NCI National Clinical Trials Network

EA9181

ECOG-ACRIN cancer research group

For Patients with Acute Lymphoblastic Leukemia

Please Enroll Your Eligible Patients!

EA9181 Available Through ECOG-ACRIN Cancer Research Group

A Phase III Randomized Trial of Steroids + Tyrosine Kinase Inhibitor (TKI) Induction with Chemotherapy or Blinatumomab for Newly Diagnosed BCR-ABL-positive Acute Lymphoblastic Leukemia (ALL) in Adults

Patient Population

See protocol Section 3 for complete eligibility criteria

Eligibility Criteria for Pre-registration (Step 0):

- Age ≥ 18 and ≤ 75; ECOG PS 0-3
- Must be newly diagnosed with B-ALL or suspected to have ALL (must have BCR-ABL1 positive disease)
- Must not have a diagnosis of BCR/ABL T-ALL
- Must not have received chemotherapy for B-ALL
- Must not have unstable epilepsy that requires treatment
- Patients with lymphoid blast crisis CML are not eligible

Eligibility Criteria for Registration to Step 1:

- Must have a diagnosis of Ph+ ALL that has been determined locally, and bone marrow/peripheral blood sent and receipt confirmed for central confirmation
- Must not have known significant organ dysfunction defined per protocol (labs obtained ≤ 28 days prior to Step 1 registration; see protocol for details)
- Patients with HIV, HBV, HCV are eligible per protocol
- No active concomitant malignancy (see protocol)
- If applicable, patient must be NYHA class 2B or better
- Investigators must confirm which TKI the patient is to receive

Eligibility Criteria for Randomization to Step 2:

- Must have completed at least 7 and no more than 21 days of protocol treatment on Arm A prior to Step 2 randomization (see protocol for details)
- For patients under 70, intended chemotherapy regimen must be determined prior to randomization
- No active CNS involvement by leukemic blasts (see protocol for details)
- Must have resolved serious infectious/medical complications related to therapy

Eligibility Criteria for Registration to Step 3:

- Institution has received centralized MRD results confirming positive status

Treatment Plan

See protocol Section 5 for complete treatment details

Step 1– Single Arm Steroid + TKI Pre-Induction:

- **Arm A:** Prednisone 60 mg/m² PO (max dose 140 mg) daily days 1-21 + TKI (dasatinib 140 mg PO ***or*** ponatinib 30 mg PO, days 1-21) daily
- Spinal fluid examination– performed prior to Step 1 registration OR within 3 days of starting treatment

Step 2 Randomization– Induction Therapy:

- To be initiated within 7 days of Step 2 randomization
- **Arm B:** Chemotherapy arm (4 cycles + continuous therapy with TKI [dasatinib/ponatinib]); see protocol for fit patients ages 18-70 or patients > 70/unfit
- **Arm C:** Blinatumomab arm (2 cycles + continuous therapy with TKI)
  - ◊ Dexamethasone 20 mg PO/IV day 1; Blinatumomab 9 mcg/day continuous IV days 1-7 followed by 28 mcg/day continuous IV days 8-28, followed by 14 day treatment-free interval
- Patients must have achieved CR or CRi in order to begin intensification therapy; high dose methotrexate is to be administered after MRD testing

Step 3 Registration– Re-induction:

- **Arm D:** Patients treated on Arm B who at the end of induction remain MRD positive will receive blinatumomab based re-induction (i.e., Arm C regimen)
- **Arm E:** Patients treated on Arm C who at the end of induction remain MRD positive will receive chemotherapy based re-induction (i.e., Arm B regimen)
- Patients who received induction and re-induction but remained with detectable disease will proceed to follow-up and are treated per investigator discretion (see protocol)

Patients with a MRD Negative Status:

- Following Step 2 or 3, patients will proceed to follow-up treatment per physician discretion with recommendations for allo-HCT or consolidation followed by maintenance therapy (see protocol)

Study Chair:
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Study Co-Chair:
Jacob M. Rowe, MD

