

PBTC-042 - A SUMMARY FOR PATIENTS AND FAMILIES

Title: PBTC-042- A Phase 1 Study of CDK 4-6 inhibitor PD-0332991 in children with recurrent, progressive, or refractory central nervous system tumors.

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-042?

Patients with histologically-confirmed primary diagnosis of a central nervous system (CNS) tumor that is either recurrent or refractory and for which there is no known curative therapy may be eligible for PBTC-042. Patients with low grade gliomas are excluded. Eligible patients must be between the ages of 4-21. Female patients may not be pregnant or nursing. Patients must have received no more than 2 prior chemotherapy regimens and/or focal radiotherapy for their brain tumor. 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 > 2 weeks prior to enrollment. Patients who are receiving Decadron should be stable or decreasing for at least 1 week prior to starting therapy. All colony forming growth factor(s) should be discontinued for at least one week prior to enrollment. 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-042. 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 40 people from all over the U.S. will take part in PBTC-042.

WHAT IS THE PURPOSE OF THIS STUDY?

Tumor cells grow and divide rapidly and uncontrollably. In normal cells, specific proteins and their enzymes called cyclin dependent kinases (CDK4 and 6) tightly control the process of cell division. In cancer cells, the two kinases (CDK4 and 6) are out of control and drive the cell to divide and form cancer. In this study, we are testing an experimental drug, PD-0332991, that works by inhibiting the CDK4 and 6 proteins.

The purpose of this research study is to investigate an experimental drug, PD-0332991, given orally for 21 consecutive days followed by a 7 day break. The drug PD-0332991 has been previously studied in adults, but is not yet FDA approved. It is our hope that the drug PD-0332991 will be a safe and effective treatment for childhood brain tumors.

The purposes of the study, PBTC-042, are:

- To find the highest dose of PD-0332991 that can be given without causing severe side effects.
- To learn what side effects may occur when PD-0332991 is given.
- To learn how the body handles PD-0332991 by studying the levels of the drug in the blood.

WHAT IS INVOLVED IN THIS STUDY?

Patients will receive the study drug, PD-0332991, in the form of capsules that are taken with food once a day for 21 consecutive days followed by 7 days break. This 4 week period is considered a course. You will take PD-0332991 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:

- Electrocardiogram (EKG): To monitor your heart, your study doctor will do an EKG prior to starting treatment. EKG will also be performed 3 hours after PD-0332991 is taken on days 1, 8, and 15 of Course 1, day 1 of Course 2 and 3 and then every 12 weeks and at the end of treatment.
- Pharmacokinetics (PK) blood: A total of 2 tablespoons of blood will be collected during the study to assess how the body is handling PD-0332991.

MRI of the brain with diffusion will be performed prior to treatment and course 2, 4, 6, and then every 12 weeks. 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.

Optional research tests may be requested which include Pharmacogenetics, PK after discontinuation of dexamethasone, PK of cerebral spinal fluid, and genomics testing of pre-trial tissue. The optional research tests will require an additional consent.

WHAT ARE THE RISKS OF PARTICIPATING IN PBTC-042?

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 PD-0332991 include diarrhea, nausea, anemia, bruising, bleeding, fatigue and infection. You should not become pregnant, breastfeed, or father a baby while on this study because how PD-0332991 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-042?

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:

Sridharan Gururangan, MRCP (UK)
 Preston Robert Tisch Brain Tumor Center
 Duke University Medical Center
 Durham, North Carolina 27710
 Telephone: (919) 668-6288
 Email: Sridharan.gururangan@duke.edu

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.