TPS2694 **Poster Session**

Trial in progress: A first-in-human (FIH) phase I study of PTX-912 in patients with locally advanced or metastatic solid tumors.

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Background: High-dose IL-2 (HD IL-2) received FDA approval for metastatic melanoma (mM) and metastatic renal cell carcinoma (mRCC), but its use is limited by severe systemic toxicities. While PD-1 blockade has improved overall survival in 20–30% of cancer patients, resistance remains a significant challenge. Notably, HD IL-2 has shown durable anti-tumor effects in mM and mRCC patients who have progressed on anti-PD-1 therapy. Moreover, combining IL-2 with pembrolizumab in mRCC demonstrated a durable response rate of 70%, compared to objective response rates (ORR) of 20% and 33% with IL-2 and pembrolizumab monotherapy, respectively (*Chatzkel et al., Clin Genitourin Cancer(2022)*). These findings suggest that combining IL-2 receptor (IL-2R) activation with PD-1 blockade may be a promising strategy to overcome PD-1 resistance and enhance clinical outcomes. PTX-912 is a novel, first-in-class bifunctional PD-1-proIL-2v fusion protein designed to synergize PD-1 blockade with PD-1-cis-directed IL-2R agonism specifically within the tumor microenvironment (TME), reducing systemic toxicities typically associated with high dose IL-2 therapy. **Methods:** This first-in-human (FIH), multicenter Phase I study (NCT06190886) evaluates the safety, tolerability, and preliminary efficacy of PTX-912 in patients with locally advanced or metastatic solid tumors who have had disease progression on all available standard of care and/or refused available standard of care therapies that would confer clinical benefit. Eligible patients must have measurable disease per RECIST v1.1 and may have received any number of prior therapies. Key exclusions include immunodeficiency, unresolved toxicities > Grade 1 per NCI CTCAE from prior therapy, active autoimmune disease, primary CNS or leptomeningeal involvement, history of transplant, recent major surgery, and significant cardiac or pulmonary dysfunction. The study includes dose escalation (Part 1a) and dose expansion (Part 1b) cohorts. In Part 1a, seven dose levels (DL1–7) will be tested, with DL1–3 following an accelerated titration design and DL4–7 using a standard 3+3 design. The primary objectives are to determine the maximum tolerated dose (MTD), optimal biological dose (OBD), and/or the recommended Phase II dose (RP2D) of PTX-912, assessed via dose-limiting toxicities (DLTs). Patients with melanoma, renal cell carcinoma (RCC), non-small cell lung cancer (NSCLC), or other populations identified based on Part 1a data will be enrolled in Part 1b. In Part 1a, patients will receive intravenous infusions of PTX-912 every two weeks (Q2W), followed by subsequent cycles with a 28-day DLT observation period. Study enrollment began in June 2024 in the United States at 3 centers. Cohorts 1 to 4 (6 patients) have been completed without DLT. Enrollment to cohort 5 is currently ongoing. Clinical trial information: NCT06190886. Research Sponsor: Proviva Therapeutics.