Supplemental Appendix

Supplement to: Oaknin A, Pothuri B, Gilbert L, et al. Safety, Efficacy, and Biomarker Analyses of Dostarlimab in Patients with Endometrial Cancer: Interim Results of the Phase I GARNET Study

Contents

Supplementary Table S1. Representativeness of study participants.

Cancer type(s)/subtype(s)/stage(s)/condition	Advanced or recurrent endometrial cancer
Considerations related to:	
Sex	Endometrial cancer is a cancer that affects women
Age	The prevalence of endometrial cancer increases with age
Race/ethnicity	The risk of death from endometrial cancer is higher for black women in the United States than for white women
Geography	Incidence rates and mortality rates of endometrial cancer are higher in North America and Europe than in other geographical areas
Other considerations	Between 25 and 30% of all patients with endometrial cancer have dMMR/MSI-H tumors
Overall representativeness of this study	The participants in this trial were recruited from mainly North American and European sites. This reflects the higher incidence rates seen in these areas. In addition, this trial includes not only patients with MMRp/MSS tumors, but patients with dMMR/MSI-H tumors, which are found in at least 25% of patients with endometrial cancer.

Supplementary Table S2. Demographics and baseline characteristics.

Characteristic	dMMR/MSI-H EC N = 143	MMRp/MSS EC N = 156
Age, median (range), y	65.0 (39–85)	66.0 (30–86)
ECOG performance status, n (%)		
0	56 (39.2)	83 (53.2)
1	87 (60.8)	73 (46.8)
FIGO disease stage at diagnosis, n (%)[a]		
Stage I or II	62 (43.4)	57 (36.5)
Stage III or IV	81 (56.6)	98 (62.8)
Histology, n (%)		
Grade 1 or 2 endometrioid carcinoma	92 (64.3)	36 (23.1)
Serous	7 (4.9)	63 (40.4)
Grade 3 endometrioid	21 (14.7)	14 (9.0)
Clear cell	1 (0.7)	11 (7.1)
Squamous	1 (0.7)	3 (1.9)
Undifferentiated	4 (2.8)	3 (1.9)
Carcinosarcoma	0	2 (1.3)
Mixed carcinoma	7 (4.9)	11 (7.1)
Unspecified	4 (2.8)	9 (5.8)
Other[b]	4 (2.8)	4 (2.6)
Unknown	2 (1.4)	0
Prior platinum-doublet therapy, n (%)	139 (97.2)	155 (99.4)
Prior lines of therapy, n (%)[c]		
1	90 (62.9)	72 (46.2)
2	35 (24.5)	67 (42.9)
≥3	18 (12.6)	17 (10.9)
Patients with only adjuvant or neoadjuvant therapy, n (%)	49 (34.3)	42 (26.9)
Prior radiation, n (%)	101 (70.6)	95 (60.9)

[a]One patient with MMRp EC had disease status/stage unknown.

[b]Other includes dedifferentiated, endometrial adenocarcinoma, endometrial adenocarcinoma not otherwise specified, endometrial neuroendocrine carcinoma, high grade uterine carcinoma, and undifferentiated clear cell carcinoma.

[c]Includes lines of therapy in the adjuvant setting.

dMMR, mismatch repair deficient; EC, endometrial cancer; FIGO, International Federation of Gynecology and Obstetrics; MMRp, mismatch repair proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable.

Supplementary Table S3. Objective response rate in patients who had received prior treatment only in the adjuvant or neoadjuvant setting.

dMMR/MSI-H EC Patients		
	dMMR (N = 48)	**dMMR/MSI-H (N = 49)**
ORR, n, % (95% CI)	20, 41.7% (27.6–56.8)	21, 42.9% (28.8–57.8)
Best confirmed response, n (%)		
CR	7 (14.6)	8 (16.3)
PR	13 (27.1)	13 (26.5)
SD	9 (18.8)	9 (18.4)
PD	15 (31.3)	15 (30.6)
NE	4 (8.4)	4 (8.1)
DCR, n (%)	29 (60.4)	30 (61.2)
MMRp/MSS EC Patients		
	MMRp (N = 38)	**MMRp/MSS (N = 42)**
ORR, n, % (95% CI)	9, 23.7% (11.4–40.2)	10, 23.8% (12.1–39.5)
Best confirmed response, n (%)		
CR	4 (10.5)	4 (9.5)
PR	5 (13.2)	6 (14.3)
SD	6 (15.8)	6 (14.3)
PD	20 (52.6)	23 (54.8)
NE	3 (7.9)	3 (7.1)
DCR, n (%)	15 (39.5)	16 (38.1)

