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715MO Safety and efficacy of sacituzumab tirumotecan (sac-TMT) in patients (pts) with previously treated advanced endometrial carcinoma (EC) and ovarian cancer (OC) from a phase II study

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Background: Trophoblast cell surface antigen 2 (TROP2) is highly expressed in EC and OC. Sac-TMT (also known as MK-2870/SKB264) is a TROP2 ADC developed with a hydrolytically cleavable linker to conjugate a belotecan-derivative topoisomerase I inhibitor. Here, we report the preliminary results from a Phase 2 study in pts with advanced EC and OC (KL264-01, NCT04152499).

Methods: Advanced EC and OC pts who have been previously treated with platinum-based chemo were given sac-TMT at 5 mg/kg Q2W until disease progression, unacceptable toxicity or withdrawal of consent. Tumor assessment was performed every 8 weeks per RECIST v1.1 by investigator. The TROP2 expression was scored using the semi-quantitative H-score method, and cut-off point was set to 200.

Results: As of March 5, 2024, 44 EC pts were enrolled and median follow-up time was 7.2 mo. 52.3% of pts had received $\geq$ 2 prior lines of therapy. The ORR was 34.1% (15/44, 12 confirmed) and DCR was 75%. Median PFS was 5.7 mo (95% CI: 3.7, 9.4) with 6-mo PFS rate of 47.5%. In the pts with TROP2 IHC H-score $>$ 200 (n=12) or H-score $\leq$ 200 (n=28), the ORR was 41.7% (5/12, 3 confirmed) and 35.7% (10/28, 9 confirmed) respectively. 40 OC pts were enrolled and median follow-up time was 28.2 mo. All pts had received $\geq$ 2 prior lines of therapy (80% of pts $\geq$ 3 prior lines). 87.5% of pts were platinum-resistant. The ORR was 40% (16/40, 14 confirmed) and DCR was 75%. mPFS was 6.0 mo (95% CI: 3.9, 7.3); mOS was 16.5 mo (95% CI: 10.7, NE). In the pts with TROP2 IHC H-score $>$ 200 (n=13) or H-score $\leq$ 200 (n=22), the ORR was 61.5% (8/13, 7 confirmed) and 27.3% (6/22, 6 confirmed) respectively. In the pts with platinum-resistant (n=35), mPFS was 6.0 mo (95% CI: 5.3, 7.3) and mOS was 16.1 mo (95% CI: 10.5, NE). Safety of the EC and OC pts is presented in the table.

Table: 715MO Safety summary

	EC (N = 44)	OC (N = 40)
Category		
TRAEs	44 (100%)	40 (100%)
$\geq$ Grade 3 TRAEs	32 (72.7%)	27 (67.5%)
serious TRAEs	9 (20.5%)	15 (37.5%)
TRAEs leading to discontinuation	1 (2.3%)	5 (12.5%)
$\geq$15% $\geq$ Grade 3 TRAEs		
Neutrophil count decreased	19 (43.2%)	12 (30.0%)
White blood cell count decreased	18 (40.9%)	9 (22.5%)
Anaemia	13 (29.5%)	14 (35.0%)
Stomatitis	6 (13.6%)	6 (15.0%)

Conclusions: Sac-TMT monotherapy has shown promising anti-tumor activity with a manageable safety profile in pts with heavily pre-treated advanced EC and OC.

Clinical trial identification: NCT04152499; first posted on November 5, 2019.

Legal entity responsible for the study: Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China.

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716MO Efficacy and safety of sacituzumab tirumotecan (sac-TMT) plus pembrolizumab in patients with recurrent or metastatic cervical cancer

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Background: Anti-PD-1 antibody is the standard therapy for recurrent or metastatic (R/M) cervical cancer (CC) patients (pts) after platinum-based chemotherapy. It was shown that ADC combined with PD-1/L1 antibody has a potential additive effect. Sac-TMT (also known as MK-2870/ SKB264) is a TROP2 ADC developed with novel linker to conjugate a belotecan-derivative topoisomerase I inhibitor. Here, we report the efficacy and safety results from the CC cohort in an ongoing Phase 2 basket study (SKB264-II-06, NCT05642780).

Methods: Pts with R/M CC who had progressed on or after platinum-doublet chemotherapy and received no more than 2 systemic therapies for R/M disease were enrolled. Sac-TMT 3 or 5 mg/kg Q2W+ pembrolizumab 400 mg Q6W were assessed in safety run-in period and the doses deemed well tolerated were being explored in expansion period. Tumor assessments per RECIST 1.1 were performed once every 8 weeks for the first 12 mo, and every 12 weeks thereafter.