C.3 Nontechnical Abstract

Protocol K-0009 titled "Vaccination in the Peripheral Stem Cell Transplant Setting for Acute Myelogenous Leukemia: The Use of Autologous Tumor Cells with an Allogeneic GM-CSF-producing Bystander Cell Line".

Acute myelogenous leukemia (AML) is a cancer of the bone marrow that is relatively rare, about 2.5 cases in 100,000 individuals. At diagnosis half of patients are older than 65 years and half are younger. The cause is primarily unknown, although prior chemotherapy, radiation exposure, and routine work-related exposure to benzene comprise a few causes. Signs and symptoms of AML are due to progressive replacement of the normal cells in the bone marrow with leukemia cells, and include anemia, bruising or bleeding, fever, infection, enlargement of the liver or spleen, persistent fatigue, weight loss, and bone or abdominal pain. Without treatment AML is uniformly fatal within several months.

Standard treatment for leukemia is repeated courses of chemotherapy, and this results in remission, in most cases, and may control the leukemia for a long period of time. Sometimes chemotherapy may cure the disease; however, in most patients the leukemia returns after chemotherapy. To keep the leukemia from returning, patients who are in remission may be treated with high doses of chemotherapy followed by a bone marrow or blood stem cell transplant.

In stem cell transplant, blood is collected from the vein, frozen, and stored. Patients then receive very high doses of chemotherapy, which kills the bone marrow and the leukemia cells. After this chemotherapy, patients receive their own blood cells back. These blood cells contain stem cells; they act as the "seeds" that grow to replace the bone marrow.

Since in at least half of patients, the leukemia returns even after stem cell transplant, patients in this study will receive an experimental vaccine, Leukemia Bystander GVAX®. Leukemia Bystander GVAX is made up of the patient's own leukemia cells that have been mixed with another kind of cell, called a bystander cell. Bystander cells are cells that have been engineered to carry a gene for GM-CSF (granulocyte-macrophage colony-stimulating factor). GM-CSF is normally found in some cells in the body in very small amounts and helps to activate the immune system (the body's defense system that helps fight infection and cancer). Mixing bystander cells with the patient's own leukemia cells and injecting them under the skin may help the immune system to better recognize the leukemia cells in the vaccine as cancer and to kill the remaining leukemia cells left in the body. Both the patient's own leukemia cells and the bystander cells are irradiated before they are mixed to make the vaccine; irradiating these cells will prevent them from growing after the vaccine is injected.

The bystander cell used in this vaccine is called CG9962 (K562 Bystander GVAX). This is a leukemia cell line which was genetically modified to secrete human GM-CSF. These cells are grown at Cell Genesys under controlled conditions, irradiated to prevent cell growth, and frozen in liquid nitrogen. Leukemia cells are obtained from the patient by blood draw, bone marrow aspiration, or a procedure called leukapheresis (filtering of the leukemia cells from the blood),

irradiated, frozen, and stored in liquid nitrogen. Tumor and CG9962 cells are thawed, mixed together just prior to administration, and injected under the skin.

The primary goals of the study are to evaluate the safety of Leukemia Bystander GVAX and to determine how practical and realistic this approach is. The secondary objectives are to demonstrate the ability to induce an immune response against leukemia following vaccine administration and to follow subjects to determine if and when their leukemia relapses.

There are six steps in this study: 1) collection of leukemia cells from the blood or bone marrow for use in making the vaccine; 2) induction chemotherapy designed to cause remission of the leukemia; 3) for patients in remission, consolidation chemotherapy to decrease residual body stores of leukemia cells; 4) pre-transplant vaccination; 5) stem cell transplant; and 6) post-transplant vaccinations (eight vaccinations, one every 3 weeks). Each vaccination contains 100 million tumor cells mixed with 40 million CG9962 cells (ratio of tumor : bystander cells of 5:2). Approximately 50 patients, ages 18-60 with newly diagnosed AML, will be enrolled in order to insure that at least 20 patients will participate in the study long enough to receive at least half of the post transplant vaccines.

This phase I/II study of Leukemia Bystander GVAX is currently ongoing. Enrollment is nearly complete and patient treatment and data analysis is in process. There are no plans to initiate any new trials with this vaccine product this year.