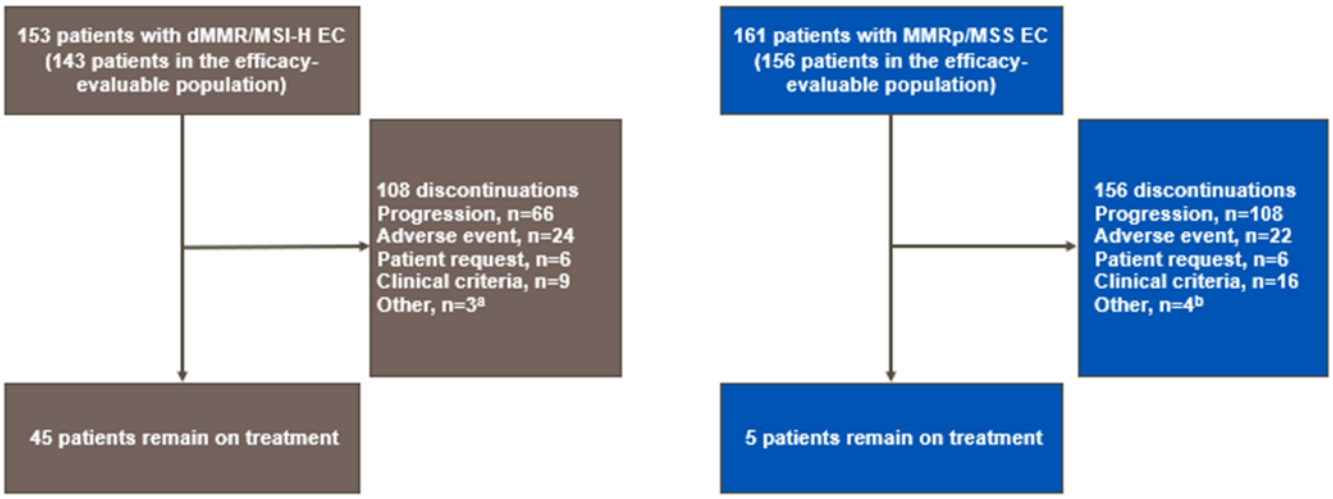
CR, complete response; DCR, disease control rate; dMMR, mismatch repair deficient; DOR, duration of response; MMRp, mismatch repair proficient; MMRunk, mismatch repair unknown; MSI-H, microsatellite instability–high; MSS, microsatellite stable; NE, not evaluable, includes patients with a best response of not done; PD, progressive disease; PR, partial response; SD, stable disease.

Supplementary Table S4. Safety.

Parameter, n (%)	dMMR/MSI-H EC (N = 153)	MMRp/MSS EC (N = 161)	Overall (N = 314)
Safety summary			
Any TEAE	152 (99.3)	161 (100)	313 (99.7)
Grade ≥3 TEAE	87 (56.9)	95 (59.0)	182 (58.0)
Any-grade TRAE	108 (70.6)	115 (71.4)	223 (71.0)
Grade ≥3 TRAE	27 (17.6)	33 (20.5)	60 (19.1)
Any irTRAE	42 (27.5)	31 (19.3)	73 (23.2)
Grade ≥3 irTRAE	16 (10.5)	9 (5.6)	25 (8.0)
Treatment-related SAE	18 (11.8)	14 (8.7)	32 (10.2)
Any TRAE leading to discontinuation	13 (8.5)	14 (8.7)	27 (8.6)
TRAE leading to death	0	0	0
Any grade TRAEs in >10% of patients			
Fatigue	21 (13.7)	35 (21.7)	56 (17.8)
Diarrhea	25 (16.3)	21 (13.0)	46 (14.6)
Nausea	19 (12.4)	24 (14.9)	43 (13.7)
Asthenia	24 (15.7)	13 (8.1)	37 (11.8)
Grade ≥3 TRAEs that occurred in >2 (0.5%) patients			
Anemia	7 (4.6)	3 (1.9)	10 (3.2)
ALT increased	3 (2.0)	3 (1.9)	6 (1.9)
Diarrhea	3 (2.0)	2 (1.2)	5 (1.6)
Amylase increased	1 (0.7)	4 (2.5)	5 (1.6)
Fatigue	1 (0.7)	3 (1.9)	4 (1.3)
AST increased	0	4 (2.5)	4 (1.3)
Hyperglycemia	1 (0.7)	3 (1.9)	4 (1.3)
Lipase increased	3 (2.0)	1 (0.6)	4 (1.3)
Pneumonitis	2 (1.3)	1 (0.6)	3 (1.0)
Grade ≥2 irTRAEs occurring in ≥2% of patients			
Hypothyroidism	13 (8.5)	13 (8.1)	26 (8.3)
ALT increased	5 (3.3)	3 (1.9)	8 (2.5)
AST increased	2 (1.3)	5 (3.1)	7 (2.2)
Arthralgia	6 (3.9)	4 (2.5)	10 (3.2)
Grade ≥3 irTRAEs occurring in ≥1% of patients			
ALT increased	3 (2.0)	3 (1.9)	6 (1.9)
AST increased	0	4 (2.5)	4 (1.3)
Pneumonitis	2 (1.3)	1 (0.6)	3 (1.0)
Any grade TRAE leading to discontinuation in ≥1% of patients			
ALT increased	2 (1.3)	3 (1.9)	5 (1.6)
AST increased	1 (0.7)	2 (1.2)	3 (1.0)
Pneumonitis	2 (1.3)	1 (0.6)	3 (1.0)

