COG ACNS1721 - A Phase 2 Study of Veliparib (ABT-888, IND # 139199) and Local Irradiation, Followed by Maintenance Veliparib and Temozolomide, in Patients with Newly Diagnosed High-Grade Glioma (HGG) without H3 K27M or BRAFV600 Mutations

Status: Completed

Eligibility Criteria

Sex: All
Age: 3 Years to 25 Years old
This study is NOT accepting healthy volunteers

Inclusion Criteria:
- Stratum 1 (IDH wild-type): Patients must be >= 3 years of age and <= 21 years of age at the time of enrollment
- Please note Stratum 1 was closed to accrual on January 24, 2020
- Stratum 2 (IDH mutant): Patients must be >= 3 years of age and <= 25 years of age at the time of enrollment
- Patients must have histological verification of diagnosis. Patients with M+ disease (defined as evidence of neuraxis dissemination) are not eligible. Cerebrospinal fluid (CSF) cytology is not required but may be obtained if clinically indicated prior to study enrollment. If cytology is positive, the patient would be considered to have metastatic disease and would, therefore, be ineligible
- Pre-operative and post-operative brain magnetic resonance imaging (MRI) with and without contrast must be obtained. The requirement for a post-operative MRI is waived for patients who undergo biopsy only. A spine MRI is not required, but may be obtained if clinically indicated. If the spine MRI is positive, the patient would be considered to have M+ disease (defined as neuraxis dissemination) and would be ineligible
- 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
- Peripheral absolute neutrophil count (ANC) >= 1,000/uL (within 7 days prior to enrollment)
- Platelet count >= 100,000/uL (transfusion independent) (within 7 days prior to enrollment)
- Hemoglobin >= 8.0 gm/dL (can be transfused) (within 7 days prior to enrollment)
- Total bilirubin <= 1.5 x upper limit of normal (ULN) (within 7 days prior to enrollment)
- 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 (within 7 days prior to enrollment):
  - 3 to < 6 years: 0.8 (male and female) maximum serum creatinine (mg/dL)
  - 6 to 10 years: 1 (male and female) maximum serum creatinine (mg/dL)
  - 10 to < 13 years: 1.2 (male and female) maximum serum creatinine (mg/dL)
  - 13 to < 16 years: 1.5 (male), 1.4 (female) maximum serum creatinine (mg/dL)
  - >= 16 years: 1.7 (male), 1.4 (female) maximum serum creatinine (mg/dL)
  - Total bilirubin <= 1.5 x upper limit of normal (ULN) for age (within 7 days prior to enrollment)
- Serum glutamate pyruvate transaminase (SGPT) alanine aminotransferase (ALT) <= 135 U/L. For the purpose of this study, the ULN for SGPT is 45 U/L
- Patients with seizures disorder may be enrolled if seizures are well-controlled (i.e., patients must not have required rescue medications for uncontrolled seizures within 14 days prior to enrollment)
- Patients must be enrolled and protocol therapy must be projected to begin no later than 31 days after definitive surgery (Day 0). If a biopsy only was performed, the biopsy date will be considered the date of definitive surgery. For patients who have a biopsy or incomplete resection at diagnosis followed by additional surgery, the date of the last resection will be considered the date of definitive surgery
- 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

Exclusion Criteria:
- Patients with the following histologies:
  - Diffuse astrocytoma (grade 2)
  - Oligodendrogliomas (any grade)
  - Pleomorphic xanthoastrocytoma (PXA, any grade)
  - Patients with primary tumor location of brainstem or spinal cord
  - Patients with M+ disease (defined as neuraxis dissemination either by imaging or by cytology)
  - Patients with treatment-related acute myeloid leukemia (AML) (t-AML)/myelodysplastic syndrome (MDS) or with features suggestive of AML/MDS
  - Prior allogeneic bone marrow transplant or double umbilical cord blood transplantation
  - Patients must not have received any prior tumor-directed therapy including radiation therapy, chemotherapy (tumor-directed therapy), molecularly targeted agents, or immunotherapy for the treatment of HGG other than surgical intervention and/or corticosteroids
  - Lumbar CSF cytology is not required, but may be performed if clinically indicated prior to study enrollment. If lumbar CSF cytology is positive, the patient is considered to have M+ disease and is ineligible
- Note: False positive cytology can occur within 10 days of surgery
- Patients with gliomatosis cerebri type 1 or 2
- Patients who are not able to receive protocol specified radiation therapy
- Patients must not be currently receiving other anti-cancer agents
- Patients with known constitutional mismatch repair deficiency syndrome (CMMR-D)/biallelic mismatch repair deficiency (bMMRD)
- Female patients who are pregnant are ineligible due to risks of fetal and teratogenic adverse events as seen in animal/human studies
- Lactating females are not eligible unless they have agreed not to breastfeed their infants
- Female patients of childbearing potential are not eligible unless they have a negative pregnancy test result has been obtained
- Sexually active patients of reproductive potential are not eligible unless they have agreed to use an effective contraceptive method for the duration of their study participation and for 6 months after the last dose of protocol-specified chemotherapy

Conditions & Interventions
**Interventions:**
Radiation: Radiation Therapy, Drug: Temozolomide, Drug: Veliparib

**Conditions:**
Anaplastic Astrocytoma, Glioblastoma, Malignant Glioma

**More Information**

**Description:** This phase II trial studies how well veliparib, radiation therapy, and temozolomide work in treating participants (≥ 3 years of age and ≤ 25) with newly diagnosed malignant glioma without H3 K27M or BRAFV600E mutations. Veliparib may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. Radiation therapy uses high energy x-rays to kill tumor cells and shrink tumors. Drugs used in chemotherapy, such as temozolomide, work in different ways to stop the growth of tumor cells, either by killing the cells, by stopping them from dividing, or by stopping them from spreading. Giving veliparib, radiation therapy, and temozolomide may work better in treating participants with newly diagnosed malignant glioma without H3 K27M or BRAFV600E mutations.

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**Phase:** Phase 2

**IRB Number:** STUDY00005445

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