

Non-Technical Abstract

Tumors arising in the brain are responsible for approximately 12,000 deaths annually in the United States. There has been little change in the outcome for adults with malignant brain tumors over the past few decades, despite improvements in surgical techniques and advances in radiation therapy. These tumors are uniformly fatal one to two years after diagnosis. The disease is devastating, due to its debilitating neurologic consequences and rapid termination in death. The patients often suffer from seizures, paralysis, incoordination, aphasia, confusion, memory loss, sensory deficits or visual loss, depending on the regions of the brain affected. In addition, they usually require large doses of corticosteroids early and late in their illness, and may experience disabling side effects of this treatment, such as edema, proximal myopathy, diabetes, fungal infections or deep vein thrombosis. Few patients in the older age group are able to work after the diagnosis. Most of the patients are incapable of self-care for several months before death. While there is some variation in the course of the disease with the type of brain tumor, no one survives glioblastomas and only a few patients are long-term survivors of anaplastic astrocytoma. Conventional brain tumor therapies are not successful because they do not distinguish tumor cells from normal cells. Creation of "artificial" differences in biochemical behavior of the tumor cells is an attractive option. This proposal seeks to make brain tumor cells sensitive to the drug ganciclovir. This will be achieved by directly injecting a virus which carries a gene for Herpes virus thymidine kinase. This gene when activated in the tumor cell will convert the relatively non-toxic drug ganciclovir to a toxic form and subsequently kill the tumor cell. In this phase I study, patients with recurrent brain tumors will receive injections of the virus into the brain tumor, followed by intravenous ganciclovir for 14 days. Patients eligible to undergo a palliative debulking procedure will receive the same treatment followed by resection on day 7. At the time of resection a second dose of virus will be administered intra-operatively into the residual, unresectable portion of the tumor, and intravenous ganciclovir will be continued for additional 14 days. Patients will be enrolled in groups of three, with each group receiving successively larger doses of adenovirus. This study will determine the toxicity of this therapy, provide evidence as to what portion of the tumor expresses the new gene, and determine the extent of virus induced injury.