NCI National Clinical Trials Network

EAA232

ECOG-ACRIN cancer research group

For Patients with High-Risk Multiple Myeloma

EAA232 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase II Trial for High-Risk Multiple Myeloma that is Refractory or in First Relapse with Daratumumab, Teclistamab (DT) versus Daratumumab, Pomalidomide, Dexamethasone (DPd) or Daratumumab, Carfilzomib, Dexamethasone (DKd)

Please Enroll Your Eligible Patients!

Patient Population

See protocol Section 3 for complete eligibility criteria

- Age ≥ 18 years, ECOG PS 0-2 (or 3 if secondary to pain), and adequate lab values ≤ 28 days prior to randomization
- Must have an identifiable dominant sequence (clonotype) established based on clonoSEQ® assay
- Must have received only one prior line of therapy, as defined per eligibility criterion 3.1.4
  - ◊ Autologous stem cell transplant is allowed provided the stem cell infusion was > 90 days prior to randomization; allogeneic SCT patients are ineligible
- Must be diagnosed with relapsed or refractory (RR) multiple myeloma, as defined per eligibility criterion 3.1.5
  - ◊ Must have high-risk multiple myeloma (HR-MM) as defined per criterion 3.1.7
  - ◊ May have primary plasma cell leukemia, secondary plasma cell leukemia, or extramedullary myeloma
- Must be daratumumab-hyaluronidase (or isatuximab) naïve, or daratumumab-hyaluronidase (or isatuximab) sensitive and > 180 days from last dose of daratumumab-hyaluronidase (or isatuximab) at randomization
- Must have measurable disease as defined by criterion 3.1.8 ≤ 28 days prior to randomization; Must have SPEP, UPEP, serum FLC assays, and bone marrow biopsy or aspirate ≤ 28 days prior to randomization
- No known allergies, hypersensitivity or intolerance to corticosteroids, monoclonal antibodies/human proteins or their excipients, or known sensitivity to mammalian-derived products
- Must not be on steroids (prednisone > 40 mg/day or equivalent) at the time of randomization
- May have received prior palliative and/or localized RT, provided that it is completed by randomization
- No evidence of active/untreated CNS positive MM (prior CNS is allowed if resolved per criterion 3.1.19)
- If applicable, must be NYHA Class 2B or better; Patients with history of COPD must have FEV1 ≥ 50% of predicted normal
- No moderate/severe persistent asthma ≤ 2 years of randomization, or active autoimmune disease

Treatment Plan

See protocol Section 5 for complete treatment details

At randomization, the investigator will select the Arm A regimen most appropriate for the patient should they be randomized to Arm A. Patients will then be randomized to Arm A or Arm B (1:1). Treatment will continue until disease progression or unacceptable toxicity.

- 1 cycle = 28 days (all regimens)

Arm A: Investigator's Choice (DPd or DKd)

- **Daratumumab-hyaluronidase + Pomalidomide + Dexamethasone (DPd)**
  - ◊ Dexamethasone 40 mg (20 mg for patients ≥ 75 years old) PO or IV Days 1, 8, 15, 22
  - ◊ Daratumumab-hyaluronidase 1800 mg/30,000 units SQ Days 1, 8, 15, & 22 (Cycles 1 & 2); Days 1 & 15 (Cycles 3-6); Day 1 (Cycles 7+)
  - ◊ Pomalidomide 4 mg PO Days 1-21
- **Daratumumab-hyaluronidase + Carfilzomib + Dexamethasone (DKd)**
  - ◊ Dexamethasone 20 or 40 mg PO or IV options (see Section 5.1.1)
  - ◊ Daratumumab-hyaluronidase 1800 mg/30,000 units SQ (same as above)
  - ◊ Carfilzomib: two IV dosing options (see Section 5.1.1)

Arm B: Daratumumab-hyaluronidase + Teclistamab (DT)

- Daratumumab-hyaluronidase 1800 mg/30,000 units SQ (same as above)
- Teclistamab step-up dosing cycle 1 (see Section 5.1.2); 1.5 mg/kg SQ Days 1, 8, 15, & 22 (Cycle 2); 3 mg/kg SQ Days 1 & 15 (Cycles 3-6); 3 mg/kg SQ Day 1 (Cycles 7+)

Notes:

- *Arm A: Patients on pomalidomide will need a new prescription and REMs # for each cycle; medication calendars for pomalidomide and dexamethasone to be completed at each cycle*
- *Premedications (Section 5.1), dose mods/delays (Section 5.4), supportive care (Section 5.5) per protocol*

