Health-related quality-of-life in patients with newly diagnosed multiple myeloma in the FIRST trial: lenalidomide plus low-dose dexamethasone *versus* melphalan, prednisone, thalidomide

Michel Delforge,[1] Leonard Minuk,[2] Jean-Claude Eisenmann,[3] Bertrand Arnulf,[4] Letizia Canepa,[5] Alberto Fragasso,[6] Serge Leyvraz,[7] Christian Langer,[8] Yousef Ezaydi,[9] Dan T. Vogl,[10] Pilar Giraldo-Castellano,[11] Sung-Soo Yoon,[12] Charles Zarnitsky,[13] Martine Escoffre-Barbe,[14] Bernard Lemieux,[15] Kevin Song,[16] Nizar Jacques Bahlis,[17] Shien Guo,[18] Mara Silva Monzini,[19] Annette Ervin-Haynes,[19] Vanessa Houck,[19] and Thierry Facon[20]

[1]Universitair Ziekenhuis Leuven, Campus Gasthuisberg, Leuven, Belgium; [2]London Health Sciences Centre, London, ON, Canada; [3]Hôpital Emile Muller, Mulhouse, France; [4]Hôpital Saint-Louis, Paris, France; [5]Clinica Ematologica, A.O.U. San Martino di Genova, Italy; [6]Unità Operativa di Oncoematologia, Ospedale di Matera, Italy; [7]Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; [8]Klinik für Innere Medizin III, Ulm, Germany; [9]Royal Hallamshire Hospital, Sheffield, UK; [10]Abramson Cancer Center, University of Pennsylvania, Philadelphia, PA, USA; [11]CIBER Enfermedades Raras (CIBERER), Translational Research Unit, Miguel Servet University Hospital, Zaragoza, Spain; [12]Seoul National University Hospital, Korea; [13]Rhumatologie Nord, Hôpital J. Monod, Le Havre, France; [14]CHRU Hôpital de Pontchaillou, Rennes, France; [15]CHUM Hôpital Notre-Dame, Montreal, QUE, Canada; [16]Vancouver General Hospital, Vancouver, BC, Canada; [17]Tom Baker Cancer Centre – University of Calgary, Calgary, AL, Canada; [18]Evidera, Lexington, MA, USA; [19]Celgene Corporation, Summit, NJ, USA; and [20]Hôpital Claude Huriez, Lille, France

Cross-sectional and longitudinal HRQoL analyses

Changes from baseline at each time point and at PD were calculated for within-treatment and between-treatment comparisons. Change from baseline was tested for statistical significance using the 1-sample t-test for within-treatment comparisons and using the 2-sample t-test for between-treatment comparisons.

Estimation of the overall treatment effects of evaluated HRQoL domains at the population level

Overall treatment effects of evaluated HRQoL domains at the population level were estimated using all longitudinal data points, mixed-model repeated-measures analyses were performed using PROC MIXED in SAS® (SAS Institute Inc., Cary, NC, USA). The analyses used change scores as the dependent variable and included baseline scores, time, treatment, and treatment-by-time interaction as fixed effects; and intercept and time as random effects. A variance components covariance structure was used to model a different variance component for each random effect. The least-squares mean change from baseline within each treatment and the difference in least-squares mean change from baseline between treatments were estimated for each HRQoL domain, based on the fixed effects.

