

Scientific Abstract

A pilot trial of a CEA/TRICOM—based vaccine in combination with combined chemotherapy/radiotherapy in patients with unresectable stage III non-small cell lung cancer (NSCLC).

Background

Lung cancer is the leading cause of cancer death in the U.S. Approximately 80% of all lung cancers are non-small cell and 40% of patients will present with stage IIIA or IIIB, which is frequently not amenable to primary surgical treatment. Combined chemotherapy and radiotherapy unfortunately has a median overall survival time of approximately 14.3 months and the median progression-free survival of 8.8 months. Carcinoembryonic antigen (CEA) is overexpressed in virtually all adenocarcinomas of the colon and rectum and is also present on most adenocarcinomas of the lung. In light of the fact that current therapeutic strategies have had limited success, vaccine strategies may represent an additional intervention. Our current generation of vaccine, designated CEA-TRICOM, contains the transgenes for CEA as well as three costimulatory molecules. Clinical experience with CEA vaccines have demonstrated safety, superiority of a prime and boost schedule and clinical activity with significant correlation between CEA-specific T-cell responses and apparent clinical benefit. In addition, it has been shown that radiation can upregulate Fas expression on tumor cells and along with chemotherapy can potentiate T-cell mediated killing of tumor.

Objective/hypothesis

To evaluate the safety and feasibility of combining the standard chemotherapy/radiation therapy for stage III unresectable NSCLC with a CEA/TRICOM vaccine regimen. Histopathologic analysis of FAS, Class I, ICAM-1, CEA, and MUC-1 on tumor cells through bronchoscopy, before and after radiation therapy will be done.

Study Design

Ten patients with unresectable stage III NSCLC will receive vaccine with standard chemotherapy/local radiation followed by 2 cycles of standard chemotherapy. Patients will receive rV-CEA(6D)/TRICOM along with rF-GM-CSF as the primary vaccination 3 weeks prior to the start of radiation, followed by boosts with rF-CEA(6D)/TRICOM and rF-GM-CSF on a 2 week basis during radiation therapy. The vaccine boosts will be given on a 3 week basis with the final 2 cycles of standard chemotherapy. Patients may continue vaccine boosts on a 3 week basis if they do not show evidence of disease progression on CT scans.

Relevance

This trial aims to obtain safety data on the use of a CEA-based vaccine and standard radiation and chemotherapy in patients with unresectable stage III NSCLC. If this trial is successful, future trials can be designed to evaluate clinical efficacy of this regimen with standard radiation and chemotherapy in patients with stage III unresectable lung cancer.