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Sacituzumab tirumotecan in previously treated advanced or recurrent endometrial cancer: Results from the phase 3 TroFuse-005/ENGOT-en23/GOG-3095 study

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Background

Trophoblast cell-surface antigen 2 (TROP2) is overexpressed in endometrial cancer, making it a promising target. Sacituzumab tirumotecan (sac-TMT) is a TROP2-directed antibody-drug conjugate with a unique, bifunctional linker that stabilizes the drug-to-antibody ratio (7.4) in circulation and maximizes payload delivery to tumor cells. TroFuse-005/ENGOT-en23/GOG-3095 (NCT06132958) evaluated sac-TMT in advanced or recurrent endometrial cancer after immunotherapy.

Methods

Eligible participants (pts) had endometrial carcinoma, including carcinosarcoma, measurable or non-measurable disease, and prior platinum and anti–PD-1/PD-L1 therapy, separately or in combination, with up to 3 total prior lines. Pts were randomized 1:1 to sac-TMT 4 mg/kg Q2W or treatment of physician's choice (TPC; doxorubicin 60 mg/m^2 Q3W or paclitaxel 80 mg/m^2 on days 1, 8, and 15 Q4W) until progression or unacceptable toxicity. Randomization was stratified by MMR status, TROP2 expression, prior lines of therapy, and baseline disease status. Dual primary endpoints were PFS by BICR and OS; ORR by BICR was the key secondary endpoint.

Results

776 pts were randomized to sac-TMT (n=386) or TPC (n=390). At data cutoff (March 23, 2026), median follow-up was 14.0 months. Statistically significant improvements in PFS (HR, 0.59 [95% CI, 0.50–0.70]; P<0.0001) and OS (HR, 0.68 [95% CI, 0.55–0.84]; P=0.0001) were observed with sac-TMT vs TPC; ORR was also significantly improved vs TPC (Table). Grade ≥3 TRAEs occurred in 54.4% of sac-TMT and 41.4% of TPC pts (Table), with anemia most common in both groups (20.8% vs 13.4%). Global health status/QoL was maintained over time in both groups.

Conclusions

Sac-TMT provided statistically significant and clinically meaningful improvements in PFS, OS, and ORR vs TPC in previously treated advanced or recurrent endometrial cancer with manageable safety, supporting it as a new treatment option for this population.Table: LBA11

Efficacy and safety

	Sac-TMT N=386	TPC N=390
Efficacy		
Median PFS, mo (95% CI)	7.2 (5.6–7.6)	3.9 (3.7–5.3)
PFS HR (95% CI)	0.59 (0.50–0.70); P<0.0001*	
Median PFS gain vs TPC, mo	3.3	
Median OS, mo (95% CI)	19.0 (16.1–NR)	12.1 (11.0–15.2)
OS HR (95% CI)	0.68 (0.55–0.84); P=0.0001*	
Median OS gain vs TPC, mo	6.9	
Response	N=376	N=375
ORR, (%)	35.1	17.3
ORR diff., percentage points (95% CI)	17.8 (11.6–23.9); P<0.00001	
Median DoR, mo (95% CI)	11.1 (9.2–13.0)	6.9 (5.4–9.1)
≥6 mo, %	69.0	53.2
≥12 mo, %	42.9	35.1
Safety	N=384	N=367
Median tx duration, wk (range)	31.1 (0.1–96.7)	15.0 (0.1–94.1)
Any TRAE, %	97.1	89.6
Grade ≥3 TRAE, %	54.4	41.4
Discontinued due to TRAE, %	3.1	4.9
Death due to TRAE, %	0.8	0.8

*1-sided log-rank p-value.

Clinical trial identification

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