

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 3.0 for Complete Eligibility Details

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

Step 1 Randomization:

- Age \geq 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 5.0 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
- Refer to the protocol for pre and post-treatment medication
- 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>

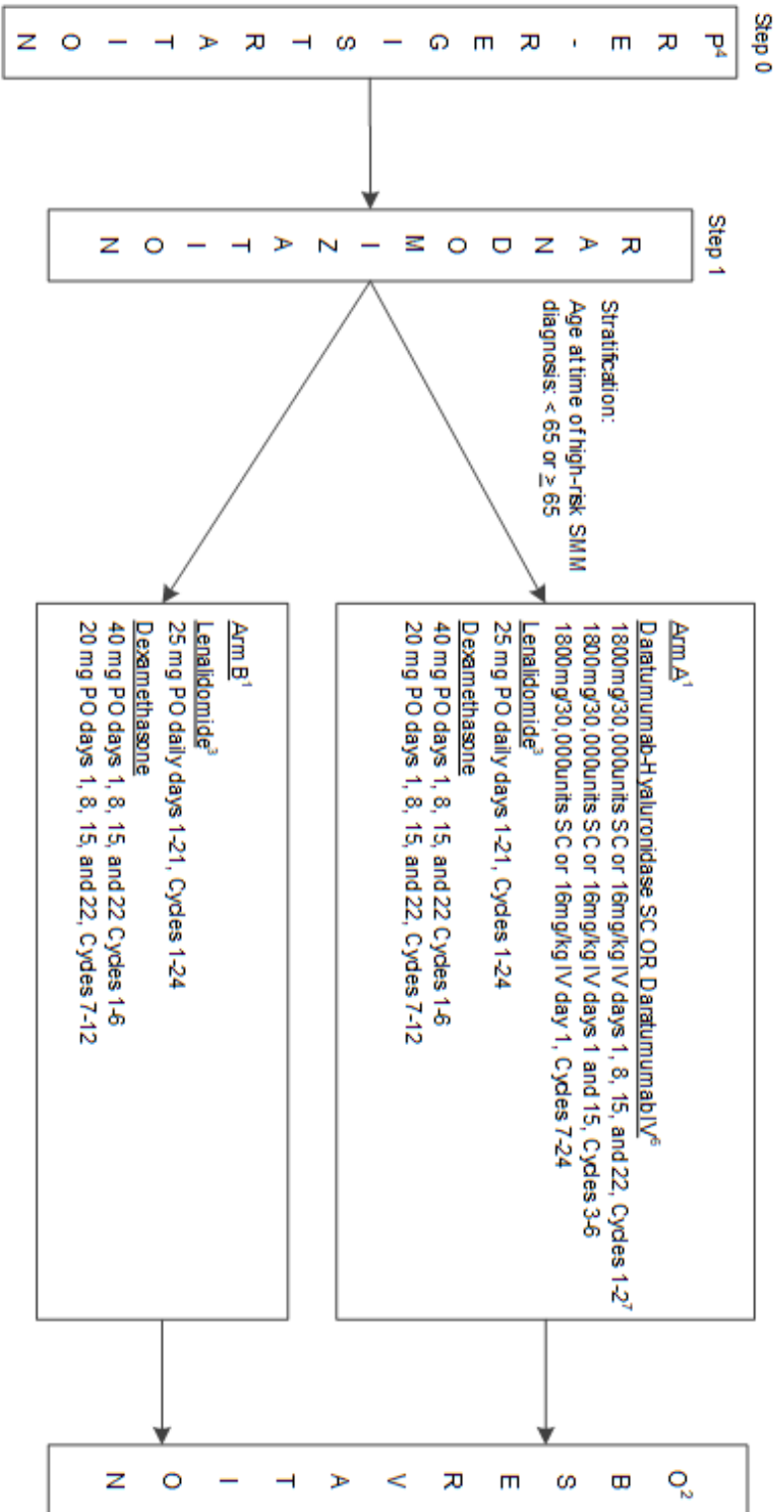
Protocol Information

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

Please Enroll Your Eligible Patients!

EAA173

Schema



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

Cycle: 28 days

- 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.
- 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.
- In patients with calculated (Cockcroft-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.
- Submission of pre-study specimens per patient consent.
- Patients must be diagnosed within the past 12 months. See Section 3.2.2 for the definition of high-risk SMM.
- 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.
- 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.