ALT, alanine transaminase, AST; aspartate transferase; dMMR, mismatch repair deficient; EC, endometrial cancer; irTRAE, immune-related TRAE; MMR, mismatch repair; MMRp, mismatch repair–proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TRAE, treatment-related adverse event.

Supplementary Figure S1. Enrollment and outcomes.



Data cutoff date: November 1, 2021.Ten (cohort A1) and 5 (cohort A2) patients were excluded from the efficacy-evaluable population because they had no measurable disease at baseline, per BICR.

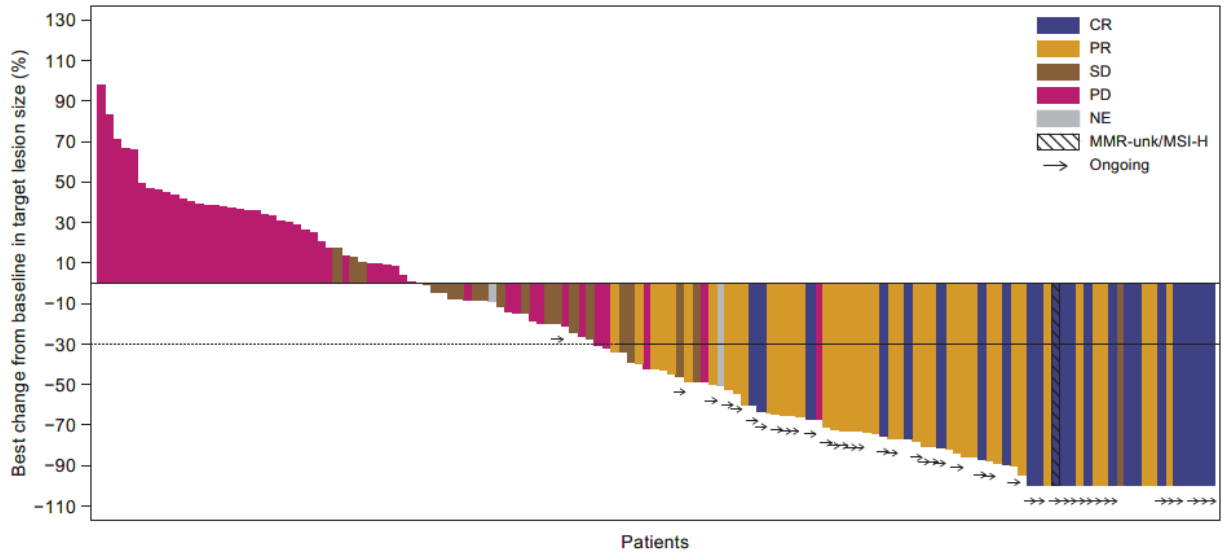
[a]Three patients in cohort A1 died of disease progression.

[b]Two patients in cohort A2 died of disease progression, 1 patient was sent to hospice care, and 1 patient discontinued because of a joint decision between patient and investigator.

