PBTC-024: Phase I Study of MK-0752 in Pediatric Patients With Recurrent or Refractory CNS Malignancies

| Type | Status | Age Range | Sponsor | Protocol ID |
|----------------|--------|---------------|---|-------------|
| Interventional | Active | 3 to 21 years | Pediatric Brain Tumor Consortium/ National Cancer Institute (NCI) | PBTC-024 |

Outline

This is a multicenter study.

Patients receive oral MK-0752 once daily on days 1-3, 8-10, 15-17, and 22-24 or days 1,8,15 and 22. Treatment repeats every 28 days for up to 19 courses in the absence of disease progression or unacceptable toxicity.

After completion of study treatment, patients are followed for 30 days.

Objectives

Primary

- To estimate the maximum tolerated dose (MTD) and recommended phase II dose of MK-0752 administered for 3
 consecutive days of every 7 days in 28 day courses to young patients with recurrent or refractory CNS
 malignancies.
- 2. To estimate the MTD and recommend a phase II dose of MK0752 administered once weekly in 28 day courses to young patients with recurrent or refractory CNS malignancies.
- 3. To compare the MK0752 systemic exposure attained with each dosage level on the different dosing regimens. malignancies.

Secondary

- 1. To characterize the pharmacokinetics of MK-0752.
- 2. To document and describe toxicities associated with MK-0752.
- 3. To preliminarily define the antitumor activity of MK-0752 within the confines of a phase I setting.

Projected Accrual

About 47 people will participate in this study at Cincinnati Children's Hospital.

Entry Criteria

Disease Characteristics:



Brain & Spinal Tumors

- Histologically confirmed primary CNS tumor.
 - Patients with intrinsic brain stem tumors do not require histologic verification, but must have radiographic evidence of progression.
- Recurrent disease or refractory to standard therapy.
- No histologically benign brain tumors (e.g., low-grade glioma).

Patient Characteristics:

Age

3 to 21 years of age.

Performance Status

Karnofsky performance status (PS) or Lansky PS 60-100%.

Life Expectancy

Not specified.

Hematopoietic

- Absolute neutrophil count ≥ 1,000/µL.
- Platelet count ≥ 100,000/µL (unsupported).
- Hemoglobin ≥ 8 g/dL (RBC transfusions allowed).

Hepatic

- Bilirubin ≤ 1.5 times upper limit of normal (ULN) for age.
- ALT ≤ 2.5 times ULN for age.
- Albumin ≥ 2.5 g/dL.

Renal

Serum creatinine normal for age OR glomerular filtration rate ≥ 70 mL/min/1.73m2.

Other

- Not pregnant or nursing.
- Negative pregnancy test.
- Fertile patients must use effective contraception.
- Sodium, potassium, magnesium, and calcium normal.
- Patients with neurological deficits are eligible provided these deficits are stable for ≥ 2 weeks prior to study registration.



Brain & Spinal Tumors

- No clinically significant systemic illness (e.g., serious infection or significant cardiac, pulmonary, hepatic, or other organ dysfunction) that would compromise the patient's ability to tolerate study therapy or would likely interfere with the study procedures or results.
- No known hypersensitivity to MK-0752.

Prior Concurrent Therapy:

Biologic Therapy

- At least 7 days since prior investigational or biologic agents.
- At least 3 weeks since prior investigational or biologic agents that have a prolonged half-life or for which the patient has experienced ≥ grade 2 myelosuppression in the treatment course preceding discontinuation of therapy.
- At least 3 half lives since prior monoclonal antibody therapy.

Chemotherapy

At least 3 weeks since prior myelosuppressive anticancer chemotherapy (6 weeks for nitrosoureas).

Radiotherapy

- At least 6 months since prior total body irradiation or craniospinal radiotherapy.
- At least 6 weeks since other prior substantial bone marrow irradiation.
- At least 2 weeks since prior local palliative radiotherapy (small volume).

Surgery

Recovered from the acute toxic effects of all prior therapy.

Other

- No prior MK-0752
- No concurrent enzyme-inducing anticonvulsant drugs (EIACDs).
- No other concurrent anticancer or investigational drug therapy.
- Concurrent dexamethasone allowed provided patient is on a stable or decreasing dose for ≥ 2 weeks prior to study registration.
- At least 6 months since prior allogeneic bone marrow transplantation (BMT).
- No evidence of active graft versus host disease.
- At least 3 months since prior autologous BMT or stem cell transplantation.
- At least 7 days since prior hematopoietic growth factors (filgrastim [G-CSF], sargramostim [GM-CSF], or erythropoietin) (14 days for long-acting formulations).

For more information contact:

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Brain & Spinal Tumors

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