

Patient-Reported Outcomes in the Subpopulation of Patients With Mismatch Repair Deficient/Microsatellite Instability–High Primary Advanced or Recurrent Endometrial Cancer Treated With Dostarlimab Plus Chemotherapy Compared With Chemotherapy Alone in the ENGOT-EN6-NSGO/GOG3031/RUBY trial

Valabrega G, Powell MA, Hietanen S, Miller E, Novak Z, Holloway R, Denschlag D, Myers T, Thijs AM, Pennington K, Gilbert L, Fleming E, Zub O, Landrum LM, Ataseven B, Gogoi R, Podzielinski I, Cloven N, Monk BJ, Sharma SS, Herzog TJ, Stuckey A, Pothuri B, Secord AA, Chase D, Vincent V, Meyers O, Garside J, Mirza MR, Black D

Supplementary Material

Supplementary Table 1. Patient-reported outcome assessments: domains and scoring.

Instrument	Domains assessed	Score	Higher score indicates
EORTC QLQ-C30 ^a	Global health status/QoL	0–100	Better HRQoL
	Functional scales: physical, role, emotional, cognitive, social	0–100	Better functioning
	Symptoms: fatigue, nausea & vomiting, pain, dyspnea, insomnia, appetite loss, constipation, diarrhea, financial difficulties	0–100	Worse symptoms
EORTC QLQ-EN24 ^b	Functional scales: sexual interest, sexual activity, sexual enjoyment	0–100	Better functioning
	Symptoms: lymphedema, urological, gastrointestinal, poor body image, vaginal, pain in back and pelvis, tingling/numbness, muscular pain, hair loss, taste change	0–100	Worse symptoms

^aAaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: A quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst.* 1993;85(5):365-76.

^bGreimel E, Nordin A, Lancelley A, et al. Psychometric validation of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Endometrial Cancer Module (EORTC QLQ-EN24). *Eur J Cancer.* 2011;47(2):183-90.

EORTC, European Organisation for Research and Treatment of Cancer; HRQoL, health-related quality of life; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-EN24, Quality of Life Questionnaire Endometrial Cancer Module; QoL, quality of life.

Supplementary Table 2. Summary of patient demographics and baseline characteristics.

Variable	dMMR/MSI-H population	
	Dostarlimab + CP N=53	Placebo + CP N=65
Age, median, (range) years	61 (45–81)	66 (39–85)
Race, n (%)		
White	44 (83.0)	56 (86.2)
Black	4 (7.5)	6 (9.2)
Asian	2 (3.8)	0
Other ^a	3 (5.7)	3 (4.6)
ECOG performance status, n (%) ^b		
0	28 (53.8)	39 (60.0)
1	24 (46.2)	26 (40.0)
BMI, median (range), kg/m ²	30.6 (20.1–54.4)	35.5 (17.9–58.1)
Disease status, n (%)		
Primary stage III	10 (18.9)	14 (21.5)
Primary stage IV	16 (30.2)	19 (29.2)
Recurrent	27 (50.9)	32 (49.2)
Prior treatment, n (%)		
Anticancer therapy	7 (13.2)	10 (15.4)
Anticancer surgery	49 (92.5)	60 (92.3)
External pelvic radiation	8 (15.1)	13 (20.0)
Histology, n (%)		
Endometrioid	44 (83.0)	56 (86.2)
Non-endometrioid ^c	9 (17.0)	9 (13.8)

^aIncludes patients identifying as American Indian or Alaska native, native Hawaiian or other Pacific Islander, unknown, or not reported. ^bCalculated based on patients with ECOG score available. ^cIncludes carcinosarcoma, clear cell adenocarcinoma, mucinous adenocarcinoma, serous adenocarcinoma, undifferentiated carcinoma, mixed carcinoma (≥10% of carcinosarcoma, clear cell, or serous histology), and other.

