (10.6)	3 (8.6)	13 (10.1)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Skin and subcutaneous tissue disorders			
Dry skin	2 (2.1)	3 (8.6)	5 (3.9)
Urticaria	4 (4.3)	0	4 (3.1)
Skin lesion	3 (3.2)	0	3 (2.3)
Alopecia	2 (2.1)	0	2 (1.6)
Eczema	1 (1.1)	1 (2.9)	2 (1.6)
Erythema	1 (1.1)	1 (2.9)	2 (1.6)
Dermatitis contact	0	1 (2.9)	1 (0.8)
Drug eruption	0	1 (2.9)	1 (0.8)
Hyperhidrosis	1 (1.1)	0	1 (0.8)
Hypertrichosis	1 (1.1)	0	1 (0.8)
Nail discolouration	1 (1.1)	0	1 (0.8)
Night sweats	1 (1.1)	0	1 (0.8)
Onychoclasis	1 (1.1)	0	1 (0.8)
Onychomadesis	0	1 (2.9)	1 (0.8)
Pain of skin	1 (1.1)	0	1 (0.8)
Papule	0	1 (2.9)	1 (0.8)
Pemphigoid	1 (1.1)	0	1 (0.8)
Prurigo	0	1 (2.9)	1 (0.8)
Rash maculo-papular	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
Source: Listing 16.1.21a, Dataset: ADAE, Program: t_sub_teae.sas, Output: t_14_3_1_23a_sub_teae.rtf,
Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Skin and subcutaneous tissue disorders			
Skin burning sensation	1 (1.1)	0	1 (0.8)
Skin reaction	1 (1.1)	0	1 (0.8)
Skin ulcer	1 (1.1)	0	1 (0.8)
Skin warm	1 (1.1)	0	1 (0.8)
Blood and lymphatic system disorders	26 (27.7)	14 (40.0)	40 (31.0)
Anaemia	23 (24.5)	12 (34.3)	35 (27.1)
Neutropenia	4 (4.3)	2 (5.7)	6 (4.7)
Leukocytosis	0	2 (5.7)	2 (1.6)
Leukopenia	2 (2.1)	0	2 (1.6)
Iron deficiency anaemia	1 (1.1)	0	1 (0.8)
Lymphopenia	1 (1.1)	0	1 (0.8)
Nervous system disorders	28 (29.8)	7 (20.0)	35 (27.1)
Headache	10 (10.6)	2 (5.7)	12 (9.3)
Dizziness	7 (7.4)	2 (5.7)	9 (7.0)
Neuropathy peripheral	2 (2.1)	2 (5.7)	4 (3.1)
Dysgeusia	3 (3.2)	0	3 (2.3)
Neuralgia	2 (2.1)	1 (2.9)	3 (2.3)
Carpal tunnel syndrome	1 (1.1)	1 (2.9)	2 (1.6)
Cognitive disorder	2 (2.1)	0	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Nervous system disorders			
Apraxia	1 (1.1)	0	1 (0.8)
Dysaesthesia	1 (1.1)	0	1 (0.8)
Dysarthria	0	1 (2.9)	1 (0.8)
Encephalopathy	1 (1.1)	0	1 (0.8)
Epilepsy	0	1 (2.9)	1 (0.8)
Facial paresis	0	1 (2.9)	1 (0.8)
Formication	1 (1.1)	0	1 (0.8)
Lethargy	1 (1.1)	0	1 (0.8)
Leukoencephalopathy	1 (1.1)	0	1 (0.8)
Paraesthesia	1 (1.1)	0	1 (0.8)
Parkinson's disease	1 (1.1)	0	1 (0.8)
Somnolence	1 (1.1)	0	1 (0.8)
Syncope	1 (1.1)	0	1 (0.8)
Tremor	1 (1.1)	0	1 (0.8)
Renal and urinary disorders	21 (22.3)	4 (11.4)	25 (19.4)
Acute kidney injury	4 (4.3)	0	4 (3.1)
Urinary incontinence	4 (4.3)	0	4 (3.1)
Dysuria	3 (3.2)	0	3 (2.3)
Haematuria	3 (3.2)	0	3 (2.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Renal and urinary disorders			
Hydronephrosis	1 (1.1)	2 (5.7)	3 (2.3)
Micturition urgency	3 (3.2)	0	3 (2.3)
Chromaturia	2 (2.1)	0	2 (1.6)
Renal colic	1 (1.1)	1 (2.9)	2 (1.6)
Urogenital fistula	2 (2.1)	0	2 (1.6)
Nephritis	1 (1.1)	0	1 (0.8)
Proteinuria	0	1 (2.9)	1 (0.8)
Renal failure	1 (1.1)	0	1 (0.8)
Tubulointerstitial nephritis	1 (1.1)	0	1 (0.8)
Urinary tract obstruction	1 (1.1)	0	1 (0.8)
Urinary tract pain	1 (1.1)	0	1 (0.8)
Urine abnormality	1 (1.1)	0	1 (0.8)
Urine odour abnormal	1 (1.1)	0	1 (0.8)
Vascular disorders	17 (18.1)	8 (22.9)	25 (19.4)
Hypertension	6 (6.4)	1 (2.9)	7 (5.4)
Deep vein thrombosis	3 (3.2)	2 (5.7)	5 (3.9)
Hot flush	3 (3.2)	2 (5.7)	5 (3.9)
Flushing	1 (1.1)	2 (5.7)	3 (2.3)
Hypotension	2 (2.1)	0	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Vascular disorders			
Lymphoedema	1 (1.1)	1 (2.9)	2 (1.6)
Thrombophlebitis superficial	1 (1.1)	1 (2.9)	2 (1.6)
Embolism	1 (1.1)	0	1 (0.8)
Peripheral venous disease	1 (1.1)	0	1 (0.8)
Shock	1 (1.1)	0	1 (0.8)
Varicose vein	1 (1.1)	0	1 (0.8)
Reproductive system and breast disorders	18 (19.1)	5 (14.3)	23 (17.8)
Pelvic pain	6 (6.4)	1 (2.9)	7 (5.4)
Vaginal discharge	4 (4.3)	1 (2.9)	5 (3.9)
Vaginal haemorrhage	4 (4.3)	1 (2.9)	5 (3.9)
Female genital tract fistula	2 (2.1)	0	2 (1.6)
Metrorrhagia	1 (1.1)	1 (2.9)	2 (1.6)
Vulvovaginal dryness	2 (2.1)	0	2 (1.6)
Breast haematoma	1 (1.1)	0	1 (0.8)
Perineal pain	0	1 (2.9)	1 (0.8)
Vulval disorder	0	1 (2.9)	1 (0.8)
Vulvovaginal pain	1 (1.1)	0	1 (0.8)
Psychiatric disorders	14 (14.9)	8 (22.9)	22 (17.1)
Insomnia	7 (7.4)	1 (2.9)	8 (6.2)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Psychiatric disorders			
Anxiety	0	5 (14.3)	5 (3.9)
Depression	2 (2.1)	2 (5.7)	4 (3.1)
Confusional state	1 (1.1)	1 (2.9)	2 (1.6)
Depressed mood	2 (2.1)	0	2 (1.6)
Agitation	1 (1.1)	0	1 (0.8)
Alcoholism	1 (1.1)	0	1 (0.8)
Bradyphrenia	1 (1.1)	0	1 (0.8)
Mood altered	1 (1.1)	0	1 (0.8)
Nervousness	0	1 (2.9)	1 (0.8)
Injury, poisoning and procedural complications	16 (17.0)	2 (5.7)	18 (14.0)
Contusion	2 (2.1)	0	2 (1.6)
Gastroenteritis radiation	2 (2.1)	0	2 (1.6)
Ligament sprain	2 (2.1)	0	2 (1.6)
Wound	2 (2.1)	0	2 (1.6)
Compression fracture	1 (1.1)	0	1 (0.8)
Fall	1 (1.1)	0	1 (0.8)
Procedural pain	1 (1.1)	0	1 (0.8)
Skin abrasion	0	1 (2.9)	1 (0.8)
Skin laceration	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Injury, poisoning and procedural complications			
Spinal compression fracture	1 (1.1)	0	1 (0.8)
Stoma site pain	1 (1.1)	0	1 (0.8)
Stress fracture	1 (1.1)	0	1 (0.8)
Tendon rupture	1 (1.1)	0	1 (0.8)
Thermal burn	0	1 (2.9)	1 (0.8)
Toxicity to various agents	1 (1.1)	0	1 (0.8)
Wound complication	1 (1.1)	0	1 (0.8)
Wound dehiscence	1 (1.1)	0	1 (0.8)