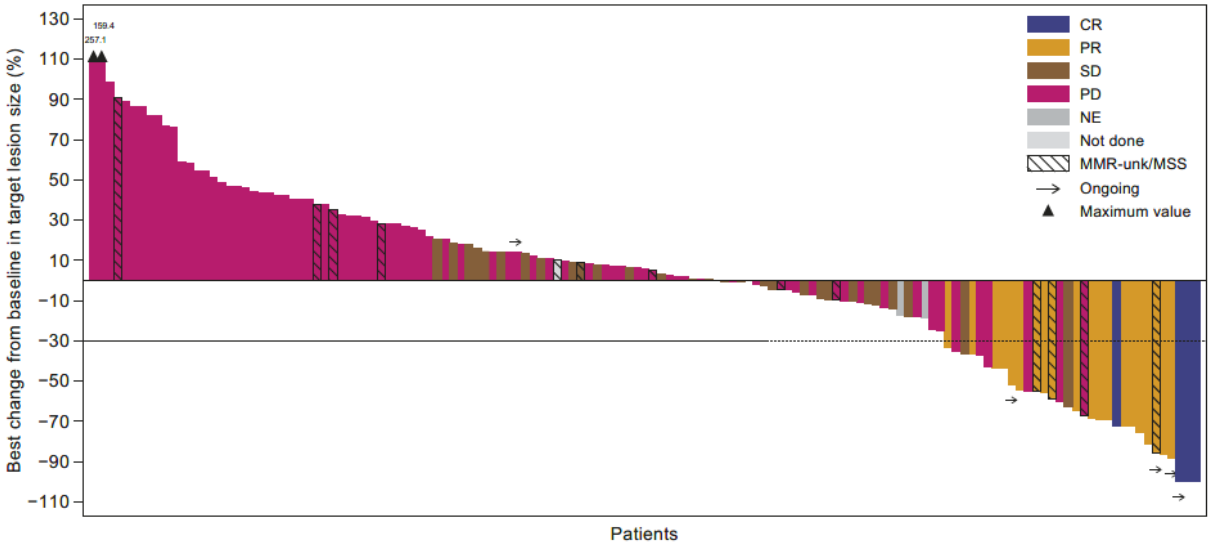
BICR, blinded independent central review; dMMR, mismatch repair–deficient; EC, endometrial cancer; MMRp, mismatch repair–proficient; MSI-H, microsatellite instability–high; MSS, microsatellite stable.

Supplementary Figure S2. Best percent volume change in target lesions based on BICR per RECIST 1.1.

A.



B.

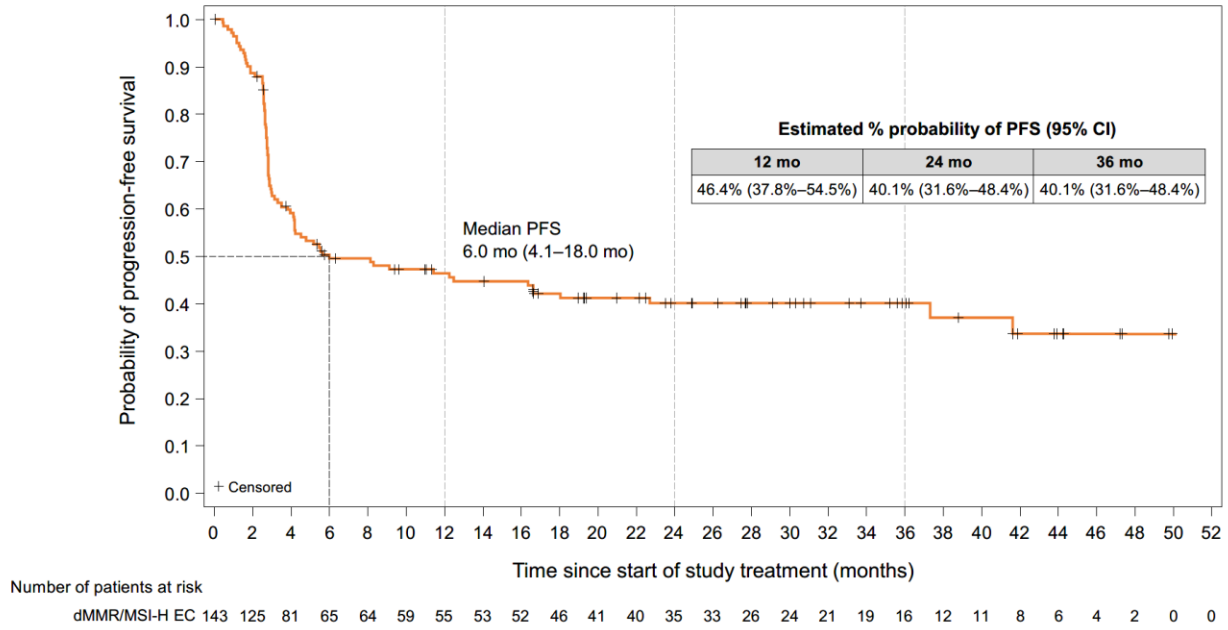


Supplementary Figure S2. Best percent change from baseline in target lesion size in patients with advanced or recurrent EC treated with dostarlimab monotherapy. **A,** patients with dMMR/MSI-H EC (Cohort A1). **B,** patients with MMRp/MSS EC (Cohort

