Background In the JAVELIN Bladder 100 trial (NCT02603432), avelumab (anti–PD-L1) first-line (1L) maintenance + best supportive care (BSC) significantly prolonged overall survival (OS) and progression-free survival (PFS) vs BSC alone in patients with advanced urothelial carcinoma (UC) that had not progressed with 1L platinum-based chemotherapy. Results led to the approval of avelumab 1L maintenance therapy in various countries worldwide and inclusion in international treatment guidelines. We hypothesized that avelumab-based combinations may further improve outcomes in this setting. The JAVELIN Bladder Medley trial will investigate such combinations as 1L maintenance therapy for advanced UC.

Methods JAVELIN Bladder Medley (NCT05327530) is a phase 2, randomized, multicenter, open-label, parallel-arm, umbrella trial. Eligible patients aged ≥18 years should have unresectable locally advanced or metastatic UC that has not progressed after 4-6 cycles of 1L chemotherapy (gemcitabine + cisplatin or carboplatin) and ECOG PS 0-1. After 4-10 weeks from end of chemotherapy, 252 patients will be randomized 1:2:2:2 to avelumab 800 mg every 2 weeks as monotherapy (control) or combined with sacituzumab govitecan (anti-Trop2/topoisomerase inhibitor conjugate) 10 mg/kg on days 1 and 8 of 21-day cycles, M6223 (anti-TIGIT) 1600 mg every 2 weeks, or NKTR-255 (IL-15 agonist) 3 μg/kg every 4 weeks. Randomization is stratified by presence of visceral metastases at start of 1L chemotherapy. Treatment will continue until progression, unacceptable toxicity, withdrawal of consent, or initiation of a new anticancer treatment. Data from the control group may be extended by combining with external data from the avelumab arm of the JAVELIN Bladder 100 trial. Primary endpoints are PFS based on investigator assessment (RECIST 1.1) and safety/tolerability of the combination regimens. Secondary endpoints include OS, objective response and duration of response based on investigator assessment (RECIST 1.1), and pharmacokinetics. The trial opened in June 2022 with sites planned to recruit in the US, Europe, Asia, and Australia.

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Trial Registration NCT05327530 (ClinicalTrials.gov)