

**Dossier zur Nutzenbewertung
gemäß § 35a SGB V**

Trastuzumab-Deruxtecan (Enhertu[®])

Daiichi Sankyo Deutschland GmbH

Modul 4 A (Anhang 4-G)

Behandlung von erwachsenen Patienten mit inoperablem oder metastasiertem HER2-positivem Brustkrebs, die bereits mindestens eine gegen HER2 gerichtete Vorbehandlung erhalten haben

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Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Global Health Status

Visit	T-DXd (N=261)						T-DM1 (N=263)					
	n	Mean (SD)	Median	Q1, Q3	Min, Max		n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	252	30.03 (21.420)	25.00	16.67, 50.00	(0.0, 100.0)		259	31.50 (21.013)	33.33	16.67, 41.67	(0.0, 91.7)	
C2D1	96	26.74 (19.381)	16.67	16.67, 41.67	(0.0, 83.3)		109	29.13 (18.202)	25.00	16.67, 33.33	(0.0, 91.7)	
CHBL	95	-0.53 (20.586)	0.00	-16.67, 8.33	(-50.0, 75.0)		108	-2.31 (18.576)	0.00	-8.33, 8.33	(-58.3, 50.0)	
C3D1	243	29.66 (18.908)	33.33	16.67, 41.67	(0.0, 100.0)		219	27.78 (17.051)	25.00	16.67, 33.33	(0.0, 75.0)	
CHBL	241	-0.31 (20.824)	0.00	-16.67, 16.67	(-66.7, 50.0)		216	-2.12 (17.782)	0.00	-16.67, 8.33	(-66.7, 50.0)	
C5D1	230	29.31 (19.636)	33.33	16.67, 41.67	(0.0, 100.0)		167	28.69 (17.273)	25.00	16.67, 41.67	(0.0, 83.3)	
CHBL	226	0.15 (21.744)	0.00	-16.67, 16.67	(-66.7, 83.3)		165	-0.15 (20.401)	0.00	-8.33, 8.33	(-83.3, 50.0)	
C7D1	210	26.71 (17.543)	25.00	16.67, 33.33	(0.0, 83.3)		152	28.84 (17.707)	29.17	16.67, 33.33	(0.0, 83.3)	
CHBL	206	-2.06 (22.649)	0.00	-16.67, 8.33	(-66.7, 75.0)		150	-0.83 (20.292)	0.00	-8.33, 8.33	(-75.0, 50.0)	
C9D1	196	28.32 (17.510)	25.00	16.67, 33.33	(0.0, 83.3)		128	29.88 (19.070)	33.33	16.67, 37.50	(0.0, 83.3)	
CHBL	192	-0.69 (21.290)	0.00	-16.67, 8.33	(-58.3, 75.0)		127	-0.26 (23.755)	0.00	-16.67, 16.67	(-66.7, 66.7)	
C11D1	191	25.35 (16.014)	25.00	16.67, 33.33	(0.0, 83.3)		114	29.17 (17.503)	33.33	16.67, 41.67	(0.0, 66.7)	
CHBL	187	-2.76 (20.949)	0.00	-16.67, 8.33	(-66.7, 66.7)		114	-3.07 (20.984)	0.00	-16.67, 16.67	(-66.7, 50.0)	
C13D1	180	26.06 (15.610)	25.00	16.67, 33.33	(0.0, 75.0)		92	29.80 (17.350)	33.33	16.67, 50.00	(0.0, 66.7)	
CHBL	176	-3.13 (21.281)	0.00	-16.67, 12.50	(-83.3, 41.7)		92	-0.82 (20.075)	0.00	-16.67, 16.67	(-66.7, 50.0)	
C15D1	166	26.20 (16.393)	16.67	16.67, 33.33	(0.0, 100.0)		76	33.22 (20.115)	33.33	16.67, 50.00	(0.0, 83.3)	
CHBL	162	-2.73 (21.540)	0.00	-16.67, 16.67	(-66.7, 66.7)		75	1.00 (23.963)	0.00	-8.33, 16.67	(-66.7, 75.0)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Global Health Status

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	26.22 (16.742)	25.00	16.67, 33.33	(0.0, 83.3)	63	30.69 (20.015)	33.33	16.67, 41.67	(0.0, 100.0)
CHBL	154	-2.16 (22.075)	0.00	-16.67, 16.67	(-83.3, 66.7)	62	-0.54 (23.419)	0.00	-8.33, 8.33	(-50.0, 100.0)
C19D1	144	28.30 (16.933)	33.33	16.67, 33.33	(0.0, 75.0)	51	29.08 (20.506)	33.33	16.67, 33.33	(0.0, 100.0)
CHBL	140	-0.12 (21.110)	0.00	-16.67, 16.67	(-66.7, 75.0)	50	-0.67 (24.096)	0.00	-16.67, 8.33	(-50.0, 83.3)
C21D1	113	26.55 (16.235)	25.00	16.67, 33.33	(0.0, 100.0)	41	27.44 (17.897)	25.00	16.67, 41.67	(0.0, 66.7)
CHBL	112	-0.97 (20.127)	0.00	-16.67, 12.50	(-66.7, 50.0)	40	-2.29 (22.723)	0.00	-16.67, 12.50	(-50.0, 58.3)
C23D1	100	27.50 (16.897)	25.00	16.67, 33.33	(0.0, 100.0)	32	27.34 (16.291)	16.67	16.67, 45.83	(0.0, 50.0)
CHBL	98	0.68 (20.989)	0.00	-16.67, 16.67	(-75.0, 50.0)	31	-3.49 (23.938)	0.00	-16.67, 8.33	(-58.3, 50.0)
C25D1	72	30.67 (17.515)	33.33	16.67, 33.33	(0.0, 91.7)	29	33.91 (21.814)	33.33	16.67, 33.33	(0.0, 91.7)
CHBL	71	1.88 (17.604)	0.00	-8.33, 16.67	(-33.3, 50.0)	28	2.38 (26.436)	0.00	-16.67, 16.67	(-50.0, 75.0)
C27D1	48	31.25 (16.080)	33.33	16.67, 41.67	(0.0, 66.7)	21	26.19 (12.987)	25.00	16.67, 33.33	(0.0, 50.0)
CHBL	47	4.61 (16.283)	0.00	0.00, 16.67	(-33.3, 41.7)	21	-3.97 (21.184)	0.00	-16.67, 8.33	(-50.0, 41.7)
C29D1	41	27.85 (15.768)	16.67	16.67, 41.67	(0.0, 58.3)	14	34.52 (21.398)	33.33	16.67, 50.00	(0.0, 75.0)
CHBL	40	3.12 (16.199)	0.00	-8.33, 16.67	(-33.3, 50.0)	14	4.76 (27.095)	4.17	0.00, 16.67	(-50.0, 58.3)
C31D1	27	27.47 (16.476)	25.00	16.67, 33.33	(0.0, 66.7)	7	30.95 (32.530)	16.67	0.00, 66.67	(0.0, 83.3)
CHBL	27	1.23 (17.094)	0.00	-8.33, 16.67	(-41.7, 33.3)	7	4.76 (42.179)	0.00	-25.00, 58.33	(-50.0, 58.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Global Health Status

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
C33D1	19	25.00 (14.699)	16.67	16.67, 33.33	(0.0, 50.0)	5	33.33 (23.570)	16.67	16.67, 50.00	(16.7, 66.7)	
CHBL	19	2.19 (18.182)	0.00	-8.33, 16.67	(-33.3, 33.3)	5	10.00 (19.896)	0.00	0.00, 16.67	(-8.3, 41.7)	
C35D1	15	30.56 (18.811)	25.00	16.67, 50.00	(0.0, 66.7)	3	27.78 (34.694)	16.67	0.00, 66.67	(0.0, 66.7)	
CHBL	15	-0.00 (17.817)	8.33	-16.67, 16.67	(-33.3, 16.7)	3	11.11 (42.763)	0.00	-25.00, 58.33	(-25.0, 58.3)	
C37D1	9	28.70 (20.031)	25.00	16.67, 33.33	(0.0, 66.7)	1	50.00 (NE)	50.00	50.00, 50.00	(50.0, 50.0)	
CHBL	9	4.63 (13.249)	0.00	0.00, 16.67	(-16.7, 25.0)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)	
C39D1	3	44.44 (9.623)	50.00	33.33, 50.00	(33.3, 50.0)	0					
CHBL	3	-2.78 (4.811)	0.00	-8.33, 0.00	(-8.3, 0.0)	0					
C41D1	2	25.00 (11.785)	25.00	16.67, 33.33	(16.7, 33.3)	0					
CHBL	2	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0					
End of Treatment	99	34.01 (19.441)	33.33	16.67, 50.00	(0.0, 83.3)	174	35.01 (19.362)	33.33	16.67, 50.00	(0.0, 100.0)	
CHBL	97	1.98 (21.340)	0.00	-8.33, 16.67	(-50.0, 66.7)	172	4.07 (22.048)	0.00	-8.33, 16.67	(-75.0, 58.3)	
40 Day Follow-Up	30	37.50 (21.637)	33.33	25.00, 50.00	(0.0, 100.0)	79	35.13 (21.709)	33.33	16.67, 50.00	(0.0, 91.7)	
CHBL	30	6.39 (23.231)	4.17	-8.33, 16.67	(-41.7, 75.0)	77	3.46 (22.876)	0.00	-8.33, 16.67	(-75.0, 58.3)	
3 Months Follow-Up	60	35.42 (22.790)	33.33	16.67, 50.00	(0.0, 83.3)	110	33.48 (18.684)	33.33	16.67, 50.00	(0.0, 83.3)	
CHBL	60	4.72 (28.139)	0.00	-16.67, 16.67	(-50.0, 75.0)	110	4.17 (22.933)	0.00	-8.33, 16.67	(-66.7, 58.3)	

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Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Global Health Status

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	45.09 (20.980)	41.67	33.33, 58.33	(0.0, 100.0)	251	43.82 (21.109)	41.67	33.33, 58.33	(0.0, 100.0)
CHBL	249	15.06 (23.503)	16.67	0.00, 33.33	(-50.0, 83.3)	248	13.07 (22.414)	16.67	0.00, 25.00	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Physical Functioning

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	253	18.42 (18.305)	13.33	6.67, 26.67	(0.0, 86.7)	259	19.07 (19.175)	13.33	6.67, 26.67	(0.0, 100.0)	
C2D1	96	20.02 (19.335)	13.33	6.67, 26.67	(0.0, 100.0)	109	18.84 (16.526)	13.33	6.67, 26.67	(0.0, 66.7)	
CHBL	95	1.42 (12.276)	0.00	-6.67, 6.67	(-33.3, 40.0)	109	-1.22 (11.730)	0.00	-6.67, 6.67	(-53.3, 33.3)	
C3D1	246	18.10 (18.261)	13.33	6.67, 26.67	(0.0, 100.0)	220	16.77 (15.675)	13.33	6.67, 26.67	(0.0, 73.3)	
CHBL	244	-0.23 (13.619)	0.00	-6.67, 6.67	(-53.3, 53.3)	217	-1.05 (14.358)	0.00	-6.67, 6.67	(-66.7, 53.3)	
C5D1	230	18.30 (18.708)	13.33	6.67, 26.67	(0.0, 100.0)	169	17.99 (16.695)	13.33	6.67, 26.67	(0.0, 80.0)	
CHBL	227	-0.01 (15.440)	0.00	-6.67, 6.67	(-66.7, 46.7)	167	0.69 (15.667)	0.00	-6.67, 6.67	(-66.7, 60.0)	
C7D1	210	16.83 (17.815)	13.33	0.00, 26.67	(0.0, 100.0)	152	17.41 (16.687)	13.33	6.67, 26.67	(0.0, 93.3)	
CHBL	207	-0.61 (16.152)	0.00	-6.67, 6.67	(-60.0, 53.3)	150	0.72 (13.303)	0.00	-6.67, 6.67	(-46.7, 33.3)	
C9D1	196	15.32 (16.033)	13.33	0.00, 20.00	(0.0, 93.3)	129	16.85 (16.161)	13.33	6.67, 26.67	(0.0, 80.0)	
CHBL	193	-1.68 (15.215)	0.00	-6.67, 6.67	(-60.0, 46.7)	128	0.78 (13.558)	0.00	-6.67, 6.67	(-40.0, 33.3)	
C11D1	192	13.92 (14.354)	13.33	0.00, 20.00	(0.0, 93.3)	114	16.80 (18.201)	13.33	0.00, 20.00	(0.0, 86.7)	
CHBL	189	-3.10 (14.579)	0.00	-6.67, 0.00	(-60.0, 40.0)	113	-0.58 (16.405)	0.00	-6.67, 6.67	(-46.7, 66.7)	
C13D1	180	15.30 (15.466)	13.33	0.00, 20.00	(0.0, 86.7)	93	17.35 (20.052)	13.33	0.00, 20.00	(0.0, 93.3)	
CHBL	177	-2.03 (14.886)	0.00	-6.67, 6.67	(-60.0, 33.3)	92	-0.51 (17.210)	0.00	-6.67, 13.33	(-53.3, 40.0)	
C15D1	166	13.49 (14.752)	13.33	0.00, 20.00	(0.0, 93.3)	76	18.09 (20.211)	13.33	0.00, 33.33	(0.0, 86.7)	
CHBL	163	-3.97 (14.771)	0.00	-13.33, 0.00	(-60.0, 40.0)	75	-0.87 (16.141)	0.00	-6.67, 6.67	(-46.7, 46.7)	

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Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Physical Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	14.01 (14.757)	13.33	0.00, 20.00	(0.0, 60.0)	63	16.08 (16.619)	13.33	6.67, 26.67	(0.0, 80.0)
CHBL	155	-3.27 (16.194)	0.00	-13.33, 0.00	(-60.0, 53.3)	63	-3.60 (16.497)	0.00	-13.33, 6.67	(-46.7, 33.3)
C19D1	144	13.66 (14.609)	13.33	0.00, 20.00	(0.0, 86.7)	50	14.50 (15.837)	13.33	0.00, 25.00	(0.0, 80.0)
CHBL	141	-2.74 (16.017)	0.00	-13.33, 6.67	(-66.7, 46.7)	50	-3.50 (16.128)	0.00	-13.33, 6.67	(-46.7, 40.0)
C21D1	113	13.16 (15.235)	13.33	0.00, 20.00	(0.0, 100.0)	41	16.26 (16.736)	13.33	6.67, 26.67	(0.0, 66.7)
CHBL	112	-3.10 (15.981)	0.00	-13.33, 6.67	(-66.7, 33.3)	41	-2.44 (18.842)	0.00	-13.33, 13.33	(-46.7, 46.7)
C23D1	100	14.00 (14.166)	13.33	0.00, 20.00	(0.0, 66.7)	32	15.21 (13.359)	13.33	0.00, 26.67	(0.0, 46.7)
CHBL	99	-1.21 (16.751)	0.00	-6.67, 6.67	(-66.7, 33.3)	32	-4.58 (19.561)	0.00	-20.00, 13.33	(-53.3, 26.7)
C25D1	72	16.30 (15.580)	13.33	0.00, 26.67	(0.0, 60.0)	29	17.24 (16.858)	6.67	6.67, 33.33	(0.0, 53.3)
CHBL	71	1.03 (15.313)	0.00	-6.67, 13.33	(-40.0, 40.0)	29	-2.76 (19.315)	0.00	-13.33, 6.67	(-53.3, 40.0)
C27D1	48	14.44 (15.273)	13.33	0.00, 20.00	(0.0, 66.7)	21	13.65 (15.843)	13.33	0.00, 26.67	(0.0, 53.3)
CHBL	47	-0.57 (18.537)	0.00	-13.33, 6.67	(-40.0, 53.3)	21	-4.76 (19.223)	-6.67	-13.33, 0.00	(-53.3, 33.3)
C29D1	41	14.59 (14.047)	13.33	0.00, 20.00	(0.0, 60.0)	14	14.29 (14.525)	10.00	0.00, 26.67	(0.0, 46.7)
CHBL	40	1.79 (15.365)	0.00	-6.67, 13.33	(-33.3, 53.3)	14	-3.81 (21.197)	0.00	-13.33, 6.67	(-53.3, 26.7)
C31D1	27	12.84 (11.387)	13.33	0.00, 20.00	(0.0, 46.7)	7	14.29 (16.523)	13.33	0.00, 33.33	(0.0, 40.0)
CHBL	27	-1.48 (14.715)	0.00	-13.33, 6.67	(-33.3, 26.7)	7	0.00 (31.032)	13.33	-20.00, 20.00	(-53.3, 40.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Physical Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	11.67 (10.116)	13.33	3.33, 16.67	(0.0, 33.3)	5	17.33 (18.619)	13.33	0.00, 33.33	(0.0, 40.0)
CHBL	20	-3.67 (15.367)	0.00	-10.00, 6.67	(-40.0, 20.0)	5	1.33 (18.499)	0.00	-13.33, 20.00	(-20.0, 20.0)
C35D1	15	10.89 (11.302)	13.33	0.00, 16.67	(0.0, 40.0)	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)
CHBL	15	-2.00 (14.896)	0.00	-6.67, 13.33	(-33.3, 13.3)	3	-4.44 (21.430)	-13.33	-20.00, 20.00	(-20.0, 20.0)
C37D1	9	10.37 (10.599)	6.67	0.00, 13.33	(0.0, 26.7)	1	13.33 (NE)	13.33	13.33, 13.33	(13.3, 13.3)
CHBL	9	0.74 (11.759)	0.00	0.00, 6.67	(-26.7, 13.3)	1	-6.67 (NE)	-6.67	-6.67, -6.67	(-6.7, -6.7)
C39D1	3	4.44 (7.698)	0.00	0.00, 13.33	(0.0, 13.3)	0				
CHBL	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
C41D1	2	6.67 (9.428)	6.67	0.00, 13.33	(0.0, 13.3)	0				
CHBL	2	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
End of Treatment	100	21.40 (22.767)	13.33	6.67, 33.33	(0.0, 100.0)	174	17.78 (16.554)	13.33	6.67, 26.67	(0.0, 80.0)
CHBL	99	1.82 (19.928)	0.00	-6.67, 6.67	(-60.0, 86.7)	172	1.25 (17.349)	0.00	-6.67, 6.67	(-80.0, 53.3)
40 Day Follow-Up	30	23.78 (24.365)	13.33	6.67, 33.33	(0.0, 93.3)	79	17.13 (19.588)	13.33	0.00, 26.67	(0.0, 93.3)
CHBL	30	6.67 (19.962)	3.33	0.00, 13.33	(-33.3, 73.3)	77	-0.50 (17.764)	0.00	-6.67, 6.67	(-73.3, 66.7)
3 Months Follow-Up	60	23.22 (23.240)	16.67	6.67, 33.33	(0.0, 100.0)	111	17.54 (20.438)	13.33	0.00, 20.00	(0.0, 100.0)
CHBL	60	2.67 (25.840)	0.00	-6.67, 6.67	(-66.7, 86.7)	111	1.44 (17.018)	0.00	-6.67, 6.67	(-33.3, 73.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Physical Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	29.20 (22.978)	26.67	13.33, 40.00	(0.0, 100.0)	251	25.95 (19.804)	20.00	13.33, 40.00	(0.0, 93.3)
CHBL	250	10.72 (18.061)	6.67	0.00, 20.00	(-53.3, 86.7)	248	7.86 (17.547)	6.67	0.00, 13.33	(-66.7, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Role Functioning

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	253	18.71 (25.657)	0.00	0.00, 33.33	(0.0, 100.0)	258	18.22 (24.109)	0.00	0.00, 33.33	(0.0, 100.0)	
C2D1	96	18.92 (24.616)	0.00	0.00, 33.33	(0.0, 100.0)	108	17.13 (21.791)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	95	2.11 (21.366)	0.00	0.00, 0.00	(-66.7, 66.7)	107	-1.40 (21.733)	0.00	0.00, 0.00	(-66.7, 83.3)	
C3D1	245	18.44 (23.792)	0.00	0.00, 33.33	(0.0, 100.0)	220	17.73 (21.043)	0.00	0.00, 33.33	(0.0, 83.3)	
CHBL	243	-0.07 (22.396)	0.00	-16.67, 0.00	(-66.7, 66.7)	216	1.54 (20.590)	0.00	0.00, 0.00	(-100.0, 66.7)	
C5D1	230	19.42 (23.768)	8.33	0.00, 33.33	(0.0, 100.0)	168	18.15 (22.176)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	227	0.81 (24.752)	0.00	0.00, 16.67	(-100.0, 66.7)	166	2.81 (23.616)	0.00	0.00, 16.67	(-100.0, 66.7)	
C7D1	210	17.94 (22.378)	16.67	0.00, 33.33	(0.0, 100.0)	151	17.55 (20.887)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	207	-0.56 (24.157)	0.00	0.00, 16.67	(-100.0, 83.3)	149	2.91 (19.733)	0.00	0.00, 16.67	(-66.7, 66.7)	
C9D1	196	16.58 (20.980)	0.00	0.00, 33.33	(0.0, 100.0)	127	15.49 (19.718)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	193	-0.52 (23.441)	0.00	-16.67, 0.00	(-100.0, 66.7)	126	0.66 (22.051)	0.00	0.00, 16.67	(-100.0, 66.7)	
C11D1	191	14.75 (21.339)	0.00	0.00, 33.33	(0.0, 100.0)	113	15.93 (20.581)	0.00	0.00, 33.33	(0.0, 66.7)	
CHBL	188	-2.93 (22.841)	0.00	-16.67, 0.00	(-100.0, 100.0)	112	-1.04 (23.064)	0.00	-8.33, 0.00	(-100.0, 66.7)	
C13D1	180	16.20 (21.318)	0.00	0.00, 33.33	(0.0, 100.0)	92	15.40 (23.471)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	177	-2.17 (22.891)	0.00	-16.67, 0.00	(-100.0, 83.3)	91	-0.73 (23.689)	0.00	0.00, 0.00	(-100.0, 66.7)	
C15D1	166	14.26 (20.619)	0.00	0.00, 33.33	(0.0, 100.0)	76	17.11 (24.033)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	163	-3.07 (23.660)	0.00	-16.67, 0.00	(-100.0, 83.3)	75	-0.00 (26.565)	0.00	-16.67, 16.67	(-100.0, 66.7)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Role Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	156	15.71 (20.846)	0.00	0.00, 33.33	(0.0, 83.3)	65	15.64 (22.220)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	154	-2.38 (25.454)	0.00	0.00, 0.00	(-100.0, 66.7)	64	-1.04 (25.350)	0.00	0.00, 0.00	(-100.0, 83.3)
C19D1	144	14.35 (17.252)	0.00	0.00, 33.33	(0.0, 66.7)	50	14.00 (20.023)	0.00	0.00, 33.33	(0.0, 83.3)
CHBL	141	-2.72 (24.367)	0.00	0.00, 0.00	(-100.0, 50.0)	50	-3.33 (25.422)	0.00	0.00, 0.00	(-100.0, 66.7)
C21D1	113	13.72 (19.573)	0.00	0.00, 33.33	(0.0, 100.0)	40	15.42 (19.017)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	112	-2.53 (18.879)	0.00	0.00, 0.00	(-66.7, 33.3)	40	-4.17 (26.887)	0.00	-16.67, 8.33	(-100.0, 50.0)
C23D1	99	14.65 (21.596)	0.00	0.00, 33.33	(0.0, 100.0)	31	16.13 (17.472)	0.00	0.00, 33.33	(0.0, 50.0)
CHBL	98	-1.36 (23.652)	0.00	0.00, 0.00	(-100.0, 66.7)	31	-3.76 (29.094)	0.00	-16.67, 16.67	(-100.0, 33.3)
C25D1	72	16.67 (20.171)	0.00	0.00, 33.33	(0.0, 66.7)	28	14.88 (23.718)	0.00	0.00, 16.67	(0.0, 100.0)
CHBL	71	-1.41 (20.845)	0.00	-16.67, 0.00	(-50.0, 33.3)	28	-5.95 (27.297)	0.00	-16.67, 8.33	(-100.0, 33.3)
C27D1	46	14.86 (21.724)	0.00	0.00, 33.33	(0.0, 83.3)	21	11.11 (17.743)	0.00	0.00, 16.67	(0.0, 66.7)
CHBL	45	-3.33 (22.077)	0.00	-16.67, 0.00	(-50.0, 66.7)	21	-1.59 (17.404)	0.00	-16.67, 0.00	(-33.3, 50.0)
C29D1	40	15.00 (18.796)	0.00	0.00, 33.33	(0.0, 66.7)	14	13.10 (14.876)	8.33	0.00, 33.33	(0.0, 33.3)
CHBL	39	0.43 (22.778)	0.00	0.00, 0.00	(-66.7, 66.7)	14	1.19 (13.812)	0.00	0.00, 0.00	(-16.7, 33.3)
C31D1	26	10.90 (17.602)	0.00	0.00, 33.33	(0.0, 50.0)	7	16.67 (25.459)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	26	-4.49 (21.374)	0.00	-16.67, 0.00	(-50.0, 50.0)	7	9.52 (26.972)	0.00	0.00, 16.67	(-16.7, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Role Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	14.17 (18.157)	0.00	0.00, 33.33	(0.0, 50.0)	5	10.00 (22.361)	0.00	0.00, 0.00	(0.0, 50.0)
CHBL	20	-3.33 (23.939)	0.00	-16.67, 0.00	(-50.0, 50.0)	5	6.67 (14.907)	0.00	0.00, 0.00	(0.0, 33.3)
C35D1	15	13.33 (15.685)	0.00	0.00, 33.33	(0.0, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
CHBL	15	1.11 (16.019)	0.00	0.00, 0.00	(-33.3, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
C37D1	9	9.26 (18.840)	0.00	0.00, 0.00	(0.0, 50.0)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)
CHBL	9	3.70 (13.889)	0.00	0.00, 0.00	(-16.7, 33.3)	1	16.67 (NE)	16.67	16.67, 16.67	(16.7, 16.7)
C39D1	3	5.56 (9.623)	0.00	0.00, 16.67	(0.0, 16.7)	0				
CHBL	3	5.56 (9.623)	0.00	0.00, 16.67	(0.0, 16.7)	0				
C41D1	2	8.33 (11.785)	8.33	0.00, 16.67	(0.0, 16.7)	0				
CHBL	2	8.33 (11.785)	8.33	0.00, 16.67	(0.0, 16.7)	0				
End of Treatment	100	21.67 (29.918)	0.00	0.00, 33.33	(0.0, 100.0)	174	19.83 (21.754)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	99	3.87 (29.046)	0.00	0.00, 16.67	(-100.0, 100.0)	171	4.09 (23.350)	0.00	0.00, 16.67	(-100.0, 66.7)
40 Day Follow-Up	30	24.44 (29.921)	16.67	0.00, 33.33	(0.0, 100.0)	79	18.57 (24.312)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	30	8.33 (26.892)	0.00	0.00, 16.67	(-33.3, 83.3)	77	2.16 (24.386)	0.00	0.00, 16.67	(-100.0, 66.7)
3 Months Follow-Up	60	22.22 (27.731)	8.33	0.00, 33.33	(0.0, 100.0)	111	19.22 (22.940)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	60	4.17 (33.139)	0.00	0.00, 16.67	(-100.0, 100.0)	111	5.71 (21.614)	0.00	0.00, 16.67	(-50.0, 83.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Role Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	34.98 (29.106)	33.33	0.00, 50.00	(0.0, 100.0)	251	30.68 (26.111)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	250	16.27 (26.884)	16.67	0.00, 33.33	(-100.0, 100.0)	247	13.97 (25.404)	0.00	0.00, 33.33	(-100.0, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Emotional Functioning

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	252	23.34 (23.370)	16.67	0.00, 33.33	(0.0, 100.0)	259	20.87 (19.437)	16.67	8.33, 33.33	(0.0, 100.0)	
C2D1	95	18.04 (21.657)	8.33	0.00, 33.33	(0.0, 83.3)	108	17.64 (19.451)	8.33	0.00, 33.33	(0.0, 91.7)	
CHBL	94	-4.91 (19.941)	0.00	-8.33, 0.00	(-83.3, 41.7)	108	-4.32 (17.259)	0.00	-12.50, 0.00	(-66.7, 50.0)	
C3D1	246	18.94 (20.775)	16.67	0.00, 33.33	(0.0, 91.7)	219	16.49 (18.274)	8.33	0.00, 25.00	(0.0, 91.7)	
CHBL	243	-4.52 (19.751)	0.00	-16.67, 8.33	(-66.7, 66.7)	216	-4.14 (18.855)	0.00	-16.67, 0.00	(-91.7, 58.3)	
C5D1	230	18.48 (19.618)	16.67	0.00, 33.33	(0.0, 100.0)	166	18.17 (17.784)	16.67	0.00, 25.00	(0.0, 91.7)	
CHBL	226	-4.74 (20.265)	0.00	-16.67, 8.33	(-66.7, 83.3)	164	-1.44 (16.905)	0.00	-8.33, 8.33	(-83.3, 66.7)	
C7D1	210	19.14 (20.684)	16.67	0.00, 33.33	(0.0, 91.7)	152	17.49 (16.934)	16.67	0.00, 25.00	(0.0, 75.0)	
CHBL	206	-4.02 (19.643)	0.00	-16.67, 0.00	(-75.0, 50.0)	150	-1.85 (17.303)	0.00	-8.33, 8.33	(-58.3, 58.3)	
C9D1	196	17.52 (20.025)	8.33	0.00, 33.33	(0.0, 91.7)	127	19.09 (19.840)	16.67	0.00, 25.00	(0.0, 100.0)	
CHBL	192	-5.15 (18.214)	0.00	-16.67, 0.00	(-66.7, 41.7)	126	0.37 (18.795)	0.00	-8.33, 8.33	(-41.7, 75.0)	
C11D1	192	17.36 (20.059)	8.33	0.00, 33.33	(0.0, 91.7)	114	17.47 (18.911)	16.67	0.00, 25.00	(0.0, 100.0)	
CHBL	188	-5.59 (19.150)	0.00	-16.67, 0.00	(-83.3, 50.0)	113	-2.97 (19.068)	0.00	-16.67, 8.33	(-66.7, 83.3)	
C13D1	180	18.89 (21.802)	16.67	0.00, 33.33	(0.0, 100.0)	93	19.62 (20.510)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	176	-5.33 (20.181)	0.00	-16.67, 0.00	(-75.0, 66.7)	92	-2.48 (21.068)	0.00	-8.33, 8.33	(-83.3, 75.0)	
C15D1	166	15.91 (20.201)	8.33	0.00, 25.00	(0.0, 91.7)	76	19.96 (20.188)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	162	-7.39 (19.253)	-8.33	-16.67, 0.00	(-75.0, 50.0)	75	-0.78 (18.132)	0.00	-8.33, 8.33	(-50.0, 75.0)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Emotional Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	16.03 (20.337)	8.33	0.00, 25.00	(0.0, 91.7)	64	18.10 (16.571)	16.67	0.00, 29.17	(0.0, 66.7)
CHBL	154	-7.18 (19.427)	0.00	-16.67, 0.00	(-75.0, 41.7)	63	-4.23 (17.827)	-8.33	-16.67, 8.33	(-50.0, 33.3)
C19D1	144	18.09 (21.315)	8.33	0.00, 33.33	(0.0, 91.7)	51	15.52 (15.186)	8.33	0.00, 25.00	(0.0, 58.3)
CHBL	140	-5.00 (21.021)	0.00	-16.67, 4.17	(-75.0, 41.7)	51	-6.37 (15.329)	-8.33	-16.67, 0.00	(-58.3, 25.0)
C21D1	113	16.74 (19.686)	8.33	0.00, 33.33	(0.0, 91.7)	41	20.12 (18.064)	16.67	8.33, 33.33	(0.0, 66.7)
CHBL	112	-6.00 (19.963)	0.00	-16.67, 0.00	(-66.7, 58.3)	41	-4.07 (20.927)	0.00	-16.67, 8.33	(-66.7, 33.3)
C23D1	100	16.67 (21.122)	8.33	0.00, 29.17	(0.0, 100.0)	32	20.14 (20.498)	12.50	4.17, 33.33	(0.0, 83.3)
CHBL	98	-4.51 (17.715)	0.00	-16.67, 0.00	(-58.3, 33.3)	32	-3.82 (20.868)	0.00	-8.33, 8.33	(-75.0, 27.8)
C25D1	72	19.56 (23.494)	12.50	0.00, 33.33	(0.0, 100.0)	28	21.73 (24.568)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	71	-4.93 (19.850)	0.00	-16.67, 8.33	(-66.7, 33.3)	28	-2.38 (22.090)	0.00	-8.33, 8.33	(-66.7, 33.3)
C27D1	48	22.74 (24.777)	16.67	0.00, 33.33	(0.0, 100.0)	21	15.08 (18.185)	8.33	0.00, 25.00	(0.0, 58.3)
CHBL	47	1.42 (17.230)	0.00	-8.33, 16.67	(-33.3, 41.7)	21	-5.95 (15.843)	0.00	-16.67, 0.00	(-50.0, 16.7)
C29D1	41	21.54 (23.421)	16.67	8.33, 33.33	(0.0, 100.0)	14	18.45 (15.393)	20.83	0.00, 33.33	(0.0, 41.7)
CHBL	40	1.67 (20.690)	0.00	-8.33, 8.33	(-50.0, 58.3)	14	-4.17 (15.929)	0.00	-8.33, 8.33	(-50.0, 16.7)
C31D1	27	18.83 (25.063)	8.33	0.00, 33.33	(0.0, 100.0)	7	13.10 (20.331)	0.00	0.00, 33.33	(0.0, 50.0)
CHBL	27	-3.70 (23.495)	0.00	-16.67, 8.33	(-66.7, 50.0)	7	-7.14 (22.786)	0.00	-25.00, 8.33	(-50.0, 16.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Emotional Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	19.17 (23.894)	16.67	0.00, 25.00	(0.0, 91.7)	5	20.00 (19.185)	25.00	0.00, 33.33	(0.0, 41.7)
CHBL	20	-5.42 (25.972)	0.00	-12.50, 4.17	(-58.3, 50.0)	5	0.00 (5.893)	0.00	0.00, 0.00	(-8.3, 8.3)
C35D1	15	17.78 (26.327)	8.33	0.00, 33.33	(0.0, 100.0)	3	8.33 (14.434)	0.00	0.00, 25.00	(0.0, 25.0)
CHBL	15	-9.44 (23.960)	-8.33	-25.00, 8.33	(-58.3, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
C37D1	9	12.04 (13.889)	8.33	0.00, 16.67	(0.0, 33.3)	1	8.33 (NE)	8.33	8.33, 8.33	(8.3, 8.3)
CHBL	9	-10.19 (22.352)	-8.33	-16.67, 0.00	(-50.0, 33.3)	1	-33.33 (NE)	-33.33	-33.33, -33.33	(-33.3, -33.3)
C39D1	3	16.67 (8.333)	16.67	8.33, 25.00	(8.3, 25.0)	0				
CHBL	3	8.33 (22.048)	16.67	-16.67, 25.00	(-16.7, 25.0)	0				
C41D1	2	8.33 (11.785)	8.33	0.00, 16.67	(0.0, 16.7)	0				
CHBL	2	0.00 (23.570)	0.00	-16.67, 16.67	(-16.7, 16.7)	0				
End of Treatment	100	20.83 (22.206)	16.67	0.00, 33.33	(0.0, 91.7)	175	20.14 (18.683)	16.67	0.00, 33.33	(0.0, 83.3)
CHBL	98	0.28 (19.873)	0.00	-8.33, 8.33	(-83.3, 50.0)	173	1.48 (20.488)	0.00	-8.33, 8.33	(-83.3, 83.3)
40 Day Follow-Up	30	26.11 (29.664)	16.67	0.00, 33.33	(0.0, 100.0)	79	20.89 (20.796)	16.67	0.00, 33.33	(0.0, 83.3)
CHBL	30	8.33 (20.295)	8.33	0.00, 16.67	(-41.7, 66.7)	77	2.16 (21.091)	0.00	-8.33, 8.33	(-66.7, 83.3)
3 Months Follow-Up	60	19.17 (18.621)	16.67	0.00, 33.33	(0.0, 66.7)	110	16.82 (20.002)	8.33	0.00, 25.00	(0.0, 91.7)
CHBL	60	1.94 (17.982)	0.00	-8.33, 16.67	(-75.0, 33.3)	110	0.45 (21.738)	0.00	-8.33, 8.33	(-50.0, 75.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Emotional Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	34.46 (24.868)	33.33	16.67, 50.00	(0.0, 100.0)	251	30.09 (22.551)	25.00	16.67, 41.67	(0.0, 100.0)
CHBL	249	11.17 (19.997)	8.33	0.00, 25.00	(-66.7, 83.3)	248	9.94 (21.310)	8.33	0.00, 25.00	(-66.7, 83.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Cognitive Functioning

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	251	16.60 (20.138)	16.67	0.00, 33.33	(0.0, 100.0)	259	14.29 (17.416)	16.67	0.00, 16.67	(0.0, 83.3)	
C2D1	95	15.61 (18.643)	16.67	0.00, 33.33	(0.0, 66.7)	108	14.66 (17.161)	16.67	0.00, 33.33	(0.0, 66.7)	
CHBL	93	-0.54 (15.039)	0.00	0.00, 0.00	(-33.3, 50.0)	108	-0.00 (16.589)	0.00	0.00, 0.00	(-66.7, 33.3)	
C3D1	246	15.38 (19.212)	16.67	0.00, 33.33	(0.0, 83.3)	219	14.61 (17.548)	16.67	0.00, 16.67	(0.0, 100.0)	
CHBL	242	-1.10 (17.541)	0.00	-16.67, 0.00	(-66.7, 66.7)	216	0.62 (17.001)	0.00	0.00, 0.00	(-66.7, 66.7)	
C5D1	230	14.93 (17.810)	16.67	0.00, 33.33	(0.0, 83.3)	166	14.76 (17.544)	16.67	0.00, 16.67	(0.0, 83.3)	
CHBL	225	-1.41 (18.278)	0.00	0.00, 0.00	(-100.0, 50.0)	164	1.12 (17.034)	0.00	0.00, 16.67	(-66.7, 50.0)	
C7D1	209	15.71 (18.965)	16.67	0.00, 33.33	(0.0, 66.7)	152	16.78 (19.794)	16.67	0.00, 33.33	(0.0, 83.3)	
CHBL	204	-1.23 (18.343)	0.00	0.00, 0.00	(-100.0, 33.3)	150	2.67 (17.062)	0.00	0.00, 16.67	(-50.0, 50.0)	
C9D1	196	15.48 (17.743)	16.67	0.00, 16.67	(0.0, 83.3)	128	14.84 (17.403)	16.67	0.00, 16.67	(0.0, 100.0)	
CHBL	191	-1.05 (15.258)	0.00	-16.67, 0.00	(-66.7, 50.0)	127	2.36 (18.272)	0.00	0.00, 16.67	(-83.3, 66.7)	
C11D1	192	14.50 (17.465)	16.67	0.00, 33.33	(0.0, 83.3)	114	14.47 (19.011)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	187	-2.23 (17.006)	0.00	-16.67, 0.00	(-100.0, 33.3)	113	0.29 (18.764)	0.00	0.00, 16.67	(-66.7, 66.7)	
C13D1	180	17.41 (19.445)	16.67	0.00, 33.33	(0.0, 83.3)	93	16.49 (19.270)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	175	-0.57 (18.213)	0.00	0.00, 16.67	(-100.0, 50.0)	92	1.81 (16.659)	0.00	0.00, 8.33	(-83.3, 66.7)	
C15D1	166	14.46 (19.724)	0.00	0.00, 33.33	(0.0, 100.0)	75	19.11 (22.874)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	161	-2.90 (19.326)	0.00	-16.67, 0.00	(-100.0, 50.0)	74	5.63 (16.385)	0.00	0.00, 16.67	(-33.3, 66.7)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Cognitive Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	156	14.32 (18.399)	8.33	0.00, 16.67	(0.0, 100.0)	64	17.19 (18.056)	16.67	0.00, 33.33	(0.0, 83.3)
CHBL	152	-2.41 (18.137)	0.00	0.00, 0.00	(-100.0, 50.0)	63	1.32 (18.036)	0.00	0.00, 16.67	(-66.7, 50.0)
C19D1	142	16.31 (19.896)	16.67	0.00, 33.33	(0.0, 100.0)	50	15.67 (18.568)	16.67	0.00, 33.33	(0.0, 66.7)
CHBL	137	-1.22 (18.484)	0.00	0.00, 0.00	(-100.0, 50.0)	50	-0.67 (15.416)	0.00	0.00, 0.00	(-66.7, 33.3)
C21D1	112	18.15 (21.523)	16.67	0.00, 33.33	(0.0, 100.0)	41	21.14 (23.577)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	111	0.90 (16.943)	0.00	0.00, 16.67	(-50.0, 33.3)	41	3.66 (19.189)	0.00	0.00, 16.67	(-50.0, 50.0)
C23D1	100	16.83 (18.876)	16.67	0.00, 33.33	(0.0, 83.3)	32	21.35 (25.128)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	98	1.19 (15.183)	0.00	0.00, 16.67	(-50.0, 33.3)	32	3.12 (22.575)	0.00	0.00, 16.67	(-50.0, 50.0)
C25D1	72	19.44 (22.378)	16.67	0.00, 33.33	(0.0, 100.0)	29	20.69 (24.257)	16.67	0.00, 33.33	(0.0, 66.7)
CHBL	71	3.05 (14.989)	0.00	0.00, 16.67	(-33.3, 50.0)	29	2.87 (22.743)	0.00	0.00, 16.67	(-50.0, 66.7)
C27D1	48	14.24 (19.139)	0.00	0.00, 25.00	(0.0, 83.3)	21	16.67 (21.082)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	47	-0.00 (12.530)	0.00	0.00, 0.00	(-33.3, 33.3)	21	0.00 (18.257)	0.00	-16.67, 16.67	(-33.3, 33.3)
C29D1	41	19.51 (20.036)	16.67	0.00, 33.33	(0.0, 100.0)	14	14.29 (17.118)	8.33	0.00, 33.33	(0.0, 50.0)
CHBL	40	6.67 (12.965)	0.00	0.00, 16.67	(-16.7, 33.3)	14	-8.33 (14.248)	0.00	-16.67, 0.00	(-33.3, 16.7)
C31D1	26	17.31 (24.258)	16.67	0.00, 16.67	(0.0, 100.0)	7	14.29 (20.250)	0.00	0.00, 33.33	(0.0, 50.0)
CHBL	26	3.85 (15.135)	0.00	0.00, 16.67	(-16.7, 50.0)	7	-4.76 (18.545)	0.00	-16.67, 16.67	(-33.3, 16.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Cognitive Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	16.67 (25.363)	8.33	0.00, 16.67	(0.0, 100.0)	5	16.67 (28.868)	0.00	0.00, 16.67	(0.0, 66.7)
CHBL	20	0.00 (16.222)	0.00	-8.33, 0.00	(-33.3, 33.3)	5	-3.33 (13.944)	0.00	-16.67, 0.00	(-16.7, 16.7)
C35D1	15	20.00 (29.005)	16.67	0.00, 33.33	(0.0, 100.0)	3	5.56 (9.623)	0.00	0.00, 16.67	(0.0, 16.7)
CHBL	15	3.33 (14.365)	0.00	0.00, 0.00	(-16.7, 33.3)	3	-5.56 (9.623)	0.00	-16.67, 0.00	(-16.7, 0.0)
C37D1	9	14.81 (17.568)	16.67	0.00, 16.67	(0.0, 50.0)	1	50.00 (NE)	50.00	50.00, 50.00	(50.0, 50.0)
CHBL	9	3.70 (13.889)	0.00	0.00, 0.00	(-16.7, 33.3)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
C39D1	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)	0				
CHBL	3	5.56 (9.623)	0.00	0.00, 16.67	(0.0, 16.7)	0				
C41D1	2	25.00 (11.785)	25.00	16.67, 33.33	(16.7, 33.3)	0				
CHBL	2	8.33 (11.785)	8.33	0.00, 16.67	(0.0, 16.7)	0				
End of Treatment	100	19.67 (20.567)	16.67	0.00, 33.33	(0.0, 83.3)	175	14.67 (18.761)	0.00	0.00, 33.33	(0.0, 83.3)
CHBL	98	5.10 (22.246)	0.00	0.00, 16.67	(-100.0, 50.0)	173	2.02 (17.071)	0.00	0.00, 16.67	(-66.7, 66.7)
40 Day Follow-Up	30	25.56 (24.264)	16.67	0.00, 33.33	(0.0, 83.3)	78	16.88 (20.189)	16.67	0.00, 33.33	(0.0, 83.3)
CHBL	30	15.56 (21.412)	16.67	0.00, 16.67	(-16.7, 83.3)	76	2.19 (20.247)	0.00	0.00, 16.67	(-66.7, 83.3)
3 Months Follow-Up	60	19.72 (22.859)	16.67	0.00, 33.33	(0.0, 100.0)	110	12.73 (15.952)	0.00	0.00, 16.67	(0.0, 66.7)
CHBL	60	5.56 (23.302)	0.00	0.00, 16.67	(-83.3, 66.7)	110	0.30 (18.477)	0.00	-16.67, 16.67	(-83.3, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Cognitive Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	29.78 (23.675)	33.33	16.67, 50.00	(0.0, 100.0)	251	25.83 (23.573)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	248	13.10 (20.000)	16.67	0.00, 25.00	(-83.3, 83.3)	248	11.90 (19.915)	16.67	0.00, 16.67	(-66.7, 83.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Social Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Baseline	251	19.39 (23.812)	16.67	0.00, 33.33	(0.0, 100.0)	260	20.00 (22.585)	16.67	0.00, 33.33	(0.0, 100.0)
C2D1	95	16.84 (24.004)	0.00	0.00, 33.33	(0.0, 100.0)	108	18.83 (22.683)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	94	-4.08 (23.146)	0.00	-16.67, 0.00	(-83.3, 100.0)	108	-2.31 (20.941)	0.00	-16.67, 0.00	(-66.7, 66.7)
C3D1	245	19.73 (23.588)	16.67	0.00, 33.33	(0.0, 100.0)	219	16.21 (22.684)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	241	0.21 (22.126)	0.00	-16.67, 0.00	(-66.7, 66.7)	217	-2.84 (21.834)	0.00	-16.67, 0.00	(-66.7, 100.0)
C5D1	230	18.77 (23.242)	16.67	0.00, 33.33	(0.0, 100.0)	166	17.77 (22.855)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	225	-0.22 (23.805)	0.00	-16.67, 16.67	(-83.3, 100.0)	165	-0.10 (21.345)	0.00	0.00, 0.00	(-83.3, 66.7)
C7D1	210	17.78 (22.088)	0.00	0.00, 33.33	(0.0, 100.0)	152	17.21 (22.321)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	205	-1.46 (23.408)	0.00	-16.67, 0.00	(-83.3, 66.7)	151	-1.55 (21.374)	0.00	-16.67, 0.00	(-66.7, 66.7)
C9D1	196	17.01 (21.281)	0.00	0.00, 33.33	(0.0, 100.0)	128	19.53 (23.017)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	191	-2.01 (22.105)	0.00	-16.67, 0.00	(-66.7, 100.0)	128	1.43 (23.665)	0.00	-8.33, 16.67	(-66.7, 83.3)
C11D1	192	15.45 (20.287)	0.00	0.00, 33.33	(0.0, 100.0)	114	17.11 (22.113)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	187	-3.21 (22.832)	0.00	-16.67, 0.00	(-83.3, 83.3)	114	-2.05 (22.299)	0.00	-16.67, 0.00	(-66.7, 66.7)
C13D1	180	18.24 (22.471)	0.00	0.00, 33.33	(0.0, 100.0)	93	20.43 (24.834)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	175	-0.29 (22.352)	0.00	0.00, 0.00	(-66.7, 83.3)	93	2.15 (23.082)	0.00	-16.67, 16.67	(-66.7, 83.3)
C15D1	166	14.96 (21.760)	0.00	0.00, 33.33	(0.0, 100.0)	76	20.18 (27.259)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	161	-4.24 (22.919)	0.00	-16.67, 0.00	(-83.3, 83.3)	76	2.19 (25.581)	0.00	0.00, 16.67	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Social Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	16.56 (22.606)	0.00	0.00, 33.33	(0.0, 100.0)	64	16.67 (22.616)	0.00	0.00, 33.33	(0.0, 83.3)
CHBL	153	-3.05 (24.291)	0.00	-16.67, 0.00	(-83.3, 83.3)	64	-0.52 (27.534)	0.00	-16.67, 16.67	(-66.7, 83.3)
C19D1	143	16.78 (22.422)	0.00	0.00, 33.33	(0.0, 100.0)	51	16.67 (24.037)	0.00	0.00, 33.33	(0.0, 83.3)
CHBL	138	-1.21 (22.391)	0.00	-16.67, 0.00	(-83.3, 66.7)	51	0.98 (26.122)	0.00	0.00, 0.00	(-83.3, 83.3)
C21D1	113	16.37 (22.711)	0.00	0.00, 33.33	(0.0, 100.0)	41	17.89 (24.264)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	111	-0.60 (24.611)	0.00	-16.67, 0.00	(-66.7, 66.7)	41	1.63 (22.914)	0.00	0.00, 0.00	(-50.0, 66.7)
C23D1	99	17.00 (20.479)	0.00	0.00, 33.33	(0.0, 66.7)	31	20.43 (30.341)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	97	-0.34 (22.946)	0.00	0.00, 0.00	(-66.7, 66.7)	31	3.76 (30.034)	0.00	0.00, 0.00	(-50.0, 100.0)
C25D1	72	19.91 (23.006)	8.33	0.00, 33.33	(0.0, 83.3)	28	19.05 (26.726)	8.33	0.00, 33.33	(0.0, 100.0)
CHBL	71	0.47 (24.065)	0.00	-16.67, 0.00	(-50.0, 83.3)	28	1.79 (24.985)	0.00	-8.33, 0.00	(-50.0, 66.7)
C27D1	48	17.36 (23.560)	0.00	0.00, 33.33	(0.0, 83.3)	21	15.87 (30.035)	0.00	0.00, 16.67	(0.0, 100.0)
CHBL	47	3.55 (23.035)	0.00	0.00, 0.00	(-50.0, 83.3)	21	-0.79 (29.569)	0.00	-16.67, 0.00	(-33.3, 100.0)
C29D1	40	13.33 (22.072)	0.00	0.00, 25.00	(0.0, 100.0)	14	10.71 (16.803)	0.00	0.00, 16.67	(0.0, 50.0)
CHBL	39	0.43 (20.763)	0.00	0.00, 0.00	(-50.0, 83.3)	14	-9.52 (18.157)	0.00	-33.33, 0.00	(-33.3, 16.7)
C31D1	26	18.59 (26.385)	0.00	0.00, 33.33	(0.0, 100.0)	7	4.76 (8.133)	0.00	0.00, 16.67	(0.0, 16.7)
CHBL	26	3.85 (25.081)	0.00	0.00, 16.67	(-50.0, 83.3)	7	-11.90 (18.545)	-16.67	-33.33, 0.00	(-33.3, 16.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Social Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	20.00 (22.031)	16.67	0.00, 33.33	(0.0, 66.7)	5	10.00 (22.361)	0.00	0.00, 0.00	(0.0, 50.0)
CHBL	20	6.67 (23.195)	0.00	0.00, 25.00	(-50.0, 50.0)	5	-13.33 (32.059)	-16.67	-33.33, 0.00	(-50.0, 33.3)
C35D1	15	16.67 (21.822)	0.00	0.00, 33.33	(0.0, 66.7)	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)
CHBL	15	2.22 (13.897)	0.00	0.00, 0.00	(-33.3, 33.3)	3	-5.56 (25.459)	0.00	-33.33, 16.67	(-33.3, 16.7)
C37D1	9	20.37 (20.031)	33.33	0.00, 33.33	(0.0, 50.0)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)
CHBL	9	12.96 (16.197)	0.00	0.00, 33.33	(0.0, 33.3)	1	16.67 (NE)	16.67	16.67, 16.67	(16.7, 16.7)
C39D1	3	22.22 (19.245)	33.33	0.00, 33.33	(0.0, 33.3)	0				
CHBL	3	16.67 (16.667)	16.67	0.00, 33.33	(0.0, 33.3)	0				
C41D1	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
CHBL	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
End of Treatment	100	20.83 (27.664)	0.00	0.00, 33.33	(0.0, 100.0)	174	19.44 (22.099)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	98	3.23 (23.161)	0.00	0.00, 16.67	(-50.0, 66.7)	172	0.68 (22.028)	0.00	-16.67, 16.67	(-100.0, 66.7)
40 Day Follow-Up	30	22.78 (32.602)	0.00	0.00, 33.33	(0.0, 100.0)	79	21.73 (24.800)	16.67	0.00, 33.33	(0.0, 83.3)
CHBL	30	8.89 (29.274)	0.00	0.00, 33.33	(-50.0, 100.0)	77	2.60 (21.471)	0.00	0.00, 16.67	(-66.7, 66.7)
3 Months Follow-Up	60	21.39 (25.690)	16.67	0.00, 33.33	(0.0, 100.0)	110	19.55 (20.797)	16.67	0.00, 33.33	(0.0, 66.7)
CHBL	60	3.61 (24.566)	0.00	0.00, 16.67	(-50.0, 66.7)	110	3.03 (19.705)	0.00	-16.67, 16.67	(-33.3, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Functional scales/Social Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	37.22 (28.661)	33.33	16.67, 50.00	(0.0, 100.0)	251	30.81 (27.044)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	248	17.74 (25.473)	16.67	0.00, 33.33	(-50.0, 100.0)	249	11.58 (26.156)	0.00	0.00, 16.67	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Fatigue

Visit	T-DXd (N=261)						T-DM1 (N=263)					
	n	Mean (SD)	Median	Q1, Q3	Min, Max		n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	253	28.33 (23.157)	33.33	11.11, 33.33	(0.0, 100.0)		259	27.54 (21.529)	33.33	11.11, 33.33	(0.0, 100.0)	
C2D1	96	30.09 (24.339)	33.33	11.11, 44.44	(0.0, 100.0)		109	28.03 (19.864)	33.33	11.11, 33.33	(0.0, 100.0)	
CHBL	95	1.40 (19.125)	0.00	-11.11, 11.11	(-33.3, 66.7)		109	-0.20 (16.072)	0.00	-11.11, 11.11	(-55.6, 55.6)	
C3D1	246	28.82 (23.126)	33.33	11.11, 33.33	(0.0, 100.0)		220	26.19 (20.414)	22.22	11.11, 33.33	(0.0, 100.0)	
CHBL	244	0.59 (21.903)	0.00	-11.11, 11.11	(-77.8, 100.0)		217	-0.13 (17.194)	0.00	-11.11, 11.11	(-55.6, 55.6)	
C5D1	230	29.37 (22.425)	33.33	11.11, 33.33	(0.0, 100.0)		168	28.57 (20.512)	33.33	11.11, 33.33	(0.0, 100.0)	
CHBL	227	1.52 (22.646)	0.00	-11.11, 11.11	(-66.7, 77.8)		166	2.81 (18.939)	0.00	-11.11, 11.11	(-44.4, 88.9)	
C7D1	210	26.03 (21.756)	22.22	11.11, 33.33	(0.0, 100.0)		151	26.78 (21.092)	33.33	11.11, 33.33	(0.0, 100.0)	
CHBL	207	-1.72 (22.822)	0.00	-11.11, 11.11	(-77.8, 55.6)		149	1.12 (16.779)	0.00	-11.11, 11.11	(-33.3, 55.6)	
C9D1	196	25.31 (19.910)	22.22	11.11, 33.33	(0.0, 88.9)		128	24.48 (18.464)	22.22	11.11, 33.33	(0.0, 100.0)	
CHBL	193	-1.99 (21.473)	0.00	-11.11, 11.11	(-66.7, 55.6)		127	-0.26 (18.961)	0.00	-11.11, 11.11	(-55.6, 66.7)	
C11D1	192	23.55 (19.499)	22.22	0.00, 33.33	(0.0, 100.0)		114	24.27 (19.586)	22.22	11.11, 33.33	(0.0, 100.0)	
CHBL	189	-3.53 (22.733)	0.00	-11.11, 11.11	(-77.8, 77.8)		113	-1.67 (20.370)	0.00	-11.11, 11.11	(-55.6, 66.7)	
C13D1	180	25.43 (21.956)	22.22	5.56, 33.33	(0.0, 100.0)		93	26.34 (21.993)	22.22	11.11, 33.33	(0.0, 100.0)	
CHBL	177	-2.64 (23.749)	0.00	-11.11, 11.11	(-77.8, 55.6)		92	0.18 (21.484)	0.00	-11.11, 11.11	(-50.0, 77.8)	
C15D1	166	21.05 (19.865)	22.22	0.00, 33.33	(0.0, 100.0)		76	26.17 (23.637)	22.22	5.56, 33.33	(0.0, 100.0)	
CHBL	163	-7.12 (23.461)	0.00	-22.22, 0.00	(-77.8, 66.7)		75	-0.74 (23.202)	0.00	-11.11, 11.11	(-66.7, 66.7)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Fatigue

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	22.22 (20.711)	22.22	0.00, 33.33	(0.0, 100.0)	65	26.24 (21.684)	22.22	11.11, 33.33	(0.0, 100.0)
CHBL	155	-4.95 (24.394)	0.00	-22.22, 11.11	(-88.9, 44.4)	64	-2.34 (22.503)	0.00	-16.67, 5.56	(-44.4, 88.9)
C19D1	144	21.95 (18.459)	22.22	0.00, 33.33	(0.0, 77.8)	50	23.11 (22.764)	22.22	0.00, 33.33	(0.0, 88.9)
CHBL	141	-4.37 (21.739)	0.00	-11.11, 11.11	(-77.8, 44.4)	50	-3.11 (18.652)	0.00	-11.11, 0.00	(-44.4, 44.4)
C21D1	113	20.60 (20.730)	22.22	0.00, 33.33	(0.0, 100.0)	41	26.29 (19.993)	22.22	11.11, 33.33	(0.0, 100.0)
CHBL	112	-5.61 (23.834)	0.00	-13.89, 5.56	(-77.8, 66.7)	41	-2.98 (17.396)	0.00	-11.11, 11.11	(-33.3, 44.4)
C23D1	100	22.78 (22.018)	22.22	0.00, 33.33	(0.0, 100.0)	32	27.78 (21.307)	33.33	11.11, 33.33	(0.0, 88.9)
CHBL	99	-1.91 (23.812)	0.00	-11.11, 11.11	(-77.8, 77.8)	32	-3.13 (18.557)	0.00	-11.11, 11.11	(-44.4, 33.3)
C25D1	72	25.62 (22.194)	22.22	0.00, 33.33	(0.0, 88.9)	29	31.80 (26.011)	33.33	11.11, 33.33	(0.0, 88.9)
CHBL	71	-0.47 (21.532)	0.00	-11.11, 11.11	(-55.6, 66.7)	29	-1.53 (22.756)	0.00	-11.11, 11.11	(-33.3, 66.7)
C27D1	48	27.55 (24.685)	27.78	0.00, 44.44	(0.0, 100.0)	21	25.93 (26.137)	22.22	0.00, 33.33	(0.0, 88.9)
CHBL	47	2.13 (24.259)	0.00	-11.11, 11.11	(-44.4, 66.7)	21	-4.76 (17.768)	0.00	-11.11, 0.00	(-44.4, 33.3)
C29D1	41	25.75 (21.864)	22.22	11.11, 33.33	(0.0, 77.8)	14	24.60 (15.209)	27.78	11.11, 33.33	(0.0, 55.6)
CHBL	40	2.22 (19.360)	0.00	-11.11, 11.11	(-55.6, 44.4)	14	-5.56 (17.296)	0.00	-11.11, 0.00	(-44.4, 22.2)
C31D1	27	23.87 (22.583)	22.22	0.00, 33.33	(0.0, 88.9)	7	28.57 (26.338)	33.33	0.00, 33.33	(0.0, 77.8)
CHBL	27	-0.82 (20.884)	0.00	-11.11, 11.11	(-66.7, 33.3)	7	-1.59 (21.687)	-11.11	-11.11, 0.00	(-22.2, 44.4)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Fatigue

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
C33D1	20	25.00 (24.417)	22.22	11.11, 33.33	(0.0, 100.0)	5	24.44 (27.666)	22.22	0.00, 33.33	(0.0, 66.7)	
CHBL	20	0.00 (23.639)	0.00	-11.11, 11.11	(-66.7, 55.6)	5	-0.00 (13.608)	0.00	-11.11, 0.00	(-11.1, 22.2)	
C35D1	15	25.19 (26.715)	22.22	0.00, 33.33	(0.0, 88.9)	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)	
CHBL	15	0.74 (21.605)	0.00	-11.11, 11.11	(-55.6, 33.3)	3	-7.41 (6.415)	-11.11	-11.11, 0.00	(-11.1, 0.0)	
C37D1	9	18.52 (18.426)	22.22	0.00, 22.22	(0.0, 55.6)	1	44.44 (NE)	44.44	44.44, 44.44	(44.4, 44.4)	
CHBL	9	2.47 (13.354)	0.00	0.00, 0.00	(-11.1, 33.3)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)	
C39D1	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)	0					
CHBL	3	3.70 (6.415)	0.00	0.00, 11.11	(0.0, 11.1)	0					
C41D1	2	27.78 (23.570)	27.78	11.11, 44.44	(11.1, 44.4)	0					
CHBL	2	5.56 (23.570)	5.56	-11.11, 22.22	(-11.1, 22.2)	0					
End of Treatment	100	30.78 (25.360)	22.22	11.11, 33.33	(0.0, 100.0)	175	26.67 (19.646)	33.33	11.11, 33.33	(0.0, 77.8)	
CHBL	99	3.25 (22.851)	0.00	-11.11, 11.11	(-44.4, 88.9)	173	1.48 (21.128)	0.00	-11.11, 11.11	(-77.8, 77.8)	
40 Day Follow-Up	30	28.15 (27.018)	22.22	11.11, 33.33	(0.0, 100.0)	79	24.05 (24.809)	22.22	0.00, 33.33	(0.0, 100.0)	
CHBL	30	2.22 (25.505)	0.00	-11.11, 22.22	(-44.4, 77.8)	77	-1.59 (26.102)	0.00	-11.11, 11.11	(-100.0, 100.0)	
3 Months Follow-Up	60	29.81 (23.636)	33.33	11.11, 44.44	(0.0, 100.0)	111	25.68 (21.149)	22.22	11.11, 33.33	(0.0, 100.0)	
CHBL	60	2.04 (23.008)	0.00	-11.11, 11.11	(-44.4, 66.7)	111	2.75 (22.732)	0.00	-11.11, 11.11	(-55.6, 88.9)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Fatigue

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	44.44 (25.468)	33.33	33.33, 66.67	(0.0, 100.0)	251	39.04 (23.415)	33.33	22.22, 55.56	(0.0, 100.0)
CHBL	250	16.13 (24.874)	11.11	0.00, 33.33	(-66.7, 100.0)	248	12.50 (21.393)	11.11	0.00, 22.22	(-77.8, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Nausea and Vomiting

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Baseline	253	5.73 (13.733)	0.00	0.00, 0.00	(0.0, 100.0)	259	5.08 (11.962)	0.00	0.00, 0.00	(0.0, 100.0)
C2D1	96	13.72 (19.041)	0.00	0.00, 16.67	(0.0, 83.3)	109	6.88 (14.020)	0.00	0.00, 16.67	(0.0, 83.3)
CHBL	95	8.07 (20.752)	0.00	0.00, 16.67	(-83.3, 83.3)	109	2.29 (13.316)	0.00	0.00, 0.00	(-50.0, 83.3)
C3D1	246	17.07 (23.373)	16.67	0.00, 33.33	(0.0, 100.0)	220	6.74 (12.988)	0.00	0.00, 16.67	(0.0, 66.7)
CHBL	244	11.41 (22.648)	0.00	0.00, 16.67	(-50.0, 100.0)	217	2.07 (13.872)	0.00	0.00, 0.00	(-50.0, 66.7)
C5D1	230	17.68 (22.494)	16.67	0.00, 33.33	(0.0, 100.0)	169	5.72 (13.855)	0.00	0.00, 0.00	(0.0, 100.0)
CHBL	227	11.89 (25.388)	0.00	0.00, 33.33	(-100.0, 100.0)	167	1.30 (14.748)	0.00	0.00, 0.00	(-50.0, 66.7)
C7D1	210	16.51 (19.496)	16.67	0.00, 33.33	(0.0, 100.0)	152	5.81 (12.616)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	207	10.95 (22.235)	0.00	0.00, 16.67	(-83.3, 100.0)	150	1.44 (14.181)	0.00	0.00, 0.00	(-66.7, 66.7)
C9D1	196	14.29 (19.971)	0.00	0.00, 16.67	(0.0, 100.0)	129	5.17 (12.290)	0.00	0.00, 0.00	(0.0, 83.3)
CHBL	193	8.55 (23.454)	0.00	0.00, 16.67	(-83.3, 100.0)	128	0.65 (13.619)	0.00	0.00, 0.00	(-66.7, 50.0)
C11D1	192	10.68 (15.917)	0.00	0.00, 16.67	(0.0, 100.0)	113	5.31 (12.048)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	189	4.76 (20.720)	0.00	0.00, 16.67	(-100.0, 100.0)	113	0.59 (14.929)	0.00	0.00, 0.00	(-66.7, 66.7)
C13D1	179	11.45 (16.118)	0.00	0.00, 16.67	(0.0, 83.3)	93	3.76 (8.198)	0.00	0.00, 0.00	(0.0, 33.3)
CHBL	176	5.11 (21.211)	0.00	0.00, 16.67	(-100.0, 83.3)	92	-1.63 (12.369)	0.00	0.00, 0.00	(-66.7, 16.7)
C15D1	166	9.44 (15.285)	0.00	0.00, 16.67	(0.0, 66.7)	76	7.68 (14.257)	0.00	0.00, 16.67	(0.0, 83.3)
CHBL	163	3.58 (17.834)	0.00	0.00, 16.67	(-100.0, 66.7)	75	1.78 (16.111)	0.00	0.00, 0.00	(-66.7, 50.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Nausea and Vomiting

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	8.70 (13.422)	0.00	0.00, 16.67	(0.0, 66.7)	65	4.36 (11.887)	0.00	0.00, 0.00	(0.0, 83.3)
CHBL	155	2.80 (18.200)	0.00	0.00, 16.67	(-100.0, 66.7)	64	-0.78 (14.678)	0.00	0.00, 0.00	(-50.0, 66.7)
C19D1	144	10.19 (16.026)	0.00	0.00, 16.67	(0.0, 66.7)	51	4.25 (8.720)	0.00	0.00, 0.00	(0.0, 33.3)
CHBL	141	4.61 (20.616)	0.00	0.00, 16.67	(-83.3, 66.7)	51	-1.31 (11.946)	0.00	0.00, 0.00	(-33.3, 33.3)
C21D1	113	10.03 (15.356)	0.00	0.00, 16.67	(0.0, 66.7)	41	5.69 (12.139)	0.00	0.00, 0.00	(0.0, 50.0)
CHBL	112	4.46 (20.745)	0.00	0.00, 16.67	(-100.0, 66.7)	41	-0.81 (15.344)	0.00	0.00, 0.00	(-50.0, 33.3)
C23D1	100	10.83 (17.628)	0.00	0.00, 16.67	(0.0, 83.3)	32	5.73 (12.421)	0.00	0.00, 0.00	(0.0, 50.0)
CHBL	99	6.06 (19.115)	0.00	0.00, 16.67	(-83.3, 66.7)	32	-1.56 (15.473)	0.00	0.00, 0.00	(-50.0, 33.3)
C25D1	72	12.50 (17.187)	0.00	0.00, 16.67	(0.0, 66.7)	29	2.87 (6.407)	0.00	0.00, 0.00	(0.0, 16.7)
CHBL	71	7.75 (16.863)	0.00	0.00, 16.67	(-33.3, 66.7)	29	-4.02 (13.841)	0.00	0.00, 0.00	(-50.0, 16.7)
C27D1	47	9.22 (12.438)	0.00	0.00, 16.67	(0.0, 33.3)	21	1.59 (5.013)	0.00	0.00, 0.00	(0.0, 16.7)
CHBL	46	5.07 (12.105)	0.00	0.00, 16.67	(-33.3, 33.3)	21	-1.59 (10.415)	0.00	0.00, 0.00	(-33.3, 16.7)
C29D1	41	8.13 (13.500)	0.00	0.00, 16.67	(0.0, 50.0)	14	2.38 (6.052)	0.00	0.00, 0.00	(0.0, 16.7)
CHBL	40	5.00 (15.191)	0.00	0.00, 16.67	(-16.7, 50.0)	14	1.19 (4.454)	0.00	0.00, 0.00	(0.0, 16.7)
C31D1	27	7.41 (13.344)	0.00	0.00, 16.67	(0.0, 50.0)	7	4.76 (8.133)	0.00	0.00, 16.67	(0.0, 16.7)
CHBL	27	3.70 (14.122)	0.00	0.00, 0.00	(-16.7, 50.0)	7	4.76 (8.133)	0.00	0.00, 16.67	(0.0, 16.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Nausea and Vomiting

