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 or Vincristine Sulfate in Patients with Relapsed or Refractory T-cell or B-cell Acute Lymphoblastic Leukemia

**Patient Population**

See Section 3.0 for Complete Eligibility Details

**Eligibility Criteria – Phase I & II: Step 0:**

Enrollment to Step 0 may occur prior to/following completion of assessments to verify patient eligibility for Step I (bone marrow and/or peripheral blood must be submitted for Phase I)

**Eligibility Criteria – Phase I (Arms A, B, C):**

- Must have a diagnosis of:
  - Relapsed/refractory B-cell/T-cell ALL after multi-agent chemotherapy
  - 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 I registration except to reduce the circulating lymphoblast count/palliation, or for ALL maintenance
- Prior HSCT allowed at least 90 days before Step I 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 ischemia
- Must not be taking any other experimental medications within 21 days prior to registration; FDA approved medications will be allowed within 14 days of registration
- No strong/moderate CYP3A inhibitors/inducers within 7 days prior to the first dose of study drug/while on study
- No history of current grade 3 or higher peripheral neuropathy; no patients with familial demyelinating disease

**Eligibility Criteria – Phase II (Arm D):**

- Relapsed/refractory B-cell/T-cell ALL, including lymphoblastic lymphoma, after at least 1 line of chemotherapy
- No patients with prior venetoclax treatment for ALL

**Treatment Plan**

See Section 5.0 for Complete Treatment Details

Cycle 1 = 42 days; cycle 2 = 28 days

**Phase I (Arm A, B, C):**

Bone marrow biopsies will be performed on Day 42 and 70 +/- 2 days

- 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):**

Bone marrow biopsies will be performed on Day 28 and 56 (+/- 2 days)

- Venetoclax 600 mg orally once daily, Days 1-28; liposomal vincristine 2.25 mg/m² IV weekly x 4 starting Day 1 OR vincristine sulfate 1.4 mg/m² IV weekly x 4 (capped at 2 mg) [effective w/Add #11 patients should be switched to vincristine sulfate]

- All patients should proceed to cycle 2 unless they have PD or achieve a CR/CRi and proceed to HSCT

  - Cycle 2 +: Venetoclax 600 mg orally once daily, Days 1-28 per cycle; liposomal vincristine 2.25 mg/m² IV weekly x 4 starting Day 1 of each cycle OR vincristine sulfate 1.4 mg/m² IV every 4 weeks

- After cycle 2, 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!