Table 1. EORTC QLQ-C30 outcomes

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Global Health Status/QoL by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1015	508	1523
Mean	51.7	50.8	51.4
Std Dev	24.36	24.16	24.29
Median	50.0	50.0	50.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.5095		
Month 1			
N	908	432	1340
Mean	52.0	52.9	52.3
Std Dev	21.36	19.96	20.92
Median	50.0	50.0	50.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4567		
Change from Baseline at Month 1			
N	879	415	1294
Mean	-0.4	1.0	0.0
Std Dev	23.96	23.68	23.87
Median	0.0	0.0	0.0
Min, Max	-91.7 , 91.7	-83.3 , 91.7	-91.7 , 91.7
p-value [1]	0.6058	0.3882	
p-value [2]	0.3176		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better global health status/QoL. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Global Health Status/QoL by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	869	411	1280
Mean	57.8	57.1	57.6
Std Dev	20.37	19.62	20.13
Median	58.3	58.3	58.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.5351		
Change from Baseline at Month 3			
N	834	396	1230
Mean	4.8	4.3	4.6
Std Dev	24.64	26.04	25.09
Median	0.0	0.0	0.0
Min, Max	-100.0 , 83.3	-83.3 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	0.0010	
p-value [2]	0.7734		
Month 6			
N	775	365	1140
Mean	59.4	58.1	59.0
Std Dev	20.01	18.72	19.61
Median	58.3	58.3	58.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2710		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better global health status/QoL. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Global Health Status/QoL by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	745	351	1096
Mean	5.6	6.1	5.8
Std Dev	24.90	25.98	25.24
Median	0.0	0.0	0.0
Min, Max	-100.0 , 91.7	-58.3 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.7930		
Month 12			
N	630	260	890
Mean	59.3	60.0	59.5
Std Dev	19.47	18.69	19.24
Median	58.3	66.7	58.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.6373		
Change from Baseline at Month 12			
N	601	252	853
Mean	4.0	6.5	4.7
Std Dev	25.90	25.90	25.91
Median	0.0	0.0	0.0
Min, Max	-91.7 , 83.3	-66.7 , 91.7	-91.7 , 91.7
p-value [1]	0.0002	<.0001	
p-value [2]	0.1974		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better global health status/QoL. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Global Health Status/QoL by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	505	184	689
Mean	61.8	60.6	61.5
Std Dev	20.23	18.03	19.66
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	8.3 , 100.0	0.0 , 100.0
p-value [2]	0.4892		
Change from Baseline at Month 18			
N	484	178	662
Mean	6.0	4.8	5.7
Std Dev	26.49	27.05	26.63
Median	0.0	0.0	0.0
Min, Max	-91.7 , 83.3	-66.7 , 83.3	-91.7 , 83.3
p-value [1]	<.0001	0.0196	
p-value [2]	0.5873		
Study Disc.			
N	482	266	748
Mean	52.9	52.1	52.7
Std Dev	23.06	23.45	23.19
Median	50.0	50.0	50.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.6482		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better global health status/QoL. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Global Health Status/QoL by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	464	257	721
Mean	2.8	0.3	1.9
Std Dev	27.31	28.07	27.58
Median	0.0	0.0	0.0
Min, Max	-75.0 , 83.3	-83.3 , 66.7	-83.3 , 83.3
p-value [1]	0.0296	0.8532	
p-value [2]	0.2553		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better global health status/QoL. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Physical Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1025	509	1534
Mean	61.5	59.9	61.0
Std Dev	27.02	28.84	27.64
Median	66.7	60.0	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2832		
Month 1			
N	917	437	1354
Mean	61.2	61.1	61.1
Std Dev	25.83	25.43	25.69
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.9367		
Change from Baseline at Month 1			
N	894	419	1313
Mean	-1.5	-0.9	-1.3
Std Dev	20.33	21.28	20.63
Median	0.0	0.0	0.0
Min, Max	-93.3 , 80.0	-66.7 , 93.3	-93.3 , 93.3
p-value [1]	0.0235	0.3947	
p-value [2]	0.5907		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better physical functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Physical Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	874	412	1286
Mean	67.7	65.3	66.9
Std Dev	24.05	23.55	23.91
Median	73.3	66.7	73.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0871		
Change from Baseline at Month 3			
N	847	396	1243
Mean	4.0	2.2	3.4
Std Dev	23.13	23.68	23.32
Median	0.0	0.0	0.0
Min, Max	-100.0 , 93.3	-66.7 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	0.0711	
p-value [2]	0.1831		
Month 6			
N	782	367	1149
Mean	70.0	67.4	69.2
Std Dev	21.58	22.41	21.87
Median	73.3	73.3	73.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0609		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better physical functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Physical Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	758	352	1110
Mean	6.2	5.3	5.9
Std Dev	24.01	24.52	24.17
Median	5.8	0.0	0.0
Min, Max	-93.3 , 73.3	-60.0 , 93.3	-93.3 , 93.3
p-value [1]	<.0001	<.0001	
p-value [2]	0.5908		
Month 12			
N	632	263	895
Mean	71.0	68.9	70.4
Std Dev	21.34	21.24	21.32
Median	73.3	73.3	73.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1873		
Change from Baseline at Month 12			
N	609	253	862
Mean	6.2	6.9	6.4
Std Dev	24.57	27.22	25.36
Median	0.0	0.0	0.0
Min, Max	-80.0 , 80.0	-60.0 , 93.3	-80.0 , 93.3
p-value [1]	<.0001	<.0001	
p-value [2]	0.7010		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better physical functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Physical Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	507	189	696
Mean	72.6	73.4	72.8
Std Dev	20.28	18.84	19.89
Median	80.0	73.3	75.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.6437		
Change from Baseline at Month 18			
N	490	183	673
Mean	6.8	8.3	7.2
Std Dev	25.18	27.10	25.70
Median	6.7	6.7	6.7
Min, Max	-77.8 , 86.7	-60.0 , 86.7	-77.8 , 86.7
p-value [1]	<.0001	<.0001	
p-value [2]	0.5062		
Study Disc.			
N	492	266	758
Mean	61.3	60.9	61.1
Std Dev	26.22	26.23	26.21
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.8638		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better physical functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1] The p-value is calculated based on a one-sample t-test.
[2] The p-value is calculated based on a pooled t-test comparing two treatment groups.
     The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Physical Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	474	256	730
Mean	1.6	-0.1	1.0
Std Dev	28.40	27.58	28.11
Median	0.0	0.0	0.0
Min, Max	-86.7 , 93.3	-86.7 , 86.7	-86.7 , 93.3
p-value [1]	0.2087	0.9549	
p-value [2]	0.4252		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better physical functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Role Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1017	508	1525
Mean	55.4	52.3	54.4
Std Dev	34.68	36.75	35.40
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1114		
Month 1			
N	915	433	1348
Mean	52.4	52.1	52.3
Std Dev	33.58	33.33	33.49
Median	66.7	50.0	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.8529		
Change from Baseline at Month 1			
N	887	415	1302
Mean	-3.7	-2.4	-3.3
Std Dev	29.08	30.48	29.53
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0002	0.1140	
p-value [2]	0.4613		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better role functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Role Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	874	412	1286
Mean	61.2	59.7	60.7
Std Dev	31.91	31.46	31.76
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4160		
Change from Baseline at Month 3			
N	841	395	1236
Mean	4.4	4.1	4.3
Std Dev	32.92	34.23	33.33
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0001	0.0168	
p-value [2]	0.9120		
Month 6			
N	781	368	1149
Mean	65.1	62.6	64.3
Std Dev	29.42	29.78	29.54
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1857		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better role functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Role Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	751	352	1103
Mean	7.5	8.2	7.7
Std Dev	33.95	36.09	34.63
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.7418		
Month 12			
N	631	262	893
Mean	67.6	65.1	66.8
Std Dev	28.65	28.08	28.49
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2349		
Change from Baseline at Month 12			
N	605	252	857
Mean	8.6	11.8	9.5
Std Dev	35.39	38.94	36.47
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.2358		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better role functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Role Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	504	189	693
Mean	69.6	69.7	69.6
Std Dev	28.51	28.45	28.47
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.9928		
Change from Baseline at Month 18			
N	485	182	667
Mean	8.6	14.5	10.2
Std Dev	34.83	39.03	36.09
Median	0.0	16.7	0.0
Min, Max	-100.0 , 100.0	-83.3 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.0594		
Study Disc.			
N	491	266	757
Mean	54.9	52.7	54.1
Std Dev	33.62	33.58	33.60
Median	66.7	50.0	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3988		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better role functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Role Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	470	256	726
Mean	2.0	-1.0	0.9
Std Dev	37.81	38.41	38.02
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.2554	0.6845	
p-value [2]	0.3162		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better role functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Emotional Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1019	510	1529
Mean	70.7	70.4	70.6
Std Dev	23.85	24.40	24.02
Median	75.0	75.0	75.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.8159		
Month 1			
N	916	436	1352
Mean	71.3	72.3	71.6
Std Dev	24.28	23.76	24.11
Median	75.0	75.0	75.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4751		
Change from Baseline at Month 1			
N	889	419	1308
Mean	0.4	1.0	0.6
Std Dev	21.43	21.52	21.45
Median	0.0	0.0	0.0
Min, Max	-75.0 , 80.6	-75.0 , 91.7	-75.0 , 91.7
p-value [1]	0.6080	0.3321	
p-value [2]	0.6081		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better emotional functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Emotional Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	870	412	1282
Mean	75.6	73.3	74.8
Std Dev	22.11	23.28	22.51
Median	83.3	75.0	75.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0884		
Change from Baseline at Month 3			
N	838	397	1235
Mean	3.9	2.1	3.3
Std Dev	22.19	22.27	22.22
Median	0.0	0.0	0.0
Min, Max	-75.0 , 91.7	-91.7 , 66.7	-91.7 , 91.7
p-value [1]	<.0001	0.0611	
p-value [2]	0.1922		
Month 6			
N	782	365	1147
Mean	77.0	75.8	76.6
Std Dev	21.49	21.87	21.61
Median	83.3	75.0	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3855		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better emotional functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Emotional Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	754	351	1105
Mean	5.2	5.5	5.3
Std Dev	23.39	22.55	23.11
Median	0.0	0.0	0.0
Min, Max	-83.3 , 83.3	-83.3 , 83.3	-83.3 , 83.3
p-value [1]	<.0001	<.0001	
p-value [2]	0.8209		
