MEKTOVI® for the Treatment of Pediatric Adamantinomatous Craniopharyngioma

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 1 year to 39 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

1. Age: Patients must be ≥ 12 months and ≤ 39 years of age at the time of study enrollment.
2. Diagnosis: Patients with histologically-confirmed adamantinomatous craniopharyngioma (ACP) Histologic confirmation of ACP may be made on solid tumor or, if no solid tumor can be safely obtained, cyst fluid with classic ACP characteristics of thick, cholesterol-rich, greenish-brown liquid in the context of imaging features consistent with craniopharyngioma, including lobulated, cystic/solid mass with calcifications that originates in the sellar/suprasellar region.
3. Disease Status: Patients must have measurable disease.

- Stratum 1: Patients with progressive or recurrent ACP who demonstrate cystic and/or solid recurrence or progression at least 6 months post completion of radiation therapy
- Stratum 2 (NOT CURRENTLY ENROLLING): Patients with measurable ACP who have undergone surgery but have NOT previously undergone irradiation (but may have received prior systemic or intracystic therapy). Progressive disease is allowed but not required.

    1. Performance Level: Karnofsky ≥ 50% for patients > 16 years of age and Lansky ≥ 50 for patients ≤ 16 years of age (See Appendix I). Note: Neurologic deficits in patients with CNS tumors must have been stable for at least 7 days prior to study enrollment. 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.
    2. Prior Therapy: Patients must have recovered or stabilized from the acute toxic effects of prior treatments
- Biologic (anti-neoplastic agent): At least 7 days must have elapsed after the last (systemic or intracystic) dose of a biologic agent. 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. The duration of this interval must be discussed with the study chair
- Immunotherapy: At least 42 days after the completion of any type of systemic immunotherapy, e.g. tumor vaccines.
- Monoclonal antibodies: At least 21 days after the last dose of a monoclonal antibody.
- Radiation therapy: Patients must have had their last (conventional or hypofractionated) fraction of: a) Focal irradiation > 6 months prior to enrollment and b) No prior craniospinal irradiation is permitted.
- Corticosteroids: Patients receiving dexamethasone must be on a stable or decreasing dose for at least 1 week prior to enrollment
- Myelosuppressive systemic therapy: At least 21 days must have elapsed after the last systemic myelosuppressive therapy.
- Surgery: At least 6 weeks must have elapsed since major or intermediate surgery. Major surgery includes major craniotomy for tumor resection of cyst fenestration, organ resection, and exploratory laparotomy. Intermediate procedures include ventriculoperitoneal shunt placement, stereotactic brain biopsy, and intraventricular catheter placement. Minor procedures that are not excluded include skin biopsy/incision and drainage, bone marrow aspirate, and central venous catheter placement, ommaya aspirations, lumbar punctures, and nasal endoscopy to remove packing.

    1. Organ Function Requirements

Adequate Bone Marrow Function Defined as:
* Peripheral absolute neutrophil count (ANC) ≥1000/mm3
* Platelet count ≥100,000/mm3 (transfusion independent, defined as not receiving platelet transfusions for at least 7 days prior to enrollment)
* Hemoglobin >8 g/dL (may be transfused)

Adequate Renal Function Defined as:
* Creatinine clearance or radioisotope GFR > 70ml/min/1.73 m2 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 Defined as:
* Total bilirubin ≤ 1.5 × institutional upper limit of normal
* AST (SGOT) ≤ 2.5 × institutional upper limit of normal
* ALT (SGPT) ≤ 2.5 × institutional upper limit of normal

Adequate Cardiac Function Defined as:
* Left Ventricular Ejection Fraction greater than the institutional lower limit of normal by echocardiogram

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* QTc ≤ 480 msec (by Bazett formula)

Adequate Neurologic Function Defined as:
* Patients with neurological deficits should have deficits that are stable for a minimum of 1 week prior to enrollment.
* Patients with current seizure disorders may be enrolled if seizures are well-controlled on antiepileptic therapies.
7. Informed Consent: All patients and/or their parents or legally authorized representatives must sign a written informed consent. Assent, when appropriate, will be obtained according to institutional guidelines

Exclusion Criteria:

1. Pregnancy or Breast-Feeding: Pregnant or breast-feeding women will not be entered on this study due to unknown risks of fetal and teratogenic adverse events as seen in animal/human studies. Pregnancy tests must be obtained in girls who are post-menarchal. Males or females of reproductive potential may not participate unless they have agreed to use an effective contraceptive method for at least 90 days after discontinuation of drug for females and at least 60 days for males. For females of childbearing potential, agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods (bilateral tubal ligation, male sterilization, hormonal contraceptives that inhibit ovulation, hormone-releasing intrauterine devices, and copper intrauterine devices; hormonal contraceptive methods must be supplemented by a barrier method) and agreement to refrain from donating eggs are required. For males of reproductive potential, agreement to remain abstinent (refrain from heterosexual intercourse) or use a condom, and agreement to refrain from donating sperm.
2. Gastrointestinal Disease:

- Patients with a history of serious gastrointestinal disease, including inflammatory bowel disease or gastrointestinal perforation
- Patients who are unable to absorb enteral medications
- Administration via NG/NJ/G-tube is allowed

1. Concomitant Medications

- Corticosteroids: Patients receiving corticosteroids who have not been on a stable or decreasing dose of corticosteroid for at least 7 days prior to enrollment are not eligible.
- Investigational Drugs: Patients who are currently receiving another investigational drug are not eligible.
- Anti-cancer Agents: Patients who are currently receiving other anti-cancer agents are not eligible.

1. Study Specific:

- Patients who have an uncontrolled infection are not eligible.
- Patients who have received any live or attenuated vaccinations within three months prior to start of therapy are not eligible.
- Any significant concurrent medical or surgical condition that would jeopardize the patient's safety or ability to complete the study, including, but not limited to, disease of the nervous, renal, hepatic, cardiac (such as symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia), pulmonary, or endocrine system
- Patients who have a history of Human Immunodeficiency Virus, Hepatitis B Virus, Hepatitis C Virus or Tuberculosis infection are not eligible.
- Patients who have received a prior solid organ transplantation are not eligible.
- Patients who in the opinion of the investigator may not be able to comply with the safety monitoring requirements of the study are not eligible.
- Patients who have a history of alcohol, drug, or chemical abuse within 6 months of screening.
- Patients who have had surgery within the last 6 weeks or who have concerns for poor postsurgical wound healing.
- Patients who have a history of allergic reactions attributed to compounds of similar chemical or biologic composition to tocilizumab and its excipients are not eligible.

Conditions & Interventions

Interventions:
DRUG: Binimetinib Oral Tablet [Mektovi]
Conditions:
Adamantinous Craniopharyngioma, Recurrent Adamantinomatous Craniopharyngioma

More Information

Description:
MEKTOVI (binimetinib) is an oral, highly selective reversible inhibitor of mitogen-activated extracellular signal regulated kinase 1 (MEK1) and MEK2. The biological activity of binimetinib that has been evaluated bith in vitro and in vivo in a wide variety of tumor types In this Phase II, the drug will be used to treat pediatric patients diagnosed with recurrent Adamantinomatous Craniopharyngioma including patients who have undergone surgery and/or radiation therapy.

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Phase: PHASE2
IRB Number:
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