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	5.00 (10.949)	0.00	0.00, 0.00	(0.0, 33.3)	5	3.33 (7.454)	0.00	0.00, 0.00	(0.0, 16.7)
CHBL	20	2.50 (13.545)	0.00	0.00, 0.00	(-16.7, 33.3)	5	3.33 (7.454)	0.00	0.00, 0.00	(0.0, 16.7)
C35D1	15	10.00 (18.687)	0.00	0.00, 16.67	(0.0, 66.7)	3	5.56 (9.623)	0.00	0.00, 16.67	(0.0, 16.7)
CHBL	15	6.67 (16.427)	0.00	0.00, 16.67	(-16.7, 50.0)	3	5.56 (9.623)	0.00	0.00, 16.67	(0.0, 16.7)
C37D1	9	3.70 (7.349)	0.00	0.00, 0.00	(0.0, 16.7)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
CHBL	9	1.85 (5.556)	0.00	0.00, 0.00	(0.0, 16.7)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
C39D1	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
CHBL	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
C41D1	2	8.33 (11.785)	8.33	0.00, 16.67	(0.0, 16.7)	0				
CHBL	2	8.33 (11.785)	8.33	0.00, 16.67	(0.0, 16.7)	0				
End of Treatment	100	12.33 (17.825)	0.00	0.00, 33.33	(0.0, 66.7)	175	6.29 (13.905)	0.00	0.00, 0.00	(0.0, 100.0)
CHBL	99	6.73 (17.805)	0.00	0.00, 16.67	(-33.3, 50.0)	173	2.50 (15.042)	0.00	0.00, 0.00	(-66.7, 83.3)
40 Day Follow-Up	30	5.00 (13.944)	0.00	0.00, 0.00	(0.0, 66.7)	79	5.27 (15.225)	0.00	0.00, 0.00	(0.0, 100.0)
CHBL	30	0.56 (16.657)	0.00	0.00, 0.00	(-33.3, 66.7)	77	2.16 (16.301)	0.00	0.00, 0.00	(-33.3, 100.0)
3 Months Follow-Up	60	8.61 (17.491)	0.00	0.00, 16.67	(0.0, 83.3)	111	7.21 (13.600)	0.00	0.00, 16.67	(0.0, 66.7)
CHBL	60	3.61 (15.972)	0.00	0.00, 0.00	(-33.3, 83.3)	111	4.80 (14.803)	0.00	0.00, 16.67	(-33.3, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Nausea and Vomiting

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	32.94 (25.412)	33.33	16.67, 50.00	(0.0, 100.0)	251	15.07 (19.428)	16.67	0.00, 16.67	(0.0, 100.0)
CHBL	250	27.27 (24.541)	33.33	16.67, 33.33	(-50.0, 100.0)	248	10.69 (18.583)	0.00	0.00, 16.67	(-33.3, 83.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Pain

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max		n	Mean (SD)	Median	Q1, Q3	Min, Max
Baseline	253	22.66 (27.019)	16.67	0.00, 33.33	(0.0, 100.0)		258	24.55 (25.259)	16.67	0.00, 33.33	(0.0, 100.0)
C2D1	96	15.10 (18.744)	16.67	0.00, 33.33	(0.0, 83.3)		109	21.41 (19.654)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	95	-5.61 (20.137)	0.00	-16.67, 0.00	(-100.0, 33.3)		108	-2.78 (17.428)	0.00	-16.67, 0.00	(-66.7, 33.3)
C3D1	246	15.99 (20.963)	16.67	0.00, 33.33	(0.0, 100.0)		218	19.11 (20.963)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	244	-6.28 (24.691)	0.00	-16.67, 0.00	(-100.0, 83.3)		214	-3.89 (23.189)	0.00	-16.67, 0.00	(-100.0, 83.3)
C5D1	229	17.61 (22.949)	16.67	0.00, 33.33	(0.0, 100.0)		164	19.00 (20.045)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	226	-5.38 (28.919)	0.00	-16.67, 0.00	(-100.0, 100.0)		162	-1.95 (22.010)	0.00	-16.67, 0.00	(-100.0, 50.0)
C7D1	210	15.71 (20.601)	0.00	0.00, 33.33	(0.0, 100.0)		152	19.30 (22.460)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	207	-6.12 (25.655)	0.00	-16.67, 0.00	(-83.3, 50.0)		149	-1.01 (21.155)	0.00	-16.67, 0.00	(-83.3, 66.7)
C9D1	194	16.24 (21.690)	0.00	0.00, 33.33	(0.0, 100.0)		128	17.32 (19.886)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	191	-4.36 (24.510)	0.00	-16.67, 0.00	(-100.0, 50.0)		126	-4.10 (25.358)	0.00	-16.67, 0.00	(-100.0, 66.7)
C11D1	192	14.15 (18.784)	0.00	0.00, 33.33	(0.0, 100.0)		114	17.40 (21.542)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	189	-7.32 (23.650)	0.00	-16.67, 0.00	(-100.0, 50.0)		113	-5.46 (23.930)	0.00	-16.67, 0.00	(-100.0, 66.7)
C13D1	179	16.01 (20.554)	16.67	0.00, 33.33	(0.0, 100.0)		91	19.96 (24.371)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	176	-6.06 (25.657)	0.00	-16.67, 0.00	(-100.0, 66.7)		91	-3.66 (24.696)	0.00	-16.67, 0.00	(-100.0, 66.7)
C15D1	165	12.32 (19.029)	0.00	0.00, 16.67	(0.0, 100.0)		76	21.49 (21.912)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	162	-9.26 (25.672)	0.00	-16.67, 0.00	(-100.0, 50.0)		74	-5.41 (26.476)	0.00	-16.67, 0.00	(-100.0, 50.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Pain

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	12.53 (19.489)	0.00	0.00, 16.67	(0.0, 100.0)	64	18.75 (21.721)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	155	-8.06 (27.152)	0.00	-16.67, 0.00	(-100.0, 50.0)	62	-7.26 (27.097)	0.00	-16.67, 0.00	(-100.0, 66.7)
C19D1	143	13.40 (17.830)	0.00	0.00, 16.67	(0.0, 66.7)	50	20.33 (19.717)	16.67	0.00, 33.33	(0.0, 66.7)
CHBL	140	-7.62 (25.709)	0.00	-16.67, 0.00	(-100.0, 33.3)	50	-5.33 (25.520)	0.00	-16.67, 0.00	(-100.0, 33.3)
C21D1	112	13.24 (18.331)	0.00	0.00, 33.33	(0.0, 100.0)	40	23.33 (24.108)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	111	-6.46 (24.013)	0.00	-16.67, 0.00	(-83.3, 50.0)	40	-5.42 (30.983)	0.00	-16.67, 0.00	(-100.0, 83.3)
C23D1	99	13.47 (19.148)	0.00	0.00, 33.33	(0.0, 100.0)	31	18.82 (15.952)	16.67	0.00, 33.33	(0.0, 50.0)
CHBL	98	-4.93 (23.474)	0.00	-16.67, 0.00	(-100.0, 50.0)	31	-14.52 (28.134)	-16.67	-33.33, 0.00	(-100.0, 33.3)
C25D1	72	14.35 (21.723)	0.00	0.00, 16.67	(0.0, 100.0)	29	16.67 (15.430)	16.67	0.00, 33.33	(0.0, 50.0)
CHBL	71	-2.35 (22.056)	0.00	-16.67, 0.00	(-66.7, 66.7)	28	-14.88 (28.810)	-16.67	-33.33, 0.00	(-100.0, 33.3)
C27D1	48	15.28 (17.475)	16.67	0.00, 16.67	(0.0, 66.7)	21	13.49 (14.548)	16.67	0.00, 33.33	(0.0, 33.3)
CHBL	47	-1.77 (22.851)	0.00	-16.67, 16.67	(-66.7, 50.0)	21	-16.67 (21.731)	-16.67	-33.33, 0.00	(-83.3, 16.7)
C29D1	41	12.60 (19.643)	0.00	0.00, 16.67	(0.0, 66.7)	14	16.67 (16.013)	16.67	0.00, 33.33	(0.0, 50.0)
CHBL	40	-0.83 (27.203)	0.00	-16.67, 16.67	(-66.7, 66.7)	14	-13.10 (28.629)	-16.67	-33.33, 0.00	(-83.3, 33.3)
C31D1	26	5.13 (10.295)	0.00	0.00, 0.00	(0.0, 33.3)	7	19.05 (14.996)	16.67	0.00, 33.33	(0.0, 33.3)
CHBL	26	-10.26 (20.590)	0.00	-16.67, 0.00	(-66.7, 33.3)	7	-9.52 (33.134)	0.00	-33.33, 16.67	(-66.7, 33.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Pain

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	11.67 (18.810)	0.00	0.00, 25.00	(0.0, 66.7)	5	13.33 (13.944)	16.67	0.00, 16.67	(0.0, 33.3)
CHBL	20	-0.83 (22.605)	0.00	0.00, 16.67	(-50.0, 33.3)	5	-10.00 (14.907)	0.00	-16.67, 0.00	(-33.3, 0.0)
C35D1	15	6.67 (13.801)	0.00	0.00, 16.67	(0.0, 50.0)	3	5.56 (9.623)	0.00	0.00, 16.67	(0.0, 16.7)
CHBL	15	-5.56 (21.517)	0.00	-16.67, 0.00	(-33.3, 50.0)	3	-16.67 (16.667)	-16.67	-33.33, 0.00	(-33.3, 0.0)
C37D1	9	3.70 (7.349)	0.00	0.00, 0.00	(0.0, 16.7)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)
CHBL	9	-7.41 (18.840)	0.00	-16.67, 0.00	(-50.0, 16.7)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
C39D1	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
CHBL	3	-5.56 (9.623)	0.00	-16.67, 0.00	(-16.7, 0.0)	0				
C41D1	2	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
CHBL	2	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
End of Treatment	100	20.83 (23.013)	16.67	0.00, 33.33	(0.0, 83.3)	175	23.43 (22.467)	16.67	0.00, 33.33	(0.0, 83.3)
CHBL	99	-4.55 (26.171)	0.00	-16.67, 16.67	(-100.0, 66.7)	173	0.58 (22.938)	0.00	0.00, 16.67	(-100.0, 83.3)
40 Day Follow-Up	30	18.33 (28.145)	0.00	0.00, 33.33	(0.0, 100.0)	78	19.23 (23.429)	16.67	0.00, 33.33	(0.0, 83.3)
CHBL	30	-1.11 (34.166)	0.00	-16.67, 16.67	(-100.0, 83.3)	76	-4.82 (24.618)	0.00	-16.67, 0.00	(-66.7, 83.3)
3 Months Follow-Up	60	25.00 (24.453)	16.67	0.00, 33.33	(0.0, 100.0)	110	17.73 (21.804)	16.67	0.00, 33.33	(0.0, 100.0)
CHBL	60	-1.39 (31.785)	0.00	-16.67, 16.67	(-83.3, 66.7)	110	-4.09 (25.759)	0.00	-16.67, 0.00	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Pain

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	33.47 (26.560)	33.33	16.67, 50.00	(0.0, 100.0)	251	35.06 (25.151)	33.33	16.67, 50.00	(0.0, 100.0)
CHBL	250	10.80 (28.322)	16.67	0.00, 33.33	(-83.3, 100.0)	247	11.47 (24.208)	16.67	0.00, 33.33	(-100.0, 83.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Dyspnoea

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Baseline	253	15.15 (22.686)	0.00	0.00, 33.33	(0.0, 100.0)	257	15.82 (22.830)	0.00	0.00, 33.33	(0.0, 100.0)
C2D1	96	12.85 (20.157)	0.00	0.00, 33.33	(0.0, 100.0)	109	12.84 (17.514)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	95	-3.51 (20.325)	0.00	0.00, 0.00	(-66.7, 33.3)	107	-2.49 (19.800)	0.00	0.00, 0.00	(-66.7, 33.3)
C3D1	246	12.60 (21.065)	0.00	0.00, 33.33	(0.0, 100.0)	220	12.58 (21.092)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	244	-2.73 (21.207)	0.00	0.00, 0.00	(-100.0, 66.7)	216	-1.70 (21.136)	0.00	0.00, 0.00	(-66.7, 100.0)
C5D1	230	14.49 (22.303)	0.00	0.00, 33.33	(0.0, 100.0)	168	13.49 (20.388)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	227	-0.59 (24.079)	0.00	0.00, 0.00	(-66.7, 100.0)	166	0.00 (22.623)	0.00	0.00, 0.00	(-66.7, 100.0)
C7D1	210	13.17 (20.389)	0.00	0.00, 33.33	(0.0, 100.0)	151	11.26 (17.591)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	207	-1.77 (23.040)	0.00	0.00, 0.00	(-66.7, 100.0)	149	-1.12 (21.719)	0.00	0.00, 0.00	(-66.7, 66.7)
C9D1	196	11.73 (18.290)	0.00	0.00, 33.33	(0.0, 100.0)	129	11.37 (18.398)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	193	-1.90 (21.833)	0.00	0.00, 0.00	(-66.7, 66.7)	127	-2.89 (20.151)	0.00	0.00, 0.00	(-66.7, 33.3)
C11D1	192	10.76 (17.720)	0.00	0.00, 33.33	(0.0, 100.0)	114	12.57 (21.901)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	189	-4.41 (23.782)	0.00	0.00, 0.00	(-66.7, 100.0)	113	-1.18 (24.369)	0.00	0.00, 0.00	(-66.7, 100.0)
C13D1	180	12.41 (17.977)	0.00	0.00, 33.33	(0.0, 66.7)	93	10.04 (18.247)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	177	-2.45 (21.029)	0.00	0.00, 0.00	(-66.7, 66.7)	91	-3.30 (19.280)	0.00	0.00, 0.00	(-66.7, 33.3)
C15D1	166	11.04 (17.365)	0.00	0.00, 33.33	(0.0, 66.7)	76	14.91 (23.972)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	163	-3.48 (19.812)	0.00	0.00, 0.00	(-66.7, 66.7)	74	0.45 (23.727)	0.00	0.00, 0.00	(-66.7, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Dyspnoea

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	9.55 (16.474)	0.00	0.00, 33.33	(0.0, 66.7)	65	11.79 (20.776)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	155	-5.38 (21.981)	0.00	0.00, 0.00	(-66.7, 33.3)	63	-4.76 (23.076)	0.00	0.00, 0.00	(-66.7, 66.7)
C19D1	144	12.04 (18.745)	0.00	0.00, 33.33	(0.0, 100.0)	50	14.00 (23.416)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	141	-3.07 (21.786)	0.00	0.00, 0.00	(-66.7, 66.7)	50	-1.33 (23.290)	0.00	0.00, 0.00	(-66.7, 66.7)
C21D1	113	9.44 (16.348)	0.00	0.00, 33.33	(0.0, 66.7)	40	18.33 (27.164)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	112	-3.57 (21.156)	0.00	0.00, 0.00	(-66.7, 66.7)	40	0.83 (29.707)	0.00	0.00, 0.00	(-66.7, 100.0)
C23D1	100	10.67 (17.003)	0.00	0.00, 33.33	(0.0, 66.7)	31	12.90 (18.614)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	99	-4.71 (19.640)	0.00	0.00, 0.00	(-66.7, 33.3)	31	-5.38 (22.928)	0.00	-33.33, 0.00	(-66.7, 33.3)
C25D1	72	12.50 (19.730)	0.00	0.00, 33.33	(0.0, 66.7)	29	21.84 (27.133)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	71	-4.23 (21.029)	0.00	-33.33, 0.00	(-33.3, 66.7)	28	2.38 (23.880)	0.00	0.00, 0.00	(-33.3, 66.7)
C27D1	48	12.50 (21.333)	0.00	0.00, 33.33	(0.0, 66.7)	21	12.70 (16.587)	0.00	0.00, 33.33	(0.0, 33.3)
CHBL	47	0.71 (21.411)	0.00	0.00, 0.00	(-33.3, 66.7)	21	0.00 (23.570)	0.00	0.00, 0.00	(-33.3, 33.3)
C29D1	41	8.94 (16.707)	0.00	0.00, 0.00	(0.0, 66.7)	14	14.29 (21.540)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	40	-1.67 (19.900)	0.00	0.00, 0.00	(-33.3, 33.3)	14	4.76 (25.678)	0.00	0.00, 0.00	(-33.3, 66.7)
C31D1	27	12.35 (18.829)	0.00	0.00, 33.33	(0.0, 66.7)	7	14.29 (26.227)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	27	0.00 (20.672)	0.00	0.00, 0.00	(-33.3, 33.3)	7	4.76 (35.635)	0.00	-33.33, 33.33	(-33.3, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Dyspnoea

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	11.67 (16.312)	0.00	0.00, 33.33	(0.0, 33.3)	5	13.33 (29.814)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	20	1.67 (20.160)	0.00	0.00, 0.00	(-33.3, 33.3)	5	6.67 (14.907)	0.00	0.00, 0.00	(0.0, 33.3)
C35D1	15	6.67 (13.801)	0.00	0.00, 0.00	(0.0, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
CHBL	15	0.00 (12.599)	0.00	0.00, 0.00	(-33.3, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
C37D1	9	11.11 (23.570)	0.00	0.00, 0.00	(0.0, 66.7)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)
CHBL	9	7.41 (27.778)	0.00	0.00, 0.00	(-33.3, 66.7)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
C39D1	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
CHBL	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
C41D1	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
CHBL	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
End of Treatment	100	16.33 (20.919)	0.00	0.00, 33.33	(0.0, 100.0)	175	13.71 (20.275)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	99	-1.68 (24.455)	0.00	0.00, 0.00	(-100.0, 66.7)	172	0.39 (22.796)	0.00	0.00, 0.00	(-100.0, 66.7)
40 Day Follow-Up	30	15.56 (25.869)	0.00	0.00, 33.33	(0.0, 100.0)	79	15.19 (24.342)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	30	2.22 (28.945)	0.00	0.00, 0.00	(-66.7, 100.0)	77	-0.43 (23.874)	0.00	0.00, 0.00	(-66.7, 66.7)
3 Months Follow-Up	60	18.33 (25.619)	0.00	0.00, 33.33	(0.0, 100.0)	111	12.01 (17.862)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	60	1.11 (28.764)	0.00	0.00, 0.00	(-66.7, 100.0)	111	-2.10 (20.734)	0.00	0.00, 0.00	(-66.7, 33.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Dyspnoea

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	26.61 (26.287)	33.33	0.00, 33.33	(0.0, 100.0)	251	26.43 (26.602)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	250	11.33 (26.392)	0.00	0.00, 33.33	(-100.0, 100.0)	246	12.06 (26.496)	0.00	0.00, 33.33	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Sleep Disturbance

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	253	25.30 (29.269)	33.33	0.00, 33.33	(0.0, 100.0)	259	24.84 (28.993)	33.33	0.00, 33.33	(0.0, 100.0)	
C2D1	96	23.26 (27.834)	0.00	0.00, 33.33	(0.0, 100.0)	109	26.61 (23.474)	33.33	0.00, 33.33	(0.0, 100.0)	
CHBL	95	-2.46 (25.839)	0.00	0.00, 0.00	(-66.7, 33.3)	109	-0.31 (26.253)	0.00	0.00, 0.00	(-66.7, 100.0)	
C3D1	246	20.73 (26.755)	0.00	0.00, 33.33	(0.0, 100.0)	220	22.12 (26.182)	33.33	0.00, 33.33	(0.0, 100.0)	
CHBL	244	-4.37 (24.735)	0.00	0.00, 0.00	(-66.7, 66.7)	217	-1.84 (26.772)	0.00	0.00, 0.00	(-100.0, 66.7)	
C5D1	230	20.14 (25.018)	0.00	0.00, 33.33	(0.0, 100.0)	169	24.85 (28.179)	33.33	0.00, 33.33	(0.0, 100.0)	
CHBL	227	-5.43 (30.480)	0.00	-33.33, 0.00	(-100.0, 100.0)	167	1.00 (27.967)	0.00	0.00, 0.00	(-66.7, 100.0)	
C7D1	210	22.06 (26.590)	0.00	0.00, 33.33	(0.0, 100.0)	151	24.94 (28.341)	33.33	0.00, 33.33	(0.0, 100.0)	
CHBL	207	-2.42 (27.471)	0.00	0.00, 0.00	(-100.0, 66.7)	149	2.01 (28.004)	0.00	0.00, 33.33	(-66.7, 66.7)	
C9D1	196	20.07 (24.221)	0.00	0.00, 33.33	(0.0, 100.0)	129	25.06 (26.690)	33.33	0.00, 33.33	(0.0, 100.0)	
CHBL	193	-3.11 (25.945)	0.00	0.00, 0.00	(-100.0, 66.7)	128	1.30 (29.102)	0.00	0.00, 0.00	(-66.7, 100.0)	
C11D1	192	19.79 (26.235)	0.00	0.00, 33.33	(0.0, 100.0)	114	21.93 (27.275)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	189	-5.47 (25.255)	0.00	-33.33, 0.00	(-100.0, 66.7)	113	-3.83 (27.729)	0.00	-33.33, 0.00	(-66.7, 66.7)	
C13D1	180	21.48 (28.974)	0.00	0.00, 33.33	(0.0, 100.0)	93	23.66 (25.811)	33.33	0.00, 33.33	(0.0, 100.0)	
CHBL	177	-5.08 (31.471)	0.00	-33.33, 0.00	(-100.0, 100.0)	92	-2.54 (30.556)	0.00	-33.33, 0.00	(-100.0, 66.7)	
C15D1	166	18.07 (24.783)	0.00	0.00, 33.33	(0.0, 100.0)	76	27.19 (28.132)	33.33	0.00, 33.33	(0.0, 100.0)	
CHBL	163	-7.57 (25.202)	0.00	-33.33, 0.00	(-100.0, 66.7)	75	-0.00 (30.511)	0.00	-33.33, 33.33	(-66.7, 100.0)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Sleep Disturbance

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	18.47 (25.708)	0.00	0.00, 33.33	(0.0, 100.0)	65	24.62 (25.192)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	155	-6.24 (26.533)	0.00	0.00, 0.00	(-100.0, 66.7)	64	-5.21 (32.104)	0.00	-33.33, 0.00	(-100.0, 100.0)
C19D1	144	17.36 (22.976)	0.00	0.00, 33.33	(0.0, 100.0)	51	24.84 (27.360)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	141	-6.15 (26.608)	0.00	0.00, 0.00	(-66.7, 66.7)	51	-4.58 (27.503)	0.00	-33.33, 0.00	(-100.0, 66.7)
C21D1	113	20.65 (25.712)	0.00	0.00, 33.33	(0.0, 100.0)	39	26.50 (30.760)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	112	-4.46 (26.657)	0.00	-16.67, 0.00	(-66.7, 100.0)	39	-5.98 (33.221)	0.00	-33.33, 0.00	(-100.0, 100.0)
C23D1	99	18.86 (24.356)	0.00	0.00, 33.33	(0.0, 100.0)	32	28.13 (28.220)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	98	-2.38 (26.325)	0.00	0.00, 0.00	(-66.7, 66.7)	32	-6.25 (33.266)	0.00	-33.33, 0.00	(-100.0, 66.7)
C25D1	72	20.83 (23.362)	16.67	0.00, 33.33	(0.0, 66.7)	29	24.14 (30.727)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	71	-0.94 (23.212)	0.00	0.00, 0.00	(-66.7, 66.7)	29	-11.49 (33.660)	0.00	-33.33, 0.00	(-100.0, 33.3)
C27D1	48	16.67 (21.744)	0.00	0.00, 33.33	(0.0, 66.7)	20	21.67 (29.170)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	47	-3.55 (22.235)	0.00	0.00, 0.00	(-66.7, 66.7)	20	-6.67 (33.508)	0.00	-33.33, 0.00	(-66.7, 66.7)
C29D1	41	22.76 (27.324)	33.33	0.00, 33.33	(0.0, 100.0)	14	26.19 (23.310)	33.33	0.00, 33.33	(0.0, 66.7)
CHBL	40	0.83 (34.167)	0.00	-16.67, 0.00	(-66.7, 100.0)	14	0.00 (32.026)	0.00	-33.33, 33.33	(-66.7, 33.3)
C31D1	27	13.58 (21.202)	0.00	0.00, 33.33	(0.0, 66.7)	7	23.81 (25.198)	33.33	0.00, 33.33	(0.0, 66.7)
CHBL	27	-8.64 (27.100)	0.00	-33.33, 0.00	(-66.7, 66.7)	7	-4.76 (29.991)	0.00	-33.33, 33.33	(-33.3, 33.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Sleep Disturbance

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
C33D1	20	18.33 (22.878)	0.00	0.00, 33.33	(0.0, 66.7)	5	33.33 (33.333)	33.33	0.00, 66.67	(0.0, 66.7)	
CHBL	20	-3.33 (32.264)	0.00	-16.67, 0.00	(-66.7, 66.7)	5	0.00 (23.570)	0.00	0.00, 0.00	(-33.3, 33.3)	
C35D1	14	16.67 (21.681)	0.00	0.00, 33.33	(0.0, 66.7)	3	22.22 (38.490)	0.00	0.00, 66.67	(0.0, 66.7)	
CHBL	14	-0.00 (22.646)	0.00	0.00, 0.00	(-33.3, 33.3)	3	0.00 (33.333)	0.00	-33.33, 33.33	(-33.3, 33.3)	
C37D1	9	7.41 (14.699)	0.00	0.00, 0.00	(0.0, 33.3)	1	66.67 (NE)	66.67	66.67, 66.67	(66.7, 66.7)	
CHBL	9	-11.11 (16.667)	0.00	-33.33, 0.00	(-33.3, 0.0)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)	
C39D1	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0					
CHBL	3	-22.22 (19.245)	-33.33	-33.33, 0.00	(-33.3, 0.0)	0					
C41D1	2	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0					
CHBL	2	-33.33 (0.000)	-33.33	-33.33, -33.33	(-33.3, -33.3)	0					
End of Treatment	100	23.00 (28.700)	0.00	0.00, 33.33	(0.0, 100.0)	175	19.24 (22.702)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	99	-2.69 (28.839)	0.00	0.00, 0.00	(-100.0, 66.7)	173	-1.35 (27.459)	0.00	0.00, 0.00	(-100.0, 100.0)	
40 Day Follow-Up	30	28.89 (34.722)	33.33	0.00, 33.33	(0.0, 100.0)	79	18.14 (24.342)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	30	6.67 (35.450)	0.00	0.00, 33.33	(-66.7, 100.0)	77	-3.90 (32.433)	0.00	-33.33, 0.00	(-100.0, 100.0)	
3 Months Follow-Up	60	20.00 (27.583)	0.00	0.00, 33.33	(0.0, 100.0)	111	18.62 (26.086)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	60	-5.00 (31.188)	0.00	-33.33, 0.00	(-100.0, 66.7)	111	-0.90 (28.590)	0.00	0.00, 0.00	(-100.0, 100.0)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Sleep Disturbance

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	40.71 (30.832)	33.33	33.33, 66.67	(0.0, 100.0)	251	39.04 (29.487)	33.33	33.33, 66.67	(0.0, 100.0)
CHBL	250	15.60 (29.743)	0.00	0.00, 33.33	(-66.7, 100.0)	248	15.46 (29.970)	0.00	0.00, 33.33	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Appetite Loss

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	253	15.42 (25.450)	0.00	0.00, 33.33	(0.0, 100.0)	259	14.93 (23.299)	0.00	0.00, 33.33	(0.0, 100.0)	
C2D1	96	21.18 (26.543)	0.00	0.00, 33.33	(0.0, 100.0)	109	16.51 (22.962)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	95	4.91 (27.491)	0.00	0.00, 0.00	(-100.0, 100.0)	109	0.00 (23.570)	0.00	0.00, 0.00	(-100.0, 66.7)	
C3D1	246	24.66 (28.836)	33.33	0.00, 33.33	(0.0, 100.0)	220	14.09 (23.374)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	244	9.29 (27.137)	0.00	0.00, 33.33	(-66.7, 100.0)	217	0.92 (21.013)	0.00	0.00, 0.00	(-66.7, 100.0)	
C5D1	230	25.51 (28.150)	33.33	0.00, 33.33	(0.0, 100.0)	169	16.57 (25.491)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	227	9.69 (31.264)	0.00	0.00, 33.33	(-100.0, 100.0)	167	4.19 (26.931)	0.00	0.00, 0.00	(-66.7, 100.0)	
C7D1	210	22.22 (25.117)	33.33	0.00, 33.33	(0.0, 100.0)	152	15.79 (23.941)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	207	7.09 (30.160)	0.00	0.00, 33.33	(-100.0, 100.0)	150	3.56 (24.470)	0.00	0.00, 0.00	(-66.7, 100.0)	
C9D1	196	20.41 (26.423)	0.00	0.00, 33.33	(0.0, 100.0)	129	14.21 (21.154)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	193	5.01 (30.490)	0.00	0.00, 33.33	(-100.0, 100.0)	128	3.65 (23.378)	0.00	0.00, 0.00	(-66.7, 100.0)	
C11D1	192	17.36 (24.587)	0.00	0.00, 33.33	(0.0, 100.0)	114	13.16 (24.134)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	189	1.59 (31.187)	0.00	0.00, 33.33	(-100.0, 100.0)	113	1.18 (27.069)	0.00	0.00, 0.00	(-66.7, 100.0)	
C13D1	180	18.33 (25.718)	0.00	0.00, 33.33	(0.0, 100.0)	93	13.62 (21.556)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	177	1.88 (32.317)	0.00	0.00, 33.33	(-100.0, 100.0)	92	2.17 (26.522)	0.00	0.00, 0.00	(-66.7, 100.0)	
C15D1	166	14.26 (23.302)	0.00	0.00, 33.33	(0.0, 100.0)	76	13.60 (23.837)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	163	-1.23 (30.064)	0.00	0.00, 0.00	(-100.0, 100.0)	75	0.89 (25.096)	0.00	0.00, 0.00	(-66.7, 66.7)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Appetite Loss

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
C17D1	157	13.80 (22.343)	0.00	0.00, 33.33	(0.0, 100.0)	65	14.36 (22.024)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	155	-0.22 (31.209)	0.00	0.00, 0.00	(-100.0, 100.0)	64	2.60 (26.762)	0.00	0.00, 0.00	(-66.7, 100.0)	
C19D1	144	14.58 (23.560)	0.00	0.00, 33.33	(0.0, 100.0)	51	10.46 (15.621)	0.00	0.00, 33.33	(0.0, 33.3)	
CHBL	141	1.89 (31.059)	0.00	0.00, 0.00	(-100.0, 66.7)	51	-0.65 (22.598)	0.00	0.00, 0.00	(-66.7, 33.3)	
C21D1	113	13.86 (24.286)	0.00	0.00, 33.33	(0.0, 100.0)	41	11.38 (21.871)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	112	0.89 (31.147)	0.00	0.00, 0.00	(-100.0, 66.7)	41	-2.44 (21.590)	0.00	0.00, 0.00	(-66.7, 66.7)	
C23D1	100	13.00 (22.670)	0.00	0.00, 33.33	(0.0, 100.0)	32	14.58 (18.813)	0.00	0.00, 33.33	(0.0, 66.7)	
CHBL	99	0.34 (28.370)	0.00	0.00, 0.00	(-100.0, 100.0)	32	-1.04 (23.163)	0.00	0.00, 0.00	(-66.7, 33.3)	
C25D1	72	14.81 (20.085)	0.00	0.00, 33.33	(0.0, 66.7)	29	18.39 (24.537)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	71	3.76 (24.912)	0.00	0.00, 33.33	(-66.7, 66.7)	29	3.45 (27.233)	0.00	0.00, 0.00	(-33.3, 100.0)	
C27D1	48	13.19 (22.534)	0.00	0.00, 33.33	(0.0, 100.0)	21	3.17 (10.026)	0.00	0.00, 0.00	(0.0, 33.3)	
CHBL	47	6.38 (26.593)	0.00	0.00, 0.00	(-66.7, 100.0)	21	-4.76 (11.952)	0.00	0.00, 0.00	(-33.3, 0.0)	
C29D1	41	8.94 (14.952)	0.00	0.00, 33.33	(0.0, 33.3)	14	9.52 (15.627)	0.00	0.00, 33.33	(0.0, 33.3)	
CHBL	40	-0.83 (19.226)	0.00	0.00, 0.00	(-66.7, 33.3)	14	2.38 (15.821)	0.00	0.00, 0.00	(-33.3, 33.3)	
C31D1	27	4.94 (12.067)	0.00	0.00, 0.00	(0.0, 33.3)	7	14.29 (26.227)	0.00	0.00, 33.33	(0.0, 66.7)	
CHBL	27	-4.94 (22.079)	0.00	0.00, 0.00	(-66.7, 33.3)	7	9.52 (25.198)	0.00	0.00, 0.00	(0.0, 66.7)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Appetite Loss

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	8.33 (18.337)	0.00	0.00, 0.00	(0.0, 66.7)	5	20.00 (29.814)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	20	0.00 (26.491)	0.00	0.00, 0.00	(-66.7, 66.7)	5	13.33 (29.814)	0.00	0.00, 0.00	(0.0, 66.7)
C35D1	15	2.22 (8.607)	0.00	0.00, 0.00	(0.0, 33.3)	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)
CHBL	15	-8.89 (23.458)	0.00	-33.33, 0.00	(-66.7, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
C37D1	9	7.41 (14.699)	0.00	0.00, 0.00	(0.0, 33.3)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)
CHBL	9	0.00 (16.667)	0.00	0.00, 0.00	(-33.3, 33.3)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)
C39D1	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
CHBL	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
C41D1	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
CHBL	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
End of Treatment	100	21.33 (26.174)	0.00	0.00, 33.33	(0.0, 100.0)	175	15.62 (23.917)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	99	5.05 (27.505)	0.00	0.00, 33.33	(-100.0, 100.0)	173	3.08 (27.436)	0.00	0.00, 0.00	(-100.0, 100.0)
40 Day Follow-Up	30	17.78 (27.310)	0.00	0.00, 33.33	(0.0, 100.0)	79	15.61 (28.161)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	30	4.44 (25.869)	0.00	0.00, 33.33	(-66.7, 66.7)	77	2.60 (30.477)	0.00	0.00, 0.00	(-100.0, 100.0)
3 Months Follow-Up	60	21.11 (26.014)	0.00	0.00, 33.33	(0.0, 100.0)	111	10.81 (20.182)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	60	6.11 (27.095)	0.00	0.00, 33.33	(-100.0, 100.0)	111	0.60 (24.611)	0.00	0.00, 0.00	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Appetite Loss

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	42.95 (30.279)	33.33	33.33, 66.67	(0.0, 100.0)	251	30.28 (29.732)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	250	27.47 (30.338)	33.33	0.00, 33.33	(-66.7, 100.0)	248	16.40 (28.454)	0.00	0.00, 33.33	(-100.0, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Constipation

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Baseline	253	13.04 (22.445)	0.00	0.00, 33.33	(0.0, 100.0)	259	11.97 (20.503)	0.00	0.00, 33.33	(0.0, 100.0)
C2D1	96	15.63 (23.671)	0.00	0.00, 33.33	(0.0, 100.0)	108	10.80 (19.775)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	95	4.21 (24.907)	0.00	0.00, 0.00	(-100.0, 100.0)	108	0.31 (22.090)	0.00	0.00, 0.00	(-66.7, 100.0)
C3D1	246	18.97 (27.956)	0.00	0.00, 33.33	(0.0, 100.0)	220	11.97 (19.459)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	244	6.15 (27.609)	0.00	0.00, 0.00	(-100.0, 100.0)	217	1.23 (20.997)	0.00	0.00, 0.00	(-100.0, 66.7)
C5D1	226	20.80 (26.203)	0.00	0.00, 33.33	(0.0, 100.0)	168	15.87 (24.457)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	223	7.77 (28.110)	0.00	0.00, 33.33	(-100.0, 100.0)	166	5.42 (23.870)	0.00	0.00, 0.00	(-66.7, 100.0)
C7D1	210	21.27 (29.028)	0.00	0.00, 33.33	(0.0, 100.0)	152	16.67 (25.447)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	207	9.34 (30.963)	0.00	0.00, 33.33	(-66.7, 100.0)	150	6.89 (26.559)	0.00	0.00, 0.00	(-66.7, 100.0)
C9D1	196	20.24 (24.431)	0.00	0.00, 33.33	(0.0, 100.0)	128	15.89 (24.017)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	193	8.98 (28.053)	0.00	0.00, 33.33	(-100.0, 100.0)	127	5.51 (25.464)	0.00	0.00, 33.33	(-66.7, 100.0)
C11D1	192	17.53 (24.344)	0.00	0.00, 33.33	(0.0, 100.0)	114	17.54 (24.775)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	189	6.70 (26.671)	0.00	0.00, 33.33	(-66.7, 100.0)	113	5.01 (26.057)	0.00	0.00, 0.00	(-66.7, 100.0)
C13D1	179	17.13 (22.996)	0.00	0.00, 33.33	(0.0, 100.0)	92	16.30 (23.438)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	177	4.71 (28.144)	0.00	0.00, 33.33	(-100.0, 100.0)	91	2.20 (26.201)	0.00	0.00, 0.00	(-66.7, 100.0)
C15D1	166	14.26 (21.183)	0.00	0.00, 33.33	(0.0, 100.0)	75	16.00 (23.481)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	163	2.04 (24.200)	0.00	0.00, 0.00	(-100.0, 66.7)	74	2.25 (25.482)	0.00	0.00, 0.00	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Constipation

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	14.86 (22.135)	0.00	0.00, 33.33	(0.0, 100.0)	65	17.44 (27.706)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	155	4.09 (24.423)	0.00	0.00, 0.00	(-66.7, 66.7)	64	3.65 (27.931)	0.00	0.00, 0.00	(-66.7, 100.0)
C19D1	144	17.82 (22.957)	0.00	0.00, 33.33	(0.0, 100.0)	51	14.38 (22.366)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	141	6.38 (26.402)	0.00	0.00, 33.33	(-66.7, 66.7)	51	0.00 (24.037)	0.00	0.00, 0.00	(-66.7, 33.3)
C21D1	113	15.93 (22.755)	0.00	0.00, 33.33	(0.0, 100.0)	41	20.33 (26.748)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	112	4.17 (26.893)	0.00	0.00, 0.00	(-100.0, 66.7)	41	3.25 (28.679)	0.00	0.00, 0.00	(-66.7, 100.0)
C23D1	100	14.67 (21.876)	0.00	0.00, 33.33	(0.0, 100.0)	31	17.20 (25.634)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	99	3.37 (25.419)	0.00	0.00, 0.00	(-100.0, 66.7)	31	-1.08 (21.915)	0.00	0.00, 0.00	(-66.7, 33.3)
C25D1	72	16.20 (24.382)	0.00	0.00, 33.33	(0.0, 100.0)	29	14.94 (26.105)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	71	5.16 (24.331)	0.00	0.00, 33.33	(-66.7, 66.7)	29	-3.45 (22.440)	0.00	0.00, 0.00	(-66.7, 33.3)
C27D1	48	16.67 (24.792)	0.00	0.00, 33.33	(0.0, 100.0)	21	20.63 (26.825)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	47	7.09 (24.013)	0.00	0.00, 33.33	(-33.3, 66.7)	21	4.76 (19.107)	0.00	0.00, 0.00	(-33.3, 33.3)
C29D1	41	13.01 (23.426)	0.00	0.00, 33.33	(0.0, 100.0)	14	23.81 (20.375)	33.33	0.00, 33.33	(0.0, 66.7)
CHBL	40	5.00 (19.319)	0.00	0.00, 0.00	(-33.3, 66.7)	14	4.76 (22.100)	0.00	0.00, 33.33	(-33.3, 33.3)
C31D1	27	13.58 (24.909)	0.00	0.00, 33.33	(0.0, 100.0)	7	19.05 (26.227)	0.00	0.00, 33.33	(0.0, 66.7)
CHBL	27	3.70 (16.879)	0.00	0.00, 0.00	(-33.3, 33.3)	7	4.76 (23.002)	0.00	0.00, 33.33	(-33.3, 33.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Constipation

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	20.00 (31.344)	0.00	0.00, 33.33	(0.0, 100.0)	5	26.67 (27.889)	33.33	0.00, 33.33	(0.0, 66.7)
CHBL	20	6.67 (29.814)	0.00	0.00, 33.33	(-66.7, 66.7)	5	0.00 (23.570)	0.00	0.00, 0.00	(-33.3, 33.3)
C35D1	15	17.78 (27.794)	0.00	0.00, 33.33	(0.0, 66.7)	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)
CHBL	15	4.44 (30.516)	0.00	0.00, 33.33	(-66.7, 66.7)	3	-11.11 (19.245)	0.00	-33.33, 0.00	(-33.3, 0.0)
C37D1	9	18.52 (29.397)	0.00	0.00, 33.33	(0.0, 66.7)	1	66.67 (NE)	66.67	66.67, 66.67	(66.7, 66.7)
CHBL	9	7.41 (22.222)	0.00	0.00, 33.33	(-33.3, 33.3)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)
C39D1	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)	0				
CHBL	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
C41D1	2	33.33 (47.140)	33.33	0.00, 66.67	(0.0, 66.7)	0				
CHBL	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
End of Treatment	100	17.00 (24.843)	0.00	0.00, 33.33	(0.0, 100.0)	174	13.60 (22.386)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	99	2.69 (30.371)	0.00	0.00, 0.00	(-100.0, 100.0)	172	3.49 (23.379)	0.00	0.00, 0.00	(-100.0, 100.0)
40 Day Follow-Up	30	8.89 (17.361)	0.00	0.00, 0.00	(0.0, 66.7)	79	15.19 (26.038)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	30	-1.11 (25.496)	0.00	0.00, 0.00	(-66.7, 33.3)	77	6.49 (24.803)	0.00	0.00, 0.00	(-33.3, 100.0)
3 Months Follow-Up	60	15.00 (24.873)	0.00	0.00, 33.33	(0.0, 100.0)	111	10.81 (21.159)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	60	1.67 (28.407)	0.00	0.00, 0.00	(-100.0, 66.7)	111	0.00 (26.968)	0.00	0.00, 0.00	(-100.0, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Constipation

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	42.56 (32.573)	33.33	33.33, 66.67	(0.0, 100.0)	251	29.08 (29.053)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	250	29.47 (33.376)	33.33	0.00, 33.33	(-33.3, 100.0)	248	18.15 (28.258)	0.00	0.00, 33.33	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Diarrhea

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Baseline	253	9.62 (19.007)	0.00	0.00, 0.00	(0.0, 100.0)	260	8.33 (16.144)	0.00	0.00, 0.00	(0.0, 100.0)
C2D1	95	17.19 (23.752)	0.00	0.00, 33.33	(0.0, 100.0)	108	5.86 (13.541)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	94	5.32 (23.085)	0.00	0.00, 33.33	(-33.3, 66.7)	108	-3.70 (16.641)	0.00	0.00, 0.00	(-33.3, 33.3)
C3D1	246	12.87 (22.967)	0.00	0.00, 33.33	(0.0, 100.0)	219	5.33 (12.243)	0.00	0.00, 0.00	(0.0, 33.3)
CHBL	244	3.14 (25.013)	0.00	0.00, 0.00	(-100.0, 100.0)	217	-3.84 (16.374)	0.00	0.00, 0.00	(-100.0, 33.3)
C5D1	230	9.71 (19.638)	0.00	0.00, 0.00	(0.0, 100.0)	167	5.99 (15.221)	0.00	0.00, 0.00	(0.0, 100.0)
CHBL	227	0.29 (23.672)	0.00	0.00, 0.00	(-100.0, 100.0)	166	-2.41 (18.556)	0.00	0.00, 0.00	(-66.7, 100.0)
C7D1	210	9.05 (18.665)	0.00	0.00, 0.00	(0.0, 100.0)	152	4.61 (13.316)	0.00	0.00, 0.00	(0.0, 100.0)
CHBL	207	-0.97 (25.210)	0.00	0.00, 0.00	(-100.0, 100.0)	151	-3.53 (18.116)	0.00	0.00, 0.00	(-66.7, 100.0)
C9D1	195	7.18 (14.937)	0.00	0.00, 0.00	(0.0, 66.7)	128	3.39 (10.940)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	192	-2.43 (20.320)	0.00	0.00, 0.00	(-100.0, 66.7)	128	-4.17 (16.732)	0.00	0.00, 0.00	(-66.7, 66.7)
C11D1	192	5.73 (13.500)	0.00	0.00, 0.00	(0.0, 66.7)	114	4.68 (12.446)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	189	-4.59 (20.689)	0.00	0.00, 0.00	(-100.0, 66.7)	114	-3.80 (17.604)	0.00	0.00, 0.00	(-66.7, 66.7)
C13D1	179	4.66 (13.104)	0.00	0.00, 0.00	(0.0, 66.7)	93	3.94 (10.823)	0.00	0.00, 0.00	(0.0, 33.3)
CHBL	177	-5.27 (20.346)	0.00	0.00, 0.00	(-100.0, 66.7)	93	-5.02 (19.001)	0.00	0.00, 0.00	(-66.7, 33.3)
C15D1	166	5.62 (14.970)	0.00	0.00, 0.00	(0.0, 66.7)	76	4.82 (16.059)	0.00	0.00, 0.00	(0.0, 100.0)
CHBL	163	-3.89 (21.079)	0.00	0.00, 0.00	(-100.0, 66.7)	76	-3.07 (21.206)	0.00	0.00, 0.00	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Diarrhea

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	5.31 (14.864)	0.00	0.00, 0.00	(0.0, 100.0)	64	6.25 (15.573)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	155	-4.73 (22.292)	0.00	0.00, 0.00	(-100.0, 66.7)	64	-2.08 (20.466)	0.00	0.00, 0.00	(-33.3, 66.7)
C19D1	144	5.09 (13.836)	0.00	0.00, 0.00	(0.0, 66.7)	51	4.58 (13.366)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	141	-4.96 (23.209)	0.00	0.00, 0.00	(-100.0, 66.7)	51	-3.27 (16.673)	0.00	0.00, 0.00	(-66.7, 66.7)
C21D1	113	4.13 (12.703)	0.00	0.00, 0.00	(0.0, 66.7)	41	4.88 (11.928)	0.00	0.00, 0.00	(0.0, 33.3)
CHBL	112	-5.65 (24.049)	0.00	0.00, 0.00	(-100.0, 66.7)	41	-3.25 (17.958)	0.00	0.00, 0.00	(-66.7, 33.3)
C23D1	100	4.00 (11.873)	0.00	0.00, 0.00	(0.0, 66.7)	32	6.25 (15.698)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	99	-7.07 (22.473)	0.00	0.00, 0.00	(-100.0, 66.7)	32	-2.08 (18.813)	0.00	0.00, 0.00	(-33.3, 66.7)
C25D1	72	4.63 (12.886)	0.00	0.00, 0.00	(0.0, 66.7)	29	5.75 (15.607)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	71	-7.04 (21.760)	0.00	0.00, 0.00	(-100.0, 66.7)	29	-3.45 (20.596)	0.00	0.00, 0.00	(-66.7, 66.7)
C27D1	48	4.17 (14.788)	0.00	0.00, 0.00	(0.0, 66.7)	21	1.59 (7.274)	0.00	0.00, 0.00	(0.0, 33.3)
CHBL	47	-4.26 (24.688)	0.00	0.00, 0.00	(-100.0, 66.7)	21	-6.35 (13.412)	0.00	0.00, 0.00	(-33.3, 0.0)
C29D1	41	4.88 (11.928)	0.00	0.00, 0.00	(0.0, 33.3)	14	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
CHBL	40	-6.67 (25.262)	0.00	-33.33, 0.00	(-100.0, 33.3)	14	-7.14 (14.194)	0.00	0.00, 0.00	(-33.3, 0.0)
C31D1	27	4.94 (15.202)	0.00	0.00, 0.00	(0.0, 66.7)	7	4.76 (12.599)	0.00	0.00, 0.00	(0.0, 33.3)
CHBL	27	-3.70 (25.036)	0.00	0.00, 0.00	(-66.7, 66.7)	7	-4.76 (12.599)	0.00	0.00, 0.00	(-33.3, 0.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Diarrhea

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	19	1.75 (7.647)	0.00	0.00, 0.00	(0.0, 33.3)	5	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
CHBL	19	-7.02 (13.962)	0.00	0.00, 0.00	(-33.3, 0.0)	5	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
C35D1	15	2.22 (8.607)	0.00	0.00, 0.00	(0.0, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
CHBL	15	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
C37D1	9	3.70 (11.111)	0.00	0.00, 0.00	(0.0, 33.3)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
CHBL	9	0.00 (16.667)	0.00	0.00, 0.00	(-33.3, 33.3)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
C39D1	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)	0				
CHBL	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)	0				
C41D1	2	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
CHBL	2	-16.67 (23.570)	-16.67	-33.33, 0.00	(-33.3, 0.0)	0				
End of Treatment	100	8.67 (16.831)	0.00	0.00, 0.00	(0.0, 66.7)	175	4.38 (11.846)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	99	-2.02 (22.243)	0.00	0.00, 0.00	(-66.7, 66.7)	173	-3.66 (17.033)	0.00	0.00, 0.00	(-66.7, 66.7)
40 Day Follow-Up	30	2.22 (8.457)	0.00	0.00, 0.00	(0.0, 33.3)	79	6.33 (16.080)	0.00	0.00, 0.00	(0.0, 66.7)
CHBL	30	-7.78 (20.869)	0.00	0.00, 0.00	(-100.0, 0.0)	77	-3.46 (20.651)	0.00	0.00, 0.00	(-66.7, 66.7)
3 Months Follow-Up	60	5.56 (12.527)	0.00	0.00, 0.00	(0.0, 33.3)	110	7.58 (16.065)	0.00	0.00, 0.00	(0.0, 100.0)
CHBL	60	-3.89 (19.496)	0.00	0.00, 0.00	(-66.7, 33.3)	110	-1.52 (22.297)	0.00	0.00, 0.00	(-100.0, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Diarrhea

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	26.09 (27.939)	33.33	0.00, 33.33	(0.0, 100.0)	251	12.75 (19.920)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	250	16.53 (28.693)	0.00	0.00, 33.33	(-66.7, 100.0)	249	4.42 (22.463)	0.00	0.00, 0.00	(-66.7, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Financial Difficulties

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	252	23.54 (31.927)	0.00	0.00, 33.33	(0.0, 100.0)	259	24.20 (29.461)	0.00	0.00, 33.33	(0.0, 100.0)	
C2D1	95	13.68 (23.568)	0.00	0.00, 33.33	(0.0, 100.0)	106	14.47 (25.206)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	94	-4.61 (21.082)	0.00	0.00, 0.00	(-66.7, 66.7)	106	-5.66 (23.218)	0.00	0.00, 0.00	(-100.0, 66.7)	
C3D1	246	18.29 (27.182)	0.00	0.00, 33.33	(0.0, 100.0)	219	17.66 (25.796)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	243	-4.94 (24.680)	0.00	0.00, 0.00	(-100.0, 66.7)	216	-4.63 (27.453)	0.00	0.00, 0.00	(-100.0, 100.0)	
C5D1	230	16.96 (25.449)	0.00	0.00, 33.33	(0.0, 100.0)	166	17.47 (26.893)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	226	-5.46 (27.120)	0.00	0.00, 0.00	(-100.0, 100.0)	164	-2.24 (26.143)	0.00	0.00, 0.00	(-100.0, 100.0)	
C7D1	210	16.51 (26.137)	0.00	0.00, 33.33	(0.0, 100.0)	151	19.21 (26.788)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	206	-5.99 (26.784)	0.00	0.00, 0.00	(-100.0, 100.0)	149	-1.34 (24.161)	0.00	0.00, 0.00	(-66.7, 100.0)	
C9D1	196	18.71 (27.034)	0.00	0.00, 33.33	(0.0, 100.0)	127	18.64 (26.777)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	192	-3.99 (27.100)	0.00	0.00, 0.00	(-100.0, 100.0)	126	-3.70 (28.974)	0.00	0.00, 0.00	(-100.0, 100.0)	
C11D1	192	18.40 (26.584)	0.00	0.00, 33.33	(0.0, 100.0)	113	20.65 (26.844)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	188	-3.90 (29.597)	0.00	0.00, 0.00	(-100.0, 100.0)	112	-2.68 (24.968)	0.00	0.00, 0.00	(-66.7, 100.0)	
C13D1	180	17.59 (25.995)	0.00	0.00, 33.33	(0.0, 100.0)	93	21.15 (28.986)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	176	-4.92 (28.526)	0.00	0.00, 0.00	(-100.0, 100.0)	92	-0.72 (30.852)	0.00	0.00, 0.00	(-100.0, 100.0)	
C15D1	166	14.66 (24.467)	0.00	0.00, 33.33	(0.0, 100.0)	76	16.67 (27.487)	0.00	0.00, 33.33	(0.0, 100.0)	
CHBL	162	-7.41 (30.410)	0.00	-33.33, 0.00	(-100.0, 100.0)	75	-6.67 (30.999)	0.00	-33.33, 0.00	(-100.0, 100.0)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Financial Difficulties

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	17.62 (28.133)	0.00	0.00, 33.33	(0.0, 100.0)	64	19.27 (28.362)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	154	-5.41 (31.765)	0.00	0.00, 0.00	(-100.0, 100.0)	63	-4.76 (30.443)	0.00	-33.33, 0.00	(-100.0, 100.0)
C19D1	144	18.52 (28.091)	0.00	0.00, 33.33	(0.0, 100.0)	51	20.92 (30.522)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	140	-4.76 (31.374)	0.00	0.00, 0.00	(-100.0, 100.0)	51	-3.92 (34.414)	0.00	0.00, 0.00	(-100.0, 100.0)
C21D1	113	17.99 (27.830)	0.00	0.00, 33.33	(0.0, 100.0)	41	21.14 (29.586)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	112	-4.76 (32.836)	0.00	0.00, 0.00	(-100.0, 100.0)	41	-4.88 (31.235)	0.00	0.00, 0.00	(-100.0, 100.0)
C23D1	100	19.00 (28.131)	0.00	0.00, 33.33	(0.0, 100.0)	32	22.92 (31.036)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	98	-5.10 (31.149)	0.00	0.00, 0.00	(-100.0, 100.0)	32	-5.21 (35.021)	0.00	-33.33, 0.00	(-100.0, 100.0)
C25D1	72	21.76 (28.614)	0.00	0.00, 33.33	(0.0, 100.0)	29	19.54 (27.483)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	71	-3.29 (36.146)	0.00	0.00, 0.00	(-100.0, 100.0)	29	-10.34 (37.905)	0.00	-33.33, 0.00	(-100.0, 100.0)
C27D1	48	18.06 (29.940)	0.00	0.00, 33.33	(0.0, 100.0)	21	14.29 (30.861)	0.00	0.00, 0.00	(0.0, 100.0)
CHBL	47	3.55 (30.482)	0.00	0.00, 0.00	(-66.7, 100.0)	21	-11.11 (28.545)	0.00	-33.33, 0.00	(-100.0, 33.3)
C29D1	41	14.63 (22.421)	0.00	0.00, 33.33	(0.0, 66.7)	14	11.90 (16.575)	0.00	0.00, 33.33	(0.0, 33.3)
CHBL	40	2.50 (19.078)	0.00	0.00, 0.00	(-33.3, 66.7)	14	-9.52 (20.375)	0.00	-33.33, 0.00	(-33.3, 33.3)
C31D1	27	16.05 (26.747)	0.00	0.00, 33.33	(0.0, 100.0)	7	4.76 (12.599)	0.00	0.00, 0.00	(0.0, 33.3)
CHBL	27	-0.00 (20.672)	0.00	0.00, 0.00	(-33.3, 66.7)	7	-14.29 (26.227)	-33.33	-33.33, 0.00	(-33.3, 33.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Financial Difficulties

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	11.67 (19.571)	0.00	0.00, 33.33	(0.0, 66.7)	5	13.33 (18.257)	0.00	0.00, 33.33	(0.0, 33.3)
CHBL	20	-0.00 (18.732)	0.00	0.00, 0.00	(-33.3, 33.3)	5	-6.67 (14.907)	0.00	0.00, 0.00	(-33.3, 0.0)
C35D1	15	13.33 (21.082)	0.00	0.00, 33.33	(0.0, 66.7)	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)
CHBL	15	2.22 (15.258)	0.00	0.00, 0.00	(-33.3, 33.3)	3	0.00 (33.333)	0.00	-33.33, 33.33	(-33.3, 33.3)
C37D1	9	14.81 (17.568)	0.00	0.00, 33.33	(0.0, 33.3)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)
CHBL	9	7.41 (14.699)	0.00	0.00, 0.00	(0.0, 33.3)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
C39D1	3	22.22 (19.245)	33.33	0.00, 33.33	(0.0, 33.3)	0				
CHBL	3	11.11 (19.245)	0.00	0.00, 33.33	(0.0, 33.3)	0				
C41D1	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
CHBL	2	16.67 (23.570)	16.67	0.00, 33.33	(0.0, 33.3)	0				
End of Treatment	100	19.00 (28.131)	0.00	0.00, 33.33	(0.0, 100.0)	175	22.29 (28.453)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	98	-3.06 (24.911)	0.00	0.00, 0.00	(-100.0, 66.7)	173	0.39 (24.109)	0.00	0.00, 0.00	(-100.0, 66.7)
40 Day Follow-Up	30	20.00 (33.448)	0.00	0.00, 33.33	(0.0, 100.0)	79	24.05 (27.702)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	30	5.56 (30.429)	0.00	0.00, 0.00	(-66.7, 100.0)	77	-2.60 (32.339)	0.00	0.00, 0.00	(-100.0, 66.7)
3 Months Follow-Up	60	21.11 (26.014)	0.00	0.00, 33.33	(0.0, 100.0)	110	24.85 (28.712)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	60	-2.78 (28.319)	0.00	0.00, 0.00	(-100.0, 33.3)	110	-0.30 (32.085)	0.00	0.00, 0.00	(-100.0, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.4: Summary of Actual Value and Change from Baseline of EORTC QLQ-C30
 Full Analysis Set

Symptom scales/Financial Difficulties

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	33.60 (33.464)	33.33	0.00, 33.33	(0.0, 100.0)	251	31.61 (32.134)	33.33	0.00, 33.33	(0.0, 100.0)
CHBL	249	9.91 (29.935)	0.00	0.00, 33.33	(-66.7, 100.0)	248	8.47 (29.158)	0.00	0.00, 33.33	(-100.0, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to global health status and all subscales of EORTC QLQ-C30. A high score for the global health status represents a low QoL; a high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.3.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Functional scales/Body Image

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	254	25.60 (27.770)	16.67	0.00, 33.33	(0.0, 100.0)	258	27.13 (25.935)	25.00	0.00, 41.67	(0.0, 100.0)	
C2D1	96	23.90 (25.016)	25.00	0.00, 37.50	(0.0, 100.0)	108	23.38 (24.100)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	95	-5.35 (21.597)	0.00	-16.67, 0.00	(-100.0, 41.7)	108	-3.34 (16.622)	0.00	-8.33, 0.00	(-41.7, 50.0)	
C3D1	246	23.88 (25.519)	16.67	0.00, 33.33	(0.0, 100.0)	219	21.12 (23.762)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	245	-2.09 (23.465)	0.00	-8.33, 8.33	(-83.3, 66.7)	215	-4.82 (19.735)	0.00	-16.67, 0.00	(-58.3, 66.7)	
C5D1	227	24.18 (25.225)	16.67	0.00, 33.33	(0.0, 100.0)	165	22.88 (25.264)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	225	-1.36 (25.425)	0.00	-11.11, 8.33	(-100.0, 66.7)	162	-2.23 (20.450)	0.00	-8.33, 8.33	(-66.7, 75.0)	
C7D1	209	22.42 (25.505)	16.67	0.00, 33.33	(0.0, 100.0)	152	21.53 (24.776)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	207	-3.53 (23.487)	0.00	-8.33, 8.33	(-75.0, 66.7)	149	-3.90 (19.599)	0.00	-8.33, 0.00	(-66.7, 66.7)	
C9D1	196	20.96 (24.394)	16.67	0.00, 33.33	(0.0, 100.0)	127	19.55 (22.552)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	194	-4.12 (22.528)	0.00	-8.33, 0.00	(-100.0, 50.0)	125	-6.42 (22.449)	0.00	-16.67, 0.00	(-75.0, 66.7)	
C11D1	191	21.42 (24.067)	16.67	0.00, 33.33	(0.0, 100.0)	113	19.32 (23.734)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	189	-3.31 (22.391)	0.00	-8.33, 0.00	(-83.3, 50.0)	111	-7.83 (21.409)	-8.33	-16.67, 0.00	(-75.0, 58.3)	
C13D1	179	21.73 (23.952)	16.67	0.00, 33.33	(0.0, 100.0)	91	20.79 (24.795)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	177	-5.15 (22.487)	0.00	-16.67, 8.33	(-83.3, 50.0)	89	-5.81 (21.556)	0.00	-16.67, 0.00	(-58.3, 66.7)	
C15D1	165	20.25 (25.101)	16.67	0.00, 33.33	(0.0, 100.0)	75	18.67 (26.700)	8.33	0.00, 33.33	(0.0, 100.0)	
CHBL	163	-5.57 (23.506)	0.00	-16.67, 0.00	(-83.3, 58.3)	73	-5.25 (20.764)	0.00	-16.67, 0.00	(-50.0, 75.0)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Functional scales/Body Image

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	156	20.69 (24.503)	16.67	0.00, 33.33	(0.0, 100.0)	62	20.30 (26.249)	8.33	0.00, 33.33	(0.0, 100.0)
CHBL	154	-4.20 (25.168)	0.00	-16.67, 8.33	(-100.0, 58.3)	60	-2.64 (21.507)	0.00	-12.50, 0.00	(-50.0, 50.0)
C19D1	144	20.02 (24.899)	12.50	0.00, 33.33	(0.0, 100.0)	49	19.39 (26.701)	8.33	0.00, 33.33	(0.0, 100.0)
CHBL	142	-4.46 (26.083)	0.00	-8.33, 8.33	(-100.0, 58.3)	48	-2.78 (23.840)	0.00	-8.33, 0.00	(-75.0, 66.7)
C21D1	111	22.67 (26.619)	16.67	0.00, 33.33	(0.0, 100.0)	40	22.08 (33.256)	0.00	0.00, 33.33	(0.0, 100.0)
CHBL	110	-2.35 (26.882)	0.00	-8.33, 16.67	(-100.0, 58.3)	39	-2.78 (26.651)	0.00	-8.33, 0.00	(-75.0, 75.0)
C23D1	99	21.80 (25.274)	16.67	0.00, 33.33	(0.0, 91.7)	32	21.96 (29.578)	13.89	0.00, 25.00	(0.0, 100.0)
CHBL	98	-1.96 (24.894)	0.00	-8.33, 8.33	(-83.3, 66.7)	32	-3.04 (26.544)	0.00	-12.50, 4.17	(-75.0, 58.3)
C25D1	73	25.42 (26.497)	25.00	0.00, 33.33	(0.0, 100.0)	29	20.40 (28.659)	8.33	0.00, 25.00	(0.0, 100.0)
CHBL	72	-1.66 (25.122)	0.00	-8.33, 16.67	(-83.3, 50.0)	29	-4.02 (25.937)	0.00	-8.33, 0.00	(-75.0, 75.0)
C27D1	48	22.57 (26.350)	16.67	0.00, 33.33	(0.0, 100.0)	21	17.86 (31.101)	0.00	0.00, 16.67	(0.0, 100.0)
CHBL	47	1.77 (26.690)	0.00	-8.33, 16.67	(-91.7, 50.0)	21	-9.92 (24.526)	0.00	-25.00, 0.00	(-75.0, 33.3)
C29D1	41	22.49 (23.437)	22.22	0.00, 33.33	(0.0, 100.0)	14	25.00 (29.235)	20.83	0.00, 33.33	(0.0, 100.0)
CHBL	40	1.18 (25.011)	0.00	-1.39, 8.33	(-83.3, 50.0)	14	1.19 (20.375)	0.00	-8.33, 0.00	(-33.3, 33.3)
C31D1	27	23.46 (24.681)	25.00	0.00, 33.33	(0.0, 100.0)	7	16.67 (30.429)	0.00	0.00, 16.67	(0.0, 83.3)
CHBL	27	0.31 (27.588)	0.00	-8.33, 8.33	(-75.0, 66.7)	7	-1.19 (10.125)	0.00	-8.33, 0.00	(-16.7, 16.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Functional scales/Body Image

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
C33D1	19	28.07 (24.250)	25.00	0.00, 50.00	(0.0, 75.0)	5	13.33 (29.814)	0.00	0.00, 0.00	(0.0, 66.7)	
CHBL	19	4.82 (31.952)	0.00	-8.33, 16.67	(-66.7, 66.7)	5	0.00 (23.570)	0.00	0.00, 0.00	(-33.3, 33.3)	
C35D1	15	17.22 (19.020)	16.67	0.00, 33.33	(0.0, 58.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	
CHBL	15	-10.00 (26.201)	0.00	-16.67, 0.00	(-75.0, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	
C37D1	9	22.22 (23.570)	33.33	0.00, 33.33	(0.0, 66.7)	1	33.33 (NE)	33.33	33.33, 33.33	(33.3, 33.3)	
CHBL	9	6.48 (14.894)	0.00	0.00, 8.33	(-8.3, 41.7)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)	
C39D1	3	33.33 (0.000)	33.33	33.33, 33.33	(33.3, 33.3)	0					
CHBL	3	2.78 (4.811)	0.00	0.00, 8.33	(0.0, 8.3)	0					
C41D1	2	33.33 (0.000)	33.33	33.33, 33.33	(33.3, 33.3)	0					
CHBL	2	12.50 (5.893)	12.50	8.33, 16.67	(8.3, 16.7)	0					
End of Treatment	100	24.69 (27.078)	16.67	0.00, 33.33	(0.0, 100.0)	172	21.64 (24.192)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	100	0.67 (24.152)	0.00	-8.33, 8.33	(-66.7, 66.7)	170	-3.56 (21.981)	0.00	-16.67, 8.33	(-58.3, 66.7)	
40 Day Follow-Up	30	24.17 (28.730)	16.67	0.00, 33.33	(0.0, 100.0)	78	25.11 (26.266)	25.00	0.00, 33.33	(0.0, 100.0)	
CHBL	30	1.11 (23.441)	0.00	-8.33, 8.33	(-58.3, 66.7)	76	-2.96 (20.892)	0.00	-16.67, 8.33	(-58.3, 66.7)	
3 Months Follow-Up	60	19.58 (23.260)	16.67	0.00, 33.33	(0.0, 100.0)	111	19.59 (20.090)	16.67	0.00, 33.33	(0.0, 100.0)	
CHBL	60	-4.03 (19.009)	0.00	-8.33, 4.17	(-66.7, 33.3)	111	-5.03 (21.768)	0.00	-16.67, 8.33	(-100.0, 58.3)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Functional scales/Body Image

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	38.97 (29.411)	33.33	16.67, 58.33	(0.0, 100.0)	251	31.84 (27.573)	33.33	8.33, 50.00	(0.0, 100.0)
CHBL	251	13.20 (23.537)	8.33	0.00, 25.00	(-58.3, 66.7)	247	6.06 (20.792)	0.00	0.00, 16.67	(-58.3, 75.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Functional scales/Sexual Functioning

