Mirdametinib in Histiocytic Disorders

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 2 years and over
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

1. Subjects must be ≥ 2 years of age AND have a diagnosis of a histiocytic disorder that requires systemic therapy

- If patient has had a diagnostic biopsy, biopsy must be reviewed and confirmed by CCHMC pathologist as feasible
- If patient has had a biopsy but has not had molecular testing done, must have tissue available for mutational analysis
- If patient has isolated pituitary/CNS disease or situations where biopsy is not feasible, positive ddPCR blood test for mutation associated with histiocytic neoplasm with clinical features of histiocytosis is sufficient

    1. Must have measurable disease on PET scan or brain MRI
    2. Subjects must demonstrate adequate organ function as defined:
- Renal: maximum serum creatinine 2x the upper limit of normal (ULN) OR a creatinine clearance or radioisotope GFR ≥ 70ml/min/1.73 m2
- Liver: ALT ≤ 3x ULN AND normal INR (≤ 1.5)
- Hematologic: Hematology: Albumin ≥ 2.8 g/dL; Absolute neutrophil count ≥ 1.5 x 109/L; Platelets ≥ 100 x 109/L; Hemoglobin ≥ 9.0 g/dL
- Patients with organ function abnormalities outside of these thresholds deemed to be the result of histiocytic disease will be considered eligible

Exclusion Criteria:

1. Prior therapy with stipulations as described:

- Myelosuppressive Chemotherapy: Must not have received any cytotoxic chemotherapy which impacts the growth and development of cells in the bone marrow within 14 days of enrollment onto this study (i.e. cytarabine, cladribine, clofarabine, mercaptopurine, methotrexate, vinblastine)
- MEK Inhibitors: Must not have received a MEK inhibitor within 30 days (or 5 half-lives, whichever is longer) of enrollment, NOR have had disease progression on MEK inhibitor
- Steroids: Due to the increased risk of an ocular event, the use of systemic oral, inhaled, or ocular glucocorticoid therapy is prohibited within 14 days prior to first dose of mirdametinib. Throughout the treatment period, short term glucocorticoid treatment (30 days or less) is permitted. Any patients requiring long-term steroid use (more than 30 consecutive days) are not eligible. The exception to this rule is subjects with endocrine deficiencies who require physiologic steroids
- Radiation: Must not have received radiation within 14 days of study enrollment or have received radiation to the orbit at any time

    1. Risk factors for retinal vein occlusion (RVO) are listed. Exclusion should be considered by clinical discretion if they have any of the following risk factors for RVO at screening:
- Intraocular pressure (IOP) > 21 mmHg; if IOP is unable to be obtained (eg age, cooperation, tolerability), ophthalmologist's exam findings and overall assessment will be utilized. If in the ophthalmologist's assessment there are no signs of raised IOP, the subject will be considered eligible for this parameter
- Glaucoma or any significant abnormality (≥ grade 2) on ophthalmologic exam that is uncontrolled with intervention
- Serum cholesterol > 300 mg/dL
- Serum triglycerides > 300 mg/dL
- Hyperglycemia (either fasting blood glucose > 125 mg/dL OR random blood glucose > 200 mg/dL)
- Uncontrolled hypertension (participants ≤ 12 years of age with a blood pressure ≥ 95th percentile for age + 12 mmHg; participants ≥ 13 years of age with a blood pressure ≥ 140/90 mm Hg) unresolved on repeat measurement

    1. LVEF < 55% at screening OR history of clinically significant cardiac disease, unless deemed to be the direct result of disease
    2. Subjects who are pregnant or breastfeeding, or are at risk of pregnancy or fathering a baby and are unable to use acceptable methods of birth control during the length of the study

Conditions & Interventions

Interventions:
DRUG: Mirdametinib
Conditions:
Langerhans Cell Histiocytosis (LCH), Juvenile Xanthogranuloma (JXG), Rosai-Dorfman Disease (RDD), Histiocytic Disorders

More Information

More Information

Description:
The purpose of this study is to see if treatment with mirdametinib in patients with Langerhans cell histiocytosis (LCH) or other histiocytic disorders will be better than current treatments and with fewer side effects.

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