NCI National Clinical Trials Network

EAA173/DETER-SMM

For Patients with Smoldering Myeloma

EAA173 Available Through ECOG-ACRIN Cancer Research Group

Daratumumab to Enhance Therapeutic Effectiveness of Revlimid in Smoldering Myeloma (DETER-SMM)

Patient Population:

See Protocol Section 3 for Complete Eligibility Details

Step 0 Pre-registration: Must be considered a potential candidate for participation on EAA173

Step 1 Randomization:

- Age ≥ 18 years, ECOG PS 0-2, and adequate lab values
- Must be diagnosed with asymptomatic high-risk (defined per protocol) smoldering multiple myeloma (SMM) within the past 12 months
- Bone marrow aspirate and/or biopsy must be performed within 42 days of randomization and must demonstrate 10-59% clonal plasma cells
- Must have measurable disease defined per protocol
- Must have no lytic lesions, no known plasmacytoma, and no unexplained hypercalcemia (see protocol)
- No known COPD defined per protocol, or moderate/ severe persistent asthma
- No prior/concurrent systemic or radiation therapy for the treatment of myeloma; no contraindication to DVT prophylaxis/aspirin
- Must not have more than 1 focal marrow lesion on MRI of either pelvis or spine
- No concurrent use of erythropoietin
- Prior glucocorticosteroid therapy for the treatment of multiple myeloma is not permitted (but other glucocorticosteroid use is permitted per protocol)
- Must not have active, uncontrolled seizure disorder, or uncontrolled intercurrent illness (see protocol)
- Patients with monoclonal gammopathy of undetermined significance are not eligible
- No Grade 2 or higher peripheral neuropathy (CTCAE)
- No active, uncontrolled infection
- May have a history of current/previous deep vein thrombosis/pulmonary embolism but are required to take anticoagulation; should not have NYHA classification III/IV heart failure at baseline
- HIV, HBV, HCV patients are eligible per protocol

Treatment Plan:

See Protocol Section 5 for Complete Treatment Details

1 cycle= 28 days

Arm A– DRd:

- Daratumumab may be administered in either the IV or SC formulation (they are not interchangeable; see protocol for cross over details)
  - ◊ 16 mg/kg **IV** days 1, 8, 15, and 22, cycles 1-2 (split -dosing schedule may be used for first infusion); 16 mg/kg IV days 1 and 15 cycles 3-6; 16 mg/kg IV day 1 cycles 7-24
  - ◊ 1800 mg/30,000 units **SC** days 1, 8, 15, cycles 1-2, then days 1 and 15 cycles 3-6, and then day 1 for cycles 7-24
- Lenalidomide 25 mg PO daily days 1-21, cycles 1-24
  - ◊ Note: starting dose should be reduced to 10 mg for patients with creatinine clearance of 30-59 mL/min
- Dexamethasone 40 mg PO days 1, 8, 15 and 22, cycles 1-6; 20 mg PO days 1, 8, 15, and 22, cycles 7-12

Arm B– Rd:

- Lenalidomide 25 mg PO daily days 1-21, cycles 1-24
  - ◊ Note: starting dose should be reduced to 10 mg for patients with creatinine clearance of 30-59 mL/min
- Dexamethasone 40 mg PO days 1, 8, 15 and 22, cycles 1-6; 20 mg PO days 1, 8, 15, and 22, cycles 7-12

Notes:

- *Dosing is based on actual body weight*
- *Patients should complete a medication diary for lenalidomide and dexamethasone each cycle*
- *See protocol for pre and post-treatment medication details*
- *All participants must be registered to the mandatory REMS program and be willing and able to comply with the requirements of REMS; see protocol for fertility instructions*