BMI, body mass index; CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; ECOG, Eastern Cooperative Oncology Group; MSI-H, microsatellite instability-high.

Supplementary Table 3. Completion rates for each instrument.

Completion rate, n(%)	Baseline		Cycle 7		Cycle 13		End of treatment	
	Dostarlimab +CP n=53	Placebo +CP n=65	Dostarlimab +CP n=40	Placebo +CP n=48	Dostarlimab +CP n=28	Placebo +CP n=14	Dostarlimab +CP n=28	Placebo +CP n=56
EORTC QLQ-C30								
Global QoL	51 (96.2)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Functional Scales								
Physical	50 (94.3)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Role	51 (96.2)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Emotional	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Cognitive	51 (96.2)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Social	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Symptom Scales								
Fatigue	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Pain	51 (96.2)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Nausea and vomiting	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Dyspnea	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	21 (77.8) ^b	44 (78.6)
Appetite loss	51 (96.2)	62 (95.4)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	43 (78.2) ^c
Insomnia	50 (94.3)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Constipation	50 (94.3)	63 (96.9)	39 (97.5)	47 (100) ^d	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Diarrhea	51 (96.2)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Financial difficulty	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
EORTC QLQ-EN24	Dostarlimab +CP n=53	Placebo +CP n=65	Dostarlimab +CP n=40	Placebo +CP n=48	Dostarlimab +CP n=28	Placebo +CP n=14	Dostarlimab +CP n=28	Placebo +CP n=56
Functional Scales								
Sexual interest	51 (96.2)	61 (93.8)	36 (97.3) ^e	44 (100) ^f	24 (96.0) ^g	13 (100) ^h	18 (75.0) ⁱ	41 (77.4) ^j
Sexual activity	51 (96.2)	58 (89.2)	35 (97.2) ^k	44 (100) ^l	24 (96.0) ^g	13 (100) ^h	18 (75.0) ⁱ	38 (76.0) ^l
Sexual enjoyment	9 (17.0)	12 (18.5)	9 (90.0) ^m	11 (100) ⁿ	8 (88.9) ^o	2 (100) ^p	3 (33.3) ^o	9 (42.9) ^q
Symptom scales								
Lymphedema	51 (96.2)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Urological	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Gastrointestinal	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Poor body image	51 (96.2)	64 (98.5)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	20 (76.9) ^r	44 (78.6)
Sexual/vaginal	10 (18.9)	12 (18.5)	9 (90.0) ^m	11 (100) ⁿ	8 (88.9) ^o	2 (100) ^p	3 (33.3) ^o	10 (45.5) ^s

Back and pelvis pain	51 (96.2)	61 (93.8)	38 (97.4) ^t	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Tingling/numbness	51 (96.2)	61 (93.8)	39 (97.5)	48 (100)	27 (96.4)	13 (100) ^h	22 (78.6)	44 (78.6)
Muscular pain	51 (96.2)	63 (96.9)	39 (97.5)	47 (100) ^d	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)
Hair loss	51 (96.2)	63 (96.9)	37 (97.4) ^u	48 (100)	27 (96.4)	14 (100)	22 (78.6)	43 (78.2) ^c
Taste change	51 (96.2)	63 (96.9)	39 (97.5)	48 (100)	27 (96.4)	14 (100)	22 (78.6)	44 (78.6)

^aPercentages were calculated based on the number of questionnaires completed that met the minimum for scoring of the instruments per the number of patients expected to complete the questionnaire at that specific visit. Percent calculations based on a denominator (patients expected to complete) of ^bn=27, ^cn=55, ^dn=47, ^en=37, ^fn=44, ^gn=25, ^hn=13, ⁱn=24, ^jn=53, ^kn=36, ^ln=50, ^mn=10, ⁿn=11, ^on=9, ^pn=2, ^qn=21, ^rn=26, ^sn=22, ^tn=39; ^un=38.

CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; EORTC, European Organisation for Research and Treatment of Cancer; MSI-H, microsatellite instability-high; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-EN24, Quality of Life Questionnaire Endometrial Cancer Module; QoL, quality of life.

Supplementary Table 4. Overall least square mean change from baseline in the overall and MMRp/MSS populations

LSM change from baseline (SE)	Overall		MMRp/MSS	
	Dostarlimab +CP N=231	Placebo + CP N=238	Dostarlimab +CP N=182	Placebo +CP N=176
EORTC QLQ-C30				
Global QoL	-0.1 (0.94)	-0.6 (1.05)	-1.1 (1.05)	0.7 (1.14)
	0.5 (1.42) P=0.724		-1.8 (1.56) P=0.242	
Physical functioning	-3.7 (0.96)	-3.0 (1.01)	-5.3 (1.21)	-3.3 (1.40)
	-0.7 (1.39) P=0.628		-1.9 (1.74) P=0.271	
Role functioning	-3.2 (1.56)	-1.5 (1.85)	-6.1 (1.58)	-1.6 (1.81)
	-1.7 (2.26) P=0.450		-4.5 (2.44) P=0.068	
Emotional functioning	2.3 (0.97)	4.0 (1.05)	1.8 (1.04)	3.9 (1.11)
	-1.7 (1.44) P=0.232		-2.1 (1.54) P=0.175	
Cognitive functioning	-5.4 (1.06)	-4.2 (1.21)	-6.2 (1.16)	-4.1 (1.29)
	-1.3 (1.59) P=0.425		-2.0 (1.73) P=0.237	
Social functioning	-1.8 (1.39)	-0.9 (1.62)	-3.3 (1.46)	-0.1 (1.56)
	-0.9 (2.05) P=0.655		-3.2 (2.15) P=0.139	
Fatigue	2.9 (1.18)	2.7 (1.32)	4.1 (1.36)	2.4 (1.52)
	0.2 (1.75) P=0.912		1.8 (2.02) P=0.383	
Nausea and vomiting	0.5 (0.71)	-0.5 (0.80)	0.5 (0.82)	-1.4 (0.90)
	1.1 (1.06) P=0.318		1.9 (1.21) P=0.113	
Pain	-0.9 (1.45)	0.1 (1.77)	1.4 (1.40)	0.4 (1.57)
	-1.0 (1.99) P=0.622		1.1 (2.11) P=0.617	
Dyspnea	3.8 (1.11)	4.7 (1.21)	4.8 (1.27)	3.9 (1.33)
	-0.9 (1.62) P=0.580		0.9 (1.84) P=0.623	
Insomnia	-6.4 (1.65)	-8.4 (1.66)	-7.6 (1.45)	-10.0 (1.57)

