

demonstrate a statistically significant OS benefit in pts with pA/rEC and supports the use of dostarlimab+CP as a standard of care in the 1L setting.

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### 38MO Progression-free survival (PFS) in primary advanced or recurrent endometrial cancer (pA/rEC) in the overall and mismatch repair proficient (MMR/MSS) populations and in histological and molecular subgroups: Results from part 2 of the RUBY trial

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**Background:** In Part 1 of the phase 3 RUBY trial (NCT03981796) in pA/rEC, patients (pts) receiving dostarlimab (dostar)/carboplatin-paclitaxel (CP) exhibited significant benefits in PFS and overall survival versus CP alone. Outcomes may be further improved by adding a poly(ADP-ribose) polymerase inhibitor (PARPi). Here we report results from Part 2 of RUBY of dostar/CP followed by dostar/niraparib (nira; a PARPi) maintenance therapy in pts with pA/rEC.

**Methods:** Pts were randomized 2:1 to dostar 500 mg IV + CP Q3W for 6 cycles followed by dostar 1000 mg IV Q6W + nira (individualized starting dose of 200 or 300 mg) PO daily for ≤3 years from randomization or to placebo (PBO) + CP Q3W for 6 cycles followed by PBOs for ≤3 years. The primary endpoint was PFS in the overall and MMRp/MSS populations.

**Results:** 291 pts were randomized (192 dostar/CP + dostar/nira; 99 PBO/CP). PFS was significantly improved in pts receiving dostar/CP + dostar/nira vs PBO/CP in the overall and MMRp/MSS populations (Table). In pts with endometrioid carcinoma, pts with other histologies, and across most biomarker subgroups (eg, TP53mut), the hazard ratio (HR) directionally favored dostar/CP + dostar/nira in the overall and MMRp/MSS populations. The safety profile observed was consistent with those of the individual agents.

Table: 38MO PFS

	Dostar/ CP+dostar/nira	PBO/CP+PBO	HR (95% CI)
Overall, n	192	99	0.60 (0.43–0.82) P=0.0007
Median (95% CI), mo	14.5 (11.8–17.4)	8.3 (7.6–9.8)	-
MMRp/MSS, n	142	74	0.63 (0.44–0.91) P=0.0060
Median (95% CI), mo	14.3 (9.7–16.9)	8.3 (7.6–9.8)	-
Pre-specified exploratory analyses			
	No. of pts with events/No. of pts		
All pts	95/192	69/99	-
Endometrioid carcinoma	52/114	46/67	0.58 (0.39–0.87)
Other histologies	42/76	23/32	0.53 (0.32–0.88)
Molecular subgroup <sup>b</sup>			
POLeut	0/3	1/2	- <sup>a</sup>
dMMR/MSI-H	12/37	10/17	0.45 (0.20–1.05)
TP53mut	27/39	10/10	0.29 (0.13–0.63)
No specific molecular profile	37/75	31/46	0.61 (0.38–0.99)
Not evaluable	19/38	17/24	0.71 (0.37–1.37)

<sup>a</sup><20 events. <sup>b</sup>Based on whole exome sequencing.

**Conclusions:** RUBY Part 2 met its primary endpoint and is the first study to show significant and clinically meaningful improvement in PFS in the MMRp/MSS and overall populations. The trial is ongoing for OS follow-up. The safety profile observed was generally consistent with the known safety profiles of the individual agents.

These data demonstrate a potential role for PARPi maintenance in pts receiving dostar/CP, especially for MMRp/MSS tumors.

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39MO

# **Phase III ENGOT-En9/LEAP-001 study: Lenvatinib + pembrolizumab (LEN/PEMBRO) vs chemotherapy (chemo) as first-line (1L) therapy for advanced or recurrent endometrial cancer**

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**Background:** LEN/PEMBRO following prior systemic therapy in any setting, including neo/adjuvant, is a standard of care for advanced endometrial cancer (EC). The phase 3 ENGOT-en9/LEAP-001 trial (NCT03884101) compared 1L LEN/PEMBRO vs chemo in patients (pts) with advanced/recurrent EC.

**Methods:** Eligible pts had stage III–IV or recurrent, measurable/non-measurable, radiographically apparent EC, with no prior chemo or PD ≥ 6 mo after neo/adjuvant platinum-based chemo. Pts were randomized 1:1 (stratified by proficient vs deficient mismatch repair status [pMMR/dMMR] and, in the pMMR stratum, by ECOG PS [0/1], measurable disease [yes/no], and chemo/chemoradiation [yes/no]) to lenvatinib 20 mg QD plus pembrolizumab 200 mg Q3W or paclitaxel 175 mg/m<sup>2</sup> Q3W plus carboplatin AUC 6 Q3W. Dual primary endpoints were PFS (RECIST v1.1, blinded independent central review) and OS in the pMMR population and among all-comers. Secondary endpoints included ORR and safety; duration of response (DOR) was an exploratory endpoint; and efficacy outcomes assessed by tumor histology was a prespecified exploratory analysis.

**Results:** 842 pts were randomized. At final analysis (data cutoff, 2 Oct 2023), after median follow-up of 38.4 (range, 30.3–52.9) mo, statistical significance for non-inferiority (NI) OS endpoint was not achieved for LEN/PEMBRO vs chemo in the pMMR population (HR, 1.02 [95% CI, 0.83–1.26]; NI P = 0.2459875; Table). PFS and OS results for LEN/PEMBRO vs chemo by histological subtype will be presented for the pMMR population and all-comers. Treatment-related AEs occurred in 411/420 (97.9%) vs 398/411 (96.8%) treated pts in the LEN/PEMBRO vs chemo groups.

Table: 39MO				
	pMMR		All-comers	
	LEN/PEMBRO n = 320	Chemo n = 322	LEN/PEMBRO n = 420	Chemo n = 422
OS HR (95% CI)	1.02 (0.83–1.26) <sup>a</sup>		0.93 (0.77–1.12)	
PFS HR (95% CI)	0.99 (0.82–1.21)		0.91 (0.76–1.09)	
ORR (95% CI), %	50.6 (45.0–56.2)	54.7 (49.0–60.2)	55.7 (50.8–60.5)	55.5 (50.6–60.3)
Median DOR (range), mo	16.1 (1.0+ to 48.7+)	10.6 (1.1+ to 43.8+)	23.2 (1.0+ to 49.0+)	10.9 (1.1+ to 46.9+)

<sup>a</sup>1-sided NI P = 0.2459875 (nonsignificant), not crossing prespecified OS NI boundary, P = 0.0158890, so no further statistical testing of efficacy endpoints was performed per prespecified multiplicity strategy for type 1 error control.