PBTC-029B - A SUMMARY FOR PATIENTS AND FAMILIES

Title: PBTC-029B- A Phase 1 and Phase II Study of AZD6244 for Recurrent or Refractory Pediatric Low Grade Glioma

This is a brief summary of a clinical trial, a type of therapeutic research study. "You" refers to 'you' or 'your child' throughout this document. Clinical trials include only patients who choose to take part in the research study. Participation is entirely voluntary.

WHO MIGHT BE ELIGIBLE TO PARTICIPATE IN PBTC-029B?

Patients with histologically-confirmed primary diagnosis of pilocytic astrocytoma, low grade glioma, or optic pathway glioma that is either recurrent or refractory and for which there is no known curative therapy may be eligible for PBTC-029B. Eligible patients must be between the ages of 3-21. Female patients may not be pregnant or nursing. Chemotherapy must not have been received within 3 weeks prior to trial and nitrosourea within 6 weeks prior. Patients must have had the last fraction of local irradiation to primary tumor $\geq$12 months prior to registration; last fraction of craniospinal irradiation > 3 months prior to registration. Patients who are receiving Decadron should be stable or decreasing for at least 1 week prior to starting therapy. Medical and neurological condition must be stable at the time they begin to participate in the trial.

Patients will need medical tests to assess whether they can participate in PBTC-029B. These tests may include a medical history, physical examination, blood and urine tests and scans (MRI) of the brain and spine. Other tests may be required if doctors believe they are necessary. About 135 children from all over the U.S. will take part in PBTC-029B.

WHAT IS THE PURPOSE OF THIS STUDY?

Low grade gliomas are among the most common primary CNS neoplasms of childhood. Recent studies demonstrate constitutive activation of the BRAF oncogene by multiple mechanisms which can lead to increased MAP kinase signaling. We propose that inhibition of the MAP kinase MEK1 and MEK2 will have antitumor effects in BRAF activated tumors.

AZD6244 is an orally available small molecule inhibitor of the MAP kinase MEK1 and MEK2. Preclinical studies demonstrate that it results in MEK1and MEK2 inhibition. The purpose of this research study is to investigate an experimental drug, AZD6244, given orally for 28 consecutive days. The drug AZD6244 has been previously studied in animal models, but is not yet FDA approved. It is our hope the drug AZD6244 will be a safe and effective treatment for childhood brain tumors.

The purposes of the study, PBTC-029B, are:

- To test the effects of the study drug AZD6244
- To learn if a biomarker test on your DNA can identify other markers in your tumor which are specific to your type of cancer and determine if these other tumor markers relate to how your cancer responds to AZD6244

WHAT IS INVOLVED IN THIS STUDY?

Patients will receive the study drug, AZD6244, in the form of capsules that are taken by mouth twice every day for 28 consecutive days. This 4 week period is considered a course. You will take AZD6244 for up to 26 courses (approximately 2 years).

Most of the exams, tests, and procedures you will have are part of the routine medical care for your cancer. However, there are some extra tests that you will need to have if you take part in this study. The additional tests include:

- Screening for Tumor markers: Stored tumor material from a previous surgery will be sent for analysis.
- Echocardiogram (ECHO): To monitor your hearth, your study doctor will do an ECHO prior to starting treatment, every 3 months during treatment, and 30 days after stopping AZD6244.
- CPK (Creatine Phosphokinase): CPK will be done monthly and at any time you experience signs of muscle weakness.

MRI of the brain with diffusion will be performed prior to treatment and before courses 2, 4, 6, 8 and 10 and then every 12 weeks for the first 13 courses. MRI of the brain with diffusion will be performed every 12 weeks until the time of progression or completion of treatment during courses 14-26. Routine history and physical exams, including eye exams, will continue to take place. If you are of childbearing or child-fathering potential, effective birth control should be used while on study (e.g., abstinence, birth control pills, contraceptive implants, condoms) to avoid pregnancy.

WHAT ARE THE RISKS OF PARTICIPATING IN PBTC-029B?

Doctors watch study participants very carefully for any side effects or other problems. However, doctors do not know all the side effects that may occur. Side effects may be mild or very serious. The pills used in this study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. The study doctor will be testing your blood and will let you know if changes occur that may affect your health.

Common side effects of AZD6244 include diarrhea, nausea, vomiting, swelling of the body, fatigue, acne, and rash. You should not become pregnant, breastfeed, or father a baby while on this study because how AZD6244 may affect an unborn baby is unknown. You should talk to your study doctor about any side effects that you have while taking part in the study.

There may be unknown risks and discomforts involved in participating in this or any clinical trial. The health care team may give participants medicines to help lessen side effects. Doctors will notify parents and patients immediately of any important information or treatment findings discovered during the study that may affect their willingness to continue to participate.

QUESTIONS ABOUT PBTC-029B?

If you would like more information, please contact the PBTC member institution closest to you. You can also contact the doctor in charge of this study:

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OTHER INFORMATION IS AVAILABLE THROUGH

The National Cancer Institute's Cancer Information Service at 1-800-422-6237or TTY: 1-800-332-8615 or through the National Cancer Institute's websites www.Cancer.gov and www.cancer.gov/clinicaltrials. There is additional accurate and reliable information at www.cancernet.org.