A Study With Tovorafenib (DAY101) as a Treatment Option for Progressive, Relapsed, or Refractory Langerhans Cell Histiocytosis

Status: RECRUITING

Eligibility Criteria

Age: 180 days to 22 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

* 180 days- \< 22 years (at time of study enrollment) * Patient must have a body surface area of ≥ 0.3 m\^2 * Patients with progressive, relapsed, or recurrent LCH with measurable disease at study entry * Patients must have had histologic verification of LCH (from either original diagnosis or relapse/progression) at the time of study entry (must be obtained within 28 days prior to enrollment and start of protocol therapy) (repeat if necessary) * Tissue confirmation of relapse is recommended but not required * Pathology report must be submitted for central confirmation of diagnosis within 7 days of enrollment. * Formalin-fixed paraffin-embedded (FFPE) blocks or unstained slides (initial diagnosis and/or subsequent biopsies) will be required for retrospective central confirmation of diagnosis and molecular studies * Patients with mixed histiocytic disorders (e.g. LCH with juvenile xanthogranuloma) may be included * Patients must have measurable disease, documented by radiographic imaging (LCH-specific response criteria (must be obtained within 28 days prior to enrollment and start of protocol therapy) (repeat if necessary). * Patients must have progressive or refractory disease or experience relapse after at least one previous systemic treatment strategy * Pathogenic somatic mutation detected in genes encoding tyrosine kinase receptors (CSFR1, ERBB3 or ALK), RAS or RAF (may be from original or subsequent biopsy or peripheral blood/bone marrow aspirate). Clinical mutation reports may include quantitative polymerase chain reaction (PCR) (e.g. BRAFV600E) and/or Sanger or next generation sequencing. Immunohistochemistry (e.g. VE1 antibody for BRAFV600E) alone is not sufficient * Participant must be able to take an enteral dose and formulation of medication. Study medication is only available as an oral suspension or tablet, which may be taken by mouth or other enteral route such as nasogastric, jejunostomy, or gastric tube * Karnofsky \>= 50% for patients \> 16 years of age and Lansky \>= 50% for patients =\< 16 years of age * 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 * Myelosuppressive chemotherapy: Patients must not have received within 14 days of entry onto this study * Investigational agent or any other anticancer therapy not defined above: Patients must not have received any investigational agent or any other anticancer therapy (including MAPK pathway inhibitor) for at least 14 days prior to planned start of tovorafenib (DAY101) * Radiation therapy (RT): Patient must not have received RT within 2 weeks after the last dose fraction of RT * Patients must have fully recovered from any prior surgery * Patients must have fully recovered from the acute toxic effects of all prior chemotherapy, immunotherapy, targeted inhibitor, and/or radiotherapy with toxicities reduced to grade 1 or less (Common Terminology Criteria for Adverse Events \[CTCAE\] version 5.0) * Steroids: =\< 0.5 mg/kg/day of prednisone equivalent (maximum 20 mg/day) averaged during the month prior to study enrollment is permissible * Strong inducers or inhibitors of CYP2C8 are prohibited for 14 days before the first dose of tovorafenib (DAY101) and from planned administration for the duration of study participation * Medications that are breast cancer resistant protein (BCRP) substrates that have a narrow therapeutic index are prohibited for 14 days before the first dose of tovorafenib (DAY101) and for the duration of study participation * Peripheral absolute neutrophil count (ANC) \>= 750/uL unless secondary to bone marrow involvement, in such cases bone marrow involvement must be documented (must be performed within 7 days prior to enrollment, must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment) * Platelet count \>= 75,000/uL (unsupported/without transfusion within the past 7 days) (must be performed within 7 days prior to enrollment, must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment) * Patients with marrow disease must have platelet count of \>= 75,000/uL (transfusion support allowed) and must not be refractory to platelet transfusions. Bone marrow involvement must be documented * Hemoglobin \>= 8 g/dL (unsupported/without transfusion within the past 7 days). Patients with marrow disease must have hemoglobin \>= 8 g/dL (transfusion support allowed). Bone marrow involvement must be documented * Hematopoietic growth factors: At least 14 days after the last dose of a long-acting growth factor (e.g., Neulasta \[registered trademark\]) or 7 days for short-acting growth factor * A serum creatinine based on age/sex as follows (must be performed within 7 days prior to enrollment, must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment) * Age: 6 months to \< 1 year; Maximum Serum Creatinine (mg/dL):= 0.5 mg/dl (male and female) * Age: 1 to \< 2 years; Maximum Serum Creatinine (mg/dL): = 0.6 mg/dl (male and female) * Age: 2 to \< 6 years; Maximum Serum Creatinine (mg/dL): = 0.8 mg/dl (male and female) * Age: 6 to \< 10 years; Maximum Serum Creatinine (mg/dL): = 1.0 mg/dl (male and female) * Age: 10 to \< 13 years; Maximum Serum Creatinine (mg/dL): = 1.2 mg/dl (male and female) * 13 to \< 16 years; Maximum Serum Creatinine (mg/dL): = 1.5 mg/dl (male) and 1.4 mg/dl (female) * Age: \>= 16 years; Maximum Serum Creatinine (mg/dL): = 1.7 mg/dl (male) and 1.4 mg/dl (female) * OR- a 24 hour urine creatinine clearance \>= 50 mL/min/1.73 m\^2 * OR- a glomerular filtration rate (GFR) \>= 50 mL/min/1.73 m\^2. GFR must be performed using direct measurement with a nuclear blood sampling method OR direct small molecule clearance method (iothalamate or other molecule per institutional standard) * Note: Estimated GFR (eGFR) from serum creatinine, cystatin C or other estimates are not acceptable for determining eligibility * Bilirubin (sum of conjugated + unconjugated) =\< 1.5 x upper limit of normal (ULN) for age (must be performed within 7 days prior to enrollment, must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment) * Alanine aminotransferase (ALT) =\< 3 x ULN for age (must be performed within 7 days prior to enrollment, must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment) * Serum albumin \>= 2 g/dl must be performed within 7 days prior to enrollment, must be repeated prior to the start of protocol therapy if \> 7 days have elapsed from their most recent prior assessment) * For patients with liver disease caused by their histiocytic disorder (as evaluated on radiographic imaging or biopsy): patients may be enrolled with abnormal bilirubin, aspartate aminotransferase (AST), ALT and albumin with documentation of histiocytic liver disease * Fractional shortening (FS) of \>= 25% or ejection fraction of \>= 50%, as determined by echocardiography or multigated acquisition scan (MUGA) within 28 days prior to study enrollment. Depending on institutional standard, either FS or left ventricular ejection fraction (LVEF) is adequate for enrollment if only one value is measured; if both values are measured, then both values must meet criteria above (must be obtained within 28 days prior to enrollment and start of protocol therapy) (repeat if necessary) * No evidence of dyspnea at rest, no exercise intolerance, and a pulse oximetry \> 94% if there is clinical indication for determination; unless it is due to underlying pulmonary LCH * Central Nervous System Function Defined As: * Patients with seizure disorder may be enrolled if well controlled * Central nervous system (CNS) toxicity =\< Grade 2 * Human immunodeficiency virus (HIV) infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial unless antiretroviral therapy interacts with the metabolism of tovorafenib (DAY101) and cannot safely be changed to antivirals that do not interact with study medication

