Lutathera for Treatment of Recurrent or Progressive High-Grade CNS Tumors

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 4 years to 39 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
All participants must meet the following inclusion and exclusion criteria. No exceptions will be given. Imaging studies to establish eligibility must be done within three weeks prior to enrollment. All other clinical evaluations to establish eligibility (except for [68Ga]Ga-DOTATATE PET) must be done within 7 days prior to enrollment.

1. Screening Criteria

1.1 Diagnosis Patient must have a diagnosis of primary high-grade CNS tumor (any histopathologic diagnosis that is WHO grade III-IV) or meningioma (any histologic grade) that is recurrent, progressive, or refractory. Note that patients with DIPG (based on radiographic/clinical diagnosis) who have undergone biopsy will be eligible with histologic diagnosis of grade II-IV infiltrating glioma. All tumors must have histologic verification either at the time of diagnosis or recurrence, except for patients meningioma who have not previously undergone biopsy or resection.

Note: Refractory disease is defined as the presence of persistent abnormality on conventional MRI that is further distinguished by histology (biopsy or sample of lesion) or advanced imaging, OR as determined by the treating physician and discussed with the primary investigator prior to enrollment.

1.2 Prior Therapy Patients must have recurred/progressed following prior standard therapy for their tumor. Note: Patients with meningioma, atypical meningioma, or anaplastic meningioma must have received at least surgical resection or radiation.

1.3 Screening Consent Participant/legal guardian is willing to sign a screening consent for [68Ga]Ga-DOTATATE PET imaging. The screening consent is to be obtained according to institutional guidelines. Assent, when appropriate, will be obtained according to institutional guidelines.
2. Eligibility Criteria

- Phase I Age Patient must be ≥ 4 and <12 years of age at the time of enrollment. Disease Status: Patients who participate in the efficacy expansion cohort must have bi-dimensionally measurable disease, defined as at least one lesion that can be accurately measured in at least two dimensions Patients with measurable extraneural disease only are also eligible.
- Phase II Age Patient must be 12 to </=39 years at the time of enrollment.
    1. Inclusion Criteria

3.1 Uptake on [68Ga]Ga-DOTATATE PET Patients must have uptake on DOTATATE PET/CT in at least one tumor lesion (corresponding to known disease) equivalent to a Krenning score ≥2 (confirmed by central radiology review).

3.2 Prior Therapy Patients must have recovered from the acute treatment related toxicities (defined as ≤ grade 1 if not defined in eligibility criteria) of all prior chemotherapy, immunotherapy, radiotherapy, or any other treatment modality prior to entering this study.

3.3 Chemotherapy Patients must have received their last dose of known myelosuppressive anticancer therapy at least 21 days prior to enrollment or at least 42 days if nitrosourea.

3.4 Investigational/Biologic Agent

●Biologic or investigational agent (anti-neoplastic): Patient must have recovered from any acute toxicity potentially related to the agent and received their last dose of the investigational or biologic agent ≥ 7 days prior to study enrollment.

For agents that have known adverse events occurring beyond 7 days after administration, this period must be extended beyond the time during which adverse events are known to occur.

●Monoclonal Antibodies and agents with known prolonged half-lives: Patient must have recovered from any acute toxicity potentially related to the agent and received their last dose of the agent ≥ 28 days prior to study enrollment.

3.5 Radiation

Patients must have had their last fraction of:
* Craniospinal irradiation or total body irradiation or radiation to > 50% of pelvis > 3 months prior to enrollment.
* Focal irradiation > 4 weeks prior to enrollment

3.6 Stem Cell Transplant

Patient must be:
* ≥ 6 months since allogeneic stem cell transplant prior to enrollment with no evidence of active graft vs. host disease
* ≥ 3 months since autologous stem cell transplant prior to enrollment

3.7 Growth Factors Patients must be off all colony-forming growth factor(s) for at least 1 week prior to enrollment (e.g. filgrastim, sargramostim or erythropoietin). Two weeks must have elapsed if patients received long-acting formulations.

3.8 Thrombopoietin receptor agonist

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* Phase I: Patients must be off thrombopoietin receptor agonists for at least 1 week prior to enrollment (e.g. romiplostim, eltrombopag)
* Phase II: Patients can receive concurrent thrombopoietin receptor agonists

3.9 Somatostatin analogs Patients must be off long-acting somatostatin analogs for at least 4 weeks and off short-acting somastatin analogs (i.e., octreotide) for at least 24 hours.

3.10 Neurologic Status
* Patients with neurological deficits should have deficits that are stable for a minimum of 1 week prior to enrollment, documented by a detailed neurological exam.
* Patients with seizure disorders may be enrolled if seizures are well controlled.

3.11 Performance Status Karnofsky Performance Scale (KPS for > 16 years of age) or Lansky Performance Score (LPS for ≤ 16 years of age) assessed within two weeks of enrollment must be ≥ 50. Patients who are unable to walk because of neurologic deficits, but who are up in a wheelchair, will be considered ambulatory for the purpose of assessing the performance score

3.12 Organ Function

Patients must have adequate organ and marrow function, for eligibility and enrollment, as defined below:
* Adequate Bone Marrow Function as defined as:

* Absolute neutrophil count ≥ 1.0 x 109 cells/ L
* Platelets ≥100 x 109 cells/ L (unsupported, defined as no platelet transfusion within 7 days)
* Hemoglobin ≥8 g/dl (may receive transfusions)

- Adequate Renal Function as defined as:
    - Creatinine clearance or radioisotope GFR >70mL/min/1.73m2 OR
    - A serum creatinine based on (Schwartz et al. J. Peds, 106:522, 1985) age/gender as follows:

  1 to < 2 years: maximum serum creatinine 0.6 mg/dL for males and females. 2 to < 6 years: maximum serum creatinine 0.8 mg/dL for males and females. 6 to < 10 years: maximum serum creatinine 1.0 mg/dL for males and females. 10 to < 13 years: maximum serum creatinine 1.2 mg/dL for males and females. 13 to < 16 years: maximum serum creatinine 1.5 mg/dL for males and 1.4 mg/dL for females.