Eye disorders	9 (9.6)	4 (11.4)	13 (10.1)
Dry eye	1 (1.1)	3 (8.6)	4 (3.1)
Vision blurred	2 (2.1)	1 (2.9)	3 (2.3)
Cataract	2 (2.1)	0	2 (1.6)
Diplopia	1 (1.1)	0	1 (0.8)
Eye irritation	1 (1.1)	0	1 (0.8)
Iridocyclitis	1 (1.1)	0	1 (0.8)
Lacrimation increased	1 (1.1)	0	1 (0.8)
Ocular discomfort	1 (1.1)	0	1 (0.8)
Uveitis	1 (1.1)	0	1 (0.8)
Vitreous floaters	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Endocrine disorders	9 (9.6)	3 (8.6)	12 (9.3)
Hypothyroidism	9 (9.6)	1 (2.9)	10 (7.8)
Hyperthyroidism	3 (3.2)	1 (2.9)	4 (3.1)
Adrenal insufficiency	1 (1.1)	0	1 (0.8)
Glucocorticoid deficiency	0	1 (2.9)	1 (0.8)
Hypophysitis	0	1 (2.9)	1 (0.8)
Cardiac disorders	3 (3.2)	4 (11.4)	7 (5.4)
Atrial fibrillation	1 (1.1)	1 (2.9)	2 (1.6)
Tachycardia	2 (2.1)	0	2 (1.6)
Angina pectoris	1 (1.1)	0	1 (0.8)
Bradycardia	0	1 (2.9)	1 (0.8)
Myocardial infarction	1 (1.1)	0	1 (0.8)
Pericardial effusion	0	1 (2.9)	1 (0.8)
Sinus tachycardia	0	1 (2.9)	1 (0.8)
Supraventricular extrasystoles	1 (1.1)	0	1 (0.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	4 (4.3)	2 (5.7)	6 (4.7)
Tumour pain	1 (1.1)	1 (2.9)	2 (1.6)
Cancer pain	0	1 (2.9)	1 (0.8)
Colon adenoma	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.23a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Radiation by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Radiation (N=94)	No Prior Radiation (N=35)	Total (N=129)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma	1 (1.1)	0	1 (0.8)
Seborrhoeic keratosis	1 (1.1)	0	1 (0.8)
Ear and labyrinth disorders	5 (5.3)	0	5 (3.9)
Tinnitus	2 (2.1)	0	2 (1.6)
Vertigo	2 (2.1)	0	2 (1.6)
Cerumen impaction	1 (1.1)	0	1 (0.8)
Hypoacusis	1 (1.1)	0	1 (0.8)
Hepatobiliary disorders	1 (1.1)	1 (2.9)	2 (1.6)
Cholecystitis	1 (1.1)	0	1 (0.8)
Hepatic function abnormal	0	1 (2.9)	1 (0.8)
Hypertransaminasaemia	1 (1.1)	0	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Any Adverse Events	5 (100)	115 (95.0)	120 (95.2)
General disorders and administration site conditions	3 (60.0)	78 (64.5)	81 (64.3)
Fatigue	1 (20.0)	30 (24.8)	31 (24.6)
Asthenia	1 (20.0)	27 (22.3)	28 (22.2)
Pyrexia	0	13 (10.7)	13 (10.3)
Oedema peripheral	1 (20.0)	10 (8.3)	11 (8.7)
Chills	1 (20.0)	5 (4.1)	6 (4.8)
Pain	1 (20.0)	3 (2.5)	4 (3.2)
Oedema	0	3 (2.5)	3 (2.4)
Peripheral swelling	0	3 (2.5)	3 (2.4)
Chest discomfort	0	2 (1.7)	2 (1.6)
General physical health deterioration	0	2 (1.7)	2 (1.6)
Influenza like illness	0	2 (1.7)	2 (1.6)
Non-cardiac chest pain	0	2 (1.7)	2 (1.6)
Catheter site erythema	0	1 (0.8)	1 (0.8)
Catheter site pruritus	0	1 (0.8)	1 (0.8)
Complication associated with device	0	1 (0.8)	1 (0.8)
Early satiety	0	1 (0.8)	1 (0.8)
Hernia pain	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
General disorders and administration site conditions			
Hyperthermia	0	1 (0.8)	1 (0.8)
Localised oedema	1 (20.0)	0	1 (0.8)
Malaise	0	1 (0.8)	1 (0.8)
Mucosal inflammation	0	1 (0.8)	1 (0.8)
Gastrointestinal disorders	3 (60.0)	76 (62.8)	79 (62.7)
Nausea	1 (20.0)	39 (32.2)	40 (31.7)
Diarrhoea	2 (40.0)	33 (27.3)	35 (27.8)
Constipation	1 (20.0)	24 (19.8)	25 (19.8)
Vomiting	1 (20.0)	23 (19.0)	24 (19.0)
Abdominal pain	2 (40.0)	19 (15.7)	21 (16.7)
Abdominal distension	0	9 (7.4)	9 (7.1)
Dyspepsia	0	6 (5.0)	6 (4.8)
Stomatitis	0	6 (5.0)	6 (4.8)
Abdominal pain upper	0	4 (3.3)	4 (3.2)
Gastrooesophageal reflux disease	0	4 (3.3)	4 (3.2)
Abdominal pain lower	0	3 (2.5)	3 (2.4)
Colitis	0	3 (2.5)	3 (2.4)
Dry mouth	0	3 (2.5)	3 (2.4)
Haemorrhoids	0	3 (2.5)	3 (2.4)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Gastrointestinal disorders			
Mouth ulceration	0	3 (2.5)	3 (2.4)
Anal incontinence	0	2 (1.7)	2 (1.6)
Anorectal discomfort	0	2 (1.7)	2 (1.6)
Ascites	1 (20.0)	1 (0.8)	2 (1.6)
Gastritis	0	2 (1.7)	2 (1.6)
Intestinal obstruction	0	2 (1.7)	2 (1.6)
Proctalgia	0	2 (1.7)	2 (1.6)
Rectal haemorrhage	0	2 (1.7)	2 (1.6)
Anal haemorrhage	0	1 (0.8)	1 (0.8)
Cheilitis	0	1 (0.8)	1 (0.8)
Chronic gastritis	0	1 (0.8)	1 (0.8)
Colonic fistula	0	1 (0.8)	1 (0.8)
Dumping syndrome	0	1 (0.8)	1 (0.8)
Enterocolitis haemorrhagic	0	1 (0.8)	1 (0.8)
Flatulence	0	1 (0.8)	1 (0.8)
Gastric ulcer	0	1 (0.8)	1 (0.8)
Gastric ulcer perforation	0	1 (0.8)	1 (0.8)
Haematemesis	0	1 (0.8)	1 (0.8)
Haematochezia	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Gastrointestinal disorders			
Large intestine polyp	0	1 (0.8)	1 (0.8)
Lip swelling	0	1 (0.8)	1 (0.8)
Melaena	0	1 (0.8)	1 (0.8)
Odynophagia	0	1 (0.8)	1 (0.8)
Oral pain	1 (20.0)	0	1 (0.8)
Pancreatitis	0	1 (0.8)	1 (0.8)
Pancreatitis acute	0	1 (0.8)	1 (0.8)
Musculoskeletal and connective tissue disorders	1 (20.0)	54 (44.6)	55 (43.7)
Back pain	0	19 (15.7)	19 (15.1)
Arthralgia	0	18 (14.9)	18 (14.3)
Myalgia	0	13 (10.7)	13 (10.3)
Muscular weakness	0	9 (7.4)	9 (7.1)
Pain in extremity	1 (20.0)	7 (5.8)	8 (6.3)
Muscle spasms	0	5 (4.1)	5 (4.0)
Musculoskeletal pain	0	4 (3.3)	4 (3.2)
Arthritis	0	2 (1.7)	2 (1.6)
Flank pain	0	2 (1.7)	2 (1.6)
Musculoskeletal stiffness	0	2 (1.7)	2 (1.6)
Osteoarthritis	0	2 (1.7)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Musculoskeletal and connective tissue disorders			
Spinal osteoarthritis	0	2 (1.7)	2 (1.6)
