TPS2680 Poster Session

QUILT 3.076 phase 1 study of memory-like cytokine-enriched natural killer (M-CENK) cells plus N-803 in locally advanced or metastatic solid tumors.

Chaitali Singh Nangia, Tara Elisabeth Seery, Katayoun Moini, Rebecca Blanton, Kathleen Adlard, Azita Nourani, Patricia Spilman, Paul Bhar, Hui Zhang, Leonard S. Sender, Sandeep Bobby Reddy, Patrick Soon-Shiong; Chan Soon-Shiong Institute for Medicine, El Segundo, CA; ImmunityBio, Inc., San Diego, CA; ImmunityBio, Inc., Culver City, CA; ImmunityBio, Inc., Morrisville, NC; ImmunityBio, Culver City, CA; ImmunityBio, Inc., El Segundo, CA; ImmunityBio, Inc, Culver City, CA

Background: Lymphopenia and low levels of natural killer (NK) cells may contribute to poor prognosis and response to therapy in cancer patients, conditions that may be addressed by infusion of memory-like cytokine-enriched NK (M-CENK) cells stimulated ex vivo by IL-12, IL-18, and the IL-15 agonist N-803 (ANKTIVA). M-CENK cells express elevated IFN-γ and granzyme B compared to healthy donor NK cells, and display toxicity against multiple tumor cell lines including SCLC lines [Fousek 2023 JITC 11 ab358]. The phase 1 study QUILT-3.076 (NCT04898543) assesses the safety and preliminary efficacy of M-CENK cells plus N-803 in participants with locally advanced or metastatic solid tumors. **Methods:** In this first-in-human study, cohort 1 (up to n = 40) includes participants with newly diagnosed solid tumors who have not received prior 1st line treatment; cohort 2 (up to n = 21) includes participants with relapsed/refractory solid tumors who progressed after $\geq$ 2 prior therapies. Both cohorts undergo apheresis (part A), but only cohort 2 undergoes treatment with M-CENK cells and N-803 (part B). During M-CENK cell generation, cohort 2B participants receive oncologist-recommended therapy. Cohort 1 participants may subsequently enroll in cohort 2B if they have progressive disease (PD) after $\geq$ 2 prior therapies or within 12 months of receiving neoadjuvant/adjuvant chemotherapy. In part B, M-CENK cells are administered weekly up to 10 times and N-803 SC for up to 5 doses every 2 weeks prior to every other dose of M-CENK cells. Key inclusion criteria are age $\geq$ 18 years, ECOG performance status of 0 to 2, and histologically confirmed locally advanced or metastatic solid tumor, with at least 1 measurable lesion and/or non-measurable disease in accordance with RECIST v1.1. There are no exclusion criteria for part A (apheresis). Key exclusion criteria for part B are life expectancy $<$ 16 weeks, involuntary weight loss of $>$ 10%, serious uncontrolled concomitant disease, systemic autoimmune disease requiring medical treatment, and/or currently receiving or received antibiotics since enrollment. The primary objective is safety as assessed and recorded by TEAEs, SAEs, and clinically significant changes in laboratory tests and vital signs. Toxicities are graded using CTCAE v5.0 or a specified grading system for CRS. Secondary measures evaluate the quantity and quality of the investigational M-CENK cells (number of MNCs for manufacturing M-CENK cells, number of cryopreserved M-CENK aliquots, % NK cells, and number, phenotype, and function of M-CENK cells). Preliminary efficacy objectives in cohort 2B are objective response rate (RECIST v1.1 and iRECIST criteria) and progression-free and overall survival evaluated using Kaplan-Meier methods. As of January 27, 2025, 15 participants have been enrolled in cohort 1, 21 participants in cohort 2 have undergone apheresis, and 10 participants have been treated with study therapies. Clinical trial information: NCT04898543. Research Sponsor: ImmunityBio, Inc.