Study of Revumenib, Azacitidine, and Venetoclax in Pediatric and Young Adult Patients With Refractory or Relapsed Acute Myeloid Leukemia

Status: RECRUITING

Eligibility Criteria

Sex: ALL
Age: 1 year to 30 years old
Healthy Volunteers: This study is NOT accepting healthy volunteers
Inclusion Criteria: Participants must have a diagnosis of AML or ALAL and meet the criteria below:

- Refractory leukemia, defined as persistent leukemia after at least two courses of induction chemotherapy (one course for secondary AML), or relapsed leukemia, defined as the re-appearance of leukemia after the achievement of remission. Patients must have ≥5% blasts in the bone marrow as assessed by morphology or ≥1% blasts flow cytometry.

However, if an adequate bone marrow sample cannot be obtained (e.g., in a patient with acute megakaryoblastic leukemia with marrow fibrosis), patients may be enrolled if there is unequivocal evidence of leukemia with ≥5% blasts by morphology or ≥1% blasts flow cytometry in the blood.

- Presence of KMT2A rearrangement (KMT2Ar), NUP98 rearrangement (NUP98r), NPM1 mutation or fusion, PICALM::MLLT10, DEK::NUP214, UBTF-TD, KAT6A rearrangement (KAT6Ar), or SET::NUP214
- Adequate organ function, defined as total bilirubin < 1.5 × institutional upper limit of normal for age or normal conjugated bilirubin (for patients with known Gilbert's syndrome, total bilirubin <3 × the ULN) unless attributed to leukemia, calculated creatinine clearance ≥60 mL/min/1.73 m^2, and left ventricular ejection fraction ≥ 40%
- QTcF < 480 msec (average of triplicate)
- Age ≥ 1 year and ≤ 30 years. The upper age limit may be defined by each institution, but may not exceed 30 years.
- Lansky ≥ 60 for patients who are < 16 years old and Karnofsky ≥ 60% for patients who are > 16 years old.
- At least 14 days or 5 half-lives (whichever is longer) must have elapsed since the completion of myelosuppressive therapy, with the exception of low-dose therapy used for cytoreduction according to institutional standards, such as hydroxyurea or low-dose cytarabine (up to 200 mg/m^2/day). In addition, all toxicities must have resolved to grade 1 or less.
- Patients must have a leukocyte count <25,000 cells/uL. Low-dose therapy, such as hydroxyurea or cytarabine as described above, to achieve this limit is acceptable.
- For patients who have received prior HCT, there can be no evidence of GVHD and greater than 60 days must have elapsed since the HCT, and patients should be off calcineurin inhibitors for at least 28 days prior to the start of protocol therapy. Physiologic prednisone for the treatment of adrenal insufficiency is acceptable..
- Patients must be taking posaconazole or voriconazole, which must be started at least 24 hours prior to the start of therapy.
- Patients of reproductive potential must agree to use effective contraception for the duration of study participation.

Patients who meet the criteria listed above are eligible for enrollment and treatment on the trial. However, patients in first relapse who are suitable for and willing to receive intensive remission induction therapy should be offered such therapy if deemed appropriate by the treating physician.

Exclusion Criteria:

- Patients who are pregnant or breastfeeding are not eligible.
- Patients with Down syndrome, acute promyelocytic leukemia, juvenile myelomonocytic leukemia, or bone marrow failure syndromes are not eligible.
- Patients with uncontrolled infection are not eligible. Patients with infections that are controlled on concurrent anti-microbial agents are eligible.

Conditions & Interventions

Interventions:
DRUG: Cytarabine, DRUG: Methotrexate, DRUG: Revumenib, DRUG: Venetoclax, DRUG: Azacitidine, DRUG: intrathecal (IT) chemotherapy
Conditions:
Refractory Acute Myeloid Leukemia, Relapsed Acute Myeloid Leukemia, Acute Leukemia of Ambiguous Lineage

More Information

Description:
This is a research study to find out if adding a new study drug called revumenib to commonly used chemotherapy drugs is safe and if they have beneficial effects in treating patients with acute myeloid leukemia (AML) or acute leukemia of ambiguous lineage (ALAL) that did not go into remission after treatment (refractory) or has come back after treatment (relapsed), and to determine the total dose of the 3-drug combination of revumenib, azacitidine and venetoclax that can be given safely in participants also taking an anti-fungal drug. Primary Objective * To determine the safety and tolerability of revumenib + azacitidine + venetoclax in pediatric patients with relapsed or refractory AML or ALAL. Secondary Objectives * Describe the rates of complete remission (CR), complete remission with incomplete count recovery (CRi), and overall survival for patients treated with revumenib + azacitidine + venetoclax at the recommended phase 2 dose (RP2D).

Contact(s): - cancer@cchmc.org
Principal Investigator:
Principal Investigator ID:

Phase: PHASE1
IRB Number:
System ID: NCT06177067
