ABT1301-Patient information sheet

Pilot Study of MLN0128 in Preoperative Recurrent Glioblastoma (GBM) Patients

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 MLN0128. The objective of this study is to assess how well MLN0128 crosses the blood brain barrier.

You will be assigned to either Cohort A or B:

Cohort A: 5-10 patients with recurrent GBM who require surgical resection will receive a pre-operative course of MLN0128 at a dose of 5 mg taken by mouth daily for 7-9 days. This dose is the recommended dose of daily MLN0128 as determined in a Millennium-sponsored phase I study. The last dose will be administered 2-4 hours before surgery.

Cohort B (to open only if Cohort A does not meets its primary endpoint): 5-10 patients with recurrent GBM who require surgical resection will receive a single pre-operative 30 mg dose of MLN0128, taken by mouth. This dose is the recommended dose of weekly MLN0128 as determined in recent Millennium-sponsored studies. The single dose will be administered 2-4 hours before surgery.

At surgery fresh tumor tissue will be collected for correlative studies. Following recovery from surgery, all patients will receive MLN0128 post-operatively at either 5 mg QD in Cohort A and at 30 mg weekly in Cohort B.

Capsules should not be opened.
Grapefruit and grapefruit juice should be avoided while on this protocol.

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
- An electrocardiogram (EKG – a recording of the electrical activity of the heart) will be done to check your heart function.
- 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. This will be repeated throughout the study.

- 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.

Additional research procedures to be performed before starting study treatment:

- Research Sample Blood tests will be drawn prior to start of (approximately 2 tablespoons).

Research Blood Samples:
As part of this study, we will be collecting extra blood samples in order to check the amount and activity of MLN0128 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.

On days of scheduled pharmacokinetic sampling, the MLN0128 dose must be taken in the outpatient clinic (prior to bevacizumab administration), to allow for the post-dosing PK samples:

Table 9.5.1.1 Blood collection plan for Part 1 participants

Study Time Point	Time	PK Sample Number
Baseline	• Baseline, prior to the initial presurgical dose	01
Day of Surgery	• Before tumor resection	02
	• After tumor resection	03
Cycle 1, Post Surgery Cohort A: any time during Week 2 (Days 8-14) Cohort B: Week 1, Days 1-2	• 5 minutes prior to dose	04
	• 0.5 hour after dosing (±5 minutes)	05
	• 1 hour after dosing (±5 minutes)	06
	• 2 hours after dosing (±5 minutes)	07
	• 4 hours after dosing (±5 minutes)	08
	• 6 hours after dosing (±5 minutes)	09
	• 8 hours after dosing (±5 minutes)	10
	• 24 hours after taking the prior dose (±5 minutes)	11

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