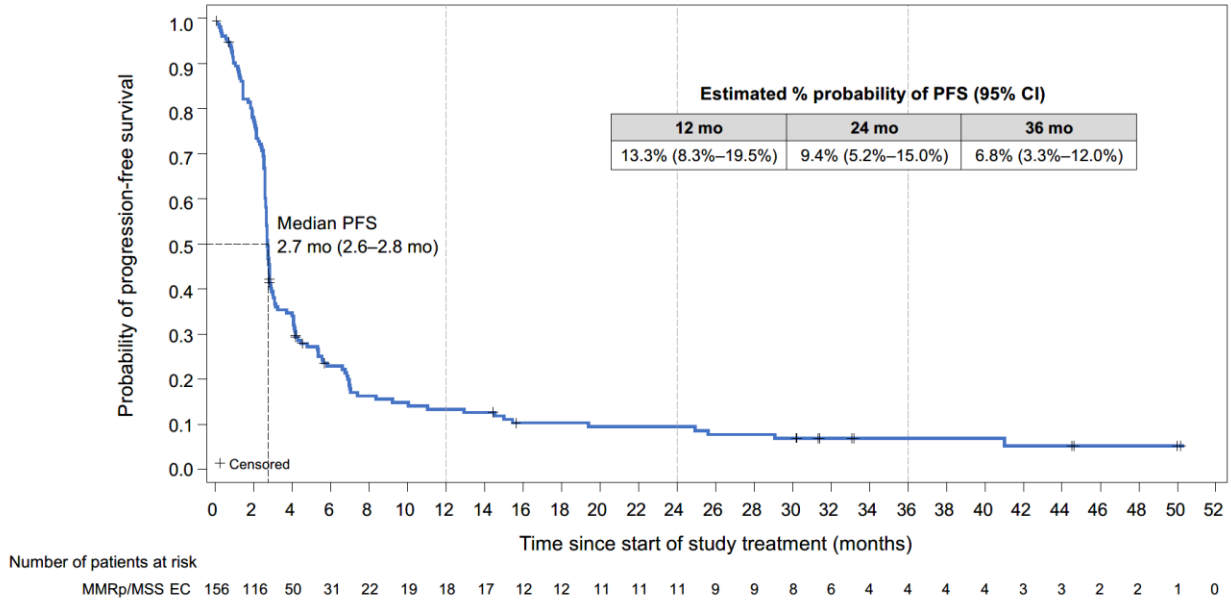
A2). CR, complete response; dMMR, mismatch repair deficient; EC, endometrial cancer; MMRunk, mismatch repair unknown; MSI-H, microsatellite instability–high; MSS, microsatellite stable; NE, not evaluable; PD, progressive disease; PR, partial response; SD, stable disease.

Supplementary Figure S3. Progression-free survival by cohort.

A.



B.

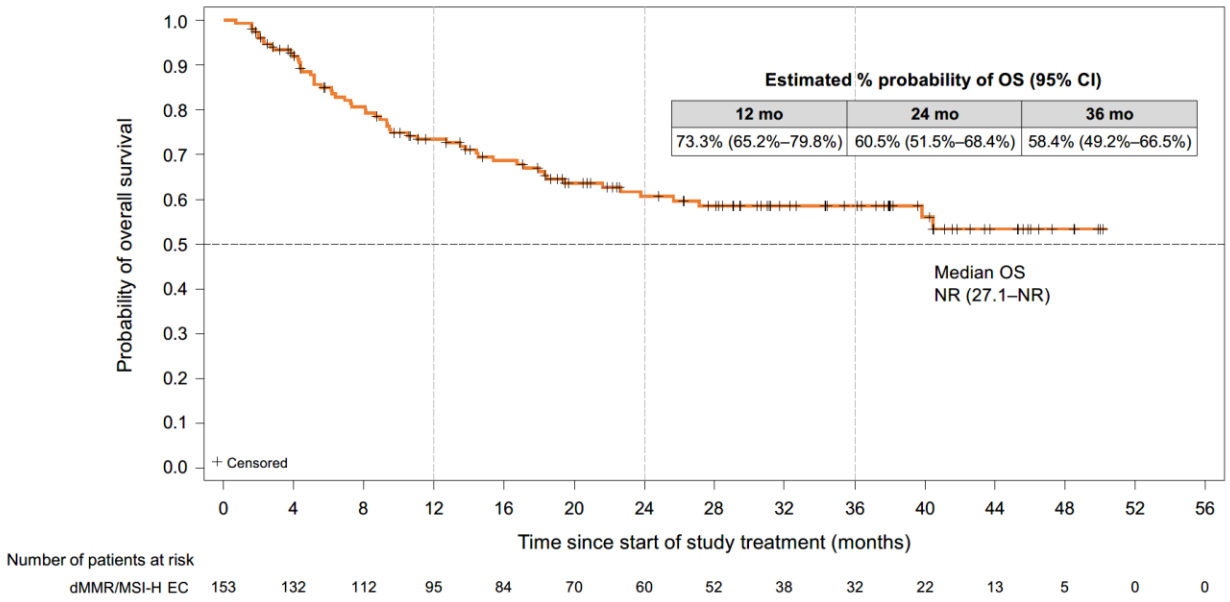


Supplementary Figure S3. Progression-free survival (PFS) in patients with advanced or recurrent EC treated with dostarlimab monotherapy. **A,** patients with dMMR/MSI-H