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Exclusion Criteria:

* LCH arising along with other hematologic malignancy (e.g. mixed LCH with acute lymphoblastic leukemia) or any history of non-histiocytic malignancy * Disease scenarios as below will be excluded * Skin-limited disease * Gastrointestinal (GI) tract involvement only (those that have disease that can be determined by endoscopic biopsies only) * LCH-associated neurodegeneration (LCH-ND) without parenchymal lesions or other systemic lesions * Patients with activating mutations in MAP2K1 are not eligible for this study due to drug target specificity. Mutation status will be submitted to study team within 7 days of enrollment * Refractory nausea and vomiting, malabsorption, or external biliary shunt that would preclude adequate absorption of tovorafenib (DAY101) * Uncontrolled systemic bacterial, viral, or fungal infection * Major surgical procedure or significant traumatic injury within 14 days prior to study enrollment, or anticipation of need for major surgical procedure during the course of the study. Placement of a vascular access device or minor surgery is permitted within fourteen (14) days of study enrollment (provided that the wound has healed) *

History of significant bowel resection that would preclude adequate absorption or other significant malabsorptive disease * Ophthalmologic considerations: Patients with known significant ophthalmologic conditions or known risk factors for retinal vein occlusion (RVO) or central serous retinopathy (CSR) are not eligible * History of solid organ or hematopoietic bone marrow transplantation * Clinically significant active cardiovascular disease, or history of myocardial infarction, or deep vein thrombosis/pulmonary embolism within 6 months prior to enrollment, ongoing cardiomyopathy, or current prolonged QT interval \> 440 ms based on triplicate electrocardiogram (ECG) average * History of Grade \>= 2 CNS hemorrhage or history of any CNS hemorrhage within 28 days of study entry * History of any drug reaction with eosinophilia and systemic symptoms (DRESS) syndrome or Stevens Johnsons syndrome (SJS) or who are allergic to tovorafenib (DAY101) or any of its components * CTCAE version (V). 5.0 Grade 3 symptomatic creatinine kinase (CPK) elevation (\> 5 x ULN) * Female patients who are pregnant are ineligible. A pregnancy test is required for female patients of childbearing potential * Lactating females who plan to breastfeed their infants are ineligible * Sexually active patients of reproductive potential who have not agreed to use an effective contraceptive method for the duration of their study participation are ineligible. Women of childbearing potential must use non-hormonal contraception during tovorafenib treatment and for at least 28 days after the last dose. Men should use effective contraception and must not father a child while taking tovorafenib and for 14 days after the last dose

Conditions & Interventions

Interventions:
PROCEDURE: Biospecimen Collection, PROCEDURE: Bone Marrow Aspiration, PROCEDURE: Bone Marrow Biopsy, PROCEDURE: Computed Tomography, PROCEDURE: Echocardiography Test, PROCEDURE: FDG-Positron Emission Tomography and Computed Tomography Scan, PROCEDURE: Lumbar Puncture, PROCEDURE: Multigated Acquisition Scan, DRUG: Tovorafenib
Conditions:
Recurrent Langerhans Cell Histiocytosis, Refractory Langerhans Cell Histiocytosis

More Information

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