were observed in a type, frequency and degree similar to other treatment arms. After repeated dosing, 1 patient demonstrated grade 1 arthritis; 1 patient demonstrated self-limited, transient grade 2 elevated LFTs; 1 patient developed grade 3 rashes, which responded quickly to oral steroid and did not recur after re-dosing. Interestingly, two out of 10 resected patients demonstrated CAP grade 2 pathologic responses in the resected PDACs after a single neoadjuvant treatment; this was not observed with other treatment cohorts (GVAX alone or GVAX+nivolumab) in this neoadjuvant platform trial. Nine out of 10 resected patients remain disease free after a median follow up of 12 months. Immunology endpoints are being analyzed by multiplex immunohistochemistry, DNA sequencing for neoantigen loads, and RNA/TCR sequencing.

Conclusions Previous observations of liver toxicity with urelumab or other T cells agonists and severe immune-related adverse events were not observed in this trial, suggesting urelumab (8 mg) is safe as neoadjuvant/adjuvant therapy in this resectable PDAC patient population. Immune and clinical efficacy of anti-CD137 agonist-based combinations warrant further investigation.

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Trial Registration NCT02451982

Ethics Approval The study was approved by the Johns Hopkins Medical Institution Institutional Review Board, approved number IRB00050517

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Combination immunotherapies

MCLA-145 (CD137xPD-L1): A POTENT CD137 AGONIST AND IMMUNE CHECKPOINT INHIBITOR THAT DOES NOT SHOW SIGNS OF PERIPHERAL TOXICITY

Abstract 812 Figure 1

Study Schema

In MCLA-145, triggered by a neighboring target cell expressing PD-L1, may provide both improved efficacy and safety. MCLA-145 is currently undergoing clinical investigation (NCT03922204).

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EVALUATING THE POTENTIAL OF HARNESSING ANTI-LEUKEMIA T CELLS FOR THE TREATMENT OF T CELL ACUTE LYMPHOBLASTIC LEUKEMIAS (T-ALL)

Background T cell Acute Lymphoblastic Leukemia (T-ALL) is a devastating malignancy found primarily in pediatric populations. Standard of care for T-ALL has not progressed from intensive regimens of chemotherapy. Another therapeutic strategy for treating T-ALL is to harness anti-leukemia T cells by immunotherapy. Currently, whether T-ALL is sufficiently immunogenic to generate anti-leukemia T cells is unknown. Furthermore, it is unclear how differences in the immune milieu of distinct tissue types (lymphoid vs non-lymphoid) that become infiltrated by T-ALL impacts T cell interactions with leukemia.

Methods These studies utilized primary T-ALL cells from a murine model that were transplanted into immune-competent, congenic (CD45.1) recipient mice. Tissues were evaluated by flow cytometry at distinct stages of disease to help determine if T cells respond to T-ALL. In addition, frozen tissue sections were analyzed using NanoString’s GeoMX Digital Spatial Profiling platform to evaluate T cells in specific regions of varying proximity to T-ALL.

Results Drastic changes to the composition of the TME were found at distinct stages of tumor burden. Evaluation of changes to the hosts’ (CD45.1+) T cells revealed a higher frequency of CD8 T cells with an activated phenotype. Furthermore, this increase largely correlated with tumor burden (figure 1). As this may represent anti-leukemia T cell responses, we next determined if they could be harnessed with immunotherapies directed against T cell co-signaling receptors. Although PD1 and OX40 monotherapies had no discernable effect, the combination of anti-PD1 with anti-