Tendon pain	0	2 (1.7)	2 (1.6)
Coccydynia	0	1 (0.8)	1 (0.8)
Joint range of motion decreased	0	1 (0.8)	1 (0.8)
Joint swelling	0	1 (0.8)	1 (0.8)
Limb discomfort	0	1 (0.8)	1 (0.8)
Muscle discomfort	0	1 (0.8)	1 (0.8)
Muscle tightness	0	1 (0.8)	1 (0.8)
Neck pain	0	1 (0.8)	1 (0.8)
Osteopenia	0	1 (0.8)	1 (0.8)
Osteoporosis	0	1 (0.8)	1 (0.8)
Pain in jaw	0	1 (0.8)	1 (0.8)
Rheumatoid arthritis	0	1 (0.8)	1 (0.8)
Scoliosis	0	1 (0.8)	1 (0.8)
Spinal stenosis	0	1 (0.8)	1 (0.8)
Infections and infestations	2 (40.0)	51 (42.1)	53 (42.1)
Urinary tract infection	0	19 (15.7)	19 (15.1)
Upper respiratory tract infection	0	9 (7.4)	9 (7.1)
Bronchitis	0	6 (5.0)	6 (4.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Infections and infestations			
Nasopharyngitis	0	6 (5.0)	6 (4.8)
Pneumonia	1 (20.0)	5 (4.1)	6 (4.8)
Sepsis	0	4 (3.3)	4 (3.2)
Cellulitis	0	2 (1.7)	2 (1.6)
Cystitis	0	2 (1.7)	2 (1.6)
Gastroenteritis	0	2 (1.7)	2 (1.6)
Oral candidiasis	0	2 (1.7)	2 (1.6)
Pharyngitis	0	2 (1.7)	2 (1.6)
Pyelonephritis	0	2 (1.7)	2 (1.6)
Rhinitis	0	2 (1.7)	2 (1.6)
Vaginal infection	0	2 (1.7)	2 (1.6)
Abdominal infection	0	1 (0.8)	1 (0.8)
Bacteraemia	1 (20.0)	0	1 (0.8)
Conjunctivitis	0	1 (0.8)	1 (0.8)
Demodicidosis	0	1 (0.8)	1 (0.8)
Ear infection	0	1 (0.8)	1 (0.8)
Gastroenteritis viral	0	1 (0.8)	1 (0.8)
Gastrointestinal viral infection	0	1 (0.8)	1 (0.8)
Genital infection	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Infections and infestations			
Herpes virus infection	0	1 (0.8)	1 (0.8)
Infected lymphocele	0	1 (0.8)	1 (0.8)
Lower respiratory tract infection	0	1 (0.8)	1 (0.8)
Oral herpes	0	1 (0.8)	1 (0.8)
Sinusitis	0	1 (0.8)	1 (0.8)
Vulvovaginal candidiasis	0	1 (0.8)	1 (0.8)
Wound infection	0	1 (0.8)	1 (0.8)
Investigations	4 (80.0)	44 (36.4)	48 (38.1)
Alanine aminotransferase increased	0	9 (7.4)	9 (7.1)
Aspartate aminotransferase increased	0	9 (7.4)	9 (7.1)
Blood creatinine increased	2 (40.0)	7 (5.8)	9 (7.1)
Weight decreased	1 (20.0)	8 (6.6)	9 (7.1)
Amylase increased	0	6 (5.0)	6 (4.8)
Weight increased	1 (20.0)	4 (3.3)	5 (4.0)
Gamma-glutamyltransferase increased	0	4 (3.3)	4 (3.2)
Lipase increased	0	4 (3.3)	4 (3.2)
Blood alkaline phosphatase increased	0	3 (2.5)	3 (2.4)
Transaminases increased	1 (20.0)	2 (1.7)	3 (2.4)
Blood lactate dehydrogenase increased	0	2 (1.7)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Investigations			
Lymphocyte count decreased	0	2 (1.7)	2 (1.6)
Activated partial thromboplastin time prolonged	0	1 (0.8)	1 (0.8)
Blood bilirubin increased	0	1 (0.8)	1 (0.8)
Blood corticotrophin decreased	0	1 (0.8)	1 (0.8)
Blood iron decreased	0	1 (0.8)	1 (0.8)
Blood potassium decreased	0	1 (0.8)	1 (0.8)
Blood thyroid stimulating hormone decreased	0	1 (0.8)	1 (0.8)
Blood thyroid stimulating hormone increased	0	1 (0.8)	1 (0.8)
Blood urea increased	0	1 (0.8)	1 (0.8)
Blood urine present	0	1 (0.8)	1 (0.8)
Electrocardiogram QT prolonged	0	1 (0.8)	1 (0.8)
Haemoglobin decreased	0	1 (0.8)	1 (0.8)
Mean platelet volume decreased	0	1 (0.8)	1 (0.8)
Neutrophil count decreased	0	1 (0.8)	1 (0.8)
Neutrophil count increased	0	1 (0.8)	1 (0.8)
Nitrite urine present	0	1 (0.8)	1 (0.8)
Serum ferritin decreased	0	1 (0.8)	1 (0.8)
Thyroxine increased	0	1 (0.8)	1 (0.8)
White blood cell count decreased	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Investigations			
White blood cell count increased	1 (20.0)	0	1 (0.8)
Respiratory, thoracic and mediastinal disorders	5 (100)	37 (30.6)	42 (33.3)
Cough	1 (20.0)	18 (14.9)	19 (15.1)
Productive cough	0	9 (7.4)	9 (7.1)
Dyspnoea	1 (20.0)	7 (5.8)	8 (6.3)
Pulmonary embolism	0	4 (3.3)	4 (3.2)
Nasal congestion	0	3 (2.5)	3 (2.4)
Rhinorrhoea	1 (20.0)	2 (1.7)	3 (2.4)
Dysphonia	0	2 (1.7)	2 (1.6)
Oropharyngeal pain	0	2 (1.7)	2 (1.6)
Pneumonitis	1 (20.0)	1 (0.8)	2 (1.6)
Sneezing	1 (20.0)	1 (0.8)	2 (1.6)
Throat irritation	1 (20.0)	1 (0.8)	2 (1.6)
Aspiration	0	1 (0.8)	1 (0.8)
Choking sensation	0	1 (0.8)	1 (0.8)
Dyspnoea exertional	0	1 (0.8)	1 (0.8)
Epistaxis	0	1 (0.8)	1 (0.8)
Hiccups	1 (20.0)	0	1 (0.8)
Hypoxia	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Respiratory, thoracic and mediastinal disorders			
Increased bronchial secretion	0	1 (0.8)	1 (0.8)
Increased upper airway secretion	0	1 (0.8)	1 (0.8)
Interstitial lung disease	0	1 (0.8)	1 (0.8)
Pleural effusion	0	1 (0.8)	1 (0.8)
Pulmonary infarction	0	1 (0.8)	1 (0.8)
Sputum retention	0	1 (0.8)	1 (0.8)
Wheezing	0	1 (0.8)	1 (0.8)
Metabolism and nutrition disorders	2 (40.0)	39 (32.2)	41 (32.5)
Decreased appetite	1 (20.0)	15 (12.4)	16 (12.7)
Hypomagnesaemia	1 (20.0)	9 (7.4)	10 (7.9)
Hypokalaemia	1 (20.0)	7 (5.8)	8 (6.3)
Hyponatraemia	0	6 (5.0)	6 (4.8)
Dehydration	1 (20.0)	4 (3.3)	5 (4.0)
Hyperglycaemia	0	3 (2.5)	3 (2.4)
Hyperkalaemia	0	3 (2.5)	3 (2.4)
Hypoalbuminaemia	1 (20.0)	2 (1.7)	3 (2.4)
Hypercalcaemia	0	2 (1.7)	2 (1.6)
Folate deficiency	0	1 (0.8)	1 (0.8)
Hyperamylasaemia	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Metabolism and nutrition disorders			
Hyperglycaemic hyperosmolar nonketotic syndrome	0	1 (0.8)	1 (0.8)
Hypocalcaemia	0	1 (0.8)	1 (0.8)
Hypophosphataemia	0	1 (0.8)	1 (0.8)
Increased appetite	0	1 (0.8)	1 (0.8)
