v.06/10/26

NCI National Clinical Trials Network

EAA242

ECOG-ACRIN cancer research group

For Patients with Multiple Myeloma in Early Relapse

EAA242 Available Through ECOG-ACRIN Cancer Research Group

Phase Ib/II Fixed Duration Study of Teclistamab/Pomalidomide (TP) versus Carfilzomib/ Pomalidomide/Dexamethasone (KPd) in Early Relapse of Multiple Myeloma

Please Enroll Your Eligible Patients!

Patient Population

See protocol Section 3 for complete eligibility criteria

- ≥ 18 years of age, ECOG PS 0-2, adequate lab values
- Must have an identifiable dominant sequence (clonotype) established based on clonoSEQ® assay for Phase II only
- Must have multiple myeloma (MM), with original MM diagnosis meeting both of these IMWG criteria:
  1. Bone marrow plasmacytosis with ≥ 10% of plasma cells or sheets of plasma cells or biopsy-proven plasmacytoma *or* tissue biopsy of any bone lesion or extramedullary plasmacytoma if applicable (positive/ negative for clonal plasma cells)
  2. One or more of the symptomatic myeloma-defining events per protocol that prompted initiation of therapy as well as end-organ damage

  Note: Patients with smoldering myeloma & monoclonal gammopathy of undetermined significance are not eligible (see protocol for details)
- Must have experienced relapse disease, defined as relapse after one line of lenalidomide therapy (single agent, or with dexamethasone, or with CD38 antibody +/- dexamethasone); can be progressive disease (per protocol)
- Must have received ≤ 2 lines of IMWG-defined therapy (induction +/- transplant + maintenance = single line); must have received an immunomodulatory drug (lenalidomide) + a CD38 antibody (daratumumab or isatuximab); must not have received prior BCMA therapy
- No non-protocol concurrent chemotherapy for the study disease/ancillary investigational therapy while on study
- Must have measurable disease per protocol ≤ 28 days prior to registration/randomization (exception: patients with bone/soft tissue plasmacytoma[s] ≥ 2 cm or who have bone marrow plasma cells ≥ 30% are eligible)
- Not known to be refractory to carfilzomib/pomalidomide
- No peripheral neuropathy > Grade 2 at the time of registration/randomization
- Must have adequate cardiac function per criterion 3.1.20
- No known allergies/hypersensitivity/intolerance to corticosteroids/monoclonal antibodies/human proteins, or their excipients, or known sensitivity to mammalian-derived products
- No current CNS involvement (past involvement permitted)

Treatment Plan

See protocol Section 5 for complete treatment details

Cycle = 28 days; +/- 7-day visit window is allowed for holidays/inclement weather; Treatment will continue until progression or unacceptable toxicity (all Arms), or maximum of 2 years (Arms A, B, C)

Phase Ib: Arms A + B (TP)

- **Teclistamab**:
  - ◊ Step-up dose 1 (C1D1) = 0.06 mg/kg SQ
  - ◊ Step-up dose 2 (C1D4) = 0.3 mg/kg SQ
  - ◊ 1.5 mg/kg SQ weekly on Cycle 1 Days 7, 14, and 21; Cycle 2 Days 1, 8, 15, and 22
  - ◊ 3 mg/kg SQ on Cycles 3-6 Days 1 and 15; Cycles 7+ Day 1 (q4W) *(note: may switch to q4W dosing beginning Cycle 7 if patient has confirmed VGPR or better)*
- **Pomalidomide**: 2 mg PO QD starting C2D1, on Days 1-21 each cycle (fallback dose level = 1 mg)

Phase II will open only after pomalidomide dose determined in Phase Ib:

Phase II: Arm C (TP)

- **Teclistamab**: same dosing/schedule as Arms A/B
- **Pomalidomide**: 2 mg or 1 mg (PO) dose TBD in Phase Ib; same schedule as Arms A/B

Phase II: Arm D (KPd)

