

NON-TECHNICAL ABSTRACT

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The overall objective of this study is to perform a Phase I Clinical Trial in recurrent colon carcinoma patients evaluating the safety of multiple intradermal immunizations with irradiated tumor cells admixed with irradiated fibroblasts genetically modified to express the gene for IL-2 an immunostimulatory protein. Two of the three colon tumor cell lines contained in the vaccine have also been genetically modified to express on their surface the B7.1 (CD80) another immunostimulatory molecule. Evaluation of these approaches in clinical trials is supported by studies in animal tumor models indicating synergistic activities between these different types of genetically engineered vaccines. Colorectal carcinoma is one of the most common cancers in the United States and Europe with an annual incidence of greater than 150,000 in the U.S. Most patients are treated with tumor resection and do not have clinically detectable tumor following surgery. However, the majority of patients have microscopic metastases and eventually relapse with clinically overt disease in the liver or abdominal cavity. These findings combined with the demonstration of enhanced anti-tumor immunity following tumor immunizations with cells genetically modified to express IL-2 and/or B7.1 (CD80) in several animal tumor systems provide the rationale for our study. Patients will receive immunizations with increasing doses of IL-2 transduced fibroblasts and a fixed dose of tumor cells. The patients will be monitored for toxicity, anti-tumor responses and the induction of anti-tumor immunity. The results of the Phase I trial should permit an assessment of the safety of this form of immunogene therapy.