

A Phase I Study of Active Immunotherapy with Autologous Dendritic Cells with CEA-6D Expressing Fowlpox-Tricom in Patients with Advanced or Metastatic Malignancies Expressing CEA

NON-TECHNICAL ABSTRACT

Cancer is the second leading cause of death in the United States. The highest cancer mortality occurs in both men and women with lung cancer, gastrointestinal malignancies, and breast cancer. While standard options such as chemotherapy, radiation, and surgery have improved modestly improved survival, relapse and progression of disease remain major problems suggesting the continued need to evaluate other new anti-tumor strategies, such as immunotherapy. Clinically effective cancer immunotherapy has been a long term objective of many investigators. The identification and cloning of a number of tumor associated and tumor specific antigens directly addressed that fact that human cancer cells do express antigens. Recent clinical developments such as the demonstrated anti-tumor activity of specific monoclonal antibodies have contributed to renewed enthusiasm in immunotherapy. In addition, cellular therapies such as donor lymphocyte infusion in chronic myelogenous leukemia and non-myeloablative bone marrow allograft for renal cell carcinoma have shown remarkable clinical promise. Advances in our basic understanding of immunity, and the requirements for the induction of specific immune responses has led to a variety of exciting active specific immunotherapy approaches, so called therapeutic cancer vaccines. To address the question of whether active immunotherapy has a therapeutic role, there is a great need to address the basic hypothesis of whether induction of an immune response results in clinical benefit.

No major organ or auto-immune toxicity was seen in multiple phase I clinical trials of recombinant vectors expressing full length CEA, clinical trials of CAP-1 peptide pulsed DC or clinical trials of CEA modified DC. Studies in murine models indicate that DC pulsed with a modified peptide (CAP-1-6D) can induce cytotoxic T lymphocytes (CTL), and DC modified with TRICOM are superior to unmodified DC. We have demonstrated that human DC infected with rF-CEA(6D)/TRICOM can induce CEA specific CTLs *in vitro*.

The overall objective of this phase I study is to evaluate the safety and feasibility of one, two, or three cycles of TRICOM modified DC expressing CEA-6D. One cycle of immunotherapy consists of a leukapheresis to obtain peripheral blood DC precursors and *in vitro* generation of the DC from these precursors followed by 1 injection every three weeks for a total of 4 injections of rF-CEA (6D)/TRICOM modified DC.