

NON-TECHNICAL ABSTRACT

Survival for patients with stage IV, relapsed or refractory melanoma is extremely poor with essentially no long term survivors. Immunotherapy, including antibody directed at GD2 on these tumors, has demonstrated anti-melanoma efficacy. We intend to provide lymphodepleting chemotherapy with subsequent infusion of autologous, GD2 chimeric antigen receptor transduced, vaccine specific CTL enriched, activated T-cells (tvs-CTL) to provide adoptive cellular immunotherapy targeting melanoma. Expression of the GD2-specific CAR gene in the tvs-CTL should render the CTL capable of expansion and persistence through stimulation via the native vaccine specific T-cell receptors by repeated vaccination after infusion, and capable of tumor cytotoxicity via the chimeric antigen receptor. We will evaluate the toxicity, vaccine reactivity and tumor reactivity of the allogeneic tvs-CTL.

To make these vaccine-specific CTL enriched lines, we first vaccinate patients at the diagnosis of stage IV melanoma, if their melanoma is BRAF V600 E negative, with common vaccines (Tdap, HepB, & PCV). If patient's tumor is BRAF V600E positive, they will be vaccinated if they fail vemurafenib (a BRAF V600 E inhibitor) therapy. Approximately 10-14 days later, or at the initiation of upfront melanoma therapy with ipilimumab, blood is harvested and sent to the Center for Cell and Gene Therapy (CAGT) at Baylor College of Medicine. T-cells are activated and expanded at CAGT, then transduced with a retroviral construct delivering the gene for the GD2 specific chimeric antigen receptor. The cells will then be tested to make sure they kill tumor cells but not patient cells and freeze them. We would anticipate infusion of the cells to the patient after they complete upfront therapy or if the patient should be refractory to upfront therapy or if they relapse. We would re-vaccinate with the 3 vaccines approximately 3-4 days prior to infusion. .

These modified T-cells will be given directly into the blood stream through a central line or a vein. Subjects will be treated in the clinic or hospital room and will be monitored closely for several hours after infusion. We will collect samples of blood from peripheral blood at regular intervals. We will look for the safety, the persistence and the function of the cells we put into the patients. Ultimately, we hope to get evidence that these CAR modified T cells are safe and effective at fighting melanoma.