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	250	89.47 (20.539)	100.00	83.33, 100.00	(0.0, 100.0)	253	90.78 (16.618)	100.00	83.33, 100.00	(33.3, 100.0)	
C2D1	93	92.11 (17.130)	100.00	83.33, 100.00	(0.0, 100.0)	105	92.38 (13.873)	100.00	83.33, 100.00	(33.3, 100.0)	
CHBL	91	1.47 (13.977)	0.00	0.00, 0.00	(-33.3, 100.0)	104	0.48 (12.605)	0.00	0.00, 0.00	(-33.3, 50.0)	
C3D1	240	91.81 (16.561)	100.00	83.33, 100.00	(0.0, 100.0)	210	91.83 (15.659)	100.00	83.33, 100.00	(16.7, 100.0)	
CHBL	237	2.04 (16.072)	0.00	0.00, 0.00	(-66.7, 100.0)	206	1.05 (14.074)	0.00	0.00, 0.00	(-66.7, 50.0)	
C5D1	221	92.61 (15.098)	100.00	100.00, 100.00	(16.7, 100.0)	158	90.61 (18.377)	100.00	83.33, 100.00	(0.0, 100.0)	
CHBL	217	2.84 (18.027)	0.00	0.00, 0.00	(-83.3, 100.0)	155	-0.22 (15.074)	0.00	0.00, 0.00	(-66.7, 50.0)	
C7D1	203	91.95 (16.108)	100.00	83.33, 100.00	(0.0, 100.0)	148	89.98 (19.121)	100.00	83.33, 100.00	(0.0, 100.0)	
CHBL	200	2.08 (17.519)	0.00	0.00, 0.00	(-33.3, 100.0)	144	0.12 (16.898)	0.00	0.00, 0.00	(-83.3, 66.7)	
C9D1	189	91.89 (16.543)	100.00	100.00, 100.00	(0.0, 100.0)	123	90.65 (17.486)	100.00	83.33, 100.00	(16.7, 100.0)	
CHBL	186	1.08 (17.639)	0.00	0.00, 0.00	(-66.7, 100.0)	121	0.28 (15.212)	0.00	0.00, 0.00	(-50.0, 66.7)	
C11D1	182	92.67 (16.001)	100.00	100.00, 100.00	(0.0, 100.0)	107	89.88 (20.057)	100.00	83.33, 100.00	(0.0, 100.0)	
CHBL	179	2.89 (18.001)	0.00	0.00, 0.00	(-50.0, 100.0)	106	-0.31 (16.900)	0.00	0.00, 0.00	(-66.7, 66.7)	
C13D1	170	91.67 (17.224)	100.00	100.00, 100.00	(0.0, 100.0)	85	89.02 (19.679)	100.00	83.33, 100.00	(16.7, 100.0)	
CHBL	167	1.50 (16.139)	0.00	0.00, 0.00	(-50.0, 100.0)	85	-0.39 (16.662)	0.00	0.00, 0.00	(-83.3, 33.3)	
C15D1	161	93.69 (14.784)	100.00	100.00, 100.00	(16.7, 100.0)	69	89.61 (17.410)	100.00	83.33, 100.00	(33.3, 100.0)	
CHBL	158	3.90 (16.525)	0.00	0.00, 0.00	(-33.3, 66.7)	68	-0.25 (13.957)	0.00	0.00, 0.00	(-33.3, 33.3)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Functional scales/Sexual Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	147	92.97 (14.974)	100.00	100.00, 100.00	(33.3, 100.0)	59	87.57 (22.014)	100.00	66.67, 100.00	(0.0, 100.0)
CHBL	144	3.47 (15.876)	0.00	0.00, 0.00	(-50.0, 66.7)	59	-2.26 (16.798)	0.00	0.00, 0.00	(-66.7, 33.3)
C19D1	138	92.27 (16.625)	100.00	100.00, 100.00	(33.3, 100.0)	46	82.97 (24.213)	100.00	66.67, 100.00	(16.7, 100.0)
CHBL	135	4.20 (17.482)	0.00	0.00, 0.00	(-50.0, 66.7)	46	-5.07 (18.213)	0.00	0.00, 0.00	(-83.3, 33.3)
C21D1	104	90.71 (17.197)	100.00	83.33, 100.00	(33.3, 100.0)	39	74.79 (32.415)	100.00	50.00, 100.00	(0.0, 100.0)
CHBL	102	3.10 (16.033)	0.00	0.00, 0.00	(-50.0, 50.0)	39	-11.54 (27.613)	0.00	-16.67, 0.00	(-83.3, 33.3)
C23D1	92	91.67 (19.219)	100.00	100.00, 100.00	(0.0, 100.0)	30	80.56 (30.033)	100.00	66.67, 100.00	(0.0, 100.0)
CHBL	90	3.15 (17.824)	0.00	0.00, 0.00	(-50.0, 50.0)	30	-3.33 (22.489)	0.00	0.00, 0.00	(-83.3, 33.3)
C25D1	71	89.20 (21.473)	100.00	83.33, 100.00	(0.0, 100.0)	29	82.18 (26.701)	100.00	66.67, 100.00	(33.3, 100.0)
CHBL	70	2.62 (18.957)	0.00	0.00, 0.00	(-50.0, 50.0)	29	-2.30 (17.092)	0.00	0.00, 0.00	(-50.0, 33.3)
C27D1	47	87.94 (21.339)	100.00	66.67, 100.00	(0.0, 100.0)	21	81.75 (27.841)	100.00	66.67, 100.00	(33.3, 100.0)
CHBL	46	2.90 (15.438)	0.00	0.00, 0.00	(-50.0, 33.3)	21	-4.76 (17.593)	0.00	0.00, 0.00	(-50.0, 33.3)
C29D1	38	95.18 (13.922)	100.00	100.00, 100.00	(33.3, 100.0)	14	89.29 (24.114)	100.00	100.00, 100.00	(16.7, 100.0)
CHBL	37	5.86 (14.281)	0.00	0.00, 16.67	(-16.7, 33.3)	14	-3.57 (9.649)	0.00	0.00, 0.00	(-33.3, 0.0)
C31D1	27	94.44 (17.903)	100.00	100.00, 100.00	(33.3, 100.0)	7	92.86 (13.113)	100.00	83.33, 100.00	(66.7, 100.0)
CHBL	26	3.21 (11.565)	0.00	0.00, 0.00	(-16.7, 33.3)	7	-4.76 (8.133)	0.00	-16.67, 0.00	(-16.7, 0.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Functional scales/Sexual Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	19	94.74 (16.715)	100.00	100.00, 100.00	(33.3, 100.0)	5	100.00 (0.000)	100.00	100.00, 100.00	(100.0, 100.0)
CHBL	19	3.51 (13.122)	0.00	0.00, 0.00	(-16.7, 33.3)	5	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
C35D1	14	100.00 (0.000)	100.00	100.00, 100.00	(100.0, 100.0)	3	100.00 (0.000)	100.00	100.00, 100.00	(100.0, 100.0)
CHBL	14	4.76 (10.187)	0.00	0.00, 0.00	(0.0, 33.3)	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
C37D1	9	96.30 (11.111)	100.00	100.00, 100.00	(66.7, 100.0)	1	100.00 (NE)	100.00	100.00, 100.00	(100.0, 100.0)
CHBL	9	-0.00 (8.333)	0.00	0.00, 0.00	(-16.7, 16.7)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
C39D1	3	100.00 (0.000)	100.00	100.00, 100.00	(100.0, 100.0)	0				
CHBL	3	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)	0				
C41D1	2	83.33 (23.570)	83.33	66.67, 100.00	(66.7, 100.0)	0				
CHBL	2	-8.33 (11.785)	-8.33	-16.67, 0.00	(-16.7, 0.0)	0				
End of Treatment	93	95.16 (14.863)	100.00	100.00, 100.00	(0.0, 100.0)	165	93.84 (14.164)	100.00	100.00, 100.00	(33.3, 100.0)
CHBL	92	3.08 (15.613)	0.00	0.00, 0.00	(-33.3, 100.0)	161	2.48 (13.464)	0.00	0.00, 0.00	(-50.0, 50.0)
40 Day Follow-Up	29	95.40 (14.013)	100.00	100.00, 100.00	(33.3, 100.0)	75	93.56 (17.735)	100.00	100.00, 100.00	(0.0, 100.0)
CHBL	29	0.57 (7.019)	0.00	0.00, 0.00	(-16.7, 16.7)	72	1.39 (13.342)	0.00	0.00, 0.00	(-50.0, 50.0)
3 Months Follow-Up	59	94.07 (15.087)	100.00	100.00, 100.00	(33.3, 100.0)	106	92.77 (16.105)	100.00	100.00, 100.00	(0.0, 100.0)
CHBL	59	3.11 (21.769)	0.00	0.00, 0.00	(-33.3, 100.0)	104	2.08 (13.073)	0.00	0.00, 0.00	(-33.3, 33.3)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Functional scales/Sexual Functioning

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	252	96.76 (11.499)	100.00	100.00, 100.00	(0.0, 100.0)	248	95.97 (11.297)	100.00	100.00, 100.00	(33.3, 100.0)
CHBL	247	7.42 (18.680)	0.00	0.00, 0.00	(-66.7, 100.0)	241	5.26 (13.439)	0.00	0.00, 0.00	(-33.3, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Systemic Therapy Side Effects

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	254	15.62 (15.765)	9.52	4.76, 23.81	(0.0, 76.2)	259	14.41 (13.129)	11.11	4.76, 19.05	(0.0, 81.0)	
C2D1	96	16.87 (15.309)	14.29	4.76, 23.81	(0.0, 61.9)	109	15.36 (12.464)	14.29	4.76, 19.05	(0.0, 52.4)	
CHBL	95	1.55 (12.588)	0.00	-4.76, 9.52	(-33.3, 52.4)	109	-0.56 (11.108)	0.00	-4.76, 4.76	(-38.1, 33.3)	
C3D1	246	19.99 (16.556)	14.29	9.52, 28.57	(0.0, 76.2)	220	17.58 (14.026)	14.29	9.52, 23.81	(0.0, 66.7)	
CHBL	245	4.39 (13.918)	4.76	-4.76, 14.29	(-42.9, 52.4)	217	3.63 (10.866)	4.76	0.00, 9.52	(-33.3, 38.1)	
C5D1	229	20.59 (16.056)	19.05	9.52, 28.57	(0.0, 81.0)	168	18.90 (15.052)	19.05	9.52, 28.57	(0.0, 66.7)	
CHBL	227	5.14 (16.060)	4.76	-4.76, 14.29	(-47.6, 47.6)	166	5.06 (11.584)	4.76	-4.76, 9.52	(-23.8, 61.9)	
C7D1	210	19.65 (16.912)	14.29	4.76, 28.57	(0.0, 85.7)	152	17.36 (14.864)	14.29	4.76, 23.81	(0.0, 71.4)	
CHBL	208	4.02 (15.317)	4.76	-4.76, 14.29	(-47.6, 42.9)	150	3.33 (12.044)	0.00	-4.76, 9.52	(-33.3, 47.6)	
C9D1	196	16.76 (14.375)	14.29	4.76, 23.81	(0.0, 76.2)	129	15.97 (13.633)	14.29	4.76, 23.81	(0.0, 71.4)	
CHBL	194	1.84 (14.016)	4.76	-4.76, 9.52	(-57.1, 28.6)	128	2.77 (11.858)	0.00	-4.76, 9.52	(-47.6, 38.1)	
C11D1	191	16.43 (14.821)	14.29	4.76, 23.81	(0.0, 76.2)	114	15.87 (13.990)	14.29	4.76, 23.81	(0.0, 76.2)	
CHBL	189	0.76 (14.593)	0.00	-4.76, 9.52	(-57.1, 42.9)	113	1.85 (13.281)	0.00	-4.76, 9.52	(-47.6, 57.1)	
C13D1	180	15.81 (14.878)	10.32	4.76, 23.81	(0.0, 76.2)	93	16.42 (14.127)	14.29	4.76, 27.78	(0.0, 57.1)	
CHBL	178	0.23 (15.152)	0.00	-4.76, 4.76	(-61.9, 52.4)	92	2.35 (13.507)	0.00	-4.76, 9.52	(-61.9, 38.1)	
C15D1	166	14.69 (13.139)	11.90	4.76, 23.81	(0.0, 76.2)	76	16.79 (15.366)	14.29	4.76, 23.81	(0.0, 85.7)	
CHBL	164	-0.90 (14.345)	0.00	-9.52, 4.76	(-66.7, 42.9)	75	2.91 (14.167)	0.00	-4.76, 14.29	(-47.6, 38.1)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Systemic Therapy Side Effects

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	14.96 (13.853)	9.52	4.76, 23.81	(0.0, 76.2)	64	17.71 (15.838)	14.29	4.76, 28.57	(0.0, 81.0)
CHBL	155	-0.33 (14.043)	0.00	-9.52, 9.52	(-57.1, 38.1)	63	3.48 (14.570)	0.00	-4.76, 14.29	(-33.3, 61.9)
C19D1	145	15.60 (13.203)	9.52	4.76, 23.81	(0.0, 57.1)	50	16.70 (18.713)	9.52	4.76, 23.81	(0.0, 90.5)
CHBL	143	0.30 (14.108)	0.00	-4.76, 9.52	(-47.6, 38.1)	50	3.09 (18.734)	0.00	-4.76, 9.52	(-52.4, 71.4)
C21D1	112	16.28 (13.808)	14.29	4.76, 23.81	(0.0, 57.1)	41	17.11 (16.718)	14.29	4.76, 23.81	(0.0, 71.4)
CHBL	111	1.07 (13.170)	0.00	-4.76, 9.52	(-47.6, 42.9)	41	2.25 (18.257)	4.76	-9.52, 9.52	(-47.6, 52.4)
C23D1	100	15.36 (13.814)	11.90	4.76, 23.81	(0.0, 57.1)	32	18.04 (14.754)	19.05	4.76, 23.81	(0.0, 57.1)
CHBL	99	1.47 (13.373)	0.00	-4.76, 9.52	(-52.4, 28.6)	32	2.71 (17.286)	0.00	-7.14, 14.29	(-42.9, 38.1)
C25D1	74	15.91 (14.578)	14.29	4.76, 23.81	(0.0, 57.1)	29	15.93 (13.425)	14.29	4.76, 28.57	(0.0, 42.9)
CHBL	73	2.95 (11.759)	0.00	-4.76, 9.52	(-19.0, 42.9)	29	0.82 (16.001)	0.00	-4.76, 14.29	(-33.3, 33.3)
C27D1	49	15.81 (15.182)	14.29	4.76, 23.81	(0.0, 71.4)	21	13.38 (9.945)	14.29	4.76, 19.05	(0.0, 28.6)
CHBL	48	2.94 (10.183)	0.00	-2.38, 9.52	(-28.6, 29.4)	21	1.36 (14.455)	0.00	-4.76, 9.52	(-38.1, 28.6)
C29D1	41	14.46 (12.391)	14.29	4.76, 23.81	(0.0, 47.6)	14	16.67 (13.041)	11.90	4.76, 28.57	(0.0, 38.1)
CHBL	40	3.52 (9.899)	4.76	0.00, 9.52	(-23.8, 23.8)	14	4.42 (17.666)	4.76	-9.52, 14.29	(-28.6, 38.1)
C31D1	27	12.38 (11.451)	9.52	0.00, 19.05	(0.0, 38.9)	7	10.88 (11.893)	9.52	0.00, 23.81	(0.0, 28.6)
CHBL	27	1.26 (9.756)	0.00	-4.76, 9.52	(-19.0, 29.4)	7	4.08 (16.594)	0.00	-14.29, 23.81	(-14.3, 23.8)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Systemic Therapy Side Effects

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	12.67 (11.504)	13.81	0.00, 19.05	(0.0, 40.0)	5	15.24 (18.257)	9.52	0.00, 23.81	(0.0, 42.9)
CHBL	20	1.95 (11.605)	0.00	-4.76, 9.05	(-19.0, 30.5)	5	3.81 (13.214)	0.00	0.00, 14.29	(-14.3, 19.0)
C35D1	15	12.70 (10.749)	9.52	0.00, 23.81	(0.0, 28.6)	3	9.52 (16.496)	0.00	0.00, 28.57	(0.0, 28.6)
CHBL	15	2.54 (8.975)	0.00	-4.76, 9.52	(-9.5, 19.0)	3	3.17 (19.245)	0.00	-14.29, 23.81	(-14.3, 23.8)
C37D1	9	14.29 (11.419)	14.29	4.76, 23.81	(0.0, 33.3)	1	38.10 (NE)	38.10	38.10, 38.10	(38.1, 38.1)
CHBL	9	4.23 (11.026)	0.00	-4.76, 14.29	(-9.5, 23.8)	1	9.52 (NE)	9.52	9.52, 9.52	(9.5, 9.5)
C39D1	3	9.52 (8.248)	4.76	4.76, 19.05	(4.8, 19.0)	0				
CHBL	3	4.76 (4.762)	4.76	0.00, 9.52	(0.0, 9.5)	0				
C41D1	2	16.67 (16.836)	16.67	4.76, 28.57	(4.8, 28.6)	0				
CHBL	2	7.14 (16.836)	7.14	-4.76, 19.05	(-4.8, 19.0)	0				
End of Treatment	100	20.00 (18.720)	14.29	4.76, 28.57	(0.0, 76.2)	174	15.65 (12.829)	14.29	4.76, 23.81	(0.0, 66.7)
CHBL	100	5.95 (15.185)	4.76	-4.76, 14.29	(-33.3, 52.4)	172	3.03 (12.212)	0.00	-4.76, 9.52	(-33.3, 47.6)
40 Day Follow-Up	30	15.08 (15.872)	11.90	4.76, 23.81	(0.0, 61.9)	79	16.33 (15.309)	14.29	4.76, 23.81	(0.0, 71.4)
CHBL	30	2.06 (14.674)	2.38	-9.52, 9.52	(-28.6, 28.6)	77	3.29 (13.496)	0.00	-4.76, 9.52	(-23.8, 47.6)
3 Months Follow-Up	60	16.19 (15.165)	14.29	4.76, 23.81	(0.0, 81.0)	111	13.56 (12.067)	9.52	4.76, 19.05	(0.0, 61.9)
CHBL	60	2.62 (15.961)	0.00	-4.76, 9.52	(-38.1, 57.1)	111	0.98 (12.782)	0.00	-4.76, 9.52	(-28.6, 47.6)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Systemic Therapy Side Effects

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	30.07 (17.500)	28.57	14.29, 42.86	(0.0, 85.7)	251	24.81 (16.169)	23.81	14.29, 33.33	(0.0, 90.5)
CHBL	251	14.54 (14.671)	14.29	4.76, 23.81	(-33.3, 52.4)	248	10.97 (13.207)	9.52	4.76, 19.05	(-33.3, 71.4)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Breast Symptoms

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	253	18.08 (22.033)	8.33	0.00, 25.00	(0.0, 100.0)	257	19.02 (23.245)	8.33	0.00, 33.33	(0.0, 100.0)	
C2D1	95	11.67 (15.395)	8.33	0.00, 16.67	(0.0, 100.0)	107	14.17 (19.433)	8.33	0.00, 16.67	(0.0, 100.0)	
CHBL	94	-5.50 (12.315)	0.00	-16.67, 0.00	(-41.7, 25.0)	107	-5.19 (14.072)	0.00	-8.33, 0.00	(-50.0, 33.3)	
C3D1	246	9.69 (14.261)	0.00	0.00, 16.67	(0.0, 83.3)	219	11.23 (17.060)	8.33	0.00, 16.67	(0.0, 100.0)	
CHBL	244	-8.54 (17.664)	0.00	-16.67, 0.00	(-100.0, 33.3)	214	-6.18 (18.374)	0.00	-8.33, 0.00	(-91.7, 75.0)	
C5D1	229	10.23 (13.942)	8.33	0.00, 16.67	(0.0, 66.7)	165	11.35 (16.400)	8.33	0.00, 16.67	(0.0, 75.0)	
CHBL	226	-8.22 (19.586)	0.00	-16.67, 0.00	(-100.0, 50.0)	161	-4.71 (17.236)	0.00	-8.33, 0.00	(-75.0, 50.0)	
C7D1	209	9.57 (14.759)	0.00	0.00, 16.67	(0.0, 91.7)	152	10.42 (15.172)	8.33	0.00, 16.67	(0.0, 100.0)	
CHBL	206	-7.97 (20.434)	0.00	-16.67, 0.00	(-100.0, 66.7)	149	-6.52 (18.690)	0.00	-8.33, 0.00	(-91.7, 25.0)	
C9D1	194	6.49 (10.380)	0.00	0.00, 8.33	(0.0, 50.0)	126	10.25 (15.281)	8.33	0.00, 16.67	(0.0, 100.0)	
CHBL	191	-10.17 (19.410)	0.00	-16.67, 0.00	(-100.0, 41.7)	126	-6.92 (21.613)	0.00	-13.89, 0.00	(-91.7, 33.3)	
C11D1	190	7.68 (11.968)	0.00	0.00, 8.33	(0.0, 66.7)	114	12.28 (19.526)	8.33	0.00, 16.67	(0.0, 100.0)	
CHBL	188	-8.82 (18.647)	0.00	-16.67, 0.00	(-100.0, 58.3)	112	-5.63 (20.160)	0.00	-8.33, 0.00	(-91.7, 33.3)	
C13D1	179	7.15 (12.082)	0.00	0.00, 8.33	(0.0, 58.3)	92	11.41 (18.927)	0.00	0.00, 16.67	(0.0, 100.0)	
CHBL	176	-9.67 (19.541)	0.00	-16.67, 0.00	(-83.3, 50.0)	91	-7.39 (19.450)	0.00	-8.33, 0.00	(-83.3, 33.3)	
C15D1	166	6.53 (11.824)	0.00	0.00, 8.33	(0.0, 75.0)	76	10.96 (18.867)	0.00	0.00, 16.67	(0.0, 100.0)	
CHBL	163	-8.49 (18.413)	0.00	-16.67, 0.00	(-91.7, 41.7)	75	-8.41 (22.562)	0.00	-16.67, 0.00	(-100.0, 50.0)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Breast Symptoms

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	7.06 (12.417)	0.00	0.00, 8.33	(0.0, 75.0)	65	10.04 (14.745)	8.33	0.00, 16.67	(0.0, 66.7)
CHBL	155	-8.60 (19.003)	0.00	-16.67, 0.00	(-100.0, 25.0)	64	-9.94 (23.339)	0.00	-16.67, 0.00	(-100.0, 25.0)
C19D1	145	6.61 (12.024)	0.00	0.00, 8.33	(0.0, 66.7)	49	9.01 (12.711)	0.00	0.00, 16.67	(0.0, 50.0)
CHBL	142	-7.98 (18.906)	0.00	-16.67, 0.00	(-100.0, 58.3)	49	-13.89 (24.670)	-8.33	-25.00, 0.00	(-100.0, 33.3)
C21D1	111	6.16 (10.403)	0.00	0.00, 8.33	(0.0, 41.7)	40	12.92 (23.186)	4.17	0.00, 12.50	(0.0, 100.0)
CHBL	110	-8.11 (19.139)	0.00	-16.67, 0.00	(-100.0, 33.3)	40	-11.81 (27.396)	-8.33	-16.67, 0.00	(-100.0, 33.3)
C23D1	100	7.31 (12.288)	0.00	0.00, 8.33	(0.0, 58.3)	31	10.22 (15.170)	0.00	0.00, 16.67	(0.0, 58.3)
CHBL	98	-6.92 (19.896)	0.00	-16.67, 0.00	(-100.0, 50.0)	31	-15.32 (27.647)	-8.33	-16.67, 0.00	(-100.0, 16.7)
C25D1	74	6.87 (14.750)	0.00	0.00, 8.33	(0.0, 83.3)	28	7.14 (10.809)	0.00	0.00, 12.50	(0.0, 33.3)
CHBL	72	-9.03 (21.926)	0.00	-16.67, 0.00	(-100.0, 50.0)	28	-16.07 (27.492)	-8.33	-20.83, 0.00	(-83.3, 16.7)
C27D1	49	5.73 (9.237)	0.00	0.00, 8.33	(0.0, 33.3)	21	5.56 (8.471)	0.00	0.00, 8.33	(0.0, 33.3)
CHBL	47	-7.51 (20.164)	0.00	-16.67, 0.00	(-91.7, 25.0)	21	-13.49 (25.614)	-8.33	-16.67, 0.00	(-91.7, 16.7)
C29D1	41	5.49 (9.430)	0.00	0.00, 8.33	(0.0, 41.7)	14	6.55 (11.866)	0.00	0.00, 8.33	(0.0, 33.3)
CHBL	40	-6.46 (19.565)	0.00	-12.50, 0.00	(-100.0, 25.0)	14	-8.33 (17.296)	-8.33	-16.67, 0.00	(-58.3, 16.7)
C31D1	27	3.70 (7.430)	0.00	0.00, 8.33	(0.0, 33.3)	7	2.38 (4.066)	0.00	0.00, 8.33	(0.0, 8.3)
CHBL	27	-10.80 (19.722)	0.00	-16.67, 0.00	(-91.7, 8.3)	7	-14.29 (20.813)	-8.33	-16.67, 0.00	(-58.3, 0.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Breast Symptoms

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	2.92 (6.210)	0.00	0.00, 0.00	(0.0, 16.7)	5	11.67 (21.731)	0.00	0.00, 8.33	(0.0, 50.0)
CHBL	20	-10.83 (23.894)	-4.17	-16.67, 0.00	(-100.0, 16.7)	5	-5.00 (7.454)	0.00	-8.33, 0.00	(-16.7, 0.0)
C35D1	15	2.22 (4.947)	0.00	0.00, 0.00	(0.0, 16.7)	2	0.00 (0.000)	0.00	0.00, 0.00	(0.0, 0.0)
CHBL	15	-11.11 (25.524)	-8.33	-8.33, 0.00	(-100.0, 8.3)	2	-8.33 (11.785)	-8.33	-16.67, 0.00	(-16.7, 0.0)
C37D1	9	3.70 (7.349)	0.00	0.00, 0.00	(0.0, 16.7)	1	41.67 (NE)	41.67	41.67, 41.67	(41.7, 41.7)
CHBL	9	-4.63 (10.300)	-8.33	-8.33, 0.00	(-16.7, 16.7)	1	-8.33 (NE)	-8.33	-8.33, -8.33	(-8.3, -8.3)
C39D1	3	5.56 (9.623)	0.00	0.00, 16.67	(0.0, 16.7)	0				
CHBL	3	0.00 (16.667)	0.00	-16.67, 16.67	(-16.7, 16.7)	0				
C41D1	2	4.17 (5.893)	4.17	0.00, 8.33	(0.0, 8.3)	0				
CHBL	2	-4.17 (17.678)	-4.17	-16.67, 8.33	(-16.7, 8.3)	0				
End of Treatment	100	10.81 (16.052)	0.00	0.00, 20.83	(0.0, 75.0)	174	16.04 (21.298)	8.33	0.00, 25.00	(0.0, 91.7)
CHBL	100	-9.53 (18.779)	0.00	-16.67, 0.00	(-83.3, 41.7)	172	-1.94 (16.156)	0.00	-8.33, 0.00	(-58.3, 66.7)
40 Day Follow-Up	29	13.51 (22.206)	8.33	0.00, 16.67	(0.0, 100.0)	78	13.25 (21.169)	0.00	0.00, 16.67	(0.0, 100.0)
CHBL	29	-3.45 (21.880)	-8.33	-16.67, 0.00	(-41.7, 75.0)	74	-2.59 (17.224)	0.00	-8.33, 0.00	(-41.7, 75.0)
3 Months Follow-Up	60	15.00 (17.880)	8.33	0.00, 25.00	(0.0, 66.7)	110	11.06 (17.382)	4.17	0.00, 16.67	(0.0, 100.0)
CHBL	60	-5.69 (20.840)	0.00	-16.67, 4.17	(-83.3, 58.3)	110	-7.27 (17.049)	0.00	-16.67, 0.00	(-66.7, 41.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Breast Symptoms

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	19.62 (19.816)	16.67	8.33, 33.33	(0.0, 100.0)	251	21.55 (23.183)	16.67	8.33, 33.33	(0.0, 100.0)
CHBL	250	1.36 (19.969)	0.00	-8.33, 8.33	(-100.0, 75.0)	246	2.96 (17.675)	0.00	0.00, 8.33	(-66.7, 75.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Arm Symptoms

Visit	T-DXd (N=261)						T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max	
Baseline	253	20.29 (24.108)	11.11	0.00, 33.33	(0.0, 100.0)	259	18.32 (23.120)	11.11	0.00, 33.33	(0.0, 100.0)	
C2D1	96	14.12 (18.345)	11.11	0.00, 22.22	(0.0, 100.0)	110	15.86 (20.106)	11.11	0.00, 22.22	(0.0, 100.0)	
CHBL	95	-6.55 (14.082)	0.00	-11.11, 0.00	(-66.7, 11.1)	110	-1.82 (14.161)	0.00	-11.11, 0.00	(-55.6, 33.3)	
C3D1	246	13.82 (19.276)	11.11	0.00, 22.22	(0.0, 100.0)	219	16.84 (20.370)	11.11	0.00, 22.22	(0.0, 100.0)	
CHBL	244	-6.51 (16.975)	0.00	-11.11, 0.00	(-77.8, 33.3)	216	-1.03 (15.643)	0.00	0.00, 0.00	(-66.7, 66.7)	
C5D1	229	15.24 (19.124)	11.11	0.00, 22.22	(0.0, 100.0)	166	19.65 (21.940)	11.11	0.00, 33.33	(0.0, 100.0)	
CHBL	226	-5.01 (17.746)	0.00	-11.11, 0.00	(-77.8, 44.4)	164	2.34 (17.032)	0.00	0.00, 11.11	(-55.6, 55.6)	
C7D1	210	13.99 (18.733)	11.11	0.00, 22.22	(0.0, 100.0)	153	17.25 (19.818)	11.11	0.00, 22.22	(0.0, 100.0)	
CHBL	207	-5.77 (17.745)	0.00	-11.11, 0.00	(-66.7, 55.6)	151	0.55 (19.434)	0.00	0.00, 11.11	(-77.8, 44.4)	
C9D1	195	13.33 (16.982)	11.11	0.00, 22.22	(0.0, 88.9)	127	19.25 (22.021)	11.11	0.00, 33.33	(0.0, 100.0)	
CHBL	192	-4.63 (18.097)	0.00	-11.11, 0.00	(-77.8, 44.4)	127	0.96 (19.848)	0.00	0.00, 11.11	(-77.8, 44.4)	
C11D1	191	12.62 (16.802)	11.11	0.00, 22.22	(0.0, 88.9)	114	17.50 (20.947)	11.11	0.00, 33.33	(0.0, 88.9)	
CHBL	189	-5.94 (17.699)	0.00	-11.11, 0.00	(-66.7, 33.3)	113	-1.82 (19.536)	0.00	-11.11, 11.11	(-66.7, 44.4)	
C13D1	180	14.14 (19.926)	0.00	0.00, 22.22	(0.0, 88.9)	92	18.18 (21.416)	11.11	0.00, 33.33	(0.0, 100.0)	
CHBL	177	-5.02 (19.852)	0.00	-11.11, 0.00	(-77.8, 77.8)	91	-2.14 (19.062)	0.00	-11.11, 5.56	(-66.7, 44.4)	
C15D1	166	11.75 (16.878)	0.00	0.00, 22.22	(0.0, 88.9)	76	20.18 (24.526)	11.11	0.00, 33.33	(0.0, 100.0)	
CHBL	163	-6.71 (22.183)	0.00	-11.11, 0.00	(-88.9, 44.4)	75	-0.15 (22.334)	0.00	-11.11, 11.11	(-66.7, 66.7)	

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Arm Symptoms

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C17D1	157	12.88 (17.947)	0.00	0.00, 22.22	(0.0, 100.0)	65	18.80 (22.731)	11.11	0.00, 22.22	(0.0, 100.0)
CHBL	155	-5.95 (20.740)	0.00	-22.22, 0.00	(-77.8, 55.6)	64	-2.60 (19.371)	0.00	-11.11, 5.56	(-77.8, 44.4)
C19D1	145	11.72 (16.604)	0.00	0.00, 22.22	(0.0, 100.0)	50	19.00 (21.534)	11.11	0.00, 33.33	(0.0, 77.8)
CHBL	142	-5.95 (22.677)	0.00	-11.11, 0.00	(-77.8, 55.6)	50	-4.33 (20.491)	0.00	-11.11, 0.00	(-66.7, 44.4)
C21D1	112	13.39 (18.030)	5.56	0.00, 22.22	(0.0, 100.0)	41	21.41 (26.456)	11.11	0.00, 22.22	(0.0, 100.0)
CHBL	111	-5.51 (19.296)	0.00	-22.22, 0.00	(-66.7, 44.4)	41	-3.25 (25.367)	0.00	-11.11, 11.11	(-77.8, 66.7)
C23D1	100	13.22 (18.054)	11.11	0.00, 22.22	(0.0, 100.0)	32	20.14 (22.121)	11.11	0.00, 33.33	(0.0, 88.9)
CHBL	98	-5.22 (22.348)	0.00	-22.22, 0.00	(-77.8, 55.6)	32	-3.82 (19.060)	0.00	-11.11, 5.56	(-66.7, 33.3)
C25D1	74	11.86 (18.604)	0.00	0.00, 22.22	(0.0, 100.0)	29	13.41 (17.911)	0.00	0.00, 22.22	(0.0, 66.7)
CHBL	72	-7.10 (22.710)	0.00	-22.22, 0.00	(-77.8, 55.6)	29	-9.20 (17.586)	0.00	-22.22, 0.00	(-66.7, 22.2)
C27D1	49	12.47 (17.367)	0.00	0.00, 22.22	(0.0, 55.6)	21	12.70 (16.587)	11.11	0.00, 22.22	(0.0, 55.6)
CHBL	47	-6.86 (25.119)	0.00	-11.11, 0.00	(-77.8, 44.4)	21	-5.29 (23.470)	0.00	-11.11, 0.00	(-77.8, 33.3)
C29D1	41	16.26 (16.311)	11.11	0.00, 22.22	(0.0, 55.6)	14	17.46 (20.308)	11.11	0.00, 33.33	(0.0, 66.7)
CHBL	40	0.56 (19.482)	0.00	-11.11, 11.11	(-66.7, 44.4)	14	-1.59 (14.360)	0.00	-11.11, 0.00	(-33.3, 22.2)
C31D1	27	11.93 (13.756)	11.11	0.00, 22.22	(0.0, 44.4)	7	9.52 (7.667)	11.11	0.00, 11.11	(0.0, 22.2)
CHBL	27	-2.88 (21.702)	0.00	0.00, 11.11	(-77.8, 22.2)	7	0.00 (9.072)	0.00	-11.11, 11.11	(-11.1, 11.1)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Arm Symptoms

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C33D1	20	16.11 (17.834)	11.11	0.00, 22.22	(0.0, 66.7)	5	20.00 (26.527)	11.11	11.11, 11.11	(0.0, 66.7)
CHBL	20	0.00 (23.639)	0.00	-5.56, 11.11	(-66.7, 33.3)	5	-2.22 (9.296)	0.00	-11.11, 0.00	(-11.1, 11.1)
C35D1	15	11.11 (14.548)	0.00	0.00, 22.22	(0.0, 44.4)	3	7.41 (12.830)	0.00	0.00, 22.22	(0.0, 22.2)
CHBL	15	-5.93 (20.517)	0.00	-22.22, 11.11	(-44.4, 22.2)	3	0.00 (19.245)	-11.11	-11.11, 22.22	(-11.1, 22.2)
C37D1	9	8.64 (12.143)	0.00	0.00, 11.11	(0.0, 33.3)	1	66.67 (NE)	66.67	66.67, 66.67	(66.7, 66.7)
CHBL	9	-9.88 (12.963)	0.00	-22.22, 0.00	(-33.3, 0.0)	1	0.00 (NE)	0.00	0.00, 0.00	(0.0, 0.0)
C39D1	3	3.70 (6.415)	0.00	0.00, 11.11	(0.0, 11.1)	0				
CHBL	3	-3.70 (16.973)	0.00	-22.22, 11.11	(-22.2, 11.1)	0				
C41D1	2	11.11 (0.000)	11.11	11.11, 11.11	(11.1, 11.1)	0				
CHBL	2	-0.00 (15.713)	-0.00	-11.11, 11.11	(-11.1, 11.1)	0				
End of Treatment	100	17.67 (21.252)	11.11	0.00, 33.33	(0.0, 100.0)	174	16.28 (20.156)	11.11	0.00, 22.22	(0.0, 100.0)
CHBL	100	-3.44 (18.732)	0.00	-11.11, 11.11	(-77.8, 44.4)	172	0.45 (20.299)	0.00	-11.11, 11.11	(-66.7, 100.0)
40 Day Follow-Up	30	21.85 (29.539)	11.11	0.00, 33.33	(0.0, 100.0)	78	17.81 (23.712)	11.11	0.00, 22.22	(0.0, 100.0)
CHBL	30	2.59 (21.577)	0.00	0.00, 11.11	(-44.4, 66.7)	76	0.29 (19.624)	0.00	-11.11, 11.11	(-55.6, 66.7)
3 Months Follow-Up	60	17.96 (22.604)	11.11	0.00, 33.33	(0.0, 100.0)	110	13.54 (19.472)	11.11	0.00, 22.22	(0.0, 100.0)
CHBL	60	-2.96 (19.285)	0.00	-11.11, 0.00	(-66.7, 77.8)	110	-3.64 (18.985)	0.00	-11.11, 0.00	(-66.7, 66.7)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.6: Summary of Actual Value and Change from Baseline of EORTC QLQ-BR45
 Full Analysis Set

Symptom scales/Arm Symptoms

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Worst post-baseline	253	28.28 (23.928)	22.22	11.11, 44.44	(0.0, 100.0)	251	27.89 (24.793)	22.22	11.11, 44.44	(0.0, 100.0)
CHBL	250	8.00 (19.921)	11.11	0.00, 22.22	(-55.6, 77.8)	248	9.86 (20.206)	11.11	0.00, 22.22	(-55.6, 100.0)

Notes: Visit is based on window rule specified in SAP.

Linear transformations are applied to all subscales of EORTC QLQ-BR45. A high score for a functional scale represents a low/unhealthy level of functioning; a high score for a symptom scale/item represents a high level of symptomatology/problems.

Source Data: adam.adqs; Listing 16.2.8.5.2.

Table 14.3.6.3: Summary of Actual Value and Change from Baseline of EQ-5D-5L Index Score and EQ VAS
 Full Analysis Set

Health Scale (VAS)

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
Baseline	252	74.3 (18.81)	80.0	60.0, 90.0	(20, 100)	259	75.2 (19.89)	80.0	65.0, 90.0	(0, 100)
C2D1	96	79.8 (15.60)	80.0	70.0, 90.0	(40, 100)	110	79.1 (14.23)	80.0	70.0, 90.0	(30, 100)
CHBL	94	3.0 (12.23)	0.0	0.0, 10.0	(-30, 50)	108	4.3 (10.90)	0.0	0.0, 10.0	(-30, 40)
C3D1	245	76.9 (16.25)	80.0	65.0, 90.0	(20, 100)	220	80.0 (14.08)	80.0	70.0, 90.0	(40, 100)
CHBL	242	2.7 (16.56)	0.0	-5.0, 10.0	(-50, 70)	218	3.0 (14.30)	0.0	-5.0, 10.0	(-30, 85)
C5D1	230	76.7 (16.33)	80.0	70.0, 90.0	(10, 100)	169	77.6 (15.52)	80.0	70.0, 90.0	(20, 100)
CHBL	226	2.4 (16.59)	0.0	-10.0, 10.0	(-50, 70)	167	0.4 (17.85)	0.0	-10.0, 8.0	(-50, 90)
C7D1	209	77.9 (15.00)	80.0	70.0, 90.0	(40, 100)	151	78.3 (15.59)	80.0	70.0, 90.0	(20, 100)
CHBL	206	3.3 (17.22)	0.0	-5.0, 10.0	(-50, 80)	149	1.3 (15.70)	0.0	-5.0, 7.0	(-60, 85)
C9D1	195	78.9 (15.19)	80.0	70.0, 90.0	(30, 100)	129	77.8 (16.84)	80.0	70.0, 90.0	(30, 100)
CHBL	193	4.2 (16.26)	0.0	-5.0, 10.0	(-50, 60)	128	1.6 (18.10)	0.0	-5.0, 8.5	(-45, 100)
C11D1	192	80.2 (13.70)	80.0	70.0, 90.0	(30, 100)	113	78.3 (14.63)	80.0	70.0, 90.0	(35, 100)
CHBL	190	5.1 (15.76)	2.0	-1.0, 10.0	(-40, 60)	113	3.2 (17.68)	0.0	-5.0, 10.0	(-40, 100)
C13D1	180	79.1 (13.37)	80.0	70.0, 90.0	(40, 100)	92	77.9 (15.18)	80.0	70.0, 90.0	(40, 100)
CHBL	178	5.4 (16.44)	3.0	-5.0, 15.0	(-55, 60)	91	2.6 (17.97)	0.0	-5.0, 10.0	(-40, 80)

Notes: EQ-5D-5L is scored according to the UK Crosswalk Value Set.

A linear transformation is applied to health scale which is measured according to a 0-100mm Visual Analog Scale (VAS). A high VAS score represents worse overall self-rated health status.

Visit is based on window rule specified in SAP.

Source Data: adam.adqs; Listing 16.2.8.5.1.

Table 14.3.6.3: Summary of Actual Value and Change from Baseline of EQ-5D-5L Index Score and EQ VAS
 Full Analysis Set

Health Scale (VAS)

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C15D1	166	79.6 (13.25)	80.0	70.0, 90.0	(40, 100)	76	76.8 (17.10)	80.0	67.5, 90.0	(35, 100)
CHBL	164	5.5 (16.29)	2.5	-5.0, 15.0	(-50, 50)	75	2.9 (20.57)	0.0	-10.0, 10.0	(-40, 100)
C17D1	157	80.3 (13.03)	80.0	70.0, 90.0	(20, 100)	65	77.4 (16.35)	80.0	70.0, 90.0	(40, 99)
CHBL	155	5.5 (16.05)	5.0	-5.0, 15.0	(-50, 55)	64	2.7 (22.74)	0.0	-7.5, 14.5	(-55, 85)
C19D1	145	79.0 (14.50)	80.0	70.0, 90.0	(40, 100)	51	80.1 (14.11)	80.0	70.0, 90.0	(40, 100)
CHBL	143	3.9 (16.27)	2.0	-5.0, 15.0	(-50, 50)	50	5.5 (22.39)	0.0	-5.0, 10.0	(-30, 100)
C21D1	113	78.7 (15.89)	80.0	70.0, 90.0	(5, 100)	41	79.8 (16.13)	80.0	70.0, 95.0	(40, 100)
CHBL	112	3.4 (18.05)	1.5	-5.0, 15.0	(-65, 50)	40	6.6 (24.15)	1.5	-6.5, 12.5	(-30, 100)
C23D1	100	78.3 (15.61)	80.0	70.0, 90.0	(5, 100)	32	78.7 (13.76)	80.0	70.0, 90.0	(50, 100)
CHBL	99	3.2 (16.90)	0.0	-10.0, 10.0	(-50, 50)	31	6.4 (23.12)	0.0	-5.0, 15.0	(-25, 80)
C25D1	74	77.1 (14.95)	80.0	70.0, 90.0	(40, 100)	28	80.6 (14.80)	82.5	72.5, 90.0	(50, 100)
CHBL	73	3.4 (13.14)	0.0	-5.0, 10.0	(-25, 40)	27	8.1 (28.64)	3.0	-5.0, 15.0	(-30, 100)
C27D1	48	76.9 (14.05)	78.5	70.0, 90.0	(50, 100)	21	80.4 (13.91)	80.0	75.0, 90.0	(45, 100)
CHBL	47	1.4 (12.83)	0.0	-6.0, 10.0	(-25, 40)	21	4.4 (16.50)	0.0	-5.0, 10.0	(-30, 40)

Notes: EQ-5D-5L is scored according to the UK Crosswalk Value Set.

A linear transformation is applied to health scale which is measured according to a 0-100mm Visual Analog Scale (VAS). A high VAS score represents worse overall self-rated health status.

Visit is based on window rule specified in SAP.

Source Data: adam.adqs; Listing 16.2.8.5.1.

Table 14.3.6.3: Summary of Actual Value and Change from Baseline of EQ-5D-5L Index Score and EQ VAS
 Full Analysis Set

Health Scale (VAS)

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
C29D1	40	75.3 (15.00)	75.0	62.5, 90.0	(50, 100)	14	75.6 (16.52)	77.5	65.0, 85.0	(50, 100)
CHBL	39	0.7 (14.48)	0.0	-6.0, 5.0	(-30, 40)	14	-4.4 (10.04)	-5.0	-10.0, 0.0	(-25, 20)
C31D1	27	78.8 (14.83)	80.0	70.0, 95.0	(50, 100)	7	78.6 (21.66)	82.0	60.0, 98.0	(40, 100)
CHBL	27	3.9 (12.13)	0.0	-5.0, 10.0	(-10, 40)	7	-9.3 (20.29)	-8.0	-30.0, 3.0	(-40, 20)
C33D1	20	78.8 (14.04)	80.0	70.0, 90.0	(50, 100)	5	77.0 (16.05)	85.0	65.0, 90.0	(55, 90)
CHBL	20	6.5 (13.04)	0.0	0.0, 17.5	(-10, 30)	5	-12.0 (13.04)	-10.0	-25.0, -5.0	(-25, 5)
C35D1	15	78.7 (15.75)	85.0	65.0, 90.0	(50, 100)	3	81.7 (20.21)	85.0	60.0, 100.0	(60, 100)
CHBL	15	4.7 (16.85)	0.0	-10.0, 10.0	(-10, 50)	3	-11.7 (16.07)	-5.0	-30.0, 0.0	(-30, 0)
C37D1	9	76.1 (17.81)	70.0	70.0, 95.0	(50, 100)	1	80.0 (NE)	80.0	80.0, 80.0	(80, 80)
CHBL	9	-2.2 (7.12)	0.0	-10.0, 0.0	(-10, 10)	1	0.0 (NE)	0.0	0.0, 0.0	(0, 0)
C39D1	3	66.7 (15.28)	70.0	50.0, 80.0	(50, 80)	0				
CHBL	3	-3.3 (5.77)	0.0	-10.0, 0.0	(-10, 0)	0				
C41D1	2	72.5 (3.54)	72.5	70.0, 75.0	(70, 75)	0				
CHBL	2	-5.0 (7.07)	-5.0	-10.0, 0.0	(-10, 0)	0				

Notes: EQ-5D-5L is scored according to the UK Crosswalk Value Set.

A linear transformation is applied to health scale which is measured according to a 0-100mm Visual Analog Scale (VAS). A high VAS score represents worse overall self-rated health status.

Visit is based on window rule specified in SAP.

Source Data: adam.adqs; Listing 16.2.8.5.1.

Table 14.3.6.3: Summary of Actual Value and Change from Baseline of EQ-5D-5L Index Score and EQ VAS
 Full Analysis Set

Health Scale (VAS)

Visit	T-DXd (N=261)					T-DM1 (N=263)				
	n	Mean (SD)	Median	Q1, Q3	Min, Max	n	Mean (SD)	Median	Q1, Q3	Min, Max
End of Treatment	99	74.6 (18.07)	80.0	65.0, 90.0	(20, 100)	175	74.8 (16.36)	75.0	65.0, 90.0	(5, 100)
CHBL	98	-1.1 (19.09)	0.0	-10.0, 10.0	(-65, 65)	173	-2.6 (15.63)	-2.0	-10.0, 5.0	(-60, 40)
40 Day Follow-Up	30	69.8 (22.72)	75.0	50.0, 85.0	(10, 100)	79	72.5 (19.21)	80.0	60.0, 90.0	(5, 100)
CHBL	30	-8.4 (23.85)	-7.5	-15.0, 0.0	(-75, 50)	78	-4.3 (16.51)	-4.0	-10.0, 5.0	(-60, 30)
3 Months Follow-Up	60	72.9 (18.98)	80.0	62.5, 90.0	(20, 99)	111	76.3 (16.98)	80.0	70.0, 90.0	(8, 100)
CHBL	59	-1.7 (24.75)	0.0	-10.0, 10.0	(-80, 70)	111	-2.2 (16.04)	0.0	-10.0, 10.0	(-62, 40)

Notes: EQ-5D-5L is scored according to the UK Crosswalk Value Set.
 A linear transformation is applied to health scale which is measured according to a 0-100mm Visual Analog Scale (VAS). A high VAS score represents worse overall self-rated health status.
 Visit is based on window rule specified in SAP.
 Source Data: adam.adqs; Listing 16.2.8.5.1.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Global Health Status	Subjects (%) with Events Deterioration	146 (55.9)	135 (51.3)	
	Median time to first deterioration (months) [a]: 95% CI	6.9 (4.4,10.4)	7.2 (5.7,10.3)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.9861 (0.7776,1.2504)
	Stratified log-rank p-value [c]			0.8854
	Deterioration rate [d] at 3 Months	61.1	67.5	
	95% CI	[54.7 , 66.8]	[61.2 , 73.0]	
	Deterioration rate [d] at 6 Months	51.5	56.3	
	95% CI	[45.1 , 57.5]	[49.7 , 62.4]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	47.4	44.6	
95% CI	[41.0 , 53.5]	[37.6 , 51.4]	
Deterioration rate [d] at 12 Months	42.2	37.5	
95% CI	[35.8 , 48.5]	[30.2 , 44.9]	
Deterioration rate [d] at 18 Months	38.1	31.2	
95% CI	[31.4 , 44.8]	[22.2 , 40.5]	
Deterioration rate [d] at 24 Months	31.1	20.1	
95% CI	[20.9 , 41.9]	[8.2 , 35.5]	
Deterioration rate [d] at 36 Months	31.1	20.1	
95% CI	[20.9 , 41.9]	[8.2 , 35.5]	
Deterioration rate [d] at 48 Months	31.1	20.1	
95% CI	[20.9 , 41.9]	[8.2 , 35.5]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Physical Functioning	Subjects (%) with Events Deterioration	109 (41.8)	104 (39.5)	
	Median time to first deterioration (months) [a]: 95% CI	NE (14.3,NE)	12.0 (8.3,NE)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.8725 (0.6644,1.1457)
	Stratified log-rank p-value [c]			0.3259
	Deterioration rate [d] at 3 Months	74.5	74.2	
	95% CI	[68.6 , 79.4]	[68.2 , 79.3]	
	Deterioration rate [d] at 6 Months	64.3	65.8	
	95% CI	[58.0 , 69.9]	[59.2 , 71.5]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	61.2	54.8	
95% CI	[54.8 , 67.0]	[47.5 , 61.5]	
Deterioration rate [d] at 12 Months	58.6	50.0	
95% CI	[52.0 , 64.5]	[42.1 , 57.3]	
Deterioration rate [d] at 18 Months	52.6	46.4	
95% CI	[45.5 , 59.3]	[36.4 , 55.8]	
Deterioration rate [d] at 24 Months	52.6	34.8	
95% CI	[45.5 , 59.3]	[15.4 , 55.1]	
Deterioration rate [d] at 36 Months	52.6	34.8	
95% CI	[45.5 , 59.3]	[15.4 , 55.1]	
Deterioration rate [d] at 48 Months	52.6	34.8	
95% CI	[45.5 , 59.3]	[15.4 , 55.1]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Role Functioning	Subjects (%) with Events Deterioration	130 (49.8)	138 (52.5)	
	Median time to first deterioration (months) [a]: 95% CI	11.6 (6.2,23.7)	6.3 (4.7,8.9)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.7532 (0.5904,0.9608)
	Stratified log-rank p-value [c]			0.0218
	Deterioration rate [d] at 3 Months	70.5	65.1	
	95% CI	[64.4 , 75.7]	[58.7 , 70.8]	
	Deterioration rate [d] at 6 Months	57.2	51.0	
	95% CI	[50.8 , 63.1]	[44.3 , 57.3]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	54.1	42.6	
95% CI	[47.6 , 60.1]	[35.7 , 49.4]	
Deterioration rate [d] at 12 Months	49.2	37.0	
95% CI	[42.6 , 55.5]	[29.6 , 44.3]	
Deterioration rate [d] at 18 Months	43.2	28.7	
95% CI	[36.0 , 50.3]	[19.7 , 38.3]	
Deterioration rate [d] at 24 Months	37.1	21.5	
95% CI	[24.5 , 49.6]	[9.5 , 36.7]	
Deterioration rate [d] at 36 Months	37.1	21.5	
95% CI	[24.5 , 49.6]	[9.5 , 36.7]	
Deterioration rate [d] at 48 Months	37.1	21.5	
95% CI	[24.5 , 49.6]	[9.5 , 36.7]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Emotional Functioning	Subjects (%) with Events Deterioration	117 (44.8)	107 (40.7)	
	Median time to first deterioration (months) [a]: 95% CI	16.7 (12.9,19.4)	11.1 (8.4,15.2)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.7993 (0.6110,1.0457)
	Stratified log-rank p-value [c]			0.1006
	Deterioration rate [d] at 3 Months	78.4	75.4	
	95% CI	[72.7 , 83.0]	[69.5 , 80.4]	
	Deterioration rate [d] at 6 Months	70.6	64.9	
	95% CI	[64.6 , 75.9]	[58.3 , 70.8]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	64.1	53.1	
95% CI	[57.8 , 69.8]	[45.6 , 60.0]	
Deterioration rate [d] at 12 Months	58.7	49.5	
95% CI	[52.1 , 64.7]	[41.7 , 56.8]	
Deterioration rate [d] at 18 Months	46.6	40.1	
95% CI	[38.6 , 54.3]	[30.3 , 49.6]	
Deterioration rate [d] at 24 Months	38.2	40.1	
95% CI	[28.3 , 48.0]	[30.3 , 49.6]	
Deterioration rate [d] at 36 Months	38.2	40.1	
95% CI	[28.3 , 48.0]	[30.3 , 49.6]	
Deterioration rate [d] at 48 Months	38.2	40.1	
95% CI	[28.3 , 48.0]	[30.3 , 49.6]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Cognitive Functioning	Subjects (%) with Events Deterioration	138 (52.9)	135 (51.3)	
	Median time to first deterioration (months) [a]: 95% CI	10.3 (8.6,14.5)	8.3 (4.8,10.3)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.7777 (0.6103,0.9912)
	Stratified log-rank p-value [c]			0.0410
	Deterioration rate [d] at 3 Months	74.3	64.9	
	95% CI	[68.3 , 79.2]	[58.5 , 70.5]	
	Deterioration rate [d] at 6 Months	62.7	52.4	
	95% CI	[56.4 , 68.4]	[45.7 , 58.6]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	53.3	45.5	
95% CI	[46.7 , 59.4]	[38.5 , 52.2]	
Deterioration rate [d] at 12 Months	47.3	38.9	
95% CI	[40.7 , 53.6]	[31.4 , 46.3]	
Deterioration rate [d] at 18 Months	39.2	30.5	
95% CI	[32.2 , 46.1]	[21.4 , 40.1]	
Deterioration rate [d] at 24 Months	34.1	21.8	
95% CI	[25.4 , 43.1]	[11.0 , 34.9]	
Deterioration rate [d] at 36 Months	34.1	21.8	
95% CI	[25.4 , 43.1]	[11.0 , 34.9]	
Deterioration rate [d] at 48 Months	34.1	21.8	
95% CI	[25.4 , 43.1]	[11.0 , 34.9]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Social Functioning	Subjects (%) with Events Deterioration	147 (56.3)	126 (47.9)	
	Median time to first deterioration (months) [a]: 95% CI	7.3 (5.6,11.8)	8.4 (5.8,11.7)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			1.0375 (0.8160,1.3189)
	Stratified log-rank p-value [c]			0.7737
	Deterioration rate [d] at 3 Months	66.6	69.7	
	95% CI	[60.4 , 72.1]	[63.5 , 75.1]	
	Deterioration rate [d] at 6 Months	54.3	54.7	
	95% CI	[47.8 , 60.2]	[48.0 , 60.9]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	47.2	47.1	
95% CI	[40.7 , 53.3]	[40.0 , 53.8]	
Deterioration rate [d] at 12 Months	42.9	40.9	
95% CI	[36.4 , 49.2]	[33.3 , 48.4]	
Deterioration rate [d] at 18 Months	35.5	36.5	
95% CI	[28.1 , 42.9]	[27.7 , 45.4]	
Deterioration rate [d] at 24 Months	31.2	30.4	
95% CI	[23.0 , 39.9]	[18.0 , 43.7]	
Deterioration rate [d] at 36 Months	31.2	30.4	
95% CI	[23.0 , 39.9]	[18.0 , 43.7]	
Deterioration rate [d] at 48 Months	31.2	30.4	
95% CI	[23.0 , 39.9]	[18.0 , 43.7]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Symptom Scales/Fatigue	Subjects (%) with Events Deterioration	150 (57.5)	153 (58.2)	
	Median time to first deterioration (months) [a]: 95% CI	5.6 (3.0,9.9)	3.6 (2.8,5.5)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.8394 (0.6688,1.0534)
	Stratified log-rank p-value [c]			0.1259
	Deterioration rate [d] at 3 Months	56.1	52.9	
	95% CI	[49.7 , 62.0]	[46.4 , 58.9]	
	Deterioration rate [d] at 6 Months	48.3	40.9	
	95% CI	[42.0 , 54.3]	[34.6 , 47.2]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	44.3	36.7	
95% CI	[38.0 , 50.4]	[30.3 , 43.1]	
Deterioration rate [d] at 12 Months	41.6	34.0	
95% CI	[35.3 , 47.8]	[27.5 , 40.7]	
Deterioration rate [d] at 18 Months	35.9	31.8	
95% CI	[29.0 , 42.9]	[24.4 , 39.4]	
Deterioration rate [d] at 24 Months	33.2	27.2	
95% CI	[25.0 , 41.5]	[17.4 , 38.0]	
Deterioration rate [d] at 36 Months	33.2	27.2	
95% CI	[25.0 , 41.5]	[17.4 , 38.0]	
Deterioration rate [d] at 48 Months	33.2	27.2	
95% CI	[25.0 , 41.5]	[17.4 , 38.0]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Symptom Scales/Nausea and Vomiting	Subjects (%) with Events Deterioration	191 (73.2)	116 (44.1)	
	Median time to first deterioration (months) [a]: 95% CI	2.8 (1.6,3.0)	9.7 (8.3,13.9)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			1.9759 (1.5649,2.4948)
	Stratified log-rank p-value [c]			<.0001
	Deterioration rate [d] at 3 Months	45.4	72.8	
	95% CI	[39.1 , 51.4]	[66.7 , 77.9]	
	Deterioration rate [d] at 6 Months	34.1	63.3	
	95% CI	[28.3 , 40.0]	[56.8 , 69.2]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	28.4	51.6	
95% CI	[22.9 , 34.1]	[44.4 , 58.3]	
Deterioration rate [d] at 12 Months	27.8	43.1	
95% CI	[22.3 , 33.6]	[35.4 , 50.6]	
Deterioration rate [d] at 18 Months	21.2	41.4	
95% CI	[15.5 , 27.6]	[33.3 , 49.3]	
Deterioration rate [d] at 24 Months	12.1	41.4	
95% CI	[5.5 , 21.6]	[33.3 , 49.3]	
Deterioration rate [d] at 36 Months	12.1	41.4	
95% CI	[5.5 , 21.6]	[33.3 , 49.3]	
Deterioration rate [d] at 48 Months	12.1	41.4	
95% CI	[5.5 , 21.6]	[33.3 , 49.3]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Symptom Scales/Pain	Subjects (%) with Events Deterioration	142 (54.4)	137 (52.1)	
	Median time to first deterioration (months) [a]: 95% CI	8.5 (5.6,14.5)	6.9 (5.3,9.8)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.8691 (0.6855,1.1020)
	Stratified log-rank p-value [c]			0.2381
	Deterioration rate [d] at 3 Months	68.1	66.1	
	95% CI	[61.9 , 73.5]	[59.7 , 71.7]	
	Deterioration rate [d] at 6 Months	53.6	52.7	
	95% CI	[47.2 , 59.6]	[46.0 , 58.9]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	48.6	43.9	
95% CI	[42.2 , 54.8]	[36.9 , 50.6]	
Deterioration rate [d] at 12 Months	44.6	37.4	
95% CI	[38.1 , 50.8]	[30.1 , 44.8]	
Deterioration rate [d] at 18 Months	37.3	29.7	
95% CI	[29.9 , 44.6]	[21.6 , 38.3]	
Deterioration rate [d] at 24 Months	31.9	29.7	
95% CI	[20.8 , 43.6]	[21.6 , 38.3]	
Deterioration rate [d] at 36 Months	31.9	29.7	
95% CI	[20.8 , 43.6]	[21.6 , 38.3]	
Deterioration rate [d] at 48 Months	31.9	29.7	
95% CI	[20.8 , 43.6]	[21.6 , 38.3]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Common Symptoms/Dyspnoea Subjects (%) with Events Deterioration	101 (38.7)	98 (37.3)	
Median time to first deterioration (months) [a]: 95% CI	NE (15.8,NE)	15.2 (11.7,NE)	
Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.8352 (0.6294,1.1082)
Stratified log-rank p-value [c]			0.2100
Deterioration rate [d] at 3 Months	79.2	79.5	
95% CI	[73.7 , 83.8]	[73.8 , 84.1]	
Deterioration rate [d] at 6 Months	70.7	66.8	
95% CI	[64.6 , 76.0]	[60.3 , 72.5]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	67.1	59.1	
95% CI	[60.9 , 72.6]	[52.1 , 65.5]	
Deterioration rate [d] at 12 Months	62.4	57.2	
95% CI	[55.8 , 68.3]	[49.9 , 63.8]	
Deterioration rate [d] at 18 Months	54.9	46.8	
95% CI	[47.4 , 61.9]	[36.4 , 56.5]	
Deterioration rate [d] at 24 Months	51.3	40.9	
95% CI	[42.6 , 59.3]	[27.1 , 54.3]	
Deterioration rate [d] at 36 Months	51.3	40.9	
95% CI	[42.6 , 59.3]	[27.1 , 54.3]	
Deterioration rate [d] at 48 Months	51.3	40.9	
95% CI	[42.6 , 59.3]	[27.1 , 54.3]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Common Symptoms/Insomnia			
Subjects (%) with Events Deterioration	115 (44.1)	112 (42.6)	
Median time to first deterioration (months) [a]: 95% CI	19.4 (10.7,NE)	12.7 (7.2,NE)	
Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.8567 (0.6584,1.1147)
Stratified log-rank p-value [c]			0.2434
Deterioration rate [d] at 3 Months	74.1	70.5	
95% CI	[68.2 , 79.0]	[64.3 , 75.8]	
Deterioration rate [d] at 6 Months	65.1	58.3	
95% CI	[58.9 , 70.7]	[51.7 , 64.3]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	59.4	53.3	
95% CI	[52.9 , 65.3]	[46.4 , 59.7]	
Deterioration rate [d] at 12 Months	55.8	50.1	
95% CI	[49.3 , 61.9]	[42.9 , 56.9]	
Deterioration rate [d] at 18 Months	51.3	46.9	
95% CI	[44.2 , 57.9]	[38.9 , 54.6]	
Deterioration rate [d] at 24 Months	45.2	46.9	
95% CI	[34.8 , 55.0]	[38.9 , 54.6]	
Deterioration rate [d] at 36 Months	45.2	46.9	
95% CI	[34.8 , 55.0]	[38.9 , 54.6]	
Deterioration rate [d] at 48 Months	45.2	46.9	
95% CI	[34.8 , 55.0]	[38.9 , 54.6]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Common Symptoms/Appetite Loss	Subjects (%) with Events Deterioration	160 (61.3)	115 (43.7)	
	Median time to first deterioration (months) [a]: 95% CI	4.2 (2.9,5.6)	10.3 (6.6,20.5)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			1.4397 (1.1302,1.8339)
	Stratified log-rank p-value [c]			0.0034
	Deterioration rate [d] at 3 Months	54.5	69.7	
	95% CI	[48.1 , 60.4]	[63.4 , 75.1]	
	Deterioration rate [d] at 6 Months	41.8	58.8	
	95% CI	[35.7 , 47.9]	[52.1 , 64.9]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	40.5	52.1	
95% CI	[34.3 , 46.5]	[45.0 , 58.6]	
Deterioration rate [d] at 12 Months	37.8	47.3	
95% CI	[31.6 , 43.9]	[39.8 , 54.5]	
Deterioration rate [d] at 18 Months	31.9	45.2	
95% CI	[25.4 , 38.6]	[36.9 , 53.1]	
Deterioration rate [d] at 24 Months	31.9	33.9	
95% CI	[25.4 , 38.6]	[19.7 , 48.6]	
Deterioration rate [d] at 36 Months	31.9	33.9	
95% CI	[25.4 , 38.6]	[19.7 , 48.6]	
Deterioration rate [d] at 48 Months	31.9	33.9	
95% CI	[25.4 , 38.6]	[19.7 , 48.6]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Common Symptoms/Constipation	Subjects (%) with Events Deterioration	154 (59.0)	122 (46.4)	
	Median time to first deterioration (months) [a]: 95% CI	5.6 (4.2,8.3)	8.5 (5.7,12.6)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			1.2398 (0.9747,1.5770)
	Stratified log-rank p-value [c]			0.0826
	Deterioration rate [d] at 3 Months	64.5	72.8	
	95% CI	[58.2 , 70.1]	[66.7 , 78.0]	
	Deterioration rate [d] at 6 Months	47.1	56.2	
	95% CI	[40.7 , 53.2]	[49.5 , 62.4]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	41.0	48.6	
95% CI	[34.7 , 47.2]	[41.6 , 55.4]	
Deterioration rate [d] at 12 Months	39.3	43.9	
95% CI	[33.0 , 45.5]	[36.4 , 51.1]	
Deterioration rate [d] at 18 Months	33.7	38.3	
95% CI	[26.9 , 40.6]	[29.5 , 47.1]	
Deterioration rate [d] at 24 Months	25.3	32.0	
95% CI	[11.9 , 41.1]	[19.1 , 45.6]	
Deterioration rate [d] at 36 Months	25.3	32.0	
95% CI	[11.9 , 41.1]	[19.1 , 45.6]	
Deterioration rate [d] at 48 Months	25.3	32.0	
95% CI	[11.9 , 41.1]	[19.1 , 45.6]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Common Symptoms/Diarrhea	Subjects (%) with Events Deterioration	106 (40.6)	62 (23.6)	
	Median time to first deterioration (months) [a]: 95% CI	NE (17.1,NE)	NE (17.8,NE)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			1.7317 (1.2619,2.3763)
	Stratified log-rank p-value [c]			0.0006
	Deterioration rate [d] at 3 Months	70.1	87.5	
	95% CI	[64.0 , 75.3]	[82.6 , 91.1]	
	Deterioration rate [d] at 6 Months	62.2	82.7	
	95% CI	[55.8 , 67.9]	[77.1 , 87.0]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	59.9	73.3	
95% CI	[53.5 , 65.8]	[66.4 , 79.0]	
Deterioration rate [d] at 12 Months	58.4	68.3	
95% CI	[51.9 , 64.4]	[60.4 , 74.9]	
Deterioration rate [d] at 18 Months	56.2	61.7	
95% CI	[49.2 , 62.7]	[49.4 , 71.9]	
Deterioration rate [d] at 24 Months	51.2	61.7	
95% CI	[41.5 , 60.0]	[49.4 , 71.9]	
Deterioration rate [d] at 36 Months	51.2	61.7	
95% CI	[41.5 , 60.0]	[49.4 , 71.9]	
Deterioration rate [d] at 48 Months	51.2	61.7	
95% CI	[41.5 , 60.0]	[49.4 , 71.9]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Common Symptoms/Financial Difficulties	Subjects (%) with Events Deterioration	87 (33.3)	84 (31.9)	
	Median time to first deterioration (months) [a]: 95% CI	NE (19.7,NE)	NE (12.7,NE)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.7964 (0.5865,1.0813)
	Stratified log-rank p-value [c]			0.1413
	Deterioration rate [d] at 3 Months	86.0	82.1	
	95% CI	[81.0 , 89.7]	[76.7 , 86.4]	
	Deterioration rate [d] at 6 Months	75.8	74.6	
	95% CI	[70.0 , 80.7]	[68.5 , 79.8]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 09 - Analysis of time to first deterioration of EORTC QLQ-C30 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	70.5	66.7	
95% CI	[64.4 , 75.8]	[59.8 , 72.8]	
Deterioration rate [d] at 12 Months	67.9	59.4	
95% CI	[61.5 , 73.4]	[51.5 , 66.5]	
Deterioration rate [d] at 18 Months	62.6	52.0	
95% CI	[55.6 , 68.9]	[41.9 , 61.0]	
Deterioration rate [d] at 24 Months	50.5	52.0	
95% CI	[34.4 , 64.6]	[41.9 , 61.0]	
Deterioration rate [d] at 36 Months	50.5	52.0	
95% CI	[34.4 , 64.6]	[41.9 , 61.0]	
Deterioration rate [d] at 48 Months	50.5	52.0	
95% CI	[34.4 , 64.6]	[41.9 , 61.0]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

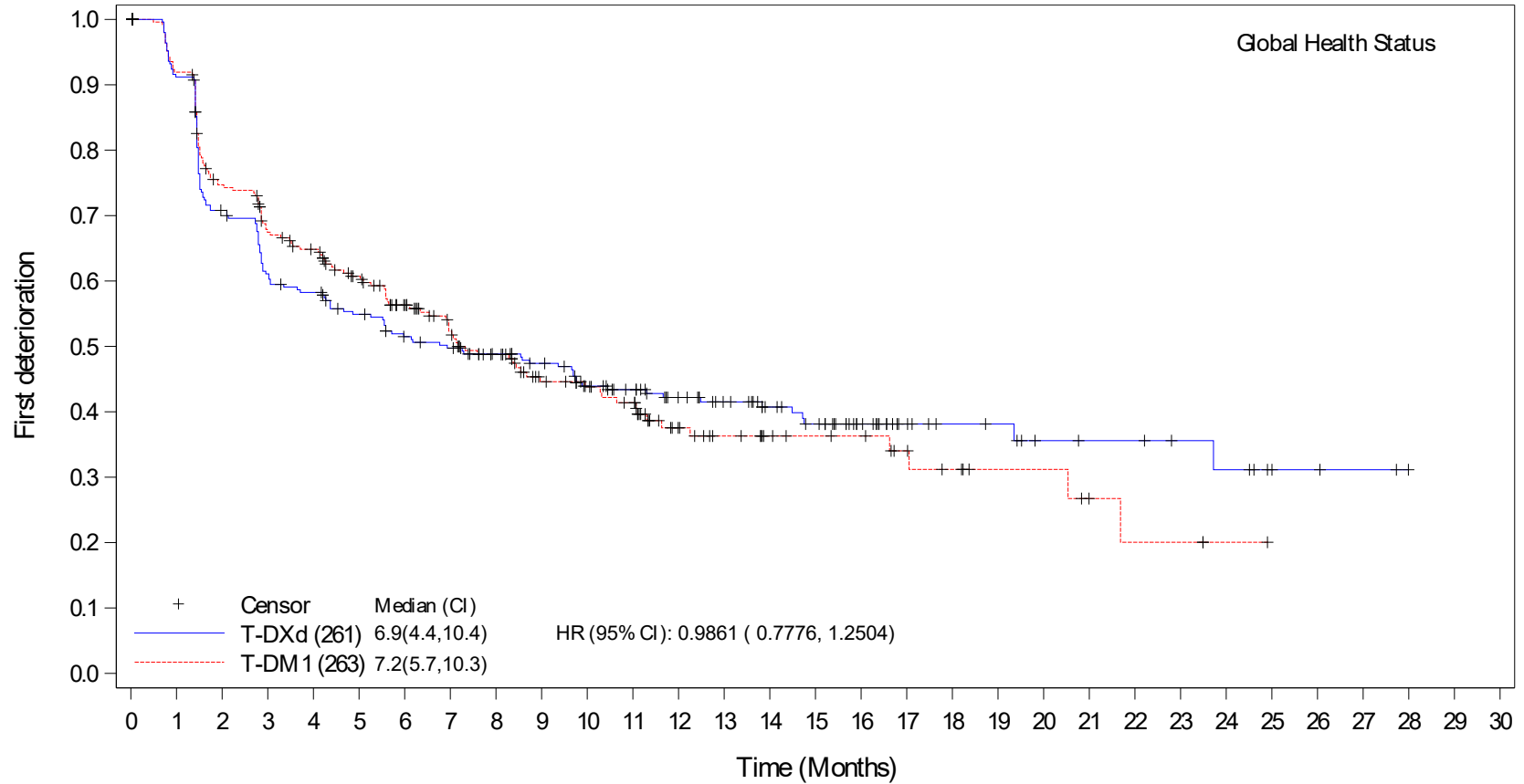
[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