Month 12			
N	633	262	895
Mean	77.3	75.9	76.8
Std Dev	21.18	22.33	21.52
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3758		
Change from Baseline at Month 12			
N	606	254	860
Mean	4.7	5.1	4.9
Std Dev	23.16	22.37	22.92
Median	0.0	0.0	0.0
Min, Max	-50.0 , 91.7	-83.3 , 75.0	-83.3 , 91.7
p-value [1]	<.0001	0.0003	
p-value [2]	0.8245		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better emotional functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Emotional Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	507	185	692
Mean	77.7	76.7	77.4
Std Dev	21.78	22.34	21.92
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.5891		
Change from Baseline at Month 18			
N	488	179	667
Mean	4.4	5.1	4.6
Std Dev	24.51	22.99	24.10
Median	0.0	0.0	0.0
Min, Max	-83.3 , 100.0	-66.7 , 83.3	-83.3 , 100.0
p-value [1]	<.0001	0.0036	
p-value [2]	0.7634		
Study Disc.			
N	486	265	751
Mean	72.1	70.8	71.6
Std Dev	24.56	25.28	24.81
Median	75.0	75.0	75.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4823		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better emotional functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Emotional Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	468	256	724
Mean	3.2	-0.0	2.1
Std Dev	23.98	24.72	24.28
Median	0.0	0.0	0.0
Min, Max	-75.0 , 91.7	-83.3 , 77.8	-83.3 , 91.7
p-value [1]	0.0037	0.9944	
p-value [2]	0.0855		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better emotional functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Cognitive Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1019	510	1529
Mean	80.0	78.3	79.4
Std Dev	22.92	23.24	23.03
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1789		
Month 1			
N	917	436	1353
Mean	78.7	77.7	78.4
Std Dev	23.94	23.72	23.87
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4784		
Change from Baseline at Month 1			
N	890	419	1309
Mean	-1.4	-1.8	-1.6
Std Dev	20.43	24.07	21.66
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-83.3 , 83.3	-100.0 , 100.0
p-value [1]	0.0356	0.1288	
p-value [2]	0.7863		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better cognitive functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Cognitive Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	871	412	1283
Mean	81.5	78.2	80.5
Std Dev	21.97	23.82	22.63
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0135		
Change from Baseline at Month 3			
N	839	397	1236
Mean	0.5	-1.5	-0.1
Std Dev	21.97	24.02	22.66
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.5128	0.2108	
p-value [2]	0.1458		
Month 6			
N	782	367	1149
Mean	81.3	78.7	80.4
Std Dev	21.56	22.41	21.86
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0636		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better cognitive functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Cognitive Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	754	353	1107
Mean	0.0	-0.3	-0.1
Std Dev	21.21	23.55	21.98
Median	0.0	0.0	0.0
Min, Max	-100.0 , 83.3	-83.3 , 66.7	-100.0 , 83.3
p-value [1]	1.0000	0.7922	
p-value [2]	0.8157		
Month 12			
N	634	262	896
Mean	80.6	78.9	80.1
Std Dev	21.34	22.67	21.74
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3078		
Change from Baseline at Month 12			
N	607	254	861
Mean	-1.4	-0.6	-1.2
Std Dev	22.75	22.97	22.81
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-83.3 , 66.7	-100.0 , 100.0
p-value [1]	0.1226	0.6824	
p-value [2]	0.6236		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better cognitive functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Cognitive Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	507	185	692
Mean	80.6	79.7	80.3
Std Dev	20.83	22.37	21.24
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.6446		
Change from Baseline at Month 18			
N	488	179	667
Mean	-2.5	-0.7	-2.0
Std Dev	23.40	23.99	23.56
Median	0.0	0.0	0.0
Min, Max	-83.3 , 100.0	-83.3 , 66.7	-83.3 , 100.0
p-value [1]	0.0190	0.7166	
p-value [2]	0.3714		
Study Disc.			
N	487	265	752
Mean	75.7	73.7	75.0
Std Dev	24.97	25.39	25.12
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3078		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better cognitive functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Cognitive Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	469	256	725
Mean	-3.6	-7.1	-4.9
Std Dev	24.77	25.15	24.94
Median	0.0	0.0	0.0
Min, Max	-100.0 , 83.3	-83.3 , 83.3	-100.0 , 83.3
p-value [1]	0.0016	<.0001	
p-value [2]	0.0733		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better cognitive functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Social Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1008	503	1511
Mean	69.3	66.9	68.5
Std Dev	31.69	32.99	32.14
Median	83.3	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1661		
Month 1			
N	916	436	1352
Mean	66.4	66.4	66.4
Std Dev	31.46	29.81	30.93
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.9935		
Change from Baseline at Month 1			
N	880	414	1294
Mean	-3.2	-1.4	-2.6
Std Dev	28.29	30.52	29.02
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0007	0.3621	
p-value [2]	0.2798		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better social functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Social Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	870	410	1280
Mean	71.6	70.4	71.3
Std Dev	29.40	27.53	28.81
Median	83.3	66.7	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4939		
Change from Baseline at Month 3			
N	829	389	1218
Mean	1.3	2.4	1.7
Std Dev	30.13	30.70	30.31
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 83.3	-100.0 , 100.0
p-value [1]	0.2052	0.1175	
p-value [2]	0.5496		
Month 6			
N	781	367	1148
Mean	75.2	71.1	73.9
Std Dev	25.83	28.17	26.66
Median	83.3	66.7	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0154		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better social functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Social Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	748	348	1096
Mean	4.6	3.4	4.2
Std Dev	30.54	35.24	32.09
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	0.0688	
p-value [2]	0.5764		
Month 12			
N	634	262	896
Mean	75.5	73.4	74.9
Std Dev	26.40	27.28	26.66
Median	83.3	75.0	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2861		
Change from Baseline at Month 12			
N	603	252	855
Mean	3.3	5.8	4.1
Std Dev	33.64	33.68	33.65
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-83.3 , 100.0	-100.0 , 100.0
p-value [1]	0.0149	0.0065	
p-value [2]	0.3270		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better social functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Social Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	507	185	692
Mean	76.4	73.9	75.7
Std Dev	25.57	27.62	26.14
Median	83.3	83.3	83.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2614		
Change from Baseline at Month 18			
N	486	177	663
Mean	3.7	6.0	4.3
Std Dev	33.37	35.20	33.85
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0148	0.0239	
p-value [2]	0.4349		
Study Disc.			
N	487	264	751
Mean	67.3	64.5	66.3
Std Dev	31.51	32.08	31.72
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2441		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better social functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Social Functioning by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	461	254	715
Mean	0.9	-3.5	-0.6
Std Dev	33.45	33.20	33.40
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.5465	0.0963	
p-value [2]	0.0906		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better social functioning. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Fatigue by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1025	512	1537
Mean	44.8	46.0	45.2
Std Dev	27.84	28.37	28.01
Median	44.4	44.4	44.4
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4290		
Month 1			
N	916	436	1352
Mean	47.1	47.2	47.1
Std Dev	26.29	25.33	25.97
Median	44.4	44.4	44.4
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.9498		
Change from Baseline at Month 1			
N	893	421	1314
Mean	3.5	2.8	3.3
Std Dev	24.69	25.44	24.92
Median	0.0	0.0	0.0
Min, Max	-66.7 , 88.9	-88.9 , 77.8	-88.9 , 88.9
p-value [1]	<.0001	0.0259	
p-value [2]	0.6318		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe fatigue. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Fatigue by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	875	413	1288
Mean	39.8	42.0	40.5
Std Dev	25.49	24.52	25.20
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1501		
Change from Baseline at Month 3			
N	848	400	1248
Mean	-2.9	-1.8	-2.6
Std Dev	26.69	28.53	27.29
Median	0.0	0.0	0.0
Min, Max	-88.9 , 100.0	-88.9 , 88.9	-88.9 , 100.0
p-value [1]	0.0014	0.1995	
p-value [2]	0.5084		
Month 6			
N	783	368	1151
Mean	37.7	40.0	38.4
Std Dev	23.16	24.51	23.61
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1186		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe fatigue. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Fatigue by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	759	355	1114
Mean	-4.8	-4.5	-4.7
Std Dev	27.47	29.09	27.98
Median	0.0	0.0	0.0
Min, Max	-88.9 , 100.0	-88.9 , 77.8	-88.9 , 100.0
p-value [1]	<.0001	0.0040	
p-value [2]	0.8532		
Month 12			
N	632	263	895
Mean	37.9	39.3	38.3
Std Dev	23.37	22.64	23.16
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3980		
Change from Baseline at Month 12			
N	609	255	864
Mean	-3.3	-3.9	-3.5
Std Dev	28.09	29.56	28.51
Median	0.0	0.0	0.0
Min, Max	-88.9 , 100.0	-88.9 , 55.6	-88.9 , 100.0
p-value [1]	0.0036	0.0351	
p-value [2]	0.7810		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe fatigue. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Fatigue by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	503	189	692
Mean	38.4	36.3	37.8
Std Dev	23.47	23.27	23.42
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3080		
Change from Baseline at Month 18			
N	486	184	670
Mean	-1.5	-4.3	-2.3
Std Dev	29.49	30.05	29.65
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-77.8 , 66.7	-100.0 , 100.0
p-value [1]	0.2492	0.0512	
p-value [2]	0.2748		
Study Disc.			
N	492	266	758
Mean	45.9	47.3	46.4
Std Dev	27.92	29.14	28.34
Median	44.4	44.4	44.4
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4929		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe fatigue. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Fatigue by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	474	258	732
Mean	-0.8	2.7	0.4
Std Dev	29.37	30.15	29.68
Median	0.0	0.0	0.0
Min, Max	-88.9 , 77.8	-77.8 , 100.0	-88.9 , 100.0
p-value [1]	0.5608	0.1495	
p-value [2]	0.1277		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe fatigue. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Pain by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1025	512	1537
Mean	44.7	45.3	44.9
Std Dev	33.65	35.37	34.22
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.7340		
Month 1			
N	922	438	1360
Mean	39.5	36.6	38.6
Std Dev	31.51	31.84	31.63
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1108		
Change from Baseline at Month 1			
N	899	423	1322
Mean	-4.9	-7.8	-5.8
Std Dev	31.28	30.93	31.19
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.1166		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe pain. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Pain by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	876	412	1288
