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 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 is required to be performed within 28 days prior to 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
- No prior or concurrent systemic or radiation therapy for the treatment of myeloma; no contraindication to 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
- Must not have Grade 2 or higher peripheral neuropathy (CTCAE)
- No active, uncontrolled infection
- Patients 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 patients with undetectable HIV viral loads tested within 6 months are eligible
- Should not have a history of allergic reactions attributed to compounds of similar chemical/biologic composition to daratumumab, lenalidomide, or dexamethasone

Treatment Plan:
See Protocol Section 5.0 for Complete Treatment Details

1 cycle= 28 days

Arm A – DRd:
- Daratumumab 16 mg/kg IV days 1, 8, 15, and 22, cycles 1-2; 16 mg/kg IV days 1 and 15 cycles 3-6; 16 mg/kg IV day 1 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-infusion 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

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

Protocol Information

Please Enroll Your Eligible Patients!
Daratumumab to Enhance Therapeutic Effectiveness of Revlimid in Smoldering Myeloma (DETER-SMM)

Schema

ARM A
Daratumumab
16 mg/kg IV days 1, 8, 15, and 22,
Cycles 1-2
16 mg/kg IV days 1 and 15 Cycles 3-6
16 mg/kg IV day 1 cycles 7-24
Lenalidomide
25 mg PO daily days 1-21, Cycles 1-24
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
Lenalidomide
25 mg PO daily days 1-21, Cycles 1-24
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

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

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 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 3.1.2 for the definition of high-risk SMM.