Study of Talazoparib in Combination With Chemotherapy in Relapsed Pediatric AML to Determine Safety and Efficacy

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: Up to 21 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria:

1. Aged ≤ 21 years.
2. Acute myeloid leukemia (AML) OR acute leukemia of ambiguous lineage (acute undifferentiated leukemia or mixed phenotype acute leukemia), specified as either refractory (persistent leukemia after at least 2 courses of induction chemotherapy) or relapsed, and further defined as any one of the criteria below:

    1. Bone marrow specimen ≥ 5% leukemic blasts by flow, as assessed by Hematologics Inc.
    2. A single bone marrow specimen with at least 2 tests demonstrates ≥ 1% leukemic blasts by flow cytometry (as assessed by Hematologics Inc), AND at least one of the following:

* Karyotypic abnormality with at least 1 metaphase similar or identical to diagnosis
* FISH abnormality identical to one present at diagnosis
* PCR or NGS-based demonstration of leukemogenic lesion identical to diagnosis

1. Rising MRD > 0.1% by flow cytometry on ≥ 2 serial samples, as assessed by Hematologics Inc.
2. If an adequate bone marrow sample is not obtained, subjects may be enrolled if there is unequivocal evidence of leukemia based on ≥ 5% blasts in the peripheral blood
    1. > 60 days has passed since hematopoietic stem cell transplant.
    2. Patients who have undergone previous allogeneic stem cell transplantation who are otherwise eligible must also be without evidence of any active graft versus host disease (GVHD), and off calcineurin inhibitors for at least 28 days (four weeks) prior to therapy. A physiologic dose of prednisone up to 3 mg/m2 (and a maximum of 7.5 mg) or equivalent other steroid dose is allowable.
    3. A minimum of 14 days has passed since completion of myelosuppressive therapy or gemtuzumab ozogamicin and all nonhematologic toxicities have resolved to Grade 0 or 1.
    4. A minimum of 24 hours has elapsed since the patient has completed any low-dose or non-myelosuppressive therapy (e.g., hydroxyurea or low-dose cytarabine (up to 100 mg/m2).
    5. Lansky (subjects ≤ 16 years old) or Karnofsky (subjects > 16 years old) score ≥ 50.
    6. WBC ≤ 50,000/uL. This may be achieved using cytoreductive therapy such as hydroxyurea or low-dose cytarabine (up to 100 mg/m2/dose)
    7. Total bilirubin ≤ 2.0 x institutional upper limit of normal (ULN) for age.
    8. AST/ALT ≤ 5 x ULN for age
    9. Left ventricular ejection fraction ≥ 40% or ECHO shortening fraction ≥ 25%.
    10. Estimated serum creatinine ≥ 60 mL/min/1.73m2

Exclusion Criteria:

1. Patients receiving or planning to receive ANY concurrent cancer therapy, including chemotherapy, radiation therapy, immunotherapy or biologic therapy.
2. Patients with down syndrome.
3. Patients with Acute Promyelocytic leukemia (APL) or Juvenile Myelomonocytic Leukemia (JMML).
4. Patients with Bone Marrow Failure Syndrome.
5. Pregnant subjects or those unwilling to use an effective method of birth control.
6. Female subjects with infants who do NOT agree to abstain from breastfeeding.
7. Inability or unwillingness of legal guardian/representative to give written informed consent.
8. Patients with uncontrolled systemic fungal, bacterial, viral or other infection.

Conditions & Interventions

Interventions:
DRUG: Talazoparib, DRUG: Topotecan, DRUG: Gemcitabine
Conditions:
Acute Myeloid Leukemia
Keywords:
PARP Inhibitor

More Information

Description:
This is a Phase 1, open label, multicenter, dose finding study with dose expansion intended to evaluate the safety and tolerability of talazoparib in combination with conventional chemotherapy. Preliminary estimates of efficacy will be obtain through a dose expansion cohort receiving the

maximum tolerated dose from the dose escalation phase of the study. This study aims to determine the safety of talazoparib in combination with conventional chemotherapy and to establish the maximum tolerated dose of all 3 drugs when given in combination. A preliminary estimate of efficacy through a dose expansion phase is a secondary aim.

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Phase: PHASE1
IRB Number:
System ID: NCT05101551
