636 **BASECAMP-1: A MASTER PRESCREENING STUDY TO IDENTIFY PATIENTS WITH HIGH-RISK OR METASTATIC SOLID TUMORS WITH HLA LOSS OF HETEROZYGOSITY (LOH) IN PREPARATION FOR TMOD CAR T-CELL THERAPY TRIALS**

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Background Chimeric antigen receptor (CAR) T-cell therapy has been challenging in solid tumors due to an absence of tumor-specific targets and the resultant on-target, off-tumor toxicity. Tmod, a novel logic-gated CAR T-cell therapy, utilizes a blocking receptor to discriminate tumor from normal cells, thus mitigating on-target, off-tumor toxicity (figure 1).[1 2] The blocker recognizes human leukocyte antigen (HLA), an antigen that is subject to LOH.[3 4] Among advanced colorectal, pancreatic, and non-small cell lung cancers, HLA LOH occurs in 15.6%, 19.6%, and 23.1% of patients, respectively (Tempus Database).[5] However, HLA LOH can only be therapeutically exploited if patients are identifiable through a feasible clinical workflow.

BASECAMP-1 is an ongoing prescreening study to: 1) Identify patients with tumor-associated HLA LOH and eligible for Tmod CAR T-cell therapy, and 2) Obtain leukapheresis in preparation for the autologous CAR T-cell therapy trials EVEREST-1 (A2B530 targeting carcinoembryonic antigen; NCT05736731) and EVEREST-2 (A2B694 targeting mesothelin).

Methods BASECAMP-1 (NCT04981119) eligibility has 2 parts (figure 2). Patients with metastatic solid tumors or at high risk of relapse will be screened for germline HLA-A*02. Tumor tissue from patients with germline HLA-A*02:01 heterozygosity will be analyzed for somatic tumor HLA-A*02:01 LOH via Tempus next-generation sequencing testing. In addition, patients may be identified via the Tempus AWARE program. AWARE analyzes tissue from patients submitted to Tempus as part of the patient's routine clinical workup. Institutional investigators are then informed of molecular results and can communicate with treating physicians regarding enrollment opportunities. Patients with tumors demonstrating HLA-A*02 LOH may be screened for subsequent leukapheresis, and banked T cells will be available for the EVEREST-1 and EVEREST-2 studies.

Results As of June 1, 2023, 664 patients were consented at 9 institutions (figure 3). HLA status was determined for 584 patients; 234 were identified as HLA-A*02:01 heterozygous (40%). LOH results were available for 117 patients; 13 were LOH positive (11%).

In addition, the AWARE program has been deployed since January 2022. We have identified 52 patients across sites with study-specific disease types with HLA-A*02:01 LOH; of these, 13 are currently being screened, 23 have been found ineligible, and 16 have consented. This demonstrated the feasibility of leveraging a diagnostic during routine clinical workup to identify rare, molecularly defined patients for personalized clinical studies.

Trial Registration NCT04981119

Please note, this trial is a screening/non-interventional clinical trial.

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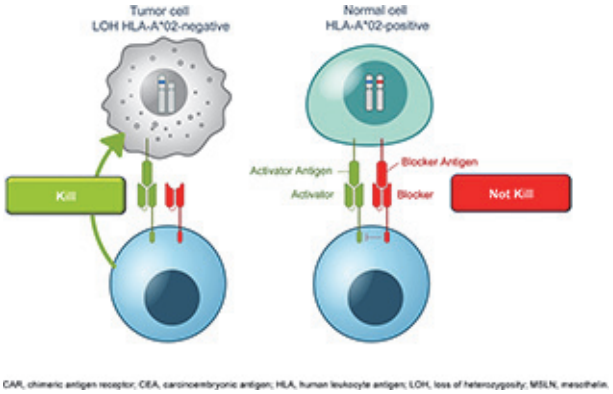
Ethics Approval This study was approved by site IRBs



Abstract 636 Figure 1 Logic-gated CAR T with the goal to reduce toxicity: CEA and MSLN (activators) and HLA-A*02 (blocker)

Abstract 636 Figure 2 Study Schema for BASECAMP-1

Abstract 636 Figure 3 BASECAMP-1 Progress to Date and Screening Process Details (June 1, 2023)

http://dx.doi.org/10.1136/jitc-2023-SITC2023.0636