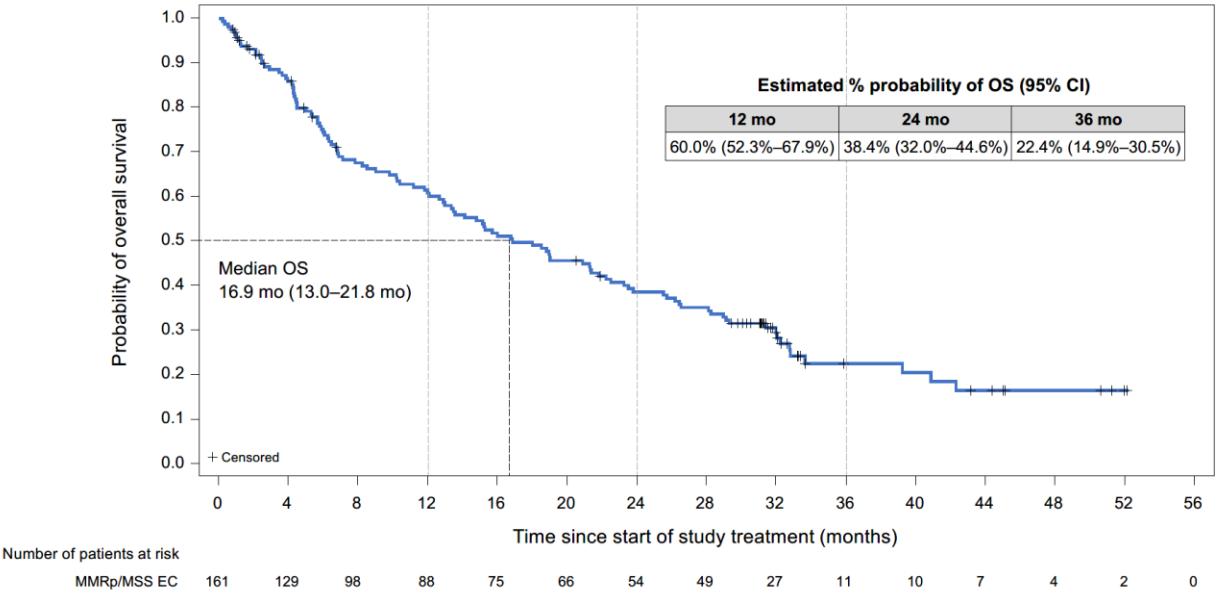
EC (Cohort A1). **B,** patients with MMRp/MSS EC (Cohort A2). dMMR, mismatch repair deficient; MMRp, mismatch repair proficient; MMRunk, mismatch repair unknown; MSI-H, microsatellite instability–high; MSS, microsatellite stable.

Supplementary Figure S4. Overall survival by cohort.

A.



B.

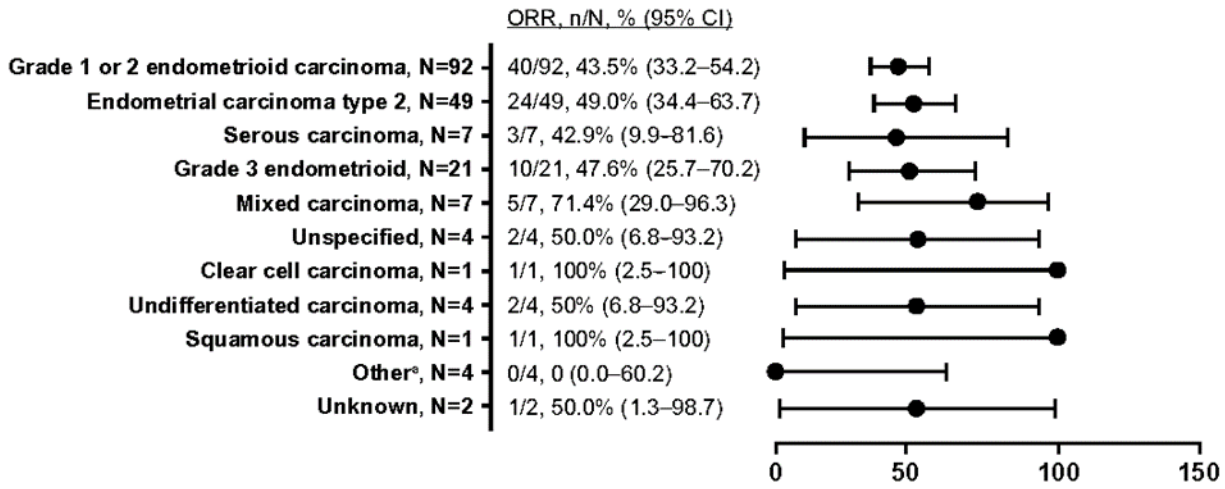


Supplementary Figure S4. Overall survival (OS) in patients with advanced and recurrent EC treated with dostarlimab monotherapy. **A,** patients with dMMR/MSI-H EC (Cohort A1). **B**, patients with MMRp/MSS EC (Cohort A2). dMMR, mismatch repair

