Version 09/16/21 (Add. #2)

NCI National Clinical Trials Network

EAA181/EQUATE

For Patients with Newly Diagnosed Multiple Myeloma

EAA181 Available Through ECOG-ACRIN Cancer Research Group

Effective Quadruplet Utilization after Treatment Evaluation (EQUATE):
A Randomized Phase 3 Trial for Newly Diagnosed Multiple Myeloma not Intended for Early Autologous Transplantation

Patient Population:

See Protocol Section 3.0 for Complete Eligibility Details

Step 0 Pre-Registration:

- Age ≥ 18 years; ECOG PS 0-2 (PS 3 allowed if secondary to pain); able to have a diagnostic bone marrow aspirate
- Must have suspected/confirmed newly diagnosed MM (IMWG); no more than 1 cycle of treatment
- Must be ineligible for autologous stem cell transplantation/willing to delay stem cell transplantation until first relapse or later (stem cell collection is allowed)
- Must agree to register to Celegene Revlimid REMS/ comply with requirements
- No known allergies/hypersensitivity/intolerance to corticosteroids, monoclonal antibodies/human proteins, or their excipients, or known sensitivity to mammalian-derived products

Step 1 Registration:

- Dominant sequences must have been identified
- Must have standard risk MM (R-ISS) Stage I/II and measurable/evaluable disease defined per protocol; adequate lab values
- Must have received no more than 1 cycle (28 days or less) of prior chemotherapy and no more than 160 mg of prior dexamethasone (or equivalent dose of prednisone) for treatment of symptomatic myeloma; must not have been exposed to daratumumab for treatment of symptomatic myeloma; prior RT to symptomatic lesions is allowed per protocol (see protocol for SMM treatment)
- HIV, HBV, HCV patients permitted per protocol
- Must be NYHA class 2B or better/meet cardiac criteria per protocol; DVT or PE patients are permitted if they are on anti-coagulation
- No peripheral neuropathy ≥ Gr 2 (or Gr 1 with pain)
- Must not have moderate/severe persistent asthma within the past 2 years/uncontrolled asthma of any classification

Step 2 Randomization:

- Institution must have received MRD test results; adequate lab values
- Must have completed Step 1 without experiencing progression

Treatment Plan:

See Protocol Section 5.0 for Complete Treatment Details

Cycle= 28 days

Step 1– Induction (9 cycles):

- **Arm A:**
  - ◊ Daratumumab-hyaluronidase 1800 mg/30,000 units SC days 1, 8, 15, 22 cycles 1-2; days 1 and 15 cycles 3-6; day 1 cycles 7-9
  - ◊ Lenalidomide 25 mg PO daily days 1-21 cycles 1-9
  - ◊ Dexamethasone 40 mg PO days 1, 8, 15, 22 cycles 1-4; 20 mg PO days 1, 8, 15, 22 cycles 5-9

Step 2- Consolidation (9 cycles) and Maintenance (until disease progression):

- **Arm B:**
  - ◊ Consolidation (9 cycles/ study cycles 10-18):
    - ♦ Bortezomib 1.3 mg/m² SC (or IV per protocol) days 1, 8, 15 cycles 1-9
    - ♦ Daratumumab-hyaluronidase 1800 mg/30,000 units SC once every 28 days (day 1) cycles 1-9
    - ♦ Lenalidomide 15 mg PO daily days 1-21 cycles 1-9 (or dose tolerated in cycle 9)
    - ♦ Dexamethasone 12 mg PO days 1, 8, 15, 22 cycles 1-9 (or dose tolerated in cycle 9)
  - ◊ Maintenance (study cycles 19+):
    - ♦ Daratumumab-hyaluronidase 1800 mg/30,000 units SC once every 28 days (day 1)
    - ♦ Lenalidomide 10 mg PO daily days 1-21
- **Arm C:**
  - ◊ Consolidation (9 cycles/ study cycles 10-18): same as Arm B WITHOUT Bortezomib
  - ◊ Maintenance (study cycles 19+): same as Arm B

Notes:

- *See protocol for pre-medication/daratumumab injection information, and dose modifications*
- *Patients should complete a medication diary for lenalidomide and dexamethasone each cycle; see protocol for fertility instructions*
- *Stem cells can be mobilized after 4 cycles of induction*

