A Study of the Drug Selinexor With Radiation Therapy in Patients With Newly-Diagnosed Diffuse Intrinsic Pontine (DIPG) Glioma and High-Grade Glioma (HGG)

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 12 months to 21 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

- PRE ENROLLMENT: Patients must be =< 25 years of age at the time of enrollment on APEC14B1 part A central nervous system (CNS)/high grade glioma (HGG) pre-enrollment eligibility screening
    - Please note:
    - This required age range applies to pre-enrollment eligibility for all HGG patients. Individual treatment protocols may have different age criteria.
    - Non-DIPG patients with tumors that do not harbor an H3K27M-mutation and are >= 18 years of age will not be eligible to enroll on ACNS1821 (Step 1).
- PRE ENROLLMENT: Patient is suspected of having localized, newly diagnosed HGG, excluding metastatic disease, OR patient has an institutional diagnosis of DIPG
    - Please note: there are specific radiographic criteria for DIPG patient enrollment on ACNS1821 (Step 1)
    - As of February 14, 2025, stratum DIPG and stratum DMG have closed to accrual, and no patients will be enrolled on these strata after Amendment #4.
- PRE ENROLLMENT:
    - For patients with non-pontine tumors: Patients and/or their parents or legal guardians must have signed informed consent for eligibility screening on APEC14B1 Part A.
    - For patients with DIPG: Patients and/or their parents or legal guardians must have signed informed consent for ACNS1821.
    - Note: As of February 14, 2025, stratum DIPG and stratum DMG have closed to accrual, and no patients will be enrolled on these strata after Amendment #4.
- PRE ENROLLMENT:
    - For patients with non-pontine tumors only, the specimens obtained at the time of diagnostic biopsy or surgery must be submitted through APEC14B1 ASAP, preferably within 5 calendar days of definitive surgery
- STEP 1: Patients must be >= 12 months and =< 21 years of age at the time of enrollment
- STEP 1: Patients must have newly-diagnosed DIPG or HGG (including DMG).
- STEP 1: Stratum DIPG (Closed with Amendment #4)
    - As of February 14, 2025, stratum DIPG and stratum DMG have closed to accrual, and no patients will be enrolled on these strata after Amendment #4.
    - Patients with newly-diagnosed typical DIPG, defined as tumors with a pontine epicenter and diffuse involvement of at least 2/3 of the pons on at least 1 axial T2 weighted image, are eligible. No histologic confirmation is required.
    - Patients with pontine tumors that do not meet radiographic criteria for typical DIPG (e.g., focal tumors or those involving less than 2/3 of the pontine cross-sectional area with or without extrapontine extension) are eligible if the tumors are biopsied and proven to be high-grade gliomas (such as anaplastic astrocytoma, glioblastoma, high-grade glioma not otherwise specified [NOS], and/or H3 K27M-mutant) by institutional diagnosis.
- STEP 1: Stratum DMG (with H3 K27M mutation) (Closed with Amendment #4)
    - As of February 14, 2025, stratum DIPG and stratum DMG have closed to accrual, and no patients will be enrolled on these strata after Amendment #4.
    - Patients must have newly-diagnosed non-pontine H3 K27M-mutant HGG without BRAF V600 or IDH1 mutations as confirmed by Rapid Central Pathology and Molecular Screening Reviews performed on APEC14B1
    - Note: Patients need not have either measurable or evaluable disease, i.e., DMG patients may have complete resection of their tumor prior to enrollment. Primary spinal tumors are eligible for enrollment. For rare H3 K27M-mutant HGG in non-midline structures (e.g., cerebral hemispheres), these patients will be considered part of Stratum DMG.
- STEP 1: Stratum HGG (without H3 K27M mutation)
    - Patients must have newly-diagnosed non-pontine H3 K27M-wild type HGG without BRAF V600 or IDH1 mutations as confirmed by Rapid Central Pathology and Molecular Screening Reviews performed on APEC14B1
    - Please note:
    - Patients who fall in this category and who are >= 18 years of age are not eligible due to another standard-of-care regimen (radiation/temozolomide) that is available
    - Patients need not have either measurable or evaluable disease, i.e., HGG patients may have complete resection of their tumor prior to enrollment. Primary spinal tumors are eligible for enrollment
- STEP 1: Patients must have a performance status corresponding to Eastern Cooperative Oncology Group (ECOG) scores of 0, 1 or 2. Use

- STEP 1: 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 who are unable to walk because of paralysis, but who are up in a wheelchair, will be considered ambulatory for the purpose of assessing the performance score.
- STEP 1: Peripheral absolute neutrophil count (ANC) >= 1000/uL (within 7 days prior to step 1 enrollment)
- STEP 1: Platelet count >= 100,000/uL (transfusion independent) (within 7 days prior to step 1 enrollment)
- STEP 1: Hemoglobin >= 8.0 g/dL (may receive red blood cell [RBC] transfusions) (within 7 days prior to step 1 enrollment)
- STEP 1: Creatinine clearance or radioisotope glomerular filtration rate (GFR) >= 70 mL/min/1.73 m^2 (within 7 days prior to step 1 enrollment) or