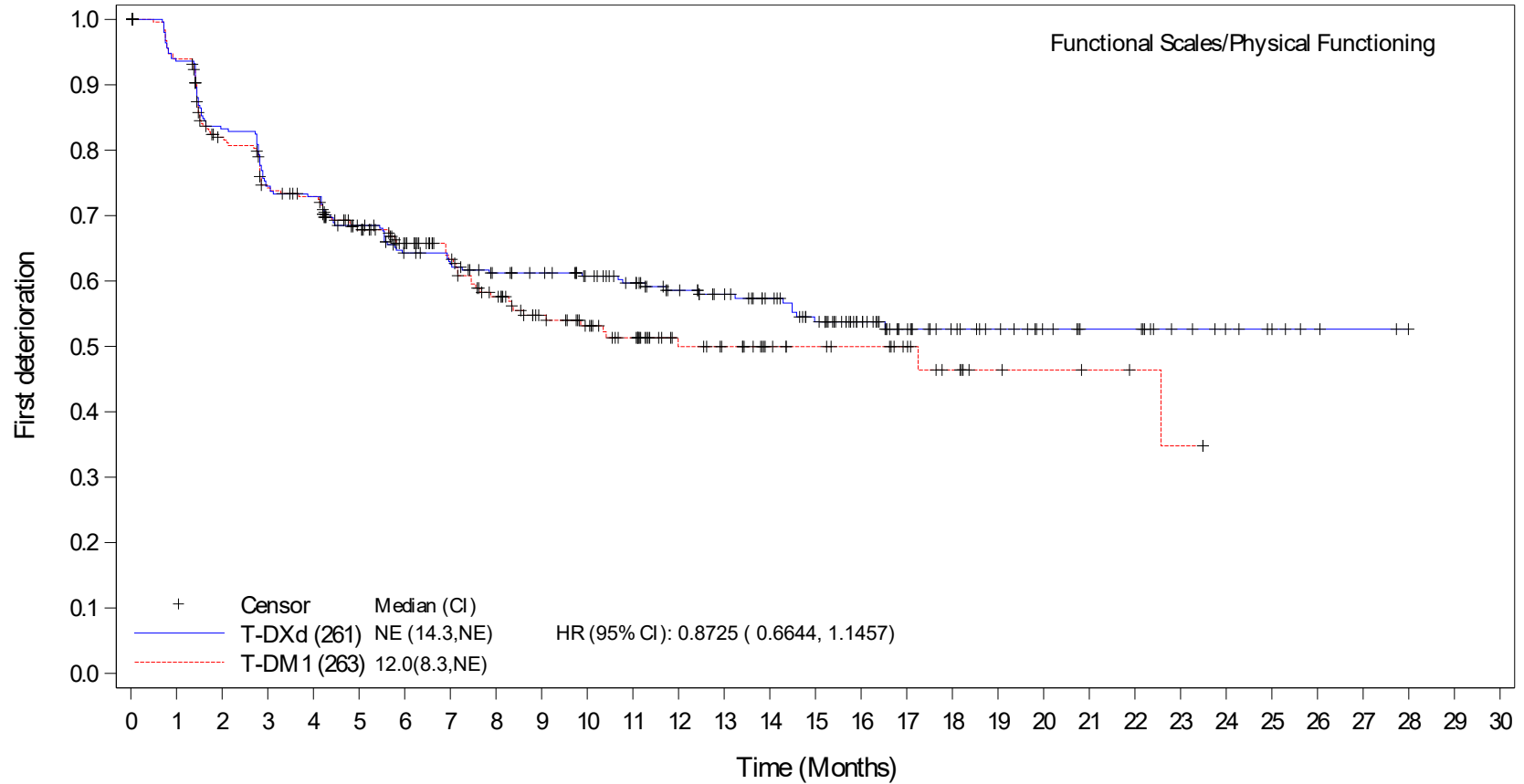
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd (261)	261	228	176	151	143	130	118	113	105	98	84	77	66	58	49	43	30	20	16	15	11	10	10	8	7	4	3	2	0
T-DM1 (263)	263	228	179	156	146	127	107	90	77	60	56	50	31	25	20	18	17	13	10	7	7	4	3	3	1	0			

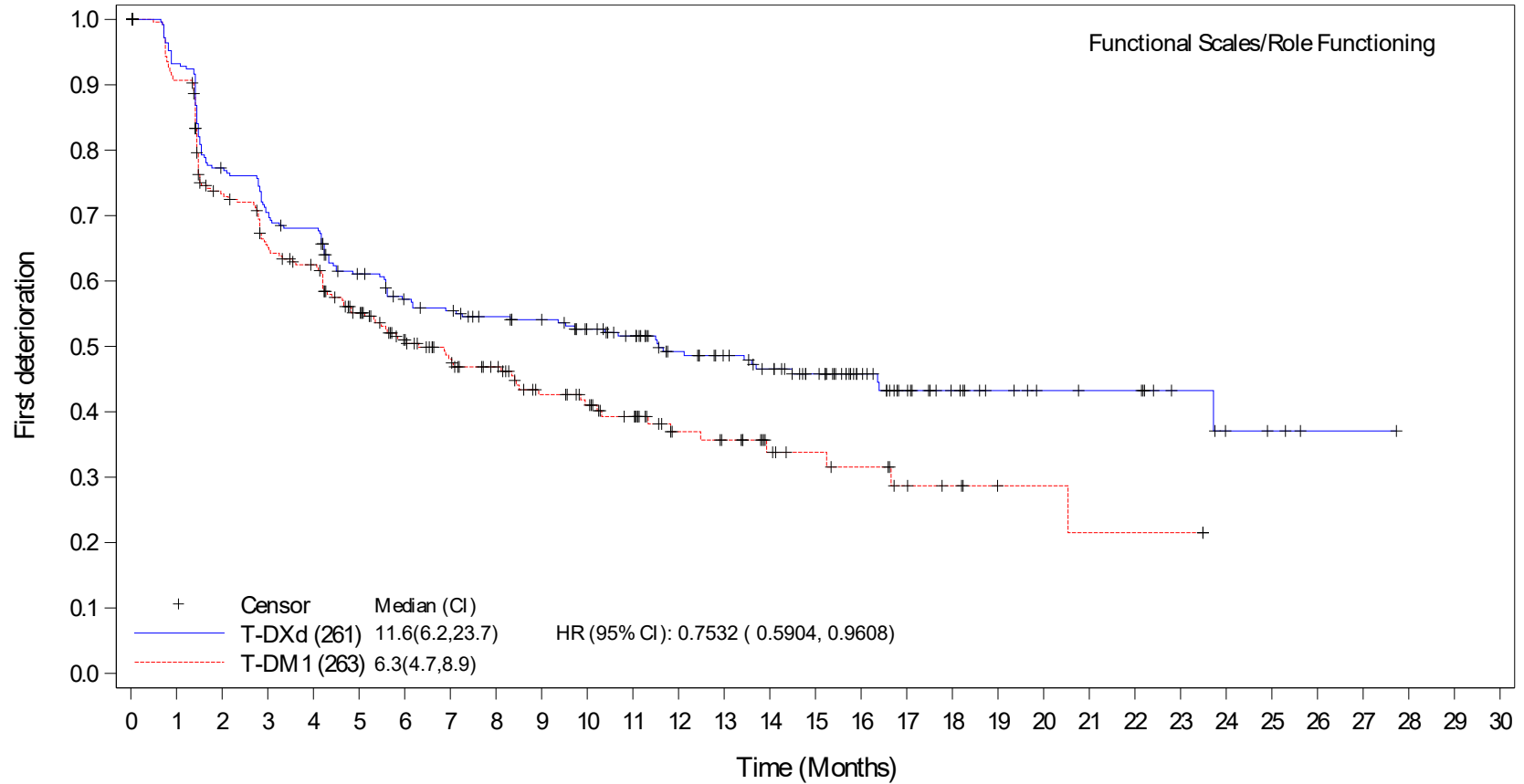
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	235	209	187	183	166	150	144	135	131	122	113	101	93	84	72	55	40	32	27	21	17	17	11	8	6	3	2	0
T-DM1 (263)	263	233	192	170	163	139	122	103	87	71	62	53	37	33	25	22	20	16	11	7	6	5	4	3	0				

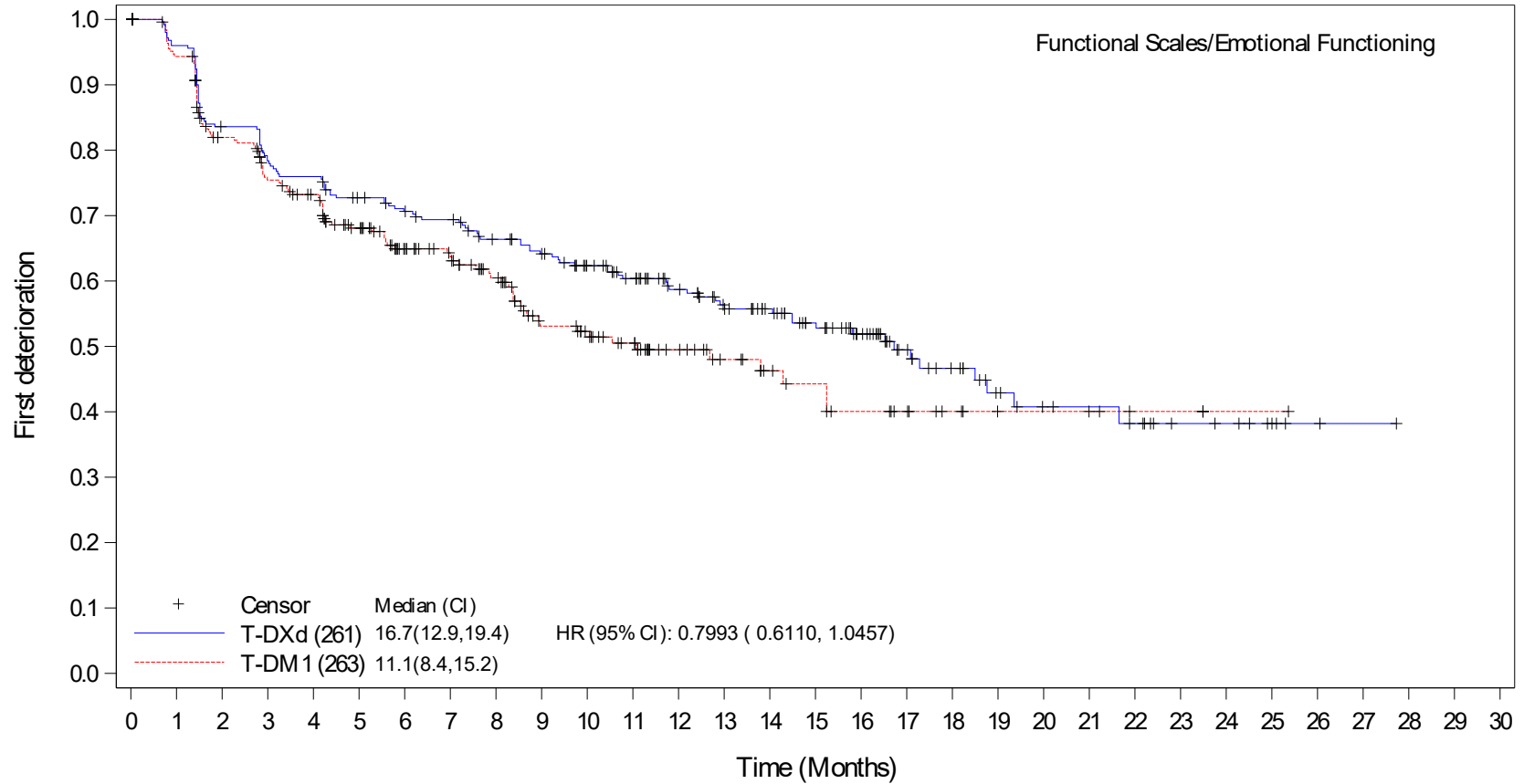
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	234	193	176	169	144	130	125	118	114	104	96	80	73	66	56	39	28	21	16	13	12	12	7	4	3	1	1	0
T-DM1 (263)	263	224	172	149	139	114	94	80	71	57	51	43	29	26	18	15	13	9	7	4	4	3	3	3	0				

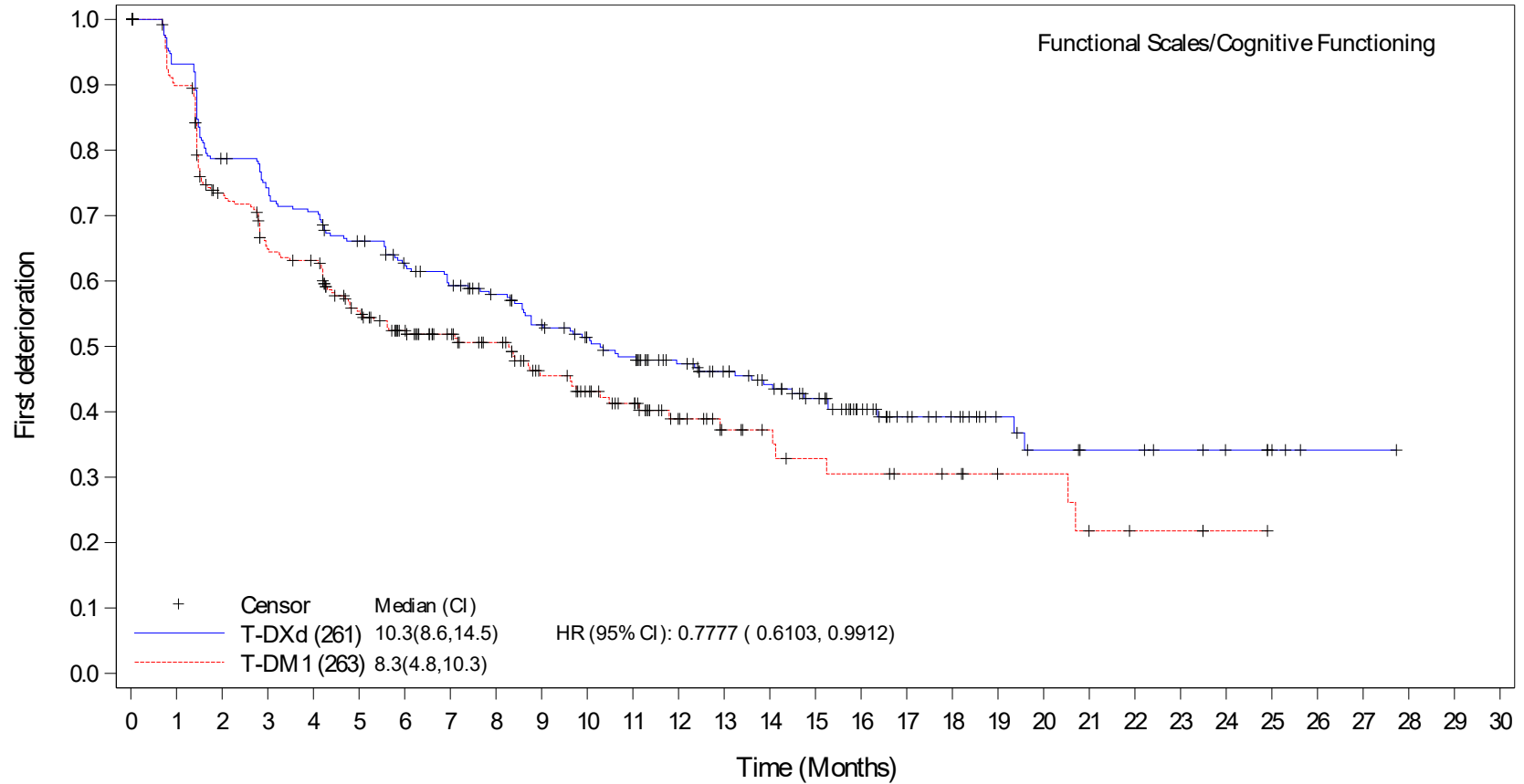
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	240	208	195	189	177	169	164	152	144	131	120	105	92	81	69	53	37	29	21	17	16	14	9	8	5	2	1	0
T-DM1 (263)	263	233	192	171	160	137	115	104	90	67	61	52	38	30	24	21	17	14	10	7	7	6	4	4	1	1	0		

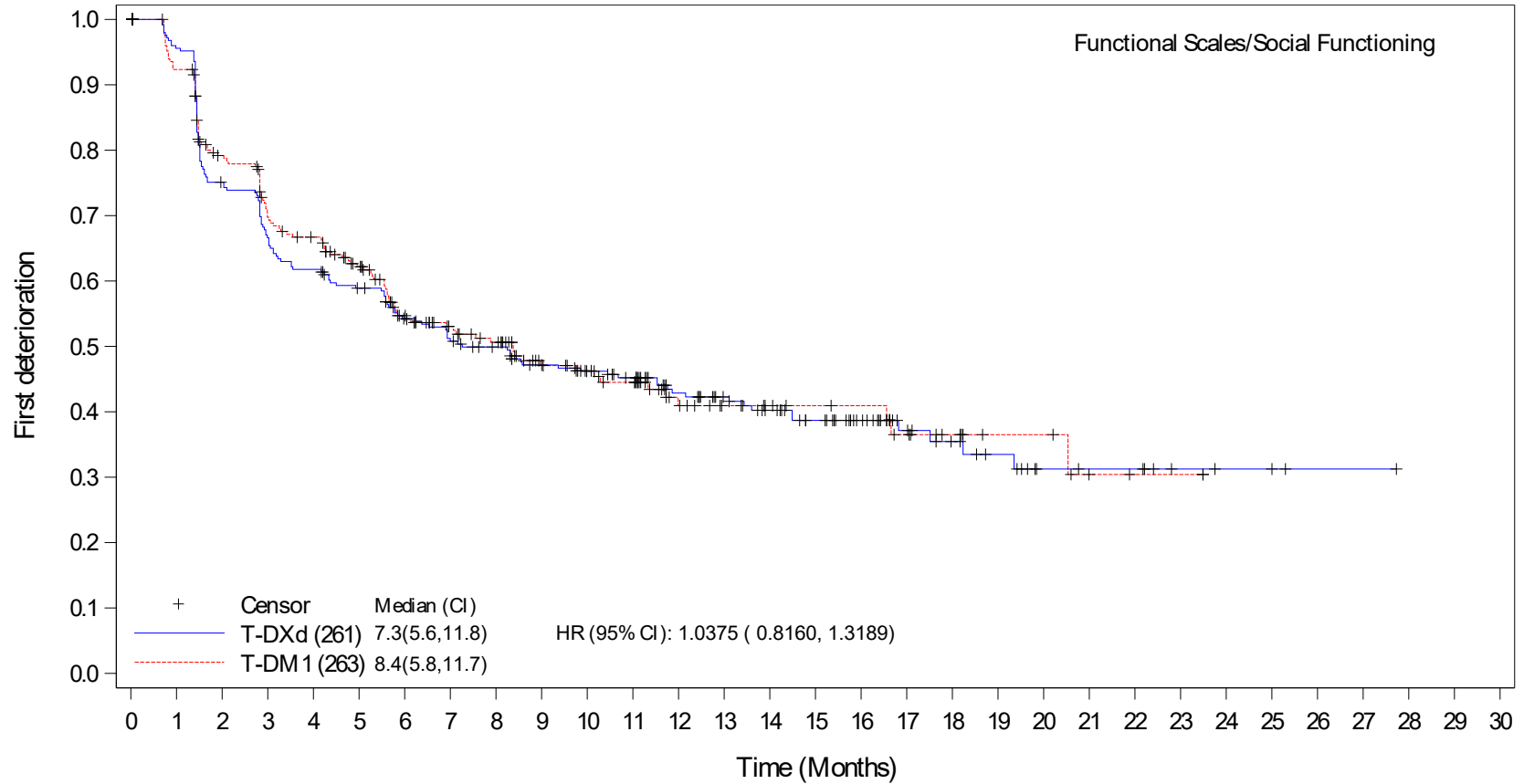
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	232	195	183	174	159	147	137	127	114	104	97	83	73	65	55	39	28	23	16	12	10	10	8	6	4	1	1	0
T-DM1 (263)	263	222	173	149	143	116	98	84	75	58	50	42	28	20	17	14	13	11	10	7	7	4	3	3	1	0			

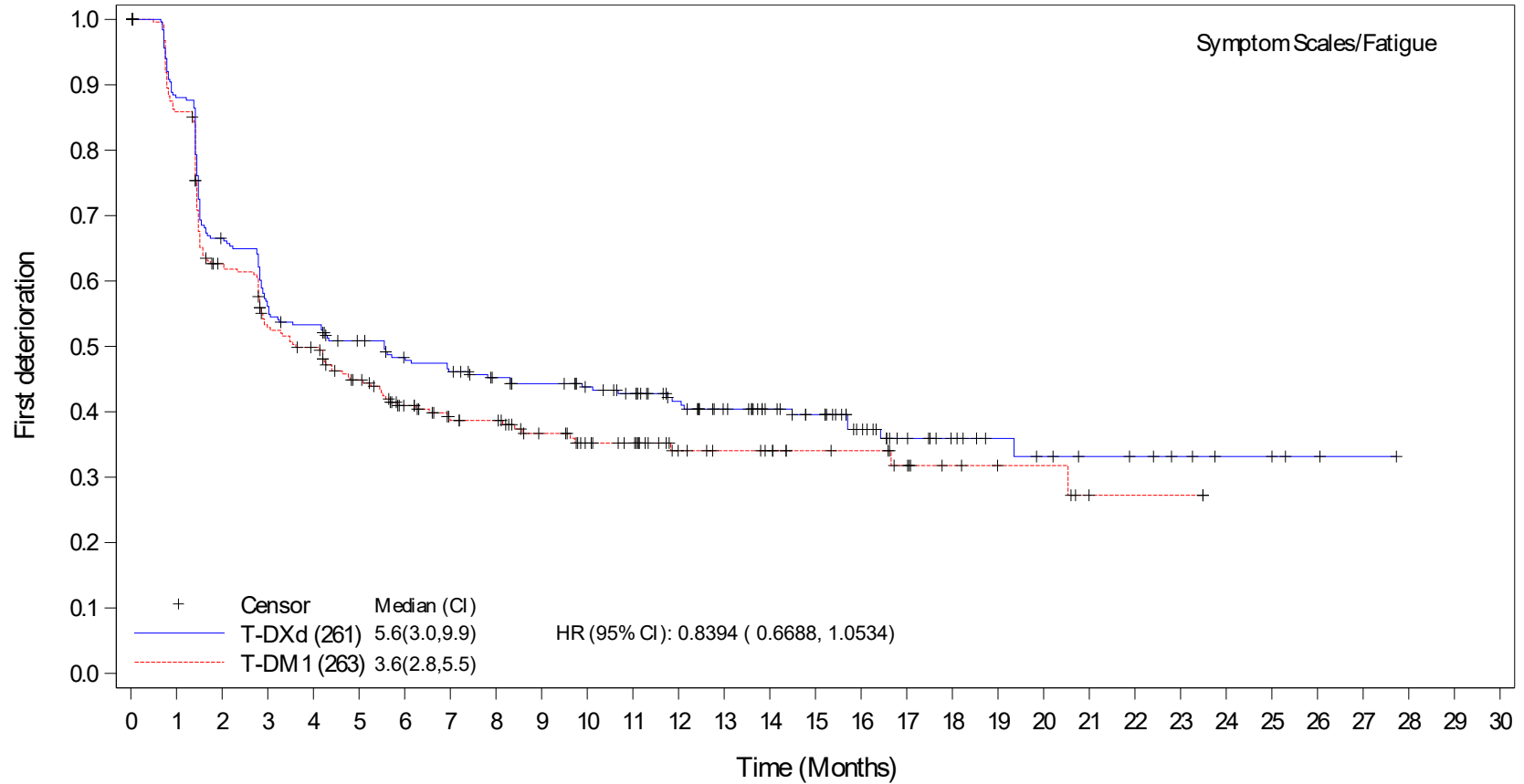
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	238	186	165	153	142	126	117	110	100	95	88	72	63	56	47	37	24	19	15	9	8	8	4	3	3	1	1	0
T-DM1 (263)	263	229	187	161	151	132	105	89	81	62	54	49	32	26	22	20	19	15	11	7	7	3	2	2	0				

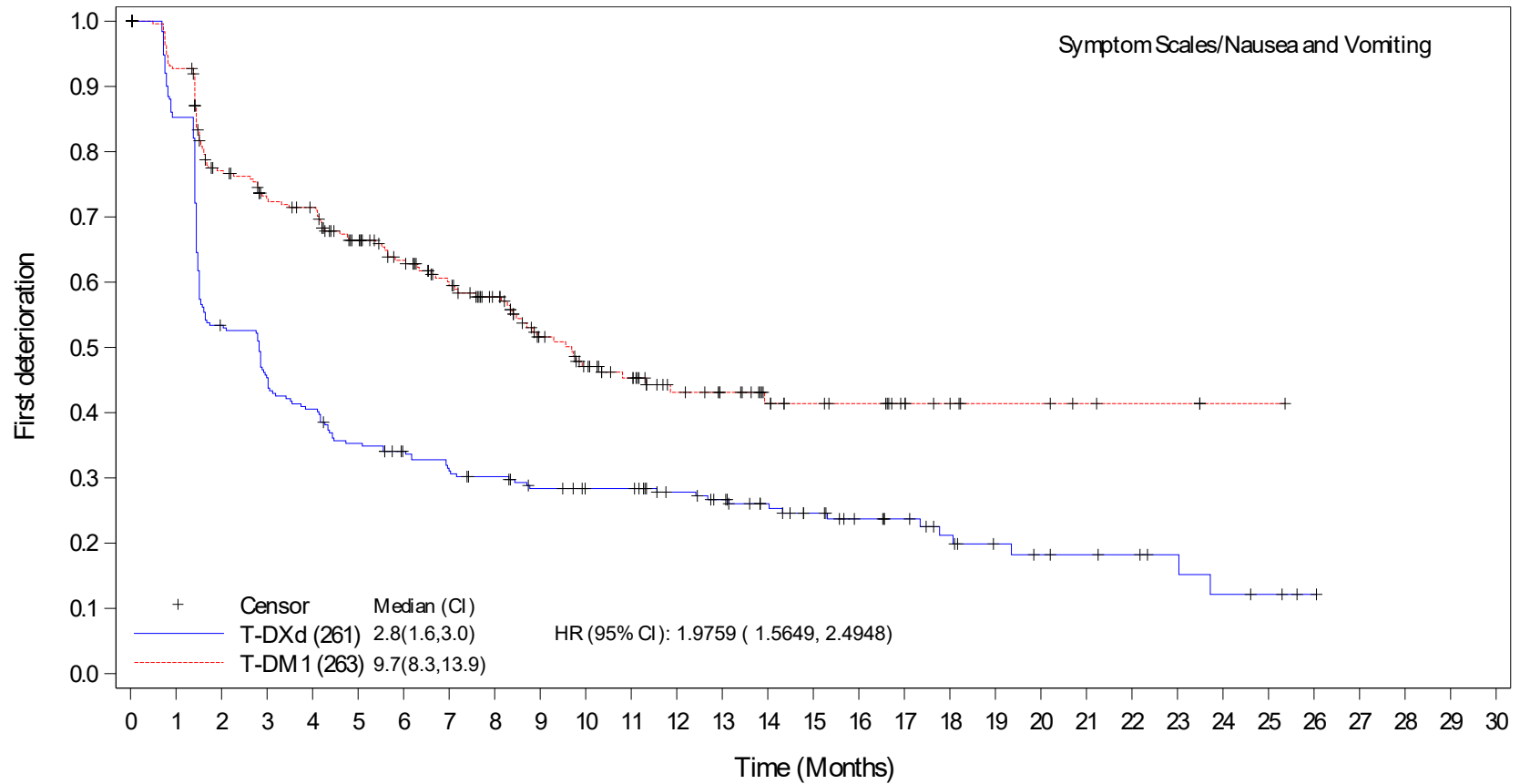
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	221	166	140	132	121	111	106	98	93	87	81	70	59	50	44	31	22	17	13	11	9	8	6	4	4	2	1	0
T-DM1 (263)	263	213	149	122	113	95	77	65	63	52	44	40	27	24	22	18	17	13	9	7	7	3	3	3	0				

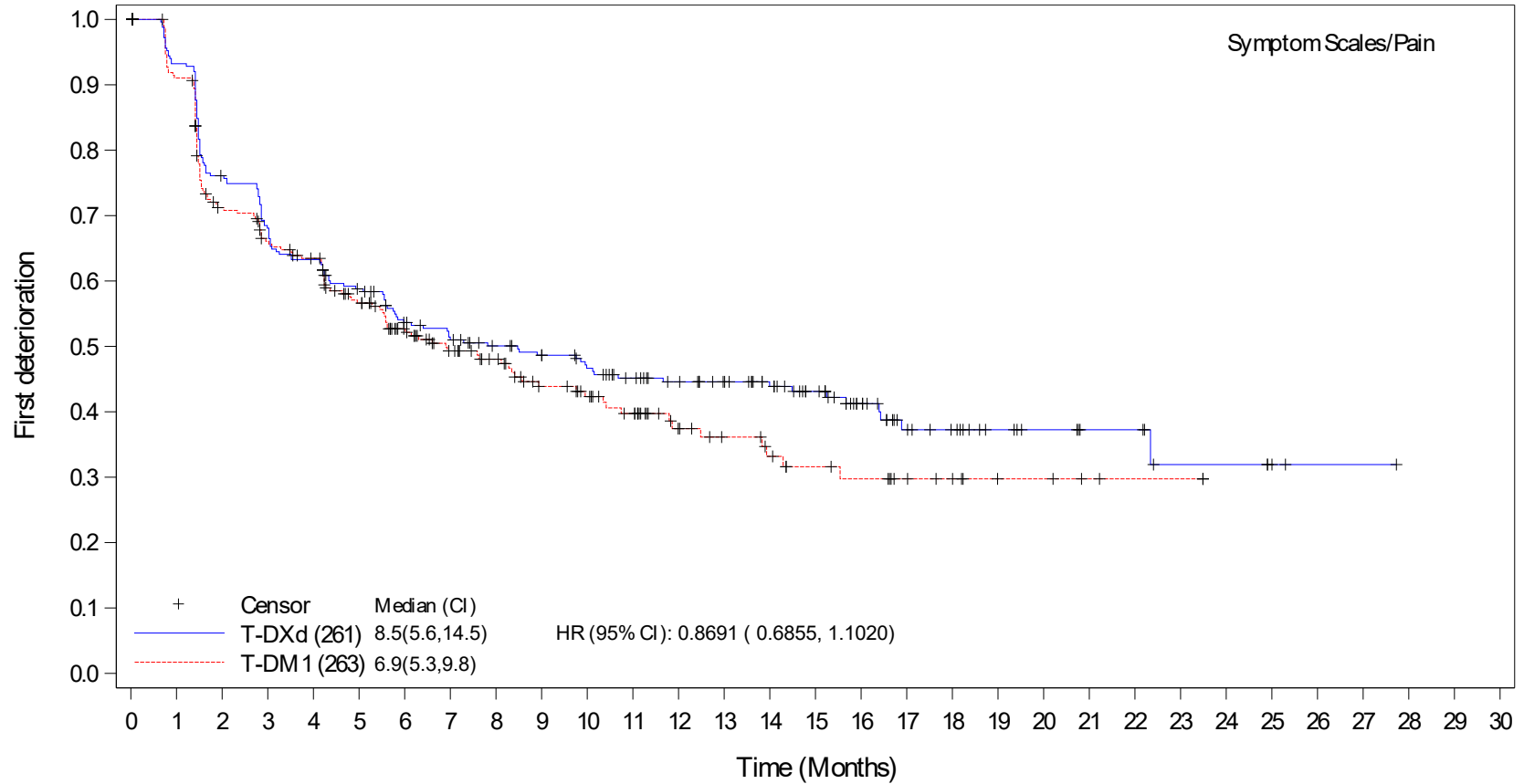
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	214	133	113	101	87	79	72	68	61	57	57	49	44	36	30	24	21	16	12	10	9	8	6	4	3	1	0
T-DM1 (263)	263	230	182	165	159	137	122	105	91	70	59	50	37	32	24	20	18	13	10	7	7	5	4	4	1	1	0	

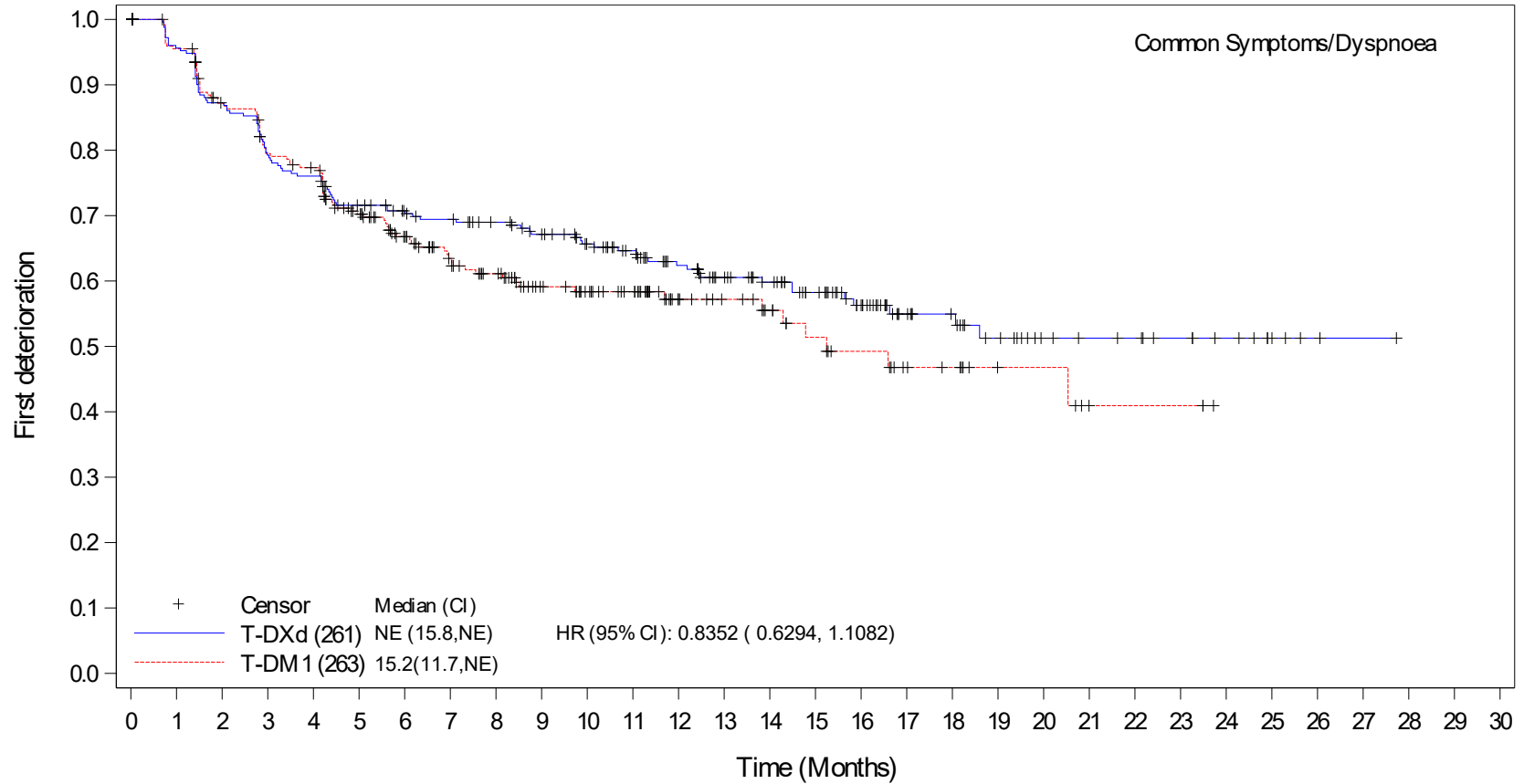
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	234	190	170	158	141	123	115	107	102	94	85	78	71	62	52	37	25	21	15	12	9	9	5	5	3	1	1	0
T-DM1 (263)	263	224	168	152	142	120	99	83	73	59	53	45	31	26	22	18	16	12	10	6	6	4	3	3	0				

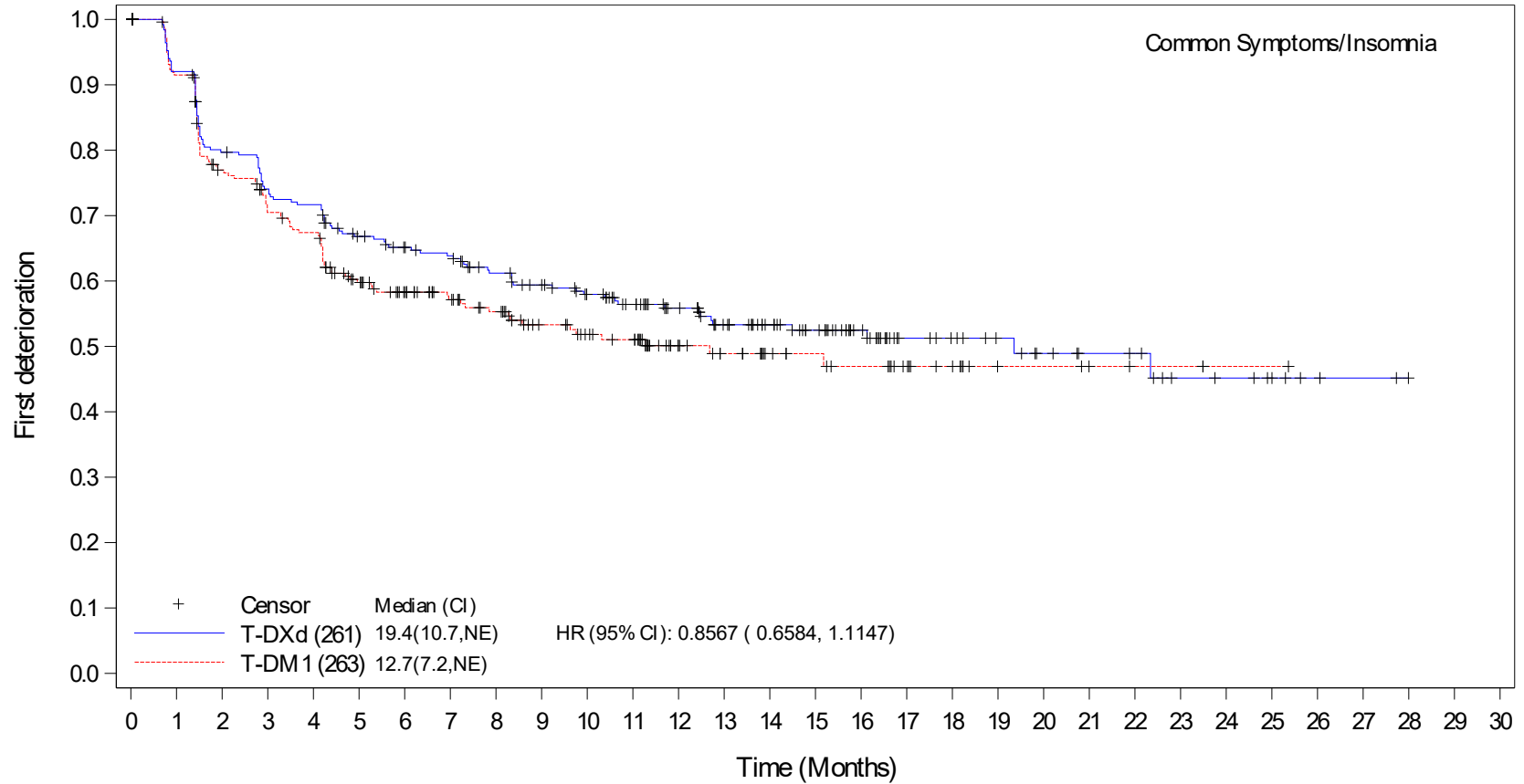
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	240	218	198	190	173	164	159	152	143	131	121	105	91	82	70	55	37	32	25	18	16	15	12	9	5	2	1	0
T-DM1 (263)	263	234	206	184	177	151	129	110	99	80	71	63	41	36	30	24	20	15	13	8	8	4	4	4	0				

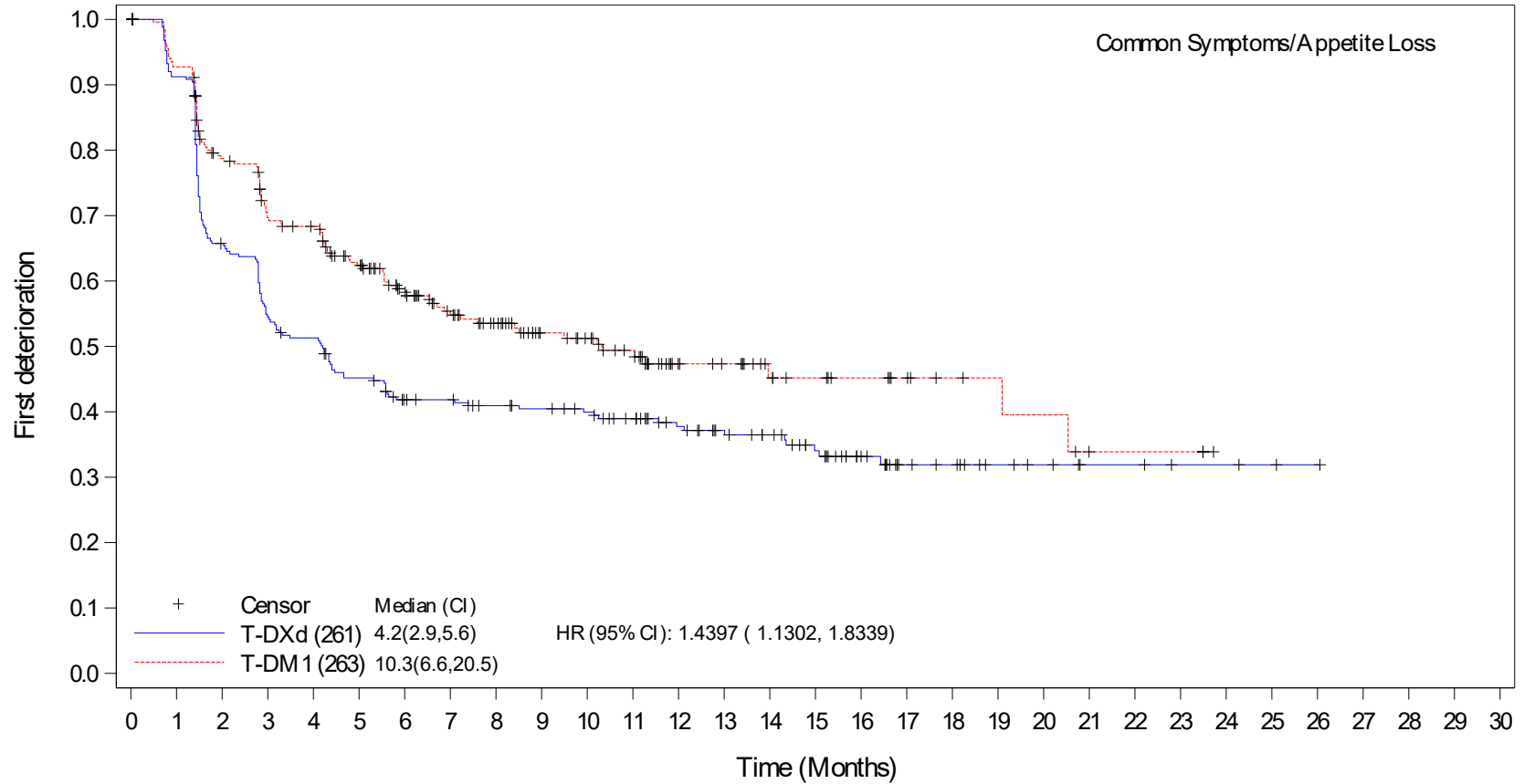
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	231	200	185	179	161	153	148	136	128	118	107	94	79	68	58	44	29	26	22	18	15	14	9	8	6	3	2	0
T-DM1 (263)	263	226	181	161	153	126	112	99	89	74	67	63	43	37	28	25	22	17	13	7	7	5	4	4	1	1	0		

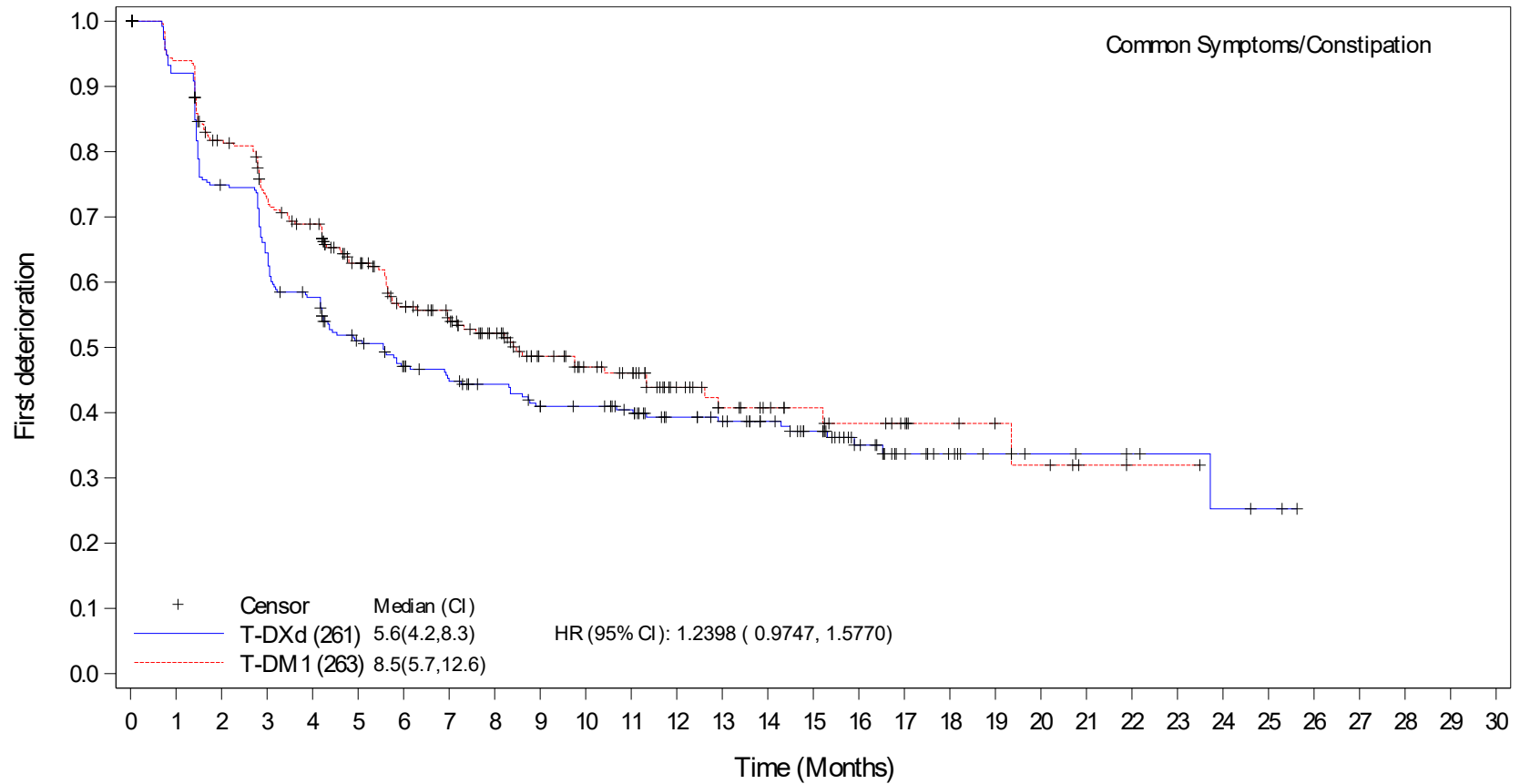
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	229	164	136	127	110	96	94	88	84	80	73	62	55	49	39	28	17	15	10	8	5	5	3	3	2	1	0
T-DM1 (263)	263	230	186	159	153	131	110	91	80	63	58	50	32	29	21	18	15	12	9	8	7	4	4	4	0			

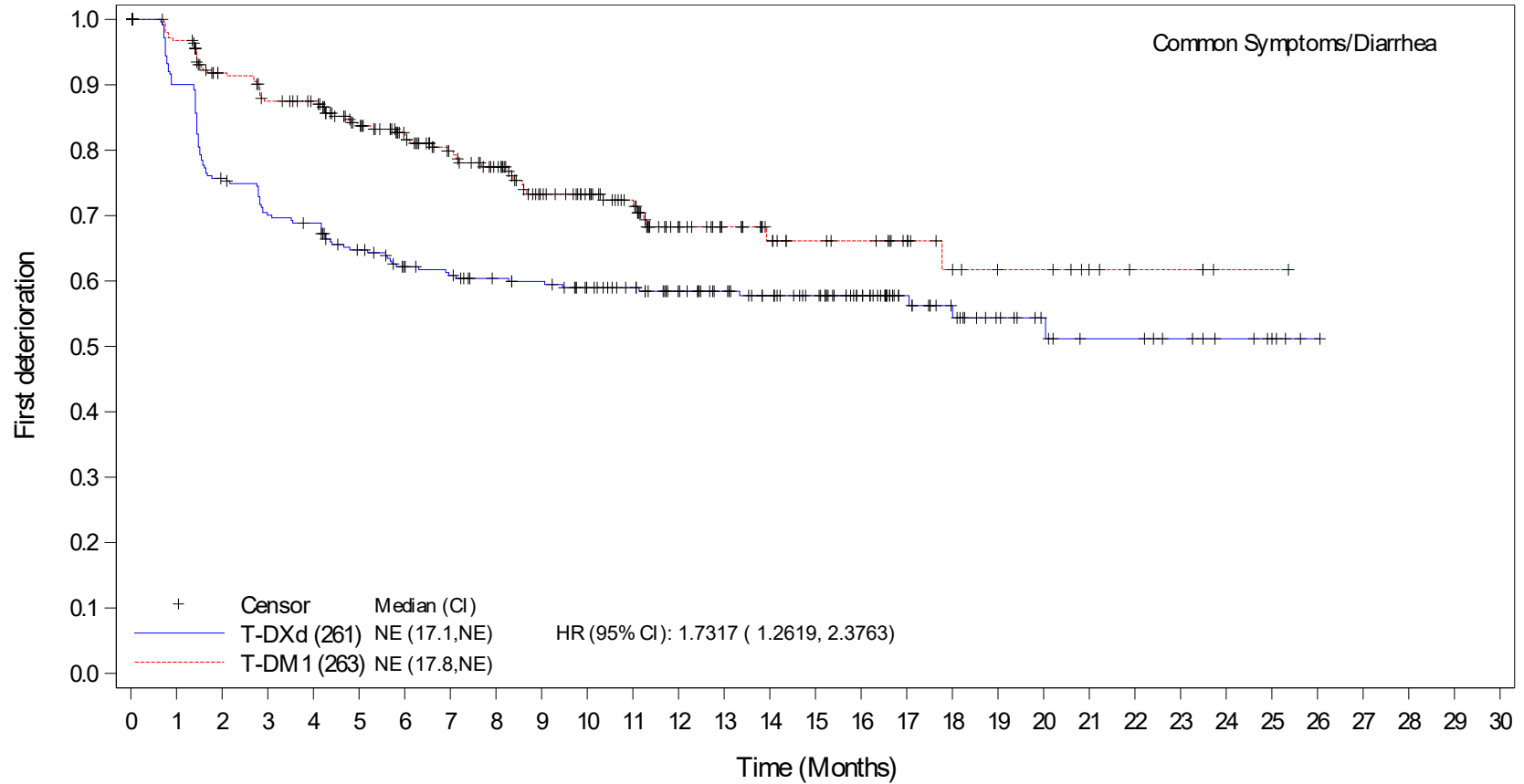
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	231	187	161	142	119	106	98	92	84	81	75	64	60	52	44	29	19	14	10	7	6	5	4	3	2	0
T-DM1 (263)	263	233	195	169	156	129	107	94	80	62	53	48	32	24	20	17	14	11	8	6	5	2	1	1	0		

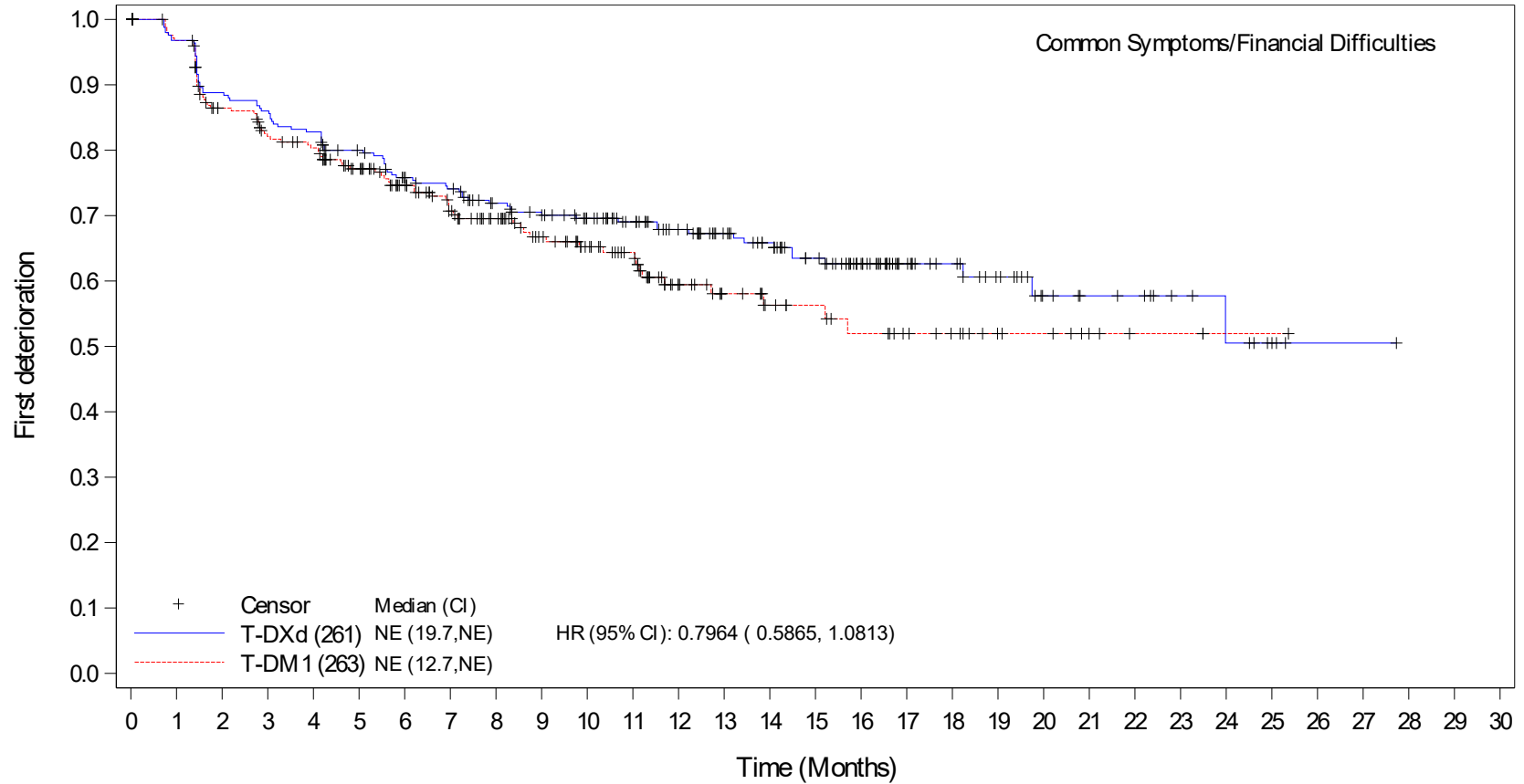
Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	226	189	174	170	154	142	137	130	126	117	110	99	90	81	72	57	38	30	22	17	13	13	10	7	5	1	0
T-DM1 (263)	263	240	214	201	195	170	152	133	120	98	88	75	51	41	31	26	24	19	14	11	11	7	5	5	1	1	0	

Figure 05 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-C30
 Full Analysis Set



Patients still at risk:

T-DXd (261)	261	242	222	215	207	193	178	172	158	150	139	127	112	98	89	76	60	40	33	26	17	14	13	9	7	4	1	1	0
T-DM1 (263)	263	239	202	187	180	160	141	123	109	92	80	70	47	37	30	27	23	19	16	11	10	6	4	4	1	1	0		

Table 11 - Analysis of time to first deterioration of EORTC BR45
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Body Image			
Subjects (%) with Events Deterioration	121 (46.4)	81 (30.8)	
Median time to first deterioration (months) [a]: 95% CI	17.3 (10.7,21.0)	NE (12.4,NE)	
Stratified Cox Proportional Hazard Model [b]: HR 95% CI			1.3507 (1.0164,1.7950)
Stratified log-rank p-value [c]			0.0391
Deterioration rate [d] at 3 Months	69.0	80.3	
95% CI	[62.8 , 74.3]	[74.7 , 84.8]	
Deterioration rate [d] at 6 Months	62.0	73.5	
95% CI	[55.6 , 67.7]	[67.3 , 78.8]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	57.6	67.6	
95% CI	[51.1 , 63.5]	[60.6 , 73.6]	
Deterioration rate [d] at 12 Months	54.3	59.8	
95% CI	[47.8 , 60.4]	[51.6 , 67.0]	
Deterioration rate [d] at 18 Months	45.8	54.9	
95% CI	[37.0 , 54.2]	[45.6 , 63.3]	
Deterioration rate [d] at 24 Months	35.1	54.9	
95% CI	[22.9 , 47.5]	[45.6 , 63.3]	
Deterioration rate [d] at 36 Months	35.1	54.9	
95% CI	[22.9 , 47.5]	[45.6 , 63.3]	
Deterioration rate [d] at 48 Months	35.1	54.9	
95% CI	[22.9 , 47.5]	[45.6 , 63.3]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Sexual Functioning	Subjects (%) with Events Deterioration	60 (23.0)	57 (21.7)	
	Median time to first deterioration (months) [a]: 95% CI	NE (NE,NE)	NE (22.6,NE)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.9309 (0.6464,1.3407)
	Stratified log-rank p-value [c]			0.7067
	Deterioration rate [d] at 3 Months	79.8	83.8	
	95% CI	[74.2 , 84.3]	[78.4 , 87.9]	
	Deterioration rate [d] at 6 Months	78.2	78.7	
	95% CI	[72.5 , 82.8]	[72.6 , 83.5]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	77.2	74.5	
95% CI	[71.4 , 82.0]	[67.8 , 80.0]	
Deterioration rate [d] at 12 Months	75.5	73.5	
95% CI	[69.4 , 80.5]	[66.5 , 79.2]	
Deterioration rate [d] at 18 Months	75.5	70.5	
95% CI	[69.4 , 80.5]	[61.3 , 77.9]	
Deterioration rate [d] at 24 Months	73.0	56.4	
95% CI	[65.2 , 79.4]	[28.2 , 77.2]	
Deterioration rate [d] at 36 Months	73.0	56.4	
95% CI	[65.2 , 79.4]	[28.2 , 77.2]	
Deterioration rate [d] at 48 Months	73.0	56.4	
95% CI	[65.2 , 79.4]	[28.2 , 77.2]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Sexual Enjoyment	Subjects (%) with Events Deterioration	23 (8.8)	11 (4.2)	
	Median time to first deterioration (months) [a]: 95% CI	13.4 (3.6,NE)	NE (NE,NE)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			3.4770 (1.3648,8.8581)
	Stratified log-rank p-value [c]			0.0064
	Deterioration rate [d] at 3 Months	66.7	85.6	
	95% CI	[50.9 , 78.4]	[72.1 , 92.8]	
	Deterioration rate [d] at 6 Months	55.6	83.1	
	95% CI	[40.0 , 68.6]	[68.9 , 91.2]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	53.2	74.6	
95% CI	[37.8 , 66.5]	[58.4 , 85.3]	
Deterioration rate [d] at 12 Months	50.4	74.6	
95% CI	[34.9 , 64.1]	[58.4 , 85.3]	
Deterioration rate [d] at 18 Months	47.1	74.6	
95% CI	[31.4 , 61.2]	[58.4 , 85.3]	
Deterioration rate [d] at 24 Months	47.1	74.6	
95% CI	[31.4 , 61.2]	[58.4 , 85.3]	
Deterioration rate [d] at 36 Months	47.1	74.6	
95% CI	[31.4 , 61.2]	[58.4 , 85.3]	
Deterioration rate [d] at 48 Months	47.1	74.6	
95% CI	[31.4 , 61.2]	[58.4 , 85.3]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Functional Scales/Future Perspective	Subjects (%) with Events Deterioration	88 (33.7)	73 (27.8)	
	Median time to first deterioration (months) [a]: 95% CI	NE (19.4,NE)	21.2 (16.7,NE)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.9846 (0.7191,1.3482)
	Stratified log-rank p-value [c]			0.9202
	Deterioration rate [d] at 3 Months	80.9	81.2	
	95% CI	[75.5 , 85.3]	[75.7 , 85.6]	
	Deterioration rate [d] at 6 Months	74.4	73.1	
	95% CI	[68.5 , 79.3]	[66.8 , 78.4]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	68.6	71.1	
95% CI	[62.4 , 74.0]	[64.5 , 76.6]	
Deterioration rate [d] at 12 Months	67.1	68.3	
95% CI	[60.7 , 72.7]	[61.2 , 74.4]	
Deterioration rate [d] at 18 Months	63.3	56.2	
95% CI	[56.4 , 69.4]	[43.2 , 67.4]	
Deterioration rate [d] at 24 Months	56.3	42.2	
95% CI	[46.4 , 65.1]	[17.5 , 65.2]	
Deterioration rate [d] at 36 Months	56.3	42.2	
95% CI	[46.4 , 65.1]	[17.5 , 65.2]	
Deterioration rate [d] at 48 Months	56.3	42.2	
95% CI	[46.4 , 65.1]	[17.5 , 65.2]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Symptom Scales/Systemic Therapy Side Effects	Subjects (%) with Events Deterioration	145 (55.6)	113 (43.0)	
	Median time to first deterioration (months) [a]: 95% CI	5.7 (4.3,11.0)	11.7 (8.3,16.7)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			1.2329 (0.9627,1.5789)
	Stratified log-rank p-value [c]			0.1004
	Deterioration rate [d] at 3 Months	61.8	70.9	
	95% CI	[55.5 , 67.5]	[64.7 , 76.2]	
	Deterioration rate [d] at 6 Months	49.1	60.8	
	95% CI	[42.8 , 55.2]	[54.2 , 66.8]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	45.1	53.7	
95% CI	[38.7 , 51.2]	[46.7 , 60.3]	
Deterioration rate [d] at 12 Months	41.8	48.8	
95% CI	[35.5 , 48.0]	[41.2 , 56.1]	
Deterioration rate [d] at 18 Months	38.9	37.2	
95% CI	[32.2 , 45.6]	[26.6 , 47.8]	
Deterioration rate [d] at 24 Months	38.9	37.2	
95% CI	[32.2 , 45.6]	[26.6 , 47.8]	
Deterioration rate [d] at 36 Months	38.9	37.2	
95% CI	[32.2 , 45.6]	[26.6 , 47.8]	
Deterioration rate [d] at 48 Months	38.9	37.2	
95% CI	[32.2 , 45.6]	[26.6 , 47.8]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Symptom Scales/Breast Symptoms	Subjects (%) with Events Deterioration	56 (21.5)	52 (19.8)	
	Median time to first deterioration (months) [a]: 95% CI	NE (NE,NE)	NE (NE,NE)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.8505 (0.5814,1.2442)
	Stratified log-rank p-value [c]			0.4025
	Deterioration rate [d] at 3 Months	92.0	89.9	
	95% CI	[87.9 , 94.8]	[85.3 , 93.1]	
	Deterioration rate [d] at 6 Months	84.6	85.4	
	95% CI	[79.5 , 88.6]	[80.1 , 89.4]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	81.4	80.2	
95% CI	[75.9 , 85.8]	[73.9 , 85.1]	
Deterioration rate [d] at 12 Months	77.6	74.1	
95% CI	[71.6 , 82.5]	[66.5 , 80.1]	
Deterioration rate [d] at 18 Months	74.4	66.8	
95% CI	[67.6 , 79.9]	[56.5 , 75.1]	
Deterioration rate [d] at 24 Months	74.4	66.8	
95% CI	[67.6 , 79.9]	[56.5 , 75.1]	
Deterioration rate [d] at 36 Months	74.4	66.8	
95% CI	[67.6 , 79.9]	[56.5 , 75.1]	
Deterioration rate [d] at 48 Months	74.4	66.8	
95% CI	[67.6 , 79.9]	[56.5 , 75.1]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Symptom Scales/Arm Symptoms	Subjects (%) with Events Deterioration	134 (51.3)	137 (52.1)	
	Median time to first deterioration (months) [a]: 95% CI	10.3 (7.7,16.7)	5.6 (4.2,9.0)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.7402 (0.5812,0.9428)
	Stratified log-rank p-value [c]			0.0140
	Deterioration rate [d] at 3 Months	76.1	63.4	
	95% CI	[70.3 , 80.9]	[56.9 , 69.1]	
	Deterioration rate [d] at 6 Months	60.5	48.4	
	95% CI	[54.1 , 66.3]	[41.8 , 54.7]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	51.4	43.6	
95% CI	[44.8 , 57.5]	[36.9 , 50.1]	
Deterioration rate [d] at 12 Months	47.6	40.0	
95% CI	[40.9 , 53.9]	[33.0 , 46.9]	
Deterioration rate [d] at 18 Months	42.5	34.3	
95% CI	[35.3 , 49.4]	[25.7 , 43.0]	
Deterioration rate [d] at 24 Months	35.5	34.3	
95% CI	[26.4 , 44.8]	[25.7 , 43.0]	
Deterioration rate [d] at 36 Months	35.5	34.3	
95% CI	[26.4 , 44.8]	[25.7 , 43.0]	
Deterioration rate [d] at 48 Months	35.5	34.3	
95% CI	[26.4 , 44.8]	[25.7 , 43.0]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Symptom Scales/Upset by Hair Loss	Subjects (%) with Events Deterioration	26 (10.0)	9 (3.4)	
	Median time to first deterioration (months) [a]: 95% CI	21.2 (4.1,NE)	21.7 (NE,NE)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			1.9780 (0.9151,4.2754)
	Stratified log-rank p-value [c]			0.0777
	Deterioration rate [d] at 3 Months	65.6	89.5	
	95% CI	[52.2 , 76.0]	[74.3 , 95.9]	
	Deterioration rate [d] at 6 Months	62.3	83.1	
	95% CI	[48.9 , 73.1]	[65.8 , 92.1]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 11 - Analysis of time to first deterioration of EORTC BR45 [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	60.2	74.8	
95% CI	[46.7 , 71.3]	[55.0 , 86.8]	
Deterioration rate [d] at 12 Months	57.7	74.8	
95% CI	[43.9 , 69.3]	[55.0 , 86.8]	
Deterioration rate [d] at 18 Months	57.7	74.8	
95% CI	[43.9 , 69.3]	[55.0 , 86.8]	
Deterioration rate [d] at 24 Months	46.2	0.0	
95% CI	[23.2 , 66.4]	[0 , 0]	
Deterioration rate [d] at 36 Months	46.2	0.0	
95% CI	[23.2 , 66.4]	[0 , 0]	
Deterioration rate [d] at 48 Months	46.2	0.0	
95% CI	[23.2 , 66.4]	[0 , 0]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

