

Phase I Study of MK-1775 with Radiation and Temozolomide in Patients with Newly Diagnosed Glioblastoma and Evaluation of Intratumoral Drug Distribution in Patients with Recurrent Glioblastoma

This research is being done because this type of tumor is almost never cured with surgery, radiation, or chemotherapy. For this reason, we are trying to find new drugs to improve treatment for this tumor. The study you are being asked to join uses an investigational drug called MK-1775.

In Arm 2 we will test the best dose of MK-1775 to give when taking standard TMZ for 5 out of every 28 days following the completion of radiation therapy. Arm 2 includes only patients who have completed radiation therapy combined with TMZ.

You will be assigned a dose of MK-1775 when you enter the study. You will be told what your dose is and it will not be increased. You will be given the same or a lower dose throughout your treatment. You will be given a lower dose if you experience side effects that require reduced dosing. We will also be looking at the side effects of MK-1775 and temozolomide.

- You will have a complete physical exam and blood tests. Your physical examination will include:
 - a medical history
 - measurement of your height, weight, blood pressure, temperature, respiratory rate, heart rate
 - performance status, which measures the degree of your ability to complete daily activities (e.g., dressing and eating)
- You will have a complete neurological exam to test your ability to think, your muscle strength, balance, and other functions of the brain.
- To measure the extent of your brain tumor, you will have an MRI (magnetic resonance imaging) scan, which is a method of obtaining pictures of internal soft bodily tissue through the use of powerful magnets and radio waves.
- As part of your screening tests, about 3 tablespoons of blood will be drawn from one of your veins to conduct laboratory tests (e.g., standard blood count including a count of your platelets, and blood chemistries). You will also be asked to have a pregnancy test if you are a woman that is able to have children. If you are pregnant you will not be permitted to participate in this study.

Arm 2 Initiation cycle RT+TMZ, no MK-1775

Arm 2 – 28-Day Cycles (up to 6 cycles)

MK-1775: Days 1 & 3 (MW) **OR** Days 1, 3, 5 **OR** Days 1-5 of each cycle

TMZ: Days 1-5 of each cycle

- Treatment cycles are 28 days (4 weeks). You will begin taking MK-1775 and temozolomide together on the same day at the beginning of each cycle (Day 1).
- MK-1775 will be taken in the form of a pill during the first 5 days of each cycle, either on Days 1 and 3; or on Days 1, 3, and 5; or on Days 1-5, depending on your assigned dose. The number of pills you take will also depend on your assigned dose. Your study doctor or nurse will provide specific dosing instructions.
- TMZ and MK-1775 must be taken on an empty stomach. You cannot eat or drink anything except water for two hours before taking your pills and for one hour after taking your pills. Medication to prevent nausea and vomiting will be prescribed by your doctor while taking temozolomide. This is part of standard care for 5-day temozolomide treatment.
- If you miss a dose or vomit after taking your dose do not replace it; missed or vomited doses should not be made up.
- **During the study**, physical and neurologic exams will be repeated and your vital signs will be measured (including temperature, heart rate, blood pressure, respiratory rate). Routine blood tests will be done. If at any point your blood counts are low, these blood tests will be repeated more often. Your blood counts will be checked at least once every week during study treatment.
- **Research Blood Samples:**
As part of this study, we will be collecting extra blood samples in order to check the amount and activity of MK-1775 in your blood. Approximately 1 teaspoon of blood will be drawn for each sample. These extra blood tests are for research purposes only and would not be part of your standard care. The costs associated with collecting and processing these blood samples will not be charged to you or your insurance company.

These blood samples will be drawn on the following days during Cycle 1.

- Day 1: 5 minutes pre-dose and then 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours and 8 hours post-dose.
- Day 2: 24 hours after MK-1775 was administered on Day 1
- Day 4: 5 minutes pre-dose and then 30 minutes, 1 hour, 2 hours, 4 hours, 6 hours and 8 hours post-dose.
- Day 5: 24 hours after MK-1775 was administered on Day 4

Contact information:

- Research nurse: Silvia Petrik, RN 410-502-5343 (email: spetrik@jhmi.edu)
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- Evening, Weekends, Holidays 410-955-4331 (ask for "Medical Oncologist on call")