Study Chair:
Muhamed Baljevic, MD

Study Co-Chair:
Shaji Kumar, MD

NCTN Study Champions:

- ***Alliance:*** Douglas Sborov, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

https://open.ctsu.org/open

1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

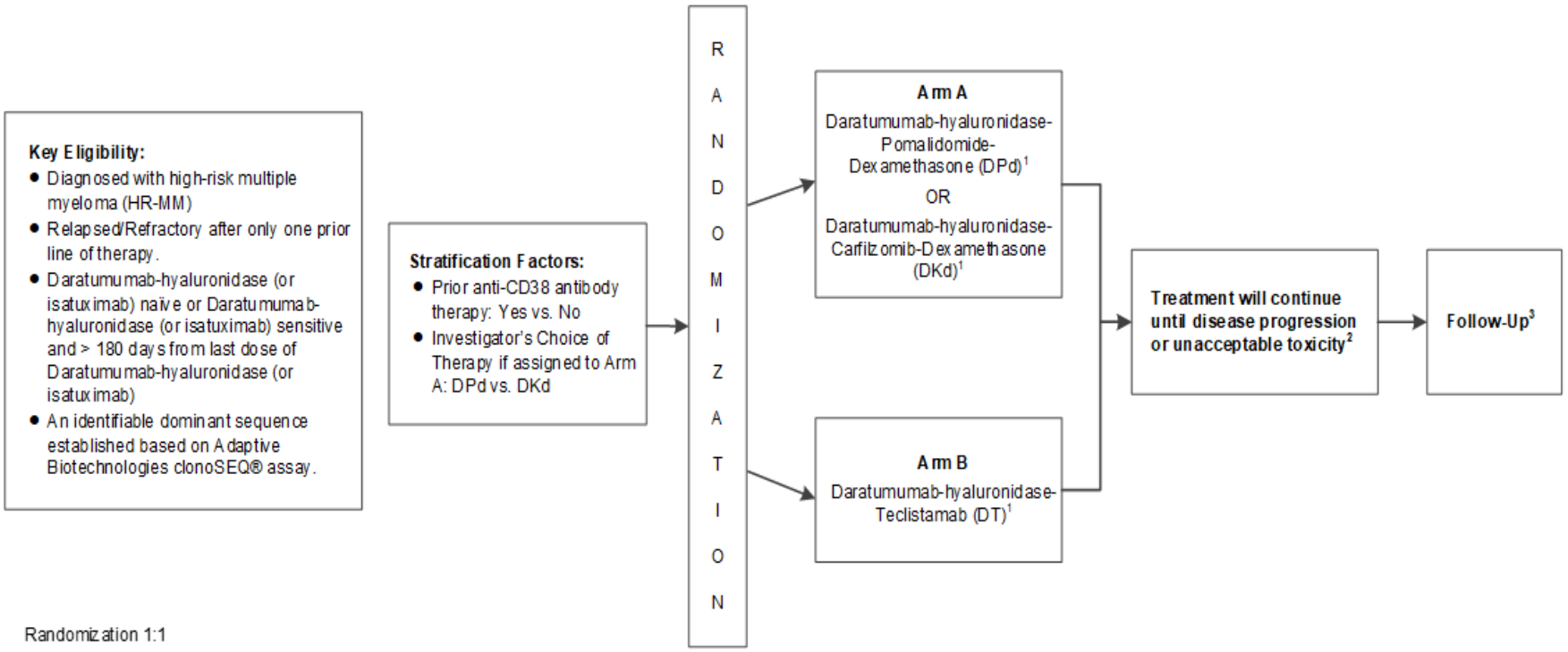
http://ecog-acrin.org (Member Login)

1-857-504-2900

v.06/22/26

EA232

Schema



Randomization 1:1
Accrual Goal N = 80
1 Cycle = 28 Days

1. Refer to Section 5.1 for detailed dosing instructions.
2. MRD test required after 6 cycles of therapy in patients achieving very good partial response or better with no measurable protein detected by SPEP/UPEP but may have serum and/or urine immunofixation positive only. Only Adaptive Biotechnologies clonoSEQ® platform accepted for this study.
3. Upon discontinuation of protocol therapy, patients will be followed for response until progression, even if non protocol therapy is initiated, and for survival according to the schedule outlined in Section 5.7.