Iron deficiency	0	1 (0.8)	1 (0.8)
Malnutrition	0	1 (0.8)	1 (0.8)
Metabolic syndrome	0	1 (0.8)	1 (0.8)
Blood and lymphatic system disorders	1 (20.0)	39 (32.2)	40 (31.7)
Anaemia	1 (20.0)	34 (28.1)	35 (27.8)
Neutropenia	0	6 (5.0)	6 (4.8)
Leukocytosis	0	2 (1.7)	2 (1.6)
Leukopenia	0	2 (1.7)	2 (1.6)
Iron deficiency anaemia	0	1 (0.8)	1 (0.8)
Lymphopenia	0	1 (0.8)	1 (0.8)
Skin and subcutaneous tissue disorders	0	40 (33.1)	40 (31.7)
Pruritus	0	18 (14.9)	18 (14.3)
Rash	0	13 (10.7)	13 (10.3)
Dry skin	0	4 (3.3)	4 (3.2)
Skin lesion	0	3 (2.5)	3 (2.4)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Skin and subcutaneous tissue disorders			
Urticaria	0	3 (2.5)	3 (2.4)
Alopecia	0	2 (1.7)	2 (1.6)
Eczema	0	2 (1.7)	2 (1.6)
Erythema	0	2 (1.7)	2 (1.6)
Dermatitis contact	0	1 (0.8)	1 (0.8)
Drug eruption	0	1 (0.8)	1 (0.8)
Hyperhidrosis	0	1 (0.8)	1 (0.8)
Hypertrichosis	0	1 (0.8)	1 (0.8)
Nail discolouration	0	1 (0.8)	1 (0.8)
Onychoclasis	0	1 (0.8)	1 (0.8)
Onychomadesis	0	1 (0.8)	1 (0.8)
Papule	0	1 (0.8)	1 (0.8)
Pemphigoid	0	1 (0.8)	1 (0.8)
Prurigo	0	1 (0.8)	1 (0.8)
Rash maculo-papular	0	1 (0.8)	1 (0.8)
Skin burning sensation	0	1 (0.8)	1 (0.8)
Skin ulcer	0	1 (0.8)	1 (0.8)
Skin warm	0	1 (0.8)	1 (0.8)
Nervous system disorders	3 (60.0)	29 (24.0)	32 (25.4)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Nervous system disorders			
Headache	0	12 (9.9)	12 (9.5)
Dizziness	1 (20.0)	8 (6.6)	9 (7.1)
Neuropathy peripheral	1 (20.0)	3 (2.5)	4 (3.2)
Dysgeusia	0	3 (2.5)	3 (2.4)
Carpal tunnel syndrome	0	2 (1.7)	2 (1.6)
Cognitive disorder	0	2 (1.7)	2 (1.6)
Neuralgia	1 (20.0)	1 (0.8)	2 (1.6)
Apraxia	0	1 (0.8)	1 (0.8)
Dysaesthesia	0	1 (0.8)	1 (0.8)
Dysarthria	0	1 (0.8)	1 (0.8)
Encephalopathy	1 (20.0)	0	1 (0.8)
Facial paresis	0	1 (0.8)	1 (0.8)
Formication	0	1 (0.8)	1 (0.8)
Leukoencephalopathy	0	1 (0.8)	1 (0.8)
Paraesthesia	0	1 (0.8)	1 (0.8)
Parkinson's disease	0	1 (0.8)	1 (0.8)
Somnolence	0	1 (0.8)	1 (0.8)
Syncope	0	1 (0.8)	1 (0.8)
Tremor	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Renal and urinary disorders	2 (40.0)	23 (19.0)	25 (19.8)
Acute kidney injury	1 (20.0)	3 (2.5)	4 (3.2)
Urinary incontinence	0	4 (3.3)	4 (3.2)
Dysuria	0	3 (2.5)	3 (2.4)
Haematuria	0	3 (2.5)	3 (2.4)
Hydronephrosis	0	3 (2.5)	3 (2.4)
Micturition urgency	0	3 (2.5)	3 (2.4)
Chromaturia	0	2 (1.7)	2 (1.6)
Renal colic	0	2 (1.7)	2 (1.6)
Urogenital fistula	0	2 (1.7)	2 (1.6)
Nephritis	0	1 (0.8)	1 (0.8)
Proteinuria	1 (20.0)	0	1 (0.8)
Renal failure	0	1 (0.8)	1 (0.8)
Tubulointerstitial nephritis	0	1 (0.8)	1 (0.8)
Urinary tract obstruction	0	1 (0.8)	1 (0.8)
Urinary tract pain	0	1 (0.8)	1 (0.8)
Urine abnormality	0	1 (0.8)	1 (0.8)
Urine odour abnormal	0	1 (0.8)	1 (0.8)
Vascular disorders	3 (60.0)	20 (16.5)	23 (18.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Vascular disorders			
Deep vein thrombosis	1 (20.0)	4 (3.3)	5 (4.0)
Hot flush	0	5 (4.1)	5 (4.0)
Hypertension	1 (20.0)	4 (3.3)	5 (4.0)
Flushing	2 (40.0)	1 (0.8)	3 (2.4)
Hypotension	0	2 (1.7)	2 (1.6)
Lymphoedema	0	2 (1.7)	2 (1.6)
Thrombophlebitis superficial	0	2 (1.7)	2 (1.6)
Embolism	0	1 (0.8)	1 (0.8)
Peripheral venous disease	0	1 (0.8)	1 (0.8)
Shock	0	1 (0.8)	1 (0.8)
Varicose vein	0	1 (0.8)	1 (0.8)
Reproductive system and breast disorders	1 (20.0)	21 (17.4)	22 (17.5)
Pelvic pain	1 (20.0)	6 (5.0)	7 (5.6)
Vaginal discharge	0	5 (4.1)	5 (4.0)
Vaginal haemorrhage	0	5 (4.1)	5 (4.0)
Female genital tract fistula	0	2 (1.7)	2 (1.6)
Metrorrhagia	0	2 (1.7)	2 (1.6)
Breast haematoma	0	1 (0.8)	1 (0.8)
Perineal pain	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Reproductive system and breast disorders			
Vulval disorder	0	1 (0.8)	1 (0.8)
Vulvovaginal dryness	0	1 (0.8)	1 (0.8)
Vulvovaginal pain	0	1 (0.8)	1 (0.8)
Psychiatric disorders	3 (60.0)	18 (14.9)	21 (16.7)
Insomnia	0	8 (6.6)	8 (6.3)
Anxiety	1 (20.0)	4 (3.3)	5 (4.0)
Depression	1 (20.0)	3 (2.5)	4 (3.2)
Confusional state	0	2 (1.7)	2 (1.6)
Depressed mood	0	2 (1.7)	2 (1.6)
Agitation	1 (20.0)	0	1 (0.8)
Alcoholism	0	1 (0.8)	1 (0.8)
Bradyphrenia	0	1 (0.8)	1 (0.8)
Nervousness	0	1 (0.8)	1 (0.8)
Injury, poisoning and procedural complications	1 (20.0)	16 (13.2)	17 (13.5)
Contusion	0	2 (1.7)	2 (1.6)
Gastroenteritis radiation	0	2 (1.7)	2 (1.6)
Wound	0	2 (1.7)	2 (1.6)
Compression fracture	0	1 (0.8)	1 (0.8)
Fall	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Injury, poisoning and procedural complications			
Ligament sprain	0	1 (0.8)	1 (0.8)
Procedural pain	0	1 (0.8)	1 (0.8)
Skin abrasion	0	1 (0.8)	1 (0.8)
Skin laceration	0	1 (0.8)	1 (0.8)
Spinal compression fracture	0	1 (0.8)	1 (0.8)
Stoma site pain	0	1 (0.8)	1 (0.8)
Stress fracture	0	1 (0.8)	1 (0.8)
Tendon rupture	0	1 (0.8)	1 (0.8)
Thermal burn	1 (20.0)	0	1 (0.8)
Toxicity to various agents	0	1 (0.8)	1 (0.8)
Wound complication	0	1 (0.8)	1 (0.8)
Wound dehiscence	0	1 (0.8)	1 (0.8)
Eye disorders	0	13 (10.7)	13 (10.3)
Dry eye	0	4 (3.3)	4 (3.2)
Vision blurred	0	3 (2.5)	3 (2.4)
Cataract	0	2 (1.7)	2 (1.6)
Diplopia	0	1 (0.8)	1 (0.8)
Eye irritation	0	1 (0.8)	1 (0.8)
Iridocyclitis	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Eye disorders			
Lacrimation increased	0	1 (0.8)	1 (0.8)
