NCI National Clinical Trials Network

EAA181/EQUATE

For Patients with Newly Diagnosed Multiple Myeloma

Please Enroll Your Eligible Patients!

EAA181 Available Through ECOG-ACRIN Cancer Research Group

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

Patient Population

See protocol Section 3 for complete eligibility criteria

Step 0 (Pre-Registration)

- Age ≥ 18 years; ECOG PS 0-2 (or 3, if secondary to pain)
- Must have suspected/confirmed newly diagnosed multiple myeloma (MM) by IMWG criteria and received no more than 1 cycle of treatment; must be ineligible for ASCT or willing to delay SCT until first relapse or later (stem cell collection is allowed)
- Must agree to register to Celgene Revlimid REMS program and comply with requirements
- No known allergies, hypersensitivity, intolerance to corticosteroids, monoclonal antibodies or human proteins/their excipients, or known sensitivity to mammalian-derived products
- Able to undergo diagnostic bone marrow aspirate if not performed previously (see criterion 3.1.8 for details)

Step 1 (Registration)

- Must have standard risk MM (R-ISS) Stage I/II; Clonality test results received with dominant sequences identified
- Must have measurable/evaluable disease per criterion 3.2.4; if measurable disease only in bone marrow, must have biopsy or aspirate ≤ 28 days prior to Step 1 registration (otherwise, bone marrow exam ≤ 90 days prior)
- SPEP, UPEP, serum FLC assay ≤ 28 days prior to registration; adequate labs ≤ 14 days prior to registration
- Must have received no more than 1 cycle (≤ 28 days) of prior chemotherapy and ≤ 160 mg of prior dexamethasone (or equivalent dose of prednisone) for treatment of symptomatic myeloma; prior RT to symptomatic lesions allowed; prior treatment for SMM allowed except lenalidomide + anti-CD38 monoclonal antibody
- Patients with cardiovascular/pulmonary history (i.e., DVT, PE, COPD, asthma, etc.) must meet criteria per protocol
- No peripheral neuropathy ≥ Grade 2 (or Grade 1 w/ pain)

Step 2 (Randomization)

- Tracking (MRD) test results received; must be MRD positive after induction (see criterion 3.3.2)
- Completed Step 1 induction without experiencing progression; adequate labs ≤ 14 days prior to registration

Treatment Plan

See protocol Section 5 for complete treatment details

Cycle= 28 days (+/- 3 day window)

Step 1: Induction/Arm A (Cycles 1-9)

- *Note: If immediate treatment is required, 1 cycle of treatment is permitted while awaiting Clonality test results*
- Daratumumab-hyaluronidase: 1800 mg/30,000 units SC; Cycles 1-2: Days 1, 8, 15, 22; Cycles 3-6: Days 1 and 15; Cycles 7-9: Day 1
- Lenalidomide: 25 mg PO QD Cycles 1-9, Days 1-21 (patients ≥ 75 years are permitted 15 mg dose)
- Dexamethasone: 40 mg PO Cycles 1-4: Days 1, 8, 15, 22; 20 mg PO Cycles 5-9: Days 1, 8, 15, 22 (patients ≥ 75 years are permitted 20 mg Cycles 1-4 and 12 mg Cycles 5-9)
- *Stem cells can be mobilized any time after 4 cycles of induction (for which treatment may be held ≤ 42 days)*

Step 2: Consolidation (9 cycles) & Maintenance

- **Arm B Consolidation (Cycles 10-18)**
  - ◊ Bortezomib: 1.3 mg/m² SC (or IV rapid push, per protocol); Cycles 10-18: Days 1, 8, 15
  - ◊ Daratumumab-hyaluronidase: 1800 mg/30,000 units SC; Cycles 10-18: Day 1
  - ◊ Lenalidomide: 15 mg PO QD (or final dose tolerated at end of induction); Cycles 10-18: Days 1-21
  - ◊ Dexamethasone: 12 mg PO (or dose tolerated in Cycle 9); Cycles 10-18: Days 1, 8, 15, 22
- **Arm C Consolidation (Cycles 10-18)**
  - ◊ Same as Arm B WITHOUT Bortezomib
- **Arms B & C Maintenance- Until Progression**
  - ◊ Daratumumab-hyaluronidase: 1800 mg/30,000 units SC; Cycles 19+: Day 1
  - ◊ Lenalidomide: 10 mg PO QD (or final dose tolerated at end of consolidation); Cycles 19+: Days 1-21

