SUMMARY FOR PATIENTS AND FAMILIES

PBTC-051 Phase I Study to Evaluate the Safety and Tolerability of the CD40 Agonistic Monoclonal Antibody APX005M in Pediatric Subjects with Recurrent/Refractory Brain Tumors and Newly Diagnosed Brain Stem Glioma

This is a brief summary of a clinical trial, a type of therapeutic research study. Clinical trials include only patients who choose, or whose parents permit them to take part in the research study. Participation is entirely voluntary.

Who might be eligible to participate in PBTC-051?
This study will enroll participants in two groups. The first group of participants (Stratum 1) will be limited to children whose tumor has grown after receiving radiation and/or chemotherapy. The second group (Stratum 2) will include participants with DIPG who have received radiation therapy and whose disease has not grown.

Stratum 1: Recurrent or refractory primary malignant CNS tumor patients must have adequate pre-trial frozen or FFPE tumor material (minimum of 10 unstained slides) available for the tumor gene mutation testing. Refractory/Recurrent patients must have recovered from the acute treatment related toxicities (defined as < grade 1) of all prior chemotherapy, immunotherapy, radiotherapy or any other treatment modality prior to entering this study. Patients must have received their last dose of known chemotherapy at least three 21 days prior to study enrollment or at least six 42 days if prior nitrosourea. Patient must have received their last dose of the biologic agent ≥ 7 days prior to study enrollment. Stratum 1 patients will enroll on the study first.

Stratum 2: Patients with DIPG who have pre-trial tumor tissue available are requested to submit tissue; however, this is not required for eligibility. DIPG patients must have not received any prior therapy for treatment of their current CNS malignancy other than radiation therapy. Stratum 2 patients will be enrolled after a safe dose is established in Stratum 1.

Patient must be ≥ 1 and ≤ 21 years of age at the time of enrollment. Patients' medical and neurological condition must be stable for a minimum of 1 week prior to enrollment. Patients requiring systemic treatment with either corticosteroids (greater than physiologic replacement, defined as dexamethasone 0.75 mg/m^2/day) or other immunosuppressive medications within 14 days of study drug administration will be excluded. Female patients may not be pregnant or nursing. Patients of childbearing or child fathering potential must be willing to use effective contraception methods (or abstain from sexual activity) while being treated on this study and for 30 days following treatment.

Patients will need medical tests to assess whether they can participate in PBTC-051. These tests may include a medical history, physical examination, blood and urine tests, ECG, Echocardiogram or MUGA scan, and scans (MRI) of the brain. Other tests may be required if doctors believe they are necessary.

Why is PBTC-051 being done?

The purpose of this study is to test the safety of the investigational study drug called APX005M in children. This study tests different doses of the drug to find out what effects, if any, it has on children. There will be about 45 people taking part in this study.

The primary goals of this study are:

- To study the effects of this drug on your body
- To determine the highest safe dose of APX005M for children
- To learn how children's bodies handle APX005M by measuring the amount of study drug in the body at different time points. This is called a pharmacokinetic (PK) study.
- To assess biomarkers (markers that may help researchers understand the disease and effectiveness of APX005M) in blood and tumor tissues
- To assess any shrinkage in your tumor

What is involved in this study?

Different doses of the study drug APX005M will be given to small groups of study participants. The first several study participants in Stratum 1 will receive the lowest dose. If the drug does not cause serious side effects, it will be given to other study participants in Stratum 1 at a higher dose. The doses will continue to increase for every group of study participants until side effects occur that require the dose to be lowered. The study will be stopped in Stratum 1 when the highest safe dose is determined in pediatric patients. Stratum 2 patients will be enrolled after a safe dose is established in Stratum 1 to determine if the same dose can be used in these participants as well.

APX005M will be given once every three weeks as an infusion into your vein over approximately one hour. You will receive the APX005M treatment for 36 courses (approximately 2 years) if you do not have serious side effects and your tumor does not grow. The study doctor will continue to watch you for side effects and follow your condition until 30 days after the last administration of study drug or until your tumor starts to grow or you start other treatment for your cancer. DIPG patients treated in Stratum 2 who are removed from treatment will be followed for up to 3 years.

Routine blood and urine tests will be performed prior to enrollment, weekly during the first two courses, prior to each infusion courses 3 through 36, and also at end of treatment. Routine history and physical exams will continue to take place. Standard MRI brain with and without contrast will be performed within 3 weeks prior to enrollment, at the end of course 2, every 3 courses through course 14, and then every 4 courses till the end of therapy, and at the time of disease progression or completion of treatment.

What are the risks of participating in PBTC-051?

Doctors watch study participants very carefully for any side effects or other problems. However, doctors do not know all the side effects which may occur. Side effects may be mild or very serious. In some cases, side effects may be long lasting or may never go away. There also is a risk of death. Many side effects may go away soon after someone stops using the APX005M.

Some of the side effects of the APX005M may include fever, chills, tiredness, vomiting, flushing, infusion reaction, flu like symptoms, bruising, bleeding, anemia, infection, dry mouth, taste changes, nausea, hiccups, diarrhea, liver damage, throat irritation, chest discomfort, headache, dizziness, numbness, high blood pressure, low blood pressure, itching; rash, hives, weight loss, allergic reactions, and lung problems (pulmonary edema), abnormal heartbeat, and heart attack.

There might be other side effects that researchers do not yet know about. If important new side effects are found, your study doctor will discuss these with you.

The health care team may give study participants medicines to help lessen side effects. Doctors will notify patients immediately of any important information or treatment findings discovered during the study that may affect their willingness to continue to participate.

What if I have more questions about PBTC-051?

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

Ira Dunkel, MD
Memorial Sloan Kettering Cancer Center
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Other information will be available through the following:
The National Cancer Institute's (NCI) Cancer Information Service at 1-800-4-CANCER (1-800-422-6237) or through the NCI's Web site such as www.cancer.gov and www.cancer.gov/clinicaltrials. There is additional accurate and reliable information at www.cancernet.org.

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