Ocular discomfort	0	1 (0.8)	1 (0.8)
Uveitis	0	1 (0.8)	1 (0.8)
Vitreous floaters	0	1 (0.8)	1 (0.8)
Endocrine disorders	0	11 (9.1)	11 (8.7)
Hypothyroidism	0	9 (7.4)	9 (7.1)
Hyperthyroidism	0	4 (3.3)	4 (3.2)
Adrenal insufficiency	0	1 (0.8)	1 (0.8)
Glucocorticoid deficiency	0	1 (0.8)	1 (0.8)
Hypophysitis	0	1 (0.8)	1 (0.8)
Cardiac disorders	0	6 (5.0)	6 (4.8)
Atrial fibrillation	0	2 (1.7)	2 (1.6)
Angina pectoris	0	1 (0.8)	1 (0.8)
Bradycardia	0	1 (0.8)	1 (0.8)
Myocardial infarction	0	1 (0.8)	1 (0.8)
Pericardial effusion	0	1 (0.8)	1 (0.8)
Sinus tachycardia	0	1 (0.8)	1 (0.8)
Supraventricular extrasystoles	0	1 (0.8)	1 (0.8)
Tachycardia	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: dMMR

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=121)	Total (N=126)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	6 (5.0)	6 (4.8)
Tumour pain	0	2 (1.7)	2 (1.6)
Cancer pain	0	1 (0.8)	1 (0.8)
Colon adenoma	0	1 (0.8)	1 (0.8)
Malignant melanoma	0	1 (0.8)	1 (0.8)
Seborrhoeic keratosis	0	1 (0.8)	1 (0.8)
Ear and labyrinth disorders	0	5 (4.1)	5 (4.0)
Tinnitus	0	2 (1.7)	2 (1.6)
Vertigo	0	2 (1.7)	2 (1.6)
Cerumen impaction	0	1 (0.8)	1 (0.8)
Hypoacusis	0	1 (0.8)	1 (0.8)
Hepatobiliary disorders	0	2 (1.7)	2 (1.6)
Cholecystitis	0	1 (0.8)	1 (0.8)
Hepatic function abnormal	0	1 (0.8)	1 (0.8)
Hypertransaminasaemia	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=0)	No Prior Bevacizumab Use (N=3)	Total (N=3)
Any Adverse Events	0	3 (100)	3 (100)
Nervous system disorders	0	3 (100)	3 (100)
Epilepsy	0	1 (33.3)	1 (33.3)
Lethargy	0	1 (33.3)	1 (33.3)
Neuralgia	0	1 (33.3)	1 (33.3)
Gastrointestinal disorders	0	2 (66.7)	2 (66.7)
Nausea	0	2 (66.7)	2 (66.7)
Bile acid malabsorption	0	1 (33.3)	1 (33.3)
Diarrhoea	0	1 (33.3)	1 (33.3)
Dry mouth	0	1 (33.3)	1 (33.3)
General disorders and administration site conditions	0	2 (66.7)	2 (66.7)
Oedema peripheral	0	2 (66.7)	2 (66.7)
Fatigue	0	1 (33.3)	1 (33.3)
Pyrexia	0	1 (33.3)	1 (33.3)
Infections and infestations	0	2 (66.7)	2 (66.7)
Candida infection	0	1 (33.3)	1 (33.3)
Fungal skin infection	0	1 (33.3)	1 (33.3)
Sinusitis	0	1 (33.3)	1 (33.3)
Upper respiratory tract infection	0	1 (33.3)	1 (33.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=0)	No Prior Bevacizumab Use (N=3)	Total (N=3)
Infections and infestations			
Urinary tract infection	0	1 (33.3)	1 (33.3)
Viral infection	0	1 (33.3)	1 (33.3)
Metabolism and nutrition disorders	0	2 (66.7)	2 (66.7)
Gout	0	1 (33.3)	1 (33.3)
Hyperammonaemia	0	1 (33.3)	1 (33.3)
Hyponatraemia	0	1 (33.3)	1 (33.3)
Hypophagia	0	1 (33.3)	1 (33.3)
Musculoskeletal and connective tissue disorders	0	2 (66.7)	2 (66.7)
Arthralgia	0	2 (66.7)	2 (66.7)
Musculoskeletal pain	0	1 (33.3)	1 (33.3)
Myalgia	0	1 (33.3)	1 (33.3)
Synovial cyst	0	1 (33.3)	1 (33.3)
Tendonitis	0	1 (33.3)	1 (33.3)
Respiratory, thoracic and mediastinal disorders	0	2 (66.7)	2 (66.7)
Cough	0	2 (66.7)	2 (66.7)
Dyspnoea	0	1 (33.3)	1 (33.3)
Vascular disorders	0	2 (66.7)	2 (66.7)
Hypertension	0	2 (66.7)	2 (66.7)
Cardiac disorders	0	1 (33.3)	1 (33.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

EC: MMR-unk/MSI-H

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=0)	No Prior Bevacizumab Use (N=3)	Total (N=3)
Cardiac disorders			
Tachycardia	0	1 (33.3)	1 (33.3)
Endocrine disorders	0	1 (33.3)	1 (33.3)
Hypothyroidism	0	1 (33.3)	1 (33.3)
Injury, poisoning and procedural complications	0	1 (33.3)	1 (33.3)
Ligament sprain	0	1 (33.3)	1 (33.3)
Investigations	0	1 (33.3)	1 (33.3)
Serum ferritin decreased	0	1 (33.3)	1 (33.3)
Psychiatric disorders	0	1 (33.3)	1 (33.3)
Mood altered	0	1 (33.3)	1 (33.3)
Reproductive system and breast disorders	0	1 (33.3)	1 (33.3)
Vulvovaginal dryness	0	1 (33.3)	1 (33.3)
Skin and subcutaneous tissue disorders	0	1 (33.3)	1 (33.3)
Dry skin	0	1 (33.3)	1 (33.3)
Night sweats	0	1 (33.3)	1 (33.3)
Pain of skin	0	1 (33.3)	1 (33.3)
Skin reaction	0	1 (33.3)	1 (33.3)
Urticaria	0	1 (33.3)	1 (33.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Any Adverse Events	5 (100)	118 (95.2)	123 (95.3)
General disorders and administration site conditions	3 (60.0)	80 (64.5)	83 (64.3)
Fatigue	1 (20.0)	31 (25.0)	32 (24.8)
Asthenia	1 (20.0)	27 (21.8)	28 (21.7)
Pyrexia	0	14 (11.3)	14 (10.9)
Oedema peripheral	1 (20.0)	12 (9.7)	13 (10.1)
Chills	1 (20.0)	5 (4.0)	6 (4.7)
Pain	1 (20.0)	3 (2.4)	4 (3.1)
Oedema	0	3 (2.4)	3 (2.3)
Peripheral swelling	0	3 (2.4)	3 (2.3)
Chest discomfort	0	2 (1.6)	2 (1.6)
General physical health deterioration	0	2 (1.6)	2 (1.6)
Influenza like illness	0	2 (1.6)	2 (1.6)
Non-cardiac chest pain	0	2 (1.6)	2 (1.6)
Catheter site erythema	0	1 (0.8)	1 (0.8)
Catheter site pruritus	0	1 (0.8)	1 (0.8)
Complication associated with device	0	1 (0.8)	1 (0.8)
Early satiety	0	1 (0.8)	1 (0.8)
Hernia pain	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
General disorders and administration site conditions			
Hyperthermia	0	1 (0.8)	1 (0.8)
Localised oedema	1 (20.0)	0	1 (0.8)
Malaise	0	1 (0.8)	1 (0.8)
Mucosal inflammation	0	1 (0.8)	1 (0.8)
Gastrointestinal disorders	3 (60.0)	78 (62.9)	81 (62.8)
Nausea	1 (20.0)	41 (33.1)	42 (32.6)
Diarrhoea	2 (40.0)	34 (27.4)	36 (27.9)
