Armoring tumor infiltrating lymphocytes (TIL) with regulatable, membrane bound IL15 for increased persistence and potency, without the use of concomitant IL2

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[1] Background

Solid tumors can be effectively treated with ex vivo expanded tumor infiltrating lymphocytes (TIL). However, the clinical use of TIL therapy is currently limited by the toxicity of concomitantly administered IL2, the reduced efficacy observed outside of melanoma and limited persistence of the cells. To this end, we have developed cytoTIL5™ as an IL2-free TIL, where activity of engineered membrane-bound IL15 (mbIL15) is regulated via a degron system ("drug responsive domain", DRD) that is pharmacologically controlled with an FDA-approved small molecule drug (cytoDRIVE® technology).

[2] cytoTIL5 persist in vivo at 3-6x greater area under the curve (AUC) than conventional TIL + IL2

[3] cytoTIL5 cells maintain TCR VB representation

[4] cytoTIL5 therapy controls allogeneic, HLA-matched melanoma PDX tumors in a MART-1-dependent manner

[5] cytoTIL5 cells infiltrate into tumors, circulate and accumulate in bone marrow, and are enriched for MART-1 TCR

[6] cytoTIL5 cells show enrichment in genes associated with enhanced infiltration and anti-tumor effecter function

[7] Tumor-infiltrating and peripheral cytoTIL5 cells demonstrate enhanced stem-like anti-tumor phenotype

[8] Conclusions

- cytoTIL5 administered without IL2 show superior in vivo persistence compared to IL2 dependent TIL
- cytoTIL5 therapy demonstrates superior tumor control in allogeneic, HLA-matched melanoma PDX model
- cytoTIL5 cells expand and infiltrate into PDX tumors and produce IFNγ and TNFα
- Anti-tumor efficacy of cytoTIL5 in allogeneic PDX model is associated with retention of conserved melanoma associated antigen MART-1
- Anti-MART-1 cytoTIL5 display increased expression of TCF-1, which in melanoma patients has been associated with response to immune checkpoint blockade, as well as progression free survival (PFS) and overall survival (OS)
- cytoTIL5 cells show a distinct profile of RNA expression consistent with their increased persistence and anti-tumor efficacy (e.g., IL2RB, GNL1, CC5, GZMB, and KLRC1)
- The University of Texas MD Anderson Cancer Center is currently enrolling patients in a Phase 1 clinical trial of OBX-115, which is being evaluated in patients with metastatic melanoma (NCT0542783).