Background Solid tumors comprise >90% of cancers. Non-small cell lung cancer (NSCLC), metastatic colorectal cancer (CRC), and pancreatic cancer are the leading causes of cancer-related mortality (5-year overall survival: 26%, 15%, and 11%, respectively).1

Chimeric antigen receptor (CAR) T-cell therapy has demonstrated clinical efficacy in hematologic malignancies.2,3 However, translating engineered T-cell therapies to solid tumors has proven to be challenging due to a lack of tumor-specific targets that can discriminate cancer cells from normal cells. Previous studies using carcinomaembryonic antigen (CEA) T-cell receptors and mesothelin (MSLN) CARs resulted in dose-limiting on-target, off-tumor toxicities.4,5

To create a therapeutic safety window, Tmod CAR T-cell therapy utilizes dual-signaling receptors to create a robust logic gate capable of killing tumor cells, while leaving healthy cells intact.6,7

The 2 receptors in Tmod CAR T-cell therapy comprise an activator that recognizes an antigen on the surface of tumor cells that may also be present on normal cells, such as CEA and MSLN, and a blocker that recognizes a second surface antigen from an allele lost only in tumor cells (figure 1).8,9

Human leukocyte antigen (HLA) loss of heterozygosity (LOH) offers a definitive tumor versus normal discriminator target for CAR T-cell therapy.10 The frequency of HLA LOH among advanced NSCLC, CRC, and pancreatic cancers in the Tempus real-world dataset is 16.3% with a range of 15.6%-23.1%.11 LOH can be reliably detected using the Tempus XT-Onco next-generation sequencing (NGS) assay.12,13 Different activator/blocker combinations can be engineered with the Tmod platform technology and may be applied to T cells and natural killer cells in autologous and allogeneic settings.

BASECAMP-1 is a currently enrolling observational study with key objectives: 1) To identify patients with somatic HLA LOH eligible for Tmod CAR T-cell therapy, and 2) Subsequent apheresis and manufacturing feasibility for the future EVEREST CEA or MSLN Tmod CAR T-cell studies.

Methods BASECAMP-1 (NCT04987119) patient eligibility has 2 parts (figure 2): 1) Patients will be initially screened to identify germline HLA-A*02 heterozygosity by central NGS. If HLA-A*02 heterozygosity is confirmed, primary archival tumor tissue will be analyzed for somatic mutations by xT-Onco NGS testing; 2) If the tumor demonstrates HLA-A*02:01 LOH and the patient is eligible after screening, the patient will undergo apheresis. Banked T cells will be available for the autologous EVEREST Tmod CAR T-cell therapy interventional study to reduce waiting time at relapse.

Trial Registration ClinicalTrials.gov, NCT04987119

REFERENCES

Ethics Approval The study was approved by site IRBs

Abstract 639 Figure 1

![Abstract 639 Figure 1](http://dx.doi.org/10.1136/jitc-2022-SITC2022.0639)