Constipation	1 (20.0)	24 (19.4)	25 (19.4)
Vomiting	1 (20.0)	23 (18.5)	24 (18.6)
Abdominal pain	2 (40.0)	19 (15.3)	21 (16.3)
Abdominal distension	0	9 (7.3)	9 (7.0)
Dyspepsia	0	6 (4.8)	6 (4.7)
Stomatitis	0	6 (4.8)	6 (4.7)
Abdominal pain upper	0	4 (3.2)	4 (3.1)
Dry mouth	0	4 (3.2)	4 (3.1)
Gastrooesophageal reflux disease	0	4 (3.2)	4 (3.1)
Abdominal pain lower	0	3 (2.4)	3 (2.3)
Colitis	0	3 (2.4)	3 (2.3)
Haemorrhoids	0	3 (2.4)	3 (2.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Gastrointestinal disorders			
Mouth ulceration	0	3 (2.4)	3 (2.3)
Anal incontinence	0	2 (1.6)	2 (1.6)
Anorectal discomfort	0	2 (1.6)	2 (1.6)
Ascites	1 (20.0)	1 (0.8)	2 (1.6)
Gastritis	0	2 (1.6)	2 (1.6)
Intestinal obstruction	0	2 (1.6)	2 (1.6)
Proctalgia	0	2 (1.6)	2 (1.6)
Rectal haemorrhage	0	2 (1.6)	2 (1.6)
Anal haemorrhage	0	1 (0.8)	1 (0.8)
Bile acid malabsorption	0	1 (0.8)	1 (0.8)
Cheilitis	0	1 (0.8)	1 (0.8)
Chronic gastritis	0	1 (0.8)	1 (0.8)
Colonic fistula	0	1 (0.8)	1 (0.8)
Dumping syndrome	0	1 (0.8)	1 (0.8)
Enterocolitis haemorrhagic	0	1 (0.8)	1 (0.8)
Flatulence	0	1 (0.8)	1 (0.8)
Gastric ulcer	0	1 (0.8)	1 (0.8)
Gastric ulcer perforation	0	1 (0.8)	1 (0.8)
Haematemesis	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Gastrointestinal disorders			
Haematochezia	0	1 (0.8)	1 (0.8)
Large intestine polyp	0	1 (0.8)	1 (0.8)
Lip swelling	0	1 (0.8)	1 (0.8)
Melaena	0	1 (0.8)	1 (0.8)
Odynophagia	0	1 (0.8)	1 (0.8)
Oral pain	1 (20.0)	0	1 (0.8)
Pancreatitis	0	1 (0.8)	1 (0.8)
Pancreatitis acute	0	1 (0.8)	1 (0.8)
Musculoskeletal and connective tissue disorders	1 (20.0)	56 (45.2)	57 (44.2)
Arthralgia	0	20 (16.1)	20 (15.5)
Back pain	0	19 (15.3)	19 (14.7)
Myalgia	0	14 (11.3)	14 (10.9)
Muscular weakness	0	9 (7.3)	9 (7.0)
Pain in extremity	1 (20.0)	7 (5.6)	8 (6.2)
Muscle spasms	0	5 (4.0)	5 (3.9)
Musculoskeletal pain	0	5 (4.0)	5 (3.9)
Arthritis	0	2 (1.6)	2 (1.6)
Flank pain	0	2 (1.6)	2 (1.6)
Musculoskeletal stiffness	0	2 (1.6)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Musculoskeletal and connective tissue disorders			
Osteoarthritis	0	2 (1.6)	2 (1.6)
Spinal osteoarthritis	0	2 (1.6)	2 (1.6)
Tendon pain	0	2 (1.6)	2 (1.6)
Coccydynia	0	1 (0.8)	1 (0.8)
Joint range of motion decreased	0	1 (0.8)	1 (0.8)
Joint swelling	0	1 (0.8)	1 (0.8)
Limb discomfort	0	1 (0.8)	1 (0.8)
Muscle discomfort	0	1 (0.8)	1 (0.8)
Muscle tightness	0	1 (0.8)	1 (0.8)
Neck pain	0	1 (0.8)	1 (0.8)
Osteopenia	0	1 (0.8)	1 (0.8)
Osteoporosis	0	1 (0.8)	1 (0.8)
Pain in jaw	0	1 (0.8)	1 (0.8)
Rheumatoid arthritis	0	1 (0.8)	1 (0.8)
Scoliosis	0	1 (0.8)	1 (0.8)
Spinal stenosis	0	1 (0.8)	1 (0.8)
Synovial cyst	0	1 (0.8)	1 (0.8)
Tendonitis	0	1 (0.8)	1 (0.8)
Infections and infestations	2 (40.0)	53 (42.7)	55 (42.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Infections and infestations			
Urinary tract infection	0	20 (16.1)	20 (15.5)
Upper respiratory tract infection	0	10 (8.1)	10 (7.8)
Bronchitis	0	6 (4.8)	6 (4.7)
Nasopharyngitis	0	6 (4.8)	6 (4.7)
Pneumonia	1 (20.0)	5 (4.0)	6 (4.7)
Sepsis	0	4 (3.2)	4 (3.1)
Cellulitis	0	2 (1.6)	2 (1.6)
Cystitis	0	2 (1.6)	2 (1.6)
Gastroenteritis	0	2 (1.6)	2 (1.6)
Oral candidiasis	0	2 (1.6)	2 (1.6)
Pharyngitis	0	2 (1.6)	2 (1.6)
Pyelonephritis	0	2 (1.6)	2 (1.6)
Rhinitis	0	2 (1.6)	2 (1.6)
Sinusitis	0	2 (1.6)	2 (1.6)
Vaginal infection	0	2 (1.6)	2 (1.6)
Abdominal infection	0	1 (0.8)	1 (0.8)
Bacteraemia	1 (20.0)	0	1 (0.8)
Candida infection	0	1 (0.8)	1 (0.8)
Conjunctivitis	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Infections and infestations			
Demodicidosis	0	1 (0.8)	1 (0.8)
Ear infection	0	1 (0.8)	1 (0.8)
Fungal skin infection	0	1 (0.8)	1 (0.8)
Gastroenteritis viral	0	1 (0.8)	1 (0.8)
Gastrointestinal viral infection	0	1 (0.8)	1 (0.8)
Genital infection	0	1 (0.8)	1 (0.8)
Herpes virus infection	0	1 (0.8)	1 (0.8)
Infected lymphocele	0	1 (0.8)	1 (0.8)
Lower respiratory tract infection	0	1 (0.8)	1 (0.8)
Oral herpes	0	1 (0.8)	1 (0.8)
Viral infection	0	1 (0.8)	1 (0.8)
Vulvovaginal candidiasis	0	1 (0.8)	1 (0.8)
Wound infection	0	1 (0.8)	1 (0.8)
Investigations	4 (80.0)	45 (36.3)	49 (38.0)
Alanine aminotransferase increased	0	9 (7.3)	9 (7.0)
Aspartate aminotransferase increased	0	9 (7.3)	9 (7.0)
Blood creatinine increased	2 (40.0)	7 (5.6)	9 (7.0)
Weight decreased	1 (20.0)	8 (6.5)	9 (7.0)
Amylase increased	0	6 (4.8)	6 (4.7)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Investigations			
Weight increased	1 (20.0)	4 (3.2)	5 (3.9)
Gamma-glutamyltransferase increased	0	4 (3.2)	4 (3.1)
Lipase increased	0	4 (3.2)	4 (3.1)
Blood alkaline phosphatase increased	0	3 (2.4)	3 (2.3)
Transaminases increased	1 (20.0)	2 (1.6)	3 (2.3)
Blood lactate dehydrogenase increased	0	2 (1.6)	2 (1.6)
Lymphocyte count decreased	0	2 (1.6)	2 (1.6)
Serum ferritin decreased	0	2 (1.6)	2 (1.6)
Activated partial thromboplastin time prolonged	0	1 (0.8)	1 (0.8)
Blood bilirubin increased	0	1 (0.8)	1 (0.8)
Blood corticotrophin decreased	0	1 (0.8)	1 (0.8)
Blood iron decreased	0	1 (0.8)	1 (0.8)
Blood potassium decreased	0	1 (0.8)	1 (0.8)
Blood thyroid stimulating hormone decreased	0	1 (0.8)	1 (0.8)
Blood thyroid stimulating hormone increased	0	1 (0.8)	1 (0.8)
