COG ACNS1833 - A Phase 3 Randomized Non-Inferiority Study of Carboplatin and Vincristine versus Selumetinib (NSC# 748727, IND# 77782) in Newly Diagnosed or Previously Untreated Low-Grade Glioma (LGG) not associated with BRAFV600E Mutations or Systemic Neurofibromatosis Type 1 (NF1)

Status: Recruiting

Eligibility Criteria

Sex: All
Age Group: 2 years to 21 years old

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) 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 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/gender 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 should be stable and should 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 gender 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 4 weeks prior to enrollment For all patients, a magnetic resonance imaging (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 4 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 have signed an appropriate consent form and Health Insurance Portability and Accountability Act (HIPAA) authorization form (if applicable) All patients and/or their parents or legal guardians must sign a written informed consent All patients have been consented and enrolled on APEC14B1 (NCT02402244) followed by enrollment on the ACNS1833 Pre-Enrollment Eligibility Screening (Step 0) on the same day to complete the Rapid Central Review All institutional, Food and Drug Administration (FDA), and National Cancer Institute (NCI) requirements for human studies must be met

Exclusion Criteria:

Patients must not have received any prior tumor-directed therapy including chemotherapy, radiation therapy, immunotherapy, or bone marrow transplant. Prior surgical intervention 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 12 weeks after stopping study therapy are not eligible. Note: Women of child-bearing potential and males with sexual partners who are pregnant or who could become pregnant (i.e., women of child-bearing potential) should use effective methods of contraception for the duration of the study and for 12 weeks after stopping study therapy to avoid pregnancy and/or potential adverse effects on the developing embryo 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: Magnetic Resonance Imaging, Other: Quality-of-Life Assessment, Other: Questionnaire Administration, Drug: Selumetinib Sulfate, Drug: Vincristine Sulfate

More Information

Description: The overall goal of this phase 3 non-inferiority study is to assess if selumetinib works as well as the standard treatment using carboplatin and vincristine (called CV) for subjects with low-grade glioma (LGG).
Study Contact: Allison Fullenkamp - fulle631@umn.edu
Principal Investigator: Christopher Moertel, MD
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