MM-547

MagnetisMM-32: Evaluation of Elranatamab vs EPd, PVd, or Kd in Patients with Relapsed or Refractory Multiple Myeloma and Prior Anti-CD38–directed Therapy

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Objective

To evaluate elranatamab monotherapy vs elotuzumab-pomalidomide-dexamethasone (EPd), pomalidomide-bortezomib-dexamethasone (PVd), or carfilzomib-dexamethasone (Kd) in patients with RRMM to determine whether elranatamab has superior clinical benefit

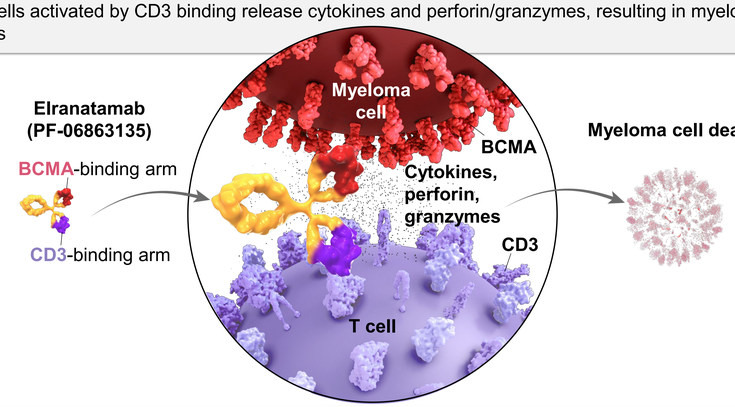
Background

- Elranatamab (ELRA) is a humanized bispecific antibody that targets both B-cell maturation antigen (BCMA)-expressed on myeloma cells and CD3-expressed on T cells (**Figure 1**)[1]
- Data from the phase 2, registrational MagnetisMM-3 trial (NCT04649359) demonstrated that ELRA monotherapy in patients with RRMM induced deep and durable responses with a manageable safety profile[1]
  - ELRA is approved for the treatment of adult patients with RRMM who have received ≥1 immunomodulatory agent (IMiD), ≥1 proteasome inhibitor (PI), and ≥1 anti-CD38 monoclonal antibody (mAb)[2,3]
- The mechanism of action of ELRA may benefit patients already exposed to PIs, IMiDs, and anti-CD38 mAbs in early lines of therapy (LOTs)
- The MagnetisMM-32 study will compare ELRA monotherapy with regimens commonly used in RRMM such as EPd, PVd, and Kd[4,5]

Figure 1. Elranatamab mechanism of action

Elranatamab[1,2]

- BsAb that binds BCMA on myeloma cells and CD3 on T cells
- T-cells activated by CD3 binding release cytokines and perforin/granzymes, resulting in myeloma cell lysis



BCMA=B-cell maturation antigen; BsAb=bispecific antibody

Methods

STUDY DESIGN

- MagnetisMM-32 (NCT06152575) is a phase 3, open-label, multicenter, randomized study (**Figure 2**)
- Patients will receive subcutaneous (SC) ELRA or investigator's choice of EPd, PVd, or Kd until disease progression, unacceptable toxicity, withdrawal of consent, loss to follow-up, or study termination
  - Patients treated with SC ELRA will receive 2 step-up priming doses followed by weekly doses in a 28-day cycle
  - Patients who achieve a partial response or better for at least 2 months will be eligible for a reduced dosing frequency
  - PVd, Kd, and EPd are approved for first and/or subsequent relapses, are CD38 antibody-free regimens, and offer the investigators a choice based on the treatment history of the enrolled patients[4,5]
- Eligible patients (**Table 1**) will be randomized 1:1, stratified by prior LOT (1 vs 2 vs 3-4) and ISS disease stage (1-2 vs 3)
- Primary and key secondary endpoints are shown in **Table 2**
  - Progression-free survival (PFS; primary endpoint) and overall survival (OS; key secondary endpoint) will be compared statistically between treatment arms by stratified log-rank tests

