Non Technical Abstract

Glioblastoma (GBM), the most aggressive brain tumor, is a rare but universally deadly form of cancer. GBM is among the most challenging of all cancers to treat because they aggressively invade normal brain tissue. Despite surgery, radiation, and chemotherapy, the median survival of patients with glioblastoma multiforme is less than one year. Improvement in this dismal prognosis requires new treatment approaches.

One new approach for treating gliomas is the use of a common cold virus called adenovirus. The natural form of this virus causes minimal and self-limiting disease in people. We have modified this virus by removing one region and by altering its ability to infect cells. The result of these modifications is that the new virus, called Delta-24-RGD4C, can infect and kill tumor cells while sparing normal cells. We have demonstrated using animal models that this viral therapy results in regression of brain tumors grown in mice. In addition, the side effects of this virus were minimal.

The phase I protocol proposed in this application is designed to study the safety of administering Delta-24-RGD4C to patients. Patients enrolled in this study will be treated with intratumoral injections of Delta-24-RGD4C virus to determine the maximum tolerated dose (MTD). A second group of patients will undergo a stereotactic injection of Delta-24-RGD4C virus via a permanently implanted catheter into the center of the tumor. After 14 days, the tumor will be surgically removed, and biological specimens will be evaluated for pathological and molecular changes. By monitoring patients throughout this study, the phase I trial will provide the basic information about the safety and biological effect of injecting Delta-24-RGD4C into human brain tumors. It is anticipated that the experiments described herein would establish the safety and provide an indication of the efficacy of this approach in human subjects with high grade gliomas and provide a rational basis to move to future phase II / III clinical trials.