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ESMO VIRTUAL PLENARY ABSTRACT

VP2-2023: Dostarlimab + chemotherapy for the treatment of primary advanced or recurrent (A/R) endometrial cancer (EC): A placebo (PBO)-controlled randomised phase III trial (ENGOT-EN6-NSGO/GOG-3031/RUBY)

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BACKGROUND

Carboplatin-paclitaxel (CP) is standard of care (SOC) for first-line treatment of primary A/R EC; median OS is <3 yrs. Use of anti−PD-1s with chemo has improved outcomes in multiple tumour types. RUBY (NCT03981796) evaluated the efficacy and safety of the anti−PD-1 dostarlimab (D)+CP in A/R EC compared with CP alone.

METHODS

RUBY is a phase III, global, randomised, double-blind, multicentre, PBO-controlled study. Pts with primary advanced stage III or IV or first recurrent EC were randomised 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 yrs. Primary endpoints were PFS by investigator assessment per RECIST v1.1 and OS. Graphical method was used for hypothesis testing of PFS in the dMMR/MSI-H population, then the overall population, and OS in the overall population. A prespecified exploratory analysis of PFS in MMR proficient (MMRp)/MS stable (MSS) pts was also performed. Safety was assessed.

RESULTS

Of 494 pts randomised (245 D+CP; 249 PBO+CP), 23.9% had dMMR/MSI-H tumours (53 D+CP; 65 PBO+CP), 47.8% had recurrent disease; 18.6% and 33.6% had primary stage III and IV disease, respectively. PFS and OS results are presented in the table. Discontinuation of dostarlimab or PBO due to a TEAE occurred in 17.4% pts receiving D+CP and 9.3% pts receiving PBO+CP. The safety profile of D+CP was generally consistent with the safety profile of each drug.

CONCLUSIONS

D+CP showed statistically significant and clinically meaningful PFS benefits in the dMMR/MSI-H and overall populations vs CP alone. A clinically relevant benefit in PFS was also observed in the MMRp/MSS population. An early trend toward improved OS was observed in all populations. The combination of dostarlimab+CP represents a new SOC for pts with newly diagnosed primary A/R EC.

CLINICAL TRIAL IDENTIFICATION

NCT03981796.

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LEGAL ENTITY RESPONSIBLE FOR THE STUDY

GSK.

Table: VP2-2023

		HR (95% CI) P	% Probability at 24 mo (95% CI)
PFS	dMMR/MSI-H		
	D+CP	0.28	61.4 (46.3–73.4)
	PBO+CP	(0.162–0.495)	15.7 (7.2–27.0)
		<0.0001	
	Overall		
	D+CP	0.64	36.1 (29.3–42.9)
	PBO+CP	(0.507–0.800)	18.1 (13.0–23.9)
		<0.0001	
	MMRp/MSS[a]		
	D+CP	0.76	28.4 (21.2–36.0)
	PBO+CP	(0.592–0.981)	18.8 (12.8–25.7)
		NA	
OS	Overall[b]		
	D+CP	0.64	71.3 (64.5–77.1)
	PBO+CP	(0.464–0.870)	56.0 (48.9–62.5)
		0.0021[e]	
	dMMR/MSI-H[c]		
	D+CP	0.30	83.3 (66.8–92.0)
	PBO+CP	(0.127–0.699)	58.7 (43.4–71.2)
		NA	
	MMRp/MSS[d]		
	D+CP	0.73	67.7 (59.8–74.4)
	PBO+CP	(0.515–1.024)	55.1 (46.8–62.5)
		NA	

[a]No hypothesis testing of PFS in MMRp/MSS was planned. Maturity:
[b]≈33%.
[c]≈26%.
[d]≈36%.
[e]*P*-value ≤0.00177 required for statistical significance at this analysis.

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DISCLOSURE

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M.A. Powell: Financial Interests, Personal, Advisory Role: GSK, Tesaro, Merck, Eisai, SeaGen, Clovis Oncology, AstraZeneca.

All other authors have declared no conflicts of interest.

NOTE

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