Figure 2. MagnetisMM-32 study design

Patient population
- RRMM
- Prior treatment with an anti-CD38 antibody and lenalidomide

Stratification criteria
- Prior LOT (1 vs 2 vs 3-4)
- ISS disease stage (1-2 vs 3)

N≈492

Randomization 1:1

- 2 step-up priming doses of SC ELRA, followed by SC ELRA weekly in 28-day cycles
- Investigator's choice of EPd, PVd, or Kd

ELRA=elranatamab; EPd=elotuzumab-pomalidomide-dexamethasone; ISS=International Staging System; Kd=carfilzomib-dexamethasone; LOT=line of therapy; PVd=pomalidomide-bortezomib-dexamethasone; RRMM=relapsed or refractory multiple myeloma; SC=subcutaneous.

Table 1.

Key inclusion criteria	Key exclusion criteria
• Age ≥18 years • MM per IMWG criteria • ECOG PS ≤2 • 1-4 prior LOTs[a] • Received ≥2 consecutive cycles of an anti-CD38 antibody-containing regimen in any prior line and ≥2 consecutive cycles of a lenalidomide-containing regimen in any prior line • Progressive disease or refractory to last LOT per IMWG criteria	• SCT ≤12 weeks prior to enrollment, or active GVHD • Active, uncontrolled infection • Ongoing Grade ≥3 peripheral sensory or motor neuropathy; history of any Grade ≥3 peripheral motor polyneuropathy • Prior BCMA-directed or CD3-redirecting therapy • Individuals who have never achieved ≥PR with any treatment during the disease course • Unable to receive EPd, PVd, or Kd

[a] Patients with 4 prior LOTs will be restricted to a maximum of 10%.
BCMA=B-cell maturation antigen; ECOG PS=Eastern Cooperative Oncology Group performance status; EPd=elotuzumab-pomalidomide-dexamethasone; GVHD=graft versus host disease; IMWG=International Myeloma Working Group; Kd=carfilzomib-dexamethasone; LOT=line of therapy; MM=multiple myeloma; PR=partial response; PVd=pomalidomide-bortezomib-dexamethasone; SCT=stem cell transplant

Table 2. Study endpoints

Primary endpoint
• PFS by BICR per IMWG criteria
Key secondary endpoint
• OS
Other secondary endpoints
• *By investigator per IMWG criteria* – PFS – PFS on next LOT • *By BICR per IMWG criteria* – Complete response rate – Duration of response – Duration of complete response – MRD negativity rate and duration – Objective response rate – Time to response – Very good partial response rate • Safety • Pharmacokinetics • Immunogenicity • Health-related QOL outcomes

BICR=blinded independent central review; IMWG=International Myeloma Working Group; LOT=line of therapy; MRD=minimal residual disease; OS=overall survival; PFS=progression-free survival; QOL=quality of life

Study status

- The study plans to enroll ≈492 patients at ≈120 sites across ≈20 countries
- Enrollment is ongoing

References: 1. Lesokhin AM, et al. Nat Med 2023;29:2259-2267. **2.** ELREXFIO (elranatamab-bcmm). Prescribing information. Pfizer; 2023. **3.** ELREXFIO (elranatamab-bcmm). Summary of product characteristics. Pfizer; 2024. **4.** Moreau P, et al. Lancet Oncol 2021;22:e105-118. **5.** Dimopoulos MA, et al. Ann Oncol 2021;32:309-322.

Acknowledgments: This study was sponsored by Pfizer. Medical writing support was provided by Robyn Roth, PhD, of Nucleus Global and was funded by Pfizer.

Disclosures: SI: research funding from AbbVie, Amgen, Insight, Novartis, Zenyaku-Kogyo. **MH, AY, GF:** employment and stock ownership at Pfizer. **FH:** consulting for Merck Sharp & Dohme; employment with Pfizer. **SS:** no conflicts of interest.

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Presented at the Society of Hematology Oncology (SOHO) Annual Meeting | September 4-7, 2024 | Houston, Texas, USA