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MonumenTAL-6: A Phase 3 Study of Talquetamab + Pomalidomide or Talquetamab + Teclistamab vs Elotuzumab + Pomalidomide + Dexamethasone (EPd) or Pomalidomide + Bortezomib + Dexamethasone (PVd) in Patients With Relapsed/Refractory Multiple Myeloma Who Received 1–4 Prior Lines of Therapy, Including Lenalidomide and an Anti-CD38 Monoclonal Antibody

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Current status

MonumenTAL-6 opened for enrollment in January 2024

Registration

MonumenTAL-6 is a randomized, open-label, multicenter, phase 3 study

Results will provide insights into the efficacy of the combination of bispecific antibodies to exploit their individual MOAs to overcome treatment resistance in patients with RRMM and prior exposure to lenalidomide and an anti-CD38 mAb

ClinicalTrials.gov, NCT06208150

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Poster

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Introduction

- Immunomodulatory drugs (IMiDs), proteasome inhibitors, and anti-CD38 monoclonal antibodies (mAbs) are standards of care for newly diagnosed multiple myeloma (MM); however, most patients ultimately relapse[1-4]
- Current regimens for relapsed/refractory MM (RRMM) and prior exposure to lenalidomide and anti-CD38 mAbs include EPd and PVd, but outcomes could be improved[5-9]
- Talquetamab (Tal), targeting GPRC5D, and teclistamab (Tec), targeting BCMA, are the first T-cell redirecting bispecific antibodies approved as monotherapies for triple-class exposed RRMM[10-13]
- Use of these immunotherapies in earlier lines of therapy (LOT), either with a dual-antigen targeting approach (**Figure 1**) or by enhancing their activity with an IMiD (pomalidomide [Pom]; **Figure 2**), may provide deeper, more durable responses and improve quality of life
- This study compares the efficacy of Tal + Pom or Tal + Tec vs investigator's choice of EPd or PVd in patients with RRMM with 1–4 prior LOT, including lenalidomide and an anti-CD38 mAb

Figure 1: Proposed Tal + Tec MOA

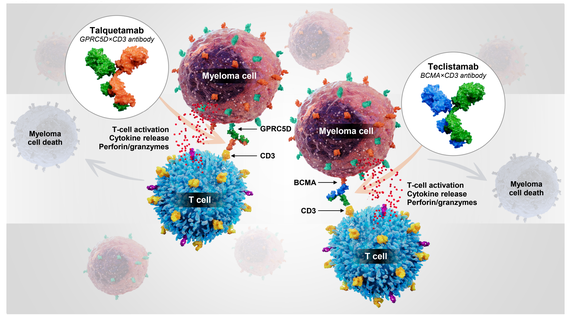
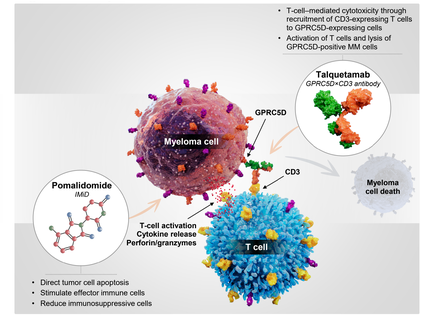


Figure 2: Proposed Tal + Pom MOA



BCMA, B-cell maturation antigen; GPRC5D, G protein–coupled receptor class C group 5 member D; MOA, mechanism of action.

Methods

Study design and patients

- MonumenTAL-6 is a randomized, open-label, multicenter, phase 3 study (**Figure 3**)
- Eligibility includes patients aged ≥18 years with documented MM per International Myeloma Working Group (IMWG) criteria, with measurable disease at screening
  - Must have an ECOG PS of 0–2, received 1–4 prior LOT (including lenalidomide and an anti-CD38 mAb in any prior LOT), and have progressive disease on or after their last therapy
  - Patients refractory to anti-CD38 mAbs are permitted
  - No prior exposure to Pom, Tec, or GPRC5D-directed therapies
- This study is actively recruiting, with more than 190 locations in 27 countries (**Figure 4**)