- **Carfilzomib**:
  - ◊ 20 mg/m² IV on Cycle 1 Days 1 and 2
  - ◊ 56 mg/m² IV on Cycle 1 Days 8 and 15; Cycle 2 Days 1, 8, and 15; Cycles 3+ Days 1 and 15
- **Pomalidomide**: 4 mg PO QD on Days 1-21
- **Dexamethasone**:
  - ◊ 40 mg PO or IV on Cycles 1-4 Days 1, 8, 15, and 22 (or 20 mg for older patients/patients with comorbidities)
  - ◊ 20 mg PO or IV on Cycles 5+ Days 1, 8, 15, and 22

Note: See Sections 5.1 for treatment details including required pre-meds, AEs/toxicity management (inc. CRS/ICANS), prophylaxis, pomalidomide fertility instructions, etc.; 5.4.1 for teclistamab restart after dose delay; 5.4.2 for dose mods for patients with hepatic impairment prior to treatment initiation

Study Chair:
Murali Janakiram, MD

Study Co-Chair:
Ajay Kumar Nooka, MD, MPH

NCTN Study Champions:
- ***Alliance:*** Samuel Rubinstein, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])

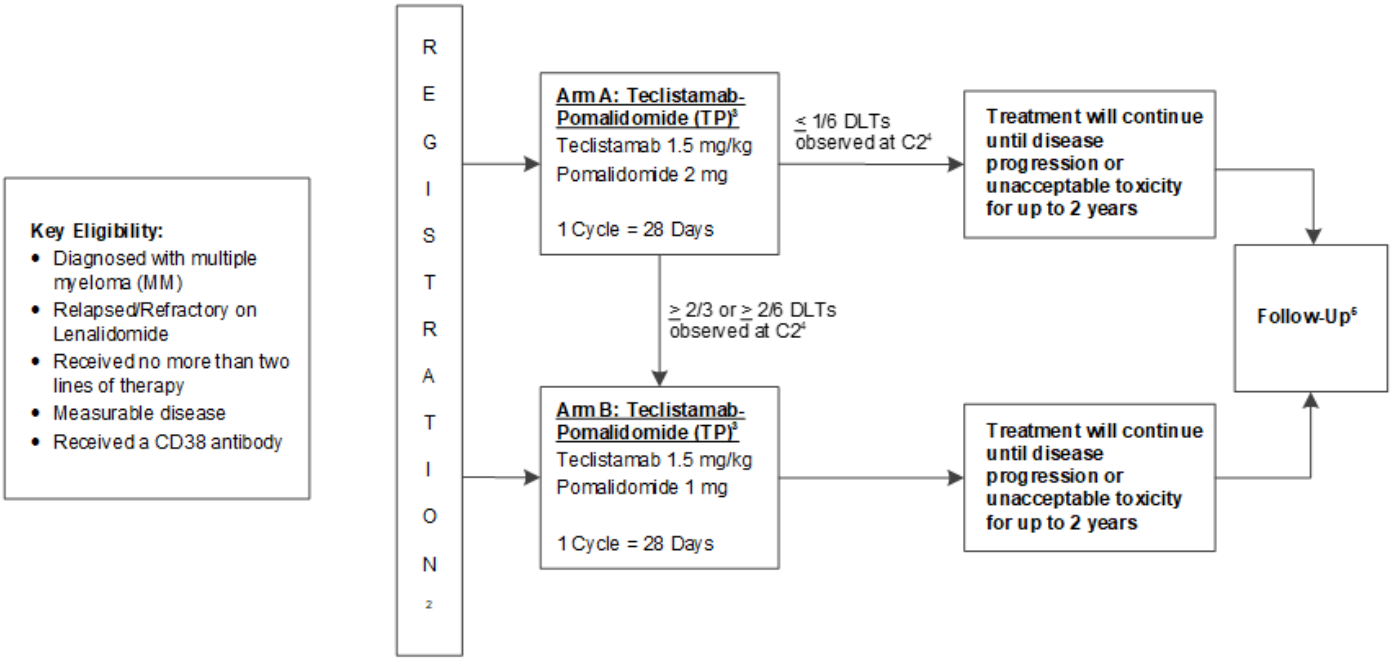
https://open.ctsu.org/open 1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)

