NCI National Clinical Trials Network

EA9213

ECOG-ACRIN cancer research group

For Patients with T Cell Acute Lymphoblastic Leukemia/Lymphoma

Please Enroll Your Eligible Patients!

EA9213 Available Through ECOG-ACRIN Cancer Research Group

A Phase II Study of Daratumumab-Hyaluronidase for Chemotherapy-Relapsed/Refractory Minimal Residual Disease (MRD) in T Cell Acute Lymphoblastic Leukemia/Lymphoma (T-ALL/T-LBL)

Patient Population

See protocol Section 3 for complete eligibility criteria

Step 0 (Pre-registration):

- *Note: Must be able to undergo diagnostic bone marrow aspirate following Step 0, if not performed previously*
- Must be ≥ 12 years of age and weight ≥ 40 kg
- Must have documented T cell acute lymphoblastic leukemia (ALL) or lymphoblastic lymphoma (LBL), and must be in first or later morphologic CR, CRh, or CRi after ≥ 2 blocks of intensive chemotherapy
  - ◊ Patients ≥ 65 years of age that are unfit for 2 blocks of intensive chemotherapy may enroll after 1 cycle of therapy as long as they are in CR, CRh, or CRi ≥ 28 days after initiation of ALL/LBL-directed therapy

Step 1 (Registration):

- Patients in morphologic CR, CRh, or CRi must have persistent or recurrent MRD ≥ 10^{-4} that has been determined by central flow cytometry at Children's Hospital of Los Angeles or determined by Adaptive clonoSEQ testing with result of ≥ 1 residual clonal cell per million nucleated cells
- Prior allogeneic stem cell transplant (SCT) acceptable, but may not have GVHD requiring ongoing immunosuppressive therapy (prednisone ≤ 10 mg QD is acceptable)
- Patients ≥ 18 years of age: ECOG PS 0-2; patients < 18 years of age: Lansky Performance Score ≥ 50
- Adequate organ and marrow function on labs ≤ 7 days prior to Step 1 registration
- Patients with prior CNS involvement are eligible as long as they do not have active CNS involvement at the time of Step 1 registration; patients with extramedullary involvement outside the CNS are eligible if they are asymptomatic from the lesions
- Patients who have controlled intermittent asthma or controlled mild persistent asthma are eligible
- Must have adequate cardiac function (per criterion 3.2.16) and pulmonary function (per criterion 3.2.17)

Treatment Plan

See protocol Section 5 for complete treatment details

Note: Pre-and post-medications per protocol

Course 1 (Days 1-28)- Daratumumab:

- 1,800 mg/30,000 units SQ q1 week x 4 doses (Days 1, 15, 22, 28)

Day 29 MRD Assessment (Bone Marrow Aspirate):

- MRD neg.: proceed to allogeneic SCT or **Course 1B**
  - ◊ May receive donor lymphocyte infusion and continue daratumumab per physician discretion
- MRD pos.: proceed to **Course 1A** (Options 1-3)
  - ◊ If complete MRD response not achieved, may discontinue study treatment for allogeneic SCT
- Progressive disease: discontinue study treatment if morphologic and/or flow cytometric evidence of T-ALL/T-LBL in the bone marrow with ≥ 5% blasts
- Daratumumab may not be given after allogeneic SCT

Course 1A or 1B (Days 36-63):

- **Course 1A, Option 1**: Daratumumab (SQ), cytarabine [ARAC] (IV&IT), methotrexate [MTX] (IV&IT)
  - ◊ Peds pts: MTX, hydrocortisone, ARAC (all IT)
- **Course 1A, Option 2:** Daratumumab (SQ), escalating MTX (IV), vincristine (IV), pegaspargase (IV or IM) [pts ≥ 22 years old] *or* calaspargase pegol (IV) [pts < 22 years old], MTX (IT)
- **Course 1A, Option 3:** Daratumumab (SQ), nelarabine (IV)
- **Course 1B:** Daratumumab (SQ)

Day 64 MRD Assessment (Bone Marrow Aspirate):

- MRD neg.: if not undergoing allogenic SCT, may proceed to **Course 2**
- MRD pos.: off treatment, proceed to follow-up

Course 2- Daratumumab:

- 1,800 mg/30,000 units SQ q2 weeks (+/-3 days) for 8 doses (Days 1, 15, 29, 43, 57, 71, 85, 99)

Study Chair:
Shira Dinner, MD

Study Co-Chair:
Talha Badar, MD

COG Co-Chair:
Teena Bhatla, MD

NCTN Study Champions:
- ***Alliance:*** Madelyn Burkart, MD
- ***SWOG:*** Ryan D. Cassaday, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