Mean	30.3	31.4	30.7
Std Dev	27.77	28.92	28.14
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4968		
Change from Baseline at Month 3			
N	849	399	1248
Mean	-13.3	-12.1	-12.9
Std Dev	33.30	31.98	32.87
Median	-16.7	0.0	-16.7
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.5689		
Month 6			
N	787	368	1155
Mean	28.8	31.3	29.6
Std Dev	26.22	29.75	27.40
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1429		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe pain. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	763	355	1118
Mean	-15.3	-13.4	-14.7
Std Dev	34.54	34.45	34.51
Median	-16.7	0.0	-16.7
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.3946		
Month 12			
N	633	263	896
Mean	28.2	29.5	28.6
Std Dev	25.54	26.43	25.80
Median	33.3	16.7	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.5119		
Change from Baseline at Month 12			
N	610	255	865
Mean	-14.4	-14.3	-14.4
Std Dev	34.23	32.85	33.81
Median	-16.7	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.9817		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe pain. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Pain by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	507	188	695
Mean	28.6	28.0	28.5
Std Dev	26.64	26.05	26.46
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.7846		
Change from Baseline at Month 18			
N	490	183	673
Mean	-13.4	-14.7	-13.7
Std Dev	35.14	32.81	34.50
Median	-16.7	0.0	-16.7
Min, Max	-100.0 , 100.0	-100.0 , 66.7	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.6733		
Study Disc.			
N	491	267	758
Mean	39.8	39.7	39.8
Std Dev	31.70	32.91	32.11
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.9731		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe pain. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Pain by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	473	259	732
Mean	-7.9	-6.0	-7.2
Std Dev	38.37	37.09	37.91
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 83.3	-100.0 , 100.0
p-value [1]	<.0001	0.0099	
p-value [2]	0.5075		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe pain. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Nausea/Vomiting by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1024	512	1536
Mean	9.2	9.5	9.3
Std Dev	19.15	18.88	19.06
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.8130		
Month 1			
N	919	439	1358
Mean	9.6	12.6	10.6
Std Dev	18.23	22.50	19.76
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0081		
Change from Baseline at Month 1			
N	895	424	1319
Mean	0.6	4.0	1.7
Std Dev	21.70	22.91	22.14
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.3971	0.0004	
p-value [2]	0.0101		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe nausea and vomiting. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Nausea/Vomiting by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	875	412	1287
Mean	6.4	7.1	6.6
Std Dev	14.36	16.12	14.95
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4471		
Change from Baseline at Month 3			
N	848	399	1247
Mean	-1.8	-1.2	-1.6
Std Dev	20.70	19.89	20.44
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0103	0.2245	
p-value [2]	0.6195		
Month 6			
N	782	368	1150
Mean	5.7	4.4	5.3
Std Dev	13.46	11.99	13.02
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1348		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe nausea and vomiting. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Nausea/Vomiting by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	758	355	1113
Mean	-2.7	-3.9	-3.1
Std Dev	20.12	19.57	19.95
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0003	0.0002	
p-value [2]	0.3175		
Month 12			
N	632	263	895
Mean	4.4	4.5	4.4
Std Dev	10.19	12.18	10.81
Median	0.0	0.0	0.0
Min, Max	0.0 , 66.7	0.0 , 83.3	0.0 , 83.3
p-value [2]	0.8520		
Change from Baseline at Month 12			
N	608	255	863
Mean	-2.9	-3.9	-3.2
Std Dev	18.03	19.09	18.34
Median	0.0	0.0	0.0
Min, Max	-100.0 , 66.7	-100.0 , 50.0	-100.0 , 66.7
p-value [1]	<.0001	0.0014	
p-value [2]	0.5003		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe nausea and vomiting. Month 1 for MPT arm corresponds to week 6 assessment.
[1] The p-value is calculated based on a one-sample t-test.
[2] The p-value is calculated based on a pooled t-test comparing two treatment groups.
     The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Nausea/Vomiting by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	505	189	694
Mean	5.0	3.2	4.5
Std Dev	11.44	11.98	11.61
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0728		
Change from Baseline at Month 18			
N	488	184	672
Mean	-2.5	-3.9	-2.9
Std Dev	19.05	19.44	19.15
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0040	0.0072	
p-value [2]	0.3979		
Study Disc.			
N	491	266	757
Mean	8.7	8.4	8.6
Std Dev	18.45	17.63	18.15
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.8128		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe nausea and vomiting. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Nausea/Vomiting by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	473	258	731
Mean	-2.2	1.0	-1.1
Std Dev	23.23	21.46	22.66
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-83.3 , 83.3	-100.0 , 100.0
p-value [1]	0.0382	0.4690	
p-value [2]	0.0689		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe nausea and vomiting. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Dyspnea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1017	506	1523
Mean	26.2	27.3	26.6
Std Dev	29.63	31.77	30.35
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4986		
Month 1			
N	906	438	1344
Mean	28.2	29.5	28.6
Std Dev	30.09	31.01	30.39
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4595		
Change from Baseline at Month 1			
N	879	417	1296
Mean	2.2	4.2	2.9
Std Dev	30.37	32.04	30.92
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0292	0.0072	
p-value [2]	0.2770		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe dyspnea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Dyspnea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	871	406	1277
Mean	23.8	26.8	24.7
Std Dev	27.40	30.01	28.28
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0814		
Change from Baseline at Month 3			
N	840	390	1230
Mean	-1.3	2.0	-0.3
Std Dev	30.68	32.49	31.29
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.2028	0.2329	
p-value [2]	0.0838		
Month 6			
N	777	366	1143
Mean	23.0	24.3	23.4
Std Dev	26.43	28.89	27.24
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4589		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe dyspnea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Dyspnea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	747	351	1098
Mean	-2.6	0.1	-1.8
Std Dev	31.41	30.29	31.07
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0222	0.9532	
p-value [2]	0.1750		
Month 12			
N	625	261	886
Mean	21.0	23.0	21.6
Std Dev	26.35	27.41	26.67
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3023		
Change from Baseline at Month 12			
N	597	253	850
Mean	-2.6	-1.6	-2.3
Std Dev	30.11	32.76	30.91
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0376	0.4434	
p-value [2]	0.6705		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe dyspnea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Dyspnea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	501	188	689
Mean	23.2	23.2	23.2
Std Dev	26.91	29.22	27.54
Median	33.3	0.0	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.9977		
Change from Baseline at Month 18			
N	482	182	664
Mean	0.6	0.4	0.5
Std Dev	30.69	32.68	31.23
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.6925	0.8800	
p-value [2]	0.9452		
Study Disc.			
N	488	265	753
Mean	28.1	34.8	30.5
Std Dev	30.44	32.66	31.38
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0051		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe dyspnea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Dyspnea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	466	255	721
Mean	0.0	7.8	2.8
Std Dev	33.94	33.72	34.04
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-66.7 , 100.0	-100.0 , 100.0
p-value [1]	1.0000	0.0003	
p-value [2]	0.0030		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe dyspnea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1023	511	1534
Mean	29.2	27.8	28.7
Std Dev	31.92	30.92	31.59
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4113		
Month 1			
N	914	436	1350
Mean	31.4	15.7	26.3
Std Dev	31.45	26.10	30.71
Median	33.3	0.0	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 1			
N	890	421	1311
Mean	2.7	-10.5	-1.6
Std Dev	33.82	30.47	33.35
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 66.7	-100.0 , 100.0
p-value [1]	0.0192	<.0001	
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe insomnia. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Insomnia by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	869	411	1280
Mean	27.7	17.6	24.5
Std Dev	28.98	27.86	29.00
Median	33.3	0.0	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 3			
N	842	399	1241
Mean	-0.6	-8.9	-3.2
Std Dev	34.32	35.28	34.84
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.6395	<.0001	
p-value [2]	<.0001		
Month 6			
N	781	366	1147
Mean	27.7	14.8	23.6
Std Dev	27.80	25.55	27.74
Median	33.3	0.0	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe insomnia. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Insomnia by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	756	353	1109
Mean	-1.6	-11.6	-4.8
Std Dev	33.14	32.96	33.40
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.1883	<.0001	
p-value [2]	<.0001		
Month 12			
N	626	260	886
Mean	26.8	15.8	23.6
Std Dev	27.72	26.10	27.70
Median	33.3	0.0	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 12			
N	603	253	856
Mean	0.1	-9.6	-2.8
Std Dev	33.64	31.00	33.16
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.9678	<.0001	
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe insomnia. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Insomnia by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	502	187	689
Mean	26.8	17.8	24.4
Std Dev	29.37	27.05	29.02
Median	33.3	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0003		
Change from Baseline at Month 18			
N	484	182	666
Mean	0.4	-6.0	-1.4
Std Dev	36.40	34.42	35.96
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.8029	0.0189	
p-value [2]	0.0388		
Study Disc.			
N	488	262	750
Mean	28.6	25.4	27.5
Std Dev	29.83	31.11	30.30
Median	33.3	0.0	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1808		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe insomnia. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Insomnia by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	469	254	723
Mean	-3.2	-4.5	-3.6
Std Dev	33.64	36.98	34.83
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0401	0.0556	
p-value [2]	0.6418		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe insomnia. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Appetite Loss by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1021	510	1531
Mean	27.4	28.2	27.7
Std Dev	33.62	35.21	34.15
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.6487		
Month 1			
N	916	439	1355
Mean	28.3	27.7	28.1