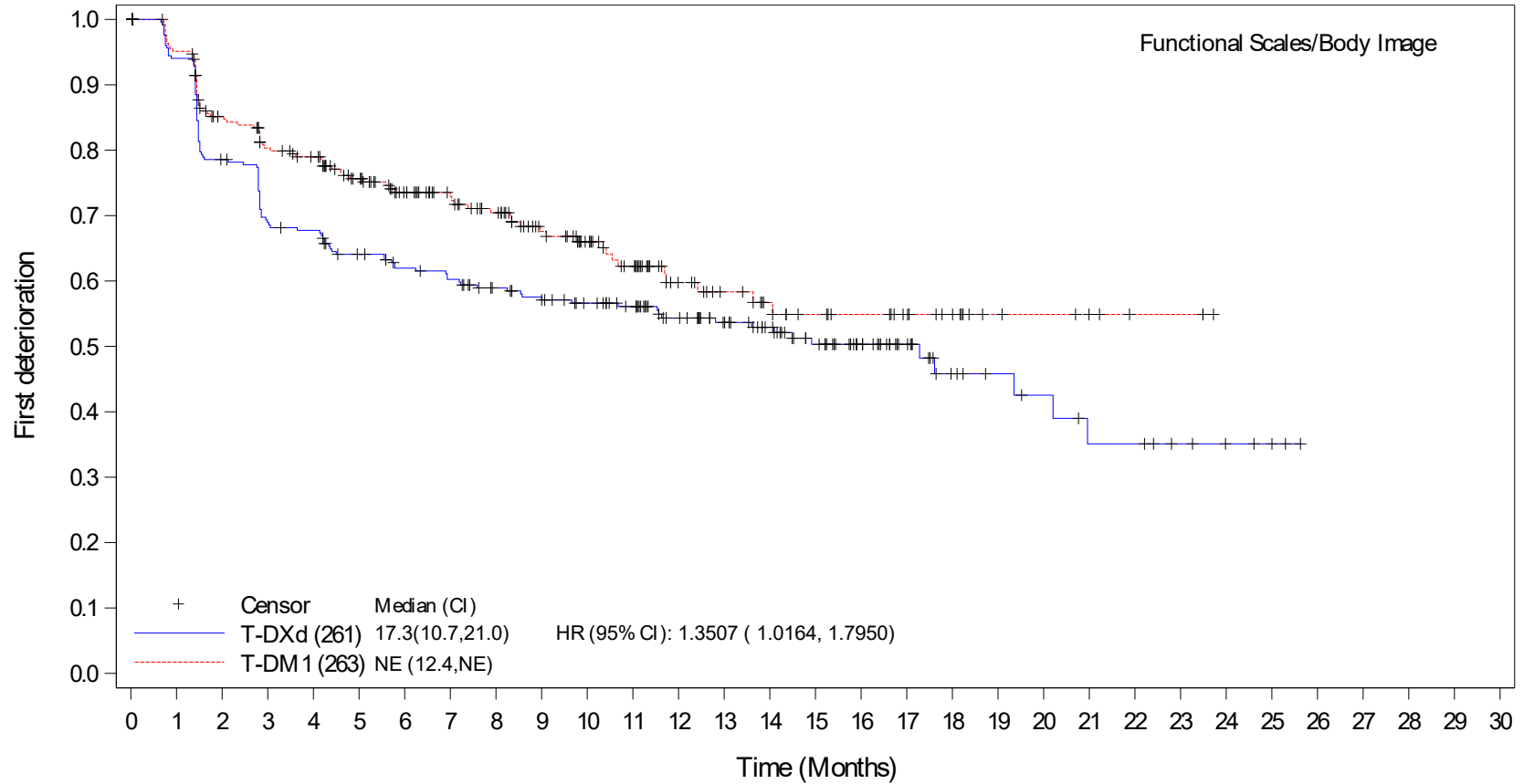
[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

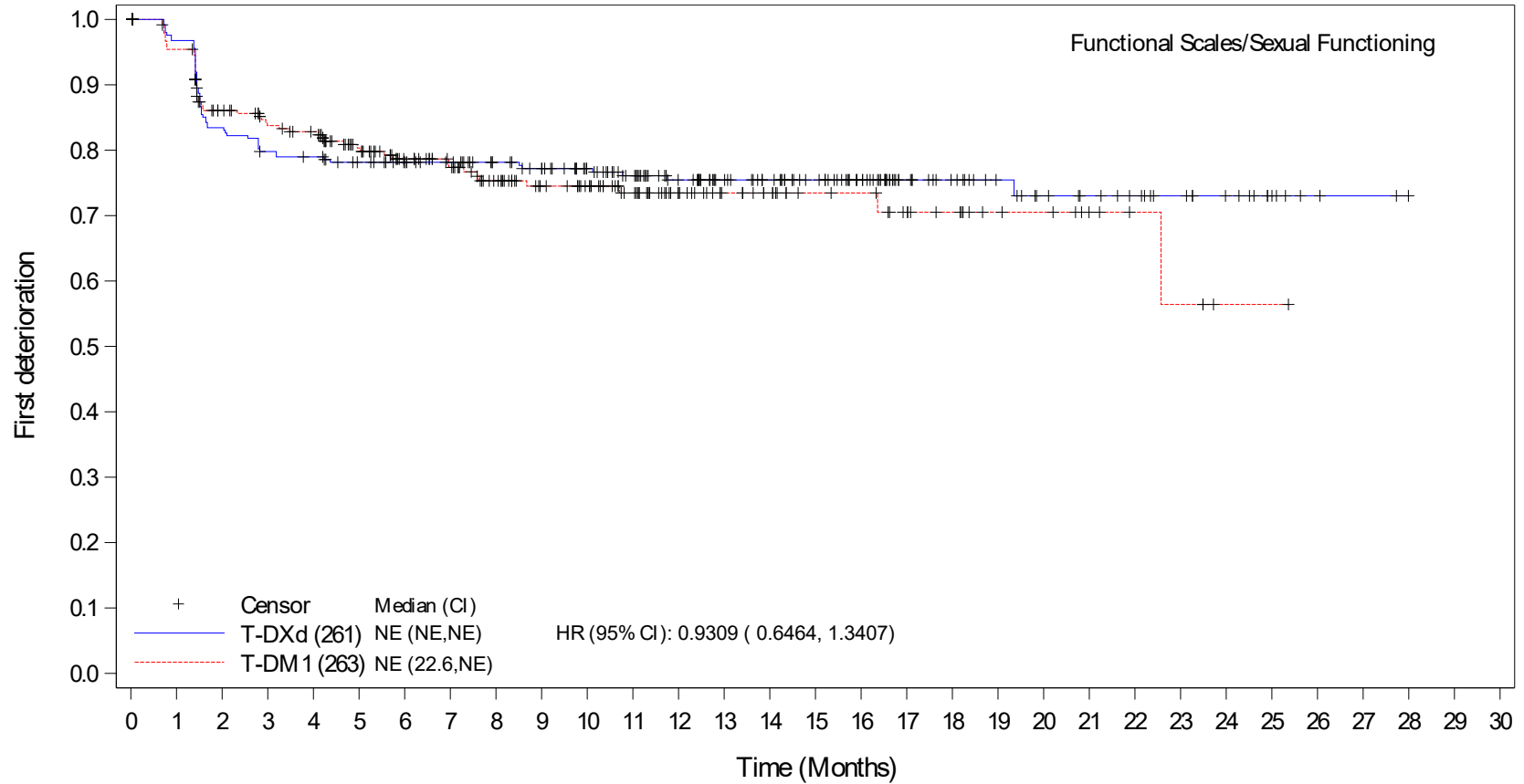
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	237	197	172	168	154	145	140	130	124	115	107	90	78	67	54	40	28	17	14	12	9	9	6	4	3	0
T-DM1 (263)	263	234	197	180	172	152	133	119	108	89	76	64	44	37	31	26	23	19	15	9	8	6	4	4	0		

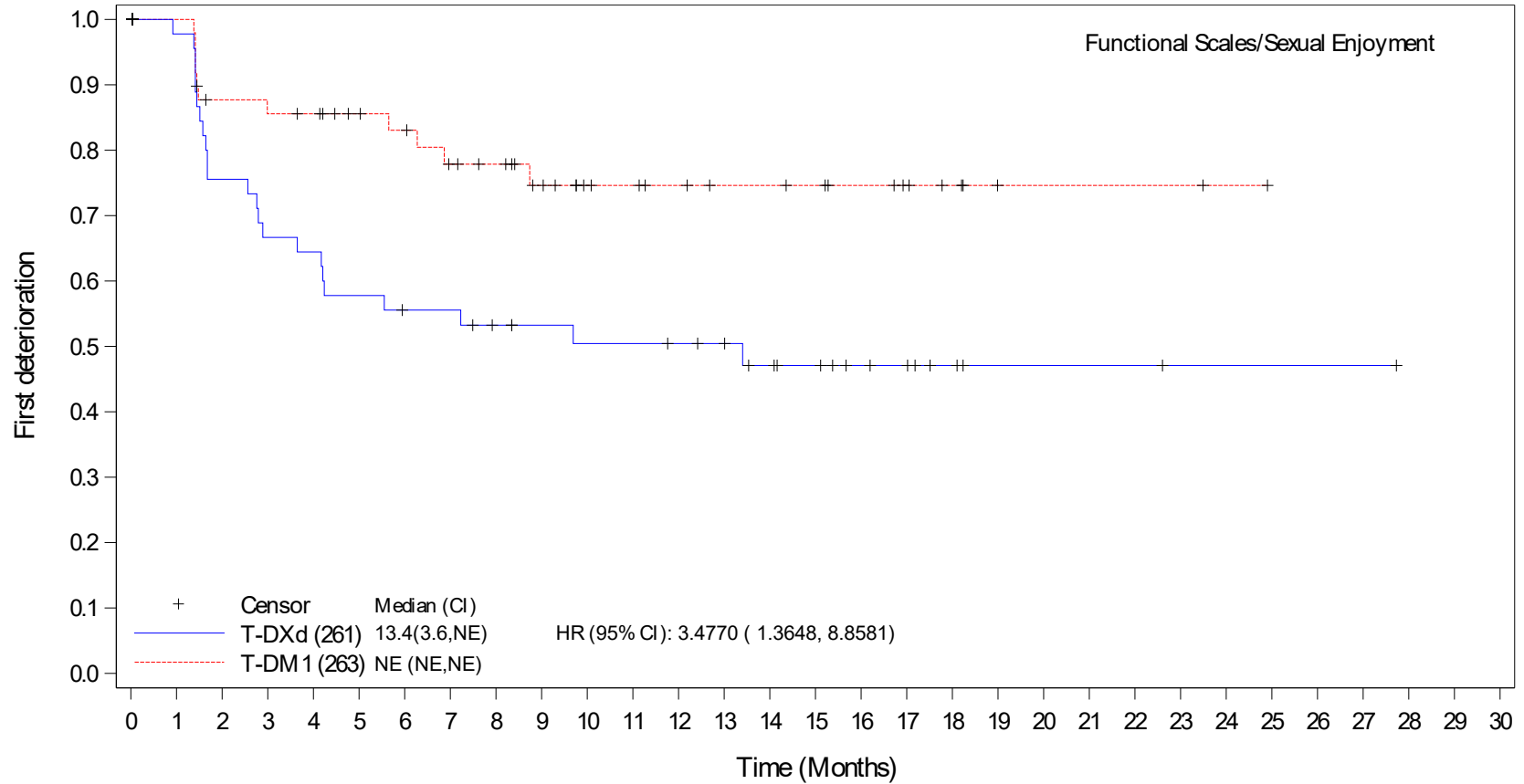
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd (261)	261	240	206	196	193	185	179	174	164	158	145	133	116	101	92	81	66	45	38	31	26	23	20	16	12	7	3	2	0
T-DM1 (263)	263	229	193	180	174	151	132	120	104	89	82	68	50	40	34	27	26	21	17	12	11	7	5	4	1	1	0		

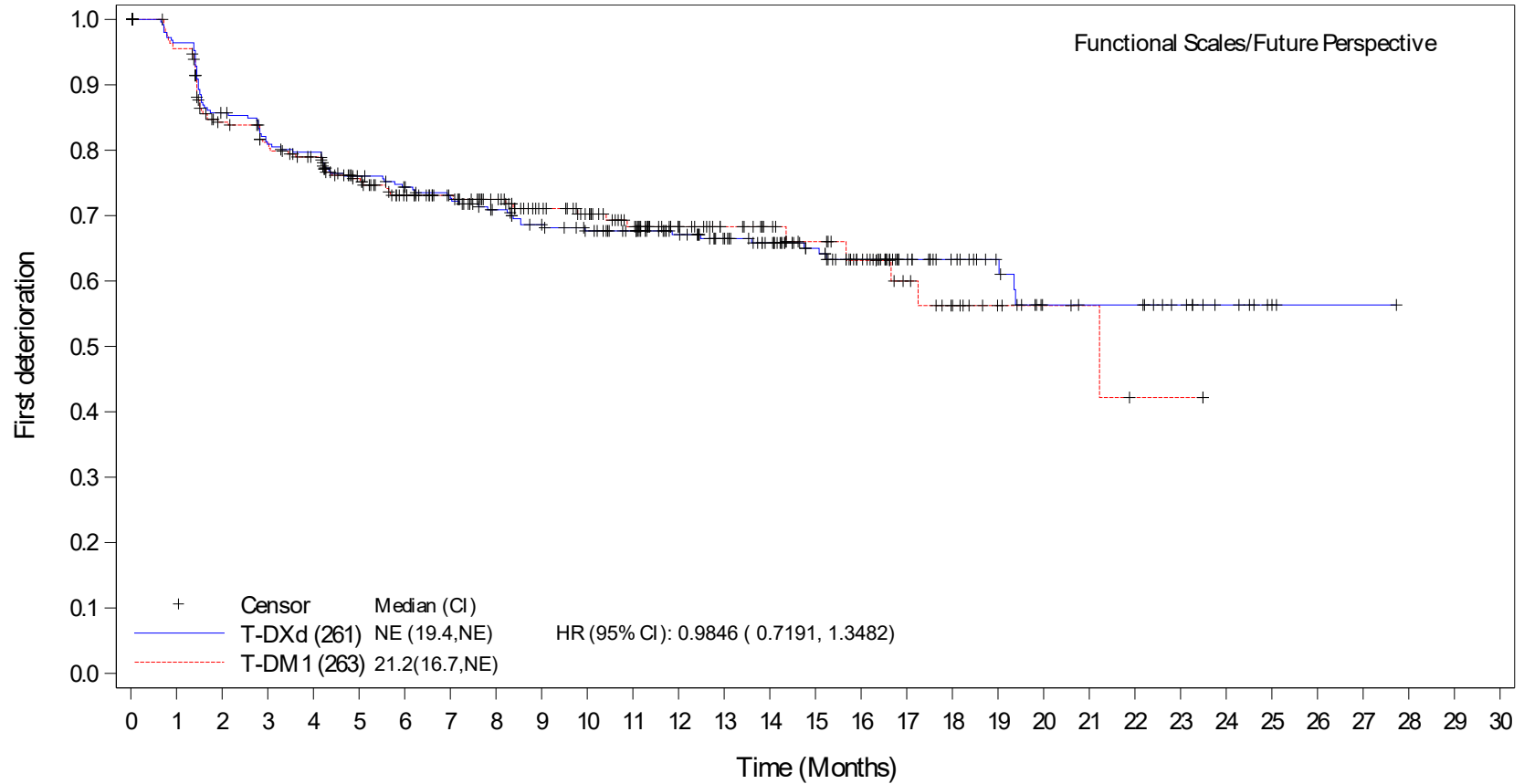
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd (261)	261	44	34	30	29	26	24	24	21	19	18	18	17	16	13	11	8	7	4	2	2	2	2	1	1	1	1	1	0
T-DM1 (263)	263	49	41	40	39	35	33	29	27	22	17	16	14	12	12	11	9	7	5	2	2	2	2	2	1	0			

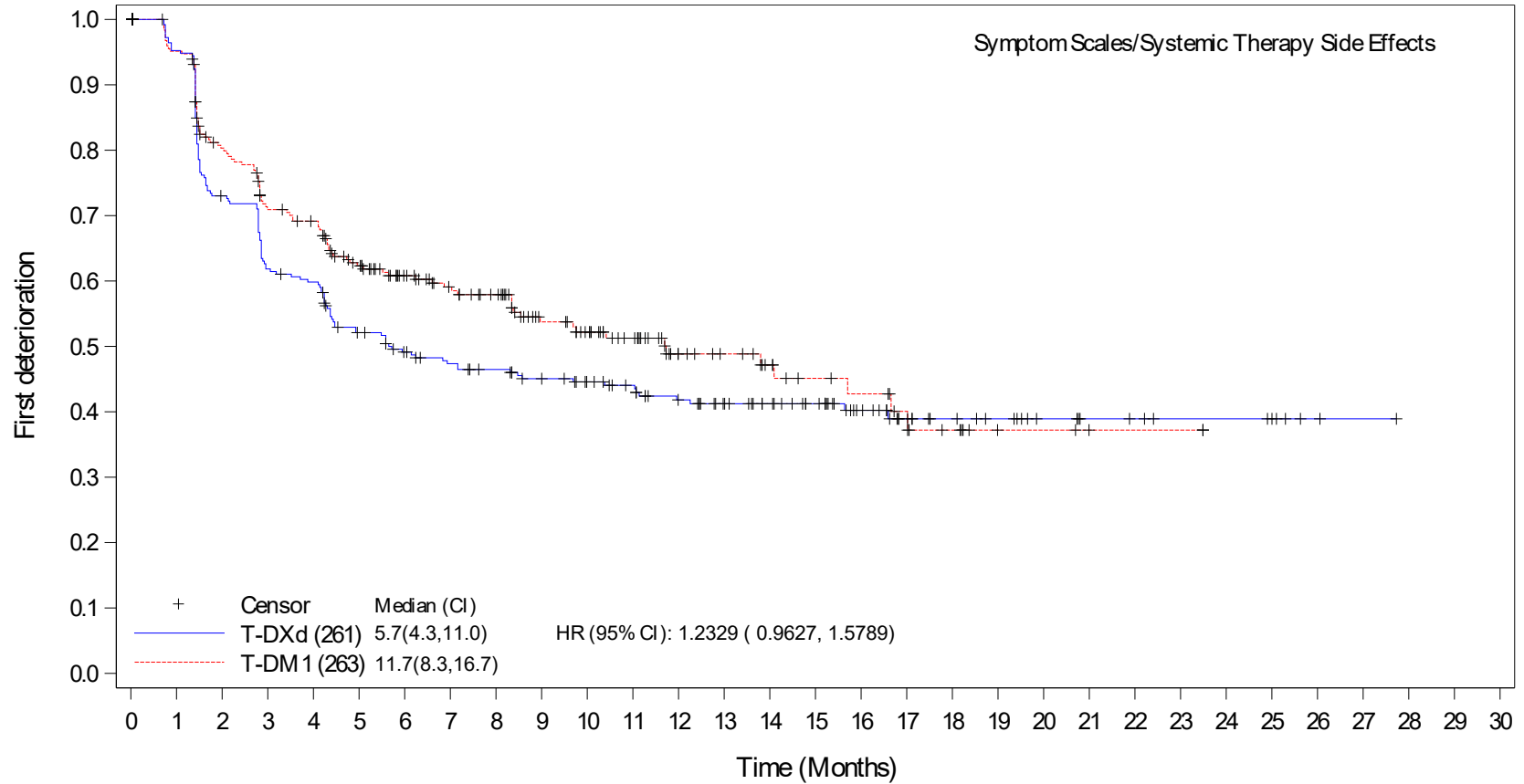
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd (261)	261	243	215	202	198	182	175	169	157	148	140	132	118	105	94	77	62	44	35	28	18	17	17	12	7	3	1	1	0
T-DM1 (263)	263	235	195	182	171	152	134	120	108	91	81	68	48	39	32	26	22	17	12	6	5	4	2	2	0				

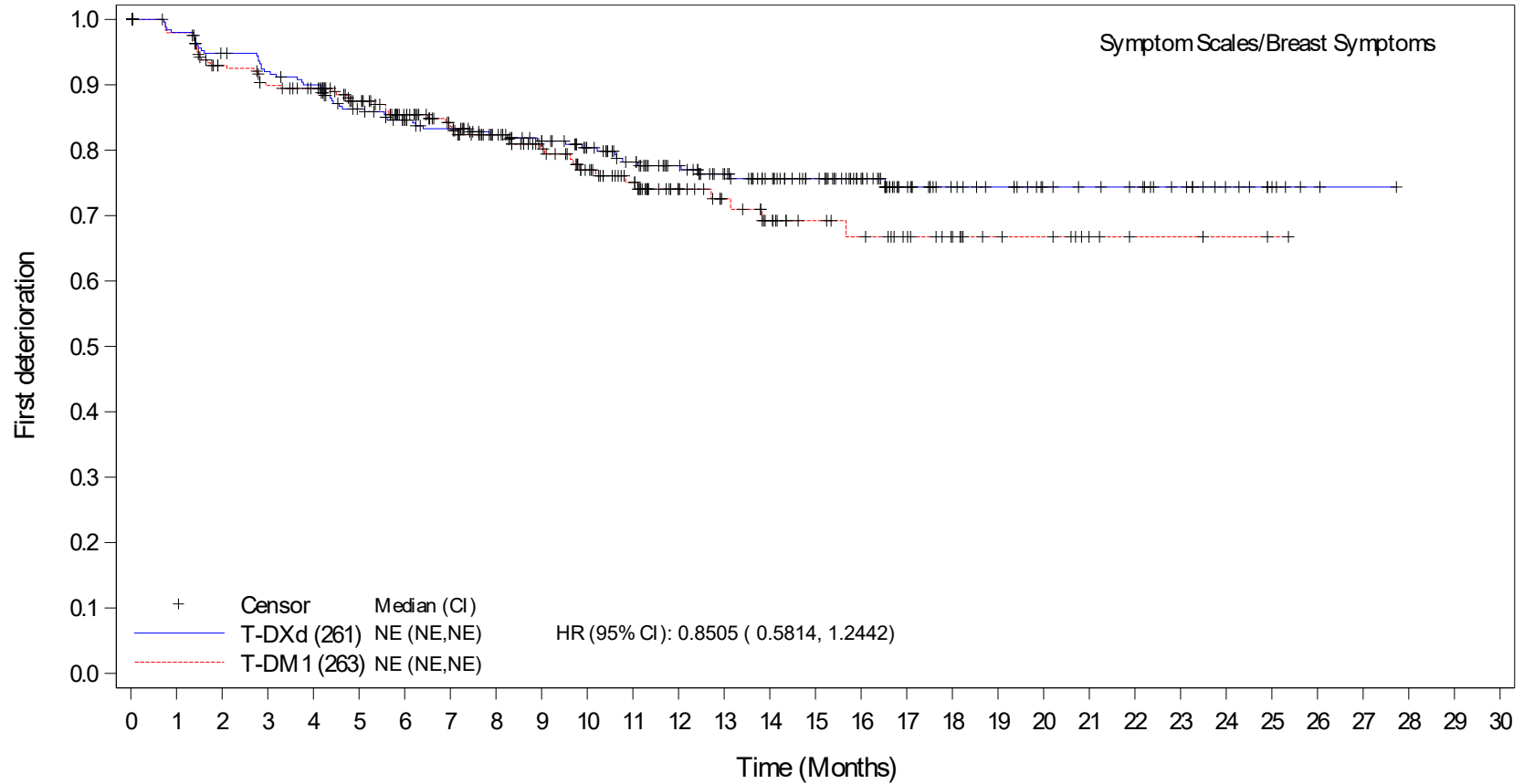
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	240	183	155	149	125	113	106	101	94	87	81	71	63	56	49	36	26	21	18	13	10	9	7	7	6	2	1	0
T-DM1 (263)	263	235	190	162	155	131	112	100	92	71	63	52	35	31	25	20	18	14	10	5	5	3	3	3	0				

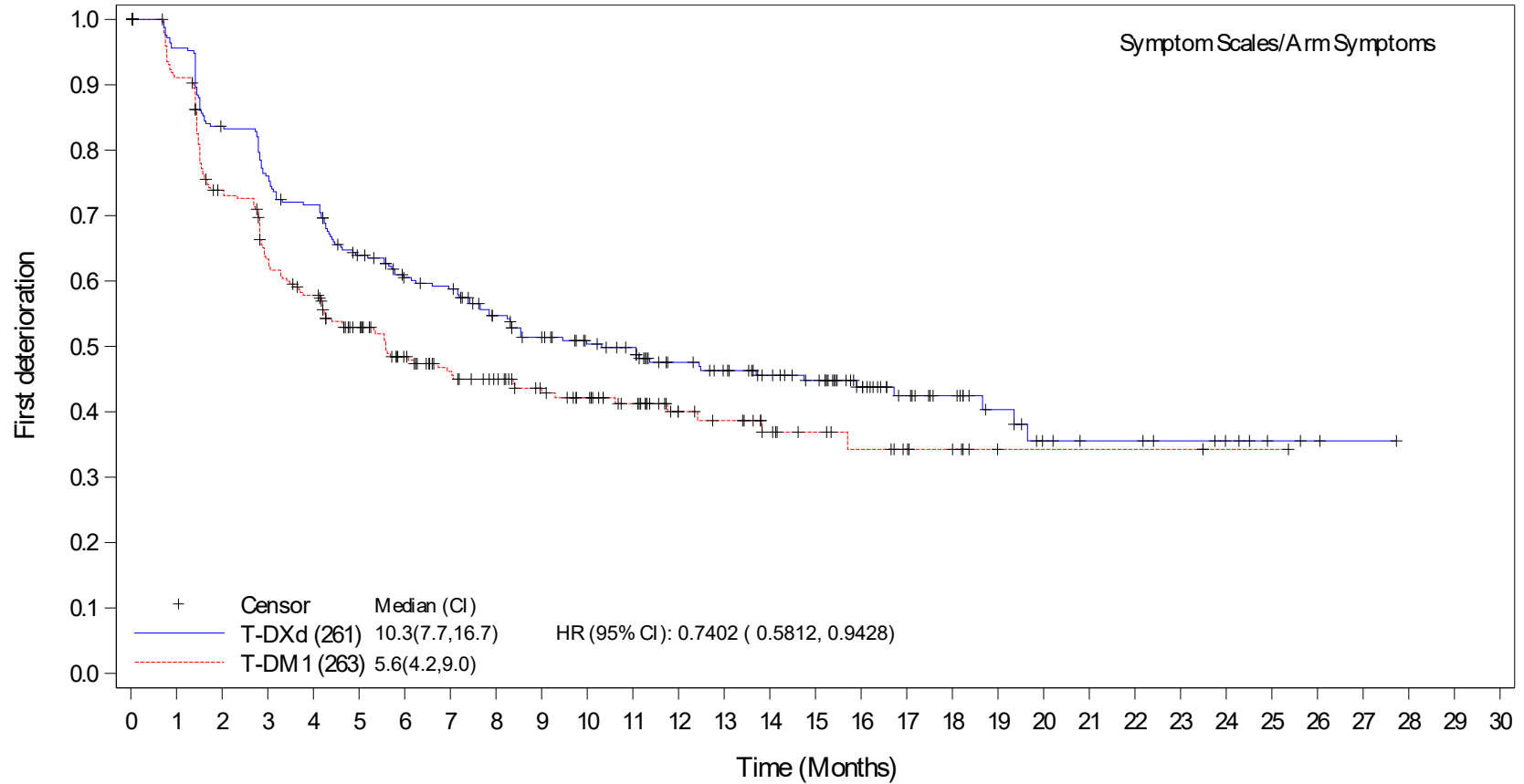
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	246	237	229	223	206	194	187	174	167	153	140	126	111	96	83	67	46	36	32	25	23	21	16	10	6	2	1	0
T-DM1 (263)	263	240	215	203	196	175	154	135	121	105	89	75	54	45	37	30	27	22	17	12	11	6	4	4	2	1	0		

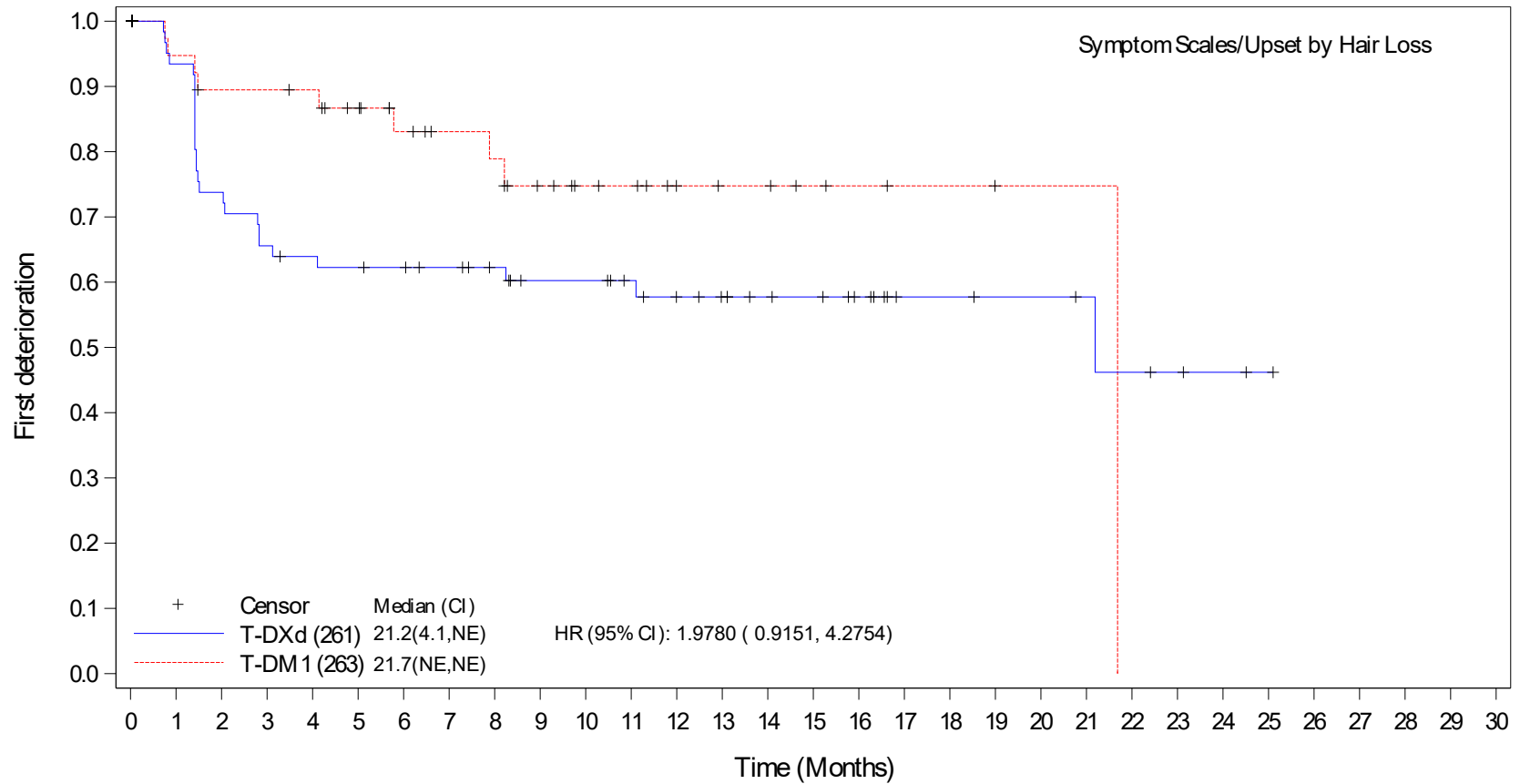
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	240	209	190	178	154	139	134	117	106	96	91	76	70	62	56	42	31	25	18	12	10	10	8	6	3	2	1	0
T-DM1 (263)	263	225	177	149	134	112	92	78	70	60	53	44	30	27	20	16	13	10	8	3	3	3	3	3	1	1	0		

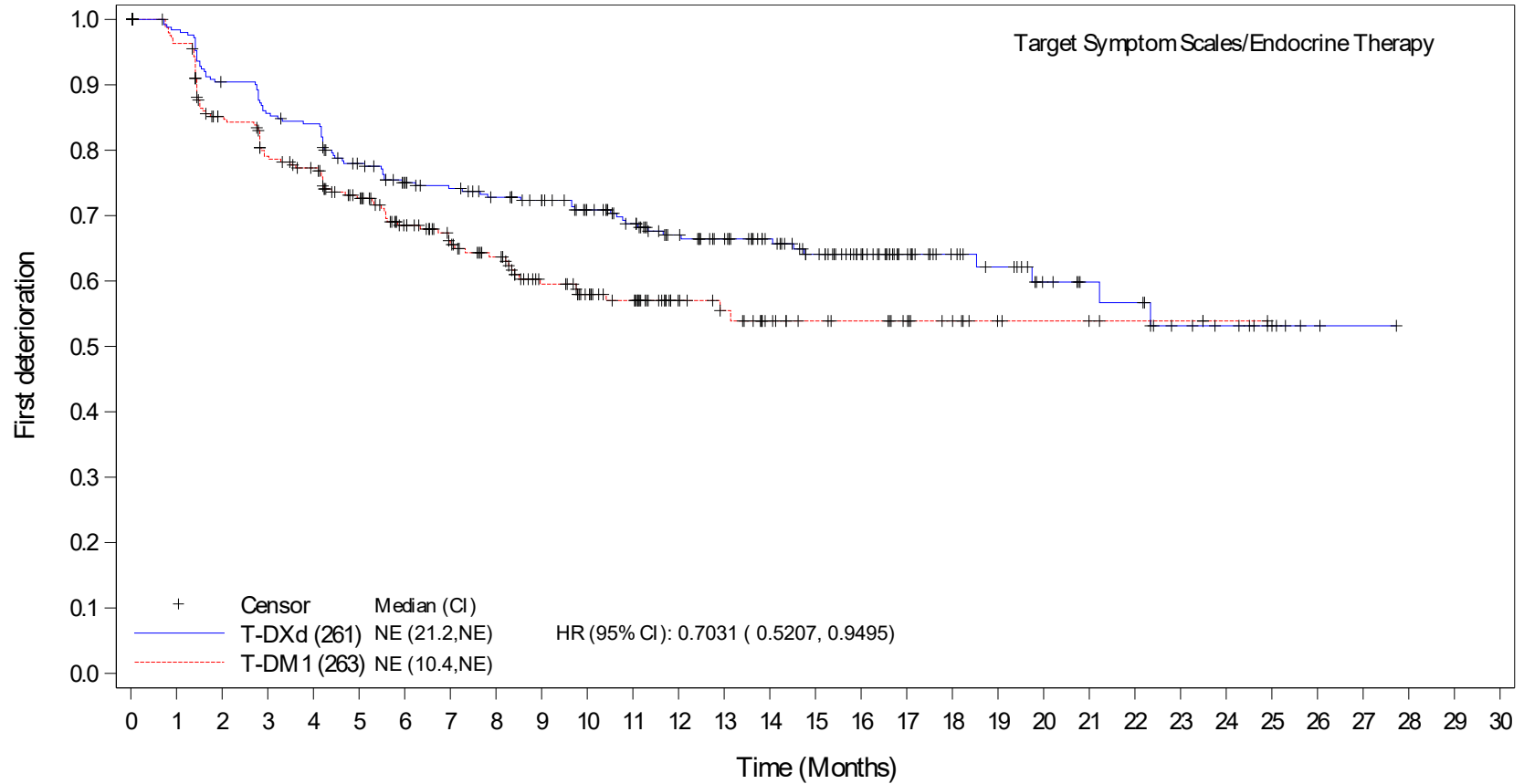
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd (261)	261	57	45	40	38	37	36	34	31	27	27	24	21	19	16	15	12	7	7	6	6	5	4	3	2	1	0
T-DM1 (263)	263	36	33	33	32	28	23	20	19	15	12	11	7	6	6	4	3	2	2	1	1	1	0				

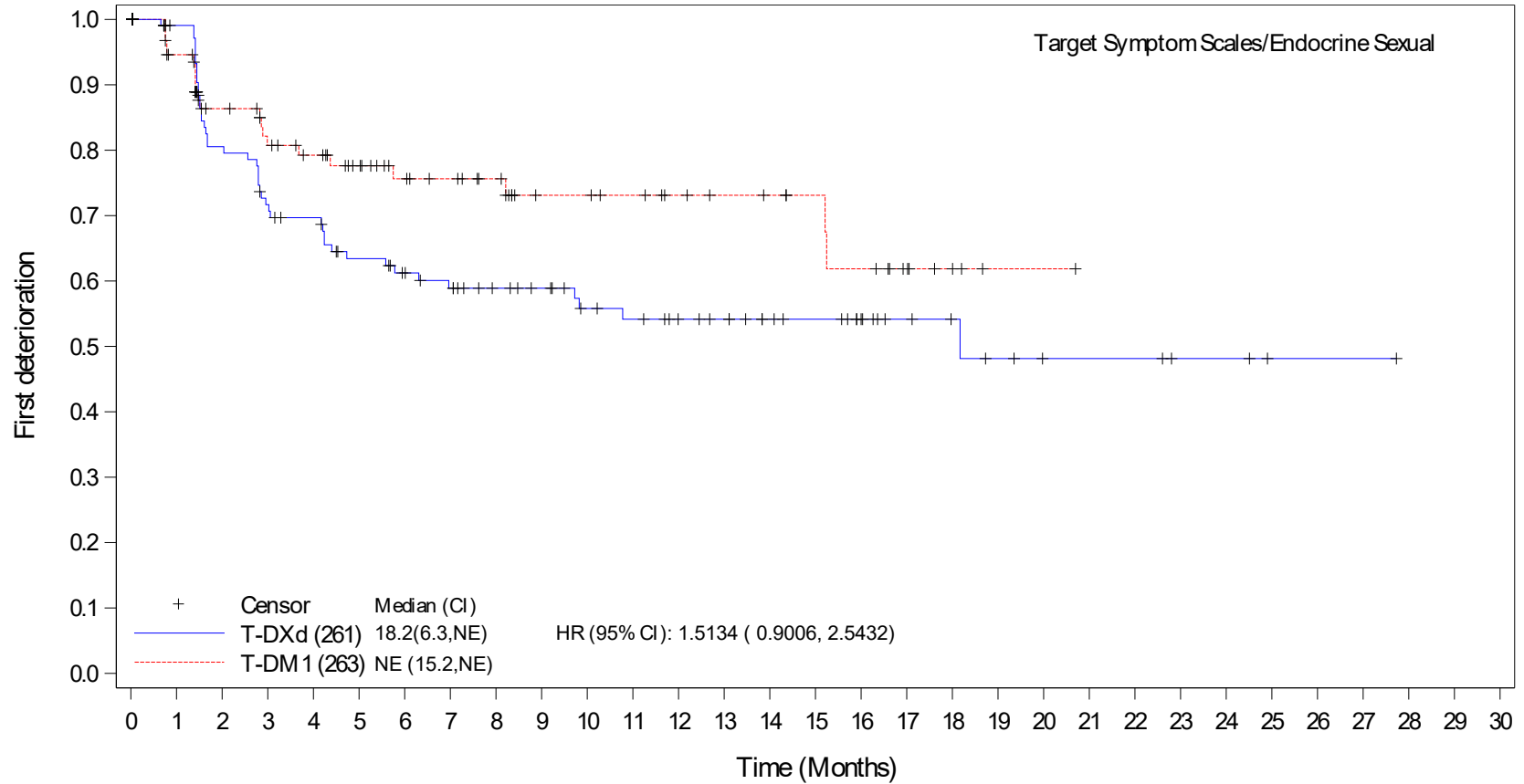
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	247	226	214	209	188	174	168	160	153	140	128	112	102	89	77	63	46	36	31	23	19	18	12	10	6	2	1	0
T-DM1 (263)	263	236	198	179	170	149	126	109	98	79	68	60	40	35	26	21	19	15	11	6	5	4	3	3	1	0			

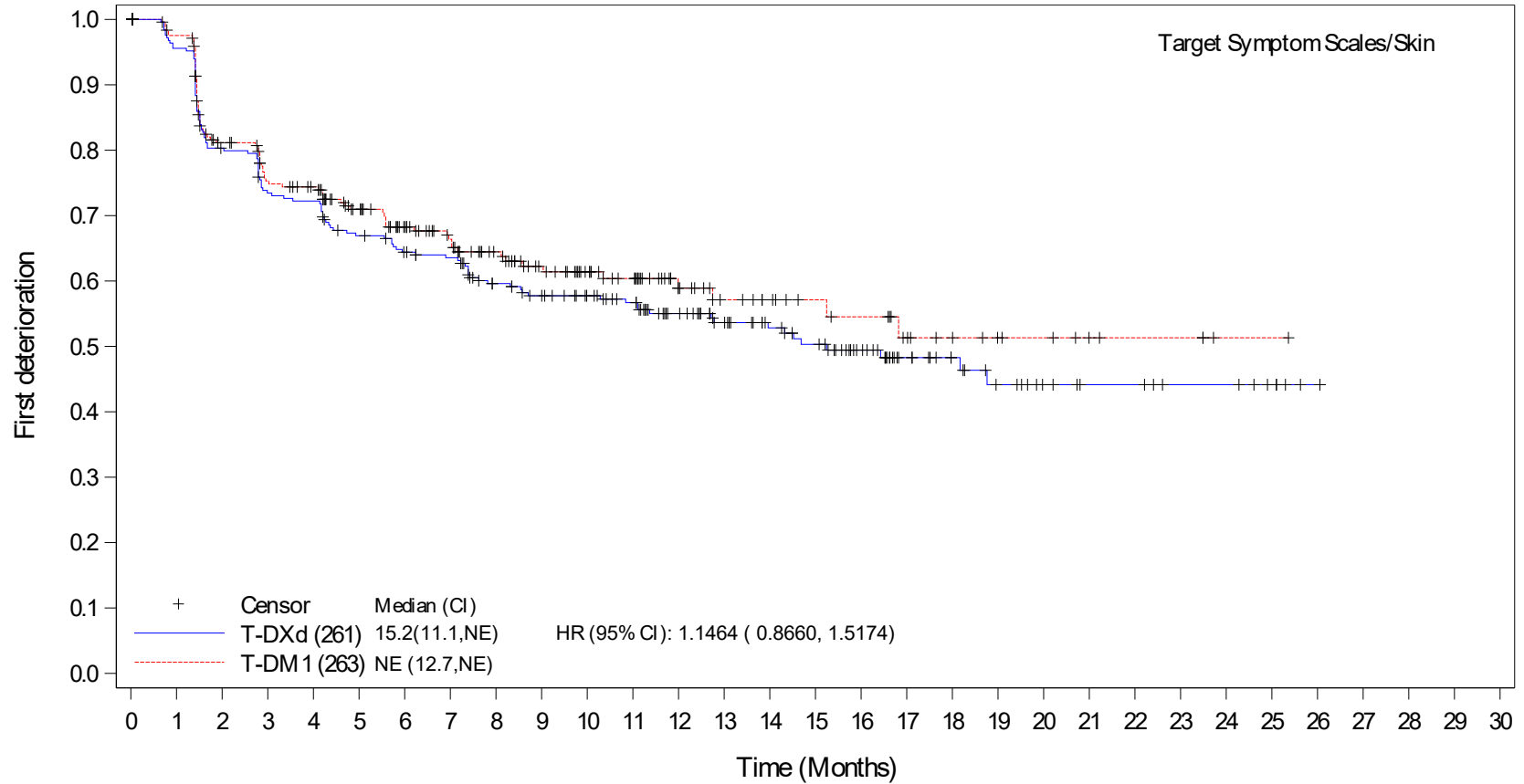
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd (261)	261	102	82	72	68	59	54	50	44	41	35	33	29	27	22	20	16	11	9	7	5	5	5	3	3	1	1	1	0
T-DM1 (263)	263	85	65	57	52	45	38	35	31	23	23	21	18	16	15	13	11	7	4	1	1	0							

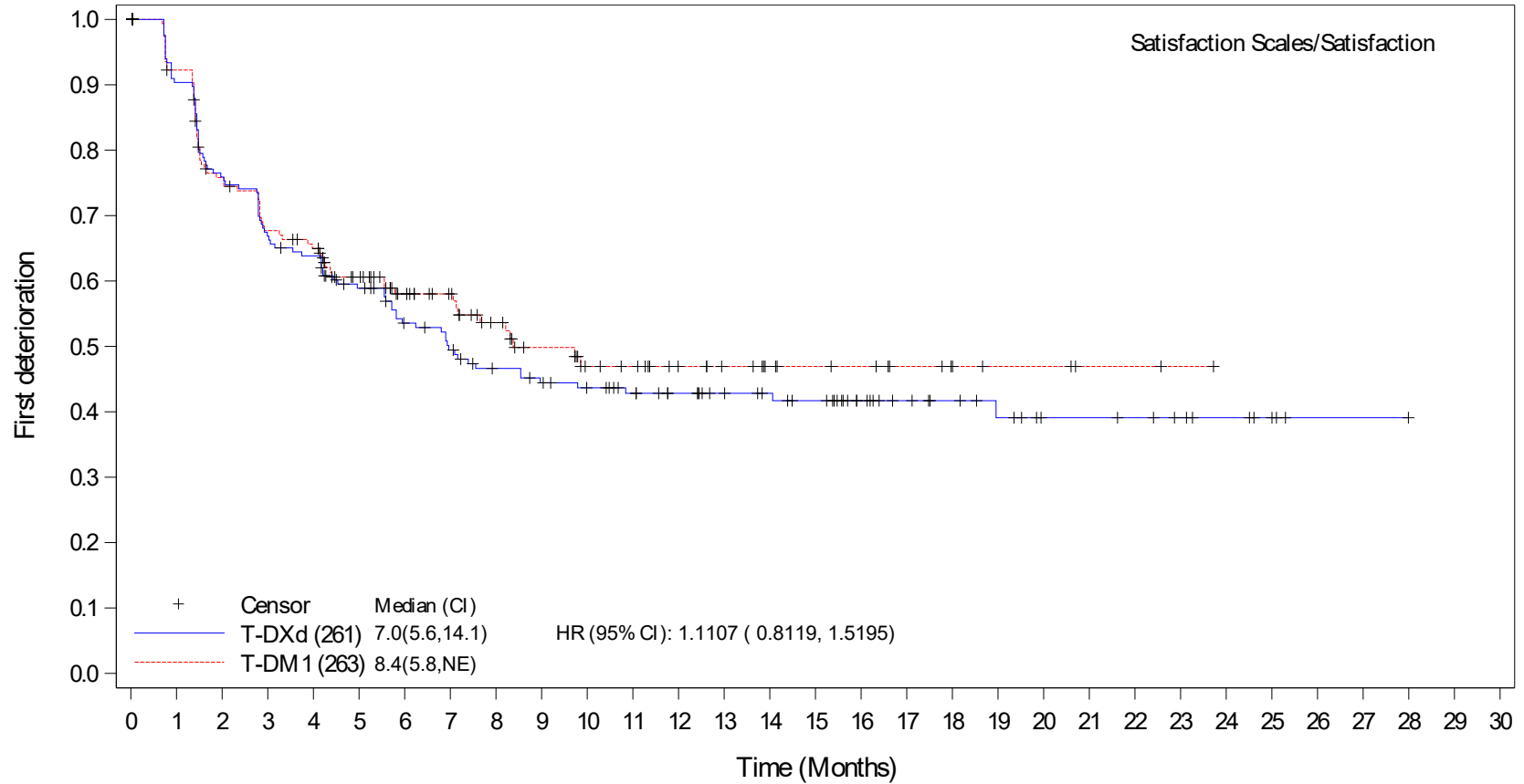
Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	238	199	181	178	162	153	148	130	122	114	106	89	76	66	59	47	32	25	19	14	11	11	8	8	5	1	0
T-DM1 (263)	263	237	185	166	159	136	118	104	90	75	64	56	38	30	26	22	20	15	12	9	8	5	4	4	1	1	0	

Figure 07 - Kaplan-Meier Plot of Time to First deterioration of EORTC QLQ-BR23
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	150	126	111	105	92	79	72	64	60	56	51	46	41	38	35	26	21	18	15	11	11	10	8	6	4	1	1	0
T-DM1 (263)	263	142	113	100	94	78	63	55	44	36	29	27	21	18	14	12	11	8	6	4	4	2	2	1	0				

Table 13 - Analysis of time to first deterioration of EQ-5D-5L
Full Analysis Set

		T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
EQ-5D-5L Score VAS	Subjects (%) with Events Deterioration	134 (51.3)	132 (50.2)	
	Median time to first deterioration (months) [a]: 95% CI	12.1 (5.8,18.2)	8.4 (5.5,9.9)	
	Stratified Cox Proportional Hazard Model [b]: HR 95% CI			0.8542 (0.6686,1.0914)
	Stratified log-rank p-value [c]			0.2067
	Deterioration rate [d] at 3 Months	67.1	67.3	
	95% CI	[60.9 , 72.5]	[61.0 , 72.9]	
	Deterioration rate [d] at 6 Months	56.1	55.4	
	95% CI	[49.7 , 62.0]	[48.8 , 61.6]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Table 13 - Analysis of time to first deterioration of EQ-5D-5L [continued]
Full Analysis Set

	T-DXd (N=261)	T-DM1 (N=263)	T-DXd vs T-DM1
Deterioration rate [d] at 9 Months	53.4	46.5	
95% CI	[47.0 , 59.4]	[39.5 , 53.2]	
Deterioration rate [d] at 12 Months	50.0	40.4	
95% CI	[43.5 , 56.1]	[33.2 , 47.5]	
Deterioration rate [d] at 18 Months	43.7	30.3	
95% CI	[36.9 , 50.4]	[21.1 , 40.0]	
Deterioration rate [d] at 24 Months	38.1	30.3	
95% CI	[28.6 , 47.5]	[21.1 , 40.0]	
Deterioration rate [d] at 36 Months	30.5	30.3	
95% CI	[16.2 , 46.0]	[21.1 , 40.0]	
Deterioration rate [d] at 48 Months	30.5	30.3	
95% CI	[16.2 , 46.0]	[21.1 , 40.0]	

Notes: Time to first deterioration is defined as the time from randomization until the date of the first clinically meaningful symptom deterioration. Deterioration is defined as an increase of 10 or more points each scale/subscale. Death is censored in this analysis.

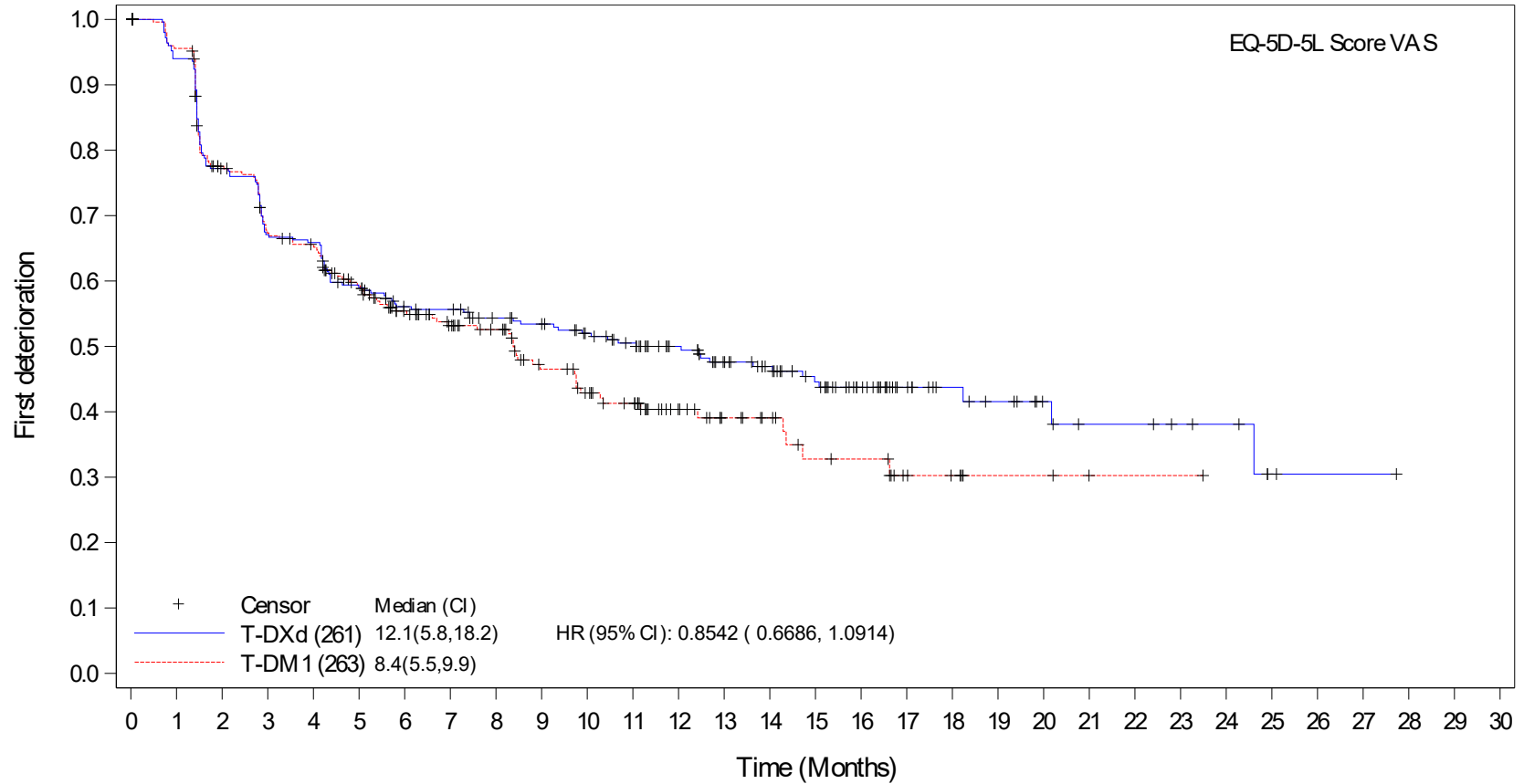
[a] Median time to first deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for deterioration rate at the specified time point are from Kaplan-Meier analysis.

Figure 09 - Kaplan-Meier Plot of Time to First deterioration of EQ-5D-5L-VAS
 Full Analysis Set



Patients still at risk:

T-DXd(261)	261	235	192	166	163	144	132	130	120	116	107	99	86	74	65	54	39	26	20	17	12	9	9	7	6	2	1	1	0
T-DM1 (263)	263	237	184	156	149	126	105	92	84	66	57	50	34	25	21	15	14	8	6	3	3	1	1	1	0				

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Global Health Status

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	108 (41.4)	104 (39.5)	
Stratified Log-rank p-value [a]			0.2677
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			0.8586
95% CI			[0.6541 , 1.1270]
Median time to deterioration (months) [b]	17.5	15.2	
95% CI	[13.6 , NE]	[10.0 , 20.5]	
Rate of deterioration at 3 Months [c]	78.7	77.4	
95% CI	[73.1 , 83.3]	[71.6 , 82.1]	
Rate of deterioration at 6 Months [c]	70.0	68.5	
95% CI	[63.8 , 75.3]	[62.1 , 74.1]	
Rate of deterioration at 9 Months [c]	63.2	58.3	
95% CI	[56.8 , 69.0]	[51.2 , 64.8]	
Rate of deterioration at 12 Months [c]	59.0	52.5	
95% CI	[52.3 , 65.1]	[44.9 , 59.6]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Global Health Status

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	49.5 [41.4 , 57.2]	44.1 [34.1 , 53.6]	
Rate of deterioration at 24 Months [c] 95% CI	46.9 [37.7 , 55.6]	34.7 [21.3 , 48.5]	
Rate of deterioration at 36 Months [c] 95% CI	46.9 [37.7 , 55.6]	34.7 [21.3 , 48.5]	
Rate of deterioration at 48 Months [c] 95% CI	46.9 [37.7 , 55.6]	34.7 [21.3 , 48.5]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Physical Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	82 (31.4)	75 (28.5)	
Stratified Log-rank p-value [a]			0.2301
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.8238 [0.5983 , 1.1342]
Median time to deterioration (months) [b] 95% CI	NE [19.5 , NE]	21.0 [17.2 , NE]	
Rate of deterioration at 3 Months [c] 95% CI	86.1 [81.1 , 89.8]	84.6 [79.3 , 88.6]	
Rate of deterioration at 6 Months [c] 95% CI	77.9 [72.2 , 82.5]	77.5 [71.5 , 82.4]	
Rate of deterioration at 9 Months [c] 95% CI	75.2 [69.3 , 80.2]	68.1 [61.1 , 74.1]	
Rate of deterioration at 12 Months [c] 95% CI	73.2 [67.1 , 78.4]	63.8 [55.9 , 70.7]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Physical Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c]	60.9	57.2	
95% CI	[52.9 , 68.0]	[46.3 , 66.7]	
Rate of deterioration at 24 Months [c]	56.7	47.7	
95% CI	[47.3 , 65.1]	[28.0 , 64.9]	
Rate of deterioration at 36 Months [c]	56.7	47.7	
95% CI	[47.3 , 65.1]	[28.0 , 64.9]	
Rate of deterioration at 48 Months [c]	56.7	47.7	
95% CI	[47.3 , 65.1]	[28.0 , 64.9]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Role Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	94 (36.0)	104 (39.5)	
Stratified Log-rank p-value [a]			0.0143
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.7028 [0.5292 , 0.9333]
Median time to deterioration (months) [b] 95% CI	NE [16.4 , NE]	13.8 [10.0 , 20.5]	
Rate of deterioration at 3 Months [c] 95% CI	80.5 [75.0 , 84.9]	76.4 [70.5 , 81.2]	
Rate of deterioration at 6 Months [c] 95% CI	74.7 [68.8 , 79.6]	67.0 [60.5 , 72.7]	
Rate of deterioration at 9 Months [c] 95% CI	71.6 [65.5 , 76.8]	59.2 [52.1 , 65.7]	
Rate of deterioration at 12 Months [c] 95% CI	65.8 [59.3 , 71.6]	51.4 [43.6 , 58.7]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Role Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	56.8 [49.2 , 63.7]	42.8 [32.4 , 52.8]	
Rate of deterioration at 24 Months [c] 95% CI	54.8 [46.5 , 62.4]	29.3 [13.9 , 46.7]	
Rate of deterioration at 36 Months [c] 95% CI	54.8 [46.5 , 62.4]	29.3 [13.9 , 46.7]	
Rate of deterioration at 48 Months [c] 95% CI	54.8 [46.5 , 62.4]	29.3 [13.9 , 46.7]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Emotional Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	80 (30.7)	67 (25.5)	
Stratified Log-rank p-value [a]			0.2032
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.8045 [0.5758 , 1.1239]
Median time to deterioration (months) [b] 95% CI	25.6 [19.4 , NE]	NE [15.2 , NE]	
Rate of deterioration at 3 Months [c] 95% CI	89.6 [85.1 , 92.8]	88.4 [83.6 , 91.8]	
Rate of deterioration at 6 Months [c] 95% CI	85.1 [80.0 , 89.0]	82.8 [77.3 , 87.1]	
Rate of deterioration at 9 Months [c] 95% CI	78.9 [73.2 , 83.6]	74.3 [67.4 , 79.9]	
Rate of deterioration at 12 Months [c] 95% CI	74.2 [67.9 , 79.4]	68.0 [60.1 , 74.6]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Emotional Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c]	62.5	56.0	
95% CI	[54.6 , 69.4]	[45.3 , 65.5]	
Rate of deterioration at 24 Months [c]	56.6	56.0	
95% CI	[46.7 , 65.3]	[45.3 , 65.5]	
Rate of deterioration at 36 Months [c]	21.2	56.0	
95% CI	[1.7 , 55.6]	[45.3 , 65.5]	
Rate of deterioration at 48 Months [c]	21.2	56.0	
95% CI	[1.7 , 55.6]	[45.3 , 65.5]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Cognitive Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	97 (37.2)	104 (39.5)	
Stratified Log-rank p-value [a]			0.0016
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.6344 [0.4775 , 0.8428]
Median time to deterioration (months) [b] 95% CI	19.6 [15.4 , NE]	14.1 [10.1 , 20.7]	
Rate of deterioration at 3 Months [c] 95% CI	87.1 [82.3 , 90.7]	76.9 [71.1 , 81.7]	
Rate of deterioration at 6 Months [c] 95% CI	77.6 [71.9 , 82.4]	65.9 [59.4 , 71.6]	
Rate of deterioration at 9 Months [c] 95% CI	71.8 [65.6 , 77.0]	60.6 [53.7 , 66.9]	
Rate of deterioration at 12 Months [c] 95% CI	66.8 [60.3 , 72.5]	53.7 [46.0 , 60.8]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Cognitive Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c]	56.0	40.5	
95% CI	[48.2 , 63.0]	[29.1 , 51.6]	
Rate of deterioration at 24 Months [c]	44.0	27.8	
95% CI	[32.9 , 54.6]	[12.9 , 44.9]	
Rate of deterioration at 36 Months [c]	44.0	27.8	
95% CI	[32.9 , 54.6]	[12.9 , 44.9]	
Rate of deterioration at 48 Months [c]	44.0	27.8	
95% CI	[32.9 , 54.6]	[12.9 , 44.9]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Social Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	106 (40.6)	96 (36.5)	
Stratified Log-rank p-value [a]			0.3230
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.8689 [0.6558 , 1.1512]
Median time to deterioration (months) [b] 95% CI	18.2 [15.1 , NE]	15.2 [11.7 , NE]	
Rate of deterioration at 3 Months [c] 95% CI	78.7 [73.1 , 83.3]	79.3 [73.6 , 83.9]	
Rate of deterioration at 6 Months [c] 95% CI	70.0 [63.8 , 75.3]	71.0 [64.6 , 76.4]	
Rate of deterioration at 9 Months [c] 95% CI	66.0 [59.7 , 71.6]	63.1 [56.1 , 69.3]	
Rate of deterioration at 12 Months [c] 95% CI	62.9 [56.4 , 68.7]	53.8 [45.6 , 61.2]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Functional Scales/Social Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	50.3 [42.2 , 57.8]	44.6 [34.5 , 54.1]	
Rate of deterioration at 24 Months [c] 95% CI	46.6 [37.6 , 55.0]	44.6 [34.5 , 54.1]	
Rate of deterioration at 36 Months [c] 95% CI	46.6 [37.6 , 55.0]	44.6 [34.5 , 54.1]	
Rate of deterioration at 48 Months [c] 95% CI	46.6 [37.6 , 55.0]	44.6 [34.5 , 54.1]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Symptom Scales/Fatigue

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	119 (45.6)	119 (45.2)	
Stratified Log-rank p-value [a]			0.0579
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.7802 [0.6021 , 1.0109]
Median time to deterioration (months) [b] 95% CI	16.0 [13.1 , 20.7]	11.3 [6.9 , 16.7]	
Rate of deterioration at 3 Months [c] 95% CI	71.3 [65.3 , 76.5]	69.0 [62.8 , 74.4]	
Rate of deterioration at 6 Months [c] 95% CI	63.4 [57.1 , 69.1]	58.0 [51.4 , 64.0]	
Rate of deterioration at 9 Months [c] 95% CI	60.7 [54.3 , 66.5]	51.7 [44.7 , 58.2]	
Rate of deterioration at 12 Months [c] 95% CI	58.6 [52.0 , 64.5]	46.6 [39.0 , 53.8]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Symptom Scales/Fatigue

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	46.7 [38.9 , 54.1]	40.7 [31.6 , 49.7]	
Rate of deterioration at 24 Months [c] 95% CI	33.1 [20.3 , 46.5]	35.6 [23.7 , 47.8]	
Rate of deterioration at 36 Months [c] 95% CI	33.1 [20.3 , 46.5]	35.6 [23.7 , 47.8]	
Rate of deterioration at 48 Months [c] 95% CI	33.1 [20.3 , 46.5]	35.6 [23.7 , 47.8]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Symptom Scales/Nausea and Vomiting

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	145 (55.6)	72 (27.4)	
Stratified Log-rank p-value [a]			<.0001
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			2.2169
95% CI			[1.6684 , 2.9458]
Median time to deterioration (months) [b]	7.9	NE	
95% CI	[4.4 , 12.5]	[NE , NE]	
Rate of deterioration at 3 Months [c]	62.1	86.4	
95% CI	[55.8 , 67.8]	[81.4 , 90.1]	
Rate of deterioration at 6 Months [c]	53.2	78.7	
95% CI	[46.8 , 59.2]	[72.7 , 83.5]	
Rate of deterioration at 9 Months [c]	46.6	71.3	
95% CI	[40.2 , 52.7]	[64.5 , 77.1]	
Rate of deterioration at 12 Months [c]	44.5	63.1	
95% CI	[38.2 , 50.7]	[55.2 , 70.0]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Symptom Scales/Nausea and Vomiting

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c]	39.1	62.0	
95% CI	[32.1 , 46.0]	[53.9 , 69.0]	
Rate of deterioration at 24 Months [c]	31.2	62.0	
95% CI	[21.0 , 42.0]	[53.9 , 69.0]	
Rate of deterioration at 36 Months [c]	31.2	62.0	
95% CI	[21.0 , 42.0]	[53.9 , 69.0]	
Rate of deterioration at 48 Months [c]	31.2	62.0	
95% CI	[21.0 , 42.0]	[53.9 , 69.0]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Symptom Scales/Pain

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	103 (39.5)	93 (35.4)	
Stratified Log-rank p-value [a]			0.3762
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.8811 [0.6631 , 1.1708]
Median time to deterioration (months) [b] 95% CI	18.5 [16.4 , NE]	21.0 [10.7 , NE]	
Rate of deterioration at 3 Months [c] 95% CI	81.2 [75.8 , 85.6]	80.1 [74.5 , 84.7]	
Rate of deterioration at 6 Months [c] 95% CI	72.2 [66.2 , 77.4]	72.1 [65.8 , 77.4]	
Rate of deterioration at 9 Months [c] 95% CI	67.7 [61.4 , 73.2]	62.8 [55.7 , 69.1]	
Rate of deterioration at 12 Months [c] 95% CI	60.8 [54.1 , 66.8]	54.5 [46.5 , 61.7]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Symptom Scales/Pain

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	53.4 [45.5 , 60.6]	51.5 [43.0 , 59.4]	
Rate of deterioration at 24 Months [c] 95% CI	49.7 [40.8 , 58.0]	42.9 [26.1 , 58.7]	
Rate of deterioration at 36 Months [c] 95% CI	44.2 [31.2 , 56.3]	42.9 [26.1 , 58.7]	
Rate of deterioration at 48 Months [c] 95% CI	44.2 [31.2 , 56.3]	42.9 [26.1 , 58.7]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Dyspnoea

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	69 (26.4)	64 (24.3)	
Stratified Log-rank p-value [a]			0.1822
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			0.7881
95% CI			[0.5545 , 1.1201]
Median time to deterioration (months) [b]	NE	20.5	
95% CI	[NE , NE]	[16.1 , NE]	
Rate of deterioration at 3 Months [c]	88.4	87.9	
95% CI	[83.8 , 91.8]	[83.0 , 91.4]	
Rate of deterioration at 6 Months [c]	81.9	81.9	
95% CI	[76.5 , 86.2]	[76.3 , 86.3]	
Rate of deterioration at 9 Months [c]	79.7	76.0	
95% CI	[74.1 , 84.2]	[69.6 , 81.3]	
Rate of deterioration at 12 Months [c]	77.1	72.2	
95% CI	[71.2 , 82.0]	[64.8 , 78.2]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Dyspnoea

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	65.7 [57.3 , 72.8]	58.7 [46.6 , 68.9]	
Rate of deterioration at 24 Months [c] 95% CI	62.2 [52.8 , 70.2]	48.7 [32.1 , 63.4]	
Rate of deterioration at 36 Months [c] 95% CI	62.2 [52.8 , 70.2]	48.7 [32.1 , 63.4]	
Rate of deterioration at 48 Months [c] 95% CI	62.2 [52.8 , 70.2]	48.7 [32.1 , 63.4]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Insomnia

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	70 (26.8)	77 (29.3)	
Stratified Log-rank p-value [a]			0.0116
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			0.6545
95% CI			[0.4693 , 0.9129]
Median time to deterioration (months) [b]	NE	NE	
95% CI	[NE , NE]	[NE , NE]	
Rate of deterioration at 3 Months [c]	87.2	83.8	
95% CI	[82.4 , 90.8]	[78.6 , 87.9]	
Rate of deterioration at 6 Months [c]	83.2	74.0	
95% CI	[77.9 , 87.3]	[67.8 , 79.1]	
Rate of deterioration at 9 Months [c]	78.7	69.0	
95% CI	[73.0 , 83.3]	[62.2 , 74.7]	
Rate of deterioration at 12 Months [c]	74.3	64.4	
95% CI	[68.1 , 79.4]	[57.0 , 71.0]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Insomnia

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c]	69.8	60.6	
95% CI	[63.0 , 75.7]	[52.2 , 67.9]	
Rate of deterioration at 24 Months [c]	63.4	60.6	
95% CI	[53.5 , 71.6]	[52.2 , 67.9]	
Rate of deterioration at 36 Months [c]	63.4	60.6	
95% CI	[53.5 , 71.6]	[52.2 , 67.9]	
Rate of deterioration at 48 Months [c]	63.4	60.6	
95% CI	[53.5 , 71.6]	[52.2 , 67.9]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Appetite Loss

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	119 (45.6)	78 (29.7)	
Stratified Log-rank p-value [a]			0.0100
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			1.4637
95% CI			[1.0963 , 1.9542]
Median time to deterioration (months) [b]	16.4	19.1	
95% CI	[9.8 , NE]	[13.8 , NE]	
Rate of deterioration at 3 Months [c]	68.5	86.3	
95% CI	[62.3 , 73.8]	[81.3 , 90.1]	
Rate of deterioration at 6 Months [c]	58.9	77.0	
95% CI	[52.5 , 64.8]	[71.0 , 82.0]	
Rate of deterioration at 9 Months [c]	56.7	70.9	
95% CI	[50.2 , 62.6]	[64.1 , 76.6]	
Rate of deterioration at 12 Months [c]	55.1	64.3	
95% CI	[48.6 , 61.1]	[56.4 , 71.1]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Appetite Loss

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	49.2 [42.0 , 56.0]	52.8 [41.6 , 62.9]	
Rate of deterioration at 24 Months [c] 95% CI	44.7 [35.8 , 53.2]	41.1 [24.7 , 56.9]	
Rate of deterioration at 36 Months [c] 95% CI	44.7 [35.8 , 53.2]	41.1 [24.7 , 56.9]	
Rate of deterioration at 48 Months [c] 95% CI	44.7 [35.8 , 53.2]	41.1 [24.7 , 56.9]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Constipation