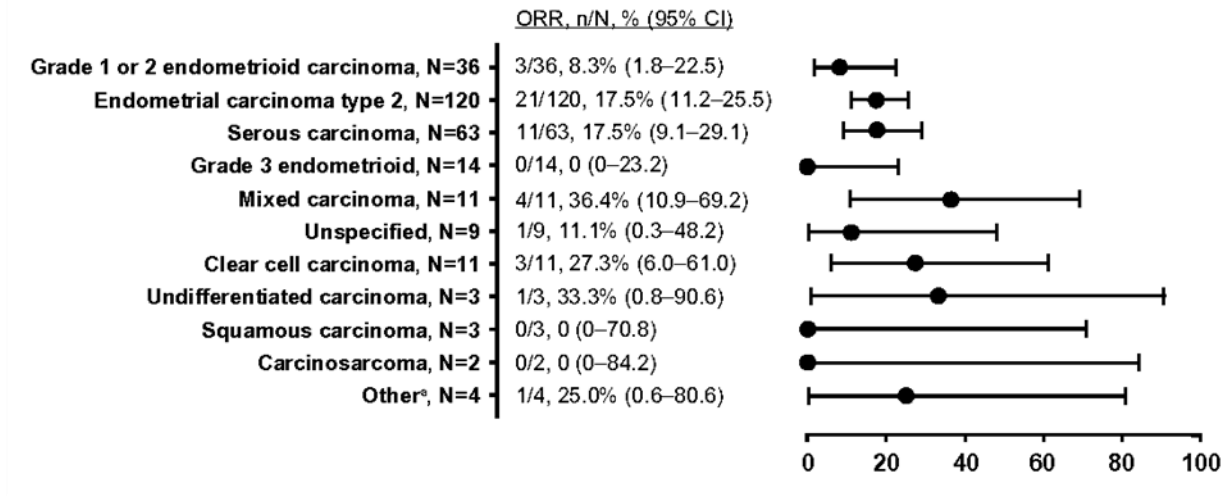
deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MMRunk, mismatch repair unknown; MSI-H, microsatellite instability–high; MSS, microsatellite stable.

Supplementary Figure S5. Objective response rate by tumor histology.

A.



B.



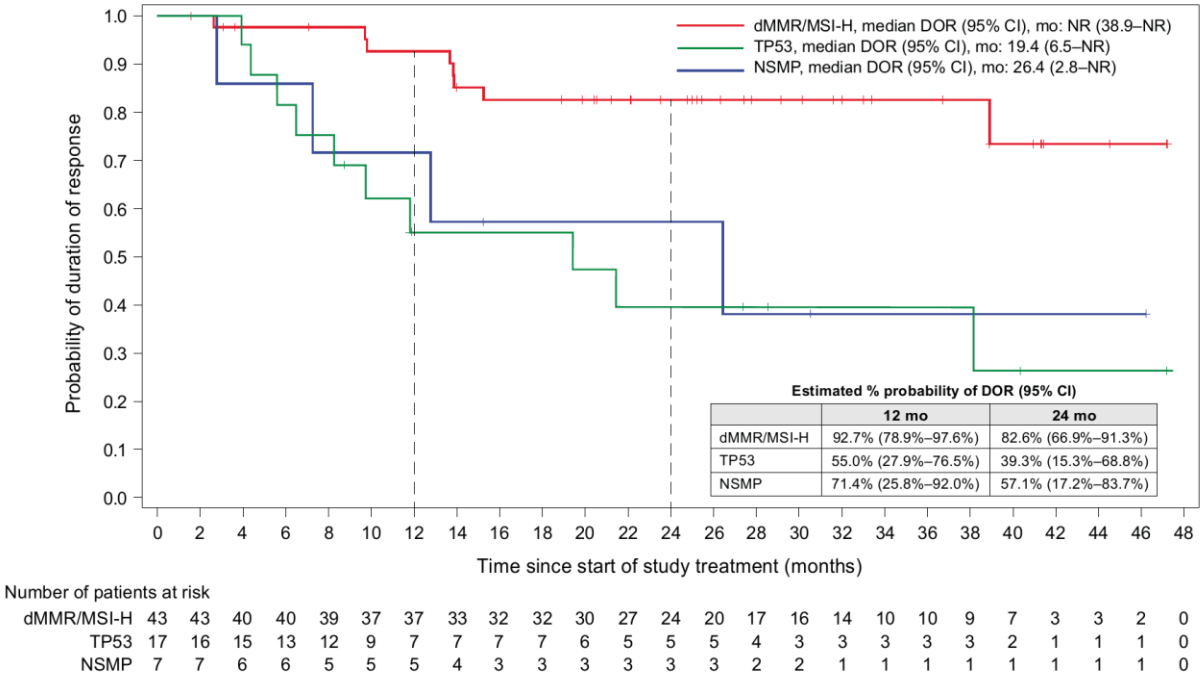
[a]Other includes dedifferentiated, endometrial adenocarcinoma, endometrial adenocarcinoma NOS, endometrial neuroendocrine carcinoma, high-grade uterine carcinoma, and undifferentiated clear cell carcinoma

