

C.3 Nontechnical Abstract

Protocol K-0015 titled "A Phase I/II Study of Vaccination with Irradiated Autologous Lung Tumor Cells Mixed with a GM-CSF Secreting Bystander Cell Line (Lung Bystander GVAX[®]) in Advanced Stage Non-small Cell Lung Cancer (NSCLC)".

Lung cancer is the leading cause of cancer death for men and women in the United States. Non-small-cell lung carcinoma (NSCLC) accounts for 75% to 80% of these cases. Although the incidence of this disease may be declining in American men, it has been steadily increasing in American women, following the steady rise in tobacco use. The worldwide increase in tobacco consumption, moreover, is likely to be associated with a global increase in lung cancer deaths during the 21st century.

Immunotherapy is a type of treatment for cancer that is based on the idea that the immune system (the system in the body that fights infection) can be activated to destroy cancer cells that have grown undetected. A vaccine is a way of delivering an antigen (something that stimulates the immune system) to the immune system so that it recognizes the antigen as foreign and destroys any cells bearing that antigen.

The Lung Bystander GVAX Vaccine consists of two components: 1) the patient's processed tumor cells and 2) K562 Bystander GVAX cells. The K562 cells are modified human leukemia cells that are engineered to carry a gene for GM-CSF (Granulocyte Macrophage Colony Stimulating Factor). The gene for GM-CSF is inserted in the K562 cells by a plasmid (piece of bacteria). GM-CSF is a substance called a cytokine, which is normally found in some cells in the human body in very small amounts. The K562 cells carrying the GM-CSF gene will produce large amounts of GM-CSF at the vaccine site to help activate the patient's immune system. Because the K562 cells will be injected with the patient's NSCLC cells, the patient's immune system may be triggered to react against the tumor cells and kill them. The goal of the vaccine is to create an army of a specialized white blood cells which can recognize and attack NSCLC cells after vaccination.

Approximately 40 adults with advanced stage NSCLC (Stage IIIA, IIIB, or IV) with accessible tumor source for production of the vaccine will be enrolled in this study at approximately 5 sites. In order to obtain NSCLC cells with which to make the vaccine specific for the patient, he/she will need to undergo a surgical procedure to remove some or all of the tumor. The tumor cells that are removed during surgery and that are not needed by pathology will be sent to a laboratory where they will be processed so they can be mixed with the K562 cells. Some normal cells in the body produce GM-CSF in very small amounts. Mixing the patient's tumor cells with the K562 cells (the cells that produce GM-CSF) will result in large amounts of GM-CSF at the vaccine site that will help activate the immune system against the patient's cancer. Before the cells are injected back into the patient, they will be irradiated to prevent them from growing, and frozen. Irradiation does not appear to affect the ability of these cells to produce GM-CSF. However, the radiated tumor cells will all die within a couple of weeks. If cell preparation for Lung Bystander GVAX vaccine fails in any way, the patient will not be treated with vaccine and will be told right away and offered other treatment options.

Approximately 2 to 4 weeks after the removal of tumor cells, the patient will receive Lung Bystander GVAX vaccinations at one of five doses, depending on the amount of tumor that was removed during surgery. Tumor cells will be mixed with K562 Bystander GVAX cells at a ratio of 2 tumor cells to 1 K562 cells in the final vaccine. The five doses are: Dose level 1 (5 million tumor cells plus 2.5 million K562 cells), Dose level 2 (10 million tumor cells plus 5 million K562 cells), Dose level 3 (20 million tumor cells plus 10 million K562 cells), Dose level 4 (40 million tumor cells plus 20 million K562 cells), or Dose Level 5 (80 million tumor cells plus 40 million K562 cells). Vaccines will be injected every 2

weeks for a minimum of 3 and a maximum of 12 vaccinations. During the study, patients will be monitored for any clinical or laboratory side effects that may develop following vaccine treatment.

In order to determine if the patient's immune system has developed the ability to react specifically against his/her lung tumor cells, a small number of the patient's own lung tumor cells will be injected under the skin two times during the course of the study (at first and third vaccination). As before, these cells will be irradiated so that they will not be able to grow again in the patient's body. The patient will be asked to return to the clinic 48 hours following the first and third vaccination to assess the reaction and for a skin biopsy of the vaccine injection site. In addition, the patient's immune system will be monitored to measure immune response against the tumor.

The clinical activity of the vaccine will be monitored by radiology studies performed prior to, and approximately 3 months following the first vaccination, and periodically thereafter. These will include CT scans of the chest and abdomen, bone scans, and any additional radiological studies necessary to evaluate the disease.

In addition, patients who receive the two highest vaccine doses will undergo more intensive monitoring to measure levels of GM-CSF secreted by the vaccine into the blood. This will allow us to determine how long the vaccine cells survive in the patient.

This study is closed to enrollment and all vaccine treatments have been completed.