



**MAXINE DUNITZ NEUROSURGICAL INSTITUTE**

8631 West Third Street – 800E  
Los Angeles, California 90048  
Tel: (310) 423-7900 ♦ Fax: (310) 423-0810

---

**A PHASE I/II CLINICAL TRIAL TO EVALUATE DOSE LIMITING TOXICITY AND EFFICACY OF INTRALESIONAL ADMINISTRATION OF REOLYSIN FOR THE TREATMENT OF PATIENTS WITH HISTOLOGICALLY CONFIRMED RECURRENT MALIGNANT GLIOMAS (IRB #13574)**

Glioblastoma Multiforme (GBM) and malignant glioma (MG) are lethal cancers of the central nervous system. Conventional treatments with surgery, radiotherapy and chemotherapy may provide palliation (symptom relief) and extend survival for a short time. One promising new approach is the use of oncolytic viruses, such as reovirus, to kill brain tumor cells. Oncolytic viruses are those which specifically destroy cancer cells by replicating in the tumor cells and causing the tumor cells to rupture or by signaling the body's immune system to target and kill the cancer cells.

The new experimental treatment called REOLYSIN uses an oncolytic virus called reovirus. Reovirus is a common, naturally occurring virus that does not cause disease in humans and has been shown to be associated with only minor flu-like symptoms. We know from research that it can selectively replicate in and kill cancer cells, while leaving healthy cells unharmed.

This is a Phase I/II multi-center study. REOLYSIN will be infused directly into the brain tumor to find out about the side effects, safety and maximum tolerated dose of the treatment. The Phase I portion of the trial will evaluate escalating doses of REOLYSIN (at five different dose levels) to determine a maximum tolerated dose. The purpose of the Phase II portion of the study is to assess tumor response. Recording the number of patients surviving to 6 months will be a secondary objective.

The Phase I portion of the study will enroll three to six patients into each dose level and therefore a maximum of 30 patients is planned. In the Phase II portion of the study, a maximum of 14 patients will be entered at the top dose reached in the Phase I.

Patients with malignant gliomas who have disease that is worsening or recurring despite "standard therapy" of surgery and radiotherapy, and who may or may not have had chemotherapy or other forms of treatment will be eligible for the study if they meet entry requirements. For Phase I, patients with any malignant glioma who have either a first, second, or third recurrence may be included. For Phase II, only patients with a first recurrence of glioblastoma multiforme will be eligible. Recurrence will be defined by MRI (use of a magnetic field to produce an image of the tumor). Histologic (examination of tumor tissue) confirmation of recurrence is required. An MRI must demonstrate progressive enhancing disease no earlier than six weeks after the completion of radiotherapy. Tumors must be evaluable, accessible to intralesional treatment, and deemed unlikely to be at risk for entry into specific areas of the brain including the ventricles, basal ganglia or foramen magnum during treatment and surgery (for example by the stereotactic needle or catheter). Patients must be on a stable dose of corticosteroids and without progressive symptoms for at least two weeks prior to study entry. Patients must be fully recovered from any prior therapy before enrolling in the study and must have a life expectancy of at least 8 weeks. Patients that are pregnant or may become pregnant, patients that are breast feeding and patients that may be immunosuppressed are not eligible for the study

Each patient enrolled in the study will receive a single infusion of REOLYSIN into the lesion over 72 hours. Patients will remain in hospital for at least 90 hours after initiation of infusion. Following REOLYSIN administration, each patient will be followed for at least 12 weeks (Phase I) and at least 6 months (Phase II) with regular evaluation visits (weekly and then monthly). Evaluations will include tumor measurements, serial neurologic exams and quality of life measures (using the Karnofsky Performance Status scale). Subjects will also undergo serial blood sampling for evaluation of the presence of virus, hematology and biochemistry.

Contact Person:

John Yu, MD

Director, Surgical Neuro-oncology

Co-Director, Gamma Knife Center

yuj@cshs.org

(310) 423-7900