TPS2676 **Poster Session**

A phase 1, first-in-human study of IB-T101, an OUTLAST CAR-T product for the treatment of CD70-positive clear cell renal carcinoma.

Matthias Schroff, Bo Liu, Warren Anderson, Mathew Esquivel, Adam Pecoraro, Kate Fagan-Solis, Yuning Lei, Jun Cui, Yarong Liu, Kevin Carbajal, Maximilian Richter; Inceptor Bio, Morrisville, NC; Tongji Hospital, Tongji Medical College, Huazhong University of Science & Technology, Wuhan, China; Grit Biotechnology, Shanghai, China

Background: Relapsed or treatment-resistant clear cell renal cell carcinoma (ccRCC) poses a significant, unmet medical challenge, as patients contend with scarce therapeutic alternatives and unfavorable clinical prognoses. CD70 is expressed in the majority of ccRCC and presents an attractive target for chimeric antigen receptor T cell (CAR-T) therapy. IB-T101, an autologous CAR-T expanded under OUTLAST conditioning, targets CD70 for the treatment of ccRCC. OUTLAST conditioning has been demonstrated to result in CAR-T cells that exhibit an early memory T cell phenotype, are resistant to suppressive signals from the tumor microenvironment, and exhibit increased persistence. The effects of OUTLAST conditioning are expected to lead to superior clinical outcomes for IB-T101 CAR-T cells in the ccRCC solid tumor setting.
Methods: Here we report an in-progress phase 1, first-in-human, open label, investigator-initiated clinical trial aimed at evaluating the safety and efficacy of IB-T101 in ccRCC. Patients eligible for inclusion had previously relapsed following VEGF targeting therapies alone or in combination with an immune checkpoint inhibitor. Autologous patient T cells are transduced with a lentiviral vector encoding a CD70-targeting CAR and are CRISPR Cas9 gene edited to knock out endogenous CD70, followed by expansion under OUTLAST conditioning. Escalating doses of IB-T101 CAR-T cells ($150 - 500 \times 10^6$) will be infused following lymphodepletion. Primary endpoints of the study will assess the safety and tolerability of IB-T101. Additional objectives of the study are to assess the anti-tumor activity and the pharmacokinetics of IB-T101. Correlative assessments will include pre-treatment biopsies to assess the level of CD70 expression in the tumor. Research Sponsor: None.