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Randomised phase II study of ubamatamab ± cemiplimab in patients (pts) with platinum-resistant ovarian cancer (OC)

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Background

Ubamatamab, a MUC16×CD3 bispecific antibody, bridges MUC16+ tumour cells and T cells to promote cytotoxicity. In phase 1 of this study (NCT03564340), ubamatamab ± cemiplimab had an acceptable safety profile and durable activity at a range of doses in pts with advanced OC.

Methods

Pts with platinum-resistant OC treated with 1–4 prior lines of therapy were randomised 1:1:1 to receive ubamatamab 250 mg or 800 mg, or ubamatamab 250 mg + cemiplimab 350 mg (all IV Q3W after ubamatamab step-up dosing). Primary endpoint: objective response rate (ORR; RECIST 1.1). Secondary endpoints: duration of response (DOR), progression-free survival (PFS) and treatment-emergent AEs (TEAEs).

Results

Overall, 150 pts were enrolled (median [med] age: 62 years; med prior lines of therapy: 3; high-grade serous OC: 93%). Med treatment duration: 15 weeks. Responses to ubamatamab monotherapy were only seen in pts without liver mets, where ORR and med DOR were higher with 800 mg (23% and 10.5 months) than 250 mg (17% and 5.7 months), respectively (Table). Addition of cemiplimab did not improve efficacy. Of pts with available MUC16 IHC (n=121), 87% had ≥75% MUC16+ tumour cells and 1/16 (6%) with <75% MUC16+ tumour cells responded to treatment (1 responder with <75% MUC16+ tumour cells = 65%). The most common TEAEs were cytokine release syndrome (85%) and pain (73%); these were primarily observed during step-up dosing and were Grade 1/2. Grade ≥3 treatment-related TEAEs (TRAEs) were reported in 40% of pts in each arm; >50% occurred during step-up dosing. Grade ≥3 TRAEs in >5% of pts were neutropenia (14%) and anaemia (8%). In total, 5% of pts discontinued treatment due to a TEAE.

Conclusions

Ubamatamab 800 mg Q3W had the most promising clinical activity, with durable responses observed in pts without liver mets and with high MUC16 expression. A MUC16+ tumour cell threshold may support biomarker-driven patient selection. Ubamatamab demonstrated an acceptable safety profile after step-up dosing.Table: 1078P

Liver mets present (n)	Ubamatamab 250 mg			Ubamatamab 800 mg			Ubamatamab 250 mg + cemiplimab 350 mg		
	All pts (50)	Yes (9)	No (41)	All pts (50)	Yes (11)	No (39)	All pts (50)	Yes (11)	No (39)
ORR, n (%)	7* (14)	0	7* (17)	9 (18)	0	9 (23)	6† (12)	1 (9)	5 (13)
Med DOR (95% CI),‡ months	5.7 (2.8–NE)	10.5 (2.5–NE)	NE (2.8–NE)						

Liver mets present (n)	Ubamatamab 250 mg			Ubamatamab 800 mg			Ubamatamab 250 mg + cemiplimab 350 mg		
	All pts (50)	Yes (9)	No (41)	All pts (50)	Yes (11)	No (39)	All pts (50)	Yes (11)	No (39)
Med PFS (95% CI), months	2.9 (2.6–4.0)	1.6 (0.5–2.9)	2.9 (2.6–4.2)	2.9 (2.6–3.9)	1.5 (1.1–2.6)	3.5 (2.8–4.4)	2.8 (1.6–3.0)	1.7 (1.2–2.9)	2.9 (1.6–4.2)

Data cutoff: 15 Jan 2025. Med follow-up: 4.9 months. *Includes 1 partial response after data cutoff; †Includes 1 immune partial response (iRECIST); ‡DOR not mature in ubamatamab 800 mg (now 3 pts responding >12 months) and ubamatamab 250 mg + cemiplimab arms.

Clinical trial identification

NCT03564340.

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Legal entity responsible for the study

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Disclosure

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