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 ≥ 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 anti-coagulation; should not have NYHA classification III/IV heart failure at baseline
- HIV, HBV, HCV patients are eligible per protocol

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

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

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

Please Enroll Your Eligible Patients!
Schema

- Step 0
  - Age at time of initiation of SMR
  - Tumor histology
  - Performance status
  - O2

- Step 1
  - Randomize
  - Am B
  - 20 mg PO days 1, 8, 15, and 22, cycles 1-2
  - 40 mg PO days 1, 8, 15, and 22, cycles 1-6
  - 60 mg PO days 1, 8, 15, and 22, cycles 1-4
  - Ledakomolide

- Step 2
  - Percentage of patients with high-risk secondary malignant myeloma

- Note
  - This protocol is intended for use only in patients who have not received prior chemotherapy for myeloma or plasma cell dyscrasias.

- Other
  - Please refer to section 5.1 for dosage and treatment details.
  - Important: Patients must be included within the part 12 months. See section 3.2 for the definition of high-risk SMR.

- Other
  - Substitution or study assessments per patient consent.

- Other
  - A standard 15-year risk-to-benefit ratio for tolerance of this drug may not be assumed.

- Other
  - This protocol is not intended for use in patients with plasmacytoma or myeloma in situ.

- Other
  - Non-refractory therapy is not permitted, and factors that influence the decision to proceed with therapy include response to prior therapy and other risk factors.

- Other
  - Treatment failure criteria for this protocol: 15 months of progression-free survival or death due to disease-related causes.

- Other
  - This protocol is for investigational therapy only and is not intended for use in the clinical setting.

- Other
  - This protocol is not intended for use in patients with multiple myeloma who have not received prior chemotherapy.