

I. Scientific Abstract

Anti-CEA Immunoglobulin-T Cell Receptor (α CEA-IgTCR)-Modified T Cells in Cancer Therapy

This is an open label, dose escalation, phase I safety study of anti-CEA IgTCR-modified T cells in patients with CEA-expressing adenocarcinomas. The chimeric IgTCR transgene consists of an anti-CEA-sFv antibody fragment fused to the ζ -signalling chain of the T cell receptor. Expression of the transgene specifically re-directs naive T cells to respond against CEA-expressing tumor cells. Preclinical studies have shown that IgTCR-modified T cells were able to respond to the target antigen with cytokine release, proliferation, and cytotoxicity. Patient T cells will be collected by pheresis, transduced with IgTCR retroviral vectors, expanded in culture and then reinfused into the patient. Patients will initially receive 1×10^9 cells and then undergo biweekly dose escalation until a total of four doses or until grade III toxicity. The goal of the study is to estimate maximum tolerated dose or to administer 4 consecutive doses of 1×10^{11} cells. Patients will be monitored for safety and tolerability, pharmacokinetics/pharmacodynamics of antiCEA-IgTCR transduced T cells, and other immunologic and oncologic parameters that may indicate anti-tumor efficacy. In addition to safety and efficacy, other specific aims are to test various improvements in IgTCR vector design. These include the use of a humanized transgene (to reduce vector immunogenicity), employing gene-modified CD4 cells (to provide *in vivo* IL2), and to test new retroviral vectoring techniques in a clinical setting.