MADRID 2026 ESMO congress

4739RO

Sacituzumab tirumotecan (sac-TMT) + pembrolizumab (pembro) for locally advanced or metastatic urothelial carcinoma (la/mUC): Results from a phase 2 study (2870-002/SKB264-II-06)

X. Bian[1], F. Zhou[2], F. Yuan[3], S. Zuo[4], H. Guo[5], A. Drosik-Kwasniewska[6], S. Jiang[7], B. Hu[8], T. Lin[9], T. Yang[10], Z. Yu[11], K. Jiang[12], J. Pikiel[13], M. Edmondson[14], A. Lai[15], T. Keenan[16], Z. Mei[17], Y. Zhou[17], J. Ge[17], D. Ye[1]

[1] Department of Urology, Fudan University Shanghai Cancer Center, Shanghai, China, [2] Department of Urology, Sun Yat-sen University Cancer Center, Guangzhou, China, [3] Department of Urologic Oncology Surgery, Chongqing University Cancer Hospital (Chongqing Cancer Institute and Chongqing Cancer Hospital), Chongqing, China, [4] Department of Oncology, Jilin Cancer Hospital, Changchun, Jilin, China, [5] Department of Urology, Nanjing Drum Tower Hospital, The Affiliated Hospital of Nanjing University Medical School, Nanjing University, Nanjing, China, [6] Department of Oncology, Pratia MCM Krakow, Krakow, Poland, [7] Department of Urology, Hunan Cancer Hospital, Yuelu District, Changsha, China, [8] Department of Urology, Liaoning Cancer Hospital & Institute, Dadong District, Shenyang, China, [9] Department of Urology, Sun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China, [10] Department of Urology, The Affiliated Cancer Hospital of Zhengzhou University, Henan Cancer Hospital, Zhengzhou, China, [11] Department of Urology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou, China, [12] Department of Oncology, The Second Affiliated Hospital of Dalian Medical University, Dalian, China, [13] Department of Oncology, Szpitale Pomorskie, Szpital Morski, Gdynia, Poland, [14] Biostatistics and Research Decision Science, Merck & Co., Inc., Rahway, United States of America, [15] Department of Oncology, Merck & Co., Inc., Rahway, United States of America, [16] Oncology Clinical Development, Merck & Co., Inc., Rahway, United States of America[17] Clinical Research Center, Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China

Background

Pembro + enfortumab vedotin is approved for la/mUC, with an ORR of 67.7% and median PFS of 12.5 mo. Sac-TMT is a TROP2-directed ADC with a unique, bifunctional linker that maximizes delivery of a belotecan-derived topoisomerase I payload to tumor cells. In the phase 1/2 2870-001/KL264-01 study (NCT04152499), sac-TMT 5 mg/kg Q2W monotherapy had antitumor activity in participants (pts) with previously treated la/mUC, irrespective of TROP2. We present updated results of sac-TMT + pembro from the la/mUC cohort of the phase 2, multicohort 2870-002/SKB264-II-06 study (NCT05642780).

Methods

Eligible pts were cisplatin-ineligible and had previously untreated la/mUC. Prior (neo)adjuvant platinum-based therapy or nivolumab was permitted if pts had disease recurrence >12 mo after completion of therapy. Pts received IV sac-TMT 4 or 5 mg/kg on days 1, 15, and 29 + IV pembro 400 mg on day 1 of each 42-d cycle until PD or unacceptable toxicity. Primary endpoints were ORR per RECIST v1.1 and safety.

Results

As of November 17, 2025, 40 pts had received sac-TMT (4 mg/kg, n=26; 5 mg/kg, n=14) + pembro. Median study follow-up was 20.5 (range, 17.5–27.7) mo. Median age was 66.5y, 88% had ECOG PS ≤1, and 60% had upper tract UC. Confirmed ORR was 68%; responses were observed irrespective of TROP2 and PD-L1 (Table). Median (range) DOR was 19.4 (2.0–23.0+) mo. Median (95% CI) PFS was 11.2 (5.8–NR) mo. Median OS was NR. 24 pts (60%) had ≥1 grade 3/4 treatment-related AE; the most frequently occurring were anemia (15%), decreased neutrophil count (15%), and stomatitis (10%). No fatal treatment-related AEs occurred. Updated data will be presented.Table: 4739RO

	Sac-TMT + PembroN=40
Confirmed ORR	68 (51–81)
Confirmed ORR by TROP2 H-score[a]	
< median[b]	72[c] (47–90)
≥ median[b]	68[d] (43–87)
Confirmed ORR by PD-L1 status	
CPS < 10	72[e] (53–86)
CPS ≥ 10	50[f] (16–84)

Data are reported as % (95% CI). [a]Analyzed in pts with available TROP2 or PD-L1 IHC: [c]n = 18, [d]n = 19, [e]n = 32, [f]n = 8. [b]Median TROP2 H-score was 270.

Conclusions

Sac-TMT + pembro had promising antitumor activity, irrespective of TROP2 and PD-L1 expression, in cisplatin-ineligible pts with previously untreated la/mUC. Safety was manageable and consistent with that of each agent. These data form the basis for a planned global phase 3 study in UC.

Clinical trial identification

NCT05642780.

Editorial acknowledgement

Medical writing assistance was provided by Rachael Smith, PhD, of ICON plc (Blue Bell, PA, USA). This assistance was funded by Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Legal entity responsible for the study

Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., Chengdu, China.

Funding

Pharmaceutical, biotech, or other commercial company: Sponsored by Sichuan Kelun-Biotech Biopharmaceutical Co., Ltd., and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.

Disclosure

M. Edmondson: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc., Rahway, NJ, USA.. A. Lai: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc., Rahway, NJ, USA.. T. Keenan: Financial Interests, Personal, Full or part-time Employment: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA; Financial Interests, Personal, Stocks/Shares: Merck & Co., Inc., Rahway, NJ, USA.. Z. Mei: Financial Interests, Personal, Full or part-time Employment: Sichuan Biokin Pharmaceutical. Y. Zhou: Financial Interests, Personal, Full or part-time Employment: Sichuan Biokin Pharmaceutical. J. Ge: Financial Interests, Personal, Full or part-time Employment: Sichuan Biokin Pharmaceutical. All other authors have declared no conflicts of interest.

© European Society for Medical Oncology