http://ecog-acrin.org (Member Login) 1-857-504-2900

EAA242

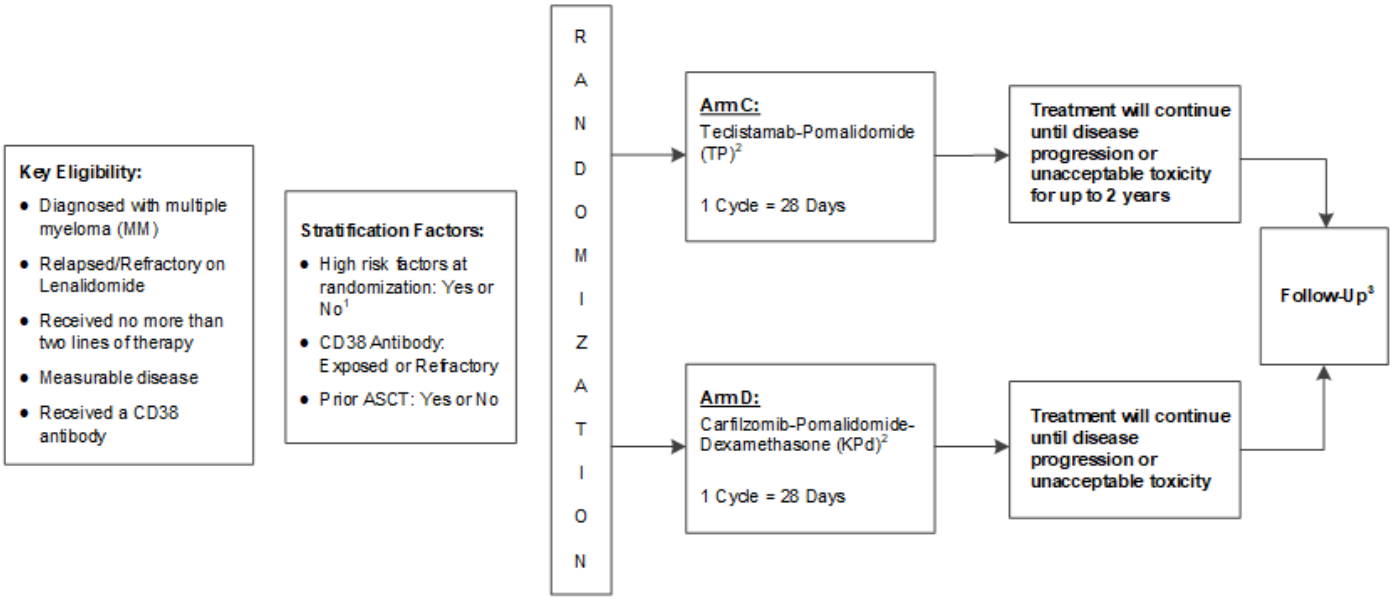
Phase Ib Schema



Phase Ib Accrual Goal N[1] = 6 - 12

1. Phase 1b will have up to 12 patients (6 per dose level).
2. Patient enrollment for this study will be facilitated using the Slot-Reservation System in conjunction with the Registration System in the Oncology Patient Enrollment Network (OPEN). See Section 4 for additional information on the Slot-Reservation System.
3. Refer to Section 5.1 for detailed step up dosing for Teclistamab that occurs on Day 1, 4, and 7 of the first cycle.
   NOTE: Pomalidomide will begin on Cycle 2 Day 1.
4. Refer to Section 5.1.1 and 9.1.1 for DLT definitions and the safety run-in outline to determine the recommended Pomalidomide Phase II dose (RP2D).
5. Refer to Section 5.7 and 7 for follow-up schedule.

Phase II Schema



Randomization = 1:1
Phase II Accrual Goal N[1] = 150

1. High risk is defined as: Translocation (14;16), and/or translocation (14;20), and/or deletion (17p) by fluorescence in-situ hybridization (FISH) or cytogenetics and/or 1q21 amplification by FISH analysis. Refer to Section 4.3.5.
2. Refer to Section 5.1 for detailed dosing instruction.
   NOTE: Arm C will have step up dosing for Teclistamab that occurs on Day 1, 4, and 7 of the first cycle and Pomalidomide will begin on Cycle 2 Day 1.
3. Refer to Section 5.7 and 7 for follow-up schedule.