Study Chair:
Shaji Kumar, MD

Co-Chair:
Michael A. Thompson, MD, PhD, FASCO

Patient Enrollment

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

Protocol Information

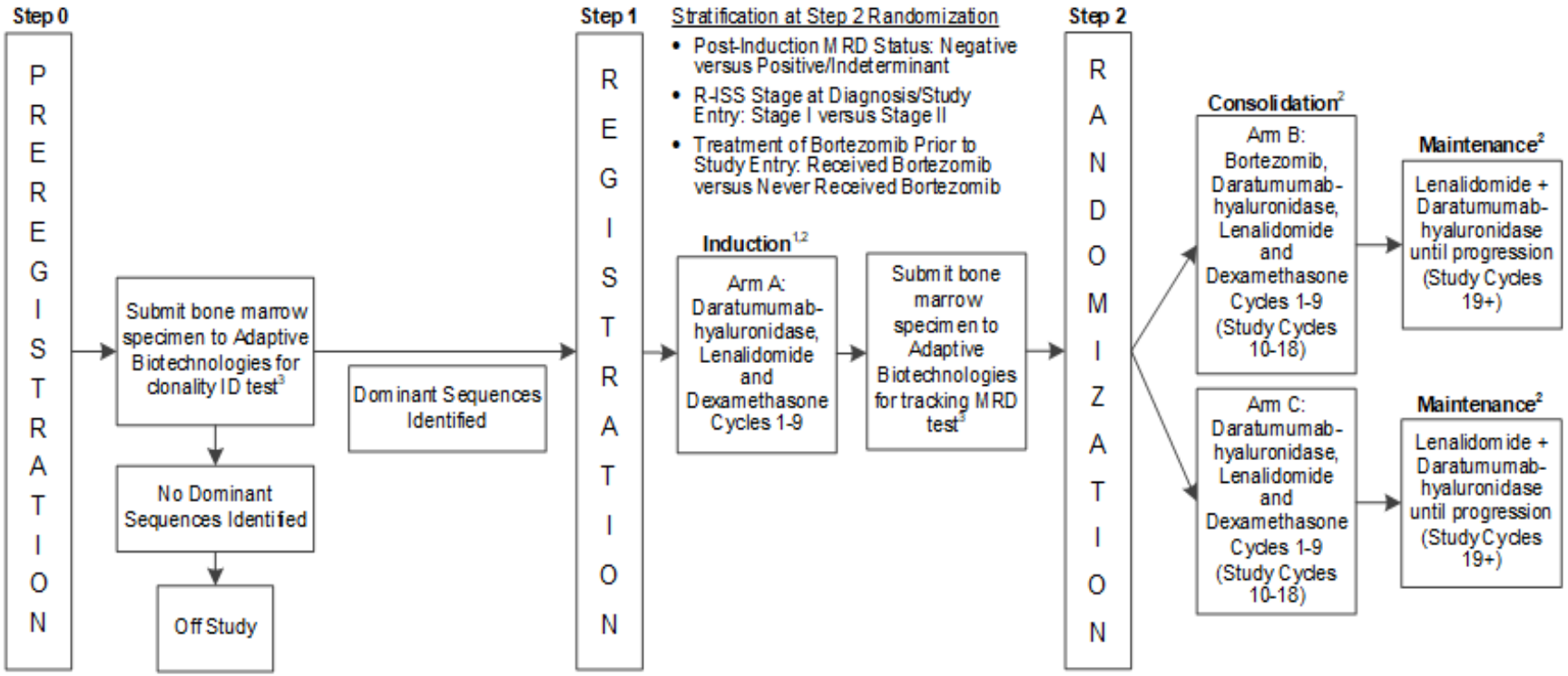
ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

ECOG-ACRIN cancer research group

EA181

Schema



Accrual Goal:
Step 1 = 1450
Cycle Duration: 28 days (4 weeks)

1. Patients can mobilize stem cells any time after 4 cycles of induction therapy. If stem cells are harvested, patients can be off treatment for up to 35 days for completion of stem cell collection. While stem cell collection is strongly recommended for patients who are considered eligible for transplant, it is not mandated.
2. Refer to Section 5.1 for detailed dosing instructions.
3. Institutions will be notified of the results of the Clonality ID and tracking MRD tests. Patients for whom dominant sequences were identified must submit bone marrow specimen for MRD test.