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	114 (43.7)	84 (31.9)	
Stratified Log-rank p-value [a]			0.3462
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			1.1457
95% CI			[0.8613 , 1.5240]
Median time to deterioration (months) [b]	16.5	NE	
95% CI	[13.1 , 22.6]	[NE , NE]	
Rate of deterioration at 3 Months [c]	79.2	80.3	
95% CI	[73.7 , 83.8]	[74.8 , 84.8]	
Rate of deterioration at 6 Months [c]	68.8	69.8	
95% CI	[62.6 , 74.2]	[63.4 , 75.3]	
Rate of deterioration at 9 Months [c]	62.9	64.4	
95% CI	[56.4 , 68.6]	[57.5 , 70.4]	
Rate of deterioration at 12 Months [c]	58.6	60.9	
95% CI	[52.0 , 64.7]	[53.5 , 67.5]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Constipation

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	46.2 [38.2 , 53.9]	59.5 [51.8 , 66.4]	
Rate of deterioration at 24 Months [c] 95% CI	36.0 [22.4 , 49.7]	59.5 [51.8 , 66.4]	
Rate of deterioration at 36 Months [c] 95% CI	36.0 [22.4 , 49.7]	59.5 [51.8 , 66.4]	
Rate of deterioration at 48 Months [c] 95% CI	36.0 [22.4 , 49.7]	59.5 [51.8 , 66.4]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Diarrhea

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	49 (18.8)	36 (13.7)	
Stratified Log-rank p-value [a]			0.6458
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			1.1080
95% CI			[0.7170 , 1.7121]
Median time to deterioration (months) [b]	NE	NE	
95% CI	[NE , NE]	[NE , NE]	
Rate of deterioration at 3 Months [c]	89.2	95.4	
95% CI	[84.7 , 92.5]	[91.8 , 97.4]	
Rate of deterioration at 6 Months [c]	85.9	91.9	
95% CI	[81.0 , 89.7]	[87.5 , 94.9]	
Rate of deterioration at 9 Months [c]	85.5	86.0	
95% CI	[80.5 , 89.3]	[80.2 , 90.2]	
Rate of deterioration at 12 Months [c]	80.7	82.1	
95% CI	[75.0 , 85.3]	[75.1 , 87.3]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Diarrhea

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c]	77.7	73.0	
95% CI	[71.2 , 82.9]	[61.0 , 81.9]	
Rate of deterioration at 24 Months [c]	77.7	73.0	
95% CI	[71.2 , 82.9]	[61.0 , 81.9]	
Rate of deterioration at 36 Months [c]	77.7	73.0	
95% CI	[71.2 , 82.9]	[61.0 , 81.9]	
Rate of deterioration at 48 Months [c]	77.7	73.0	
95% CI	[71.2 , 82.9]	[61.0 , 81.9]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Financial Difficulties

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	58 (22.2)	64 (24.3)	
Stratified Log-rank p-value [a]			0.0214
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.6552 [0.4553 , 0.9428]
Median time to deterioration (months) [b] 95% CI	NE [24.0 , NE]	NE [17.8 , NE]	
Rate of deterioration at 3 Months [c] 95% CI	90.8 [86.5 , 93.8]	89.6 [85.1 , 92.9]	
Rate of deterioration at 6 Months [c] 95% CI	85.5 [80.5 , 89.3]	83.5 [78.1 , 87.8]	
Rate of deterioration at 9 Months [c] 95% CI	82.9 [77.6 , 87.1]	75.6 [69.0 , 81.0]	
Rate of deterioration at 12 Months [c] 95% CI	78.1 [72.2 , 83.0]	67.4 [59.4 , 74.2]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 57 Analysis of time to definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

Common Symptoms/Financial Difficulties

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	75.2 [68.7 , 80.5]	58.8 [47.5 , 68.5]	
Rate of deterioration at 24 Months [c] 95% CI	61.6 [43.6 , 75.4]	58.8 [47.5 , 68.5]	
Rate of deterioration at 36 Months [c] 95% CI	61.6 [43.6 , 75.4]	58.8 [47.5 , 68.5]	
Rate of deterioration at 48 Months [c] 95% CI	61.6 [43.6 , 75.4]	58.8 [47.5 , 68.5]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

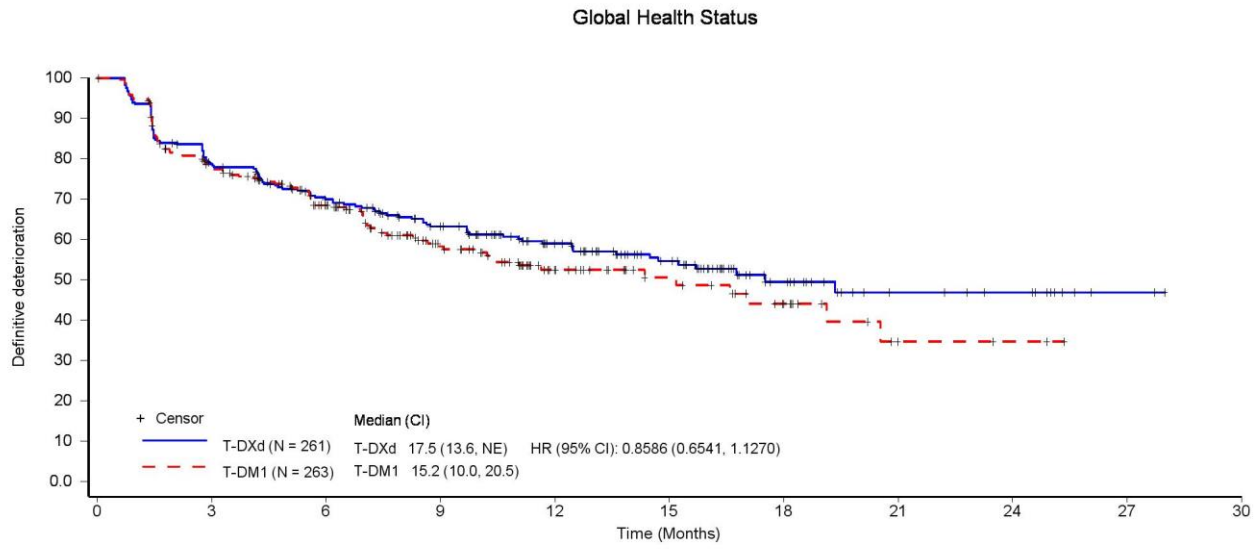
[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

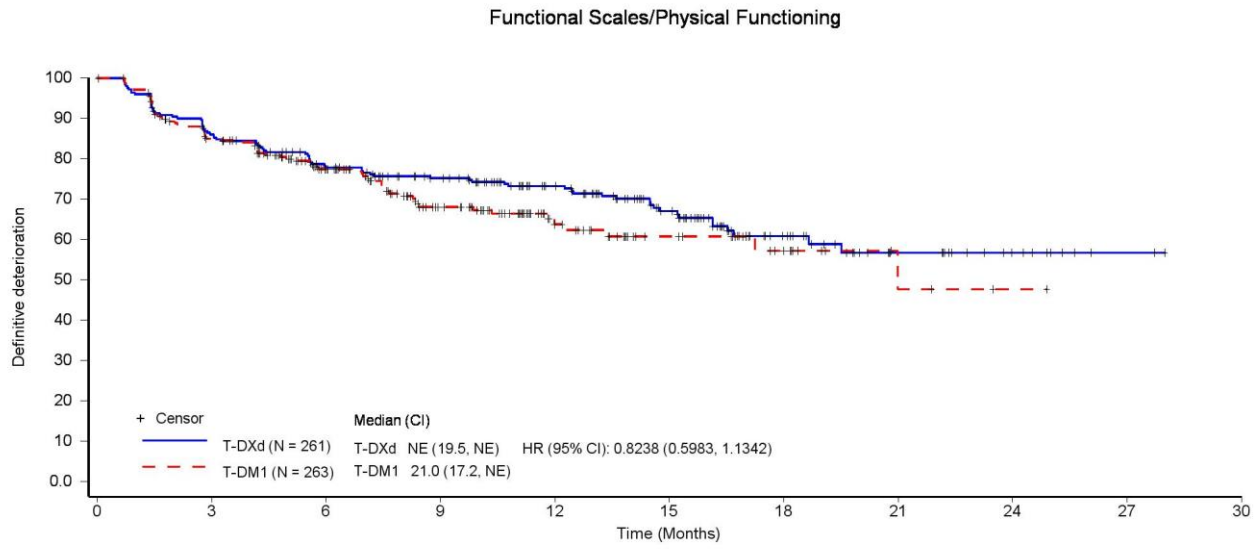


Patients still at risk:

T-DXd (N = 261)	261	194	162	132	96	64	26	13	10	2	0
T-DM1 (N = 263)	263	179	133	81	44	26	16	5	2	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

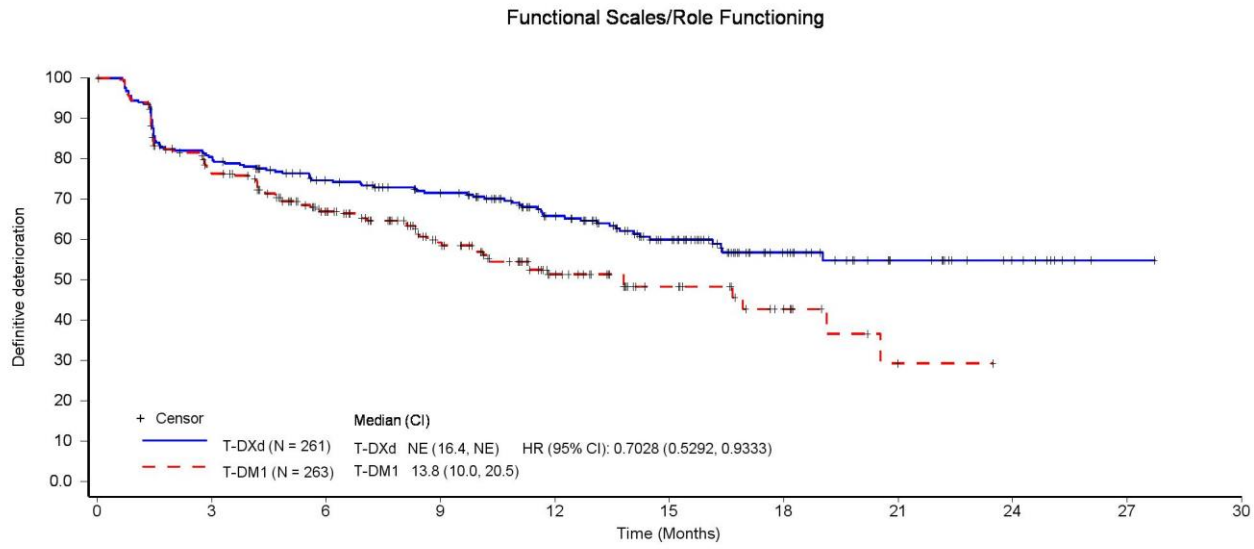


Patients still at risk:

T-DXd (N = 261)	261	216	183	161	126	84	36	18	9	2	0
T-DM1 (N = 263)	263	194	146	91	46	26	14	5	1	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

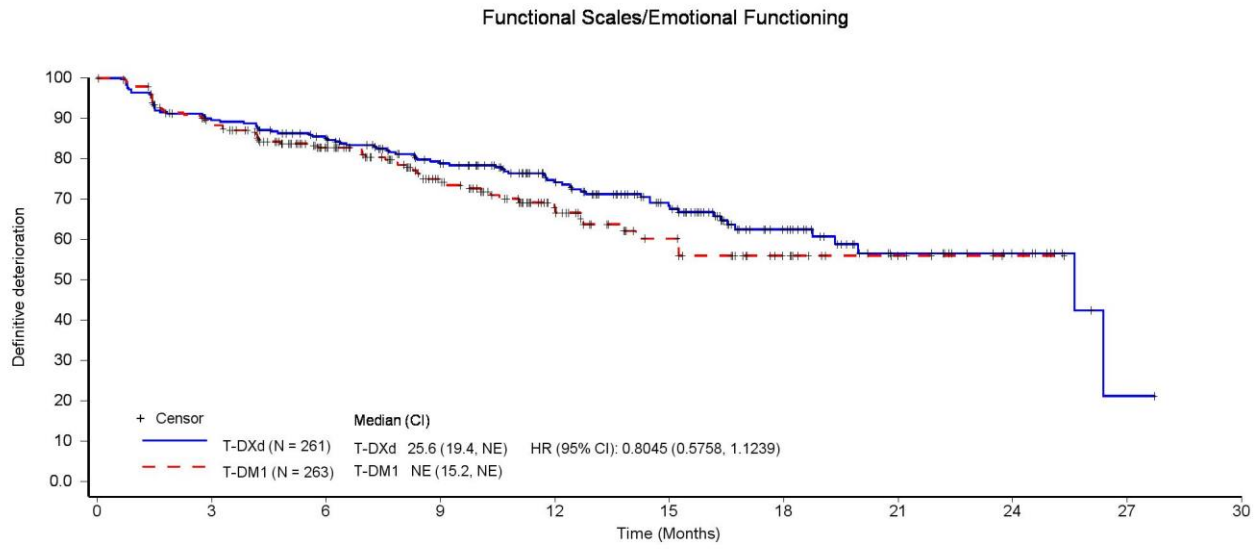


Patients still at risk:

T-DXd (N = 261)	261	201	172	154	116	77	36	19	10	1	0
T-DM1 (N = 263)	263	175	127	82	45	23	12	3	0	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

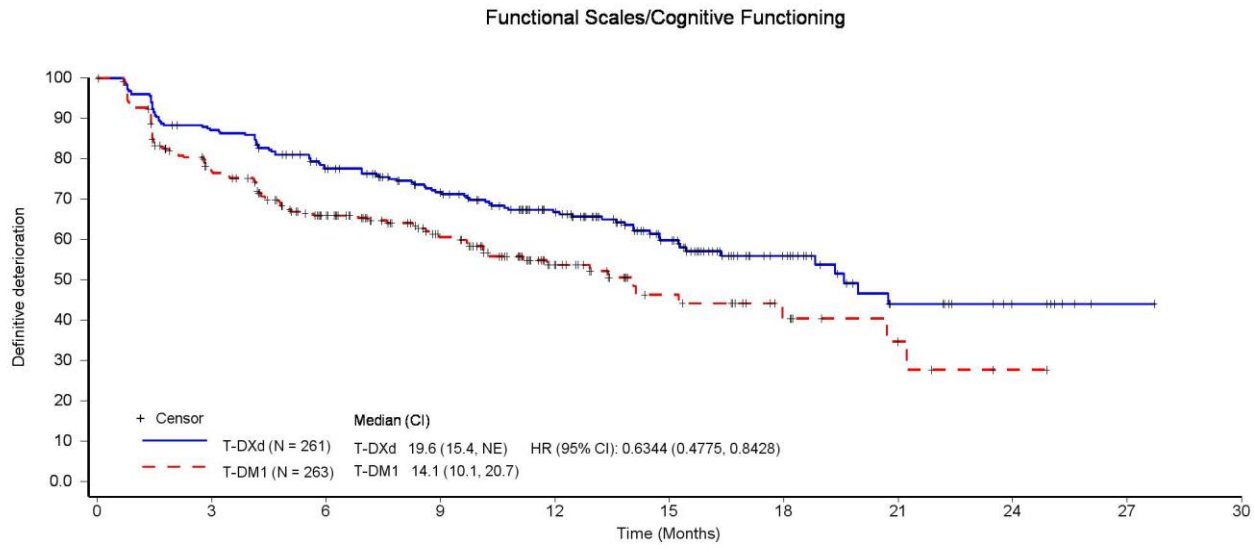


Patients still at risk:

T-DXd (N = 261)	261	223	202	171	132	90	43	21	12	1	0
T-DM1 (N = 263)	263	202	153	98	54	30	16	7	1	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

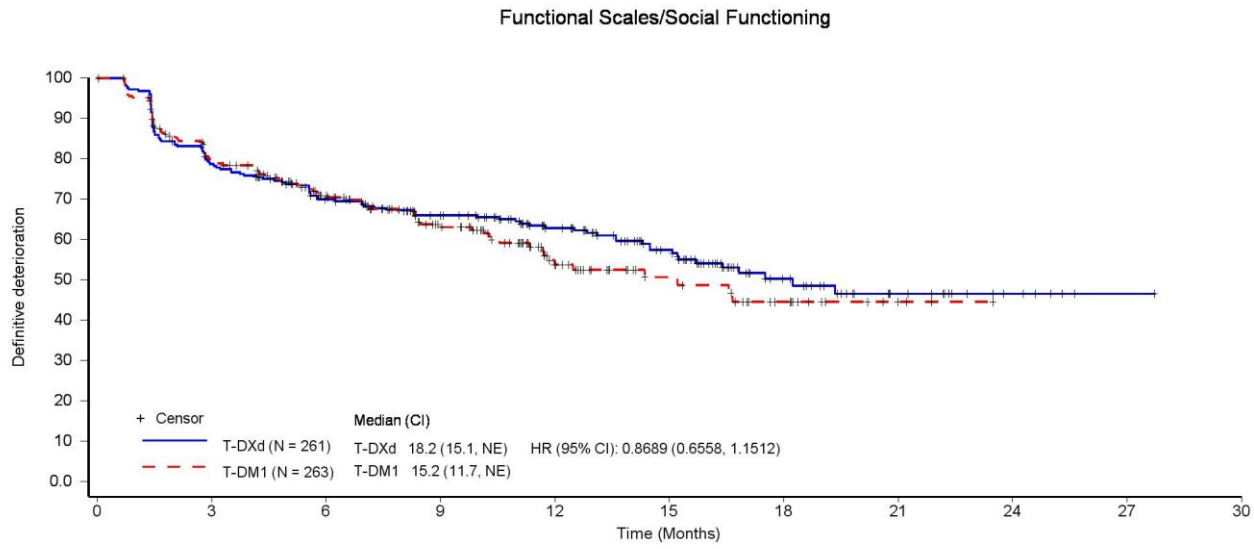


Patients still at risk:

T-DXd (N = 261)	261	215	182	153	119	74	33	15	8	1	0
T-DM1 (N = 263)	263	177	126	83	42	21	11	5	1	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

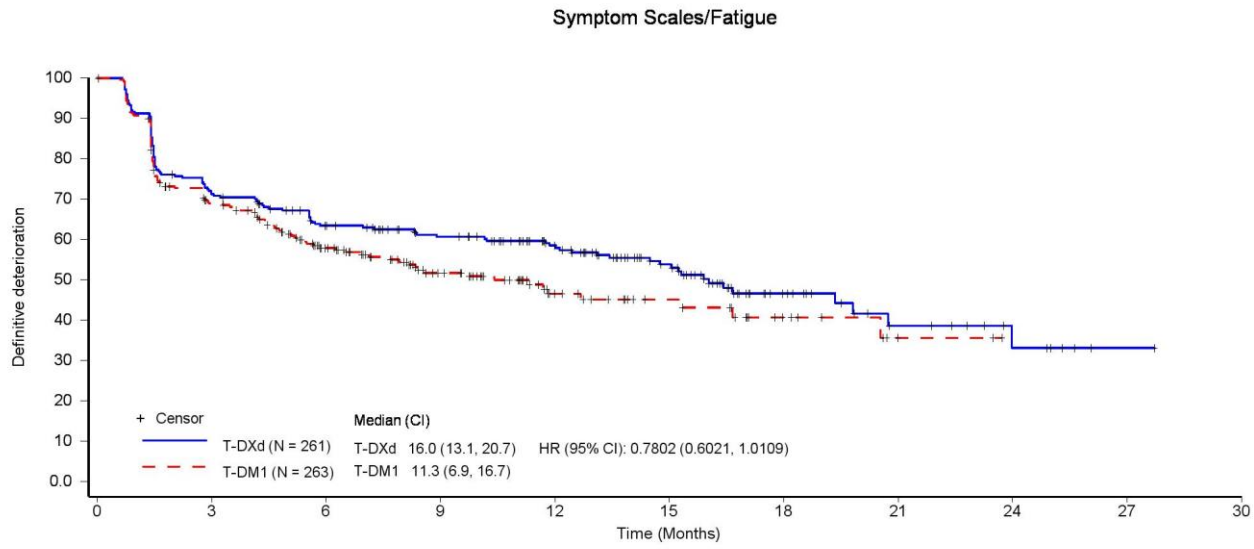


Patients still at risk:

T-DXd (N = 261)	261	195	162	143	110	74	31	15	6	1	0
T-DM1 (N = 263)	263	183	139	91	46	26	15	5	0	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

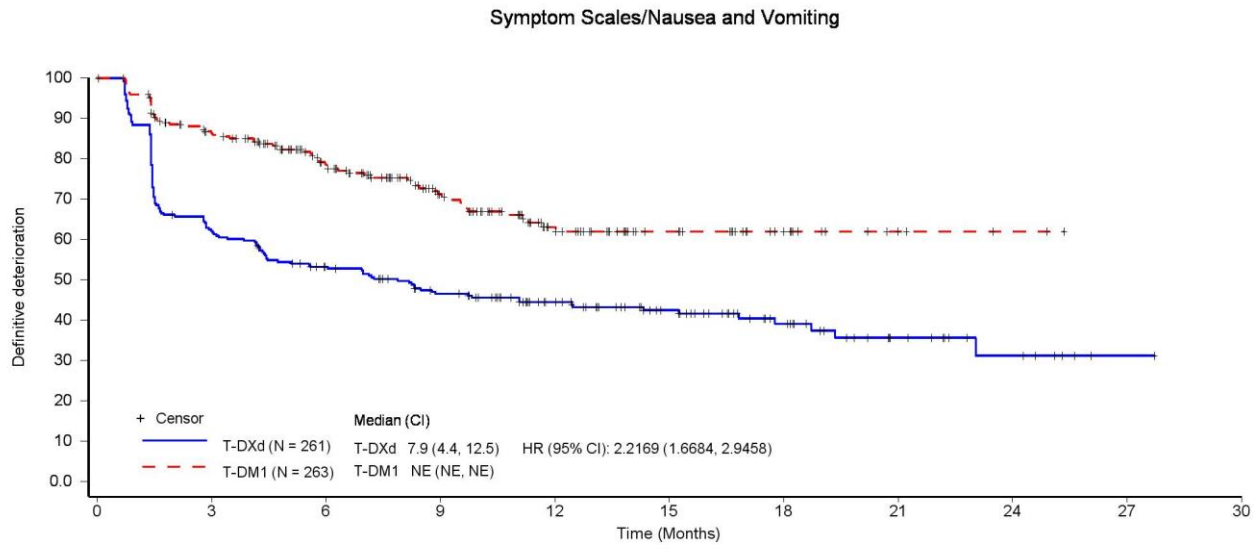


Patients still at risk:

T-DXd (N = 261)	261	178	148	128	101	65	24	12	6	1	0
T-DM1 (N = 263)	263	160	111	68	35	22	11	4	0	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

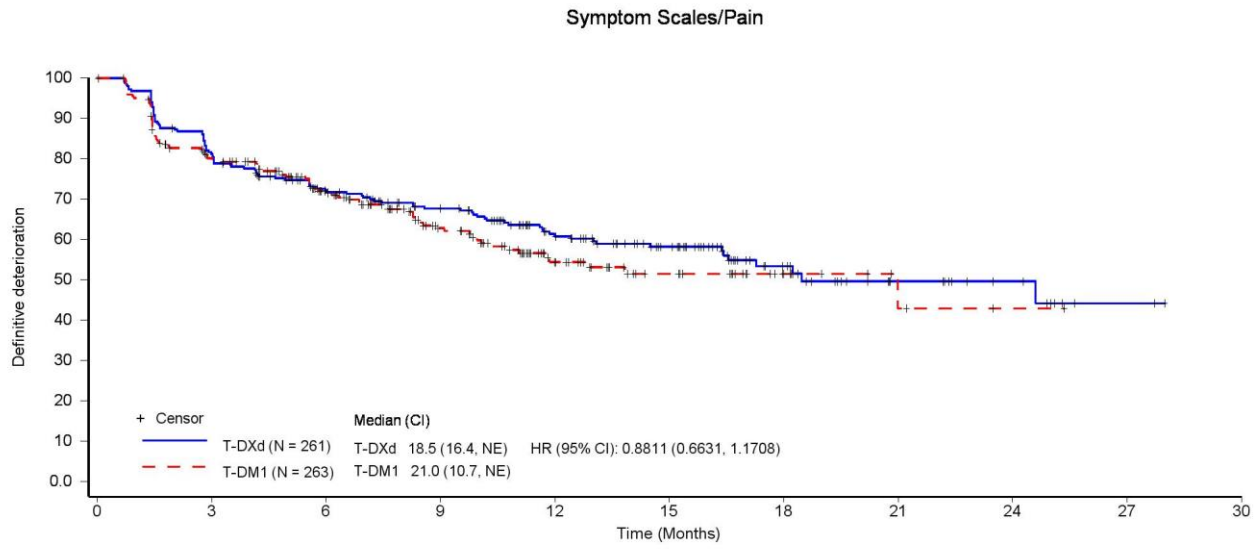


Patients still at risk:

T-DXd (N = 261)	261	155	124	99	74	50	29	14	7	1	0
T-DM1 (N = 263)	263	197	149	99	55	29	16	6	2	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

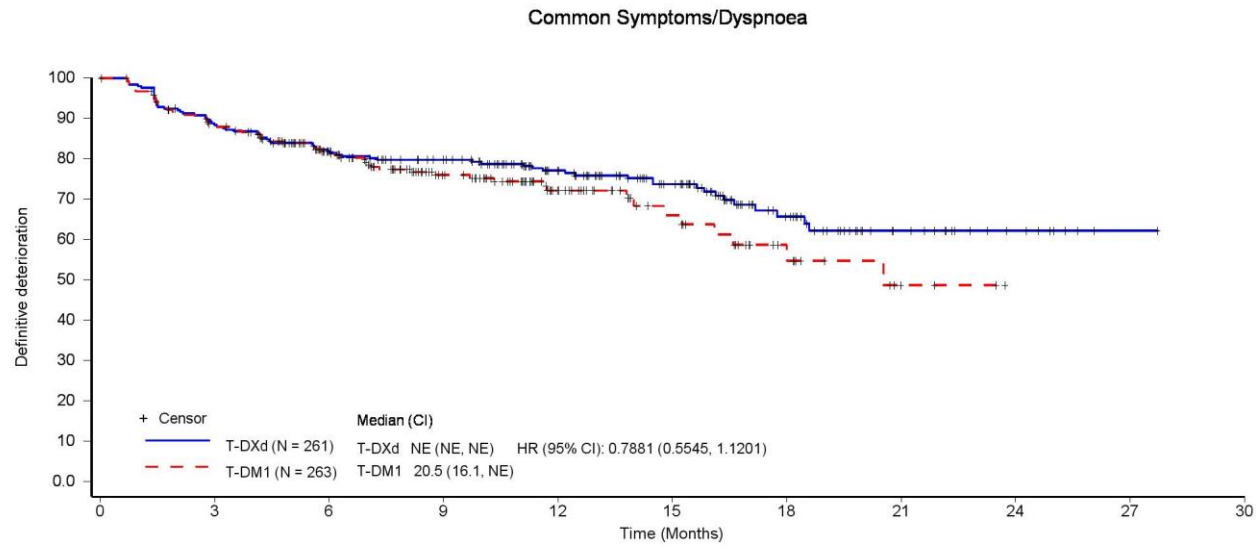


Patients still at risk:

T-DXd (N = 261)	261	203	166	143	105	75	32	16	10	2	0
T-DM1 (N = 263)	263	184	136	88	47	27	14	5	1	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

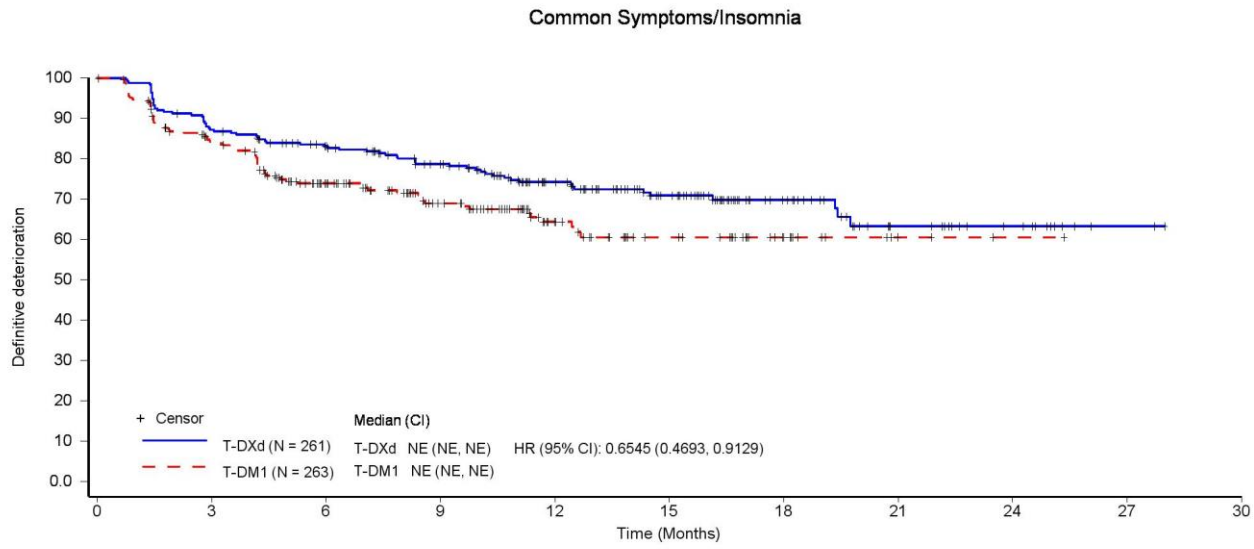


Patients still at risk:

T-DXd (N = 261)	261	221	191	172	132	93	43	20	9	1	0
T-DM1 (N = 263)	263	203	157	103	56	29	15	5	0	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

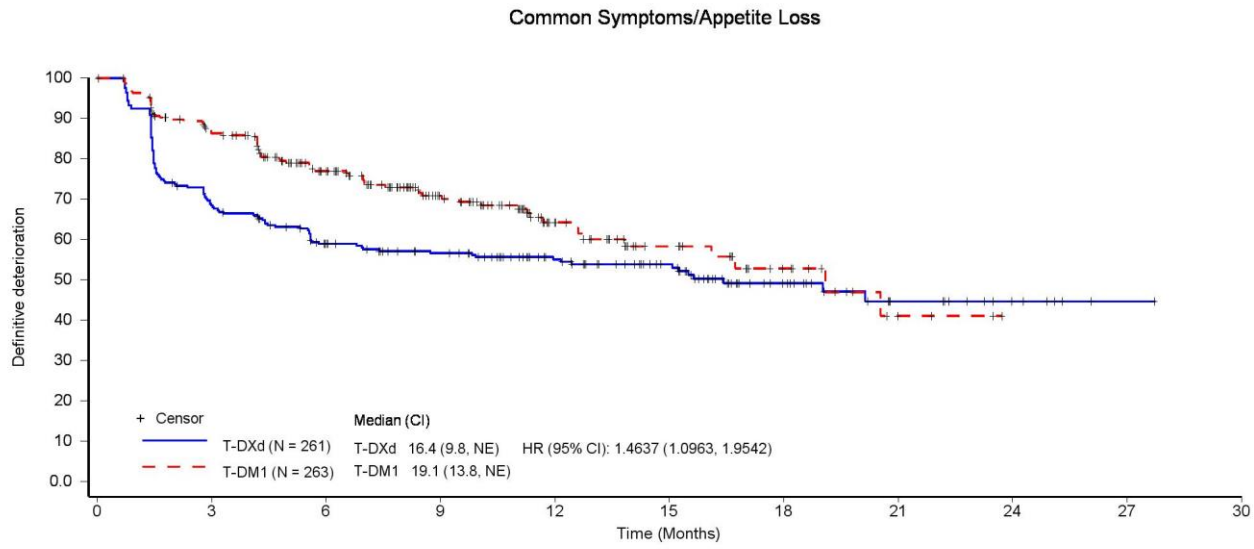


Patients still at risk:

T-DXd (N = 261)	261	218	194	170	129	85	41	21	13	2	0
T-DM1 (N = 263)	263	192	143	99	52	29	15	5	1	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

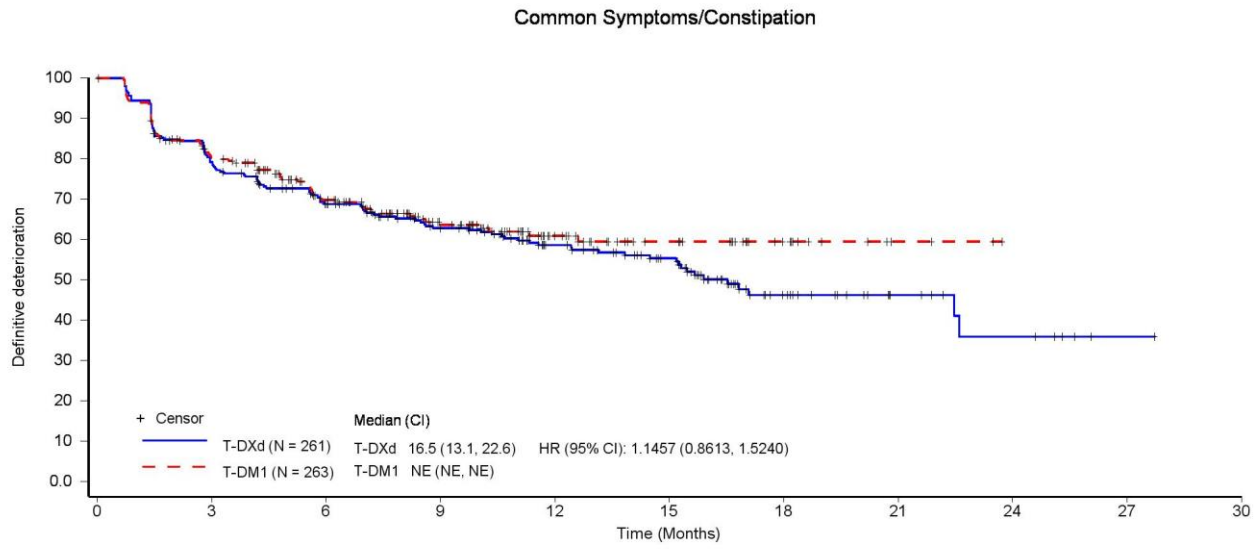


Patients still at risk:

T-DXd (N = 261)	261	170	135	118	92	66	30	14	6	1	0
T-DM1 (N = 263)	263	198	147	93	48	26	13	5	0	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

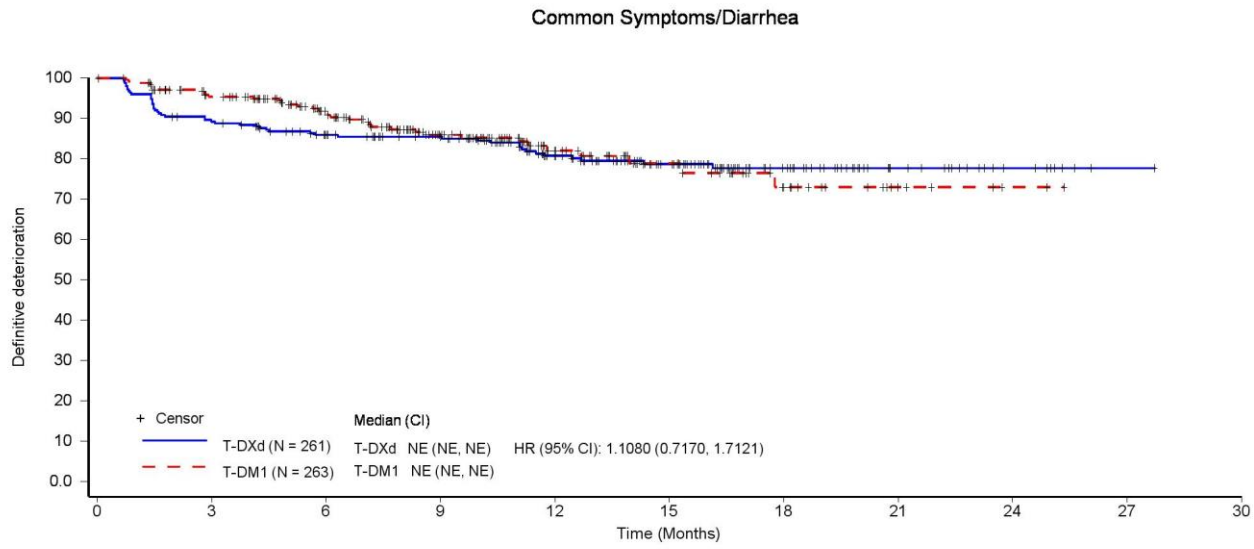


Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 261)	261	197	158	132	98	71	27	12	7	1	0
T-DM1 (N = 263)	263	187	134	88	49	28	14	5	0	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set

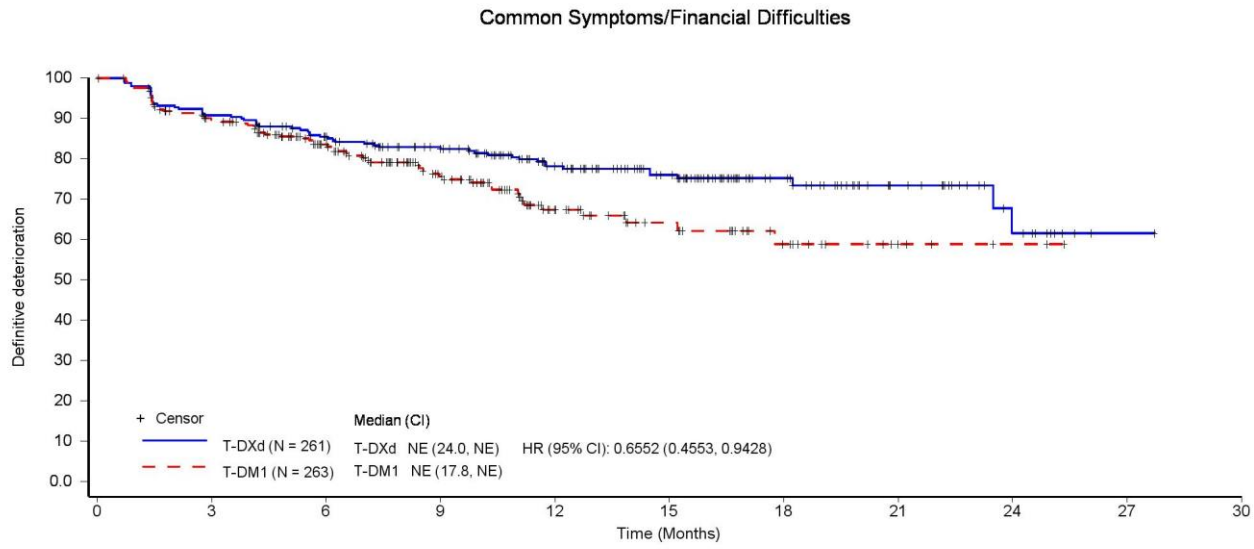


Patients still at risk:

T-DXd (N = 261)	261	222	199	183	138	95	43	21	10	1	0
T-DM1 (N = 263)	263	217	170	117	65	36	20	8	2	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 36 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-C30 – Threshold 10 – Full Analysis Set



Patients still at risk:

T-DXd (N = 261)	261	227	201	177	132	95	44	24	10	1	0
T-DM1 (N = 263)	263	204	158	105	52	31	17	7	2	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Functional Scales/Body Image	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	83 (31.8)	57 (21.7)	
Stratified Log-rank p-value [a]			0.4838
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			1.1321 [0.8030 , 1.5963]
Median time to deterioration (months) [b] 95% CI	23.7 [19.4 , NE]	25.4 [NE , NE]	
Rate of deterioration at 3 Months [c] 95% CI	84.9 [79.8 , 88.8]	87.5 [82.7 , 91.1]	
Rate of deterioration at 6 Months [c] 95% CI	78.3 [72.6 , 82.9]	82.5 [76.8 , 86.9]	
Rate of deterioration at 9 Months [c] 95% CI	74.8 [68.8 , 79.7]	77.2 [70.6 , 82.4]	
Rate of deterioration at 12 Months [c] 95% CI	72.3 [66.1 , 77.5]	71.1 [63.1 , 77.6]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Functional Scales/Body Image

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c]	60.0	67.0	
95% CI	[51.3 , 67.6]	[57.5 , 74.9]	
Rate of deterioration at 24 Months [c]	49.4	67.0	
95% CI	[35.2 , 62.1]	[57.5 , 74.9]	
Rate of deterioration at 36 Months [c]	49.4	0.0	
95% CI	[35.2 , 62.1]	[0.0 , 0.0]	
Rate of deterioration at 48 Months [c]	49.4	0.0	
95% CI	[35.2 , 62.1]	[0.0 , 0.0]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Functional Scales/Sexual Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	57 (21.8)	49 (18.6)	
Stratified Log-rank p-value [a]			0.9282
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			0.9791
95% CI			[0.6660 , 1.4393]
Median time to deterioration (months) [b]	NE	NE	
95% CI	[NE , NE]	[NE , NE]	
Rate of deterioration at 3 Months [c]	84.2	86.8	
95% CI	[79.1 , 88.2]	[81.8 , 90.5]	
Rate of deterioration at 6 Months [c]	81.3	83.6	
95% CI	[75.8 , 85.6]	[78.1 , 87.9]	
Rate of deterioration at 9 Months [c]	78.9	78.9	
95% CI	[73.2 , 83.6]	[72.5 , 84.0]	
Rate of deterioration at 12 Months [c]	77.7	76.4	
95% CI	[71.8 , 82.5]	[69.4 , 81.9]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Functional Scales/Sexual Functioning

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	74.3 [67.1 , 80.2]	71.6 [61.9 , 79.2]	
Rate of deterioration at 24 Months [c] 95% CI	71.9 [63.2 , 78.9]	71.6 [61.9 , 79.2]	
Rate of deterioration at 36 Months [c] 95% CI	71.9 [63.2 , 78.9]	71.6 [61.9 , 79.2]	
Rate of deterioration at 48 Months [c] 95% CI	71.9 [63.2 , 78.9]	71.6 [61.9 , 79.2]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Functional Scales/Sexual Enjoyment

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	16 (6.1)	7 (2.7)	
Stratified Log-rank p-value [a]			0.0406
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			3.1457
95% CI			[1.0127 , 9.7713]
Median time to deterioration (months) [b]	NE	NE	
95% CI	[13.4 , NE]	[18.0 , NE]	
Rate of deterioration at 3 Months [c]	75.6	91.8	
95% CI	[60.2 , 85.6]	[79.6 , 96.8]	
Rate of deterioration at 6 Months [c]	75.6	91.8	
95% CI	[60.2 , 85.6]	[79.6 , 96.8]	
Rate of deterioration at 9 Months [c]	73.3	85.9	
95% CI	[57.7 , 83.8]	[70.7 , 93.5]	
Rate of deterioration at 12 Months [c]	68.0	85.9	
95% CI	[51.9 , 79.7]	[70.7 , 93.5]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Functional Scales/Sexual Enjoyment

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	64.9 [48.4 , 77.3]	71.6 [35.4 , 89.8]	
Rate of deterioration at 24 Months [c] 95% CI	52.0 [24.9 , 73.4]	71.6 [35.4 , 89.8]	
Rate of deterioration at 36 Months [c] 95% CI	52.0 [24.9 , 73.4]	71.6 [35.4 , 89.8]	
Rate of deterioration at 48 Months [c] 95% CI	52.0 [24.9 , 73.4]	71.6 [35.4 , 89.8]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Functional Scales/Future Perspective	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	60 (23.0)	51 (19.4)	
Stratified Log-rank p-value [a]			0.2736
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			0.8058
95% CI			[0.5476 , 1.1857]
Median time to deterioration (months) [b]	NE	NE	
95% CI	[24.3 , NE]	[21.2 , NE]	
Rate of deterioration at 3 Months [c]	89.7	89.6	
95% CI	[85.2 , 92.8]	[85.0 , 92.9]	
Rate of deterioration at 6 Months [c]	87.2	82.9	
95% CI	[82.4 , 90.8]	[77.4 , 87.3]	
Rate of deterioration at 9 Months [c]	83.2	79.7	
95% CI	[77.9 , 87.4]	[73.6 , 84.6]	
Rate of deterioration at 12 Months [c]	80.3	78.0	
95% CI	[74.6 , 84.8]	[71.4 , 83.2]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Functional Scales/Future Perspective

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	74.2 [67.3 , 79.8]	66.0 [52.4 , 76.6]	
Rate of deterioration at 24 Months [c] 95% CI	63.5 [51.1 , 73.6]	52.8 [26.1 , 73.9]	
Rate of deterioration at 36 Months [c] 95% CI	56.5 [38.6 , 71.0]	52.8 [26.1 , 73.9]	
Rate of deterioration at 48 Months [c] 95% CI	56.5 [38.6 , 71.0]	52.8 [26.1 , 73.9]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Symptom Scales/Systemic Therapy Side Effects

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	95 (36.4)	81 (30.8)	
Stratified Log-rank p-value [a]			0.8693
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			0.9766
95% CI			[0.7226 , 1.3200]
Median time to deterioration (months) [b]	NE	16.7	
95% CI	[17.4 , NE]	[13.9 , NE]	
Rate of deterioration at 3 Months [c]	77.0	81.3	
95% CI	[71.2 , 81.7]	[75.8 , 85.7]	
Rate of deterioration at 6 Months [c]	70.8	75.8	
95% CI	[64.7 , 76.0]	[69.8 , 80.8]	
Rate of deterioration at 9 Months [c]	67.3	67.9	
95% CI	[61.0 , 72.8]	[60.9 , 74.0]	
Rate of deterioration at 12 Months [c]	64.7	62.6	
95% CI	[58.3 , 70.4]	[54.6 , 69.6]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Symptom Scales/Systemic Therapy Side Effects

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	57.3 [49.6 , 64.3]	45.8 [33.3 , 57.4]	
Rate of deterioration at 24 Months [c] 95% CI	55.5 [47.2 , 63.1]	45.8 [33.3 , 57.4]	
Rate of deterioration at 36 Months [c] 95% CI	55.5 [47.2 , 63.1]	45.8 [33.3 , 57.4]	
Rate of deterioration at 48 Months [c] 95% CI	55.5 [47.2 , 63.1]	45.8 [33.3 , 57.4]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Symptom Scales/Breast Symptoms

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	33 (12.6)	32 (12.2)	
Stratified Log-rank p-value [a]			0.2313
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.7400 [0.4513 , 1.2135]
Median time to deterioration (months) [b] 95% CI	NE [NE , NE]	NE [NE , NE]	
Rate of deterioration at 3 Months [c] 95% CI	96.0 [92.7 , 97.8]	93.3 [89.3 , 95.8]	
Rate of deterioration at 6 Months [c] 95% CI	92.7 [88.7 , 95.4]	91.3 [86.8 , 94.3]	
Rate of deterioration at 9 Months [c] 95% CI	90.4 [85.9 , 93.6]	88.0 [82.6 , 91.8]	
Rate of deterioration at 12 Months [c] 95% CI	88.9 [84.1 , 92.3]	84.1 [77.3 , 89.0]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Symptom Scales/Breast Symptoms

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	83.8 [77.3 , 88.6]	79.5 [70.8 , 85.8]	
Rate of deterioration at 24 Months [c] 95% CI	81.9 [74.1 , 87.5]	79.5 [70.8 , 85.8]	
Rate of deterioration at 36 Months [c] 95% CI	81.9 [74.1 , 87.5]	79.5 [70.8 , 85.8]	
Rate of deterioration at 48 Months [c] 95% CI	81.9 [74.1 , 87.5]	79.5 [70.8 , 85.8]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Symptom Scales/Arm Symptoms

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	95 (36.4)	104 (39.5)	
Stratified Log-rank p-value [a]			0.0063
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			0.6758
95% CI			[0.5087 , 0.8977]
Median time to deterioration (months) [b]	20.1	18.2	
95% CI	[18.7 , NE]	[8.6 , NE]	
Rate of deterioration at 3 Months [c]	88.4	76.8	
95% CI	[83.8 , 91.8]	[70.9 , 81.6]	
Rate of deterioration at 6 Months [c]	77.3	64.5	
95% CI	[71.5 , 82.0]	[57.9 , 70.3]	
Rate of deterioration at 9 Months [c]	68.3	56.6	
95% CI	[62.0 , 73.9]	[49.5 , 63.0]	
Rate of deterioration at 12 Months [c]	64.7	52.9	
95% CI	[58.1 , 70.5]	[45.4 , 59.9]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Symptom Scales/Arm Symptoms

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	58.6 [51.0 , 65.4]	51.5 [43.7 , 58.8]	
Rate of deterioration at 24 Months [c] 95% CI	48.4 [37.1 , 58.8]	38.7 [22.1 , 54.9]	
Rate of deterioration at 36 Months [c] 95% CI	36.3 [15.7 , 57.4]	19.3 [1.9 , 50.7]	
Rate of deterioration at 48 Months [c] 95% CI	36.3 [15.7 , 57.4]	19.3 [1.9 , 50.7]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Symptom Scales/Upset by Hair Loss

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events			
Deterioration	23 (8.8)	3 (1.1)	
Stratified Log-rank p-value [a]			0.0068
Stratified Cox Proportional Hazard Model [a]			
Hazard Ratio			4.7108
95% CI			[1.3785 , 16.099]
Median time to deterioration (months) [b]	NE	NE	
95% CI	[12.4 , NE]	[NE , NE]	
Rate of deterioration at 3 Months [c]	72.1	94.7	
95% CI	[59.1 , 81.7]	[80.6 , 98.7]	
Rate of deterioration at 6 Months [c]	68.8	94.7	
95% CI	[55.6 , 78.8]	[80.6 , 98.7]	
Rate of deterioration at 9 Months [c]	66.8	90.6	
95% CI	[53.4 , 77.2]	[72.9 , 97.0]	
Rate of deterioration at 12 Months [c]	64.3	90.6	
95% CI	[50.4 , 75.2]	[72.9 , 97.0]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 59 Analysis of time to definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

Symptom Scales/Upset by Hair Loss

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	61.6 [47.3 , 73.1]	90.6 [72.9 , 97.0]	
Rate of deterioration at 24 Months [c] 95% CI	53.9 [34.5 , 69.9]	90.6 [72.9 , 97.0]	
Rate of deterioration at 36 Months [c] 95% CI	53.9 [34.5 , 69.9]	90.6 [72.9 , 97.0]	
Rate of deterioration at 48 Months [c] 95% CI	53.9 [34.5 , 69.9]	90.6 [72.9 , 97.0]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

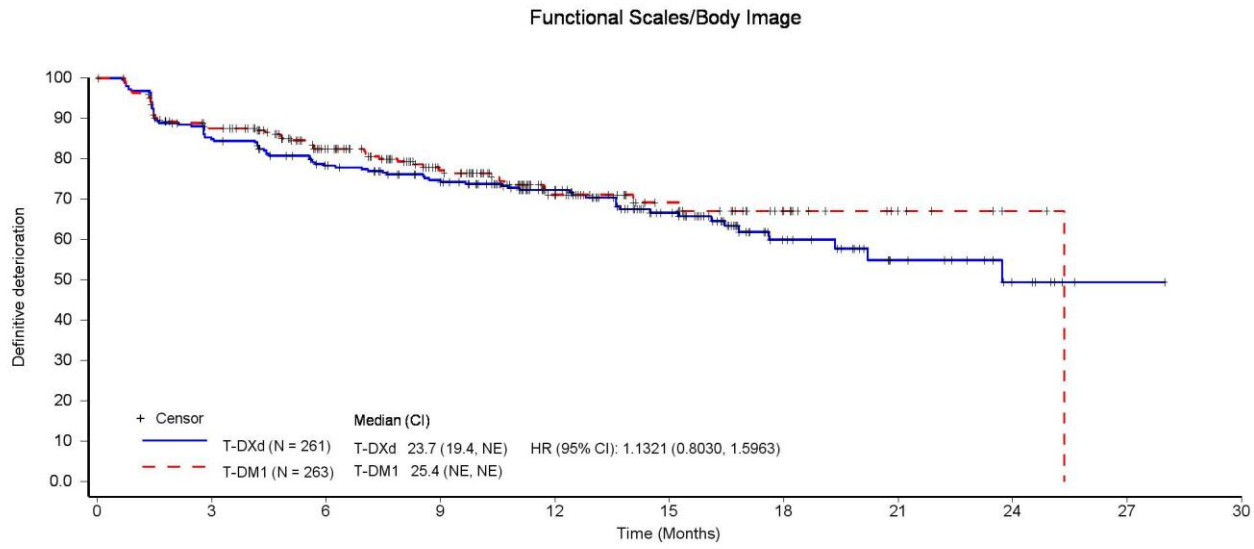
[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Figure 38 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

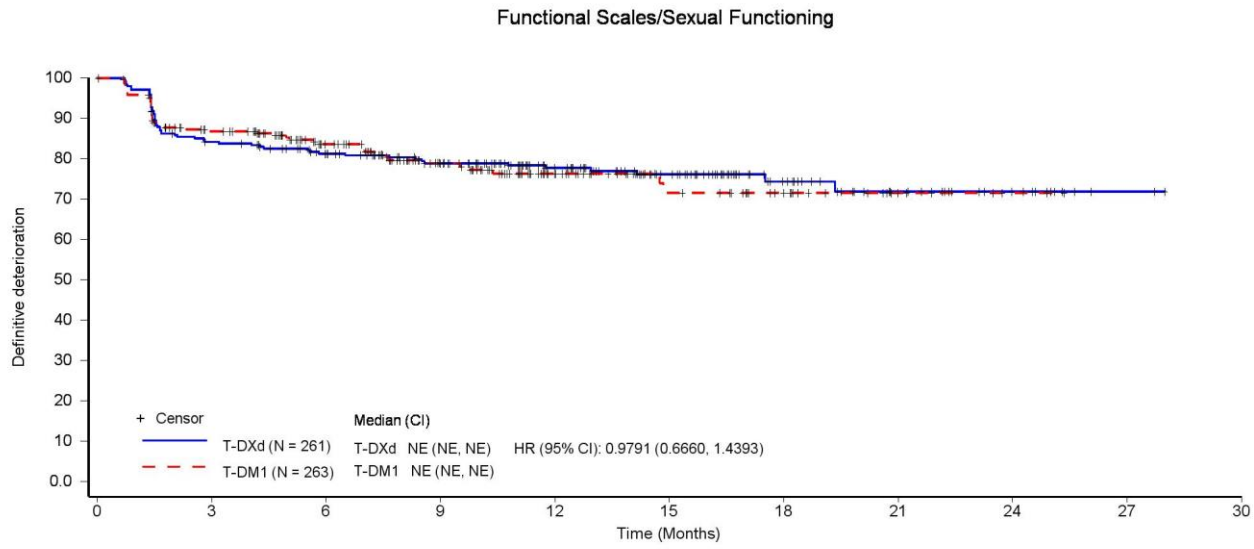


Patients still at risk:

T-DXd (N = 261)	261	212	184	163	121	77	30	16	7	1	0
T-DM1 (N = 263)	263	196	148	101	52	32	18	8	2	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 38 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

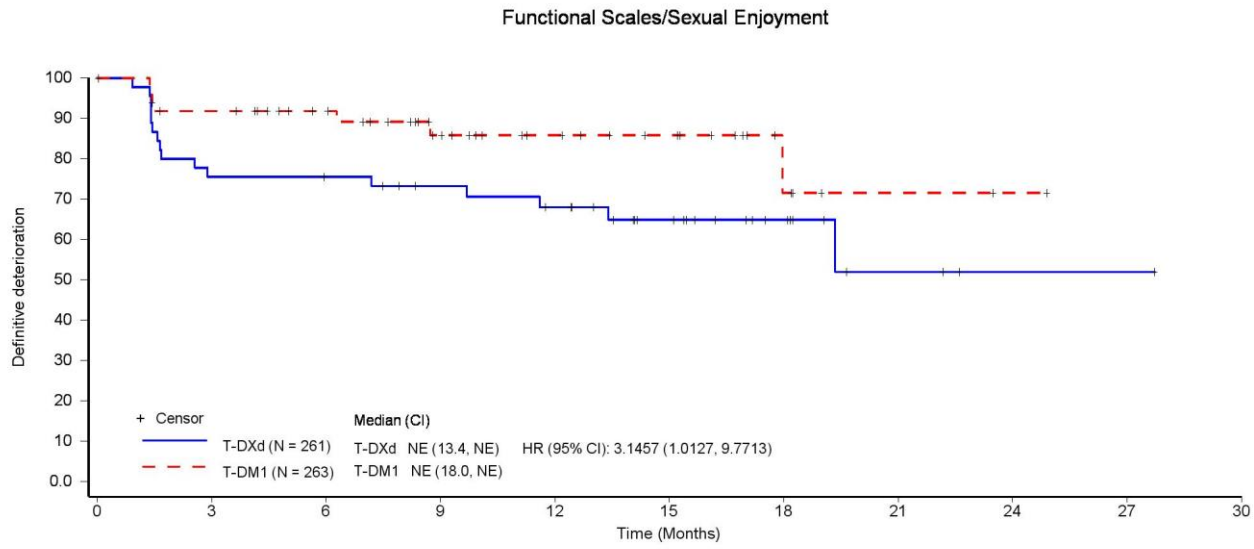


Patients still at risk:

T-DXd (N = 261)	261	206	186	161	119	82	38	23	12	2	0
T-DM1 (N = 263)	263	186	142	98	56	30	19	7	2	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 38 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

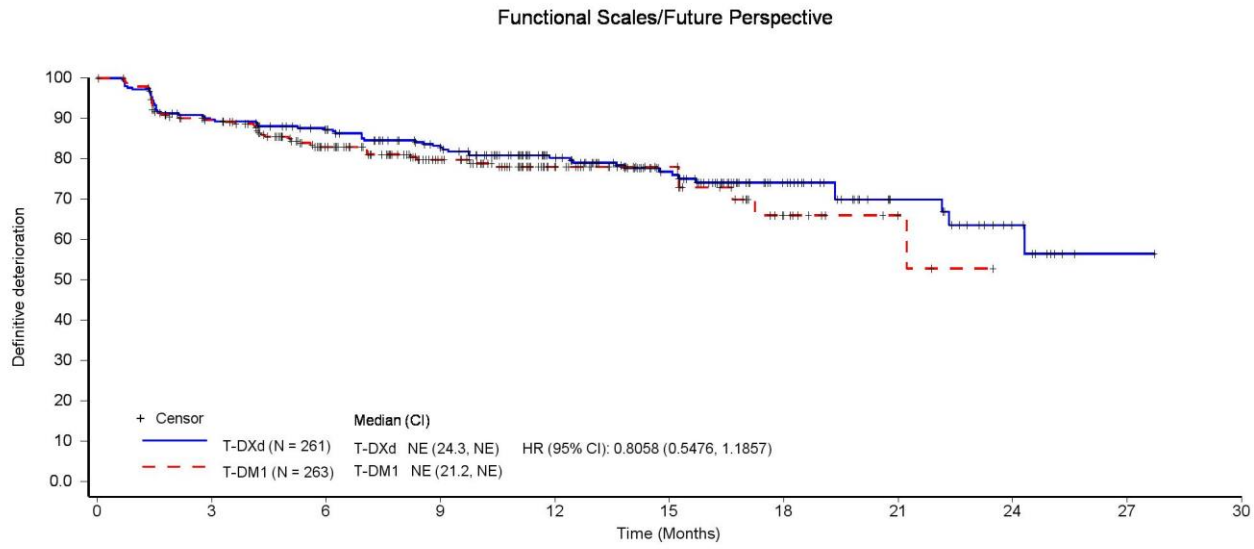


Patients still at risk:

T-DXd (N = 261)	261	34	33	28	25	17	9	3	1	1	0
T-DM1 (N = 263)	263	43	36	25	17	13	5	2	1	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 38 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

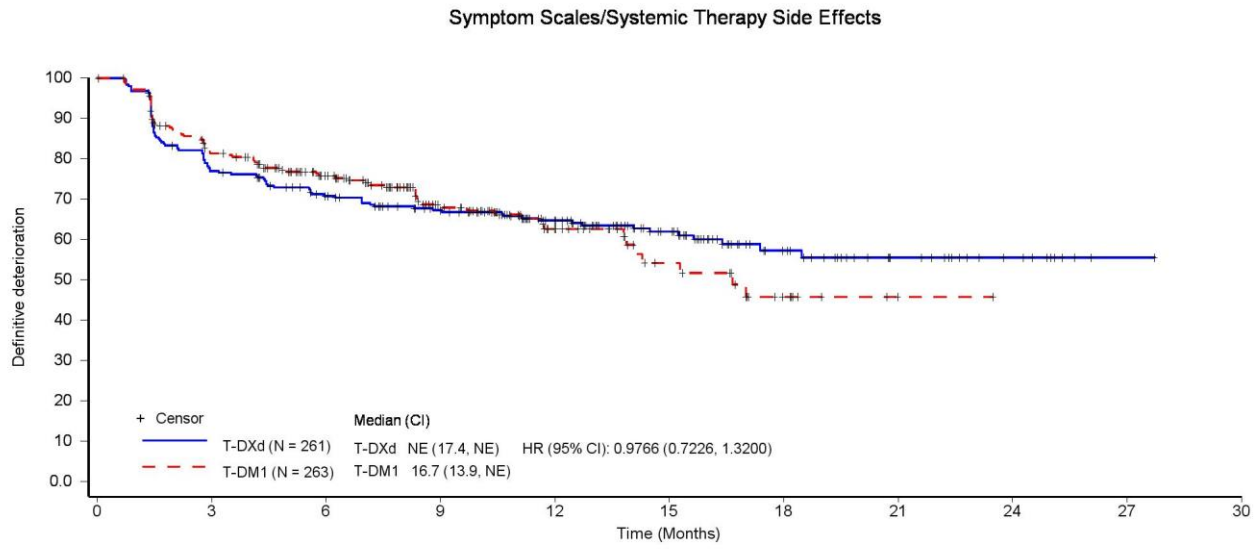


Patients still at risk:

T-DXd (N = 261)	261	224	204	178	136	91	44	23	10	1	0
T-DM1 (N = 263)	263	201	153	104	56	32	14	5	0	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 38 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

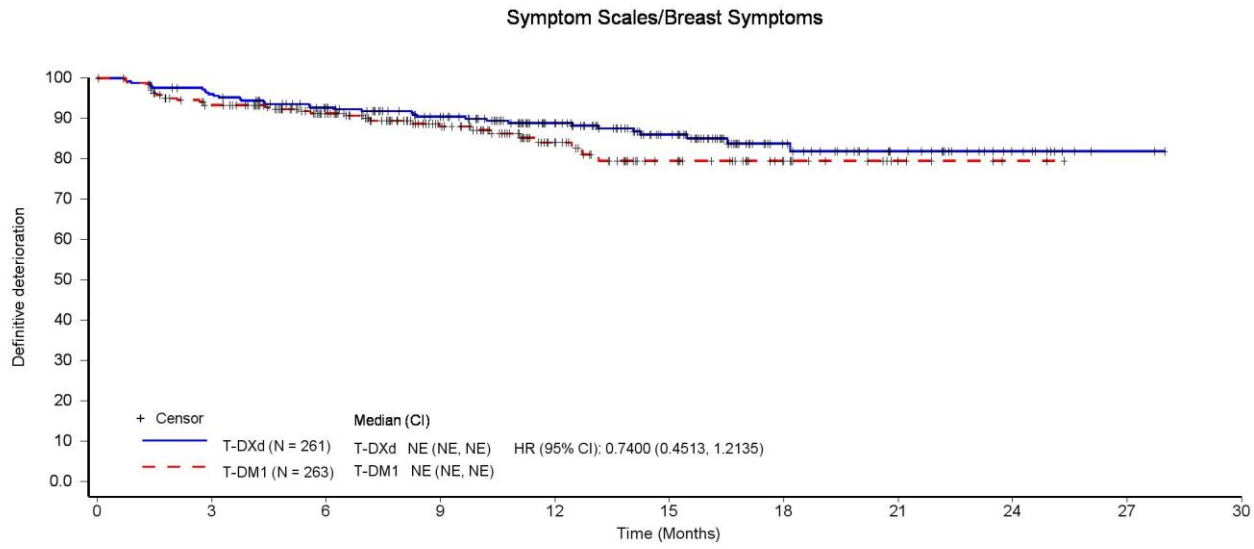


Patients still at risk:

T-DXd (N = 261)	261	193	166	144	114	74	34	18	9	1	0
T-DM1 (N = 263)	263	187	144	89	43	22	10	3	0	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 38 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

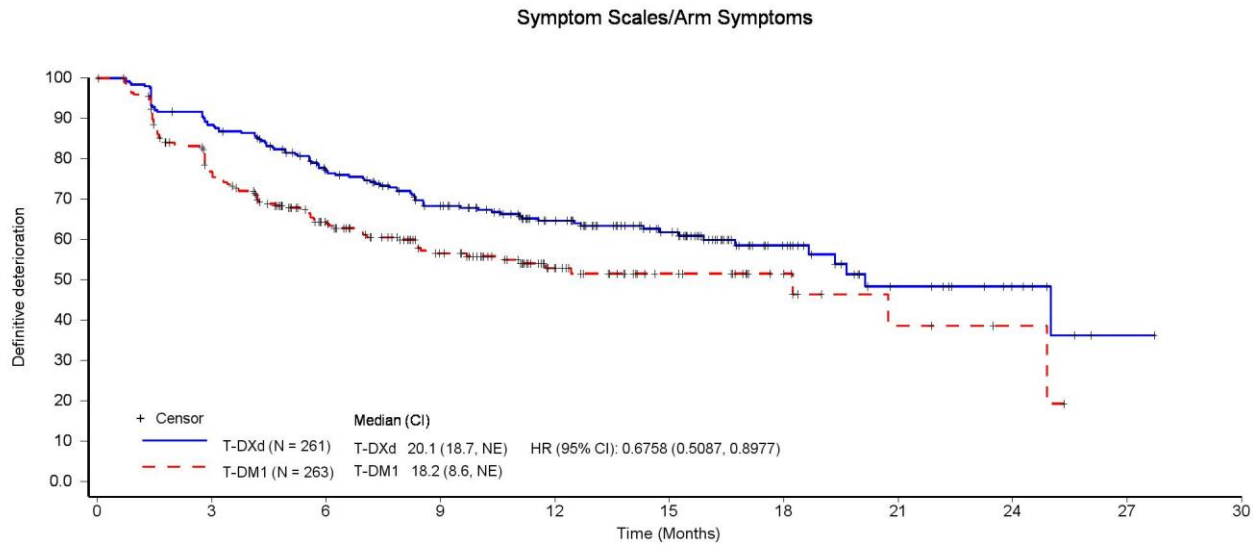


Patients still at risk:

T-DXd (N = 261)	261	239	214	189	146	98	44	27	12	2	0
T-DM1 (N = 263)	263	209	165	115	62	33	18	7	2	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 38 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set

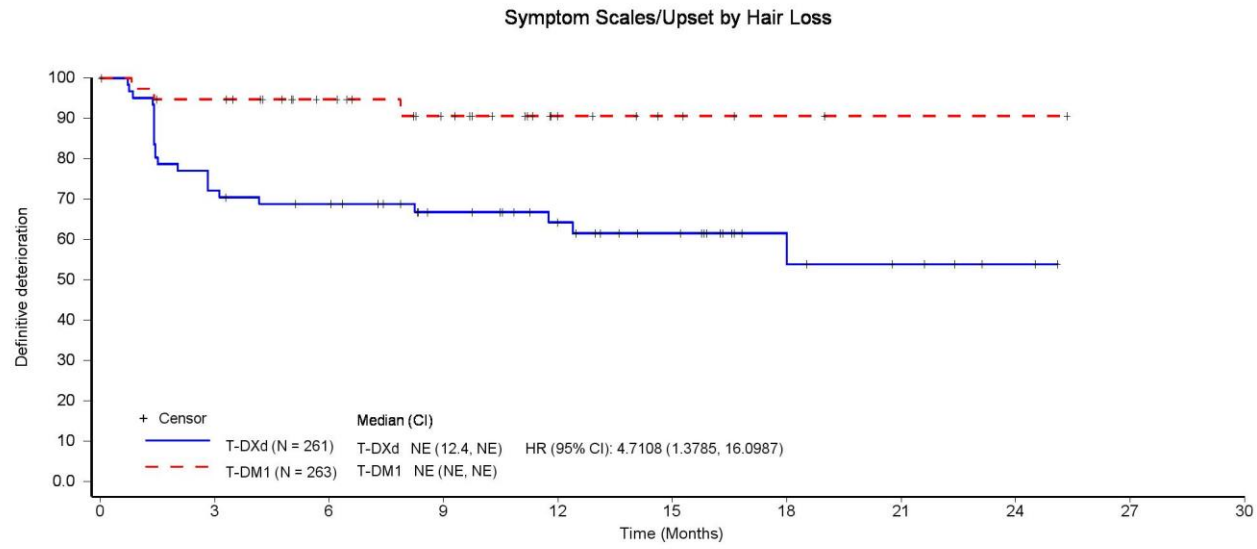


Patients still at risk:

T-DXd (N = 261)	261	221	179	146	110	75	32	14	7	1	0
T-DM1 (N = 263)	263	178	123	81	42	22	12	5	2	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Figure 38 Kaplan-Meier Plot of Time to Definitive deterioration of EORTC QLQ-BR23 – Threshold 10 – Full Analysis Set



Patients still at risk:

T-DXd (N = 261)	261	44	40	31	24	17	8	5	2	0	0
T-DM1 (N = 263)	263	35	26	19	7	4	2	1	1	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Table 61 Analysis of time to definitive deterioration of EQ-5D-5L VAS – Threshold 10 – Full Analysis Set

EQ-5D-5L VAS

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Subjects (%) with Events Deterioration	94 (36.0)	103 (39.2)	
Stratified Log-rank p-value [a]			0.0108
Stratified Cox Proportional Hazard Model [a] Hazard Ratio 95% CI			0.6896 [0.5171 , 0.9196]
Median time to deterioration (months) [b] 95% CI	24.6 [17.9 , NE]	12.5 [10.3 , NE]	
Rate of deterioration at 3 Months [c] 95% CI	81.2 [75.7 , 85.5]	81.1 [75.5 , 85.5]	
Rate of deterioration at 6 Months [c] 95% CI	75.0 [69.1 , 79.9]	70.6 [64.2 , 76.0]	
Rate of deterioration at 9 Months [c] 95% CI	71.8 [65.7 , 77.0]	59.9 [52.8 , 66.3]	
Rate of deterioration at 12 Months [c] 95% CI	67.9 [61.5 , 73.4]	51.9 [44.2 , 59.1]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Table 61 Analysis of time to definitive deterioration of EQ-5D-5L VAS – Threshold 10 – Full Analysis Set

EQ-5D-5L VAS

	T-DXd (N=261)	T-DM1 (N=263)	Analysis T-DXd vs T-DM1
Rate of deterioration at 18 Months [c] 95% CI	57.3 [49.2 , 64.5]	44.5 [35.5 , 53.1]	
Rate of deterioration at 24 Months [c] 95% CI	51.1 [41.2 , 60.1]	35.6 [19.3 , 52.4]	
Rate of deterioration at 36 Months [c] 95% CI	43.8 [28.1 , 58.5]	35.6 [19.3 , 52.4]	
Rate of deterioration at 48 Months [c] 95% CI	43.8 [28.1 , 58.5]	35.6 [19.3 , 52.4]	

Notes: Time to definitive deterioration is defined as the time from randomization until the date of the first symptom deterioration, out of the two consecutive visits for which a deterioration should be observed. Deterioration is defined as an increase of 10 or more points each scale.

