491 **BASECAMP-1: AN OBSERVATIONAL STUDY TO IDENTIFY RELAPSED SOLID TUMOR PATIENTS WITH HUMAN LEUKOCYTE ANTIGEN (HLA) LOSS OF HETEROZYGOSITY (LOH) AND LEUKAPHERESIS FOR FUTURE CAR T-CELL THERAPY**

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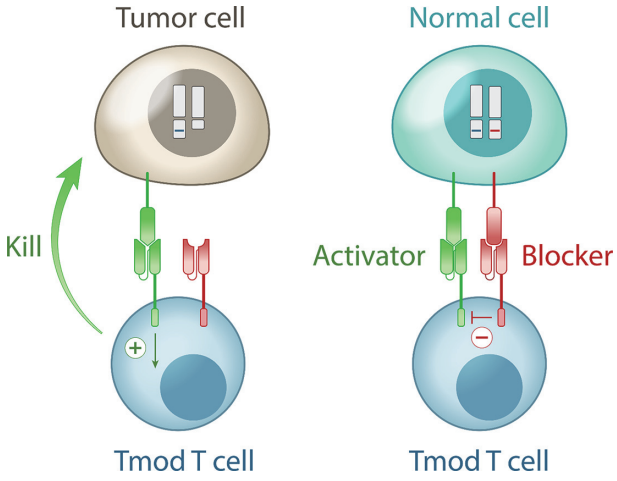
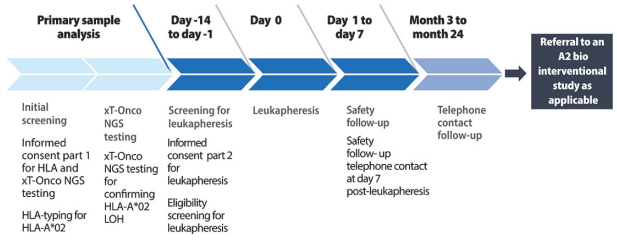
Background Solid tumors comprise >90% of cancers. Metastatic colorectal cancer, non-small cell lung cancer, and pancreatic cancer are among the leading causes of cancer-related mortality (5-year overall survival: 14%, 6%, and 3%, respectively).[1]Chimeric antigen receptor (CAR) T-cell therapy demonstrated clinical outcomes in hematologic malignancies.[2 3] However, translating engineered T-cell therapies to solid tumors proves difficult due to a lack of tumor-specific targets that discriminate cancer cells from normal cells. In previous studies, the use of a carcinoembryonic antigen T-cell receptors and mesothelin CARs both resulted in dose-limiting on-target, off-tumor toxicities.[4 5] Tmod™ CAR T-cell therapy addresses these challenges by leveraging dual receptors to create a robust AND NOT signal integrator capable of killing tumor cells, while leaving healthy cells intact (figure 1).[6] Tmod platform technology is a versatile system that may be applied to T cells and natural killer cells in autologous and allogeneic settings.HLA LOH offers a definitive tumor versus normal discriminator target for CAR T-cell therapy.[6 7] The 2 receptors comprise an activator that recognizes an antigen present on the surface of normal and tumor cells and a blocker that recognizes a second surface antigen from an allele lost only in tumor cells. HLA LOH has been observed in ~13% across all solid tumors and up to 33% of pancreatic cancers.[8] New technologies have shown higher HLA LOH rates; however, it is unclear whether patients with HLA LOH in their primary tumor tissues are at higher risk for recurrence. BASECAMP-1 is an observational study with key objectives: 1) To determine and identify patients with somatic HLA LOH eligible for Tmod CAR T-cell therapy, and 2) Subsequent leukapheresis and manufacturing feasibility for future Tmod CAR T-cell trials.

Methods BASECAMP-1 (NCT04981119) patient eligibility has 2 parts (figure 2): 1) Patients will be initially screened to identify germline HLA-A*02 heterozygosity by central next-generation sequencing (NGS). If HLA-A*02 heterozygosity is confirmed, primary archival tumor tissue will be analyzed by xT-Onco NGS testing[9] to determine if somatic tumor HLA-A*02 LOH is present; 2) If the tumor demonstrates HLA-A*02 LOH and the patient screens eligible, the patient will undergo leukapheresis. Patients enrolled in the study who undergo leukapheresis will be evaluated for safety 7 days post-leukapheresis and followed for relapsed status. Banked T cells will be available for subsequent autologous Tmod CAR T-cell therapy at the time of relapse.



Abstract 491 Figure 1 Illustration of the Tmod T cell engaging with tumor cells with somatic loss of HLA-A*02 and with normal cells



Abstract 491 Figure 2 Study schema. HLA, human leukocyte antigen; LOH, loss of heterozygosity; NGS, next generation sequencing

Trial Registration NCT04981119

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