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WEB AD

Immunotherapy and Temodar in Glioblastoma Multiforme A Phase II Trial of Dendritic Cells Pulsed with Tumor Lysate Followed by Temozolomide Upon Recurrence in Patients with Newly Diagnosed Glioblastoma

Glioblastoma multiforme (GBM) is the most aggressive and most common primary brain tumor. A diagnosis of GBM carries with it a median survival of approximately 12 months, with 90-95% of patients surviving less than two years. The current standard treatment of surgical resection followed by radiation therapy and chemotherapy has not substantially prolonged survival and even the few treatments shown to exhibit small increases in survival primarily benefit certain (i.e., young) patient subpopulations.

Cancer vaccines represent one novel therapy for recurrent malignant tumors. The goal is for the body to recognize the tumor cells as foreign and produce its own response to fight off recurring tumor cells. A promising means of generating an immune response so the body can create this immunity is through the use of dendritic cell (DC) based vaccines.

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.

Retrospective analysis of previous studies demonstrated that a number of patients who were given a chemotherapy agent - temozolomide - after administration of the vaccine appeared to have a longer survival. In this study, we will test the hypothesis, in a more controlled analysis, that temozolomide upon tumor recurrence after dendritic cell vaccination increases survival and progression free survival from that seen by temozolomide alone. And that DC vaccination may sensitize GBM to chemotherapy and specifically to temozolomide.

This Phase II, dendritic-cell based vaccine is an investigational study meaning that the therapy is not approved by the FDA as treatment but is approved by the FDA as a research study.

You are being invited to take part in this research study because you have a high grade brain tumor.

Your participation is totally voluntary; you may choose not to participate at any time before or during the study.

INCLUSION CRITERIA

- Patients must have a histopathological diagnosis (diagnosed by pathologist after he/she examines the tumor tissue) of newly diagnosed glioblastoma multiforme.
- Patients had 95% of their brain tumor surgically removed.
- No age or gender limit, although minimal weight limitation for apheresis is 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 must have a Karnofsky performance score of at least 60%
- Patients must be off steroid for at least two weeks prior to vaccination.
- Baseline laboratory results must fall within a specified range.
- Patient must be capable of signing IRB approved Research Consent and Release of Medical Records form.

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EXCLUSION CRITERIA

- Patients whose tumor progresses (gets worse) during radiation therapy and temozolomide.
- Patients with blood disorders after during radiation therapy and temozolomide that is irreversible in 2 weeks.
- Severe lung, heart 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 if unable to have negative cultures within 3 weeks.
- Patients with a known history of an autoimmune disorder.
- Pregnancy.
- Patients positive for hepatitis B, hepatitis C, HIV I/II, syphilis, HTLV I/II, HCV.

SUMMARY OF STUDY PROCEDURES

You will undergo maximal surgical resection followed by external beam radiation therapy to 60 Gy with simultaneous temozolomide ($75 \text{ mg/m}^2/\text{d} \times 42$ days or clinically indicated dose if you are under the age of 18 years). We are testing to see if the temozolomide will help make the vaccine more effective in fighting your brain tumor. MRI of the brain will be performed before and after surgery to evaluate the degree of resection. After completion of temozolomide/radiation therapy, you will undergo leukapheresis to obtain dendritic cells. You will receive 3 vaccines at 2-week intervals. Each vaccine contains 50 million tumor lysate-pulsed dendritic cells, which will be injected intradermally in 1 ml saline in the axillary (armpit) or groin region. A registered nurse will monitor you for two hours after vaccination. Four weeks after the last vaccination, you will undergo a brain MRI and a blood test to determine whether you have produced an immune response. Six weeks after the last vaccination, you will receive temozolomide $100\text{-}200 \text{ mg/m}^2/\text{d} \times 5$ days per 28-day period. MRI of the brain scans will be performed every 2 months or every 2 cycles of chemotherapy, or as clinically indicated. If the disease remains stable, you will continue with chemotherapy. Should the disease progress (get worse) or the tumor recurs (comes back), you will be taken off the trial and further consideration will be given to surgery and/or other appropriate treatment therapies.

We think you will be in the study for about one year.

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