TPS7568

MagnetisMM-32: A Phase 3 Randomized Study of Elranatamab vs EPd, PVd, or Kd in Patients With Relapsed or Refractory Multiple Myeloma and Prior Anti-CD38–Directed Therapy

Steven Schuster,[1] Saulius Girnius,[2] Rayan Kaedbey,[3] Paola Ochoa,[4] Ludek Pour,[5] Ronan Le Calloch,[6] Tobias Slordahl,[7] Ann De Becker,[8] Fangxin Hong,[9] Margaret Hoyle,[10] Anne Yver,[11] Gregory Finn,[12] Thomas Chalopin[13]

[1]UCHealth Cancer Care and Hematology, Fort Collins, CO, USA; [2]TriHealth Cancer Institute, Cincinnati, OH, USA; [3]Segal Cancer Centre, Jewish General Hospital, McGill University, Montréal, QC, Canada; [4]Instituto Alexander Fleming, Buenos Aires, Argentina; [5]University Hosptal Brno, Czech Republic; [6]Centre Hospitalier de Cornouaille, Quimper, Concarneau, France; [7]Norwegian University of Science and Technology, Trondheim, Norway; [8]Universitair Ziekenhuis Brussel (UZB), Brussels, Belgium; [9]Pfizer Inc, Cambridge, MA, USA; [10]Pfizer Srl, Milan, Italy; [11]Pfizer Inc, Paris, France; [12]Pfizer Inc, Cambridge, MA, USA; [13]Service d'hématologie, Centre Hospitalo-Universitaire, Tours, France

Objectives

- To evaluate whether elranatamab (ELRA) can provide superior clinical benefit over elotuzumab-pomalidomide-dexamethasone (EPd), pomalidomide-bortezomib-dexamethasone (PVd), or carfilzomib-dexamethasone (Kd) in patients with relapsed or refractory multiple myeloma (RRMM)

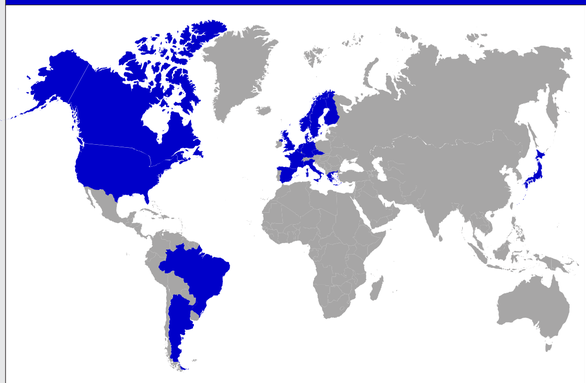
Background

- 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**)[1-3]
- 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]

STUDY STATUS

- The study is ongoing and plans to enroll ≈492 patients
- As of April 14, 2025, the study is open in 18 countries (**Figure 2**)

Figure 2. MagnetisMM-32 study sites

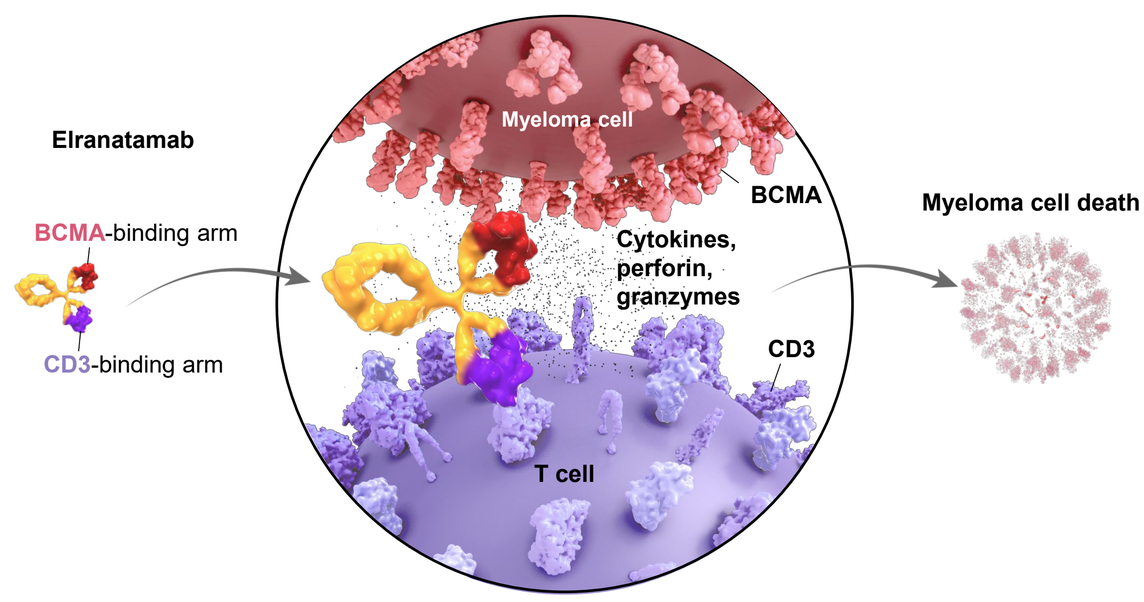


Argentina, Belgium, Brazil, Canada, Czech Republic, Denmark, Finland, France, Germany, Greece, Italy, Japan, Netherlands, Norway, Spain, Sweden, UK, and US