		2.0 (2.47) P=0.248		2.4 (2.13) P=0.257	
Appetite loss	-2.9 (1.21)		-3.6 (1.41)	-2.9 (1.20)	-2.8 (1.32)
		0.7 (1.91) P=0.716		-0.1 (1.84) P=0.969	
Constipation	-0.7 (1.18)		-2.3 (1.40)	1.7 (1.34)	-2.0 (1.51)
		1.6 (1.84) P=0.374		3.7 (2.02) P=0.066	
Diarrhea	3.3 (0.83)		1.4 (0.90)	2.4 (0.86)	1.1 (0.91)
		1.8 (1.23) P=0.134		1.3 (1.25) P=0.300	
Financial difficulties	-0.4 (1.22)		-1.9 (1.35)	0.5 (1.31)	-2.7 (1.38)
		1.5 (1.83) P=0.405		3.2 (1.92) P=0.099	
EORTC QLQ-EN24					
Sexual interest	0.3 (0.98)		3.4 (1.06)	-0.5 (1.11)	3.6 (1.18)
		-3.0 (1.45) P=0.038*		-4.1 (1.63) P=0.012*	
Sexual activity	1.7 (0.86)		2.1 (0.90)	0.1 (0.95)	1.8 (0.99)
		-0.4 (1.26) P=0.761		-1.6 (1.38) P=0.245	
Sexual enjoyment	-0.7 (3.88)		-1.2 (4.42)	-1.8 (4.26)	-2.9 (4.16)
		0.5 (5.89) P=0.939		1.2 (5.99) P=0.847	
Lymphedema	5.9 (1.15)		6.5 (1.23)	6.8 (1.30)	5.4 (1.41)
		-0.6 (1.70) P=0.724		1.4 (1.94) P=0.475	
Urological symptoms	-2.7 (0.84)		-1.3 (0.88)	-1.7 (0.94)	-0.8 (1.01)
		-1.5 (1.21) P=0.223		-0.9 (1.39) P=0.512	
Gastrointestinal symptoms	-1.2 (0.64)		-1.1 (0.71)	-1.0 (0.76)	-1.5 (0.86)
		-0.1 (0.95) P=0.881		0.5 (1.07) P=0.645	
Poor body image	9.0 (1.46)		5.7 (1.47)	9.2 (1.68)	5.0 (1.74)
		3.3 (2.07) P=0.111		4.2 (2.42) P=0.082	
Sexual/vaginal problems	6.3 (2.71)		2.0 (3.52)	6.2 (3.09)	2.2 (3.24)
		4.3 (4.43) P=0.328		4.0 (4.49) P=0.381	

Back and pelvis pain	-4.1 (1.34)	-2.6 (1.50)	-1.7 (1.49)	-1.1 (1.63)
		-1.5 (2.06) P=0.462		-0.6 (2.21) P=0.777
Tingling/numbness	31.3 (1.74)	26.0 (1.83)	31.5 (2.10)	23.8 (2.24)
		5.3 (2.53) P=0.036*		7.7 (3.13) P=0.014*
Muscular pain	14.9 (1.37)	12.8 (1.47)	14.5 (1.54)	11.8 (1.70)
		2.1 (1.98) P=0.289		2.7 (2.30) P=0.236
Hair loss	22.5 (1.39)	21.3 (1.48)	21.8 (2.16)	20.6 (2.29)
		1.2 (2.03) P=0.569		1.2 (3.17) P=0.694
Taste change	9.6 (1.63)	7.6 (1.60)	10.7 (1.73)	8.2 (1.85)
		2.0 (2.33) P=0.418		2.5 (2.57) P=0.336

*Denotes nominally significant difference between arms.

CP, carboplatin-paclitaxel; LSM, least squares mean; MMRp, mismatch repair proficient; MSS, microsatellite stable; QoL, quality of life; SE, standard error.

Supplementary Figure 1. Formulas for linear transformation of (A) EORTC QLQ-C30 and (B) QLQ-EN24 scores^{a,b}

A.

Raw score

$$RS = \frac{(I_1 + I_2 + \dots + I_n)}{n}$$

Linear transformation: functional scales^c

$$S = \left\{ 1 - \frac{(RS-1)}{range} \right\} * 100$$

Linear transformation: symptom scales / items^c

$$S = \left\{ \frac{(RS-1)}{range} \right\} * 100$$

Linear transformation: global health status / HRQoL^c

$$S = \left\{ \frac{(RS-1)}{range} \right\} * 100$$

B.

Raw Score^d

$$RS = \frac{(I_1 + I_2 + \dots + I_n)}{n}$$

Linear transformation: symptom and functional scales/items^c

$$S = \left\{ \frac{(RS-1)}{range} \right\} * 100$$

^aFayers PM, Aaronson NK, Bjordal K, et al, on behalf of the EORTC Quality of Life Group. The EORTC QLQ-C30 Scoring Manual (3rd Edition). Published by: European Organisation for Research and Treatment of Cancer, Brussels 2001.

