TPS2685 **Poster Session**

A phase 1, first-in-human study of CTIM-76, a claudin-6 (CLDN6)-directed bispecific antibody, in patients with recurrent ovarian cancer and other advanced solid tumors.

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Background: CLDN6 is an oncofetal protein expressed at high levels in many solid tumors while expressed at very low levels in adult normal tissues. The high target antigen density and slow rate of internalization makes it an attractive target in cancer therapeutics. CTIM-76, a CLDN6 x CD3 T cell engager bispecific antibody is engineered to bind with high selectivity to CLDN6 and redirect the immune system's T cells to recognize and kill CLDN6-expressing cancer cells. CTIM-76 effectively inhibited tumor growth, inducing complete responses in ovarian cancer xenograft models. The first in human study of CTIM-76 in patients with advanced ovarian, endometrial, and testicular cancers (NCT06515613) is described here. **Methods:** Part 1 dose escalation exploring 9 ascending dose levels with a 3+3 design. The first two dose levels are single patient cohorts (22.5 μg starting dose), CTIM-76 delivered as weekly iv infusions, with step dosing and steroid premedication to minimize cytokine release syndrome. Approximately 40 patients with platinum resistant ovarian cancer, or endometrial or testicular cancers relapsed after standard of care will be enrolled. Tumors from patients with ovarian or endometrial cancer require prospective CLDN6 + confirmation by IHC (10% $\geq$ 1+), testicular cancer patients will not require prospective screening due to the known uniformly high prevalence of CLDN6. The primary objective is to evaluate safety and tolerability (incidence and severity of adverse events per NCI CTCAE v5.0) and establish the recommended dose for expansion. Secondary objectives include assessment of antitumor activity (RECIST v1.1, iRECIST), pharmacokinetics, and pharmacodynamic correlates of immune activation. Part 2 will evaluate two doses in approximately 30 patients with one tumor type, with efficacy and further safety as primary objectives. This multicenter study has currently five sites open for enrollment. The first patient was dosed in January 2025. Clinical trial information: NCT06515613. Research Sponsor: None.