TPS4623 Poster Session

Neoadjuvant stereotactic radiotherapy and enfortumab vedotin: A phase I/II study for localized, cisplatin ineligible, muscle invasive bladder cancer (STAR-EV).

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Background: Patients with muscle invasive bladder cancer (MIBC) may not be candidates for cisplatin-based chemotherapy based on their comorbidities and clinical status. Based on EV-103 cohort H, patients with localized, cisplatin ineligible MIBC respond well to enfortumab vedotin (EV), with 36% pathologic complete responses (pCRs). Radiation (XRT) is also an effective therapy for MIBC, with recent retrospective data showing safety when combining XRT-EV. Therefore, we designed a trial with EV and XRT to improve pCR rates. **Methods:** STAR-EV is a single center, phase 1/2 trial open at UT Southwestern Medical Center. Patients will receive EV 1.25mg/m2 IV days 1/8 every 3 weeks for 3 cycles, with either sequential or concurrent stereotactic body XRT (SBRT) in 5 fractions. The safety lead-in phase starts with SBRT given at cycle 3 day 21 and then escalated forward to start at cycle 2 day 15 (level 1) or cycle 1 day 15 (level 2). All patients undergo radical cystectomy (RC). Dose limiting toxicities during the safety portion include non-hematologic adverse events grade 3 or higher, not completing 3 cycles of EV, delaying SBRT over 2 weeks, or delaying RC over 8 weeks. Rate of pCR is the primary endpoint for efficacy, with a goal of 60% pCR. In a Simon's two-stage design, if more than 3 pCRs are seen in the first 8 patients, 11 additional patients will be enrolled (total n = 19). The null hypothesis will be rejected if more than 10 pCRs are found. Main inclusion criteria include urothelial cancer of the bladder, cT2-4aN0M0, $>$ 50% urothelial histology, and cisplatin ineligible; main exclusion criteria include any small cell/neuroendocrine histology, prior systemic therapy for bladder cancer, prior pelvic XRT, baseline grade 2 or higher neuropathy, prior allergic reaction attributed to EV, or uncontrolled intercurrent illness. Secondary endpoints include safety of combining EV and SBRT, rate of pathologic down-staging; and exploratory objectives include quality of life, disease free survival after RC, and delay of RC $>$ 8 weeks from end of EV/SBRT. Serum and urinary biomarkers will be explored. The study is open and enrolling. Clinical trial information: NCT06394570. Research Sponsor: Astellas.