Blood urea increased	0	1 (0.8)	1 (0.8)
Blood urine present	0	1 (0.8)	1 (0.8)
Electrocardiogram QT prolonged	0	1 (0.8)	1 (0.8)
Haemoglobin decreased	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Investigations			
Mean platelet volume decreased	0	1 (0.8)	1 (0.8)
Neutrophil count decreased	0	1 (0.8)	1 (0.8)
Neutrophil count increased	0	1 (0.8)	1 (0.8)
Nitrite urine present	0	1 (0.8)	1 (0.8)
Thyroxine increased	0	1 (0.8)	1 (0.8)
White blood cell count decreased	0	1 (0.8)	1 (0.8)
White blood cell count increased	1 (20.0)	0	1 (0.8)
Respiratory, thoracic and mediastinal disorders	5 (100)	39 (31.5)	44 (34.1)
Cough	1 (20.0)	20 (16.1)	21 (16.3)
Dyspnoea	1 (20.0)	8 (6.5)	9 (7.0)
Productive cough	0	9 (7.3)	9 (7.0)
Pulmonary embolism	0	4 (3.2)	4 (3.1)
Nasal congestion	0	3 (2.4)	3 (2.3)
Rhinorrhoea	1 (20.0)	2 (1.6)	3 (2.3)
Dysphonia	0	2 (1.6)	2 (1.6)
Oropharyngeal pain	0	2 (1.6)	2 (1.6)
Pneumonitis	1 (20.0)	1 (0.8)	2 (1.6)
Sneezing	1 (20.0)	1 (0.8)	2 (1.6)
Throat irritation	1 (20.0)	1 (0.8)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Respiratory, thoracic and mediastinal disorders			
Aspiration	0	1 (0.8)	1 (0.8)
Choking sensation	0	1 (0.8)	1 (0.8)
Dyspnoea exertional	0	1 (0.8)	1 (0.8)
Epistaxis	0	1 (0.8)	1 (0.8)
Hiccups	1 (20.0)	0	1 (0.8)
Hypoxia	0	1 (0.8)	1 (0.8)
Increased bronchial secretion	0	1 (0.8)	1 (0.8)
Increased upper airway secretion	0	1 (0.8)	1 (0.8)
Interstitial lung disease	0	1 (0.8)	1 (0.8)
Pleural effusion	0	1 (0.8)	1 (0.8)
Pulmonary infarction	0	1 (0.8)	1 (0.8)
Sputum retention	0	1 (0.8)	1 (0.8)
Wheezing	0	1 (0.8)	1 (0.8)
Metabolism and nutrition disorders	2 (40.0)	41 (33.1)	43 (33.3)
Decreased appetite	1 (20.0)	15 (12.1)	16 (12.4)
Hypomagnesaemia	1 (20.0)	9 (7.3)	10 (7.8)
Hypokalaemia	1 (20.0)	7 (5.6)	8 (6.2)
Hyponatraemia	0	7 (5.6)	7 (5.4)
Dehydration	1 (20.0)	4 (3.2)	5 (3.9)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Metabolism and nutrition disorders			
Hyperglycaemia	0	3 (2.4)	3 (2.3)
Hyperkalaemia	0	3 (2.4)	3 (2.3)
Hypoalbuminaemia	1 (20.0)	2 (1.6)	3 (2.3)
Hypercalcaemia	0	2 (1.6)	2 (1.6)
Folate deficiency	0	1 (0.8)	1 (0.8)
Gout	0	1 (0.8)	1 (0.8)
Hyperammonaemia	0	1 (0.8)	1 (0.8)
Hyperamylasaemia	0	1 (0.8)	1 (0.8)
Hyperglycaemic hyperosmolar nonketotic syndrome	0	1 (0.8)	1 (0.8)
Hypocalcaemia	0	1 (0.8)	1 (0.8)
Hypophagia	0	1 (0.8)	1 (0.8)
Hypophosphataemia	0	1 (0.8)	1 (0.8)
Increased appetite	0	1 (0.8)	1 (0.8)
Iron deficiency	0	1 (0.8)	1 (0.8)
Malnutrition	0	1 (0.8)	1 (0.8)
Metabolic syndrome	0	1 (0.8)	1 (0.8)
Skin and subcutaneous tissue disorders	0	41 (33.1)	41 (31.8)
Pruritus	0	18 (14.5)	18 (14.0)
Rash	0	13 (10.5)	13 (10.1)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Skin and subcutaneous tissue disorders			
Dry skin	0	5 (4.0)	5 (3.9)
Urticaria	0	4 (3.2)	4 (3.1)
Skin lesion	0	3 (2.4)	3 (2.3)
Alopecia	0	2 (1.6)	2 (1.6)
Eczema	0	2 (1.6)	2 (1.6)
Erythema	0	2 (1.6)	2 (1.6)
Dermatitis contact	0	1 (0.8)	1 (0.8)
Drug eruption	0	1 (0.8)	1 (0.8)
Hyperhidrosis	0	1 (0.8)	1 (0.8)
Hypertrichosis	0	1 (0.8)	1 (0.8)
Nail discolouration	0	1 (0.8)	1 (0.8)
Night sweats	0	1 (0.8)	1 (0.8)
Onychoclasis	0	1 (0.8)	1 (0.8)
Onychomadesis	0	1 (0.8)	1 (0.8)
Pain of skin	0	1 (0.8)	1 (0.8)
Papule	0	1 (0.8)	1 (0.8)
Pemphigoid	0	1 (0.8)	1 (0.8)
Prurigo	0	1 (0.8)	1 (0.8)
Rash maculo-papular	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Skin and subcutaneous tissue disorders			
Skin burning sensation	0	1 (0.8)	1 (0.8)
Skin reaction	0	1 (0.8)	1 (0.8)
Skin ulcer	0	1 (0.8)	1 (0.8)
Skin warm	0	1 (0.8)	1 (0.8)
Blood and lymphatic system disorders	1 (20.0)	39 (31.5)	40 (31.0)
Anaemia	1 (20.0)	34 (27.4)	35 (27.1)
Neutropenia	0	6 (4.8)	6 (4.7)
Leukocytosis	0	2 (1.6)	2 (1.6)
Leukopenia	0	2 (1.6)	2 (1.6)
Iron deficiency anaemia	0	1 (0.8)	1 (0.8)
Lymphopenia	0	1 (0.8)	1 (0.8)
Nervous system disorders	3 (60.0)	32 (25.8)	35 (27.1)
Headache	0	12 (9.7)	12 (9.3)
Dizziness	1 (20.0)	8 (6.5)	9 (7.0)
Neuropathy peripheral	1 (20.0)	3 (2.4)	4 (3.1)
Dysgeusia	0	3 (2.4)	3 (2.3)
Neuralgia	1 (20.0)	2 (1.6)	3 (2.3)
Carpal tunnel syndrome	0	2 (1.6)	2 (1.6)
Cognitive disorder	0	2 (1.6)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Nervous system disorders			
Apraxia	0	1 (0.8)	1 (0.8)
Dysaesthesia	0	1 (0.8)	1 (0.8)
Dysarthria	0	1 (0.8)	1 (0.8)
Encephalopathy	1 (20.0)	0	1 (0.8)
Epilepsy	0	1 (0.8)	1 (0.8)
Facial paresis	0	1 (0.8)	1 (0.8)
Formication	0	1 (0.8)	1 (0.8)
Lethargy	0	1 (0.8)	1 (0.8)
Leukoencephalopathy	0	1 (0.8)	1 (0.8)
Paraesthesia	0	1 (0.8)	1 (0.8)
Parkinson's disease	0	1 (0.8)	1 (0.8)
Somnolence	0	1 (0.8)	1 (0.8)
Syncope	0	1 (0.8)	1 (0.8)
Tremor	0	1 (0.8)	1 (0.8)
Renal and urinary disorders	2 (40.0)	23 (18.5)	25 (19.4)
Acute kidney injury	1 (20.0)	3 (2.4)	4 (3.1)
Urinary incontinence	0	4 (3.2)	4 (3.1)
Dysuria	0	3 (2.4)	3 (2.3)
Haematuria	0	3 (2.4)	3 (2.3)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Renal and urinary disorders			
Hydronephrosis	0	3 (2.4)	3 (2.3)
Micturition urgency	0	3 (2.4)	3 (2.3)
Chromaturia	0	2 (1.6)	2 (1.6)
Renal colic	0	2 (1.6)	2 (1.6)
Urogenital fistula	0	2 (1.6)	2 (1.6)
Nephritis	0	1 (0.8)	1 (0.8)
Proteinuria	1 (20.0)	0	1 (0.8)
Renal failure	0	1 (0.8)	1 (0.8)
Tubulointerstitial nephritis	0	1 (0.8)	1 (0.8)
Urinary tract obstruction	0	1 (0.8)	1 (0.8)
Urinary tract pain	0	1 (0.8)	1 (0.8)
Urine abnormality	0	1 (0.8)	1 (0.8)
Urine odour abnormal	0	1 (0.8)	1 (0.8)
Vascular disorders	3 (60.0)	22 (17.7)	25 (19.4)
Hypertension	1 (20.0)	6 (4.8)	7 (5.4)
Deep vein thrombosis	1 (20.0)	4 (3.2)	5 (3.9)
Hot flush	0	5 (4.0)	5 (3.9)
Flushing	2 (40.0)	1 (0.8)	3 (2.3)
Hypotension	0	2 (1.6)	2 (1.6)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Generated on: 26AUG2020 03:09 Data extraction: 23JUL2020 Data cutoff: 01MAR2020

Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Vascular disorders			
Lymphoedema	0	2 (1.6)	2 (1.6)
Thrombophlebitis superficial	0	2 (1.6)	2 (1.6)
Embolism	0	1 (0.8)	1 (0.8)
Peripheral venous disease	0	1 (0.8)	1 (0.8)
Shock	0	1 (0.8)	1 (0.8)
Varicose vein	0	1 (0.8)	1 (0.8)
Reproductive system and breast disorders	1 (20.0)	22 (17.7)	23 (17.8)
Pelvic pain	1 (20.0)	6 (4.8)	7 (5.4)
Vaginal discharge	0	5 (4.0)	5 (3.9)
Vaginal haemorrhage	0	5 (4.0)	5 (3.9)
Female genital tract fistula	0	2 (1.6)	2 (1.6)
Metrorrhagia	0	2 (1.6)	2 (1.6)
Vulvovaginal dryness	0	2 (1.6)	2 (1.6)
Breast haematoma	0	1 (0.8)	1 (0.8)
Perineal pain	0	1 (0.8)	1 (0.8)
Vulval disorder	0	1 (0.8)	1 (0.8)
Vulvovaginal pain	0	1 (0.8)	1 (0.8)
Psychiatric disorders	3 (60.0)	19 (15.3)	22 (17.1)
Insomnia	0	8 (6.5)	8 (6.2)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Psychiatric disorders			
Anxiety	1 (20.0)	4 (3.2)	5 (3.9)
Depression	1 (20.0)	3 (2.4)	4 (3.1)
Confusional state	0	2 (1.6)	2 (1.6)
Depressed mood	0	2 (1.6)	2 (1.6)
Agitation	1 (20.0)	0	1 (0.8)
Alcoholism	0	1 (0.8)	1 (0.8)
Bradyphrenia	0	1 (0.8)	1 (0.8)
Mood altered	0	1 (0.8)	1 (0.8)
Nervousness	0	1 (0.8)	1 (0.8)
Injury, poisoning and procedural complications	1 (20.0)	17 (13.7)	18 (14.0)
Contusion	0	2 (1.6)	2 (1.6)
Gastroenteritis radiation	0	2 (1.6)	2 (1.6)
Ligament sprain	0	2 (1.6)	2 (1.6)
Wound	0	2 (1.6)	2 (1.6)
Compression fracture	0	1 (0.8)	1 (0.8)
Fall	0	1 (0.8)	1 (0.8)
Procedural pain	0	1 (0.8)	1 (0.8)
Skin abrasion	0	1 (0.8)	1 (0.8)
Skin laceration	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term (Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Injury, poisoning and procedural complications			
Spinal compression fracture	0	1 (0.8)	1 (0.8)
Stoma site pain	0	1 (0.8)	1 (0.8)
Stress fracture	0	1 (0.8)	1 (0.8)
Tendon rupture	0	1 (0.8)	1 (0.8)
Thermal burn	1 (20.0)	0	1 (0.8)
Toxicity to various agents	0	1 (0.8)	1 (0.8)
Wound complication	0	1 (0.8)	1 (0.8)
Wound dehiscence	0	1 (0.8)	1 (0.8)
Eye disorders	0	13 (10.5)	13 (10.1)
Dry eye	0	4 (3.2)	4 (3.1)
Vision blurred	0	3 (2.4)	3 (2.3)
Cataract	0	2 (1.6)	2 (1.6)
Diplopia	0	1 (0.8)	1 (0.8)
Eye irritation	0	1 (0.8)	1 (0.8)
Iridocyclitis	0	1 (0.8)	1 (0.8)
Lacrimation increased	0	1 (0.8)	1 (0.8)
Ocular discomfort	0	1 (0.8)	1 (0.8)
Uveitis	0	1 (0.8)	1 (0.8)
Vitreous floaters	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Endocrine disorders	0	12 (9.7)	12 (9.3)
Hypothyroidism	0	10 (8.1)	10 (7.8)
Hyperthyroidism	0	4 (3.2)	4 (3.1)
Adrenal insufficiency	0	1 (0.8)	1 (0.8)
Glucocorticoid deficiency	0	1 (0.8)	1 (0.8)
Hypophysitis	0	1 (0.8)	1 (0.8)
Cardiac disorders	0	7 (5.6)	7 (5.4)
Atrial fibrillation	0	2 (1.6)	2 (1.6)
Tachycardia	0	2 (1.6)	2 (1.6)
Angina pectoris	0	1 (0.8)	1 (0.8)
Bradycardia	0	1 (0.8)	1 (0.8)
Myocardial infarction	0	1 (0.8)	1 (0.8)
Pericardial effusion	0	1 (0.8)	1 (0.8)
Sinus tachycardia	0	1 (0.8)	1 (0.8)
Supraventricular extrasystoles	0	1 (0.8)	1 (0.8)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	0	6 (4.8)	6 (4.7)
Tumour pain	0	2 (1.6)	2 (1.6)
Cancer pain	0	1 (0.8)	1 (0.8)
Colon adenoma	0	1 (0.8)	1 (0.8)

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Table 14.3.1.24a Subgroup Analysis of Treatment-Emergent Adverse Events by Prior Bevacizumab by System Organ Class and Preferred Term
(Safety Analysis Set)

dMMR or (MMR-unk & MSI-H) EC: Total

System Organ Class Preferred Term [n (%)]	Prior Bevacizumab Use (N=5)	No Prior Bevacizumab Use (N=124)	Total (N=129)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma	0	1 (0.8)	1 (0.8)
Seborrhoeic keratosis	0	1 (0.8)	1 (0.8)
Ear and labyrinth disorders	0	5 (4.0)	5 (3.9)
Tinnitus	0	2 (1.6)	2 (1.6)
Vertigo	0	2 (1.6)	2 (1.6)
Cerumen impaction	0	1 (0.8)	1 (0.8)
Hypoacusis	0	1 (0.8)	1 (0.8)
Hepatobiliary disorders	0	2 (1.6)	2 (1.6)
Cholecystitis	0	1 (0.8)	1 (0.8)
Hepatic function abnormal	0	1 (0.8)	1 (0.8)
Hypertransaminasaemia	0	1 (0.8)	1 (0.8)

Note: Adverse events are coded using MedDRA version 23.0. For each system organ class and preferred term, patients are included only once, even if they experienced multiple events in that system organ class or preferred term. Treatment-emergent AEs are new AEs that begin, or any preexisting condition that worsens in severity, after at least 1 dose of study treatment has been administered and throughout the treatment period until 90 days after end of treatment(EOT) visit(or until the start of alternate anticancer therapy, whichever occurs earlier).
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