

NON-TECHNICAL ABSTRACT

In the United States, the incidence of malignant melanoma is increasing more rapidly than of any other neoplasm. The incidence rose from 1/1500 in 1935 to 1/135 in 1987, and it is projected to reach 1/75 in the year 2000. The cost of treating melanoma patients is 25 billion dollars per year. Most successes in melanoma therapy have been achieved by surgery or immunotherapy, although there is no adequate procedure for treating advanced metastatic melanoma. The pilot clinical trial proposed in this document is based on the immunotherapy procedure developed in Dr. Alan Garen's laboratory at Yale University, which tested this approach successfully in a mouse model of human melanoma. The procedure for the trial involves injecting into accessible tumors of Stage IV melanoma patients an adenoviral vector encoding an immunoconjugate molecule that targets a melanoma tumor for killing by the immune system. The tumor cells infected by the vector synthesize and secrete the immunoconjugate into the systemic circulation. The blood-borne immunoconjugate molecules bind to tumor cells and also to the blood vessels that supply the tumor cells with oxygen and nutrients, resulting in a powerful immune attack against the tumor. The patients will be monitored for signs of toxicity and also for changes in the size or number of their tumors. The aim is to control the growth and spread of tumors in the treated patients without unacceptable side effects from the treatment.