

WEB AD:

A PHASE II OPEN-LABEL, MULTIPLE-DOSE STUDY OF
INTRACAVITARY ADMINISTERED ¹³¹I-TM-601 IN ADULT
PATIENTS WITH RECURRENT HIGH-GRADE GLIOMA

LAY TITLE:

¹³¹I-TM-601 in Patients with Recurrent High Grade Glioma

The primary purposes of this phase II study is to study the safety and tolerability of three (3) and six (6) repeat doses of TM-601 when coupled to non-experimental radioactive ¹³¹I and to evaluate the effect of this drug on high-grade gliomas.

¹³¹I-TM 601 is composed of a synthetically prepared compound (TM-601) known as a polypeptide (a type of protein), which has been coupled (combined) to radioactive iodine (¹³¹I). TM-601 binds (attaches) to tumor cells through a specific receptor (specific area) found on malignant brain tumor cells, but not found in normal brain tissue. Testing in cell lines and animal models suggest that TM-601 binds to glioma cells with great affinity (likelihood). Preclinical data suggests that ¹³¹I-TM 601 may be useful in the diagnosis and treatment of malignant brain tumors. Treatment with ¹³¹I is not experimental and has been used in the treatment of malignant brain tumors in other clinical studies. It is known that radioactivity is one of the most effective treatments for glioma, but the amount of radioactivity that can be delivered is often limited by the risk of radiation damage to normal brain tissues. This limits the radiation doses that can be delivered to where the glioma cells have infiltrated (spread) into normal brain. Attaching radioactive iodine to TM-601 (¹³¹I-TM 601) may provide a way to focus and concentrate radioactivity on malignant brain tumors, resulting in efficient localized delivery of radioactivity to these tumors.

This study is the second trial sequence (phase) following the dose escalation (increase) phase of the study, which has been completed. During the first trial sequence, dose escalation phase, the dose of drug that was best tolerated by patients without causing too much toxicity (bad side effects), known as the maximum tolerated dose (MTD), was to be determined (figured out). However, the MTD was not reached in the dose escalation phase; therefore, the dose will be the pre-set dose, 40mCi per injection. A total of either 120 or 240 mCi for 3-injection and 6-injection groups respectively. Patients participating in this study will be randomized to one of the two groups (3-dose cycle versus 6-dose cycle of ¹³¹I-TM-601) by chance, like the flip of a coin.

During this randomized phase a total of 54 patients (in up to 10 clinical sites) will be randomly selected to receive either three (3) or six (6) intracavitary injections. There will be a seven (7) day interval (period) between each injection, but your physician may decide to extend this interval for up to a maximum of 28 days as well as to reduce the dose based on your clinical tolerance after the injection.

After your eligibility to participate is determined, you will also be asked to sign a consent form prior to your debulking surgery (the surgery to remove as much of the tumor as possible) allowing for the placement of a ventricular access device (VAD) at the time of surgery. The placement of this device is not standard procedure for patients having this surgery, however it is a standard device used for administering different types of drugs/medicines. The VAD will be used to deliver 131I-TM-601 to the brain. Catheter placement and patency (openness) will be verified by injecting a contrast agent - a substance that makes the x-ray better visible - (Omnipaque® or 111In-DPTA) following by x-ray prior to each 131I-TM-601 injection. You will stay under close observation for four hours after the injection. If no signs and/or symptoms of toxicity are observed you will be discharged; however, your doctor may place you on steroid (anti-swelling) medication for several days following the injection.

Physical examination, neurological examination, clinical laboratory tests, pregnancy test, brain MRI, electrocardiogram (ECG), Karnofsky Performance assessment, Spitzer QOL, disease progression/survival, concomitant medication, and adverse events may be evaluated at the following time points: 1) at screening; 2) within three days prior to the first injection; 3) prior to receiving the first injection; 4) within 3 days prior to each subsequent injection; 4) seven to 11 days following the first injection; 5) at 3-month, 6-month, 9-month, and 12-month follow-up visits. In addition, a hematological test (complete blood count with differential and platelet count) will be done 24 to 32 days following the final injection, and a 5-ml blood sample (1 teaspoon) will also be obtained at day 90 for TM-601 serum antibody testing and other non-clinical studies to be performed by the sponsor, TransMolecular, Inc.

Following the 12-month follow-up visit, you may choose to continue your care at Cedars-Sinai Medical Center and have regular follow-up appointments with your doctor to monitor your response to the therapy. Or if you choose to continue your care elsewhere, you will be contacted every 3 to 4 months and queried regarding your medical status.

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

INCLUSION CRITERIA

Disease Characteristics:

- Patient has had prior histologically (by tumor tissue analysis using the microscope) confirmed diagnosis of malignant glioma (grade 3 or 4, including anaplastic astrocytoma, gliosarcoma, glioblastoma multiforme or malignant oligoastrocytoma)
- Glioma has progressed (became larger) or recurred (new tumor appeared) following radiotherapy that was no less than 50 Gy (+/- chemotherapy; +/- surgery)
- Imaging shows recurrent (has come back) unilateral (on one side), supratentorial tumor(s) (above the tentorial area of the brain)
- There is no diffuse leptomeningeal disease

- The patient is a candidate for re-operation independent (despite) of intended treatment with ¹³¹I-TM-601
- Patient has a Karnofsky Performance Status \geq 60%
- Based on the neurosurgeon's judgment, a single surgical cavity of less than 100 cc in volume will be created and result in removal of \geq 80% of the tumor burden (volume) (based on T1 weighed gadolinium image)
- For patients with previous radio-surgery or enhanced radiotherapy, based on the neurosurgeon's judgment, the area of enhancement can be removed during surgery
- Based on the neurosurgeon's judgment, there is no anticipated physical connection between the post-resection tumor cavity and the cerebral ventricle

Patient Characteristics:

- Male or female patients 18 years of age or older
- Patient has recovered from toxicity of prior therapies; an interval of at least 12 weeks must have elapsed since the completion of the most recent course of radiation (including radiosurgery and enhanced radiotherapy), treatment with Gliadel® or the previous surgery, while at least 4 weeks must have elapsed since the completion of a non-nitrosourea containing chemotherapy regimen and at least 6 weeks since the completion of a nitrosourea containing chemotherapy regimen
- Patient has a Karnofsky Performance Status \geq 60%
- Patient's life expectancy, based on the Investigator's judgment, is at least 3 months
- Patient has no uncontrolled seizures or other neurological conditions that would interfere with evaluation
- Patient is not currently receiving, or is not anticipated to receive, concomitant anticancer agent(s) during the course of this study
- Patient is able to give voluntary written informed consent and can comply with the study protocol

EXCLUSION CRITERIA

- Patient who has concurrent malignancy except curatively treated basal or squamous cell carcinoma of the skin or carcinoma in situ of the cervix and/or breast or patients with prior malignancies that have not been disease-free for five years
- Patient with known allergy to iodine, iodine containing drugs or Omnipaque® contrast agent
- Patient with the potential for pregnancy or impregnating their partner and who do not agree to follow an acceptable birth control method to avoid conception
- Female patient of childbearing potential who has a positive serum pregnancy test or are lactating.
- Patient previously admitted to this study

RB No.: Pro00008863/ CR00001796

Approval Date: 5/1/2007

Expiration Date: 4/30/2008

Page 4 of 4

- Patient with any other condition or situation judged by the PI to preclude compliance with the objectives and procedures of this protocol

For More Information Contact:

Adam Mamelak, MD, Principal Investigator

8631 West Third Street, Suite 800E

Los Angeles, CA 90048

310-423-7900

mamelaka@cshs.org