Std Dev	33.68	34.22	33.84
Median	16.7	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.7755		
Change from Baseline at Month 1			
N	889	422	1311
Mean	2.1	1.0	1.8
Std Dev	32.66	32.35	32.55
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0556	0.5148	
p-value [2]	0.5774		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe appetite loss. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Appetite Loss by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	875	411	1286
Mean	20.7	19.5	20.3
Std Dev	29.53	29.34	29.46
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.5039		
Change from Baseline at Month 3			
N	845	396	1241
Mean	-4.6	-6.2	-5.1
Std Dev	36.84	35.03	36.26
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0003	0.0004	
p-value [2]	0.4652		
Month 6			
N	781	368	1149
Mean	16.1	12.5	15.0
Std Dev	26.88	23.62	25.92
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0266		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe appetite loss. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Appetite Loss by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	755	354	1109
Mean	-9.2	-13.5	-10.6
Std Dev	37.07	35.98	36.77
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.0706		
Month 12			
N	631	262	893
Mean	17.0	12.6	15.7
Std Dev	26.55	22.94	25.61
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0189		
Change from Baseline at Month 12			
N	606	253	859
Mean	-6.8	-10.5	-7.9
Std Dev	36.18	34.16	35.62
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.1631		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe appetite loss. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Appetite Loss by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	506	188	694
Mean	16.1	9.9	14.5
Std Dev	26.22	20.87	25.02
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0036		
Change from Baseline at Month 18			
N	487	183	670
Mean	-6.6	-12.2	-8.2
Std Dev	34.67	31.88	34.00
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 66.7	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.0590		
Study Disc.			
N	490	265	755
Mean	25.2	23.9	24.7
Std Dev	32.77	32.16	32.54
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.6089		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe appetite loss. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Appetite Loss by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	470	257	727
Mean	-4.7	-2.6	-3.9
Std Dev	37.28	37.18	37.23
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0067	0.2644	
p-value [2]	0.4704		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe appetite loss. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Constipation by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1019	510	1529
Mean	26.7	29.2	27.5
Std Dev	33.01	34.75	33.61
Median	0.0	33.3	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1665		
Month 1			
N	916	436	1352
Mean	33.5	47.0	37.9
Std Dev	35.07	36.71	36.15
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 1			
N	887	419	1306
Mean	7.3	18.4	10.8
Std Dev	36.45	41.23	38.39
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe constipation. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Constipation by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	870	412	1282
Mean	25.8	41.9	31.0
Std Dev	30.13	34.60	32.50
Median	33.3	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 3			
N	838	397	1235
Mean	0.9	13.9	5.1
Std Dev	37.27	39.30	38.40
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.4775	<.0001	
p-value [2]	<.0001		
Month 6			
N	779	367	1146
Mean	22.2	35.4	26.4
Std Dev	28.01	33.86	30.62
Median	0.0	33.3	33.3
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe constipation. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Constipation by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	750	353	1103
Mean	-3.8	6.8	-0.4
Std Dev	37.45	40.41	38.72
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0059	0.0017	
p-value [2]	<.0001		
Month 12			
N	632	263	895
Mean	20.8	31.2	23.9
Std Dev	27.90	33.71	30.08
Median	0.0	33.3	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 12			
N	605	255	860
Mean	-3.8	3.7	-1.6
Std Dev	38.44	38.28	38.52
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0153	0.1280	
p-value [2]	0.0094		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe constipation. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Constipation by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	506	185	691
Mean	18.5	24.7	20.2
Std Dev	26.74	30.65	27.95
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0100		
Change from Baseline at Month 18			
N	488	179	667
Mean	-5.2	0.0	-3.8
Std Dev	36.00	37.06	36.33
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0015	1.0000	
p-value [2]	0.1021		
Study Disc.			
N	484	266	750
Mean	20.0	24.9	21.8
Std Dev	28.38	32.25	29.88
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0317		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe constipation. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	464	257	721
Mean	-7.7	-2.2	-5.7
Std Dev	39.51	38.86	39.34
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	0.3638	
p-value [2]	0.0731		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe constipation. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Diarrhea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1017	510	1527
Mean	7.3	6.1	6.9
Std Dev	18.16	16.46	17.61
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2101		
Month 1			
N	911	433	1344
Mean	10.2	4.8	8.4
Std Dev	20.82	15.14	19.34
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 1			
N	882	416	1298
Mean	3.0	-0.6	1.8
Std Dev	25.23	18.79	23.42
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-66.7 , 100.0	-100.0 , 100.0
p-value [1]	0.0004	0.4869	
p-value [2]	0.0085		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe diarrhea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Diarrhea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	865	410	1275
Mean	11.2	3.5	8.7
Std Dev	21.31	11.94	19.15
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 3			
N	832	395	1227
Mean	3.5	-2.4	1.6
Std Dev	26.13	18.61	24.12
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0001	0.0093	
p-value [2]	<.0001		
Month 6			
N	778	365	1143
Mean	14.5	4.4	11.3
Std Dev	23.84	13.72	21.65
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe diarrhea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Diarrhea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	749	351	1100
Mean	7.1	-2.2	4.2
Std Dev	28.16	21.19	26.49
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	0.0543	
p-value [2]	<.0001		
Month 12			
N	629	261	890
Mean	17.8	3.3	13.6
Std Dev	25.74	11.59	23.47
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 66.7	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 12			
N	602	253	855
Mean	10.5	-2.5	6.6
Std Dev	30.09	17.26	27.57
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-66.7 , 66.7	-100.0 , 100.0
p-value [1]	<.0001	0.0219	
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe diarrhea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Diarrhea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	505	184	689
Mean	20.1	3.6	15.7
Std Dev	27.49	10.40	25.22
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 33.3	0.0 , 100.0
p-value [2]	<.0001		
Change from Baseline at Month 18			
N	487	178	665
Mean	12.9	-1.7	9.0
Std Dev	31.11	17.46	28.83
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-66.7 , 33.3	-100.0 , 100.0
p-value [1]	<.0001	0.1994	
p-value [2]	<.0001		
Study Disc.			
N	485	264	749
Mean	16.6	4.8	12.4
Std Dev	25.68	13.72	22.90
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe diarrhea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Diarrhea by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	467	255	722
Mean	8.4	-0.5	5.2
Std Dev	30.64	19.39	27.52
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-66.7 , 100.0	-100.0 , 100.0
p-value [1]	<.0001	0.6671	
p-value [2]	<.0001		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe diarrhea. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Financial Difficulties by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1005	502	1507
Mean	11.3	11.0	11.2
Std Dev	23.18	23.39	23.25
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.7607		
Month 1			
N	911	431	1342
Mean	12.4	10.2	11.7
Std Dev	23.56	23.05	23.41
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1148		
Change from Baseline at Month 1			
N	876	409	1285
Mean	0.9	0.5	0.8
Std Dev	21.03	22.98	21.66
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.2185	0.6672	
p-value [2]	0.7661		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe financial difficulties. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Financial Difficulties by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	861	410	1271
Mean	12.4	11.8	12.2
Std Dev	23.43	23.53	23.46
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.6700		
Change from Baseline at Month 3			
N	820	388	1208
Mean	0.7	1.9	1.1
Std Dev	22.51	21.48	22.19
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.3523	0.0839	
p-value [2]	0.3970		
Month 6			
N	778	364	1142
Mean	12.0	10.7	11.6
Std Dev	22.59	21.95	22.39
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3835		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe financial difficulties. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Financial Difficulties by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	743	345	1088
Mean	0.5	0.7	0.6
Std Dev	22.09	24.57	22.89
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.5067	0.6094	
p-value [2]	0.9263		
Month 12			
N	633	260	893
Mean	11.7	10.6	11.4
Std Dev	22.35	22.74	22.46
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.5261		
Change from Baseline at Month 12			
N	601	249	850
Mean	1.0	1.1	1.0
Std Dev	23.63	23.16	23.48
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.3007	0.4663	
p-value [2]	0.9673		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe financial difficulties. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Financial Difficulties by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	504	183	687
Mean	11.5	10.0	11.1
Std Dev	21.43	22.16	21.62
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.4251		
Change from Baseline at Month 18			
N	483	174	657
Mean	1.9	0.4	1.5
Std Dev	22.74	21.20	22.34
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 66.7	-100.0 , 100.0
p-value [1]	0.0625	0.8119	
p-value [2]	0.4332		
Study Disc.			
N	478	265	743
Mean	13.7	15.0	14.2
Std Dev	24.88	26.08	25.30
Median	0.0	0.0	0.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.5257		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe financial difficulties. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-C30 Constructed Scale and Change from Baseline in Financial Difficulties by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	452	254	706
Mean	1.1	5.0	2.5
Std Dev	25.33	24.82	25.20
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.3537	0.0015	
p-value [2]	0.0495		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents more severe financial difficulties. Month 1 for MPT arm corresponds to week 6 assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Table 2. EORTC QLQ-MY20 outcomes

