

1. SCIENTIFIC ABSTRACT:

The hypothesis of the proposed trial is that an immune response against carcinoma embryonic antigen (CEA) can be induced by the study drug, ALVAC CEA-B7.1. Prior vaccination studies attempting to immunize against CEA have demonstrated limited numbers of immune responses, and usually humoral responses. This vaccine combines the gene for CEA with B7.1, a costimulatory molecule which helps induce a T-cell response. As the best method of vaccination is unknown, three different cohorts of patients will be accrued to receive therapy as an intramuscular injection, an intradermal injection, or an intradermal injection with the adjuvant GM-CSF.

ALVAC CEA-B7.1 for these studies will be obtained from the NCI-CTEP. The agent is a canary pox viral vector, which is incapable of replicating human tissues. The genes for CEA and B7.1 have been inserted into the virus. This vector has undergone extensive toxicity testing in primates and has been approved by the RAC & FDA for clinical evaluation in patients with adenocarcinomas using ALVAC CEA by IM injection (ORDA: 9508-122). A similar cDNA for B7.1 has also been employed in a melanoma vaccine (ORDA: 93 12-063).

Preclinical studies in the laboratory of Dr. Jeffrey Schlom and others have provided the rationale for the proposed hypothesis and feasibility of the proposed clinical trial. These studies have shown that targeting of specific antigens, including tumor antigens, encoded in ALVAC vector can induce an immune response; in particular, combining the tumor antigen with B7.1 has led to a reduction in tumor growth and protection against tumor challenge in mice. The ability of inducing a CEA-specific cytotoxic T cell response in humans with adenocarcinoma has been demonstrated using a vaccinia vector and ALVAC (unpublished data, J. Schlom). Given the large number of patients with adenocarcinomas of the breast, lung, colon, rectum and cervix, an effective vaccine strategy for adenocarcinomas is worth investigating. This study provides rationale for evaluating the safety and biological effects of ALVAC CEA B7.1 in the treatment of patients with advanced adenocarcinomas who have failed conventional therapy.