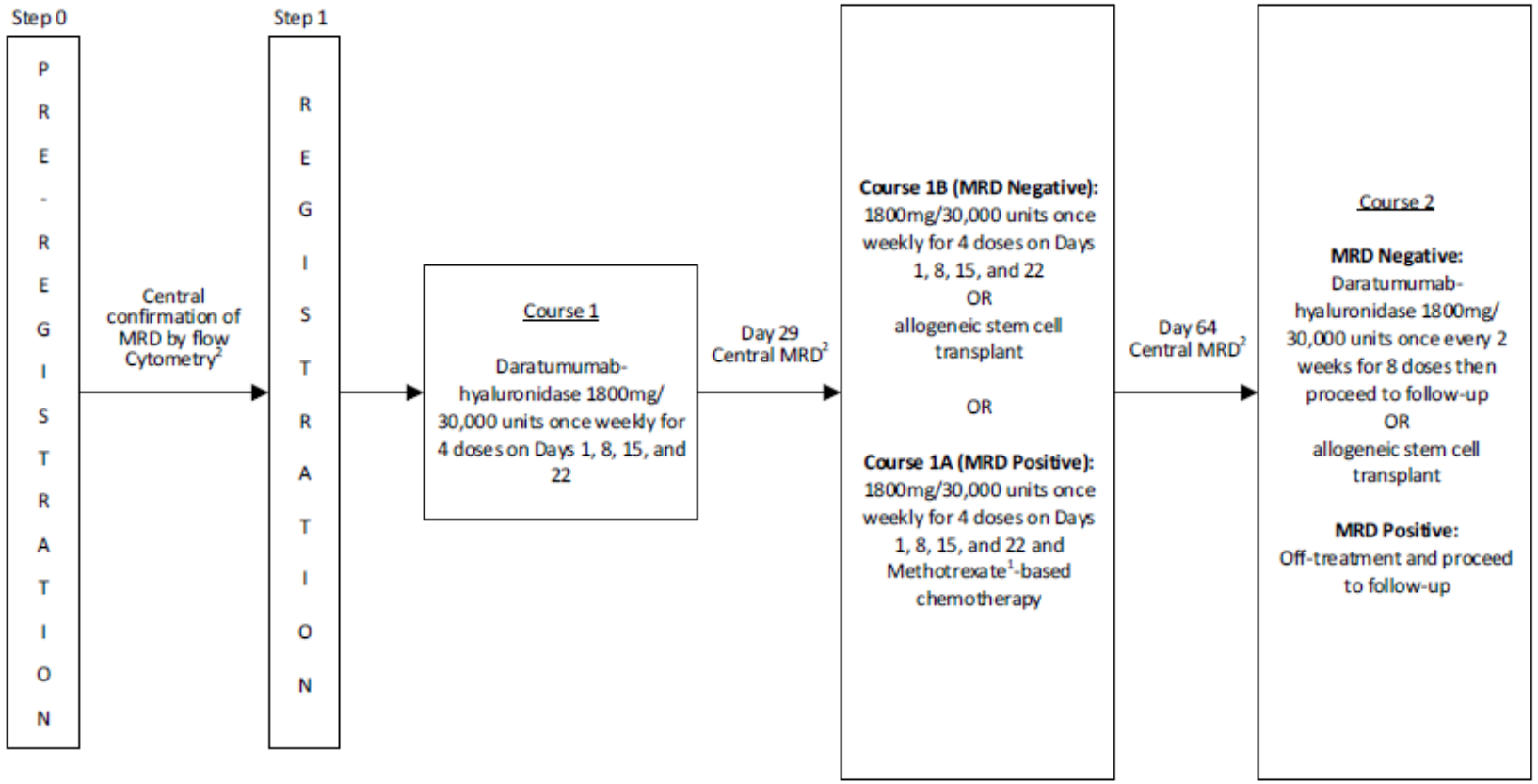
Schema



Accrual = 20

1. Refer to Section 5.1.2 for details on Methotrexate-based chemotherapy.
2. Refer to Section 10 for more information.
3. Patients with a complete MRD response on treatment can undergo allogeneic stem cell transplant at any time after Course 1 or Course 2 at the treating physician's discretion. Patients with morphologic evidence of T-ALL in the bone marrow with ≥ 5% blasts will be taken off study treatment.

3. Selection of Patients

Each of the criteria in the checklist that follows must be met in order for a patient to be considered eligible for this study. Use the checklist to confirm a patient's eligibility. For each patient, this checklist must be photocopied, completed and maintained in the patient's chart.

In calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test is done on a Monday, the Monday four weeks later would be considered Day 28.

ECOG-ACRIN Patient No. _____

Patient's Initials (L, F, M) _

Physician Signature and Date _____

NOTE: CTEP Policy does not allow for the issuance of waivers to any protocol specified criteria (http://ctep.cancer.gov/protocolDevelopment/policies_deviations.htm). Therefore, all eligibility criteria listed in Section 3 must be met, without exception. The registration of individuals who do not meet all criteria listed in Section 3 can result in the participant being censored from the analysis of the study, and the citation of a major protocol violation during an audit and require reporting to the IRB of record as non-compliance.

All questions regarding clarification of eligibility criteria must be directed to the Group's Executive Officer (EA.ExecOfficer@jimmy.harvard.edu) or the Group's Regulatory Officer (EA.RegOfficer@jimmy.harvard.edu).

