A Study of the Drugs Selumetinib vs. Carboplatin and Vincristine in Patients With Low-Grade Glioma

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 2 years to 21 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- Patients must be >= 2 years and =< 21 years at the time of enrollment
- Patients must have a body surface area (BSA) of >= 0.5 m^2 at enrollment
- Patients must have non-neurofibromatosis type 1 (non-NF1) low-grade glioma (LGG) without a BRAFV600E mutation as confirmed by Rapid Central Pathology and Molecular Screening Reviews performed on APEC14B1 (NCT02402244) Childhood Cancer Data Initiative (CCDI)-MCI, or accepted Clinical Laboratory Improvement Act (CLIA)-certified test and that has not been treated with any modality besides surgery. Note: Patients may be newly-diagnosed OR previously diagnosed, and there is no required time frame between biopsy/surgery and treatment initiation.
    - Patients with residual tumor after resection or progressive tumor after initial diagnosis (with or without surgery) who have not received treatment (chemotherapy and/or radiation) are eligible
    - Patients must have two-dimensional measurable tumor >= 1 cm^2 to be eligible
    - Patients with ependymoma are not eligible
- Eligible histologies will include all tumors considered low-grade glioma or low-grade astrocytoma (World Health Organization [WHO] grade I and II) by 5th edition WHO classification of central nervous system (CNS) tumors with the exception of subependymal giant cell astrocytoma
- Patients with metastatic disease or multiple independent primary LGG are eligible
- Creatinine clearance or radioisotope glomerular filtration rate (GFR) >= 70 mL/min/1.73 m^2 OR a serum creatinine based on age/sex as follows (performed within 7 days prior to enrollment):
    - Age: Maximum Serum Creatinine (mg/dL)
    - 2 to < 6 years: 0.8 mg/dL (male); 0.8 mg/dL (female)
    - 6 to < 10 years: 1 mg/dL (male); 1 mg/dL (female)
    - 10 to < 13 years: 1.2 mg/dL (male); 1.2 mg/dL (female)
    - 13 to < 16 years: 1.5 mg/dL (male); 1.4 mg/dL (female)
    - >= 16 years: 1.7 mg/dL (male); 1.4 mg/dL (female)
- Total bilirubin =< 1.5 x upper limit of normal (ULN) for age (performed within 7 days prior to enrollment) (children with a diagnosis of Gilbert's syndrome will be allowed on study regardless of their total and indirect [unconjugated] bilirubin levels as long as their direct [conjugated] bilirubin is < 3.1 mg/dL)
- Serum glutamic pyruvic transaminase (SGPT) (alanine aminotransferase [ALT]) =< 135 U/L (performed within 7 days prior to enrollment). For the purpose of this study, the ULN for SGPT is 45 U/L
- Albumin >= 2 g/dL (performed within 7 days prior to enrollment)
- Left ventricular ejection fraction (LVEF) >= 53% (or institutional normal; if the LVEF result is given as a range of values, then the upper value of the range will be used) by echocardiogram (performed within 4 weeks prior to enrollment)
- Corrected QT (QTc) interval =< 450 msec by electrocardiography (EKG) (performed within 4 weeks prior to enrollment)
- Absolute neutrophil count >= 1,000/uL (unsupported) (performed within 7 days prior to enrollment)
- Platelets >= 100,000/uL (unsupported) (performed within 7 days prior to enrollment)
- Hemoglobin >= 8 g/dL (may be supported) (performed within 7 days prior to enrollment)
- Patients with a known seizure disorder must be stable and must not have experienced a significant increase in seizure frequency within 2 weeks prior to enrollment
- Patients 2-17 years of age must have a blood pressure that is =< 95th percentile for age, height, and sex at the time of enrollment (with or without the use of anti-hypertensive medications)
- Patients >= 18 years of age must have a blood pressure =< 130/80 mmHg at the time of enrollment (with or without the use of anti-hypertensive medications)
- Note for patients of all ages: Adequate blood pressure can be achieved using medication for the treatment of hypertension
- All patients must have ophthalmology toxicity assessments performed within 8 weeks prior to enrollment
- For all patients, an MRI of the brain (with orbital cuts for optic pathway tumors) and/or spine (depending on the site(s) of primary disease)

with and without contrast must be performed within 8 weeks prior to enrollment

- Patients must have a performance status corresponding to Eastern Cooperative Oncology Group (ECOG) scores of 0, 1, or 2. Use Karnofsky for patients > 16 years of age and Lansky for patients =< 16 years of age
- Patients must have the ability to swallow whole capsules
- All patients and/or their parents or legal guardians must sign a written informed consent
- All institutional, Food and Drug Administration (FDA), and National Cancer Institute (NCI) requirements for human studies must be met
- All patients have signed an appropriate consent form and Health Insurance Portability and Accountability Act (HIPAA) authorization form (if applicable)
- All patients have been consented and enrolled on APEC14B1 (NCT02402244) Part A for Pre-Enrollment Eligibility Screening for ACNS1833