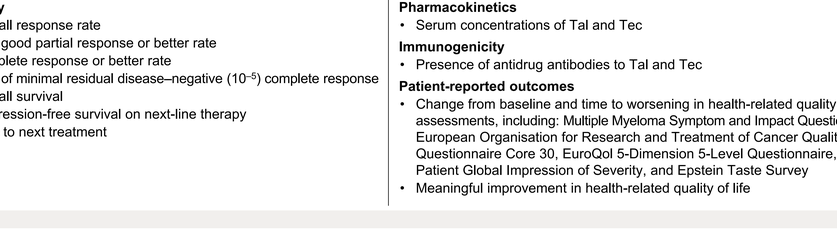
Treatment

- Patients are equally randomized to 1 of 3 cohorts: Tal + Pom (arm A), Tal + Tec (arm B), or investigator's choice of EPd or PVd (arm C) (**Figure 3**)
  - The study will be conducted in 3 phases: screening (up to 28 days before randomization), treatment, and follow-up
  - Interim analyses are planned for safety; an interim data review will also be conducted to evaluate cumulative safety data after 20 patients have been treated for ≥2 cycles or discontinued, and thereafter approximately every 6 months
  - Tal + Pom, Tal + Tec, and EPd are administered in 28-day cycles and PVd in 21-day cycles
- In arms A and B, following step-up doses of 0.01 and 0.06 mg/kg, subcutaneous (SC) Tal is administered as a single dose of 0.4 mg/kg and then 0.8 mg/kg every other week (Q2W)
  - Patients are permitted to switch Tal dosing from Q2W to every 4 weeks (Q4W) following a confirmed very good partial response or better at cycle 5
- In arm B, following step-up doses of 0.06 and 0.3 mg/kg, SC Tec is administered as 2 doses of 1.5 mg/kg and then 3.0 mg/kg Q4W from cycle 2
- A finite dosing approach is employed for both Tal and Tec for up to 26 cycles as tolerated
- In arm A, 2 mg of oral Pom is administered on cycle 2 day 1; dose may be escalated to 4 mg per investigator discretion on cycle 3 day 1 as tolerated
- In arm C, EPd is administered per approved label[5,6]
- In arm C, PVd is administered per standard doses used in clinical practice for treatment of MM[7]
- Patients receive study treatment until disease progression, death, intolerable toxicity, withdrawal of consent, or end of study, whichever occurs first

Endpoints

- Endpoints are summarized in the **Table**
  - Response is assessed per IMWG criteria
  - Qualitative patient interviews will be conducted across selected countries to better understand patient experience

Figure 3: Study overview of MonumenTAL-6



[a]Target enrollment. [b]Including lenalidomide and an anti-CD38 mAb in any prior LOT. [c]Stratified by number of prior LOT (1 vs ≥2), ISS stage at screening (I vs II or III), and investigator's choice of treatment (EPd vs PVd).
ECOG PS, Eastern Cooperative Oncology Group performance status; ISS, International Staging System.

Figure 4: Countries with open or planned study sites for MonumenTAL-6

Table: Study endpoints

Primary endpoint

- Progression-free survival

Secondary endpoints

Efficacy
- Overall response rate
- Very good partial response or better rate
- Complete response or better rate
- Rate of minimal residual disease–negative (10^{-5}) complete response
- Overall survival
- Progression-free survival on next-line therapy
- Time to next treatment

Pharmacokinetics
- Serum concentrations of Tal and Tec

Immunogenicity
- Presence of antidrug antibodies to Tal and Tec

Patient-reported outcomes
- Change from baseline and time to worsening in health-related quality of life assessments, including: Multiple Myeloma Symptom and Impact Questionnaire, European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire Core 30, EuroQol 5-Dimension 5-Level Questionnaire, Patient Global Impression of Severity, and Epstein Taste Survey
- Meaningful improvement in health-related quality of life

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Multiple Myeloma

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