Dostarlimab for primary advanced or recurrent (A/R) endometrial cancer (EC): Outcomes by blinded independent central review (BICR) of the RUBY trial (ENGOT-EN6-NSGO/GOG-3031/RUBY).

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Background: RUBY (NCT03981796) evaluated the efficacy and safety of the anti–programmed death 1 (PD-1) dostarlimab + standard of care (SOC) carboplatin paclitaxel (CP) versus CP alone in A/R EC. The primary endpoint of PFS by investigator assessment (INV) per RECIST v1.1 was significantly longer with dostarlimab+CP than placebo (PBO)+CP in the mismatch repair deficient/microsatellite instability-high (dMMR/MSI-H; HR 0.28; 95% CI 0.162–0.495) and overall populations (HR 0.64, 95% CI 0.507–0.800). Here we present secondary efficacy endpoints by BICR. **Methods:** RUBY is a phase 3, global, randomized, double-blind, multicenter, PBO-controlled study. Patients (pts) with primary advanced stage III or IV or first recurrent EC were randomized 1:1 to receive dostarlimab 500 mg, or PBO, plus carboplatin AUC 5 and paclitaxel 175 mg/m^2 Q3W (6 cycles), followed by dostarlimab 1000 mg, or PBO, monotherapy Q6W for up to 3 y. Secondary endpoints by BICR assessment per RECIST v1.1 were PFS, ORR, DOR, and DCR in the overall and dMMR/MSI-H populations. **Results:** 494 pts were randomized (245:dostarlimab+CP; 249:PBO+CP); 47.8% had recurrent disease, 18.6% and 33.6% had primary stage III and IV disease, respectively. PFS by BICR was longer with dostarlimab+CP than PBO+CP in the dMMR/MSI-H (HR 0.29; 95% CI 0.158–0.543) and overall populations (HR 0.66; 95% CI 0.517–0.853; Table). Consistent benefits were seen with dostarlimab+CP for ORR, DCR, and DOR by BICR in the dMMR/MSI-H and overall populations (Table). Safety was previously reported. **Conclusions:** Dostarlimab+CP showed clinically meaningful improvement in BICR-assessed PFS in the dMMR/MSI-H and overall populations compared with CP alone. The HRs for PFS per BICR and per INV were consistent, which supports the reliability of PFS by INV in EC trials. Benefits were seen in all BICR-assessed endpoints, which were consistent with INV. Dostarlimab+CP represents a new SOC for pts with primary A/R EC. Clinical trial information: NCT03981796. Research Sponsor: GSK.

	dMMR/MSI-H		Overall	
	Dostarlimab +CP N=53	PBO+CP N=65	Dostarlimab +CP N=245	PBO+CP N=249
PFS by INV, HR (95% CI)	0.28 (0.162–0.495) *P*<0.0001		0.64 (0.507–0.800) *P*<0.0001	
PFS by BICR, HR (95% CI)	0.29 (0.158–0.543)		0.66 (0.517–0.853)	
Probability of PFS by BICR at 24 mo, % (95% CI)	66.3 (50.8–77.9)	26.0 (13.5–40.5)	42.5 (35.2–49.6)	25.4 (18.9–32.4)
ORR by BICR, % (95% CI; n/N)[a] CR, % (n)	77.1 (62.7–88.0; 37/48)	63.3 (49.9–75.4; 38/60)	68.2 (61.6–74.2; 152/223)	59.4 (52.7–65.8; 136/229)
PR, % (n)	22.9 (11)	13.3 (8)	20.6 (46)	14.8 (34)
	54.2 (26)	50.0 (30)	47.5 (106)	44.5 (102)
DCR, % (95% CI; n/N)[a]	91.7 (80.0–97.7; 44/48)	91.7 (81.6–97.2; 55/60)	88.3 (83.4–92.2; 197/223)	86.9 (81.8–91.0; 199/229)
mDOR (95% CI), mo[a]	NE (13.1–NE)	6.9 (5.5–10.1)	12.9 (8.2–NE)	6.7 (5.7–8.3)

[a]Assessed in pts with evaluable disease at baseline.
CR, complete response; PR, partial response; NE, not estimable. *no MRI done.