For Patients with Acute Lymphoblastic Leukemia

EA9152 Available Through ECOG-ACRIN Cancer Research Group

A Phase Ib/II Study of Venetoclax (ABT-199) in Combination with Liposomal Vincristine in Patients with Relapsed or Refractory T-cell or B-cell Acute Lymphoblastic Leukemia

Patient Population
See Section 3.0 for Complete Eligibility Details

Pre-registration (Step 0)– Phase I and II:
- Diagnostic bone marrow and/or peripheral blood specimens must be submitted for centralized immunophenotyping performed at the EA LTRL and results reported to the institution

Eligibility Criteria (Step 1)– Phase I and II:
- Must have a diagnosis of:
  - Relapsed/refractory B-cell/T-cell ALL after multi-agent chemotherapy (≥ 5% marrow lymphoblasts)
  - Patients with <5% blasts may enroll in phase I provided that MRD is present, per protocol, OR
  - Relapsed lymphoblastic lymphoma
- Age ≥ 18 years, ECOG PS 0-2, and adequate lab values
- No patients with isolated testicular/CNS relapsed disease; no active CNS leukemia per protocol
- Must not have Burkitt’s lymphoma/leukemia (WHO)
- No chemo within 2 weeks before Step 1 registration except to reduce the circulating lymphoblast count/palliation, or for ALL maintenance
- Prior HSCT allowed at least 90 days before Step 1 registration (see protocol for details)
- No poorly controlled chronic viral infections; HIV patients are permitted per protocol
- No NYHA Class III/IV heart failure, uncontrolled angina, severe uncontrolled ventricular arrhythmias or electrocardiographic evidence of acute ischema
- Must not be participating in any other clinical trial or taking any other experimental medications within 21 days prior to registration
- No strong/moderate CYP3A inhibitors/inducers within 7 days prior to the first dose of study drug
- No history of/current grade 3 or higher peripheral neuropathy; no patients with familial demyelinating disease

Treatment Plan
See Section 5.0 for Complete Treatment Details

Cycle 1= 42 days; cycle 2= 28 days. Bone marrow biopsies will be performed on Day 42 and 70 +/- 2 days

Phase I (Arm A, B, C):
- Venetoclax orally once daily, with a fixed standard dose of IV liposomal vincristine 2.25 mg/m² weekly starting after a 2 week lead-in phase of venetoclax:
  - Arm A: 20, 50, 100, 200 mg on Days 1, 2, 3, 4 and 400 mg on Days 5 – 42
  - Arm B: 50, 100, 200, 400 mg on Days 1, 2, 3, 4 and 600 mg on Days 5 – 42
  - Arm C: 100, 200, 400, 600 mg on Days 1, 2, 3, 4 and 800 mg on Days 5 – 42
- All patients should proceed to cycle 2 unless they have PD or they achieve CR/CRi and proceed to HSCT; patients may continue combination therapy until HSCT can be arranged. Cycle 2 (with liposomal vincristine):
  - Arm A: 400 mg on Days 43 – 70
  - Arm B: 600 mg on Days 43 – 70
  - Arm C: 800 mg on Days 43 – 70
- If patients achieve CR/CRi, they may continue on combination therapy/venetoclax after cycle 2 per physician discretion

Phase II (Arm D):
- Venetoclax orally once daily at dose to be determined per MTD in Phase I, Days 1-42; liposomal vincristine 2.25 mg/m² IV weekly x 4 starting Day 15
- All patients should proceed to cycle 2 unless they have PD or achieve a CR or CRi and proceed to HSCT (combination therapy can continue until this is arranged):
  - Venetoclax orally once daily at dose to be determined per MTD in Phase I, Days 43-70; liposomal vincristine 2.25 mg/m² IV over weekly x 4
- Patient may continue therapy per physician discretion

Patient Enrollment
All Sites: Oncology Patient Enrollment Network (OPEN) https://open.ctsu.org

Protocol Information

Please Enroll Your Eligible Patients!