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**PHASE II TRIAL OF TUMOR LYSATE-PULSED DENDRITIC CELL  
IMMUNOTHERAPY FOR PATIENTS WITH ATYPICAL OR  
MALIGNANT, PRIMARY OR METASTATIC BRAIN TUMORS OF  
THE CENTRAL NERVOUS SYSTEM**

This study is being done to determine whether vaccinations with the subject's own immune cells called "dendritic cells" (after they are mixed with proteins from the subject's brain tumor cells) can activate the subject's immune system to fight their brain tumor. Tumor cells are taken at the time of surgery and are frozen and thawed to separate protein segments that are unique to that tumor. These proteins will be added to another culture of the subject's dendritic cells grown from their blood, combined together, then re-injected back into the subject's body.

Dendritic cells are a small group of cells contained in everyone's white blood cell population. These cells are responsible for letting the immune system know that something foreign, like bacteria, or a tumor, is in the body. Dendritic cells help the body ward off disease by alerting the immune system.

The purpose of this study is to evaluate and test the safety of subcutaneous (beneath the skin) injections of the subject's own dendritic cells that have been removed from the subject's peripheral blood and cultured with tumor protein fragments from the subject's brain tumor. We will also evaluate the proteins circulating in the blood.

Possible benefits of participation in the study include prolonged survival, better response to chemotherapy treatment, and improvement of quality of life.

**Inclusion Criteria:**

To become eligible for therapy the following criteria must be fulfilled for a patient:

- ◆ No age or gender limit, though minimal weight limitations for apheresis is about 15-20 Kg.
- ◆ Both male and female of childbearing age entering the protocol must use a medically accepted form of birth control during the study, will be required to have a negative pregnancy test for female.
- ◆ Patients with atypical malignant brain tumor will be eligible. Tumors may be primary to the CNS or Metastatic to the CNS. in 5 tumor groups of 5 patients each (in Glioblastoma Multiforme will be 30 patients):
  - metastatic tumors to brain , including ovarian, colon, other
  - recurrent or high risk medulloblastoma/ PNETs, ependymomas;
  - recurrent anaplastic gliomas
  - recurrent, newly diagnosed glioblastoma multiforme

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- recurrent meningioma and miscellaneous tumor types.
- ◆ Patients must have a Karnofsky performance score of at least 60% (See Appendix).
- ◆ Patients may be maintained on glucocorticoid therapy at the lowest possible dose.
- ◆ Baseline hematologic studies and chemistry profiles must meet the following criteria and must be performed within a week of initiating therapy:
  - hemoglobin greater than 9.9 gm/dl,
  - total granulocyte count greater than  $1000/\text{mm}^3$ ,
  - platelet count greater than  $60,000/\text{mm}^3$ ,
  - BUN less than 30 mg/dl, creatinine less than 2 mg/dl,
  - alkaline phosphatase and AST and ALT less than 2x upper limit of normal
  - a prothrombin time (PT) and activated partial thromboplastin time (PTT) no greater than 1.4x control unless therapeutically warranted.
- Tumor specimen of adequate size to yield protein concentration in sufficient quantity.
- Tumor-lysate peptide must be generated in sufficient quantity(>1 mg peptide) to pulse the APC's for vaccination.
- Patient must have no prior sensitivity to the components of the dendritic cell vaccine.
- Patient must agree to consider an autopsy in the event of death in an attempt to learn more concerning the nature of this treatment and tumor biology.
- Patient must be capable of signing IRB approved Research Consent and Release of Medical Records form.

**Exclusion Criteria:**

- Severe pulmonary, cardiac or other systemic disease associated with an unacceptable anesthetic or operative risk.
- The presence of an acute infection requiring active treatment will be criteria for delay or exclusion.
- Patients with a known history of an autoimmune disorder.
- Inability to give informed consent.
- Pregnancy.

**Patient will be in the study for about one year.**

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