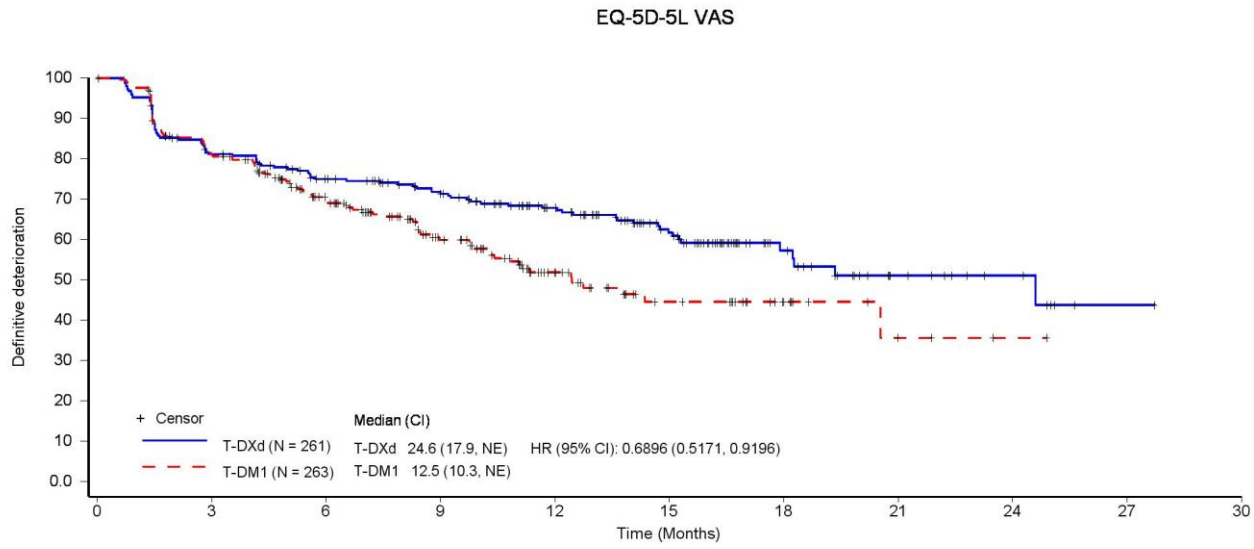
[a] Median time to definitive deterioration is from Kaplan-Meier estimate. Confidence Interval (CI) for median was computed using the Brookmeyer-Crowley method.

[b] Hazard ratio is from stratified Cox proportional hazards model, stratified by the randomization stratification factors as recorded by the IXRS.

[c] Two-sided p-value from stratified log-rank test using the same randomization stratification factors as recorded by the IXRS.

[d] Estimate and CI for time to response rate at the specified time point are from Kaplan-Meier analysis

Figure 40 Kaplan-Meier Plot of Time to Definitive deterioration of EQ-5D-5L VAS – Threshold 10 – Full Analysis Set



Patients still at risk:

T-DXd (N = 261)	261	201	175	154	119	77	30	14	8	1	0
T-DM1 (N = 263)	263	189	138	88	44	22	11	3	1	0	0

Notes: Stratified Cox proportional hazard model for Hazard ratio.
 NE: Not Estimable.

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Gastrointestinal disorders						
Any Preferred Term	237 (92.2)	152 (58.2)	8.50 (5.06, 14.27)	1.58 (1.42, 1.77)	0.340 (0.272, 0.408)	2.86 (2.33, 3.52) <0.0001
Nausea	195 (75.9)	79 (30.3)	7.25 (4.91, 10.69)	2.51 (2.06, 3.05)	0.456 (0.380, 0.533)	3.74 (2.88, 4.87) <0.0001
Vomiting	126 (49.0)	26 (10.0)	8.69 (5.42, 13.95)	4.92 (3.35, 7.24)	0.391 (0.320, 0.462)	5.47 (3.58, 8.35) <0.0001
Constipation	88 (34.2)	51 (19.5)	2.14 (1.44, 3.20)	1.75 (1.30, 2.36)	0.147 (0.072, 0.222)	1.54 (1.09, 2.17) 0.0147
Diarrhoea	75 (29.2)	18 (6.9)	5.56 (3.21, 9.63)	4.23 (2.61, 6.87)	0.223 (0.159, 0.286)	4.22 (2.52, 7.07) <0.0001
Stomatitis	40 (15.6)	10 (3.8)	4.63 (2.26, 9.47)	4.06 (2.08, 7.95)	0.117 (0.067, 0.167)	3.36 (1.68, 6.75) 0.0003

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Abdominal pain	29 (11.3)	5 (1.9)	6.51 (2.48, 17.11)	5.89 (2.32, 14.98)	0.094 (0.052, 0.136)	4.44 (1.71, 11.54) 0.0008
Dyspepsia	29 (11.3)	16 (6.1)	1.95 (1.03, 3.68)	1.84 (1.02, 3.31)	0.052 (0.003, 0.100)	1.48 (0.80, 2.74) 0.2103
Abdominal pain upper	28 (10.9)	12 (4.6)	2.54 (1.26, 5.11)	2.37 (1.23, 4.56)	0.063 (0.017, 0.109)	1.88 (0.95, 3.72) 0.0676
Gastroesophageal reflux disease	13 (5.1)	4 (1.5)	3.42 (1.10, 10.64)	3.30 (1.09, 9.99)	0.035 (0.005, 0.066)	2.45 (0.79, 7.60) 0.1109
Abdominal distension	11 (4.3)	5 (1.9)	2.29 (0.78, 6.68)	2.23 (0.79, 6.34)	0.024 (-0.006, 0.053)	1.80 (0.62, 5.23) 0.2747
Dry mouth	8 (3.1)	25 (9.6)	0.30 (0.13, 0.69)	0.32 (0.15, 0.71)	-0.065 (-0.106, -0.023)	0.25 (0.11, 0.55) 0.0002

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Investigations						
Any Preferred Term	162 (63.0)	179 (68.6)	0.78 (0.54, 1.12)	0.92 (0.81, 1.04)	-0.055 (-0.137, 0.026)	0.61 (0.49, 0.75) <0.0001
Neutrophil count decreased	75 (29.2)	25 (9.6)	3.89 (2.38, 6.36)	3.05 (2.00, 4.63)	0.196 (0.130, 0.262)	2.83 (1.80, 4.46) <0.0001
Aspartate aminotransferase increased	66 (25.7)	105 (40.2)	0.51 (0.35, 0.75)	0.64 (0.49, 0.82)	-0.145 (-0.225, -0.066)	0.44 (0.32, 0.60) <0.0001
White blood cell count decreased	58 (22.6)	14 (5.4)	5.14 (2.79, 9.49)	4.21 (2.41, 7.35)	0.172 (0.114, 0.230)	3.68 (2.05, 6.60) <0.0001
Alanine aminotransferase increased	56 (21.8)	77 (29.5)	0.67 (0.45, 0.99)	0.74 (0.55, 1.00)	-0.077 (-0.152, -0.002)	0.57 (0.40, 0.81) 0.0016
Platelet count decreased	54 (21.0)	112 (42.9)	0.35 (0.24, 0.52)	0.49 (0.37, 0.64)	-0.219 (-0.297, -0.141)	0.33 (0.23, 0.45) <0.0001

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Weight decreased	43 (16.7)	16 (6.1)	3.08 (1.68, 5.62)	2.73 (1.58, 4.72)	0.106 (0.052, 0.160)	2.10 (1.18, 3.75) 0.0099
Blood alkaline phosphatase increased	35 (13.6)	30 (11.5)	1.21 (0.72, 2.04)	1.18 (0.75, 1.87)	0.021 (-0.036, 0.078)	0.90 (0.55, 1.47) 0.6806
Blood bilirubin increased	17 (6.6)	13 (5.0)	1.35 (0.64, 2.84)	1.33 (0.66, 2.68)	0.016 (-0.024, 0.057)	0.81 (0.39, 1.69) 0.5775
Blood lactate dehydrogenase increased	17 (6.6)	35 (13.4)	0.46 (0.25, 0.84)	0.49 (0.28, 0.86)	-0.068 (-0.119, -0.017)	0.37 (0.21, 0.67) 0.0007
Lymphocyte count decreased	14 (5.4)	3 (1.1)	4.95 (1.41, 17.45)	4.74 (1.38, 16.30)	0.043 (0.012, 0.074)	3.50 (1.00, 12.27) 0.0369
Gamma-glutamyltransferase increased	12 (4.7)	11 (4.2)	1.11 (0.48, 2.57)	1.11 (0.50, 2.47)	0.005 (-0.031, 0.040)	0.87 (0.38, 1.99) 0.7467

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Blood creatinine increased	11 (4.3)	3 (1.1)	3.85 (1.06, 13.95)	3.72 (1.05, 13.19)	0.031 (0.003, 0.059)	3.13 (0.87, 11.31) 0.0664

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Electrocardiogram QT prolonged	10 (3.9)	12 (4.6)	0.84 (0.36, 1.98)	0.85 (0.37, 1.92)	-0.007 (-0.042, 0.028)	0.62 (0.27, 1.46) 0.2700

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
General disorders and administration site conditions						
Any Preferred Term	159 (61.9)	133 (51.0)	1.56 (1.10, 2.22)	1.21 (1.04, 1.41)	0.109 (0.024, 0.194)	1.03 (0.82, 1.31) 0.7663
Fatigue	74 (28.8)	52 (19.9)	1.63 (1.08, 2.44)	1.45 (1.06, 1.97)	0.089 (0.015, 0.162)	1.27 (0.89, 1.82) 0.1845
Asthenia	32 (12.5)	31 (11.9)	1.06 (0.62, 1.79)	1.05 (0.66, 1.67)	0.006 (-0.051, 0.062)	0.84 (0.51, 1.39) 0.5042
Malaise	29 (11.3)	10 (3.8)	3.19 (1.52, 6.70)	2.95 (1.47, 5.92)	0.075 (0.029, 0.120)	2.64 (1.28, 5.45) 0.0062
Pyrexia	27 (10.5)	39 (14.9)	0.67 (0.40, 1.13)	0.70 (0.44, 1.11)	-0.044 (-0.102, 0.013)	0.45 (0.27, 0.74) 0.0013
Oedema peripheral	17 (6.6)	9 (3.4)	1.98 (0.87, 4.54)	1.92 (0.87, 4.22)	0.032 (-0.006, 0.069)	1.28 (0.57, 2.92) 0.5490

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Influenza like illness	12 (4.7)	4 (1.5)	3.15 (1.00, 9.89)	3.05 (1.00, 9.32)	0.031 (0.002, 0.061)	2.11 (0.67, 6.61) 0.1909

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Skin and subcutaneous tissue disorders						
Any Preferred Term	139 (54.1)	75 (28.7)	2.92 (2.03, 4.20)	1.88 (1.51, 2.35)	0.253 (0.171, 0.336)	1.96 (1.48, 2.60) <0.0001
Alopecia	95 (37.0)	8 (3.1)	18.55 (8.78, 39.18)	12.06 (5.98, 24.30)	0.339 (0.276, 0.402)	13.50 (6.56, 27.79) <0.0001
Pruritus	21 (8.2)	18 (6.9)	1.20 (0.62, 2.31)	1.18 (0.65, 2.17)	0.013 (-0.033, 0.058)	0.86 (0.45, 1.63) 0.6432
Rash	16 (6.2)	24 (9.2)	0.66 (0.34, 1.27)	0.68 (0.37, 1.24)	-0.030 (-0.076, 0.016)	0.47 (0.25, 0.90) 0.0197
Dry skin	14 (5.4)	4 (1.5)	3.70 (1.20, 11.39)	3.55 (1.19, 10.65)	0.039 (0.008, 0.071)	2.35 (0.76, 7.21) 0.1247
Skin hyperpigmentation	11 (4.3)	0	NE (NE, NE)	NE (NE, NE)	0.043 (0.018, 0.068)	NE (NE, NE) 0.0030

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence \geq 1% in at least one arm and observed for \geq 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Metabolism and nutrition disorders						
Any Preferred Term	122 (47.5)	80 (30.7)	2.04 (1.43, 2.93)	1.55 (1.24, 1.94)	0.168 (0.085, 0.251)	1.56 (1.18, 2.07) 0.0020
Decreased appetite	75 (29.2)	44 (16.9)	2.03 (1.33, 3.10)	1.73 (1.24, 2.41)	0.123 (0.051, 0.195)	1.69 (1.16, 2.45) 0.0060
Hypokalaemia	33 (12.8)	26 (10.0)	1.33 (0.77, 2.30)	1.29 (0.79, 2.09)	0.029 (-0.026, 0.083)	0.95 (0.56, 1.59) 0.8435
Hypoalbuminaemia	20 (7.8)	12 (4.6)	1.75 (0.84, 3.66)	1.69 (0.85, 3.39)	0.032 (-0.010, 0.073)	1.31 (0.63, 2.70) 0.4657
Dehydration	11 (4.3)	0	NE (NE, NE)	NE (NE, NE)	0.043 (0.018, 0.068)	NE (NE, NE) 0.0009

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Nervous system disorders						
Any Preferred Term	116 (45.1)	98 (37.5)	1.37 (0.96, 1.94)	1.20 (0.98, 1.48)	0.076 (-0.009, 0.160)	0.93 (0.71, 1.23) 0.6296
Headache	54 (21.0)	38 (14.6)	1.56 (0.99, 2.46)	1.44 (0.99, 2.11)	0.065 (-0.001, 0.130)	1.07 (0.70, 1.63) 0.7451
Dizziness	32 (12.5)	22 (8.4)	1.54 (0.87, 2.74)	1.48 (0.88, 2.47)	0.040 (-0.012, 0.093)	1.22 (0.71, 2.11) 0.4701
Peripheral sensory neuropathy	19 (7.4)	25 (9.6)	0.75 (0.40, 1.41)	0.77 (0.44, 1.37)	-0.022 (-0.070, 0.026)	0.54 (0.30, 0.99) 0.0443
Dysgeusia	15 (5.8)	8 (3.1)	1.96 (0.82, 4.71)	1.90 (0.82, 4.41)	0.028 (-0.008, 0.063)	1.65 (0.70, 3.91) 0.2494
Neuropathy peripheral	11 (4.3)	8 (3.1)	1.41 (0.56, 3.57)	1.40 (0.57, 3.42)	0.012 (-0.020, 0.045)	0.99 (0.40, 2.49) 0.9871

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Infections and infestations						
Any Preferred Term	112 (43.6)	85 (32.6)	1.60 (1.12, 2.29)	1.34 (1.07, 1.67)	0.110 (0.027, 0.193)	1.01 (0.76, 1.35) 0.9273
Upper respiratory tract infection	20 (7.8)	15 (5.7)	1.38 (0.69, 2.77)	1.35 (0.71, 2.59)	0.020 (-0.023, 0.064)	1.06 (0.54, 2.09) 0.8566
Urinary tract infection	19 (7.4)	13 (5.0)	1.52 (0.74, 3.15)	1.48 (0.75, 2.94)	0.024 (-0.017, 0.066)	1.07 (0.52, 2.18) 0.8589
Pneumonia	18 (7.0)	9 (3.4)	2.11 (0.93, 4.79)	2.03 (0.93, 4.44)	0.036 (-0.003, 0.074)	1.33 (0.59, 2.99) 0.4901

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Respiratory, thoracic and mediastinal disorders						
Any Preferred Term	107 (41.6)	79 (30.3)	1.64 (1.14, 2.36)	1.38 (1.09, 1.74)	0.114 (0.032, 0.196)	0.96 (0.72, 1.29) 0.7990
Epistaxis	29 (11.3)	42 (16.1)	0.66 (0.40, 1.10)	0.70 (0.45, 1.09)	-0.048 (-0.107, 0.011)	0.41 (0.25, 0.67) 0.0002
Cough	27 (10.5)	26 (10.0)	1.06 (0.60, 1.87)	1.05 (0.63, 1.76)	0.005 (-0.047, 0.058)	0.79 (0.46, 1.37) 0.4003
Dyspnoea	21 (8.2)	13 (5.0)	1.70 (0.83, 3.47)	1.64 (0.84, 3.21)	0.032 (-0.011, 0.075)	1.15 (0.57, 2.32) 0.6936
Pneumonitis	18 (7.0)	1 (0.4)	19.58 (2.59, 147.79)	18.28 (2.46, 135.93)	0.066 (0.034, 0.098)	11.05 (1.47, 83.03) 0.0034
Oropharyngeal pain	13 (5.1)	6 (2.3)	2.26 (0.85, 6.05)	2.20 (0.85, 5.70)	0.028 (-0.005, 0.060)	1.53 (0.57, 4.06) 0.3946

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Interstitial lung disease	12 (4.7)	2 (0.8)	6.34 (1.41, 28.63)	6.09 (1.38, 26.96)	0.039 (0.011, 0.067)	3.59 (0.80, 16.12) 0.0750

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Blood and lymphatic system disorders						
Any Preferred Term	103 (40.1)	75 (28.7)	1.66 (1.15, 2.39)	1.39 (1.09, 1.78)	0.113 (0.032, 0.195)	1.16 (0.86, 1.57) 0.3152
Anaemia	83 (32.3)	44 (16.9)	2.35 (1.55, 3.57)	1.92 (1.39, 2.64)	0.154 (0.081, 0.227)	1.64 (1.14, 2.37) 0.0078
Neutropenia	41 (16.0)	7 (2.7)	6.89 (3.03, 15.67)	5.95 (2.72, 13.01)	0.133 (0.084, 0.182)	4.60 (2.06, 10.30) <0.0001
Leukopenia	22 (8.6)	8 (3.1)	2.96 (1.29, 6.78)	2.79 (1.27, 6.16)	0.055 (0.015, 0.095)	2.15 (0.95, 4.87) 0.0594
Lymphopenia	15 (5.8)	6 (2.3)	2.63 (1.01, 6.90)	2.54 (1.00, 6.44)	0.035 (0.001, 0.069)	1.74 (0.67, 4.52) 0.2526
Thrombocytopenia	13 (5.1)	31 (11.9)	0.40 (0.20, 0.77)	0.43 (0.23, 0.80)	-0.068 (-0.116, -0.021)	0.31 (0.16, 0.60) 0.0003

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Musculoskeletal and connective tissue disorders						
Any Preferred Term	94 (36.6)	87 (33.3)	1.15 (0.80, 1.66)	1.10 (0.87, 1.39)	0.032 (-0.050, 0.115)	0.80 (0.59, 1.07) 0.1356
Back pain	24 (9.3)	16 (6.1)	1.58 (0.82, 3.04)	1.52 (0.83, 2.80)	0.032 (-0.014, 0.078)	1.13 (0.60, 2.15) 0.7033
Myalgia	23 (8.9)	16 (6.1)	1.50 (0.78, 2.92)	1.46 (0.79, 2.70)	0.028 (-0.017, 0.074)	1.18 (0.62, 2.25) 0.6038
Arthralgia	22 (8.6)	23 (8.8)	0.97 (0.53, 1.79)	0.97 (0.56, 1.70)	-0.003 (-0.051, 0.046)	0.71 (0.39, 1.28) 0.2492
Pain in extremity	21 (8.2)	16 (6.1)	1.36 (0.69, 2.67)	1.33 (0.71, 2.50)	0.020 (-0.024, 0.065)	1.00 (0.52, 1.92) 0.9931
Musculoskeletal pain	17 (6.6)	12 (4.6)	1.47 (0.69, 3.14)	1.44 (0.70, 2.95)	0.020 (-0.019, 0.060)	0.96 (0.45, 2.03) 0.9131

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence \geq 1% in at least one arm and observed for \geq 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Muscle spasms	11 (4.3)	12 (4.6)	0.93 (0.40, 2.14)	0.93 (0.42, 2.07)	-0.003 (-0.039, 0.032)	0.58 (0.25, 1.33) 0.1929

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Vascular disorders						
Any Preferred Term	45 (17.5)	21 (8.0)	2.43 (1.40, 4.20)	2.18 (1.34, 3.55)	0.095 (0.038, 0.152)	1.66 (0.98, 2.80) 0.0569
Hypertension	14 (5.4)	6 (2.3)	2.45 (0.93, 6.47)	2.37 (0.92, 6.07)	0.031 (-0.002, 0.065)	1.84 (0.70, 4.85) 0.2099

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Eye disorders						
Any Preferred Term	41 (16.0)	30 (11.5)	1.46 (0.88, 2.42)	1.39 (0.90, 2.15)	0.045 (-0.015, 0.104)	0.92 (0.57, 1.48) 0.7323
Dry eye	9 (3.5)	10 (3.8)	0.91 (0.36, 2.28)	0.91 (0.38, 2.21)	-0.003 (-0.036, 0.029)	0.59 (0.24, 1.46) 0.2477

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Psychiatric disorders						
Any Preferred Term	39 (15.2)	35 (13.4)	1.16 (0.71, 1.89)	1.13 (0.74, 1.73)	0.018 (-0.043, 0.078)	0.80 (0.50, 1.27) 0.3388
Anxiety	18 (7.0)	6 (2.3)	3.20 (1.25, 8.20)	3.05 (1.23, 7.55)	0.047 (0.011, 0.083)	2.13 (0.84, 5.42) 0.1027
Insomnia	15 (5.8)	24 (9.2)	0.61 (0.31, 1.20)	0.63 (0.34, 1.18)	-0.034 (-0.079, 0.012)	0.45 (0.24, 0.87) 0.0156

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	HR ^[e] (95% CI) p-value
Injury, poisoning and procedural complications Any Preferred Term	32 (12.5)	27 (10.3)	1.23 (0.72, 2.12)	1.20 (0.74, 1.95)	0.021 (-0.034, 0.076)	0.79 (0.47, 1.33) 0.3712

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Cardiac disorders Any Preferred Term	21 (8.2)	11 (4.2)	2.02 (0.95, 4.28)	1.94 (0.95, 3.94)	0.040 (-0.002, 0.081)	1.34 (0.64, 2.80) 0.4418

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Ear and labyrinth disorders						
Any Preferred Term	21 (8.2)	9 (3.4)	2.49 (1.12, 5.55)	2.37 (1.11, 5.08)	0.047 (0.007, 0.087)	1.65 (0.75, 3.63) 0.2100
Vertigo	10 (3.9)	5 (1.9)	2.07 (0.70, 6.15)	2.03 (0.70, 5.86)	0.020 (-0.009, 0.049)	1.35 (0.46, 4.01) 0.5847

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Reproductive system and breast disorders Any Preferred Term	21 (8.2)	17 (6.5)	1.28 (0.66, 2.48)	1.25 (0.68, 2.32)	0.017 (-0.028, 0.061)	0.86 (0.45, 1.64) 0.6389

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence \geq 1% in at least one arm and observed for \geq 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Hepatobiliary disorders Any Preferred Term	20 (7.8)	29 (11.1)	0.68 (0.37, 1.23)	0.70 (0.41, 1.21)	-0.033 (-0.084, 0.017)	0.53 (0.29, 0.94) 0.0283
Hepatitis	5 (1.9)	10 (3.8)	0.50 (0.17, 1.48)	0.51 (0.18, 1.47)	-0.019 (-0.048, 0.010)	0.44 (0.15, 1.30) 0.1279

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Table 34 Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence \geq 1% in at least one arm and observed for \geq 10 patients - Safety Analysis Set

System Organ Class Preferred Term	T-DXd (N=257)	T-DM1 (N=261)	T-DXd vs T-DM1			HR ^[e] (95% CI) p-value
	n (%)	n (%)	OR ^[b] (95% CI)	RR ^[c] (95% CI)	ARR ^[d] (95% CI)	
Renal and urinary disorders Any Preferred Term	15 (5.8)	11 (4.2)	1.41 (0.63, 3.13)	1.38 (0.65, 2.96)	0.016 (-0.021, 0.054)	1.00 (0.46, 2.20) 0.9953

Notes: Adverse events were coded using the MedDRA dictionary, Version 23.0 and graded according to NCI CTCAE v5.0.

[a] IR: Incidence rate per person-years

[b] OR: odds-ratio; obtained via a logistic regression model

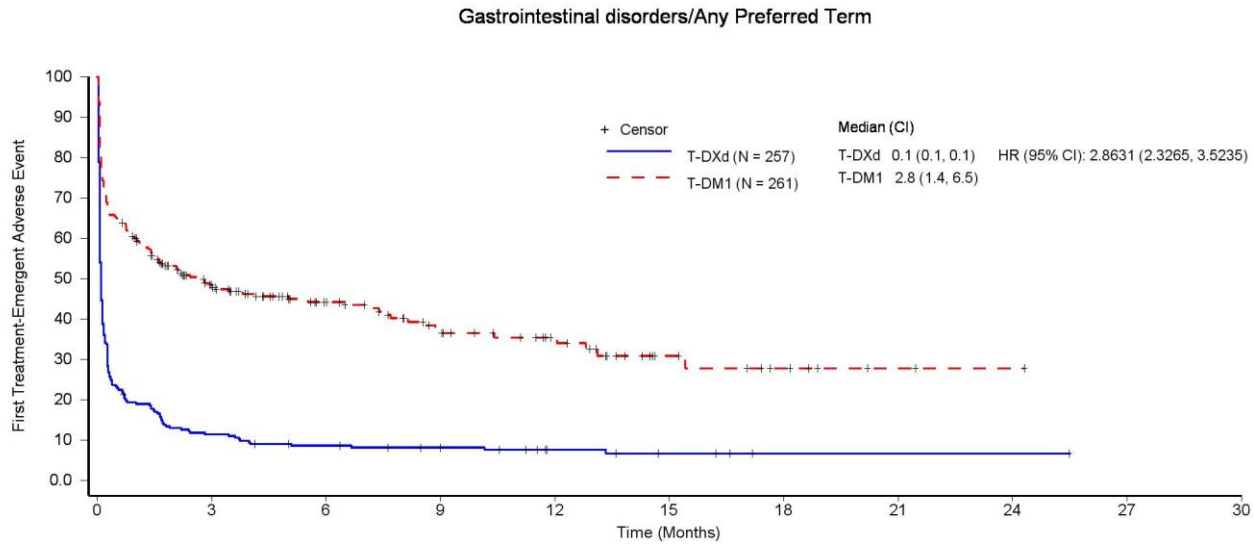
[c] RR: Relative risk; derived using the Cochran-Mantel-Haenszel method

[d] ARR: Absolute Risk Reduction; derived using the Cochran-Mantel-Haenszel method and presented on the risk scale.

[e] HR: Hazard ratio obtained from a Cox proportional hazards model, p-value from log-rank test

NE - Not Evaluable

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



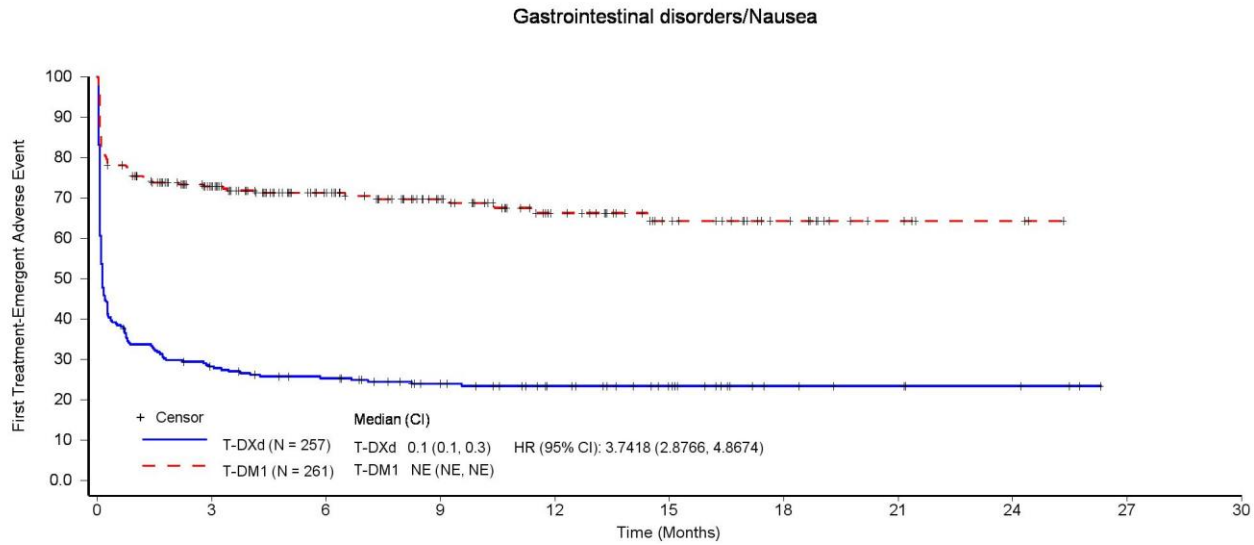
Patients still at risk:

T-DXd (N = 257)	257	29	20	16	8	5	1	1	1	0	0
T-DM1 (N = 261)	261	93	59	39	25	11	6	2	1	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



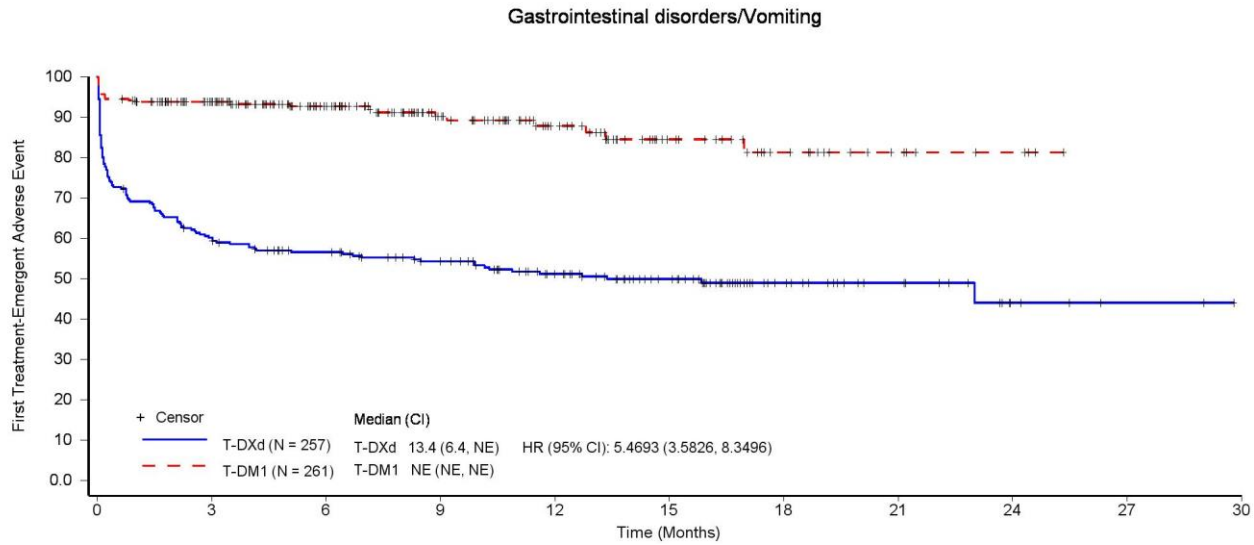
Patients still at risk:

T-DXd (N = 257)	257	70	59	46	33	21	8	6	4	0	0
T-DM1 (N = 261)	261	147	99	72	45	27	16	7	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



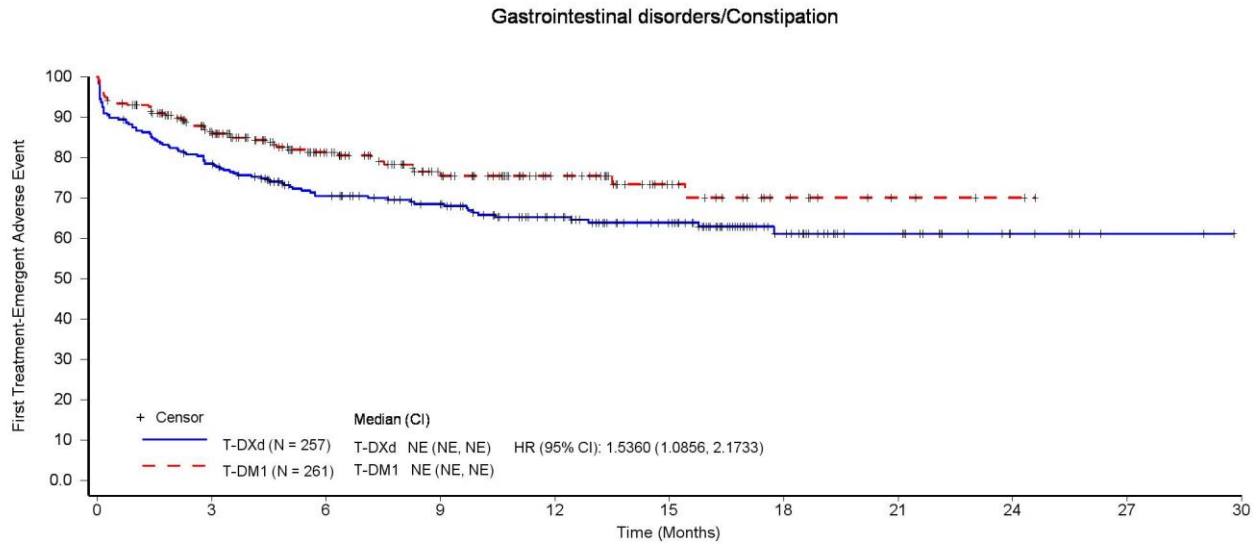
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	153	133	115	87	62	25	15	5	2	0
T-DM1 (N = 261)	261	198	140	92	58	33	20	9	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



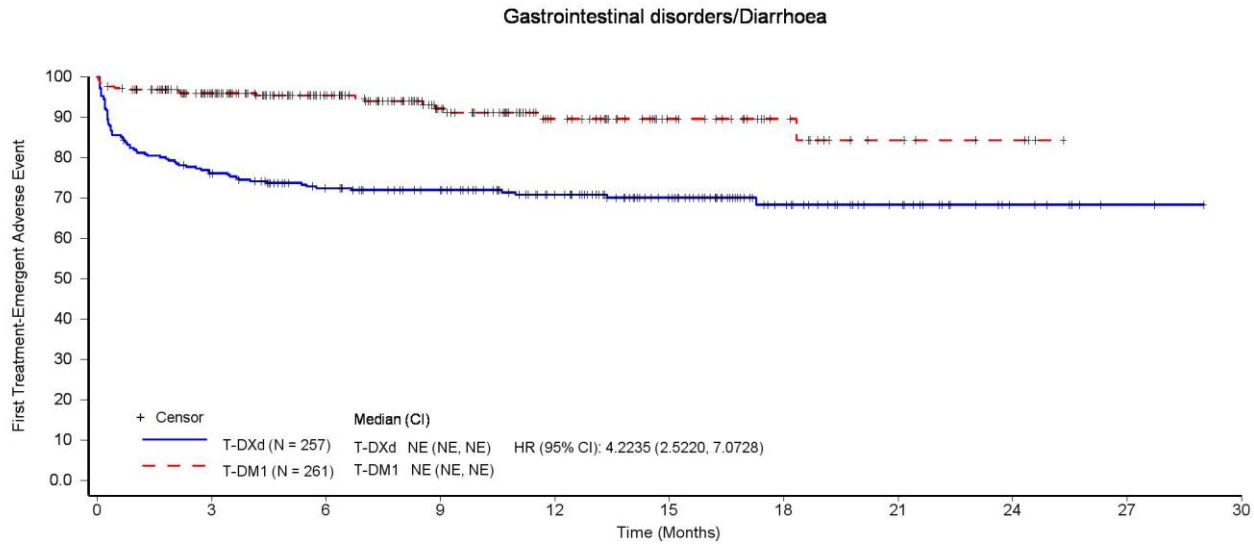
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	199	157	136	101	75	33	19	7	2	0
T-DM1 (N = 261)	261	177	116	76	47	24	12	4	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



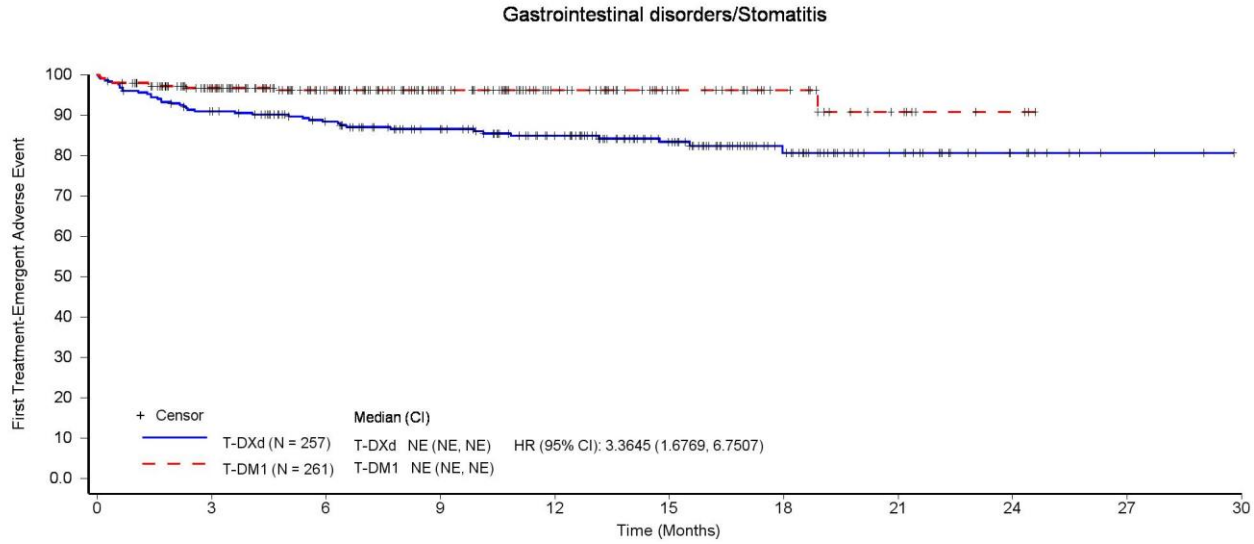
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	192	162	143	111	76	35	21	8	2	0
T-DM1 (N = 261)	261	197	142	92	54	32	18	8	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



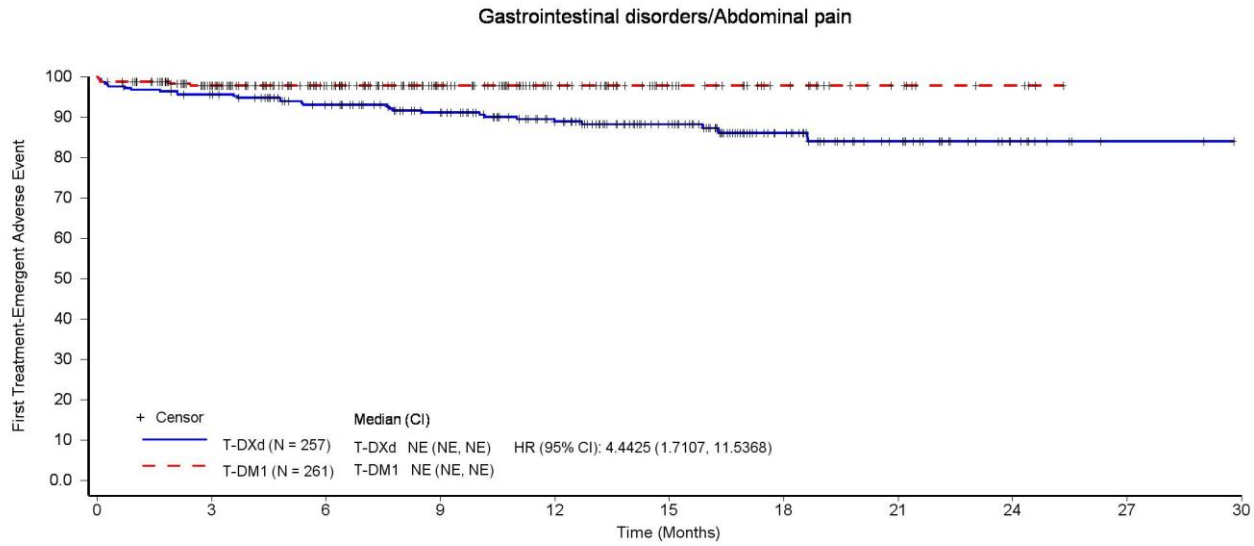
Patients still at risk:

T-DXd (N = 257)	257	228	200	172	138	95	45	24	10	3	0
T-DM1 (N = 261)	261	200	144	96	60	37	22	9	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



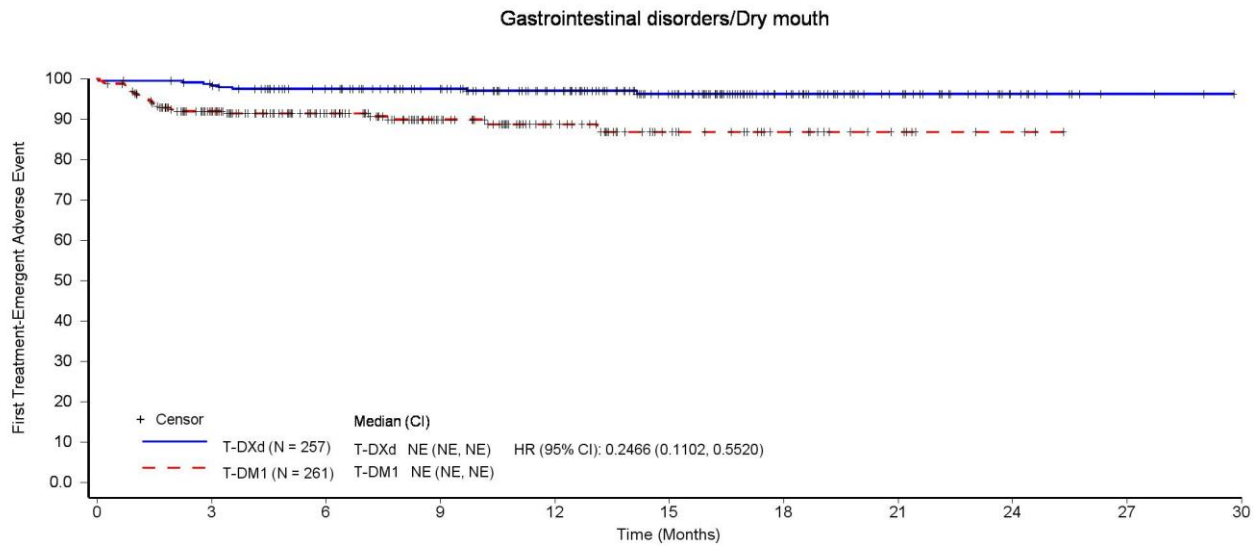
Patients still at risk:

T-DXd (N = 257)	257	240	210	182	145	103	48	27	10	2	0
T-DM1 (N = 261)	261	202	146	97	60	36	22	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



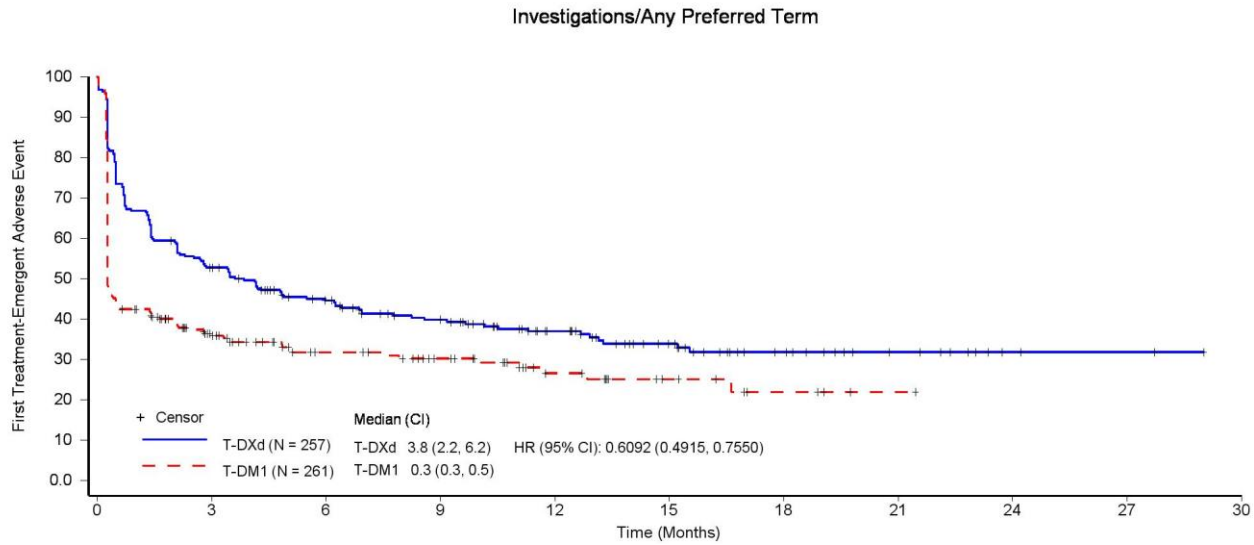
Patients still at risk:

T-DXd (N = 257)	257	247	220	195	156	110	55	31	12	3	0
T-DM1 (N = 261)	261	188	134	88	53	31	19	9	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



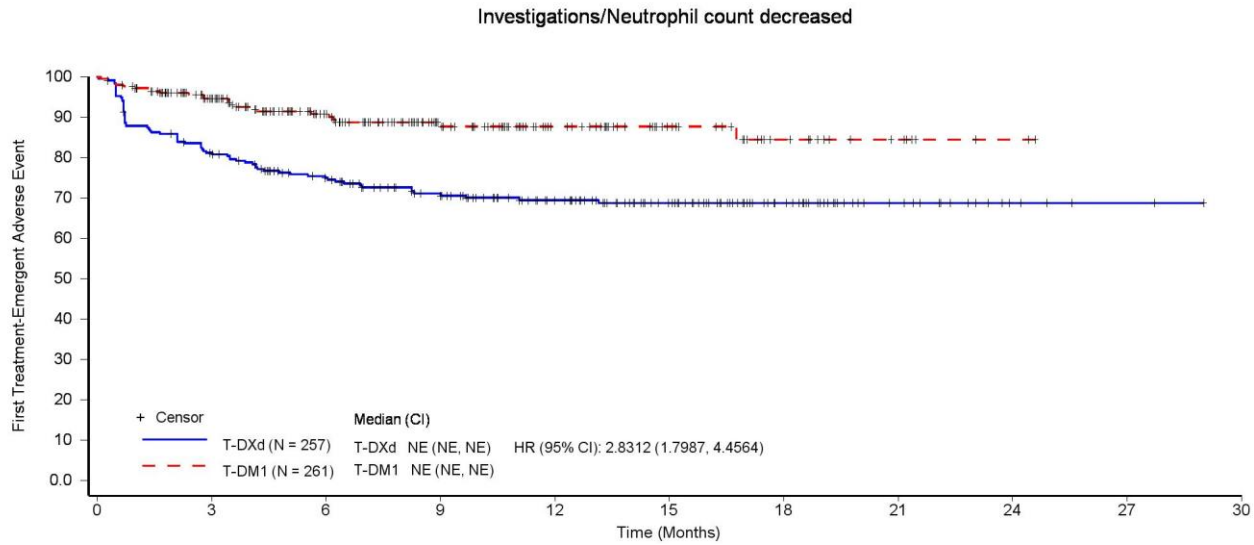
Patients still at risk:

T-DXd (N = 257)	257	134	99	78	54	35	18	10	3	2	0
T-DM1 (N = 261)	261	72	45	33	18	10	5	1	0	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



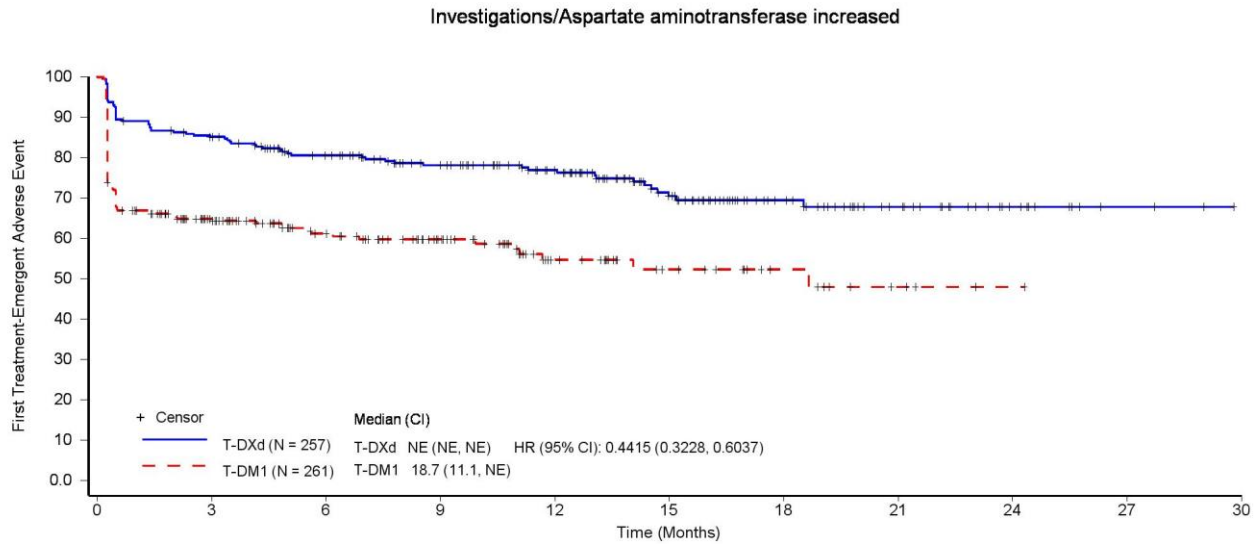
Patients still at risk:

T-DXd (N = 257)	257	205	166	137	105	72	35	16	5	2	0
T-DM1 (N = 261)	261	194	133	86	53	33	18	8	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



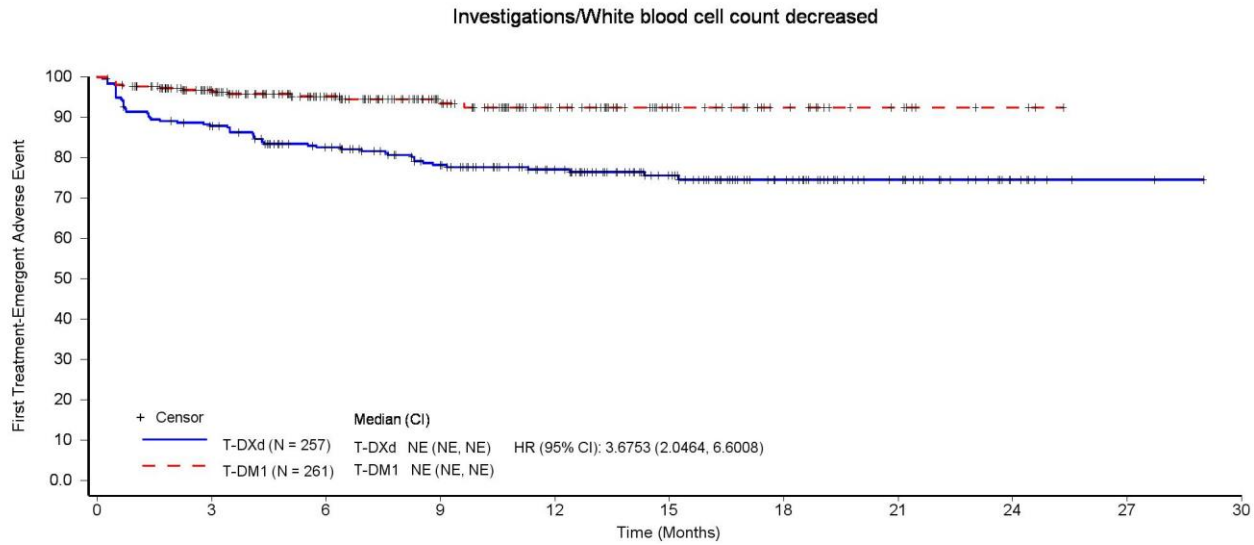
Patients still at risk:

T-DXd (N = 257)	257	214	179	154	122	75	43	25	11	3	0
T-DM1 (N = 261)	261	130	89	62	34	20	12	4	1	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



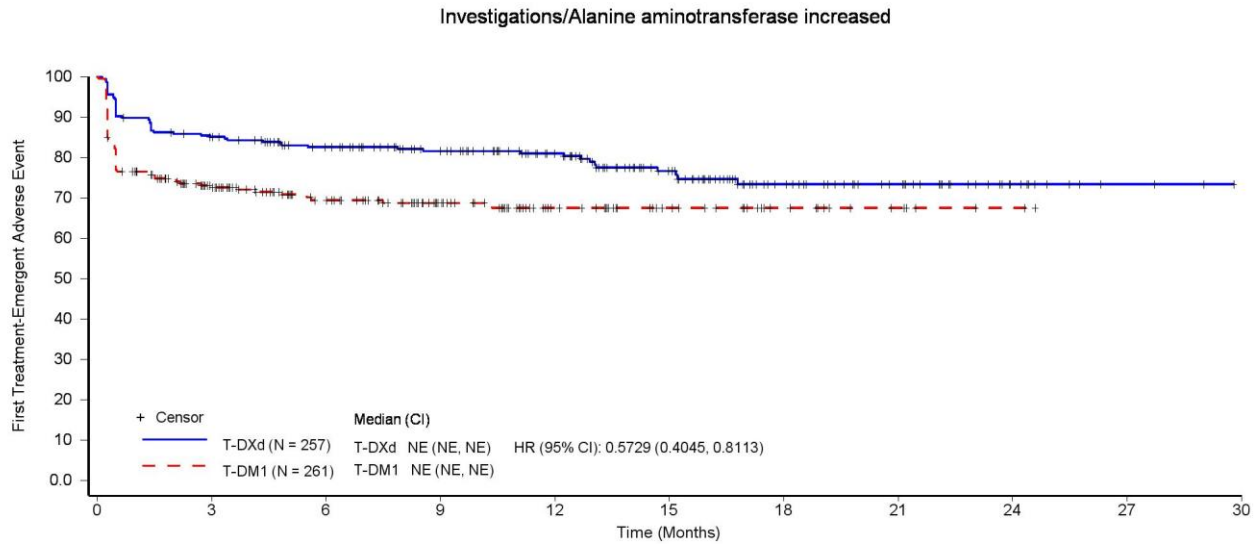
Patients still at risk:

T-DXd (N = 257)	257	222	185	155	121	81	45	25	8	2	0
T-DM1 (N = 261)	261	199	142	93	58	35	20	9	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



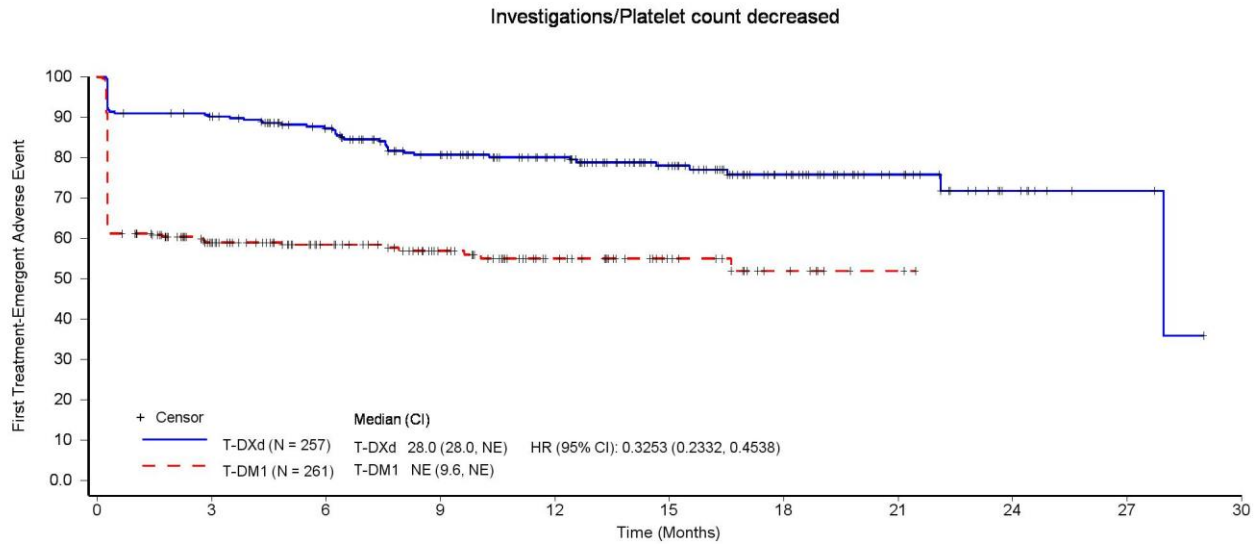
Patients still at risk:

T-DXd (N = 257)	257	214	184	161	128	83	43	28	11	3	0
T-DM1 (N = 261)	261	147	100	69	41	26	15	6	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



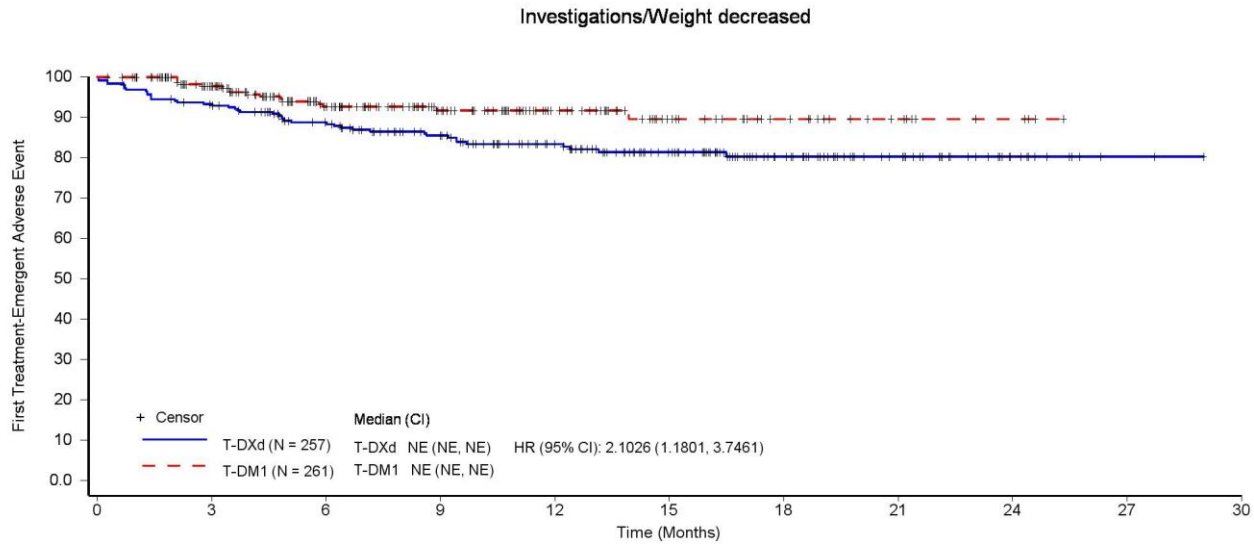
Patients still at risk:

T-DXd (N = 257)	257	226	196	160	129	87	45	24	9	3	0
T-DM1 (N = 261)	261	117	88	63	39	22	10	3	0	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



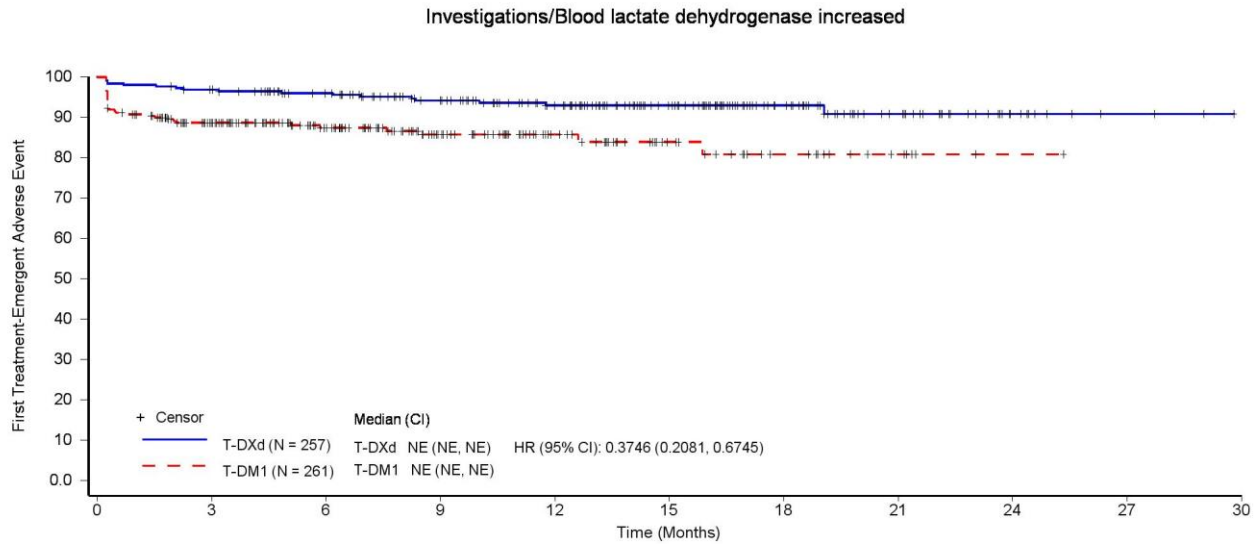
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	234	200	169	133	97	51	30	11	2	0
T-DM1 (N = 261)	261	203	138	93	58	34	21	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



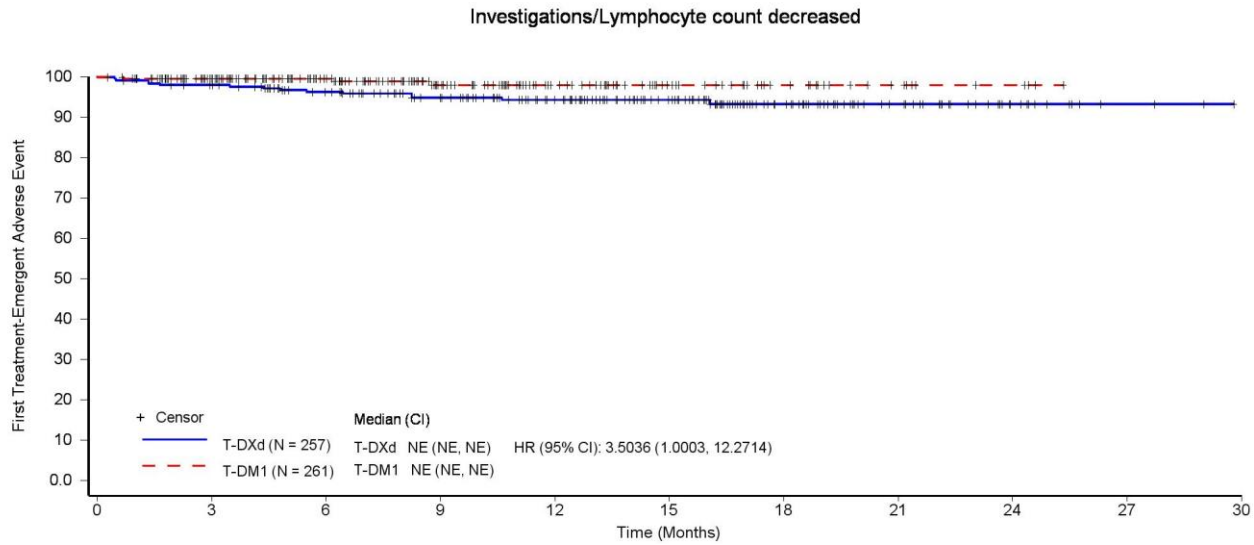
Patients still at risk:

T-DXd (N = 257)	257	246	218	188	151	105	53	29	10	3	0
T-DM1 (N = 261)	261	185	132	85	51	29	17	7	1	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



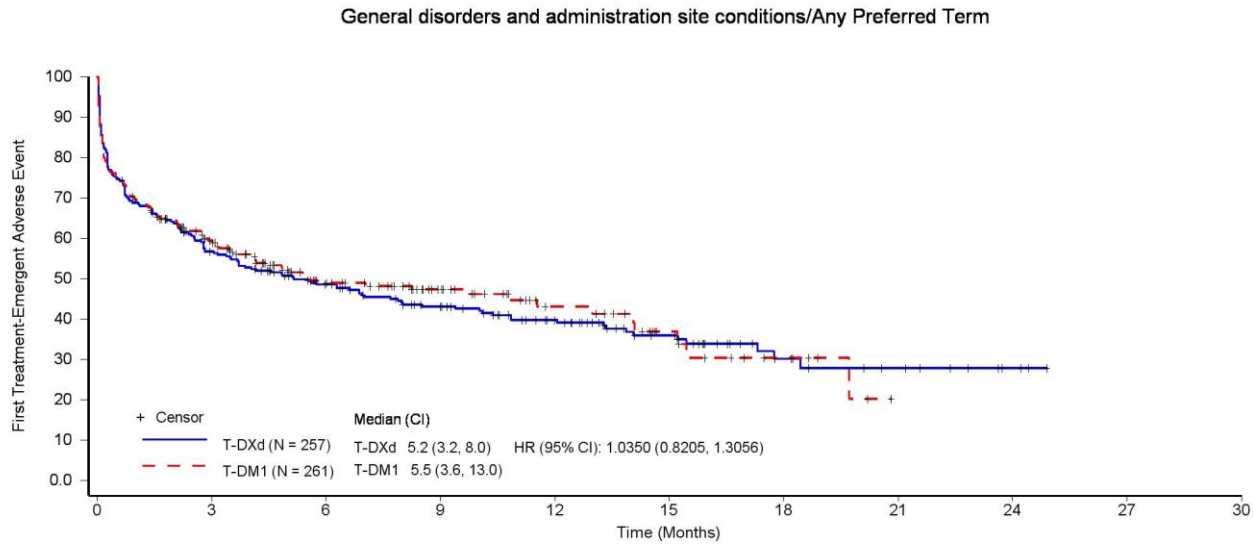
Patients still at risk:

T-DXd (N = 257)	257	246	217	189	155	110	54	30	12	3	0
T-DM1 (N = 261)	261	205	149	97	61	37	22	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



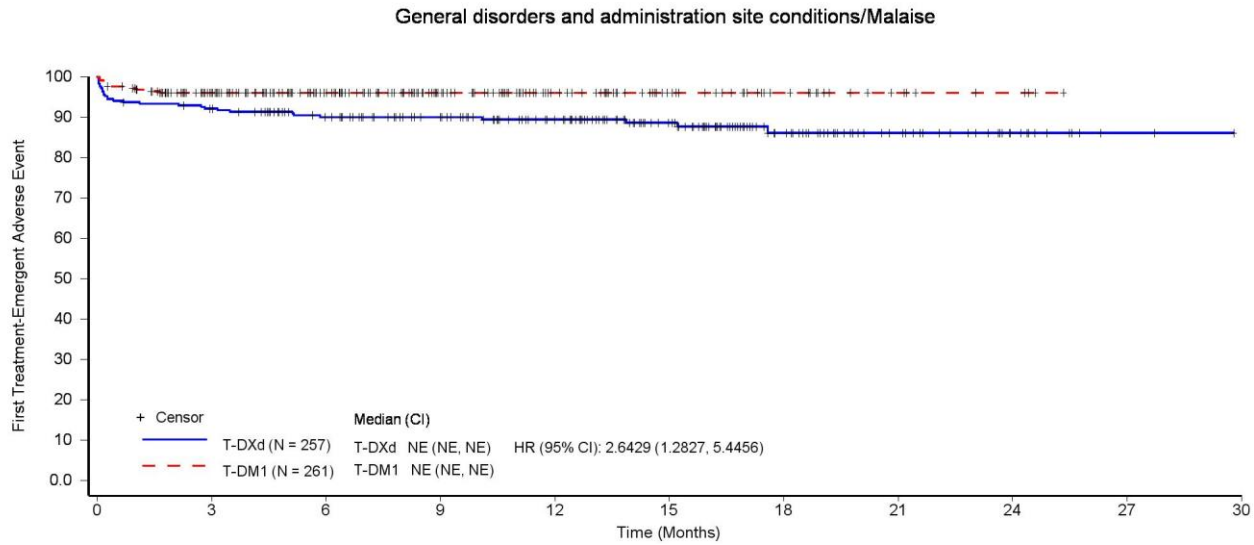
Patients still at risk:

