Background In pre-clinical studies, CAR macrophages (CAR-M) phagocytose tumor cells, activate the tumor micro-environment (TME), recruit T cells, and induce anti-tumor T cell immunity. CT-0508 is a first-in-class CAR-M product comprised of autologous monocyte-derived macrophages expressing an anti-HER2 CAR. Here we present preliminary clinical results from the CT-0508 Phase 1 FIH study.

Methods This multi-center, open-label study is evaluating CT-0508’s safety, tolerability, and manufacturing feasibility in 18 participants with advanced solid tumors overexpressing HER2 with progression on prior therapies. Monocytes are isolated from mobilized apheresis products, differentiated into macrophages, and engineered with an anti-HER2 CAR. Group 1 participants (n = 9) receive a fractionated dose on days 1, 3, 5 and Group 2 participants (n = 9) receive the full dose on day 1. CT-0508 is administered without preparative chemotherapy. Serial blood samples and biopsies (baseline and 2 post-treatment) are collected to investigate safety, pharmacokinetics, and mechanism of action.

Results Nine participants (6F/3M) have been treated, comprising breast (4), esophageal (2), cholangiocarcinoma, ovarian, and parotid gland cancers, with a median age of 58. Participants had received a median of 3 (range, 2-11) prior lines of therapy; 8 had received prior anti-HER2 therapy. CT-0508 was successfully manufactured and well tolerated with no dose-limiting toxicities. Three related SAEs occurred in 2 participants: grade 1 CRS with hospitalization for monitoring and grade 2 infusion reaction that resolved within 1 hour were reported in one participant. Grade 2 CRS with fever and hypoxia occurred in another participant and resolved within ~ 72 hours. Five additional participants experienced Grade 1-2 CRS and/or infusion reactions with rapid resolution. There were no major organ toxicities and no on-target off-tumor toxicities. Post-infusion cytokines were transiently elevated in most participants enrolled in group 1 and were self-limiting. Four of 7 participants enrolled had stable disease. CT-0508 was transiently detectable in the blood and was detected in the TME 8 days and 4 weeks after infusion. CT-0508 modulated the TME, leading to myeloid cell activation, T cell infiltration, activation, and proliferation. TCR sequencing demonstrated newly expanding T cell clones in the blood post-treatment that accumulated within the TME, suggesting expansion of tumor-reactive T cells upon CT-0508 infusion. Data from participants enrolled in group 1 will be presented.

Conclusions CT-0508 was safe and feasible to manufacture. Early correlative data demonstrate trafficking, TME modulation, and induction of anti-tumor T cell immunity. The study is actively enrolling.

Trial Registration NCT04660929

REFERENCE