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Disease Symptoms by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1022	511	1533
Mean	30.1	30.3	30.1
Std Dev	22.30	22.72	22.43
Median	27.8	27.8	27.8
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.8714		
Month 1			
N	915	435	1350
Mean	25.4	24.4	25.1
Std Dev	20.20	21.69	20.69
Median	22.2	16.7	22.2
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3713		
Change from Baseline at Month 1			
N	890	421	1311
Mean	-4.1	-4.4	-4.2
Std Dev	19.05	19.04	19.04
Median	0.0	-5.6	-2.2
Min, Max	-83.3 , 75.0	-61.1 , 55.6	-83.3 , 75.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.7403		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall disease symptom. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Disease Symptoms by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	870	410	1280
Mean	19.9	21.8	20.5
Std Dev	16.91	18.53	17.46
Median	16.7	16.7	16.7
Min, Max	0.0 , 83.3	0.0 , 83.3	0.0 , 83.3
p-value [2]	0.0648		
Change from Baseline at Month 3			
N	840	396	1236
Mean	-9.6	-7.0	-8.7
Std Dev	20.83	20.43	20.73
Median	-5.6	-5.6	-5.6
Min, Max	-100.0 , 55.6	-77.8 , 61.1	-100.0 , 61.1
p-value [1]	<.0001	<.0001	
p-value [2]	0.0402		
Month 6			
N	780	366	1146
Mean	20.5	22.1	21.0
Std Dev	17.47	19.03	17.99
Median	16.7	16.7	16.7
Min, Max	0.0 , 88.9	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1551		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall disease symptom. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Disease Symptoms by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	756	353	1109
Mean	-9.3	-7.9	-8.9
Std Dev	20.91	21.94	21.25
Median	-5.6	-5.6	-5.6
Min, Max	-94.4 , 66.7	-77.8 , 61.1	-94.4 , 66.7
p-value [1]	<.0001	<.0001	
p-value [2]	0.2904		
Month 12			
N	632	262	894
Mean	20.6	22.2	21.1
Std Dev	17.03	18.93	17.61
Median	16.7	16.7	16.7
Min, Max	0.0 , 77.8	0.0 , 86.7	0.0 , 86.7
p-value [2]	0.2405		
Change from Baseline at Month 12			
N	609	254	863
Mean	-8.3	-6.5	-7.7
Std Dev	21.02	21.58	21.19
Median	-5.6	-5.6	-5.6
Min, Max	-88.9 , 55.6	-77.8 , 55.6	-88.9 , 55.6
p-value [1]	<.0001	<.0001	
p-value [2]	0.2593		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall disease symptom. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Disease Symptoms by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	508	188	696
Mean	21.8	21.0	21.6
Std Dev	18.01	18.39	18.10
Median	16.7	16.7	16.7
Min, Max	0.0 , 83.3	0.0 , 88.9	0.0 , 88.9
p-value [2]	0.6187		
Change from Baseline at Month 18			
N	492	183	675
Mean	-7.5	-7.9	-7.6
Std Dev	23.41	21.26	22.83
Median	-5.6	-5.6	-5.6
Min, Max	-88.9 , 72.2	-66.7 , 55.6	-88.9 , 72.2
p-value [1]	<.0001	<.0001	
p-value [2]	0.8399		
Study Disc.			
N	490	266	756
Mean	28.2	27.2	27.8
Std Dev	22.46	23.09	22.68
Median	22.2	21.1	22.2
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.5529		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall disease symptom. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Disease Symptoms by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	471	259	730
Mean	-4.0	-3.7	-3.9
Std Dev	24.85	23.54	24.38
Median	-5.6	-1.1	-5.6
Min, Max	-100.0 , 83.3	-77.8 , 61.1	-100.0 , 83.3
p-value [1]	0.0005	0.0126	
p-value [2]	0.8478		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall disease symptom. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Side Effects by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1020	510	1530
Mean	19.8	20.1	19.9
Std Dev	15.59	15.87	15.68
Median	14.8	18.5	16.7
Min, Max	0.0 , 85.2	0.0 , 81.5	0.0 , 85.2
p-value [2]	0.7071		
Month 1			
N	911	433	1344
Mean	22.4	24.3	23.0
Std Dev	15.29	16.20	15.61
Median	18.5	22.2	20.0
Min, Max	0.0 , 86.7	0.0 , 90.5	0.0 , 90.5
p-value [2]	0.0380		
Change from Baseline at Month 1			
N	884	418	1302
Mean	3.3	5.6	4.0
Std Dev	14.33	15.00	14.58
Median	3.7	3.7	3.7
Min, Max	-48.9 , 59.3	-37.0 , 64.6	-48.9 , 64.6
p-value [1]	<.0001	<.0001	
p-value [2]	0.0070		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall side effect of treatment. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Side Effects by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	868	407	1275
Mean	19.8	21.9	20.5
Std Dev	14.55	15.41	14.85
Median	18.5	18.5	18.5
Min, Max	0.0 , 83.3	0.0 , 81.5	0.0 , 83.3
p-value [2]	0.0203		
Change from Baseline at Month 3			
N	838	393	1231
Mean	1.1	3.5	1.9
Std Dev	14.95	15.40	15.13
Median	0.0	3.7	2.2
Min, Max	-72.6 , 59.3	-44.4 , 56.3	-72.6 , 59.3
p-value [1]	0.0340	<.0001	
p-value [2]	0.0088		
Month 6			
N	777	365	1142
Mean	19.3	21.9	20.1
Std Dev	14.24	16.65	15.09
Median	16.7	18.5	18.5
Min, Max	0.0 , 80.0	0.0 , 94.4	0.0 , 94.4
p-value [2]	0.0072		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall side effect of treatment. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Side Effects by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	752	351	1103
Mean	0.7	2.9	1.4
Std Dev	15.02	17.28	15.80
Median	0.0	3.7	0.0
Min, Max	-53.3 , 63.3	-66.7 , 79.6	-66.7 , 79.6
p-value [1]	0.2183	0.0017	
p-value [2]	0.0276		
Month 12			
N	631	262	893
Mean	19.7	22.9	20.6
Std Dev	14.03	16.28	14.79
Median	16.7	20.4	18.5
Min, Max	0.0 , 83.3	0.0 , 76.7	0.0 , 83.3
p-value [2]	0.0030		
Change from Baseline at Month 12			
N	606	254	860
Mean	1.6	4.7	2.5
Std Dev	15.35	17.17	15.97
Median	3.0	3.7	3.7
Min, Max	-65.2 , 70.0	-77.8 , 63.3	-77.8 , 70.0
p-value [1]	0.0126	<.0001	
p-value [2]	0.0085		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall side effect of treatment. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Side Effects by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	507	187	694
Mean	19.9	21.7	20.3
Std Dev	14.62	14.85	14.69
Median	18.5	18.5	18.5
Min, Max	0.0 , 85.2	0.0 , 80.0	0.0 , 85.2
p-value [2]	0.1528		
Change from Baseline at Month 18			
N	490	182	672
Mean	2.2	4.3	2.8
Std Dev	16.49	16.37	16.47
Median	3.7	7.0	3.7
Min, Max	-76.3 , 74.1	-40.0 , 70.0	-76.3 , 74.1
p-value [1]	0.0031	0.0006	
p-value [2]	0.1530		
Study Disc.			
N	486	266	752
Mean	21.1	23.7	22.0
Std Dev	15.12	16.71	15.74
Median	18.5	20.0	18.5
Min, Max	0.0 , 80.0	0.0 , 86.7	0.0 , 86.7
p-value [2]	0.0312		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall side effect of treatment. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Side Effects by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	467	258	725
Mean	-0.3	3.8	1.1
Std Dev	15.83	16.52	16.19
Median	0.0	2.4	0.0
Min, Max	-80.0 , 57.8	-37.0 , 53.3	-80.0 , 57.8
p-value [1]	0.6617	0.0003	
p-value [2]	0.0011		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a more severe overall side effect of treatment. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Future Perspective by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	1012	509	1521
Mean	54.5	55.0	54.7
Std Dev	26.47	26.68	26.53
Median	55.6	55.6	55.6
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.7360		
Month 1			
N	907	429	1336
Mean	58.5	59.2	58.7
Std Dev	26.22	25.87	26.10
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.6128		
Change from Baseline at Month 1			
N	876	415	1291
Mean	4.3	3.3	4.0
Std Dev	21.55	23.20	22.09
Median	0.0	0.0	0.0
Min, Max	-88.9 , 77.8	-66.7 , 88.9	-88.9 , 88.9
p-value [1]	<.0001	0.0037	
p-value [2]	0.4715		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better future perspective. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Future Perspective by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	864	410	1274
Mean	64.1	61.9	63.4
Std Dev	25.50	26.84	25.95
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1581		
Change from Baseline at Month 3			
N	830	394	1224
Mean	8.8	6.3	8.0
Std Dev	23.10	25.06	23.77
Median	11.1	0.0	11.1
Min, Max	-77.8 , 88.9	-77.8 , 88.9	-77.8 , 88.9
p-value [1]	<.0001	<.0001	
p-value [2]	0.0876		
Month 6			
N	771	365	1136
Mean	66.0	63.2	65.1
Std Dev	25.36	26.91	25.89
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0846		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better future perspective. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Future Perspective by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	744	350	1094
Mean	11.0	8.0	10.1
Std Dev	24.28	25.26	24.63
Median	11.1	11.1	11.1
Min, Max	-88.9 , 88.9	-77.8 , 88.9	-88.9 , 88.9
p-value [1]	<.0001	<.0001	
p-value [2]	0.0618		
Month 12			
N	629	258	887
Mean	67.2	64.4	66.4
Std Dev	24.09	27.19	25.05
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1225		
Change from Baseline at Month 12			
N	602	249	851
Mean	11.4	10.0	11.0
Std Dev	23.17	26.30	24.12
Median	11.1	11.1	11.1
Min, Max	-55.6 , 77.8	-55.6 , 88.9	-55.6 , 88.9
p-value [1]	<.0001	<.0001	
p-value [2]	0.4119		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better future perspective. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Future Perspective by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	505	185	690
Mean	67.9	65.2	67.2
Std Dev	24.21	25.30	24.51
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1876		
Change from Baseline at Month 18			
N	484	179	663
Mean	12.2	9.5	11.5
Std Dev	24.34	21.75	23.68
Median	11.1	0.0	11.1
Min, Max	-77.8 , 100.0	-44.4 , 66.7	-77.8 , 100.0
p-value [1]	<.0001	<.0001	
p-value [2]	0.1939		
Study Disc.			
N	487	262	749
Mean	59.6	56.9	58.6
Std Dev	28.77	28.11	28.55
Median	66.7	66.7	66.7
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2188		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better future perspective. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Future Perspective by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	467	254	721
Mean	7.5	3.2	6.0
Std Dev	26.38	27.13	26.70
Median	11.1	0.0	0.0
Min, Max	-77.8 , 88.9	-77.8 , 77.8	-77.8 , 88.9
p-value [1]	<.0001	0.0584	
p-value [2]	0.0419		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better future perspective. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Body Image by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	990	504	1494
Mean	81.8	81.2	81.6
Std Dev	28.58	29.65	28.94
Median	100.0	100.0	100.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.7361		
Month 1			
N	880	426	1306
Mean	78.7	80.8	79.4
Std Dev	29.82	26.96	28.92
Median	100.0	100.0	100.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.2412		
Change from Baseline at Month 1			
N	839	408	1247
Mean	-3.0	-1.6	-2.5
Std Dev	28.35	29.97	28.89
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.0024	0.2714	
p-value [2]	0.4404		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better body image. Month 1 for MPT arm corresponds to 6 week assessment.
[1] The p-value is calculated based on a one-sample t-test.
[2] The p-value is calculated based on a pooled t-test comparing two treatment groups.
     The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Body Image by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	852	405	1257
Mean	82.4	78.0	81.0
Std Dev	26.86	28.58	27.49
Median	100.0	100.0	100.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.0078		
Change from Baseline at Month 3			
N	802	387	1189
Mean	-0.4	-3.0	-1.3
Std Dev	26.91	29.38	27.75
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.6619	0.0442	
p-value [2]	0.1303		
Month 6			
N	763	364	1127
Mean	82.0	79.3	81.2
Std Dev	25.49	29.26	26.78
Median	100.0	100.0	100.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1082		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better body image. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Body Image by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	723	347	1070
Mean	0.1	-2.8	-0.8
Std Dev	28.83	33.07	30.28
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.9315	0.1175	
p-value [2]	0.1457		
Month 12			
N	619	254	873
Mean	81.5	79.0	80.8
Std Dev	25.61	28.05	26.36
Median	100.0	100.0	100.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1984		
Change from Baseline at Month 12			
N	576	242	818
Mean	-0.9	-2.6	-1.4
Std Dev	30.60	31.96	31.00
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.4963	0.2039	
p-value [2]	0.4617		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better body image. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Body Image by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	496	183	679
Mean	82.3	80.3	81.7
Std Dev	24.78	27.32	25.48
Median	100.0	100.0	100.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.3815		
Change from Baseline at Month 18			
N	463	174	637
Mean	-1.3	-1.1	-1.3
Std Dev	29.56	33.60	30.69
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.3460	0.6524	
p-value [2]	0.9572		
Study Disc.			
N	482	258	740
Mean	79.3	75.6	78.0
Std Dev	29.37	31.57	30.19
Median	100.0	100.0	100.0
Min, Max	0.0 , 100.0	0.0 , 100.0	0.0 , 100.0
p-value [2]	0.1083		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better body image. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd is the comparison of combined Rd and Rd18 versus MPT.

