TPS2679 **Poster Session**

Safety and efficacy of HLA-G–targeted CAR T cells (IVS-3001) in patients with advanced HLA-G–positive solid tumors: Clinical trial in progress.

Samer Ali Srour, Nizar M. Tannir, Amir A. Jazaeri, Matthew T. Campbell, Yago Nieto, Cara L Haymaker, Ying Yuan, Israa Salih, Yali Yang, Valérie Doppler, Julie Garibal, Marie Escande, Qi Melissa Yang, Jake Kushner, Jane Koo, Serdar A Gurses, David S. Hong, Siqing Fu, Funda Meric-Bernstam, Aung Naing; The University of Texas MD Anderson Cancer Center, Houston, TX; INVECTYS SA, Paris, France; CTMC, Houston, TX

Background: Immunotherapies have transformed cancer treatment, yet only a small proportion of patients experiences durable responses. IVS-3001 is an innovative autologous chimeric antigen receptor (CAR) T-cell therapy specifically targeting Human Leukocyte Antigen (HLA-G). HLA-G is an immune-modulatory checkpoint molecule expressed on various solid tumors, positioning it as an ideal a tumor-specific targeted antigen. Our third-generation CAR construct features enhanced T cell activation and persistence against HLA-G. By harnessing IVS-3001 to target HLA-G and revitalize immune cells, we aim to overcome the suppressive tumor microenvironment and improve antitumor activity, potentially leading to better outcomes for patients with advanced solid tumors who otherwise have no standard options known to confer clinical benefit. **Methods:** Study NCT05672459 is a First-in-Human, phase 1/2a, safety and efficacy study of IVS-3001 in subjects with previously treated advanced HLA-G-positive solid tumors. Phase 1 ($n \leq 24$ patients) is a Bayesian Optimal Interval Design (BOIN) with primary objective to determine the safety, tolerability and the recommended phase 2 dose. The primary objective for phase 2 ($n \leq 90$ patients) is to evaluate the anti-tumor activity of IVS-3001. The secondary objectives of the study are to evaluate i) pharmacokinetic profile of IVS-3001 (persistence, expansion); ii) the clinical activity of IVS-3001 in selected HLA-G+ solid tumor types; iii) assess the long-term safety of IVS-3001. Exploratory endpoints include functionality of CAR-T cells, immune biomarker changes, and relationships with clinical response. Key inclusion criteria: adults with advanced solid tumors expressing HLA-G; ECOG < 2; adequate organ function. Key exclusion criteria: uncontrolled brain metastasis; prior exposure to HLA-G targeted therapy. Subjects undergo lymphodepletion with fludarabine and cyclophosphamide on days -5 to -3, followed by CAR-T cell infusion on day 0 and a 28-day monitoring period for dose limiting toxicity. Response assessment per RECIST criteria. Study is currently accruing at Dose level 3. Active recruitment and enrollment are ongoing at The University of Texas MD Anderson Cancer Center, Houston, Texas. Clinical trial information: NCT05672459. Research Sponsor: Invectys; National Cancer Institute.