Note: See protocol for lenalidomide reduced dosing for patients with CrCl 30-59 mL/min, and pre-medications/ supportive care

Study Chair:
Shaji Kumar, MD

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

NCTN Study Champions:
- ***Alliance:*** Edward Faber, DO, MS
- ***SWOG:*** Krisstina Gowin, DO

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

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

Protocol Information (ECOG-ACRIN Operations – Boston)

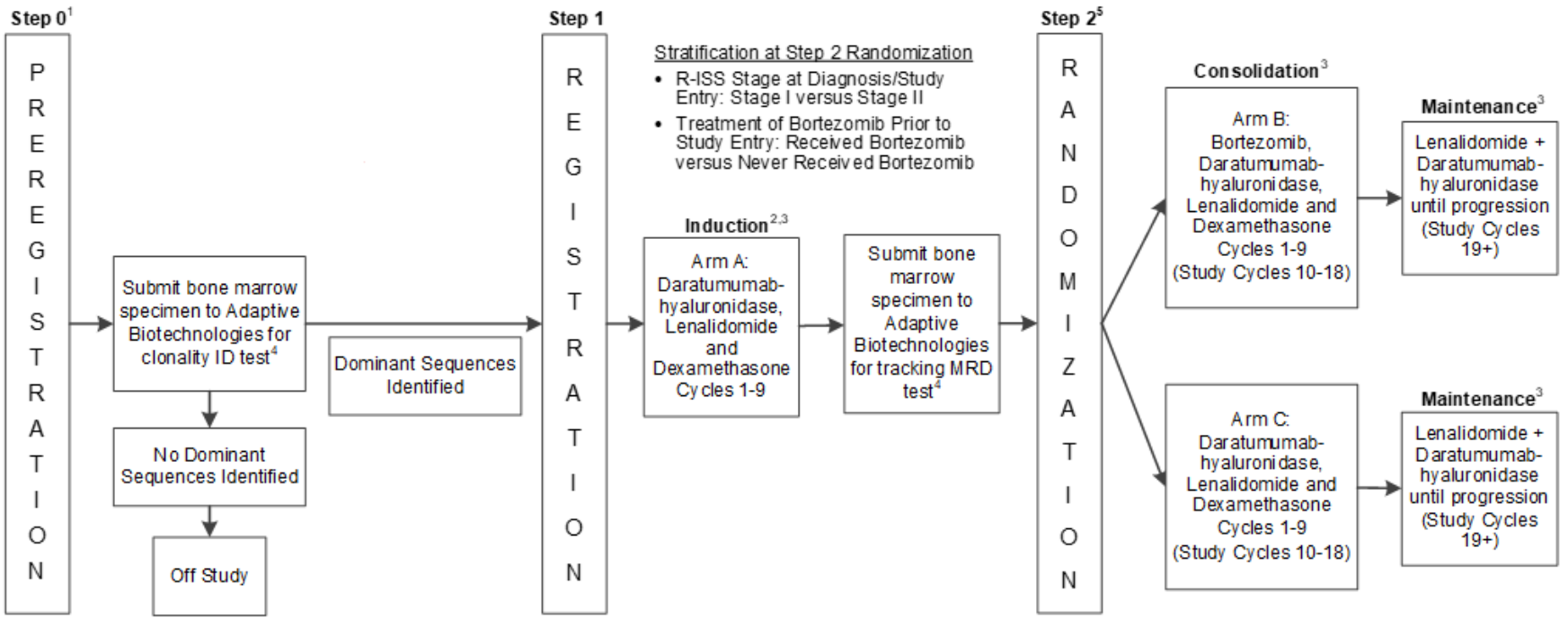
http://ecog-acrin.org (Member Login) 1-857-504-2900

v.01/29/26 (Add. #4)

ECOG-ACRIN cancer research group

EA181

Schema



Accrual Goal:
Step 1 = 542
Cycle Duration: 28 days (4 weeks)

1. Please refer to Section 5.1 for an overview of the Step 0 process.
2. 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 42 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.
3. Refer to Section 5.1 for detailed dosing instructions.
4. 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.
5. As of Addendum #4: Patients must be MRD positive after induction to be randomized to Step 2. Patients with post-induction MRD status of negative or indeterminate will not be randomized. Please refer to Section 3.3.2 for additional details.