

14J-MC-HHBD: A Phase I Trial of LY2940680 in Pediatric Patients with Recurrent or Refractory Rhabdomyosarcoma and Medulloblastoma.

PURPOSE: The purpose of this study is to find a recommended dose level of LY2940680 that can be safely given to children with medulloblastoma or rhabdomyosarcoma that has returned or doesn't respond to initial treatment. The study will also explore the changes in a cancer marker levels. Finally, the study will help document any antitumor activity.

Study Type: Interventional
Masking: Open Label
Primary Purpose: Treatment

AGES ELIGIBLE FOR STUDY: 12 Months to 21 Years

CRITERIA

Inclusion Criteria:

- For Part A: Have a diagnosis of recurrent or refractory rhabdomyosarcoma or medulloblastoma and have had histologic verification of malignancy at original diagnosis or relapse.
- For Part B: Have a diagnosis of recurrent or refractory medulloblastoma and have had histologic verification of malignancy at original diagnosis or relapse.
- Current disease state must be one for which there is no known curative therapy or therapy proven to prolong survival with an acceptable quality of life.
- Karnofsky score must be at least 50% for participants >16 years of age, and Lansky score must be at least 50% for participants 16 years of age or less. Participants who are unable to walk because of paralysis, but who are in a wheelchair, will be considered ambulatory for the purpose of assessing the performance score.
- Have fully recovered from the acute toxic effects of all prior anticancer chemotherapy.
 - Participants with solid tumors must not have received myelosuppressive chemotherapy within 3 weeks of enrollment in this study (6 weeks, if previously treated with nitrosourea).
 - Hematopoietic growth factors: At least 14 days after the last dose of a longacting growth factor (eg, Neulasta®) or 7 days for short-acting growth factor.
 - Biologic (antineoplastic agent): At least 7 days after the last dose of a biologic agent.
 - Immunotherapy: At least 6 weeks since the completion of any type of immunotherapy (eg, tumor vaccines).
 - Monoclonal antibodies: At least 3 half-lives of the antibody after the last dose of a monoclonal antibody.

- Radiation therapy (XRT): ≥ 8 weeks for local irradiation to primary tumor; ≥ 2 weeks prior to study entry for focal irradiation for symptomatic metastatic sites; ≥ 3 months for craniospinal XRT, or ≥ 24 weeks if $\geq 50\%$ radiation of pelvis; minimum of 6 weeks must have elapsed if other substantial bone marrow radiation has been received.
- Stem cell transplant: allowed if they have recovered from all acute toxicity and adequate bone marrow reserve is demonstrated. At least 8 weeks must have elapsed since autologous stem cell transplantation or ≥ 3 months for allogenic transplantation. Participants must be off all immunosuppressive therapy and have no evidence of active graft-versus-host disease.
- Have adequate organ function, including:
 - Bone marrow: Peripheral absolute neutrophil count (ANC) ≥ 500 /cubic millimeter (mm^3) and platelet count $\geq 100,000/\text{mm}^3$ (transfusion independent, defined as not receiving platelet transfusions within a 7-day period prior to enrollment).
 - Hepatic: Bilirubin (sum of conjugated + unconjugated) $\leq 1.5 \times$ upper limit of normal (ULN) for age. Serum alanine aminotransferase (ALT) and aspartate aminotransferase (AST) ≤ 2.0 times ULN for age. Serum albumin ≥ 2 grams/deciliter (g/dL).
 - Renal: Creatinine clearance or radioisotope glomerular filtration rate (GFR) ≥ 70 milliliters/minute/1.73 square meters ($\text{mL}/\text{min}/1.73 \text{ m}^2$), or a serum creatinine based on age/gender per the Schwartz formula for estimating GFR utilizing child length and stature data published by the Centers for Disease Control and Prevention (CDC).
 - Neurologic: Participants with seizure disorders may be enrolled if receiving nonenzyme-inducing anticonvulsants and if the symptoms are well controlled. They must have a stable neurologic status for at least 1 week prior to enrollment in the study.
- Must be able to swallow powder or a capsule.
- Have the presence of either measurable or nonmeasurable disease.

Exclusion Criteria:

- Have received treatment within 21 days of the initial dose of study drug with an experimental agent for noncancer indications that has not received regulatory approval for any indication.
- Receiving corticosteroids and have not been on a stable or decreasing dose of corticosteroid for the prior 7 days.
- Receiving enzyme-inducing anticonvulsants.
- Have serious preexisting medical conditions.
- Have current hematologic malignancies or acute or chronic leukemia.

- Have a known active fungal, bacterial, and/or known viral infection, including human immunodeficiency virus (HIV) or viral (A, B, or C) hepatitis (screening is not required).
- Have a second primary malignancy that, in the judgment of the investigator and sponsor, may affect the interpretation of results.
- Have \geq Grade 2 QT prolongation, that is, QTc interval of >480 milliseconds (msec) on screening electrocardiography (ECG).

For more information contact:

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