Study Chair:
Natalie Callander, MD

Co-Chair:
Sagar Lonial, MD

Patient Enrollment

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

Protocol Information

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

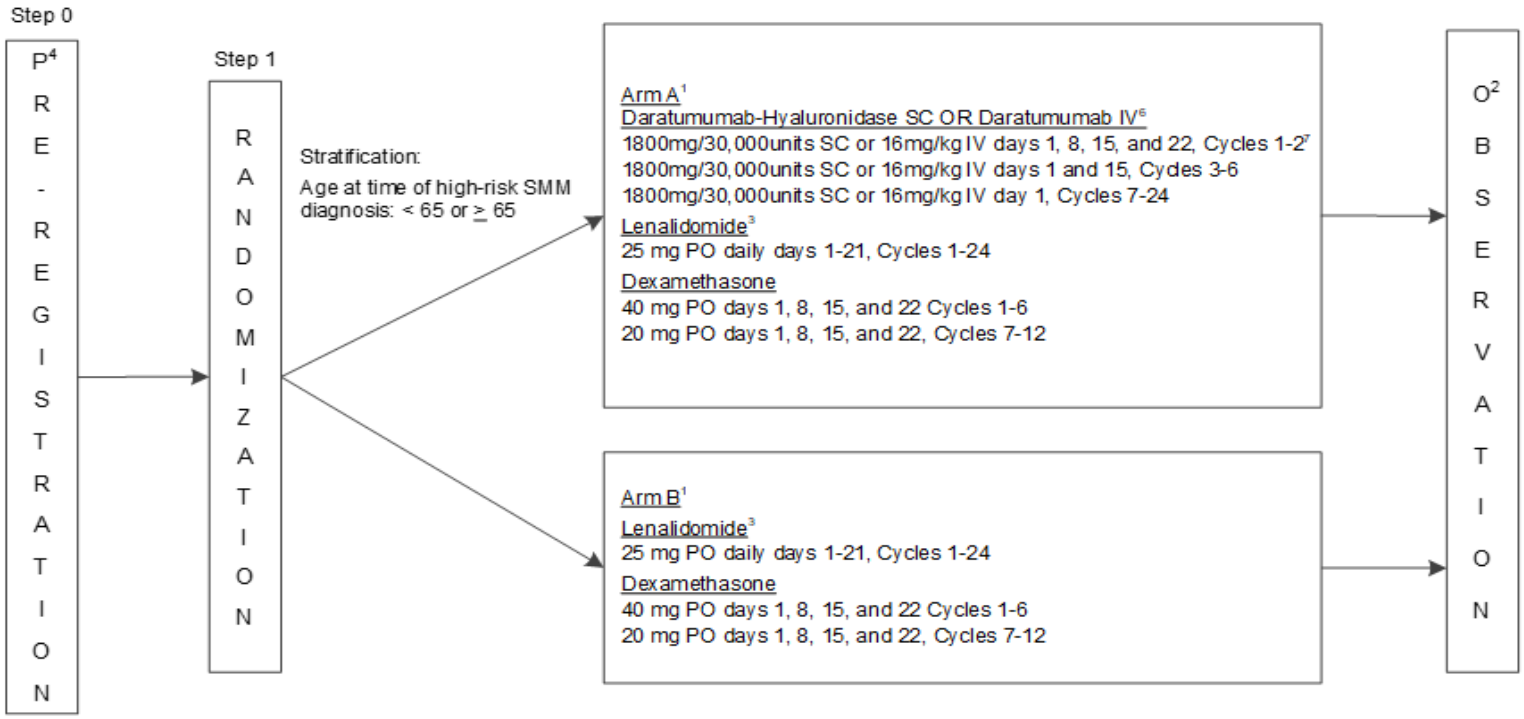
Please Enroll Your Eligible Patients!

Version 07/25/23 (Add. #4)

ECOG-ACRIN cancer research group

EA173

Schema



Accrual Goal: 288 patients with high-risk smoldering multiple myeloma.[5]

Cycle: 28 days

1. Peripheral blood stem cells for future transplants should be collected between cycles 4-6 of therapy. Therapy may be interrupted for up to 6 weeks to allow for PBSC collection. While collection following 4-6 weeks of therapy is strongly suggested, it is not required for protocol participation.
2. All patients, including those who discontinue protocol therapy early, will be followed for response until progression, even if non-protocol therapy is initiated, and for survival for 15 years from the date of randomization.
3. In patients with calculated (Cockroft-Gault) creatinine clearance of 30-59 ml/min, starting dose of lenalidomide should be reduced to 10 mg. If the clearance improves to ≥ 60 ml/min, the dose can be increased to 25 mg provided the patient has not experienced any of the toxicities that would require a dose reduction for lenalidomide.
4. Submission of pre-study specimens per patient consent.
5. Patients must be diagnosed within the past 12 months. See Section 3.2.2 for the definition of high-risk SMM.
6. Patients currently receiving IV daratumumab should cross over to SC daratumumab-hyaluronidase unless they do not tolerate daratumumab-hyaluronidase. Patients intolerant of SC daratumumab-hyaluronidase may remain on or cross over to IV daratumumab. Please refer to Section 5.1.1 for daratumumab treatment details.
7. For patients receiving IV daratumumab, split-dosing schedule may be used for first IV infusion, and will consist of 8mg/kg given on Cycle 1, days 1 and 2 only