Summary of EORTC QLQ-MY20 Constructed Scale and Change from Baseline in Body Image by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	450	250	700
Mean	-1.4	-5.6	-2.9
Std Dev	32.48	33.73	32.97
Median	0.0	0.0	0.0
Min, Max	-100.0 , 100.0	-100.0 , 100.0	-100.0 , 100.0
p-value [1]	0.3584	0.0092	
p-value [2]	0.1069		

Note: Constructed scale and change from baseline are calculated based on the mean scale linear transformation of raw score.
A higher score represents a better body image. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on a one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.

Table 3 EQ-5D Health Utility outcomes

Summary of EQ-5D Health Utility and Change from Baseline in Health Utility Score by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Baseline			
N	982	490	1472
Mean	0.5	0.5	0.5
Std Dev	0.36	0.37	0.36
Median	0.7	0.7	0.7
Min, Max	-0.6 , 1.0	-0.6 , 1.0	-0.6 , 1.0
p-value [2]	0.2490		
Month 1			
N	868	414	1282
Mean	0.6	0.6	0.6
Std Dev	0.34	0.32	0.33
Median	0.7	0.7	0.7
Min, Max	-0.6 , 1.0	-0.6 , 1.0	-0.6 , 1.0
p-value [2]	0.2122		
Change from Baseline at Month 1			
N	820	381	1201
Mean	0.0	0.0	0.0
Std Dev	0.30	0.28	0.30
Median	0.0	0.0	0.0
Min, Max	-1.2 , 1.0	-0.8 , 1.0	-1.2 , 1.0
p-value [1]	0.2007	0.0274	
p-value [2]	0.3063		

Note: Health Utility Score is derived using UK population weights
A higher score represents better health state. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on the one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd + Rd18 is the comparison of Rd + Rd18 and MPT treatment groups,

Summary of EQ-5D Health Utility and Change from Baseline in Health Utility Score by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 3			
N	829	392	1221
Mean	0.7	0.6	0.6
Std Dev	0.27	0.31	0.28
Median	0.7	0.7	0.7
Min, Max	-0.6 , 1.0	-0.6 , 1.0	-0.6 , 1.0
p-value [2]	0.0671		
Change from Baseline at Month 3			
N	772	366	1138
Mean	0.1	0.1	0.1
Std Dev	0.32	0.32	0.32
Median	0.0	0.0	0.0
Min, Max	-1.2 , 1.2	-1.2 , 1.1	-1.2 , 1.2
p-value [1]	<.0001	0.0001	
p-value [2]	0.3429		
Month 6			
N	739	350	1089
Mean	0.7	0.7	0.7
Std Dev	0.25	0.26	0.26
Median	0.7	0.7	0.7
Min, Max	-0.6 , 1.0	-0.2 , 1.0	-0.6 , 1.0
p-value [2]	0.3110		

Note: Health Utility Score is derived using UK population weights
A higher score represents better health state. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on the one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd + Rd18 is the comparison of Rd + Rd18 and MPT treatment groups,

Summary of EQ-5D Health Utility and Change from Baseline in Health Utility Score by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Month 6			
N	692	323	1015
Mean	0.1	0.1	0.1
Std Dev	0.31	0.34	0.32
Median	0.0	0.1	0.0
Min, Max	-0.8 , 1.2	-1.0 , 1.1	-1.0 , 1.2
p-value [1]	<.0001	<.0001	
p-value [2]	0.5645		
Month 12			
N	600	245	845
Mean	0.7	0.7	0.7
Std Dev	0.23	0.28	0.25
Median	0.7	0.7	0.7
Min, Max	-0.5 , 1.0	-0.3 , 1.0	-0.5 , 1.0
p-value [2]	0.0262		
Change from Baseline at Month 12			
N	561	231	792
Mean	0.1	0.1	0.1
Std Dev	0.32	0.35	0.33
Median	0.1	0.1	0.1
Min, Max	-1.1 , 1.4	-0.9 , 1.4	-1.1 , 1.4
p-value [1]	<.0001	<.0001	
p-value [2]	0.9992		

Note: Health Utility Score is derived using UK population weights
A higher score represents better health state. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on the one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd + Rd18 is the comparison of Rd + Rd18 and MPT treatment groups,

Summary of EQ-5D Health Utility and Change from Baseline in Health Utility Score by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Month 18			
N	473	182	655
Mean	0.7	0.7	0.7
Std Dev	0.24	0.22	0.24
Median	0.7	0.7	0.7
Min, Max	-0.3 , 1.0	-0.6 , 1.0	-0.6 , 1.0
p-value [2]	0.5493		
Change from Baseline at Month 18			
N	449	170	619
Mean	0.1	0.1	0.1
Std Dev	0.34	0.35	0.34
Median	0.0	0.0	0.0
Min, Max	-0.9 , 1.3	-1.1 , 1.4	-1.1 , 1.4
p-value [1]	<.0001	<.0001	
p-value [2]	0.4632		
Study Disc.			
N	450	252	702
Mean	0.6	0.6	0.6
Std Dev	0.35	0.36	0.35
Median	0.7	0.7	0.7
Min, Max	-0.6 , 1.0	-0.6 , 1.0	-0.6 , 1.0
p-value [2]	0.8741		

Note: Health Utility Score is derived using UK population weights
A higher score represents better health state. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on the one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
      The p-value under Rd + Rd18 is the comparison of Rd + Rd18 and MPT treatment groups,

Summary of EQ-5D Health Utility and Change from Baseline in Health Utility Score by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Rd (N=1076)	MPT (N=547)	Overall (N=1623)
Change from Baseline at Study Disc.			
N	417	240	657
Mean	0.0	0.0	0.0
Std Dev	0.37	0.39	0.38
Median	0.0	0.0	0.0
Min, Max	-1.1 , 1.4	-1.3 , 1.4	-1.3 , 1.4
p-value [1]	0.0191	0.3535	
p-value [2]	0.5253		

Note: Health Utility Score is derived using UK population weights
A higher score represents better health state. Month 1 for MPT arm corresponds to 6 week assessment.
[1]   The p-value is calculated based on the one-sample t-test.
[2]   The p-value is calculated based on a pooled t-test comparing two treatment groups.
       The p-value under Rd + Rd18 is the comparison of Rd + Rd18 and MPT treatment groups,

