

ABSTRACT

Lung cancer is the leading cause of cancer death among both males and females in the United States with over 160,000 deaths/year. Most cases present in an advanced stage leading to a 5-year survival of less than 10%. We propose a phase I safety trial of a gene therapy for non small cell lung cancer (NSCLC). We will use a replication defective adenovirus 5 with deletion of the E1 region and replacement with the Herpes simplex thymidine kinase gene under control of the Rous sarcoma virus LTR promoter. This adenovirus will be directly injected into advanced NSCLC (stage IIIb or IV) via a transthoracic needle and/or transbronchial needle. We will perform a second bronchoscopy within 48 hrs to obtain transbronchial biopsies to determine if the HSV.tk gene has been transduced in tumor tissue. Tumor biopsies will be evaluated using RT PCR, DNA PCR, and in situ hybridization. Following tumor injection, ganciclovir will be given intravenously for 7 days. We expect that this suicide gene approach will result in tumor cell killing, and that there will be a bystander effect leading to destruction of neighboring tumor cells. We will inject three escalating dose levels with a cohort of at least 3 patients per dose level. We plan initially to give a single dose. Safety assessments will include biochemical parameters, chest CT radiographs pre- and post-injection, measures of adenoviral antibodies, and measures of specific immunity. The adenoviral vector is the same as used in FDA and RAC approved phase I clinical trials for brain, prostate, and head and neck cancer by Dr. Savio Woo.