NCI National Clinical Trials Network

EA9152

ECOG-ACRIN cancer research group

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 1 (bone marrow and/or peripheral blood must be submitted for Phase I)

Eligibility Criteria –Phase I (Arms A, B, C)- Step 1:

- 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 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 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)- Step 1:

- 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

Study Chair:
Neil Palmisiano, MD, MS

Co-Chair:
David Claxton, MD

Patient Enrollment

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

Protocol Information

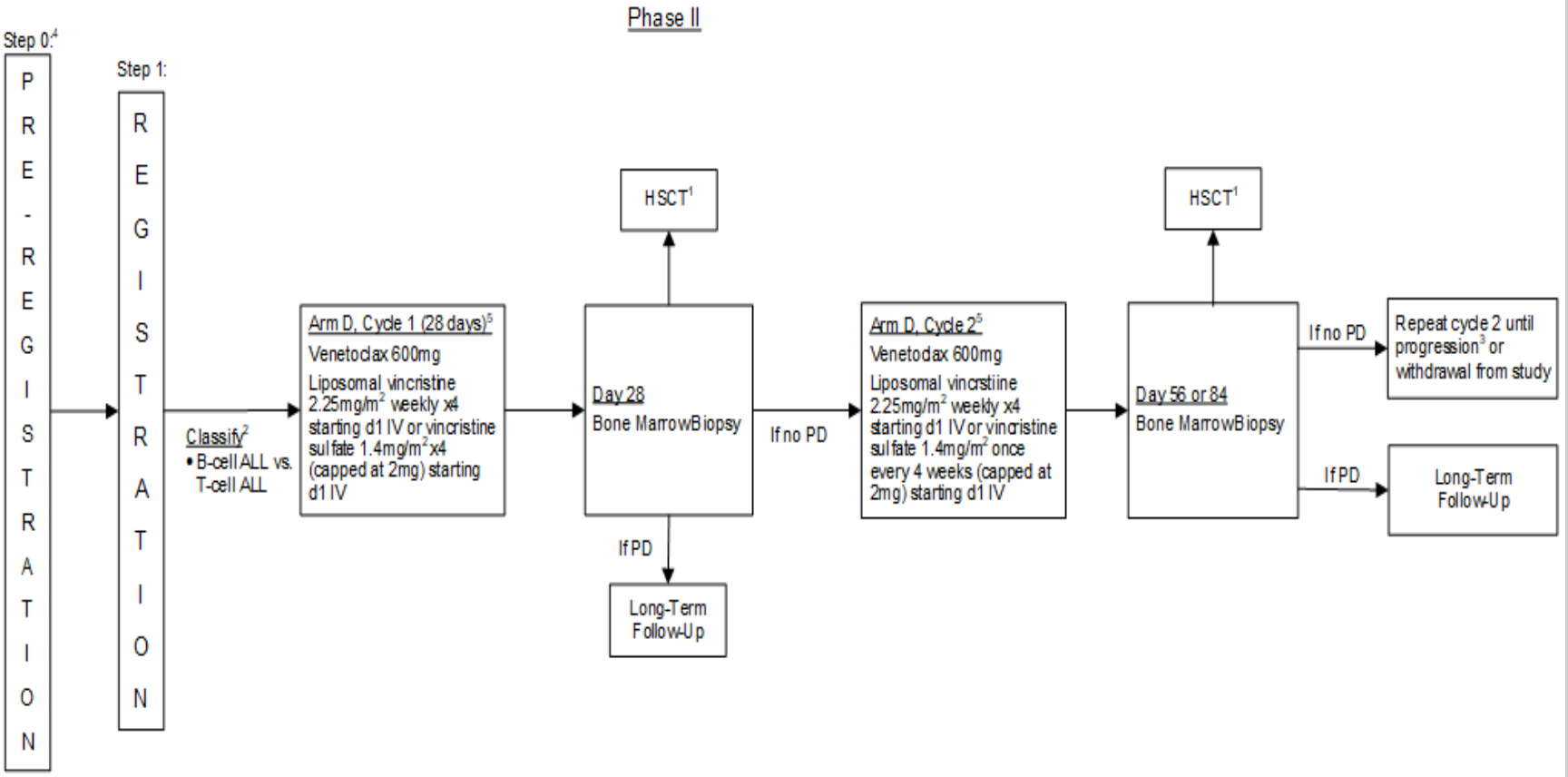
ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

Version 07/20/22 (Add. #11)

EA9152

Refer to the protocol for the Phase I schema (3-18 patients for dose escalation)



Phase II Accrual Goal: 56 patients

1. If patient demonstrates CR or CRi at day 28 or day 56 bone marrow biopsies, they may continue on combination therapy or proceed to HSCT if deemed fit for transplant and advised by treating physician. Patient may proceed to HSCT at any point at treating physician's discretion (if not day 28 or 56).
2. Patients will be classified by immunophenotype: B-cell ALL vs. T-cell ALL, with 28 patients as the accrual goal for each cohort.
3. If patient does not demonstrate any signs of progression, they may continue on combination therapy as long as they are receiving benefit per treating physician. Patients, if in CR/Cri by the end of cycle 2 may continue on combination or single agent venetoclax at the discretion of the treating physician.
4. Bone marrow and peripheral blood specimens collected for the purpose of banking.
5. In the event of liposomal vincristine shortage or discontinuation, patients actively undergoing treatment will be switched permanently to vincristine sulfate.
   NOTE: Liposomal Vincristine is no longer being manufactured