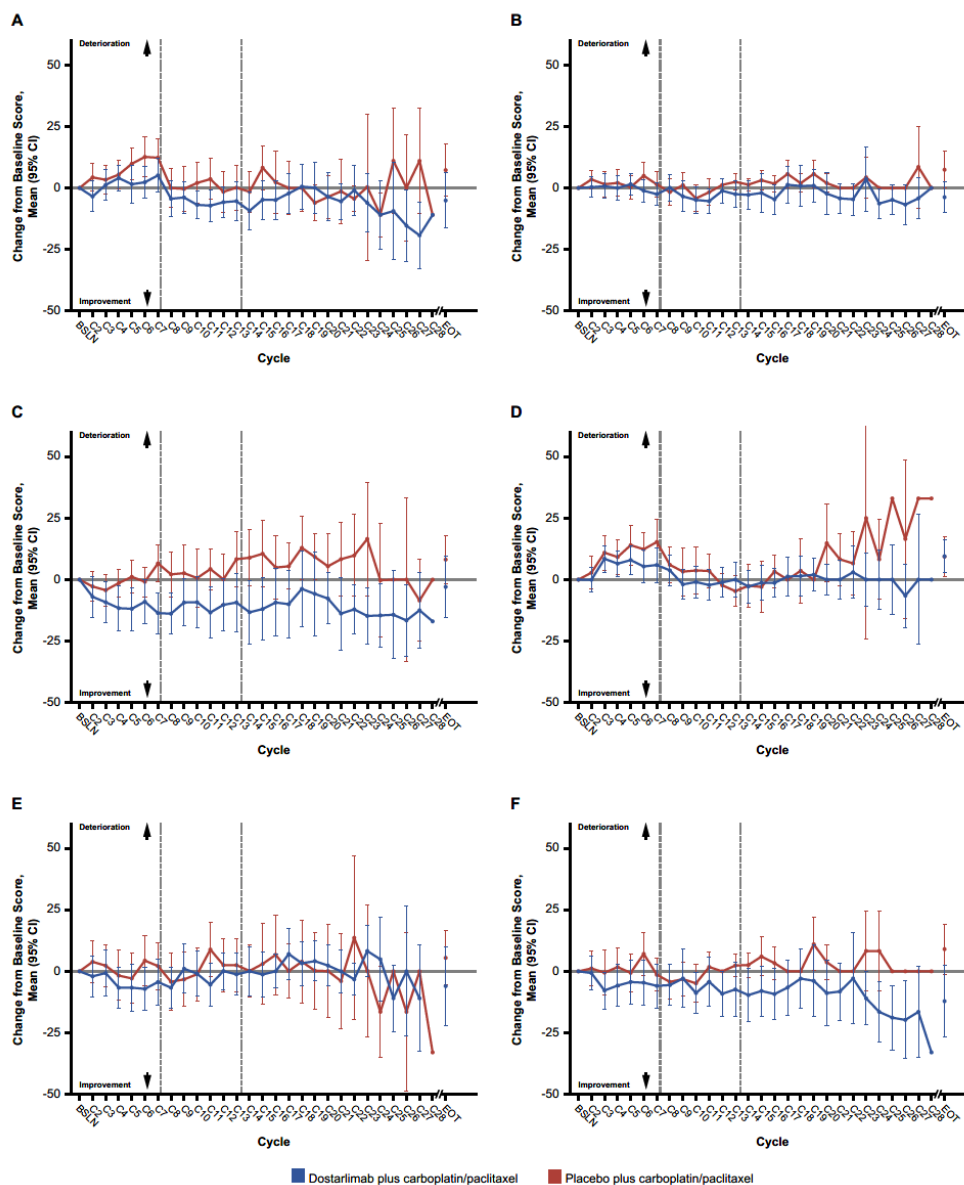
^bGreimel E, Nordin A, Lanceley A, et al. Psychometric validation of the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Endometrial Cancer Module (EORTC QLQ-EN24). *European Journal of Cancer*. 2011;47(2):183-190.

