TPS4613 Poster Session

A phase 1/2 first in human study of ADI-270, an armored allogeneic anti-CD70 chimeric antigen receptor γδ T cell therapy, in relapsed or refractory (R/R) clear cell renal cell carcinoma (ccRCC).

Sumanta Kumar Pal, Benjamin Garmezy, Helen Budworth, Xiaoyan Du, Shon Green, Kevin Nishimoto, Jackie Kennedy-Wilde, Blake T. Aftab, Julia D. Maltzman, Gregory Sumpao Vosganian, Brian I. Rini; Department of Medical Oncology, City of Hope Comprehensive Cancer Center, Duarte, CA; Sarah Cannon Research Institute, Nashville, TN; Adicet Bio, Redwood City, CA; Department of Medicine, Vanderbilt University Medical Center, Nashville, TN

Background: CD70 is a type II transmembrane protein of the tumor necrosis factor superfamily normally transiently expressed in activated lymphocytes, including B, T, NK, and mature dendritic cells. CD70 is aberrantly expressed in solid and hematologic cancers and is implicated in enhanced growth, metastasis, immune evasion, and suppression. In ccRCC, CD70 expression is increased in the tumor microenvironment and on malignant cells. Despite advancements in the treatment of patients with metastatic RCC, the 5-year survival rate is 15% and there remains an unmet need. ADI-270 is an investigational, allogeneic, CD70-targeting (CD27 receptor-based) Vδ1 γδ chimeric antigen receptor (CAR) T cell product expressing a dominant negative form of the TGFβ receptor II (dnTGFβRII) to mitigate the immunosuppressive effects of TGFβ within the tumor microenvironment. γδ T cells possess innate and adaptive immunity, a natural role in immune surveillance, and the ability to home to tissues. γδ T cells are ideal for an allogeneic cell therapy as their TCR recognizes MHC-independent antigens, thereby avoiding the risk of graft versus host disease. ADI-270 has demonstrated potent preclinical activity against CD70 expressing hematological and solid tumors expressing a range of CD70 levels both in vitro and in mouse xenograft models. Furthermore, ADI-270 demonstrated superior activity against tumors expressing low levels of CD70 when compared to scFv-based αβ CAR T cell benchmarks currently in clinical development. **Methods:** ADI-202427001 (NCT06480565) is a multi-center, phase 1 / 2 open-label, dose-escalation and -expansion study evaluating ADI-270 in adult patients with R/R ccRCC. Selected inclusion criteria include confirmed diagnosis of R/R advanced/metastatic ccRCC, previous treatment with an immune checkpoint inhibitor and a VEGF inhibitor, and Karnofsky performance status ≥ 70. Selection exclusion criteria include receipt of CD70 targeting treatment and autoimmune disease requiring systemic immunosuppressive therapy. Objectives of phase 1 include characterizing the safety and tolerability of ADI-270, identifying the recommended phase 2 dose (RP2D), and assessing cellular kinetics (CK), immunogenicity, pharmacodynamics (PD), and anti-tumor activity. Objectives of phase 2 include characterizing the anti-tumor activity, safety, immunogenicity, CK, and PD profile of ADI-270 at the RP2D. The totality of data from Phase 1 will be used to determine the RP2D for the Phase 2 part of the study. Responses will be evaluated per the RECIST 1.1 criteria. Additional efficacy analyses include duration of response, progression-free survival, and overall survival. Enrollment in study ADI-202427001 is ongoing. Clinical trial information: NCT06480565. Research Sponsor: AdicetBio, Inc.