  ≥ 16 years: maximum serum creatinine 1.7 mg/dL for males and 1.4 mg/dL for females.

- Adequate Liver Function as defined as:
    - Total bilirubin ≤ 3 times institutional upper limit of normal (ULN) for age
    - AST(SGOT)/ALT(SGPT) ≤ 3 times institutional ULN
    - Serum albumin ≥ 2g/dL
    - Coagulation parameters: INR <1.5 times ULN and aPTT <1.5 times ULN unless patients are receiving therapeutic anticoagulation which affects these parameters
- Adequate Cardiac Function as defined as:
    - Ejection fraction of ≥ 55% by echocardiogram
    - Serum electrolytes (Sodium, Potassium, Chloride) within institutional limits of normal (patients can be on enteral supplementation)

3.13 Corticosteroids Patients who are receiving dexamethasone must be on a stable or decreasing dose for at least 1 week prior to enrollment, with a maximum dexamethasone dose of 2.5mg/m2/day.

3.14 Pregnancy Status Female patients of childbearing potential must have a negative serum or urine pregnancy test within 72 hours prior to receiving the first dose of study medication. If the urine test is positive or cannot be confirmed as negative, a serum pregnancy test will be required.

3.15 Pregnancy Prevention Patients of childbearing or child fathering potential must be willing to use a medically acceptable form of birth control, which includes abstinence, while being treated on this study and for at least 7 months after drug cessation in females of childbearing potential and for at least 4 months after drug cessation in males of child fathering potential.

3.16 Informed Consent The patient or parent/guardian is able to understand the consent and is willing to sign a written informed consent document according to institutional guidelines.
4. Exclusion Criteria

4.1 Confirmed bone marrow metastatic disease Patients with confirmed metastatic disease to bone marrow are ineligible.

4.2 Presence of bulky disease Patients with bulky disease on imaging as described below are ineligible. Treating physicians are encouraged to request a rapid central imaging review to confirm fulfillment of these criteria if there are questions or concerns.

Bulky disease is defined as:
* Tumor with evidence of clinically significant uncal herniation or midline shift.
* Tumor with diameter of >5cm in one dimension on T2/FLAIR.
* Tumor that in the opinion of the site investigator shows significant mass effect in either the brain or spine.

Note that patients with metastatic or multi-focal disease (with exception of bone marrow) are eligible as long as no sites of disease meet above criteria for bulky disease.

4.3 Breast-feeding Nursing mothers are excluded from this study. There is an unknown but potential risk for adverse events in nursing infants secondary to treatment of the mother with Lutathera.

4.4 Concurrent Illness
* Patients with a history of any other malignancy, except patients with a secondary brain tumor if the patient's prior malignancy has been in remission for at least 5 years from the end of treatment.
* Patients with any clinically significant unrelated systemic illness (serious infections or significant cardiac, pulmonary, hepatic or other organ

dysfunction), that in the opinion of the investigator would compromise the patient's ability to tolerate protocol therapy, put them at additional risk for toxicity or would interfere with the study procedures or results.
* Patients with type I diabetes.

4.5 Concomitant Medications
* Patients who are receiving any other anti-cancer or investigational drug therapy are ineligible.
* Prior or current treatment with 177Lu-DOTATATE/TOC or 90Y-DOTATATE/TOC.

4.6 Prisoners will be excluded from this study.

4.7 Inability to participate: Patients who in the opinion of the investigator are unwilling or unable to return for required follow-up visits, obtain follow-up studies required to assess toxicity to therapy, or adhere to drug administration plan, other study procedures, and study restrictions.
5. Inclusion of Women and Minorities Both males and females of all races and ethnic groups are eligible for this study.

Conditions & Interventions

Interventions:
DRUG: LUTATHERA® (Lutetium Lu 177 dotatate)
Conditions:
High Grade Glioma, Meningioma, Embryonal Tumor, Medulloblastoma, Anaplastic Ependymoma, Recurrent Diffuse Intrinsic Pontine Glioma, Recurrent Malignant Glioma, Recurrent Medulloblastoma, Recurrent Primary Central Nervous System Neoplasm, Refractory Diffuse Intrinsic Pontine Glioma, Refractory Malignant Glioma, Refractory Medulloblastoma, Refractory Primary Central Nervous System Neoplasm
Keywords:
Somatostatin Receptor, DOTATATE, Lutathera

More Information

Description:
This study will evaluate the safety and efficacy of Lutathera (177Lu-DOTATATE) in patients with progressive or recurrent High-Grade Central Nervous System (CNS) tumors and meningiomas that demonstrate uptake on DOTATATE PET. The drug will be given intravenously once every 8 weeks for a total of up to 4 doses over 8 months in patients aged 4 to \<12 years (Phase I) or 12 to \

Contact(s): - cancer@cchmc.org
Principal Investigator:
Principal Investigator ID:
Phase: PHASE1
IRB Number:
System ID: NCT05278208