SWOG Co-Chair:
Kathleen W. Phelan, MD

Alliance Co-Chair:
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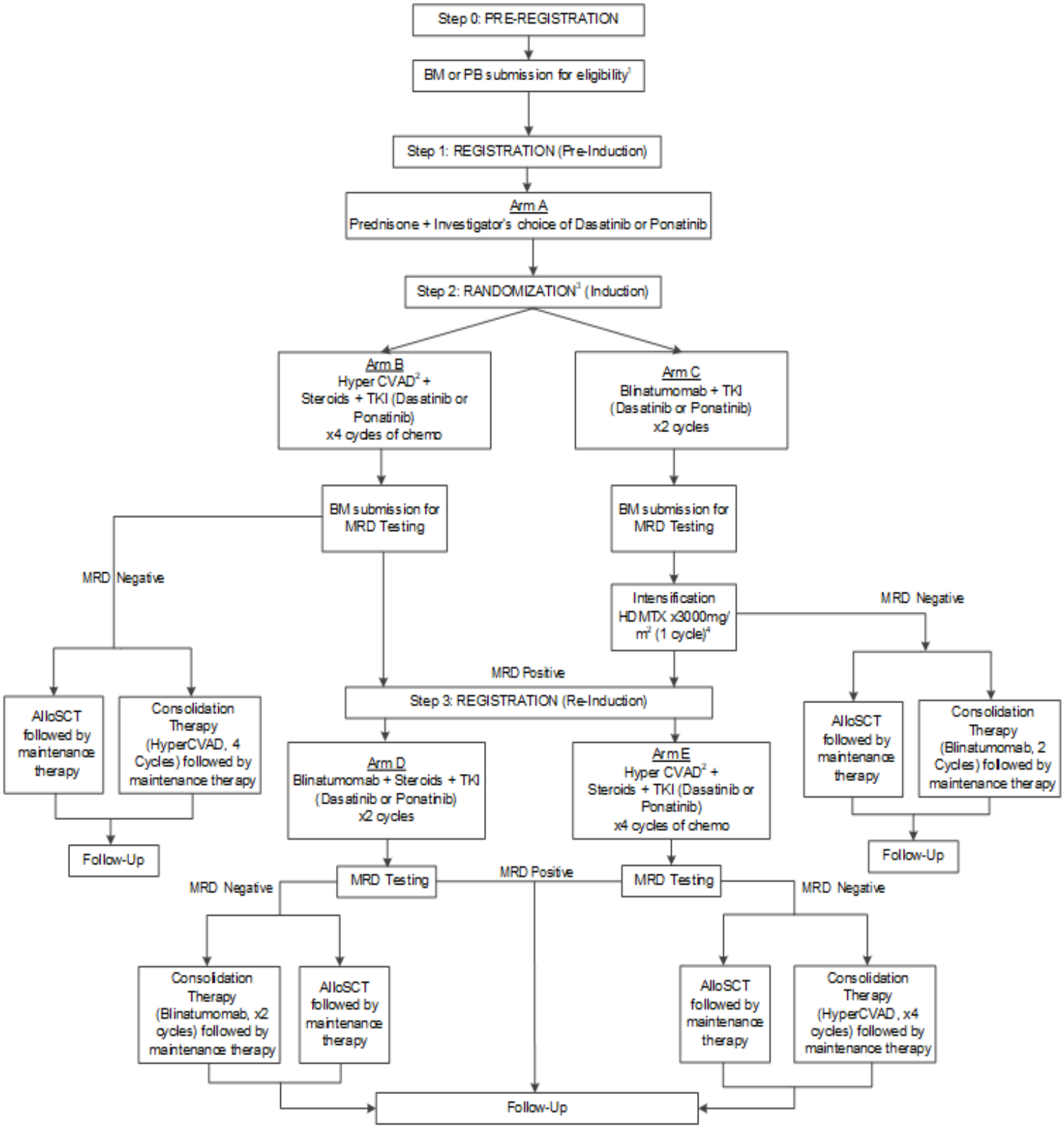
Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open 1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

Schema



Accrual: 348 patients

1: Bone marrow specimen must be submitted to ECOG-ACRIN Leukemia Bank at MD Anderson Cancer Center for the central establishment of BCR/ABL status to confirm patient's eligibility for registration to Step 1 as outlined in Section 10.1. If a diagnosis of BCR-ABL positive ALL has been established locally, the patient may be registered to Step 1without waiting for central confirmation. Peripheral Blood is only acceptable if there is circulating blasts.

2: Patients older than 70 and ***younger unfit patients*** are subject to modified Hyper-CVAD treatment only. All other patients will be treated with full Hyper-CVAD as outlined in Section 5. Type of planned Hyper-CVAD therapy is to be reported at time of registration.

3: At Step 2 Randomization, patients will be stratified by age (≤ 60 years vs 60-70 years vs > 70 years of age), TKI intended to receive (Dasatinib vs Ponatinib) and for patient age < 70 years, if patient is randomized to chemotherapy, investigators declaration of full or modified Hyper-CVAD protocol.

4: Patients must have achieved CR or CRi in order to begin intensification therapy.