REPEATED DOSING OF ANTI-CLAUDIN 18.2 CAR-T IN METASTATIC GASTROINTESTINAL CANCER

1Dan Zhao*, 1Amanda Olson, 1Mariela Blum Murphy, 1So Jung Hong, 2Hong Ma, 2Zonghai Li, 2Raffaele Baffa. 1The University of Texas MD Anderson Cancer Center; Houston, TX, USA; 2CARsgen Therapeutics, Houston, TX, USA

Background Cellular therapy for the treatment of solid tumors is challenging. In this study we proposed repeat dosing to overcome the resistance and improve the response rate. Claudin 18.2 (CLDN18.2) is a tight junction protein overexpressed in gastric cancer and other cancers. Anti-claudin 18.2 CAR-T cell product (CT041) is under development in global clinical trials. Here we report a gastric cancer patient who received repeated infusions of anti-Claudin 18.2 CAR-T cells (NCT04404595).

Methods CLDN18.2 positive patients were selected and underwent apheresis for CAR-T manufacturing. Patients received a pre-conditioning regimen of fludarabine, cyclophosphamide, and 100mg/m² nab-paclitaxel before CT041 CAR-T infusion. Safety, efficacy, and cellular kinetic profile of CT041 were evaluated. Adverse Events (AEs) were graded per CTCAE 5.0. Cytokine release syndrome (CRS) and Immune Effector Cell Associated Neurotoxicity (ICANS) were scored and managed per American Society for Transplantation and Cellular Therapy (ASTCT) and Immune Effector Cell Therapy Toxicity Assessment and Management (CARTOX). Tumor response was assessed per RECIST 1.1.

Results A 57-year-old man with metastatic gastric cancer to the liver (HER2 negative, PD-L1 CPS 10%) progressed after 5 cycles of FOLFOX+Nivolumab and 4 cycles of FOLFIRI/Ramucirumab. After the patient was tested positive for CLDN18.2, he was treated with 6×10^8 CT041 cells after pre-conditioning chemotherapy. The patient experienced G1 CRS with fever, which was resolved after one dose of tocilizumab. His monthly CT scan showed a decreased tumor at -19.2%, -24.4%, -26.9%. Three months after the first infusion, he received the second dose of 6×10^8 CT041 cells. Again, he had G1 CRS with fever, which was resolved without tocilizumab. Monthly CT scan after the second infusion reported continued decreasing tumor from the baseline -34.6%, and -41.0% (5 months after the 1st infusion). To date, 14 patients in the US have received a second infusion and 3 patients have received a third infusion on the trial. Data analysis is underway.

Conclusions Repeated dosing of anti-claudin 18.2 CAR-T cells (CT041) was safe and deepened tumor response was observed after repeated dosing.

Acknowledgements We appreciate the patients and their family members who supported this trial.

We thank the MD Anderson pharmacy team and research team.

Trial Registration https://classic.clinicaltrials.gov/ct2/show/NCT04404595

Ethics Approval This study is approved by MD Anderson cancer center IRB #021–0602. Patients were consented.

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0659