Title: PBTC-037-A phase I study of intratumoral/peritumoral herpes simplex virus-1 mutant HSV1716 in patients with refractory or recurrent high grade gliomas (HGG)

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-037?

Patients with histologically-confirmed primary diagnosis of high grade glioma that is either recurrent or refractory and for which there is no known curative therapy may be eligible for PBTC-037. Patients with metastatic disease are not eligible. Eligible patients must be between the ages of 12-21 and amenable to surgical resection. 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. Craniospinal radiation must have concluded 3 months prior to registration and Decadron dose should be stable or decreasing for at least 1 week prior to starting therapy. Patients’ 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-037. 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 24 children from all over the U.S. will take part in PBTC-037.

WHAT IS THE PURPOSE OF THIS STUDY?

Novel therapeutic approaches, such as oncolytic viral therapy, warrant clinical investigation. HSV1716 is a virus that has a gene which has been changed in such a way that it multiplies in dividing cells like in your tumor and kills the tumor cells. The purpose of this research study is to investigate an experimental drug, HSV1716, given by injection following surgical resection. The drug HSV1716 has been previously studied in a small number of children, in a variety of tumors, but is not yet FDA approved. It is our hope the drug HSV1716 will be a safe and effective treatment for childhood brain tumors.

The purposes of the study, PBTC-037, are:

- To find the highest dose of the drug HSV1716 that can be given without causing severe side effects.
- To learn what side effects may occur when the drug HSV1716 is given.
- To learn how the body processes the drug HSV1716 by studying the levels of the drug in the blood over time.
- To learn more from blood tests to help clinicians and researchers understand how the drug HSV1716 is working and to see if changes in these blood tests are related to how the tumor responds to HSV1716.
- To learn how certain tumors respond to the drug HSV1716 by studying the characteristics of these tumors in a laboratory.

WHAT IS INVOLVED IN THIS STUDY?

Patients will receive one injection of HSV1716 which will be injected into or near your tumor during surgery. You will be followed for serious events (observation period) for 56 days after the injection of HSV1716. You will continue be followed for 15 years from the time of injection.

Routine urine tests, mouth swabs, and blood tests will be performed before your surgery, and on days 4,7,14,21, 28 and 42 days after the HSV1716 injection then will continue once a month during months...
2,3,4, 8 and 12, once every 6 months for 5 years and then yearly through 15 years. HSV-1 immune status will be observed in the blood prior to injection, day +28 and 2 months post injection. Starting 12 months post injection, blood will be drawn every 6 months for 5 years and then yearly for up to 15 years post injection.

MRI of the brain will be performed within 72 hours of HSV1716 injection and 2 months following injection. Additional imaging studies (MRI diffusion and MR perfusion) will be obtained during your standard MRI of the brain. Routine history and physical exams will continue to take place. If your child is 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-037?

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 injection of HSV1716, used in this research study may affect how different parts of your body work such as your liver, kidneys, heart, and blood. Doctor will be testing your blood and will let you know if changes occur that may affect your health. Other medications may be given to lessen side effects. In some cases, side effects may be long lasting or may never go away. There is also a risk of death.

Some of the common side effects of HSV1716 include chills, fever, headache and fatigue. You should not become pregnant or father a baby while on this study because how HSV1716 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-037?

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 1-800-422-6237 or 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.