

***A Phase I/II Study of Autologous CC49-Zeta Gene-Modified T Cells and Alpha-Interferon in Patients with Advanced Colorectal Carcinomas Expressing the Tumor-Associated Antigen, TAG-72.***

**Scientific Abstract:**

Adenocarcinoma of the large bowel affects approximately 15% of the population of the Western world and is the second most common cause of cancer and cancer-related deaths in the United States. In the United States alone, 155,000 new cases of colorectal cancer are diagnosed annually, representing 15% of all cancers and resulting in 61,500 annual deaths. Despite a modest improvement in the 5-year survival rate of colon cancer patients from 41% to 54% over the past 30 years, a significant unmet medical need for more effective therapy still exists for this disease.

The proposed protocol will evaluate the use of CC49-zeta gene-modified T cells for adoptive immunotherapy of patients with colorectal cancer. Rather than isolating and expanding rare, MHC-restricted, tumor antigen-specific T cell clones, a method has been developed to rapidly generate large numbers of antigen-specific, MHC-unrestricted T cells using retroviral-mediated gene transfer to insert a tumor-targeting gene into primary CD8+ and CD4+ T cells. The tumor-targeting gene, CC49-zeta, encodes a genetically-engineered, MHC-unrestricted, chimeric receptor directed against a specific tumor antigen, TAG-72. The DNA introduced into the cells encodes a receptor that is made from an antibody that recognizes tumor-specific marker expressed on colon cancer cells, linked to a signalling chain derived from the human T cell receptor. The genetically-modified cells can be expanded *ex vivo*, resulting in the rapid generation of large numbers of high affinity tumor-specific T cells. This approach has been used to generate genetically-modified T cells specific for TAG-72, a tumor-associated antigen expressed on a wide range of adenocarcinomas.

The study is a phase I/II open label, non-randomized, inpatient dose escalation of autologous CC49-zeta gene-modified CD4+ and CD8+ T cells in patients with metastatic colorectal carcinomas expressing TAG-72.

Non-technical

Points to Consider

Clinical Protocol