

Clinical Trials in Progress

951

A PHASE 1 FIRST IN HUMAN STUDY OF ADENOVIRALLY TRANSDUCED ANTI-HER2 CAR MACROPHAGES IN SUBJECTS WITH HER2 OVEREXPRESSING SOLID TUMORS: PRELIMINARY SAFETY, PHARMACOKINETICS, AND TME REPROGRAMMING DATA

¹Kim Reiss*, ²Yuan Yuan, ³Debra Barton, ³Amy Ronczka, ³Daniel Cushing, ³Michael Klichinsky, ³Sascha Abramson, ³Rehman Qureshi, ³Thomas Condamine, ⁴Elizabeth Dees. ¹University of Pennsylvania, Philadelphia, PA, USA; ²City of Hope Comprehensive Cancer Center, Duarte, CA, USA; ³Carisma Therapeutics, Springfield, NJ, USA; ⁴UNC, Chapel Hill, NC, USA

Background CT-0508 is an autologous monocyte-derived pro-inflammatory macrophage cell product engineered with Ad5f35 to express an anti-HER2 CAR. In pre-clinical studies CT-0508 was safe and effective. This abstract contains preliminary results from the first-in-human experience with CAR macrophages (CAR-M).

Methods This First-In-Human Phase 1, multi-center, open-label study is evaluating the safety, tolerability, manufacturing feasibility, pharmacokinetics and mechanism of action of CT-0508 in 18 subjects with advanced solid tumors overexpressing HER2 who have progressed on prior therapies, including HER2 targeted therapies if indicated.

Patients receive four doses of filgrastim for monocyte mobilization prior to apheresis. CT-0508 CAR-M is manufactured from autologous apheresis products and delivered as a cryopreserved cell product. Group 1 subjects enter an intra-patient fractionated dose escalation regimen, receiving CT-0508 on D1, D3 and D5, followed by Group 2 subjects who receive CT-0508 on D1. There is no preparative chemotherapy prior to CT-0508 infusion.

Pre and post treatment biopsies and blood samples are collected to investigate correlates of safety, serum cytokines and chemokines, pharmacokinetics, TME modulation, and induction of an adaptive anti-tumor immune response.

Results To date, two subjects have been treated with CT-0508 (esophageal adenocarcinoma and extrahepatic cholangiocarcinoma). Patient product was successfully manufactured, CT-0508 treatment was well tolerated, with no dose limiting and no major organ toxicities observed.

One subject experienced Grade 2 CRS on Day 3 which resolved on the same day.

Grade 3 AEs included anemia (present at baseline for both subjects) and lymphopenia (present at baseline in one subject). One subject experienced one SAE of Grade 4 tumor bleeding which was unrelated to CT-0508, 88 days after the last infusion.

CAR-M were transiently detected in the peripheral blood following each infusion, demonstrating rapid egress from the periphery into tissues within hours. Transient cytokine/chemokine elevations were observed (peak: 2 hours, back to baseline at 48 hours). Single cell RNAseq analysis of dissociated tumor tissue samples (pre-treatment, day 8 and week 4) demonstrated dynamic TME reprogramming, with recruitment of inflammatory innate immune cells and naïve T cells at day 8, and significant CD8+ T cell infiltration, activation, and proliferation at week 4.

Conclusions CT-0508 has been administered to two subjects thus far, exhibiting safety, good tolerability, T cell repertoire modulation, and reprogramming of the TME consistent with

the induction of anti-tumor immunity. The study continues to recruit patients and updated data will be presented.

Trial Registration NCT04660929

REFERENCE

1. Klichinsky M, Ruella M, Shestova O, *et al.* Human chimeric antigen receptor macrophages for cancer immunotherapy. *Nat Biotechnol* 2020;**38**(8):947–953.

Ethics Approval Ethics approvals have been obtained from the clinical sites enrolling patients: the University of Pennsylvania (844106/IORG0000029), the University of North Carolina and City of Hope Comprehensive Cancer Center (20201732/IORG0000432).

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.951>