TPS4622 **Poster Session**

Adjuvant sacituzumab govitecan (SG) plus nivolumab (N) in patients (pts) with muscle-invasive urothelial carcinoma (UC) at high-risk for recurrence.

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Background: Pts with muscle-invasive UC of the bladder or upper genitourinary tract who undergo radical cystectomy or nephroureterectomy are at high risk for cancer recurrence if residual pathologic advanced disease is identified at the time of surgery. Emerging data demonstrates that pts with minimal residual disease following curative-intent surgery, as detected by circulating tumor DNA (ctDNA), may be at a particularly high risk of UC recurrence. Adjuvant N has been approved post curative-intent surgery, with or without prior neoadjuvant chemotherapy (NAC), in pts with muscle-invasive UC at high risk of recurrence based on results of the CheckMate 274 study, which demonstrated a disease free survival (DFS) at 6 months of 74.9% with N versus 60.3% with placebo. SG is an antibody-drug conjugate with activity in UC. Evaluating intensification of adjuvant therapy in order to reduce the chance of metastasis development is of great interest. **Methods:** This is an IRB-approved, prospective, multi-center, single-arm phase 2 study of combination therapy with SG plus N. To be eligible, pts must have documented muscle-invasive UC, with variant and mixed histology allowed, except small cell. Pts must have undergone curative-intent surgery within 180 days prior to study therapy initiation and be radiographically free of metastasis. Pts who received prior NAC must have T2-T4 or node positive disease on surgical pathology, while those without NAC must have pathologic T3-T4 or node positive disease. Pts must also be ineligible or refuse platinum-based adjuvant chemotherapy. Additional selected eligibility criteria include creatinine clearance of at least 30 ml/min and adequate bone marrow function. If eligible for the study, pts will receive SG 7.5 mg/kg on day 1 and 8 combined with Nivolumab 360 mg on day 1 given every 21 days for 4 cycles, followed by single-agent Nivolumab 480 mg on day 1 given every 28 days for an additional 11 cycles. Use of growth factor support is allowed, as per institutional practice. Primary study endpoint is investigator-assessed DFS at 6 months. Secondary study endpoints include DFS, distant metastasis-free survival (MFS), overall survival (OS), incidence of grade 3 or higher adverse events, rate of ctDNA clearance in baseline ctDNA positive patients as well as exploratory biomarker analysis. The sample size calculation was based on a one-sided one sample test for exponential hazard rate when the probability of DFS at 6-months in the experimental group is 85% and in the historical control group is 75% in order to detect a hazard ratio of 0.565 with a power of 80% at a 0.05 significance level. Projected study accrual time is 24 months and per pt follow-up time is 36 months. Out of 23 anticipated pts, 3 have been enrolled to date since study activation in 11/2024. Clinical trial information: NCT06682728. Research Sponsor: None.