NOTE: Institutions may use the eligibility checklist as source documentation if it has been reviewed, signed, and dated prior to registration by the treating physician.

NOTE: This study involves preregistration during which specimens must be submitted for centralized MRD status testing and results will determine patient's Step 1 eligibility (Section 3.2).

3.1 Preregistration (Step 0)

Patient must be able to undergo diagnostic bone marrow aspirate following preregistration if not performed previously.

NOTE: Bone marrow aspirate must be submitted to Dr. Brent Wood's laboratory at Children's Hospital Los Angeles for central assessment of the establishment of MRD status to confirm patient's eligibility for registration to Step 1.

Bone marrow must be from the first pull (initial or redirect needle) and specimens must contain sufficient blast cells. In cases where the bone marrow aspiration is not adequate or the bone marrow examination has already been performed prior to study consent and enrollment on Step 0, peripheral blood can be submitted regardless of peripheral blast percentage.

Dr. Brent Wood's laboratory at Children's Hospital Los Angeles will forward results within 48 hours (two business days) of receipt of the specimen to the submitting institution.

NOTE: If MRD status testing was performed previously as part of standard of care at Dr. Brent Wood's laboratory, eligible patients can proceed from Step 0 preregistration directly to Step 1 registration after forwarding MRD report to Dr. Brent Wood for verification and uploading report via Medidata Rave. MRD testing will not be accepted from other laboratories. Step 0 preregistration cannot be bypassed. MRD must be quantified within 14 days prior to starting daratumumab treatment on study.

_____3.1.1 Patient must be ≥ 18 years of age.

_____3.1.2 Patient must have documented T cell ALL and must be in first or later hematologic CR or CRi after a minimum of 2 blocks of intensive chemotherapy.

3.1.2.1 Patients ≥ 65 years of age that the physician judges to be unfit for 2 blocks of intensive chemotherapy may enroll after one cycle of chemotherapy as long as they are in CR or CRi at least 28 days after initiation of Leukemia directed therapy. These patient must have received at least 4 weekly doses of vincristine and steroids.

3.2 Registration (Step 1)

_____3.2.1 Patient must meet eligibility criteria outlined in Section 3.1.

_____3.2.2 Patients in hematologic CR or CRi must have persistent or recurrent MRD ≥ 10^{-4}.

_____3.2.3 Institution must have received central MRD status test results confirming persistent or recurrent MRD ≥ 10^{-4} by flow cytometry.

_____3.2.4 Patient may have undergone a prior allogeneic stem cell transplant, but patient may not have Grafts Versus Host Disease (GVHD) that requires ongoing immunosuppressive therapy. Patient may receive prednisone if the dose is ≤ 10 mg per day.

_____3.2.5 Patient must have an ECOG performance status 0-2.

_____3.2.6 Patient must not be pregnant or breast-feeding due to the potential harm to an unborn fetus and possible risk for adverse events in nursing infants with the treatment regimens being used.

All patients of childbearing potential must have a blood test or urine study within 14 days prior to Step 1 registration to rule out pregnancy.

A patient of childbearing potential is defined as anyone, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).

Patient of childbearing potential?_____(Yes or No)

If yes, Date of blood test or urine study: _____

_____ 3.2.7 Patients must not expect to conceive or father children by using an accepted and effective method(s) of contraception or by abstaining from sexual intercourse for the duration of their participation in the study and continue to 3 months after the last dose of protocol treatment. Patients must also agree to abstain from donating sperm, even if they have had a successful vasectomy, or donating eggs while on study treatment and for 3 months after the last dose of protocol treatment.

_____3.2.8 Patient must have the ability to understand and the willingness to sign a written informed consent document. Patients with impaired decision-making capacity (IDMC) who have a legally authorized representative (LAR) or caregiver and/or family member available will also be considered eligible.

_____3.2.9 Patient must have adequate organ and marrow function as defined below (these labs must be obtained ≤ 7 days prior to Step 1 registration):

- Absolute neutrophil count (ANC) ≥ 750/µL

  ANC:_____Date of Test: _____

- Platelets ≥ 75,000/µL

  Platelets:_____Date of Test: _____

  Total or Direct bilirubin ≤ 2 mg/dL

  _____Total Bilirubin:_____Direct Bilirubin: _____

  Date of Test: _____

- AST(SGOT)/ALT(SGPT) ≤ 3.0 × institutional ULN

  AST:_____Institutional ULN: _____

  Date of Test: _____

  ALT:_____Institutional ULN: _____

- _____ Creatinine ≤ 1.5 x institutional ULN or Creatinine Clearance > 30 ml/min

  Creatinine:_____Institutional ULN: _____

  Creatinine Clearance: _____

  Date of Test: _____

_____3.2.10 Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of registration are eligible for this trial.

_____3.2.11 For patients with evidence of chronic hepatitis B virus (HBV) infection, the HBV viral load must be undetectable on suppressive therapy, if indicated.

_____3.2.12 Patients with a history of hepatitis C virus (HCV) infection must have been treated and cured. For patients with HCV infection who are

currently on treatment, they are eligible if they have an undetectable HCV viral load.

_____3.2.13 Patients with prior CNS involvement are eligible as long as they do not have active CNS involvement at time of Step 1 registration.

_____3.2.14 Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

_____ 3.2.15 Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients should be class 2B or better.

_____ _____

Physician Signature Date

OPTIONAL: This signature line is provided for use by institutions wishing to use the eligibility checklist as source documentation.