Supplementary Figure S5. Objective response rate (complete or partial response) in patients with advanced and recurrent EC treated with dostarlimab monotherapy stratified by tumor histology. **A**, patients with dMMR/MSI-H EC (Cohort A1). **B,** patients with MMRp/MSS EC (Cohort A2). dMMR, mismatch repair deficient; EC, endometrial

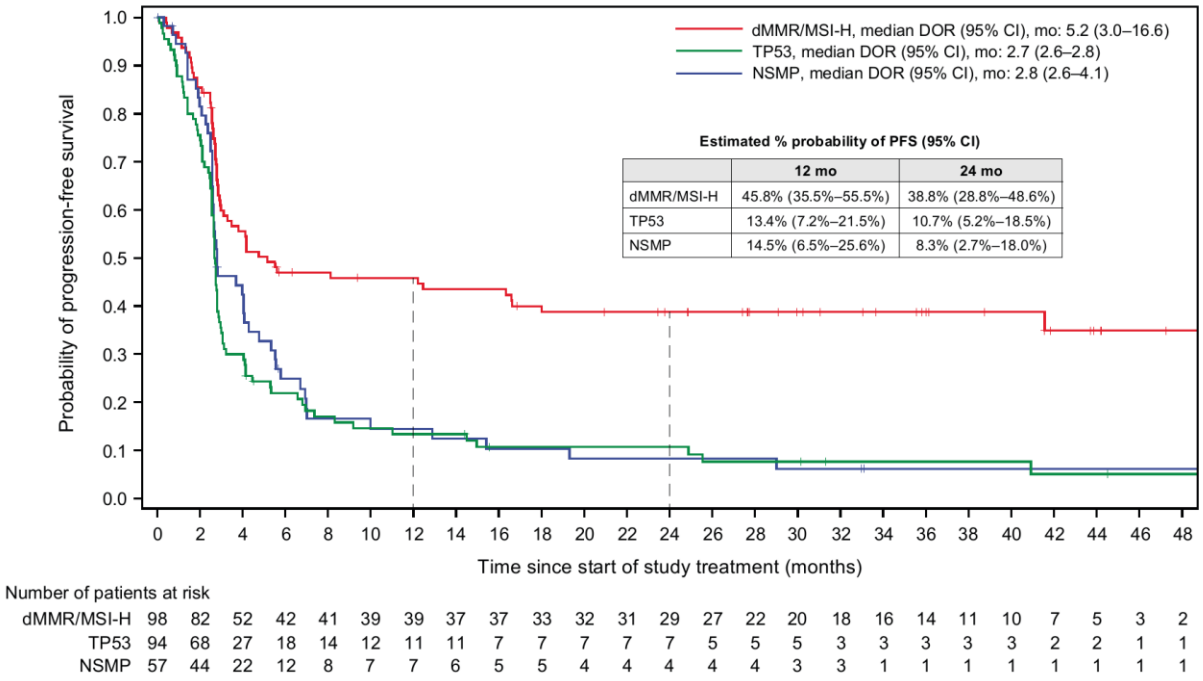
cancer; MMRp, mismatch repair proficient MSI-H; microsatellite instability–high; MSS, microsatellite stable

Supplementary Figure S6. DOR and PFS by molecular subtype.

A.



B.



Supplementary Figure S6. Response by molecular subtype in patients with dMMR/MSI-H EC (Cohort A1) and patients with MMRp/MSS EC (Cohort A2) treated with dostarlimab monotherapy. **A,** Duration of response (DOR). **B,** Progression-free

survival (PFS). dMMR, mismatch repair deficient; EC, endometrial cancer; MMRp, mismatch repair proficient; MMRunk, mismatch repair unknown; MSI-H, microsatellite instability–high; MSS, microsatellite stable; NSMP, no specific molecular profile; *TP53*mut, *TP53* mutation subtype.