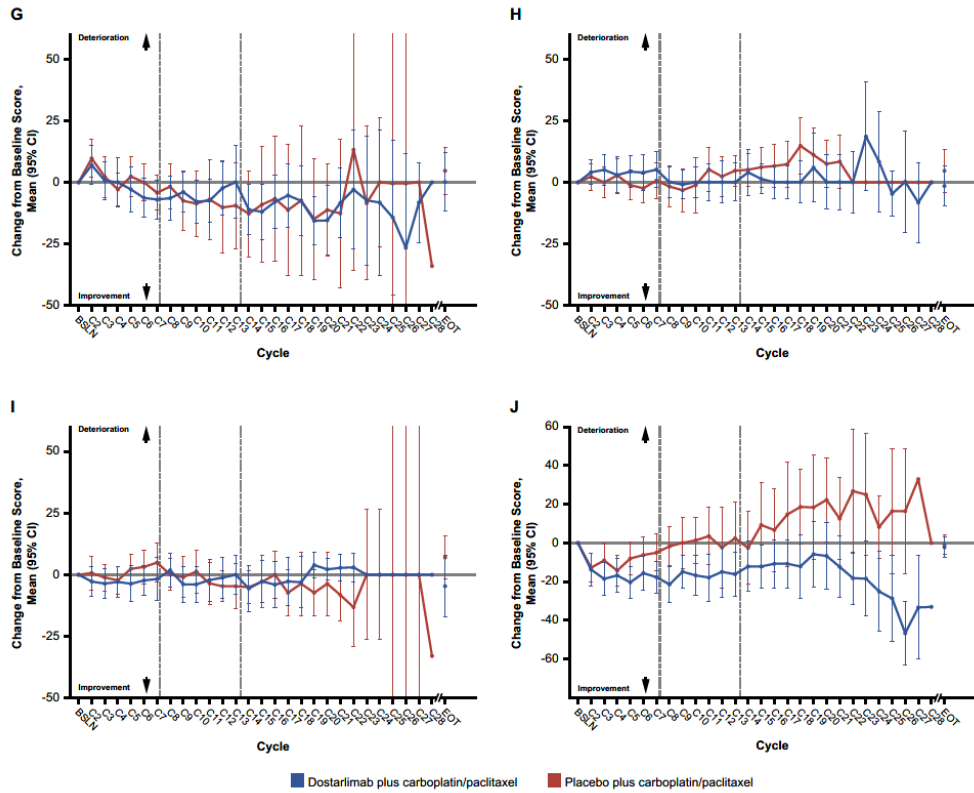
^cRange is the difference between the maximum possible value of RS and the minimum possible value.

^dFor the EORTC QLQ-EN24, for each single-item measure, the score of the item corresponds to the raw score.

EORTC, European Organisation for Research and Treatment of Cancer; I, item; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-EN24, Quality of Life Questionnaire Endometrial Cancer Module. RS, raw score; S, score.

Supplementary Figure 2. Mean change from baseline in PRO scores for symptom scales in the dMMR/MSI-H population. (A) QLQ-C30 fatigue; (B) QLQ-C30 nausea and vomiting; (C) QLQ-C30 pain; (D) QLQ-C30 dyspnea; (E) QLQ-C30 insomnia; (F) QLQ-C30 appetite loss; (G) QLQ-C30 constipation; (H) QLQ-C30 diarrhea; (I) QLQ-C30 financial difficulties; (J) QLQ-EN24 pain in back and pelvis





Error bars indicate 95% CIs.

BSLN, baseline; CP, carboplatin-paclitaxel; dMMR, mismatch repair deficient; EORTC, European Organisation for Research and Treatment of Cancer; EOT, end of treatment; MSI-H, microsatellite instability-high; PRO, patient-reported outcome; QLQ-C30, Quality of Life Questionnaire Core 30; QLQ-EN24, Quality of Life Questionnaire Endometrial Cancer Module.