T-DXd (N = 257)	257	144	112	88	62	39	15	9	3	0	0
T-DM1 (N = 261)	261	125	71	45	24	12	5	0	0	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



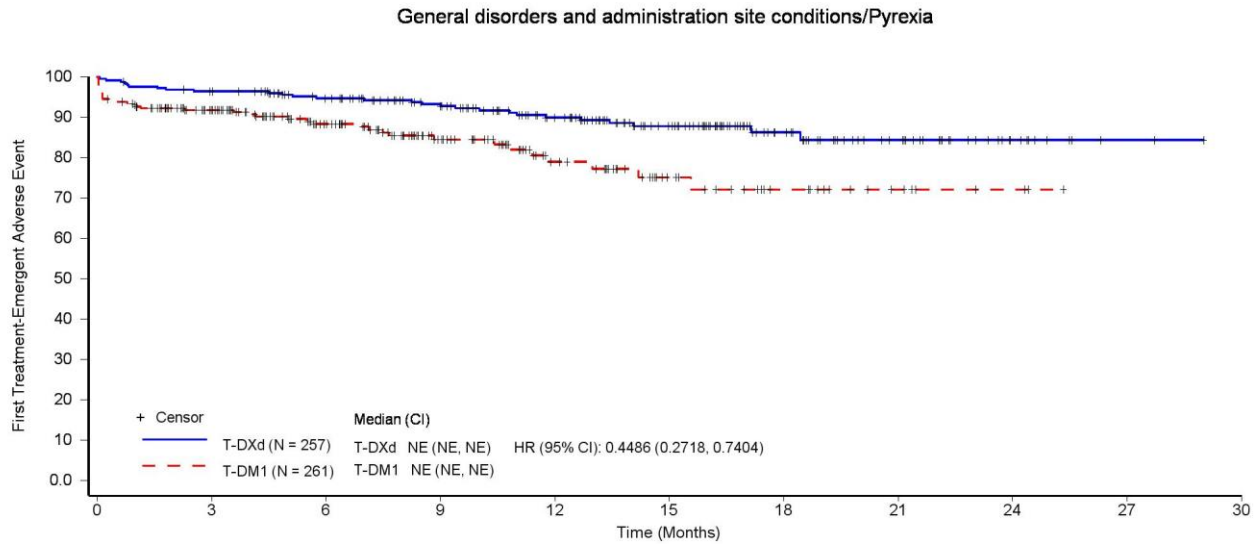
Patients still at risk:

T-DXd (N = 257)	257	232	202	179	142	99	47	26	11	2	0
T-DM1 (N = 261)	261	198	143	94	58	35	20	9	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



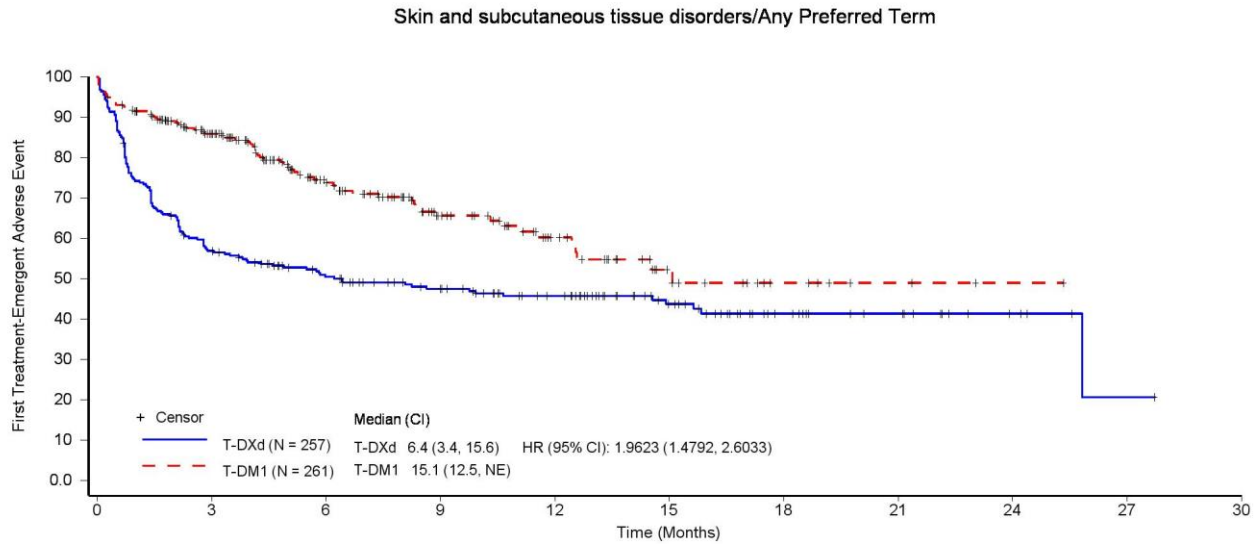
Patients still at risk:

T-DXd (N = 257)	257	243	215	187	145	102	48	28	10	2	0
T-DM1 (N = 261)	261	192	135	85	48	27	16	7	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



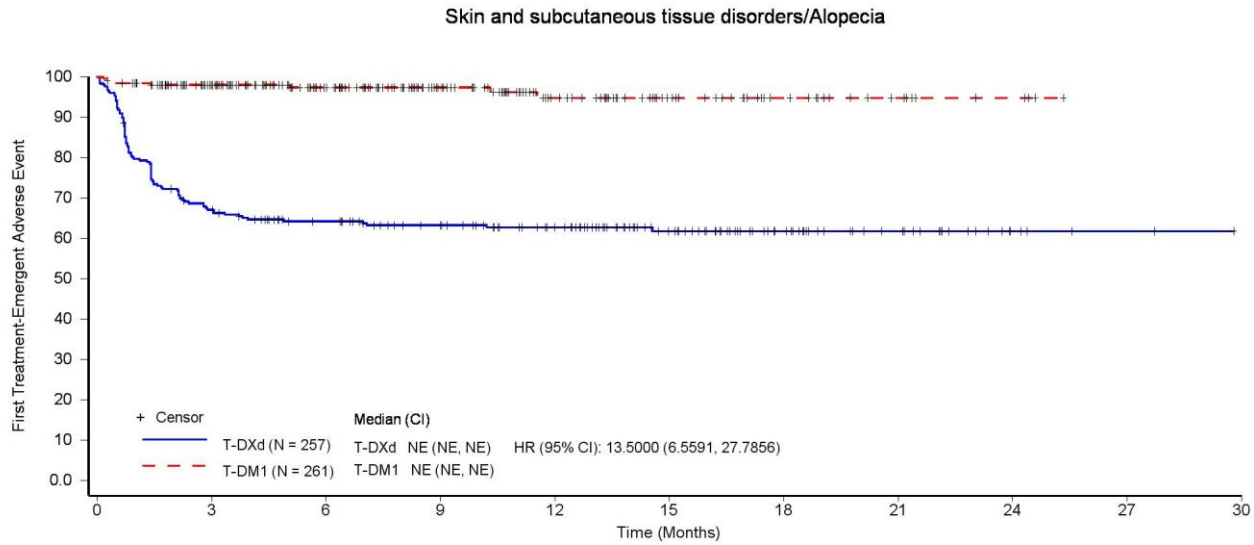
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	143	109	89	69	42	20	13	5	1	0
T-DM1 (N = 261)	261	178	109	61	35	16	7	3	1	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



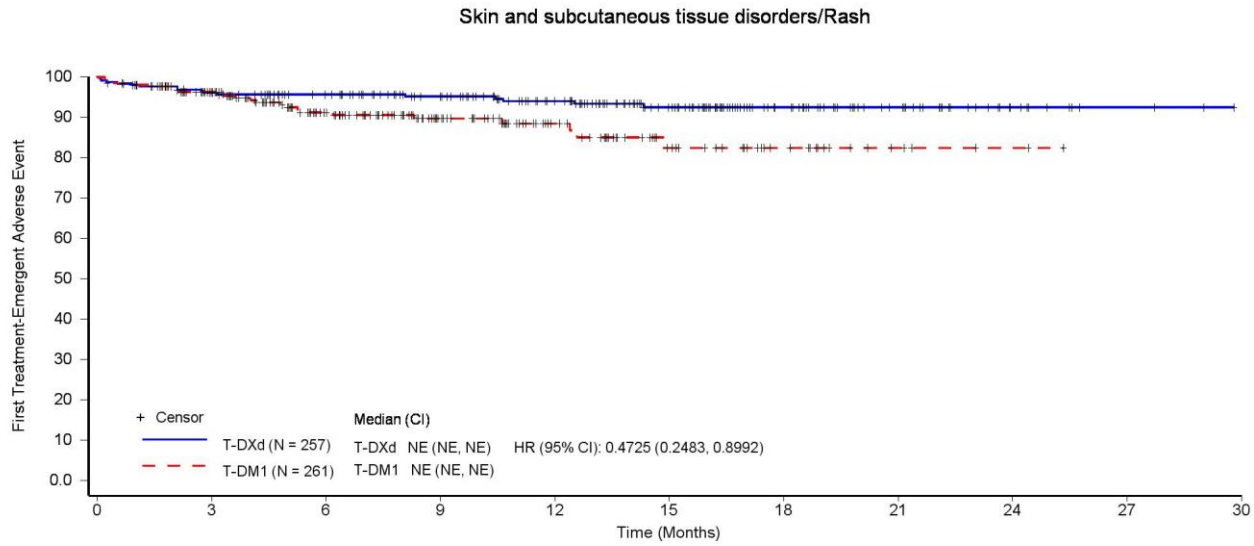
Patients still at risk:

T-DXd (N = 257)	257	169	141	124	99	62	33	19	5	2	0
T-DM1 (N = 261)	261	202	145	97	59	36	21	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



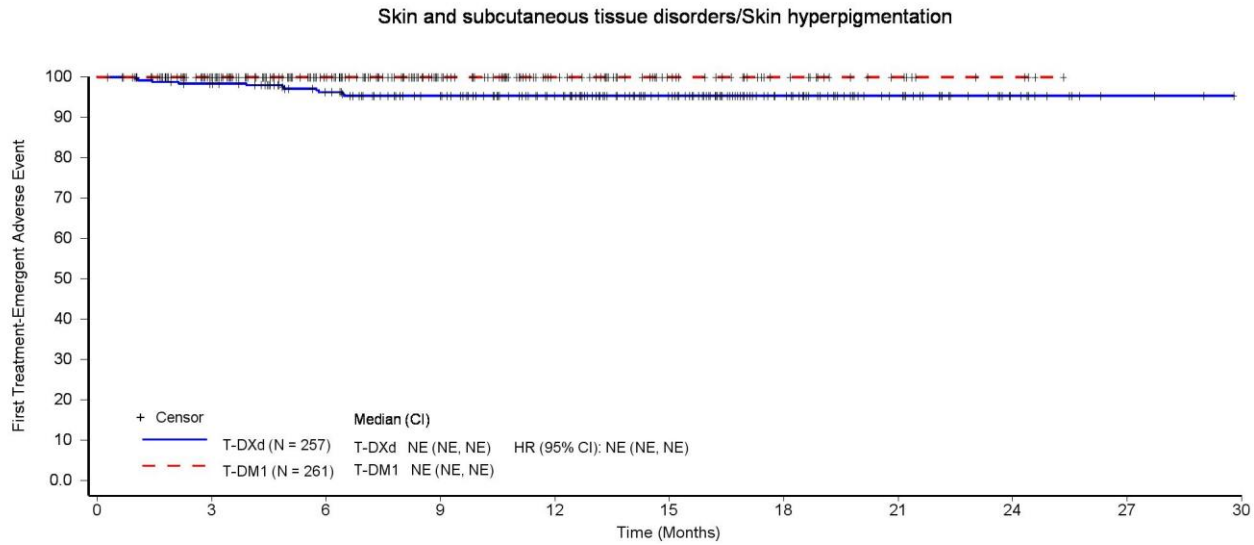
Patients still at risk:

T-DXd (N = 257)	257	241	215	188	149	103	49	28	10	3	0
T-DM1 (N = 261)	261	198	135	87	54	30	16	6	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



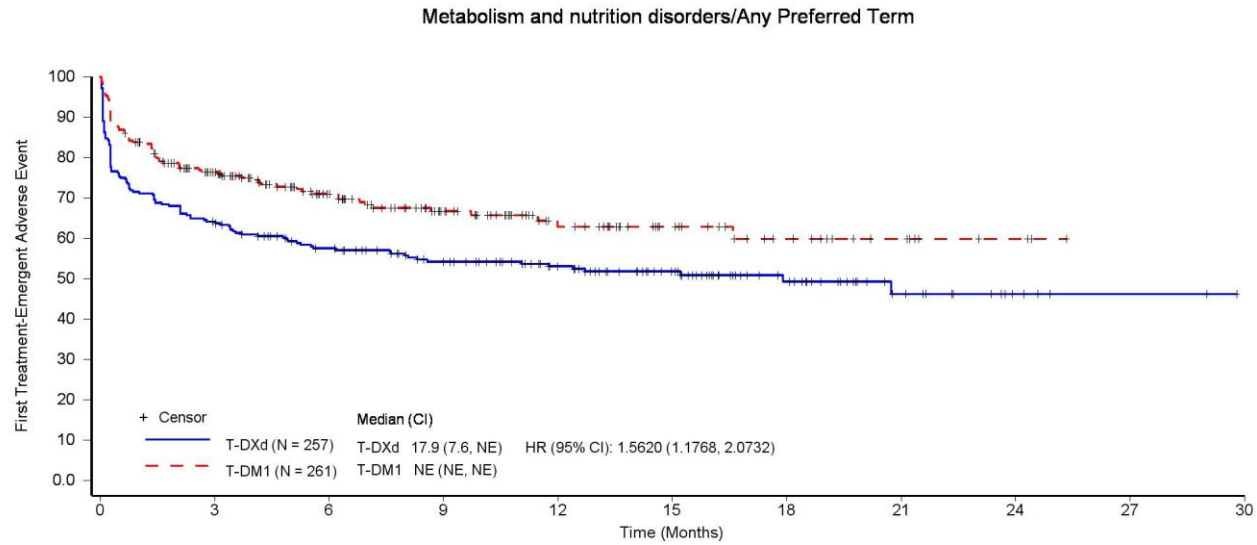
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	247	216	189	153	108	53	30	12	3	0
T-DM1 (N = 261)	261	206	149	98	61	37	22	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



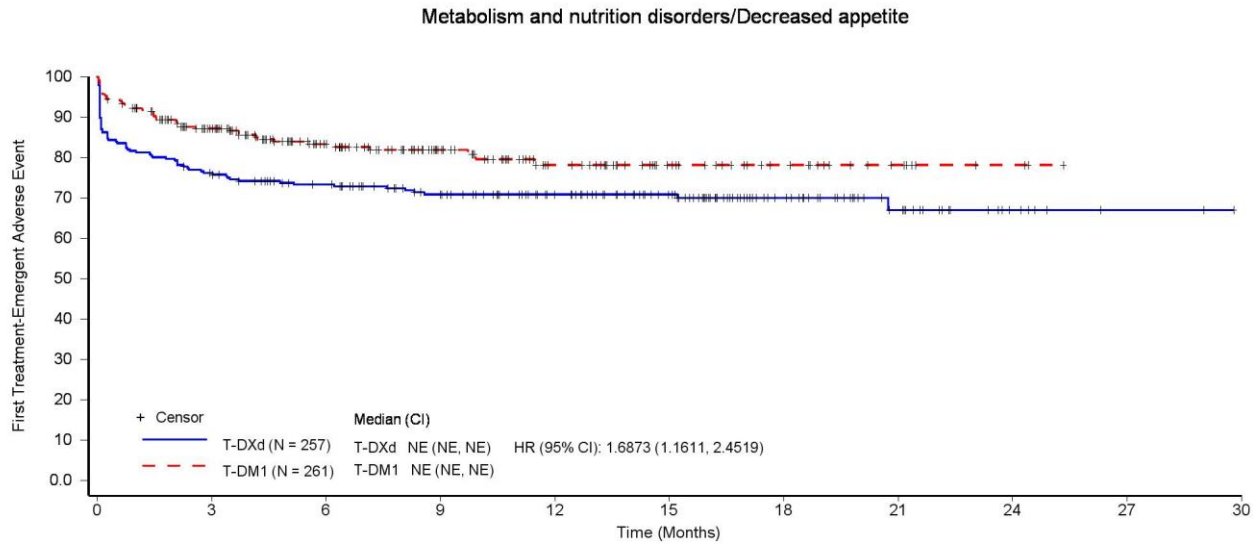
Patients still at risk:

T-DXd (N = 257)	257	163	132	110	84	57	31	14	5	2	0
T-DM1 (N = 261)	261	163	109	71	42	27	16	8	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



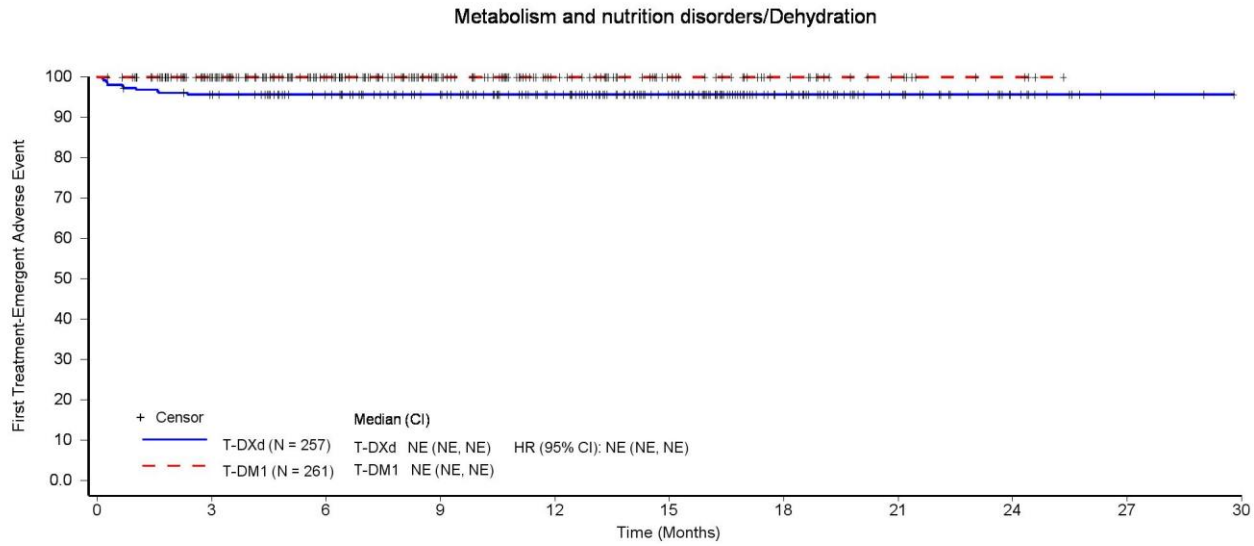
Patients still at risk:

T-DXd (N = 257)	257	193	165	140	110	81	40	21	7	2	0
T-DM1 (N = 261)	261	182	124	81	48	29	18	8	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



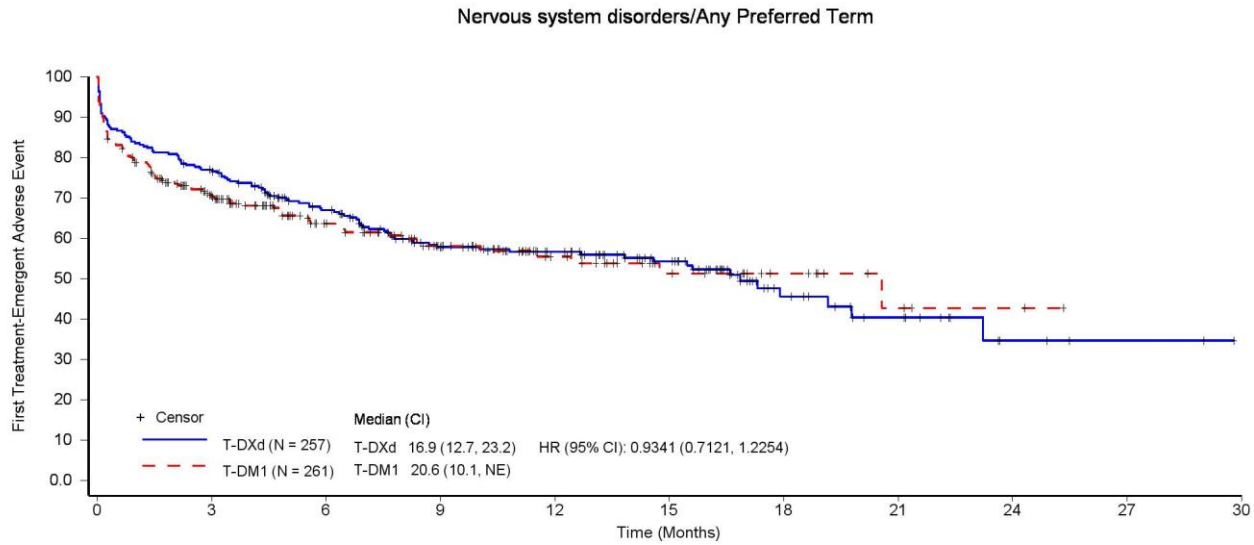
Patients still at risk:

T-DXd (N = 257)	257	242	218	194	156	110	52	28	12	3	0
T-DM1 (N = 261)	261	206	149	98	61	37	22	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



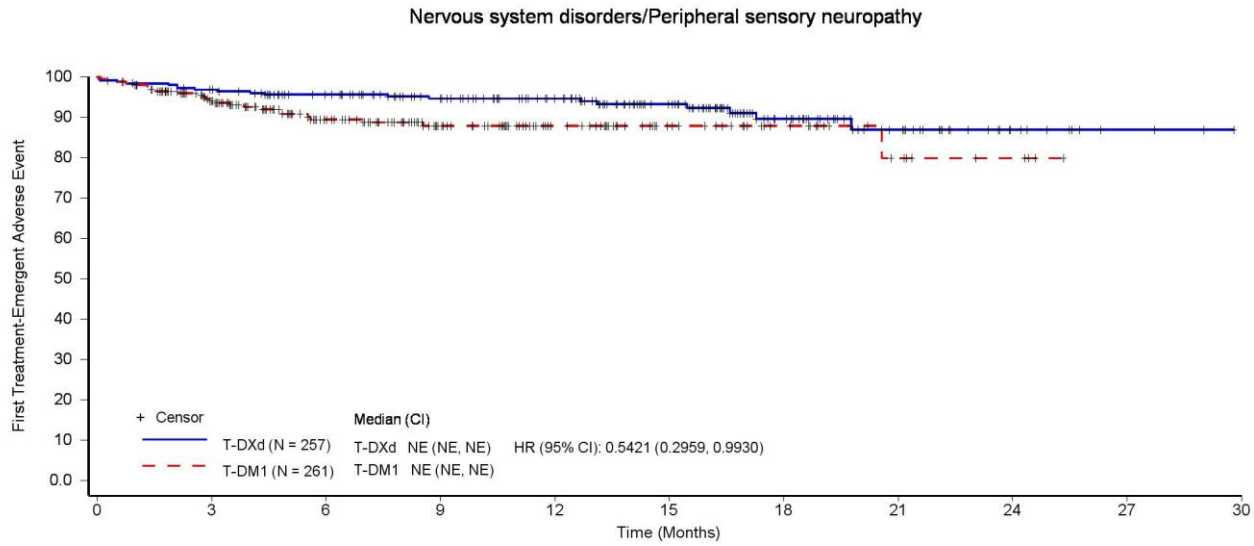
Patients still at risk:

T-DXd (N = 257)	257	194	149	112	87	61	22	13	4	2	0
T-DM1 (N = 261)	261	145	90	57	34	20	11	5	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



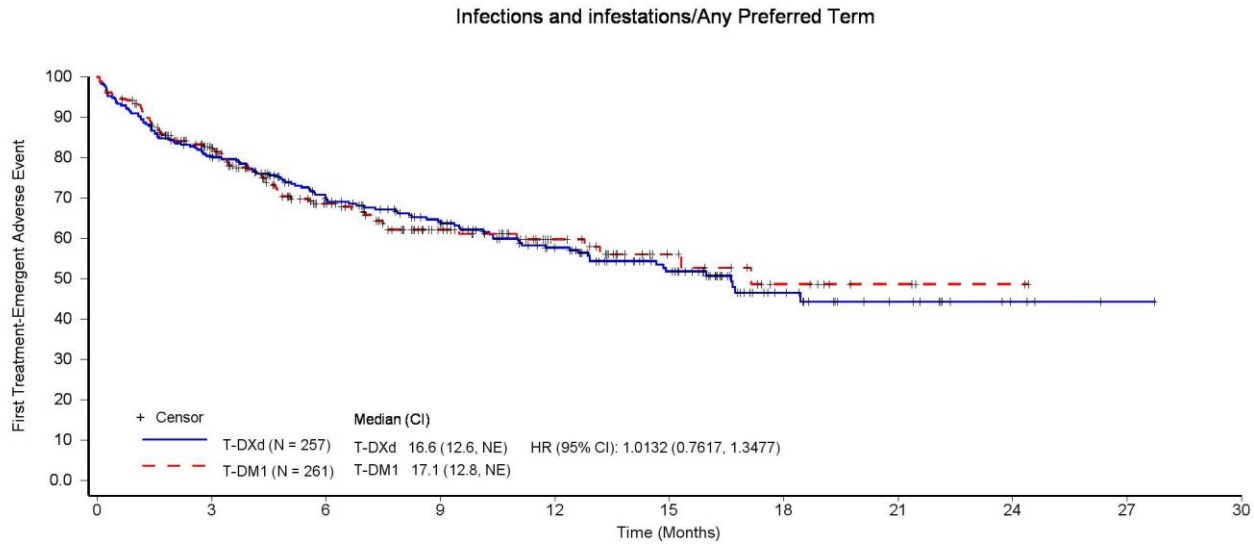
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	244	215	187	153	108	50	27	10	3	0
T-DM1 (N = 261)	261	193	132	87	54	34	21	9	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



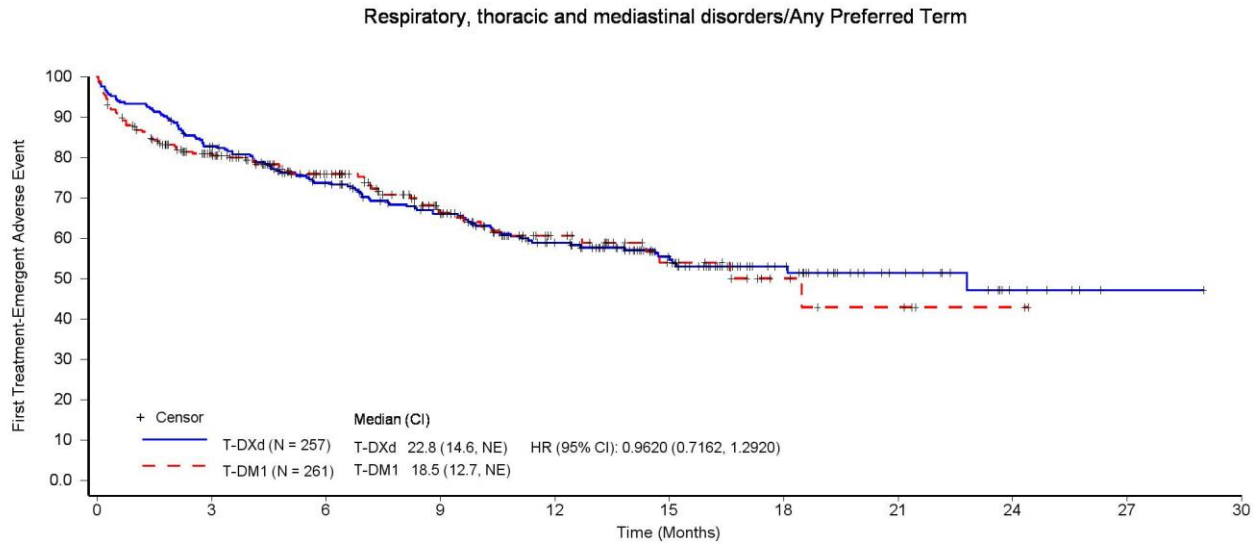
Patients still at risk:

T-DXd (N = 257)	257	204	156	128	93	61	23	12	4	1	0
T-DM1 (N = 261)	261	177	105	63	35	18	9	4	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



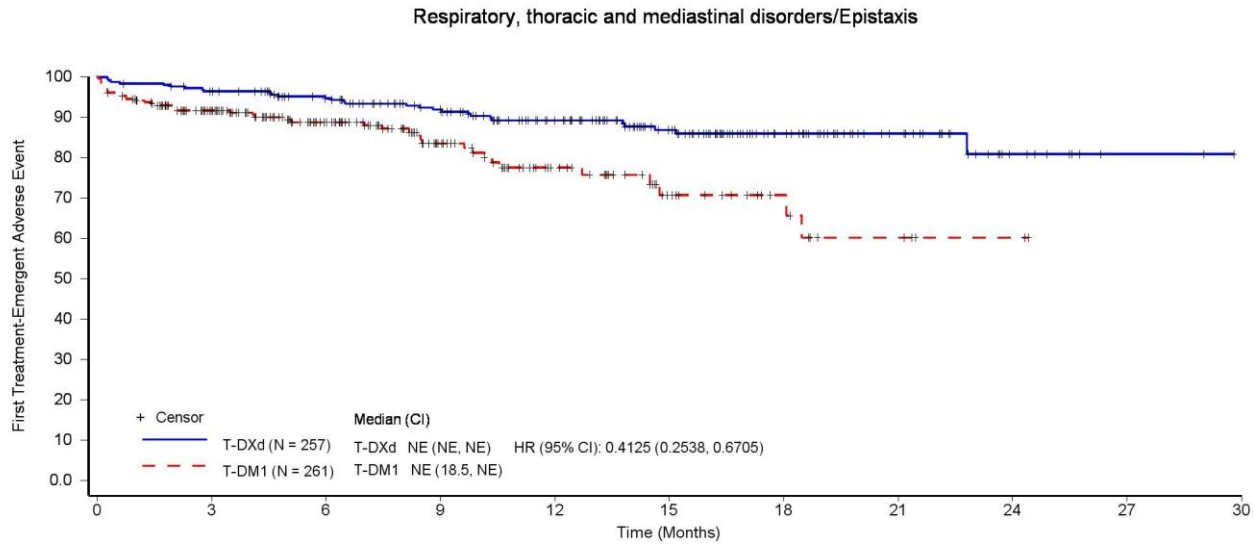
Patients still at risk:

T-DXd (N = 257)	257	210	172	141	103	70	34	17	6	1	0
T-DM1 (N = 261)	261	167	114	67	37	19	8	5	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



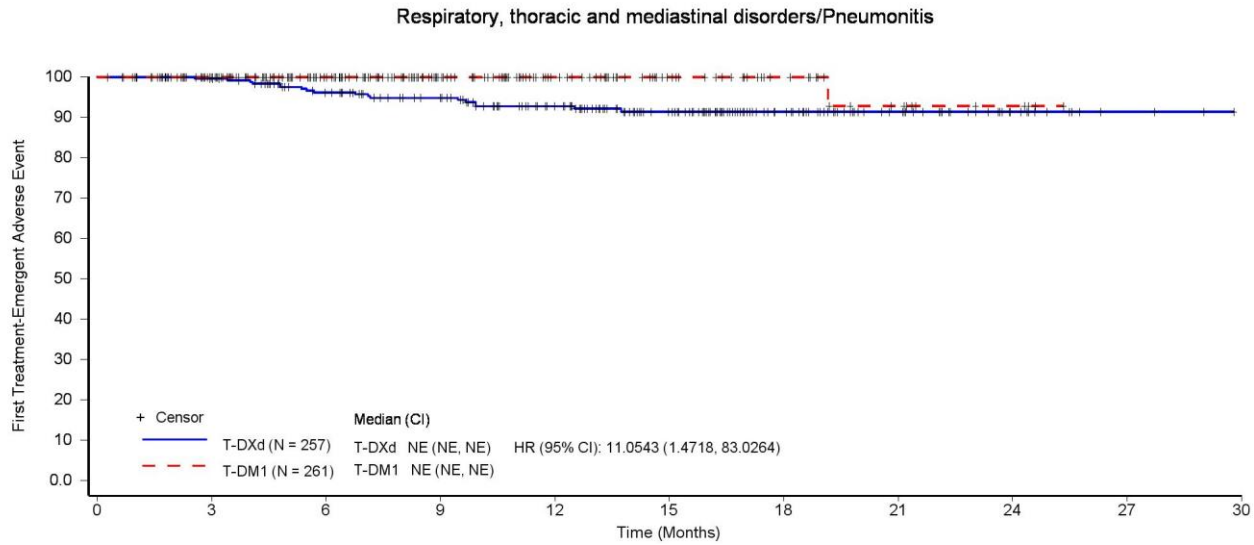
Patients still at risk:

T-DXd (N = 257)	257	243	214	184	144	98	48	27	9	2	0
T-DM1 (N = 261)	261	187	128	79	46	24	14	6	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



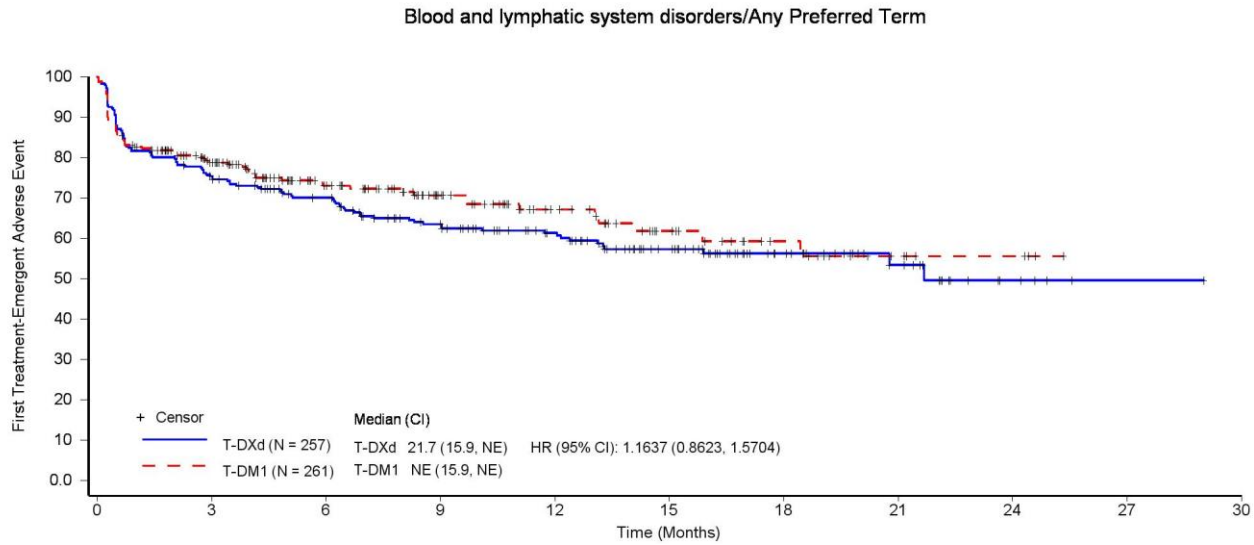
Patients still at risk:

T-DXd (N = 257)	257	250	218	196	157	111	54	30	12	3	0
T-DM1 (N = 261)	261	206	149	98	61	37	22	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



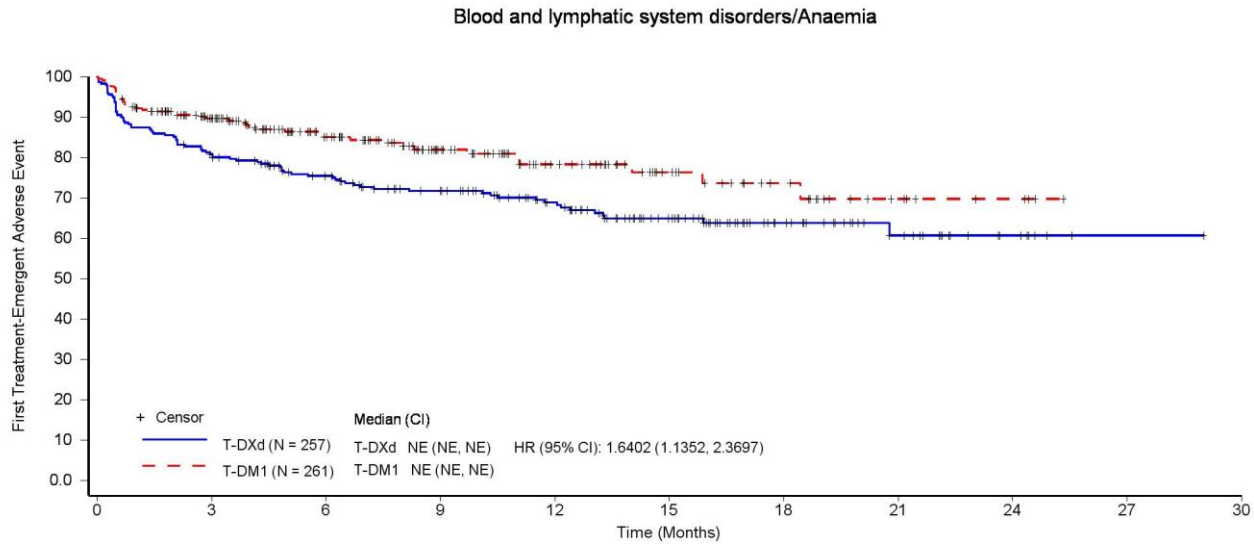
Patients still at risk:

T-DXd (N = 257)	257	192	157	126	96	68	32	18	5	1	0
T-DM1 (N = 261)	261	165	107	69	43	27	16	7	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



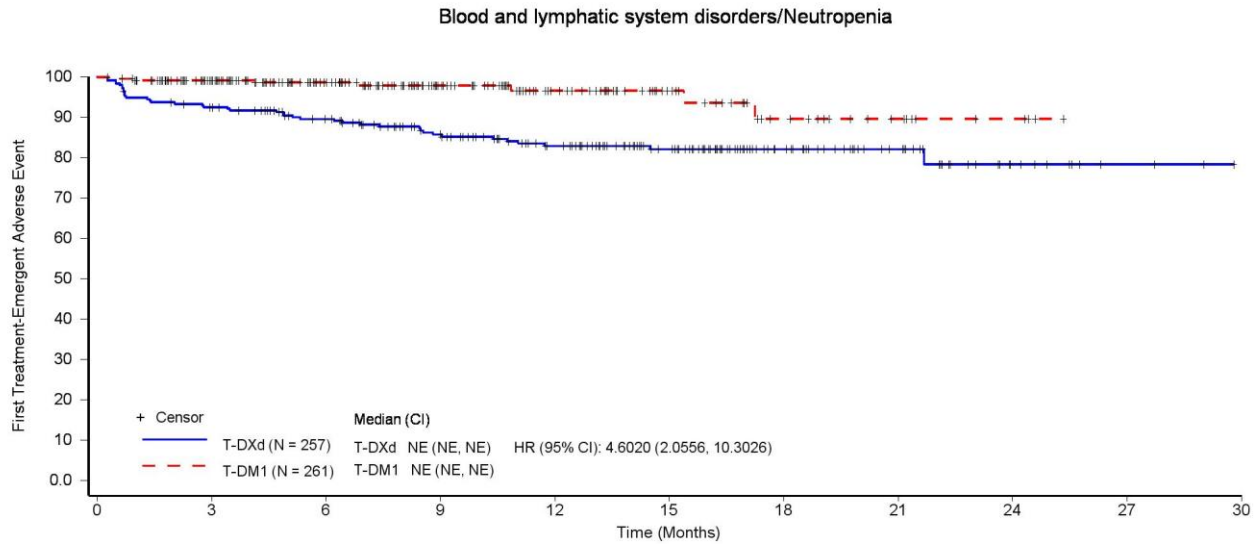
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	206	169	143	109	73	35	19	7	1	0
T-DM1 (N = 261)	261	187	128	82	51	31	20	8	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



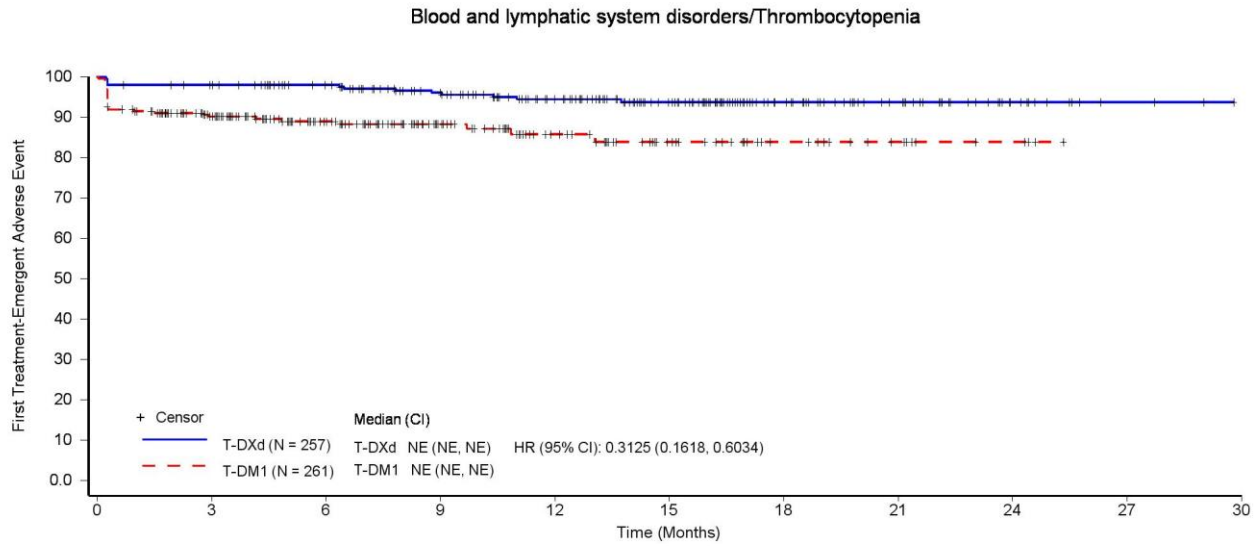
Patients still at risk:

T-DXd (N = 257)	257	232	201	170	134	98	46	28	10	3	0
T-DM1 (N = 261)	261	204	146	95	59	35	20	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



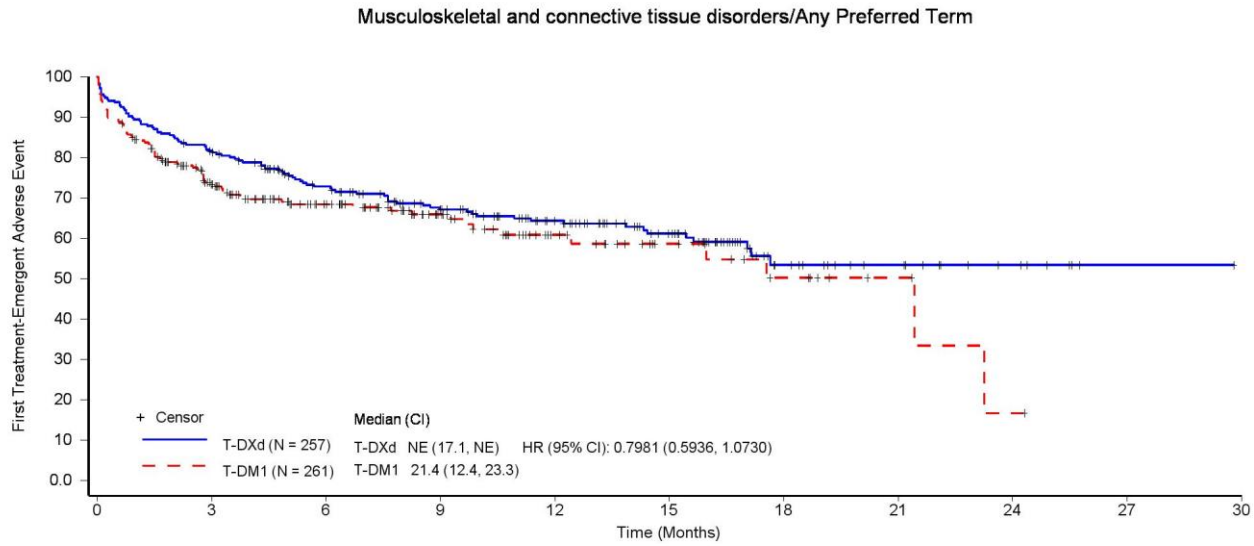
Patients still at risk:

T-DXd (N = 257)	257	246	221	191	153	108	51	31	12	3	0
T-DM1 (N = 261)	261	186	130	83	51	31	18	9	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



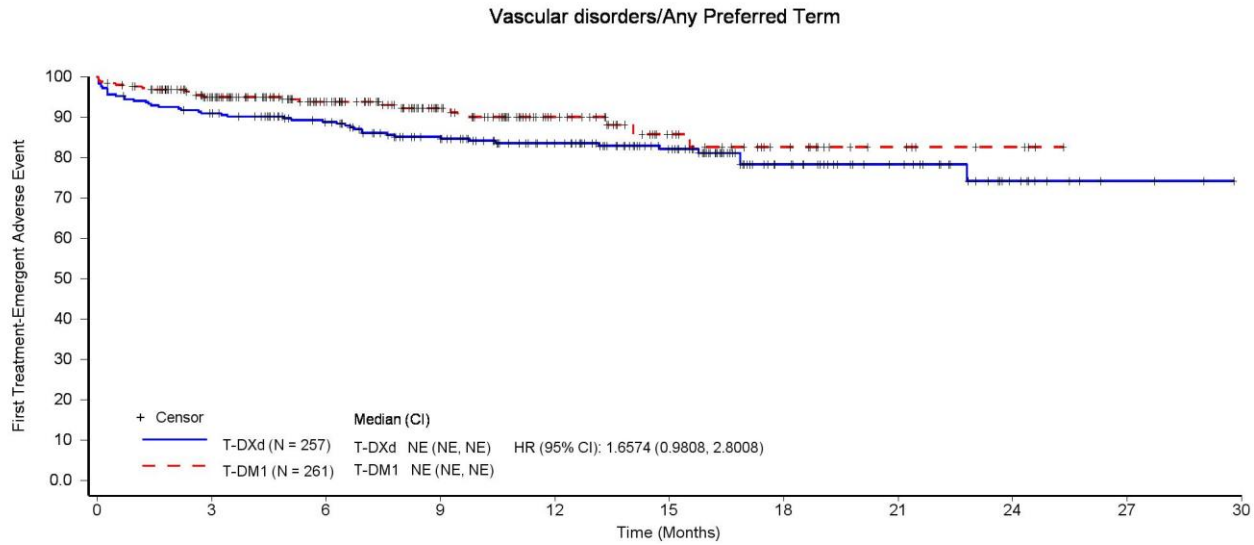
Patients still at risk:

T-DXd (N = 257)	257	208	163	132	99	68	22	14	7	1	0
T-DM1 (N = 261)	261	149	98	59	30	17	10	4	1	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



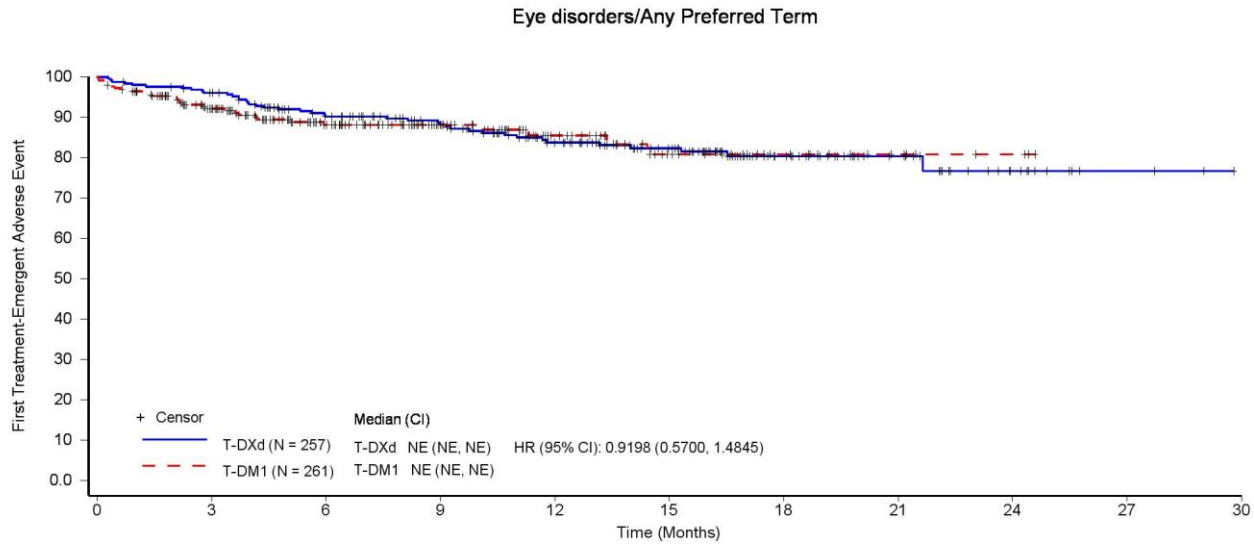
Patients still at risk:

T-DXd (N = 257)	257	229	203	171	138	96	42	27	11	3	0
T-DM1 (N = 261)	261	198	140	91	54	30	18	8	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



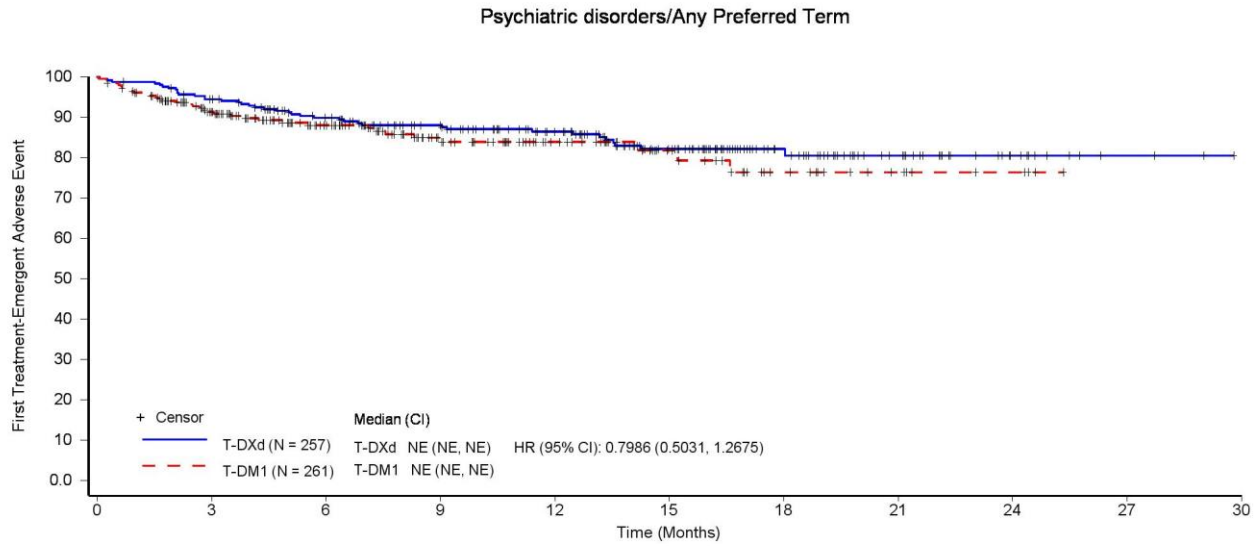
Patients still at risk:

T-DXd (N = 257)	257	241	203	175	135	101	45	26	11	3	0
T-DM1 (N = 261)	261	189	129	82	50	28	17	8	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



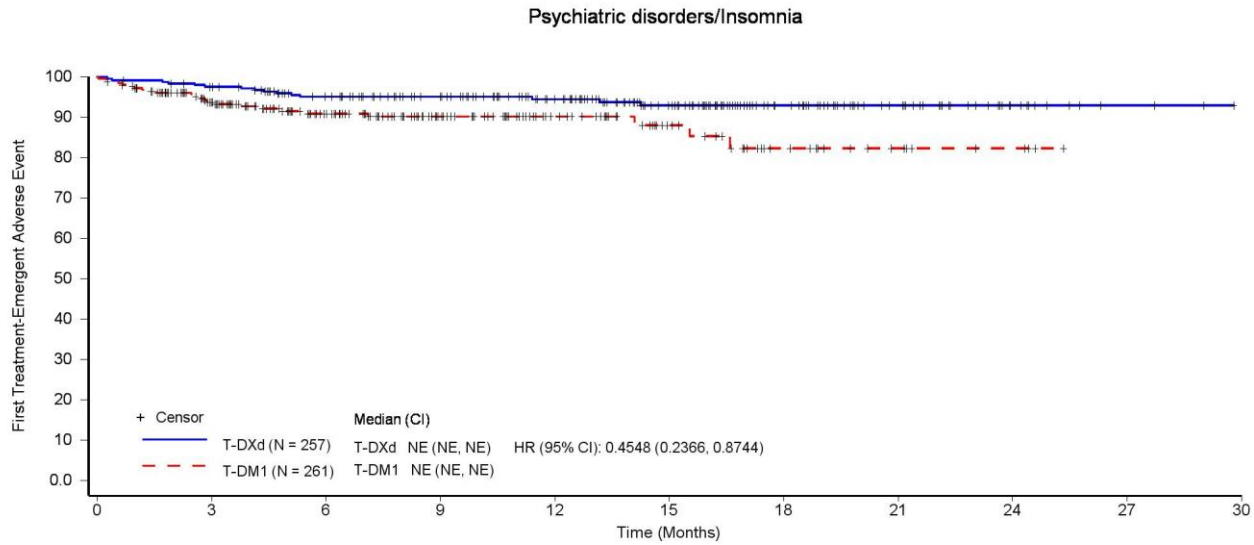
Patients still at risk:

T-DXd (N = 257)	257	238	204	175	140	96	49	27	11	3	0
T-DM1 (N = 261)	261	191	132	83	54	33	18	9	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



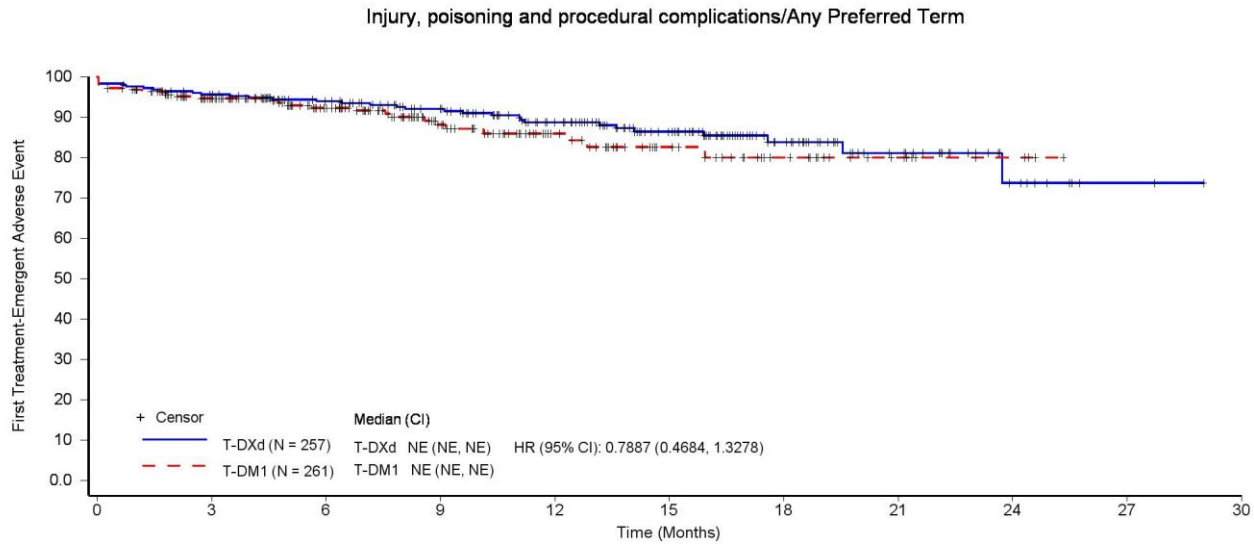
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	246	214	188	150	105	52	30	11	3	0
T-DM1 (N = 261)	261	194	135	89	56	34	18	9	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



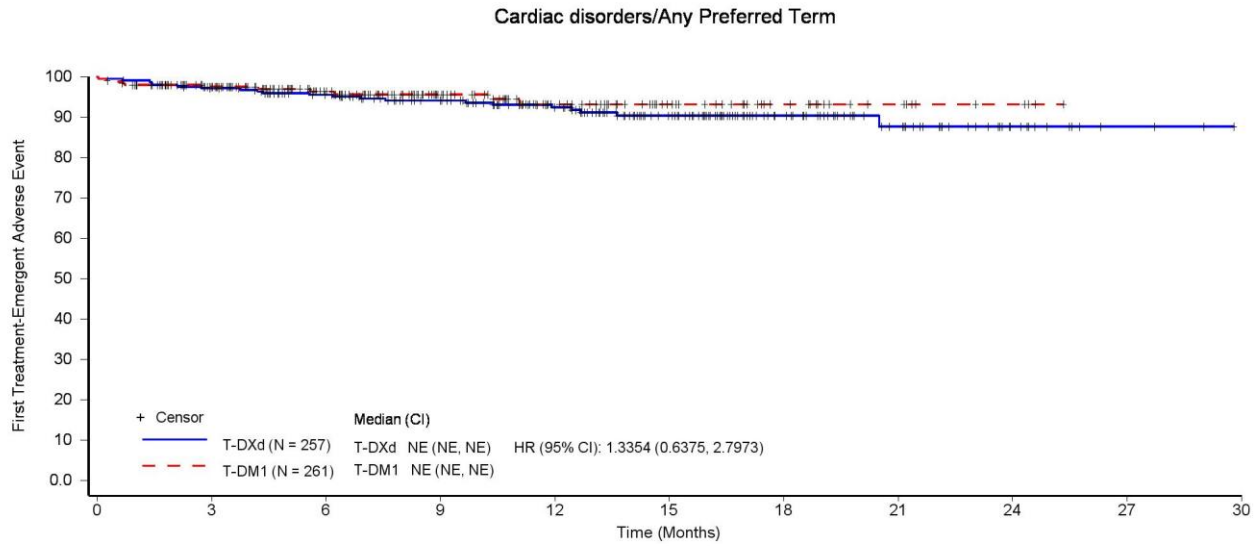
Patients still at risk:

T-DXd (N = 257)	257	240	210	183	141	97	45	25	9	2	0
T-DM1 (N = 261)	261	195	139	87	53	34	21	9	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



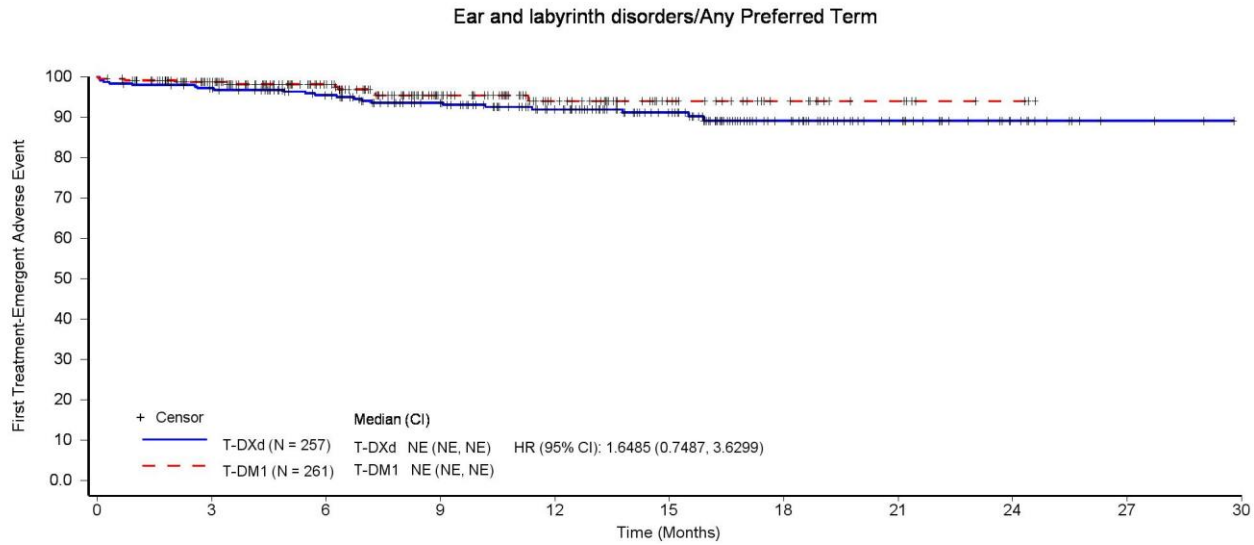
Patients still at risk:

T-DXd (N = 257)	257	244	215	187	149	101	52	30	12	3	0
T-DM1 (N = 261)	261	201	144	94	57	36	21	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



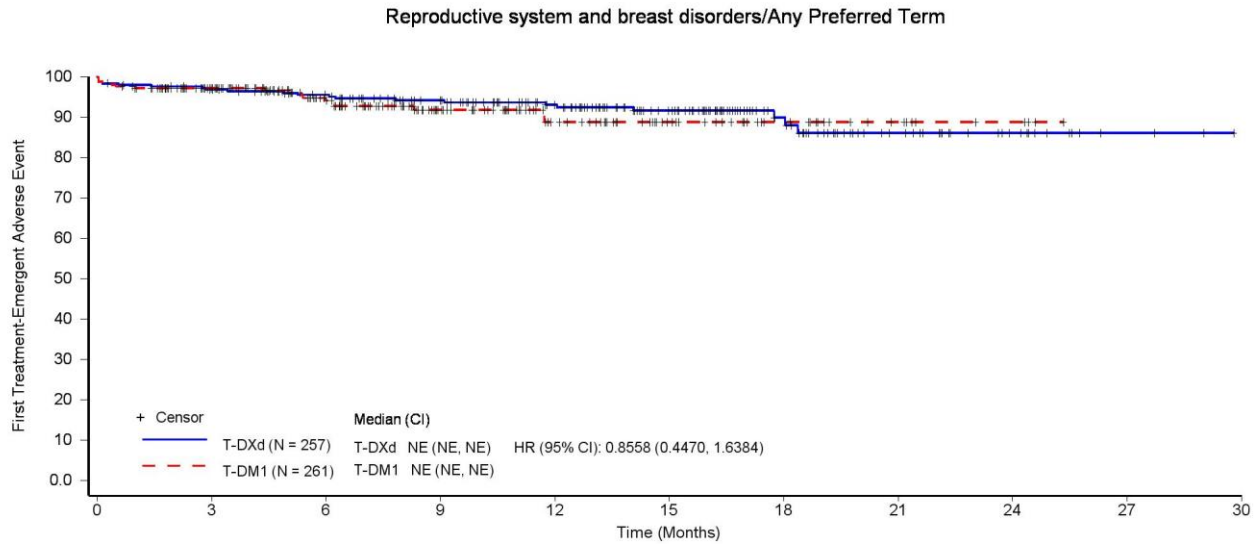
Patients still at risk:

T-DXd (N = 257)	257	244	214	184	144	104	47	27	12	3	0
T-DM1 (N = 261)	261	205	149	94	57	33	19	9	3	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



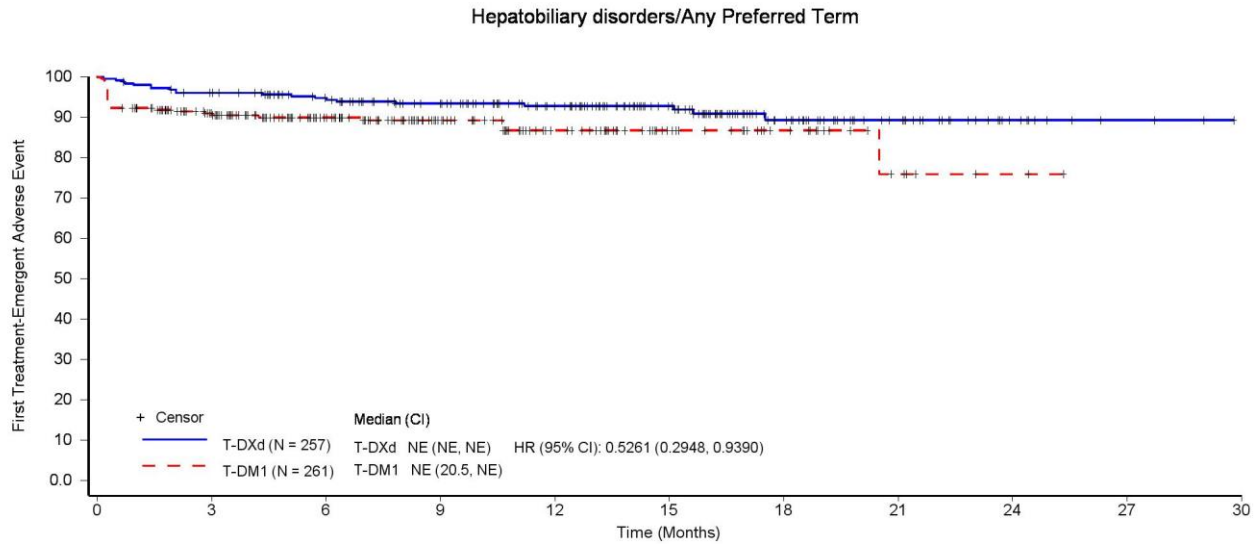
Patients still at risk:

T-DXd (N = 257)	257	244	216	189	149	103	48	25	12	3	0
T-DM1 (N = 261)	261	201	140	89	54	34	20	10	4	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



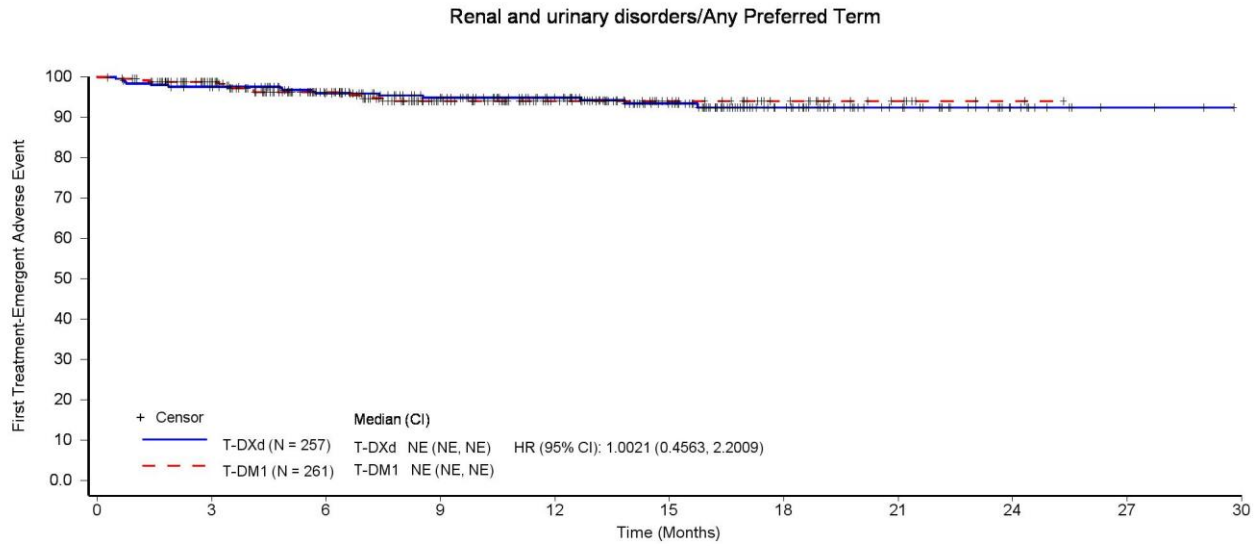
Patients still at risk:

	0	3	6	9	12	15	18	21	24	27	30
T-DXd (N = 257)	257	243	215	188	150	106	49	27	10	3	0
T-DM1 (N = 261)	261	188	134	87	54	31	18	6	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.

Figure 17 Kaplan-Meier Plot of First Treatment-Emergent Adverse Events by System Organ Class, Preferred Term with incidence $\geq 1\%$ in at least one arm and observed for ≥ 10 patients - Safety Analysis Set



Patients still at risk:

T-DXd (N = 257)	257	246	216	188	150	104	50	28	11	3	0
T-DM1 (N = 261)	261	204	144	92	57	34	20	8	2	0	0

Notes: Unstratified Cox proportional hazard model for Hazard ratio.

NE: Not Estimable.