

PR01 Targeting pancreatic cancer using non-engineered, multi-antigen specific T cells (TACTOPS). Brandon G Smaglo¹, Tao Wang¹, Benjamin L Musher¹, Premal D Lulla¹, George Van Buren II¹, William Fisher¹, Ayumi Watanabe², Manik Kuvalekar², Catherine Robertson², Amanda Brisco¹, Bambi J Grilley², Adrian P Gee², Carlos Ramos¹, George Carrum¹, Helen Heslop¹, Juan F Vera Valdes², Ann M Leen². ¹Dan L Duncan Comprehensive Cancer Center, Baylor College of Medicine, Houston, TX, USA, ²Texas Children's Hospital, Houston, TX, USA.

Introduction: To explore the benefit of immunotherapy to solid tumors, we have developed a non-engineered T cell therapy with single T cell lines that simultaneously target the tumor-associated antigens (TAAs) PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin, and administer these T cells to patients with pancreatic adenocarcinoma in a Phase I clinical trial with 3 study arms: A - patients with unresectable/metastatic disease who are responding to standard first line chemotherapy; B - patients with progressive disease or therapy intolerance after first line; C - patients with potentially resectable disease. The primary study objectives are safety and feasibility with assessment of progression-free and overall survival as secondary outcome measures.

Background and Methods: Multiantigen-targeted T cells are generated by culturing autologous PBMCs in the presence of a Th1-polarizing/pro-proliferative cytokine cocktail, and adding autologous pepmix-loaded dendritic cells as antigen presenting cells. The use of whole antigen overcomes the HLA restriction imposed by the use of transgenic TCRs specific for single peptides, while targeting multiple antigens simultaneously should reduce the risk of tumor immune evasion.

Results: To date, we have generated 35 clinical-grade multiTAA T cell lines, comprising CD3+ T cells (mean 97.2±1.3%) with a mixture of CD4+ (mean 47.2±7.4%) and CD8+ (mean 39.5±6.4%) T cells that recognize the targeted antigens PRAME, SSX2, MAGEA4, NY-ESO-1 and Survivin (range 0-323, 0-80, 0-772, 0-143 and 0-30 SFU/2x10⁵, respectively in IFN-γ ELISpot). None of the lines reacted against non-malignant autologous cells (2±3% specific lysis; E:T 20:1). To date, we have treated a total of 18 patients (9 - Arm A; 6 - Arm B; 3 - Arm C), each of whom received up to 6 monthly infusions of 1x10⁷ multiTAA-T cells/m². Of the 9 patients who have received cells in conjunction with first line chemotherapy, 2 are too early to evaluate, 2 had disease progression, and 5 have had ongoing radiographic stable disease or responses (6-9 month duration), including one complete response. Of the 6 patients treated with progressive disease (Arm B) 3 continued to progress on treatment while 3 have on-going stable disease (1-6 months). Finally, the 3 patients with potentially resectable disease received one infusion of T cells preoperatively and are still receiving their post-operative infusions and adjuvant therapy. Clinical benefit has correlated with the detection of tumor-reactive T cells in patient peripheral blood (Arms A-C) and within tumor biopsy samples (Arm C) post-infusion. T cells have exhibited activity against targeted antigens as well as non-targeted TAAs including MAGEA2B and AFP, indicating induction of antigen/epitope spreading. Notably, no patient had infusion-related systemic- or neuro-toxicity.

Conclusion: Administration of multiTAA-T cells as a therapy for pancreatic cancer appears to be feasible and safe, and may be associated with benefit to patients with pancreatic cancer.

This abstract is also being presented as Poster A18