TPS5630 **Poster Session**

SynKIR-CAR T cell advanced research (STAR)-101 phase 1 clinical trial for patients with advanced mesothelin-expressing ovarian cancer, mesothelioma, or cholangiocarcinoma.

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Background: Chimeric antigen receptor (CAR) T cells have transformed treatment of hematologic malignancy but have shown limited efficacy in solid tumors due to T cell exhaustion and lack of functional persistence. Second-generation CAR T cells targeting mesothelin via the SS1 scFv demonstrate safety and early tumor reduction but lack durable clinical benefit (1-3). SynKIR-110, a novel natural killer cell-signaling based CAR T therapy, employs a multichain signaling system designed to reduce exhaustion by activating T cells only upon tumor engagement. In vitro, SynKIR-110 matches CD3-based CAR T cells in cytokine production and tumor lysis, and in conventional CAR T-cell-resistant mesothelioma mouse xenograft models, SynKIR-110 eliminates tumors without observed toxicity (4). **Methods:** This first-in-human, Phase 1, multicenter, open-label, dose-escalation study evaluates the safety and feasibility of SynKIR-110 in patients with advanced mesothelin-expressing tumors, including ovarian cancer, cholangiocarcinoma, and mesothelioma. Participants receive non-myeloablative lymphodepletion with cyclophosphamide and fludarabine, followed by a single intravenous infusion of SynKIR-110. Up to six dose cohorts (3+3 design) will establish the maximum tolerated dose (MTD) or maximum feasible dose (MFD), with an expansion cohort at the recommended phase 2 dose to confirm safety and assess activity. Participants are followed for 12 months to evaluate best overall response, survival, drug persistence, immune function and potential correlation with pre-treatment tumor mesothelin levels, through exploratory analyses. Eligible patients must have recurrent or relapsed ovarian cancer, cholangiocarcinoma, or epithelial pleural or peritoneal mesothelioma after at least one prior systemic therapy. Additional eligibility criteria include measurable disease by iRECIST or mRECIST, ECOG performance status of 0-1, and adequate organ and bone marrow function. Cohort 1 completed without dose-limiting toxicities (DLTs). Enrollment in Cohort 2 initiated in 2025 and is ongoing. SynKIR-110 represents a promising approach to overcoming the limitations of CAR T cells in solid tumors. 1. Beatty GL et al. *Cancer Immunol Res*. 2014 Feb;2(2):112-20. PMID: 24579088. 2. Haas AR et al. *Mol Ther*. 2019 Nov 6;27(11):1919-1929. PMID: 31420241. 3. Beatty GL et al. *Gastroenterology*. 2018 Jul; 155(1):29-32. PMID: 29567081. 4. Wang E et al. *Cancer Immunol Res.* 2015 Jul;3(7):815-26. PMID: 25941351. Clinical trial information: NCT05568680. Research Sponsor: Verismo Therapeutics.