Table 4 EQ-5D Health Utility Responses

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Mobility	Baseline			
		No Problems	437 (43.5)	218 (43.6)
		Moderate Problems	519 (51.7)	251 (50.2)
		Severe Problems	48 (4.8)	31 (6.2)
		p-value [1]	0.484	
	Month 1			
		No Problems	363 (40.5)	189 (44.5)
		Moderate Problems	497 (55.5)	221 (52.0)
		Severe Problems	36 (4.0)	15 (3.5)
		p-value [1]	0.395	
	Month 3			
		No Problems	422 (49.9)	189 (47.6)
		Moderate Problems	410 (48.5)	199 (50.1)
		Severe Problems	14 (1.7)	9 (2.3)
		p-value [1]	0.582	
	Month 6			
		No Problems	396 (51.8)	187 (52.2)
		Moderate Problems	359 (46.9)	169 (47.2)
		Severe Problems	10 (1.3)	2 (0.6)
		p-value [1]	0.598	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
     and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
  [1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Mobility	Month 12			
		No Problems	340 (55.7)	130 (52.0)
		Moderate Problems	262 (43.0)	117 (46.8)
		Severe Problems	8 (1.3)	3 (1.2)
		p-value [1]	0.579	
	Month 18			
		No Problems	263 (54.1)	105 (57.4)
		Moderate Problems	219 (45.1)	77 (42.1)
		Severe Problems	4 (0.8)	1 (0.5)
		p-value [1]	0.803	
	Study Disc.			
		No Problems	196 (42.2)	100 (39.1)
		Moderate Problems	245 (52.7)	145 (56.6)
		Severe Problems	24 (5.2)	11 (4.3)
		p-value [1]	0.580	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
     and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
 [1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Self-Care	Baseline			
		No Problems	679 (68.2)	331 (66.6)
		Moderate Problems	260 (26.1)	132 (26.6)
		Severe Problems	56 (5.6)	34 (6.8)
		p-value [1]	0.604	
	Month 1			
		No Problems	608 (68.2)	297 (69.9)
		Moderate Problems	238 (26.7)	110 (25.9)
		Severe Problems	46 (5.2)	18 (4.2)
		p-value [1]	0.729	
	Month 3			
		No Problems	650 (77.1)	295 (74.1)
		Moderate Problems	167 (19.8)	91 (22.9)
		Severe Problems	26 (3.1)	12 (3.0)
		p-value [1]	0.464	
	Month 6			
		No Problems	614 (81.0)	283 (79.5)
		Moderate Problems	133 (17.5)	66 (18.5)
		Severe Problems	11 (1.5)	7 (2.0)
		p-value [1]	0.687	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
[1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Self-Care	Month 12			
		No Problems	514 (84.3)	203 (80.9)
		Moderate Problems	90 (14.8)	40 (15.9)
		Severe Problems	6 (1.0)	8 (3.2)
		p-value [1]	0.065	
	Month 18			
		No Problems	418 (87.1)	159 (87.4)
		Moderate Problems	53 (11.0)	21 (11.5)
		Severe Problems	9 (1.9)	2 (1.1)
		p-value [1]	0.864	
	Study Disc.			
		No Problems	330 (71.6)	191 (74.3)
		Moderate Problems	102 (22.1)	50 (19.5)
		Severe Problems	29 (6.3)	16 (6.2)
		p-value [1]	0.710	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
[1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Usual Activities	Baseline			
		No Problems	358 (35.9)	187 (37.8)
		Moderate Problems	469 (47.0)	204 (41.2)
		Severe Problems	170 (17.1)	104 (21.0)
		p-value [1]	0.060	
	Month 1			
		No Problems	290 (32.7)	138 (32.8)
		Moderate Problems	438 (49.3)	209 (49.6)
		Severe Problems	160 (18.0)	74 (17.6)
		p-value [1]	0.984	
	Month 3			
		No Problems	338 (40.0)	143 (35.8)
		Moderate Problems	431 (51.0)	214 (53.6)
		Severe Problems	76 (9.0)	42 (10.5)
		p-value [1]	0.317	
	Month 6			
		No Problems	322 (42.3)	153 (42.9)
		Moderate Problems	396 (52.0)	173 (48.5)
		Severe Problems	43 (5.7)	31 (8.7)
		p-value [1]	0.137	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
    and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
  [1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

Visit	Category	Rd (N=1076)	MPT (N=547)
Usual Activities	Month 12		
	No Problems	282 (46.3)	109 (43.8)
	Moderate Problems	302 (49.6)	121 (48.6)
	Severe Problems	25 (4.1)	19 (7.6)
	p-value [1]	0.107	
	Month 18		
	No Problems	234 (49.0)	91 (49.7)
	Moderate Problems	217 (45.4)	86 (47.0)
	Severe Problems	27 (5.6)	6 (3.3)
	p-value [1]	0.482	
	Study Disc.		
	No Problems	177 (38.3)	92 (35.8)
	Moderate Problems	212 (45.9)	130 (50.6)
	Severe Problems	73 (15.8)	35 (13.6)
	p-value [1]	0.463	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
    and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
   [1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Pain	Baseline			
		No Problems	212 (21.2)	110 (21.9)
		Moderate Problems	634 (63.3)	309 (61.4)
		Severe Problems	155 (15.5)	84 (16.7)
		p-value [1]	0.734	
	Month 1			
		No Problems	202 (22.6)	115 (27.0)
		Moderate Problems	587 (65.7)	271 (63.6)
		Severe Problems	105 (11.7)	40 (9.4)
		p-value [1]	0.141	
	Month 3			
		No Problems	250 (29.5)	112 (28.1)
		Moderate Problems	555 (65.4)	252 (63.3)
		Severe Problems	43 (5.1)	34 (8.5)
		p-value [1]	0.065	
	Month 6			
		No Problems	226 (29.7)	101 (28.5)
		Moderate Problems	500 (65.8)	233 (65.8)
		Severe Problems	34 (4.5)	20 (5.6)
		p-value [1]	0.653	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
[1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Pain	Month 12			
		No Problems	179 (29.3)	72 (28.9)
		Moderate Problems	409 (67.0)	163 (65.5)
		Severe Problems	22 (3.6)	14 (5.6)
		p-value [1]	0.410	
	Month 18			
		No Problems	145 (29.9)	45 (24.5)
		Moderate Problems	322 (66.4)	133 (72.3)
		Severe Problems	18 (3.7)	6 (3.3)
		p-value [1]	0.357	
	Study Disc.			
		No Problems	92 (19.9)	66 (25.8)
		Moderate Problems	315 (68.0)	157 (61.3)
		Severe Problems	56 (12.1)	33 (12.9)
		p-value [1]	0.149	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
  and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
  [1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Anxiety/Depression	Baseline			
		No Problems	427 (42.8)	200 (40.0)
		Moderate Problems	502 (50.3)	262 (52.4)
		Severe Problems	69 (6.9)	38 (7.6)
		p-value [1]	0.562	
	Month 1			
		No Problems	398 (44.5)	192 (45.0)
		Moderate Problems	438 (49.0)	213 (49.9)
		Severe Problems	58 (6.5)	22 (5.2)
		p-value [1]	0.652	
	Month 3			
		No Problems	408 (48.1)	174 (43.7)
		Moderate Problems	397 (46.8)	200 (50.3)
		Severe Problems	43 (5.1)	24 (6.0)
		p-value [1]	0.312	
	Month 6			
		No Problems	390 (51.8)	166 (46.5)
		Moderate Problems	332 (44.1)	177 (49.6)
		Severe Problems	31 (4.1)	14 (3.9)
		p-value [1]	0.230	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
    and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
  [1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.

Summary of the Responses to Each of the Five EQ-5D Dimensions by Cycle
Intent-to-Treat Population (Pooled Analyses)

	Visit	Category	Rd (N=1076)	MPT (N=547)
Anxiety/Depression	Month 12			
		No Problems	336 (55.4)	124 (49.6)
		Moderate Problems	252 (41.6)	114 (45.6)
		Severe Problems	18 (3.0)	12 (4.8)
		p-value [1]	0.173	
	Month 18			
		No Problems	265 (55.0)	104 (56.5)
		Moderate Problems	202 (41.9)	75 (40.8)
		Severe Problems	15 (3.1)	5 (2.7)
		p-value [1]	0.945	
	Study Disc.			
		No Problems	199 (43.1)	117 (46.1)
		Moderate Problems	238 (51.5)	114 (44.9)
		Severe Problems	25 (5.4)	23 (9.1)
		p-value [1]	0.079	

Note: The denominator for percentage calculation is based on the numbers of subjects who have valid data in each dimension
and each visit. Month 1 for MPT arm corresponds to 6 week assessment.
[1]: The p-values are calculated based on the Fisher exact test comparing the pooled Rd and Rd18 vs. MPT.