Exclusion Criteria:

- Patients must not have received any prior tumor-directed therapy including chemotherapy, radiation therapy, immunotherapy, or bone marrow transplant. Prior surgical intervention (with the exclusion of laser interstitial thermal therapy [LITT]) is permitted
- Patients with a concurrent malignancy or history of treatment (other than surgery) for another tumor within the last year are ineligible
- Patients with diffuse intrinsic pontine tumors as seen on MRI (> 2/3 of pons involvement on imaging) are not eligible even if biopsy reveals grade I/II histology
- Patients may not be receiving any other investigational agents
- Patients with any serious medical or psychiatric illness/condition, including substance use disorders or ophthalmological conditions, likely in the judgment of the investigator to interfere or limit compliance with study requirements/treatment
- Patients who, in the opinion of the investigator, are not able to comply with the study procedures are not eligible
- Female patients who are pregnant are not eligible since fetal toxicities and teratogenic effects have been noted for several of the study drugs. A pregnancy test is required for female patients of childbearing potential
- Lactating females who plan to breastfeed their infants are not eligible
- Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of their study participation and for 1 week after stopping study therapy are not eligible.
    - Note: Women study participants of child-bearing potential must use acceptable contraception during the study and for 1 week (7 days) after the last dose of selumetinib. Men study participants with sexual partners who are pregnant or who are of child-bearing potential must use acceptable contraception during the study and for 1 week (7 days) after the last dose of study agent. Acceptable contraception includes implants, injectables, or oral contraceptives (all combined with barrier methods), some intrauterine devices (IUDs), vasectomy or abstinence
- Known genetic disorder that increases risk for coronary artery disease. Note: The presence of dyslipidemia in a family with a history of myocardial infarction is not in itself an exclusion unless there is a known genetic disorder documented
- Symptomatic heart failure
- New York Health Association (NYHA) class II-IV prior or current cardiomyopathy
- Severe valvular heart disease
- History of atrial fibrillation
- Current or past history of central serous retinopathy
- Current or past history of retinal vein occlusion or retinal detachment
- Patients with uncontrolled glaucoma
    - If checking pressure is clinically indicated, patients with intraocular pressure (IOP) > 22 mmHg or ULN adjusted by age are not eligible
- Supplementation with vitamin E greater than 100% of the daily recommended dose. Any multivitamin containing vitamin E must be stopped prior to study enrollment even if less than 100% of the daily recommended dosing for vitamin E
- Surgery within 2 weeks prior to enrollment, with the exception of surgical biopsy, placement of a vascular access device or cerebral spinal fluid (CSF) diverting procedure such as endoscopic third ventriculostomy (ETV) and ventriculoperitoneal (VP) shunt.
    - Note: Patients must have healed from any prior surgery
- Patients who have an uncontrolled infection are not eligible

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, DRUG: Carboplatin, PROCEDURE: Echocardiography Test, PROCEDURE: Magnetic Resonance Imaging, OTHER: Questionnaire Administration, DRUG: Selumetinib Sulfate, DRUG: Vincristine Sulfate
Conditions:
Low Grade Astrocytoma, Low Grade Glioma, Metastatic Low Grade Astrocytoma, Metastatic Low Grade Glioma, WHO Grade 1 Glioma, WHO Grade 2 Glioma

More Information

Description:
This phase III trial compares the effect of selumetinib versus the standard of care treatment with carboplatin and vincristine (CV) in treating patients with newly diagnosed or previously untreated low-grade glioma (LGG) that does not have a genetic abnormality called BRAFV600E mutation and is not associated with systemic neurofibromatosis type 1. Selumetinib works by blocking some of the enzymes needed for cell growth and may kill tumor cells. Carboplatin is in a class of medications known as platinum-containing compounds. It works in a way similar to the anticancer drug

tumor cells. Carboplatin is in a class of medications known as platinum-containing compounds. It works in a way similar to the anticancer drug cisplatin, but may be better tolerated than cisplatin. Carboplatin works by killing, stopping or slowing the growth of tumor cells. Vincristine is in a class of medications called vinca alkaloids. It works by stopping tumor cells from growing and dividing and may kill them. The overall goal of this study is to see if selumetinib works just as well as the standard treatment of CV for patients with LGG. Another goal of this study is to compare the effects of selumetinib versus CV in subjects with LGG to find out which is better. Additionally, this trial will also examine if treatment with selumetinib improves the quality of life for subjects who take it.

Contact(s): - cancer@cchmc.org
Principal Investigator:
Principal Investigator ID:
Phase: PHASE3
IRB Number:
System ID: NCT04166409
