

SUMMARY FOR PATIENTS AND FAMILIES

PBTC-056 A Phase I Study of the ADAM-10 inhibitor, INCB7839 in children with recurrent/progressive high-grade gliomas to target microenvironmental neuroligin-3

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-056?

This study will enroll patients who have recurrent or progressive diffuse intrinsic pontine glioma (DIPG), H3K27M-mutant diffuse midline glioma (DMG), glioblastoma multiforme, anaplastic astrocytoma or anaplastic oligodendroglioma.

Patient must be ≥ 3 and ≤ 21 years of age at the time of enrollment. Patients' medical and neurological condition must be stable for a minimum of 7 days prior to enrollment. Patients requiring systemic treatment with dexamethasone must be on a stable or decreasing dose for at least 7 days prior to enrollment. Female patients may not be pregnant or nursing. Patients of childbearing or child fathering potential must be willing to use a medically acceptable form of birth control, which includes abstinence, while being treated on this study.

Patients will need medical tests to assess whether they can participate in PBTC-056. These tests may include a medical history, physical examination, blood and urine tests, knee X-ray (and knee MRI if clinically indicated), and scans (MRI) of the brain. Other tests may be required if doctors believe they are necessary.

Why is PBTC-056 being done?

The purpose of this study is to test the safety of the investigational study drug called INCB7839 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 28 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 INCB7839 for children
- To learn how children's bodies handle INCB7839 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 INCB7839) in blood and CSF (fluid surrounding the brain or spinal cord)
- To assess any shrinkage in your tumor

What is involved in this study?

Two different doses of the study drug INCB7839 will be given to small groups of study participants. The first several study participants will receive the dose similar to the recommended dose in adults adjusted by the body surface area. If the drug does not cause serious side effects, it will be given to other study participants as the recommended dose in pediatric patients. The dose

will decrease if side effects occur that require the dose to be lowered. The study will be stopped when the higher safe dose is determined in pediatric patients.

INCB7839 will be given orally, twice a day each day for 28-day cycles. You will receive the INCB7839 treatment for 26 cycles (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 dose of study drug or until your tumor starts to grow or you start other treatment for your cancer. Patients will be followed-up 2 years following the last dose of INCB7839.

Routine blood and urine tests will be performed prior to enrollment, weekly during the first course, prior to courses 2 through 26, 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, 4, 6, then every 12 weeks thereafter (after courses 9, 12, 15, 18, 21, 24), then after course 26 at off treatment.

What are the risks of participating in PBTC-056?

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 INCB7839.

Some of the side effects of the INCB7839 may include blood clots (in lung, arm, leg, or in a vein), nausea, vomiting, loss of appetite, flatulence, diarrhea, headache, dizziness, drowsiness, tinnitus (ringing in the ears), tiredness, fever, dehydration, pain, bleeding from the nose, difficulty breathing, rash, constipation, anemia, muscle weakness, infection, bone growth abnormality, liver damage which may cause yellowing of eyes and skin, blood clotting disorder which may cause bleeding.

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-056?

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:

Michelle Monje, MD PhD

Stanford University and Lucile Packard Children's Hospital

Phone: (650) 721-5750

E-mail: mmonje@stanford.edu

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.

This study is supported by the following funding organizations:

- The Cancer Therapy Evaluation Program (CTEP) of the National Cancer Institute (NCI)
- Incyte Corporation
- American Lebanese Syrian Associated Charities (ALSAC)