A serum creatinine based on age/sex as follows (within 7 days prior to step 1 enrollment):

- Age / Maximum Serum Creatinine (mg/dL)
    - 1 to < 2 years / male: 0.6; female: 0.6
    - 2 to < 6 years / male: 0.8; female: 0.8
    - 6 to < 10 years / male: 1; female: 1
    - 10 to < 13 years / male: 1.2; female: 1.2
    - 13 to < 16 years / male: 1.5; female: 1.4
    - >= 16 years / male: 1.7; female: 1.4
    - STEP 1: Total bilirubin =< 1.5 x upper limit of normal (ULN) for age
    - STEP 1: 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.
    - STEP 1: Serum amylase =< 1.5 x ULN
    - STEP 1: Serum lipase =< 1.5 x ULN
    - STEP 1: No evidence of dyspnea at rest, no exercise intolerance, and a pulse oximetry > 94% if there is clinical indication for determination.
    - STEP 1: Patients with seizure disorder may be enrolled if on anticonvulsants and well controlled.
    - STEP 1: Patients must be enrolled and protocol therapy must begin no later than 31 days after the date of radiographic diagnosis (in the case of non-biopsied DIPG patients only) or definitive surgery, whichever is the later date (Day 0).

For patients who have a biopsy followed by resection, the date of resection will be considered the date of definitive diagnostic surgery. If a biopsy only was performed, the biopsy date will be considered the date of definitive diagnostic surgery.

Exclusion Criteria:

- STEP 1: Patients must not have received any prior therapy for their central nervous system (CNS) malignancy except for surgery and steroid medications.
- STEP 1: Patients who are currently receiving another investigational drug are not eligible.
- STEP 1: Patients who are currently receiving other anti-cancer agents are not eligible.
- STEP 1: Patients >=18 years of age who have H3 K27M-wild type HGG.
- STEP 1: Patients who have an uncontrolled infection.
- STEP 1: Patients who have received a prior solid organ transplantation.
- STEP 1: Patients with grade > 1 extrapyramidal movement disorder.
- STEP 1: Patients with known macular degeneration, uncontrolled glaucoma, or cataracts.
- STEP 1: Patients with metastatic disease are not eligible; MRI of spine with and without contrast must be performed if metastatic disease is suspected by the treating physician.
- STEP 1: Patients with gliomatosis cerebri type 1 or 2 are not eligible, with the exception of H3 K27M-mutant bithalamic tumors.
- STEP 1: Patients who are not able to receive protocol specified radiation therapy.
- STEP 1:
    - Female patients who are pregnant are ineligible since there is yet no available information regarding human fetal or teratogenic toxicities.
    - Lactating females are not eligible unless they have agreed not to breastfeed their infants. It is not known whether selinexor is excreted in human milk.
    - Female patients of childbearing potential are not eligible unless a negative pregnancy test result has been obtained.
    - Sexually active patients of reproductive potential are not eligible unless they have agreed to use two effective methods of birth control (including a medically accepted barrier method of contraception, e.g., male or female condom) for the duration of their study participation and for 90 days after the last dose of selinexor. Abstinence is an acceptable method of birth control.

Conditions & Interventions

Interventions:
PROCEDURE: Biopsy Procedure, PROCEDURE: Magnetic Resonance Imaging, RADIATION: Radiation Therapy, DRUG: Selinexor
Conditions:
Malignant Glioma

More Information

Description:
This phase I/II trial tests the safety, side effects, and best dose of selinexor given in combination with standard radiation therapy in treating children and young adults with newly diagnosed diffuse intrinsic pontine glioma (DIPG) or high-grade glioma (HGG) with a genetic change called H3 K27M mutation. It also tests whether combination of selinexor and standard radiation therapy works to shrink tumors in this patient population. Glioma is a type of cancer that occurs in the brain or spine. Glioma is considered high risk (or high-grade) when it is growing and spreading quickly. The term, risk, refers to the chance of the cancer coming back after treatment. DIPG is a subtype of HGG that grows in the pons (a part of the brainstem that

controls functions like breathing, swallowing, speaking, and eye movements). This trial has two parts. The only difference in treatment between the two parts is that some subjects treated in Part 1 may receive a different dose of selinexor than the subjects treated in Part 2. In Part 1 (also called the Dose-Finding Phase), investigators want to determine the dose of selinexor that can be given without causing side effects that are too severe. This dose is called the maximum tolerated dose (MTD). In Part 2 (also called the Efficacy Phase), investigators want to find out how effective the MTD of selinexor is against HGG or DIPG. Selinexor blocks a protein called CRM1, which may help keep cancer cells from growing and may kill them. It is a type of small molecule inhibitor called selective inhibitors of nuclear export (SINE). Radiation therapy uses high energy to kill tumor cells and shrink tumors. The combination of selinexor and radiation therapy may be effective in treating patients with newly-diagnosed DIPG and H3 K27M-Mutant HGG.

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