**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

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

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

**Please Enroll Your Eligible Patients!**