Figure 1. Elranatamab mechanism of action

Elranatamab[1-3]

- 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



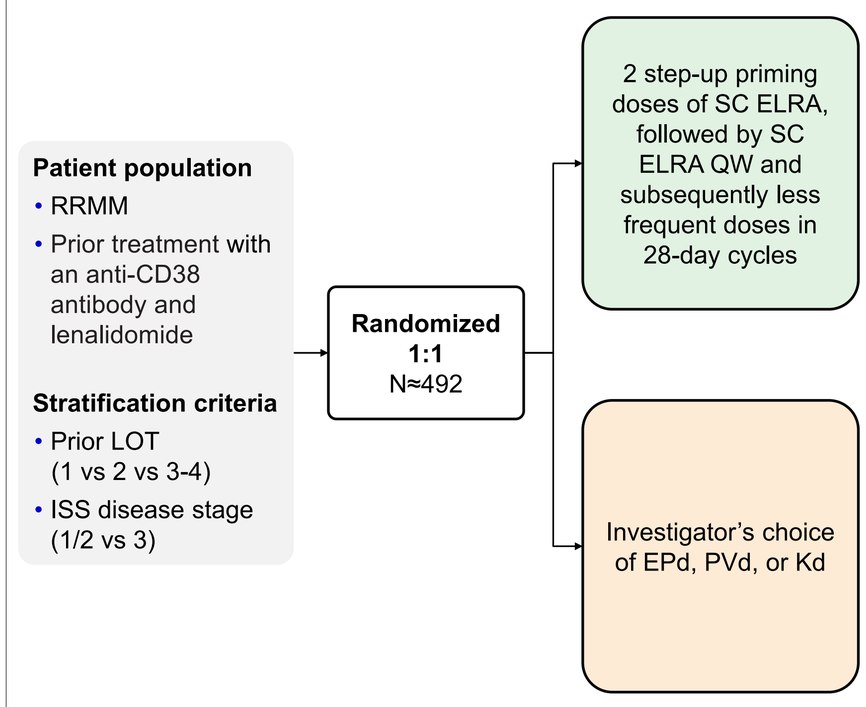
BCMA=B-cell maturation antigen; BsAb=bispecific antibody

Methods

STUDY DESIGN

- MagnetisMM-32 (NCT06152575) is a phase 3, open-label, multicenter, randomized study (**Figure 3**)

Figure 3. MagnetisMM-32 study design



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

- 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 and subsequently less frequent doses in 28-day cycles
  - 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

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 • Adequate bone marrow function	• 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 any of the Arm B regimens (EPd, PVd, or Kd) • Any other active malignancy <3 years prior to enrollment

[a] Patients with 4 prior LOT 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 – Objective response rate – Time to response – Very good partial response rate • MRD negativity rate (including sustained for ≥12 months) and duration (*per IMWG)* • 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

Electronic Poster

Please scan this quick response (QR) code with your smartphone app to view this poster. If you do not have a smartphone, access the poster via the internet at:
https://scientificpubs.congressposter.com/p/cm93t332q9n0xsgt

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: SS, SG, LP, RLC, ADB, TC: no conflicts of interest. **RK**: honoraria from Akcea, Amgen, BMS, Janssen, Merck, Sanofi, Celgene, Pfizer, and Takeda; research funding from Merck, Sanofi; current equity holder at Karyophar. **PO**: honoraria from Janssen and Sanofi; consulting or advisory role for Sanofi and Janssen; travel/accommodations/expenses from Janssen. **TS**: consulting fees from Bristol-Myers Squibb, GSK, Menarini Group, and Sanofi; honoraria or payments from Takeda, Amgen, J&J, AbbVie, and Pfizer; advisory boards for Bristol-Myers Squibb, J&J, Sanofi, and GSK. **FH:** consulting for Merck Sharp & Dohme; employment with Pfizer. **MH, AY, GF:** employment and stock ownership at Pfizer.

Contact: Steven Schuster, Steven.Schuster@uchealth.org

Presented at the 2025 ASCO Annual Meeting | May 30- June 3, 2025 | Chicago, IL