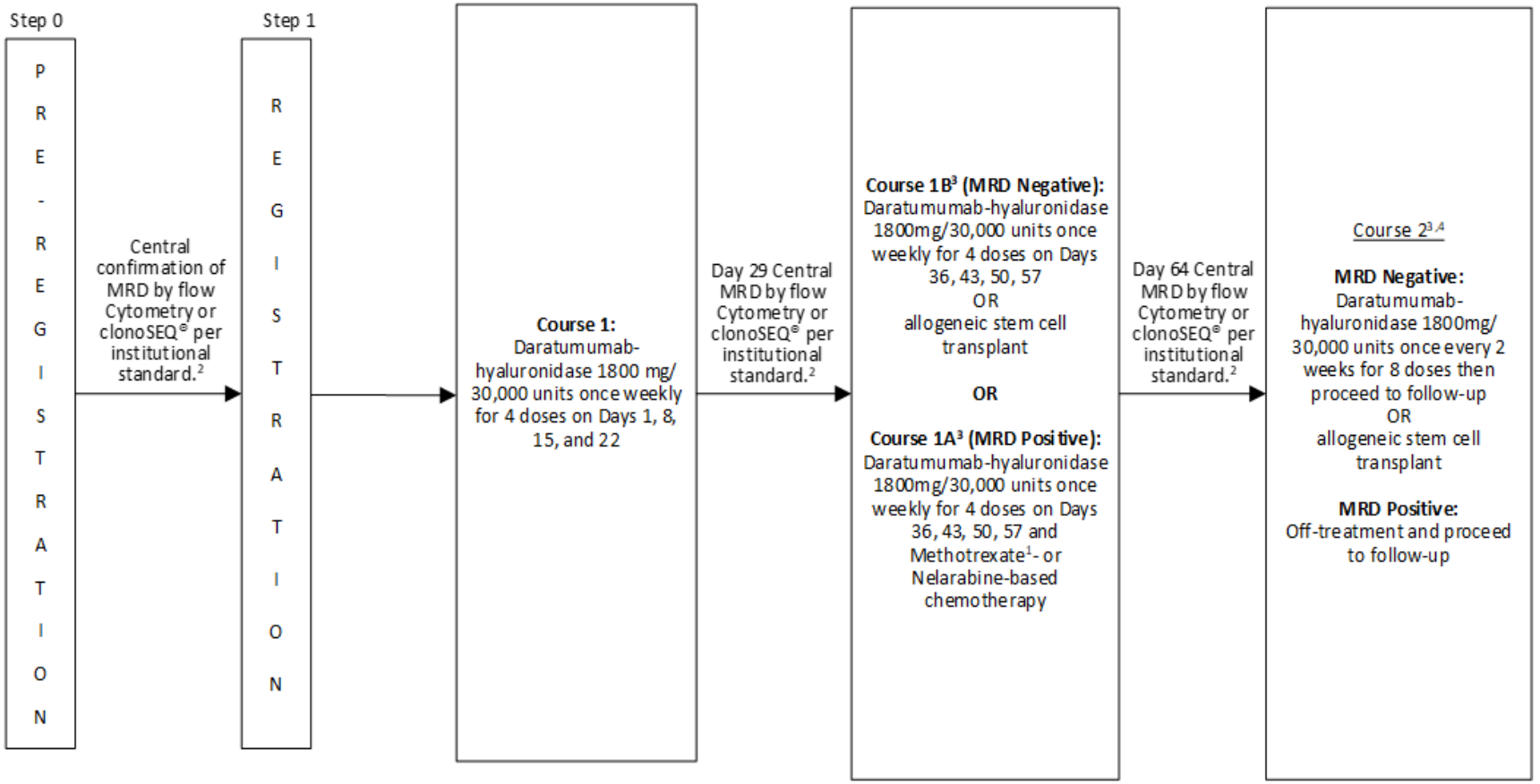
https://open.ctsu.org/open 1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

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

EA9213

Schema



Accrual = 20

1. Refer to Section 5.1.2 for details on Methotrexate-based chemotherapy.
2. All patients must have sample submitted for central MRD by flow cytometry. 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, Course 1A or Course 1B 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.
4. The start of Course 2 may be delayed until after results of the bone marrow MRD assessment are available. If blood counts have not recovered to ANC ≥ 750 µL and platelets ≥ 75,000/µL, contact the study chair to consider repeat bone marrow reassessment versus discontinuing study treatment.