TPS4627 **Poster Session**

Intravesical sacituzumab tirumotecan in participants with intermediate-risk non–muscle-invasive bladder cancer: The phase 1/2 TroFuse-027 study.

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Background: Standard treatment for patients with intermediate-risk (IR) non–muscle-invasive bladder cancer (NMIBC) is transurethral resection of bladder tumor (TURBT) with or without adjuvant intravesical chemotherapy or bacillus Calmette-Guérin. However, 30% to 50% of patients experience disease recurrence, which leads to repeated endoscopic resections and intravesical therapies that contribute to patient morbidity and decreased urinary quality of life. Therefore, novel therapies with favorable efficacy and safety profiles are needed. Trophoblast cell-surface antigen 2 (TROP2) is a transmembrane glycoprotein expressed broadly in several tumors, including all stages of bladder cancer, making it a viable therapeutic target. Sacituzumab tirumotecan (sac-TMT; MK-2870) is an antibody-drug conjugate consisting of a humanized anti-TROP2 monoclonal antibody, a linker, and a cytotoxic belotecan-derivative topoisomerase I inhibitor. In *in vivo* mouse models, intravesical sac-TMT demonstrated antitumor activity, tolerability, and minimal systemic exposure. TroFuse-027 (NCT06637423) is a nonrandomized, open-label, phase 1/2 study designed to evaluate the safety and efficacy of intravesical sac-TMT as ablative therapy in participants with IR NMIBC.
Methods: Eligible participants are adults with prior history of pathologically confirmed low-grade Ta diagnosed with recurrence by visual inspection on cystoscopy who have not yet undergone TURBT and have urine cytology negative for high-grade urothelial carcinoma. In the phase 1 dose-escalation part, approximately 32 participants will be sequentially enrolled into 4 escalating sac-TMT dose groups using the Bayesian optimal interval design with a target dose-limiting toxicity rate of 30%; 3 to 14 participants are planned for each dose group. Sac-TMT will be administered by intravesical instillation weekly for 6 weeks unless there is unacceptable toxicity or withdrawal of consent. Disease assessments (per local urine cytology, cystoscopy, and biopsy as indicated for visible tumors) will occur at week 12 in all participants, then every 12 weeks for the first year and every 24 weeks thereafter for up to 2 years unless progression to high-grade NMIBC or muscle-invasive bladder cancer occurs. Participants with low-grade Ta that persists at week 12 or recurs anytime after that will undergo TURBT and remain in efficacy follow-up. The primary objectives are to evaluate safety and tolerability and to establish the recommended phase 2 dose. Secondary objectives are pharmacokinetics and complete response rate (the proportion of participants with the absence of visible tumors at the 12-week assessment after initiating treatment) and duration of complete response per local assessment. Future studies (phase 2) will be initiated on completion of dose escalation and based on the totality of data. Clinical trial information: NCT06637423. Research Sponsor: Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA.