A PHASE I/II TRIAL INVESTIGATING SAFETY AND EFFICACY OF AUTOLOGOUS TAC01-HER2 IN RELAPSED OR REFRACTORY SOLID TUMORS

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Background Despite therapeutic developments for patients with advanced HER2+ solid tumors, significant unmet medical needs still exist. The T cell antigen coupler (TAC) technology is an approach to modifying T cells ex vivo, which allows recognition and cytotoxicity of tumor cells by co-opting the natural T cell receptor. TAC T cells demonstrate a safer profile than chimeric antigen receptor T cells. TAC01-HER2 is an autologous T-cell product comprising T cells expressing HER2 TAC.

Methods The ongoing clinical trial (NCT04727151) is evaluating the safety and preliminary anti-tumor activity of TAC01-HER2 treatment of HER2+ solid tumors. Subjects undergo leukapheresis followed by low-intensity lymphodepletion chemotherapy prior to TAC01-HER2 infusion.

In phase I dose escalation, TAC01-HER2 is administered at increasing doses (Cohorts 1–4) in adult subjects after ≥2 lines of therapy. Dose limiting toxicities (DLT) are assessed up to 28 days from TAC01-HER2 infusion.

In Phase II, dose expansion groups will further evaluate the efficacy, safety, and pharmacokinetics of the optimal TAC01-HER2 dose in gastric/GEJ tumors.

Results As of 5 June 2023, 20 patients with solid tumors have been treated in Cohorts 1–4. Three were HER2 1+ or 2+/FISH-. One DLT event of grade (G) 3 pneumonitis has been reported in 1 subject in Cohort 4. No neurotoxicity has been reported. Most subjects treated at Cohorts 3–4 experienced cytokine release syndrome (CRS) which resolved with supportive therapy. Thirteen subjects have reported a total of 26 serious adverse events, with 1 G3 pneumonitis, 4 CRS (1 G1, 3 G2 and 1 G3) and 1 G3 bronchial hyperreactivity related to TAC01-HER2.

A 67% disease control rate (DCR) was observed in Cohorts 2–4 at first restaging after TAC01-HER2 infusion. For gastric/GEJ subjects of the same Cohorts, DCR was 83%. 3 months after TAC01-HER2 infusion, DCR was 33.3% for all subjects of Cohorts 2–4 and 50% for gastric/GEJ subjects. Two patients had a partial response (PR). At Cohort 4, a PR was observed in a subject with GEJ (HER2 2+, FISH+) with 100% reduction of target lesion. This patient had progressed on 4 prior lines of therapy including trastuzumab and trastuzumab deruxtecan.

Conclusions Treatment with TAC01-HER2 showed manageable safety and promising clinical activity in a heavily pre-treated cancer population. The recommended phase 2 dose was identified as dose level 4 (6–8 x 10^6 cells/kg).

Trial Registration www.clinicaltrials.gov, NCT04727151

Ethics Approval This study obtained ethics approval from the following IRBs:

- University of Chicago, #IRB20-1944-AM005
- Dana Farber Cancer Institute, #21-062

All participants gave informed consent before participating in this study.

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