Summary for Patients and Families

Phase I/II trial of Dabrafenib, Trametinib, and Hydroxychloroquine (HCQ) for BRAF V600E-mutant or Trametinib and HCQ for BRAF fusion/duplication positive or NF1-associated recurrent or progressive gliomas in children and young adults

This study is being undertaken by the Pediatric Brain Tumor Consortium (PBTC). The PBTC is a group dedicated to improving treatment options for childhood brain tumors. PBTC is made up of eleven academic centers and children's hospitals in the United States.

The following is a summary of a clinical trial, a therapeutic research study. Clinical trials include only patients who choose or whose parents permit them to participate in the research study. Participation is entirely voluntary.

Who might be eligible to participate in PBTC-055?

Children with recurrent or progressive pediatric low-grade glioma, confirmed by laboratory tests. Patients must be 1-30 years of age with a minimum body weight of 9 kg at the time of enrollment for trials. Patients must have received prior therapy other than surgery. Before entering this study, they must have fully recovered from the acute treatment-related toxicities of all prior chemotherapy, immunotherapy, radiotherapy, or any other treatment modality.

Why is PBTC-055 being undertaken?

For pediatric low-grade glioma patients, there is a clear need to develop more effective therapies. This research will study the safety and efficacy of adding hydroxychloroquine to medications dabrafenib and trametinib in children with brain tumors previously treated with similar drugs and did not respond completely or whose tumor came back while receiving a similar agent.

What is involved in this study?

Treatment will be administered on an outpatient basis. One course consists of a 28-day cycle, and patients may continue treatment for 26 courses (approximately 2 years) if there is no excessive toxicity or disease progression. Patients will receive either hydroxychloroquine, dabrafenib, and trametinib or hydroxychloroquine and trametinib, depending upon the type of tumor. Dabrafenib, trametinib, and hydroxychloroquine will be given orally or by way of gastronomy (G)/nasogastric (NG) tube, in the form of capsules which must be taken whole, or an oral solution made from tablets. Hydroxychloroquine will only be administered by oral suspension. Within each combination, dabrafenib and hydroxychloroquine will be administered twice daily in a 28-day course. Trametinib will be administered once a day for 28 days during each course.

What are the risks of participating in PBTC-055?

There is a risk that patients may experience side effects from the study drugs. Some of the most common side effects that the study doctors know about are nausea, vomiting, diarrhea, decreased appetite, constipation, fatigue, fever, headache, alopecia,

skin rash, abdominal pain, peripheral edema, cough, and arthralgia. These medications may cause skin and ocular toxicity. There may be some risks that the study doctors do not yet know about.

There may be unknown risks and discomforts involved in participating in this or any clinical trial. In the event of adverse effects, the healthcare team may modify the treatment and/or incorporate additional medical tests to monitor adverse effects. Doctors will notify parents and patients immediately of any critical information or treatment findings discovered during the study that may affect their willingness to continue to participate.

QUESTIONS ABOUT THIS STUDY?

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.