MagnetisMM-20: Efficacy and Safety of Elranatamab Plus Carfilzomib and Dexamethasone for Relapsed/Refractory Multiple Myeloma

[1] Michael H Tomasson,[2] Eli Gabayan,[3] Syed Abbas Ali,[4] Sona Ghorashi,[4] Trish Creel,[5] Luisa Paccagnella,[6] Carolyn Lou,[7] Ola Landgren

[1]Department of Internal Medicine, University of Iowa, Iowa City, IA, USA; [2]Beverley Hills Cancer Center, Beverley Hills, CA, USA; [3]Department of Oncology, The Sydney Kimmel Comprehensive Cancer Center, Johns Hopkins University School of Medicine, Baltimore, MD, USA; [4]Pfizer Inc, New York, NY, USA; [5]Pfizer Inc, Cambridge, MA, USA; [6]Pfizer Inc, Bothell, WA, USA; [7]Sylvester Comprehensive Cancer Center, Miami, FL, USA

Objectives

- Assess the safety and tolerability of elranatamab (ELRA) in combination with carfilzomib and dexamethasone (Kd) and select a recommended phase 2 dose
- Evaluate the efficacy of ELRA in combination with Kd

Conclusions

- In BCMA-naive patients with RRMM, with a median of 2 prior lines of therapy, ELRA in combination with Kd demonstrated a predictable safety profile and clinical efficacy
- Responses deepened over time, and some responses persisted even after treatment discontinuation
- The study is ongoing and will continue to explore the combination of ELRA and Kd in a larger group of patients with 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[1]
- Data from the phase 2, registrational MagnetisMM-3 trial (NCT04649359) demonstrated that ELRA monotherapy in patients with relapsed/refractory multiple myeloma (RRMM) induced deep and durable responses with a manageable safety profile[3]
  - ELRA is approved for the treatment of adult patients with RRMM who have received ≥1 immunomodulatory agent, ≥1 proteasome inhibitor, and ≥1 anti-CD38 monoclonal antibody[2,3]
- Carfilzomib is a standard-of-care proteasome inhibitor with significant activity as a monotherapy and in combination with other agents[4]
- Given the high rate of relapse in RRMM, there is a need for new therapies and combinations that may provide synergistic activity
- Here we present dose escalation (Part 1) results from the Phase 1b MagnetisMM-20 (NCT05675449) trial of ELRA in combination with Kd in patients with RRMM

Methods

- MagnetisMM-20 is a phase 1b, open-label, multicentre study
- Eligible patients were age ≥18 years with RRMM, 1-3 prior lines of therapy (LOTs; no prior BCMA-directed therapy), and an Eastern Cooperative Oncology Group performance status (ECOG PS) ≤1
- Prior carfilzomib was allowed in patients with a partial response or better to the most recent carfilzomib-containing therapy and no relapse ≤60 days after discontinuation, with a ≥6-month carfilzomib-free interval
- The label-recommended step-up dosing regimen for ELRA including premedications was used followed by weekly (QW) dosing in 28-day cycles
  - ELRA was evaluated at 2 dose levels (DLs): ELRA 44 mg QW + Kd (DL1) and ELRA 76 mg QW + Kd (DL2)
  - If patients received ≥6 months of QW ELRA and achieved ≥PR (lasting ≥2 months), they could change to Q2W dosing at the same DL
- Carfilzomib was administered per label on day [D]1, D8, and D15 of each 28-day cycle; carfilzomib dose reductions were permitted
- Dexamethasone was administered per label QW in 28-day cycles
- The data cut off date for this analysis was September 13, 2024

Results

PATIENTS AND TREATMENT

- A total of 12 patients were treated
  - 4 patients received ELRA 44 mg QW + Kd (DL 1); 3 patients discontinued (n=1 each for adverse event, progressive disease, and withdrawal of consent)
  - 8 patients received ELRA 76 mg QW + Kd (DL 2); 4 patients discontinued (n=2 for adverse event and n=1 each for death and withdrawal of consent)
  - At the data cutoff of September 13, 2024, treatment was ongoing in 5 patients (41.7%; n=1 DL1 and n=4 DL2)
- Median duration of treatment was 8.4 months (range, 0.6-20.1)
- Median age was 66.0 years (range, 45-80) and 66.7% were male
- 25.0% of patients were Black or African American and 58.3% were White
- Baseline clinical characteristics are presented in **Table 1**

Table 1. Baseline clinical characteristics

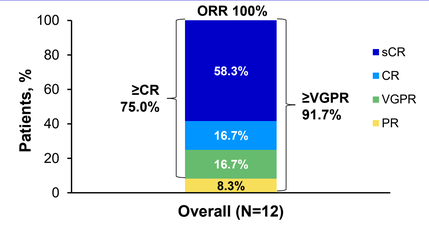
	n=12
ECOG PS, n (%)	
0	9 (75.0)
1	3 (25.0)
R-ISS disease stage, n (%)	
I	4 (33.3)
II	6 (50.0)
III	2 (16.7)
ISS disease stage, n (%)	
I	5 (41.7)
II	2 (16.7)
III	4 (33.3)
Missing	1 (8.3)
Cytogenic risk, n (%)	
Standard	9 (75.0)
High[a]	3 (25.0)
Prior lines of therapy, median (range)	2.0 (1-3)
No. of prior lines of therapy, n (%)	
1 LOT	4 (33.3)
2 LOTs	6 (50)
3 LOTs	2 (16.7)
Prior stem cell transplant, n (%)	8 (66.7)
Exposure status, n (%)	
IMiDs	11 (91.7)
PIs	10 (83.3)
Carfilzomib	1 (8.3)
Anti-CD38 antibody	7 (58.3)
Triple-class[b]	6 (50.0)
Refractory status, n (%)	
Triple-class[b]	5 (41.7)
Refractory to last line of MM therapy	12 (100)

[a] Includes t(4;14), t(14;16), and del(17p) chromosomal abnormalities; [b] Triple-class refers to ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody
ECOG PS=Eastern Cooperative Oncology Group performance status; EMD=extramedullary disease; IMiD=immunomodulatory drug; ISS=International Staging System; LOT=line of therapy; MM=multiple myeloma; PI=proteasome inhibitor; R-ISS=Revised-ISS

EFFICACY

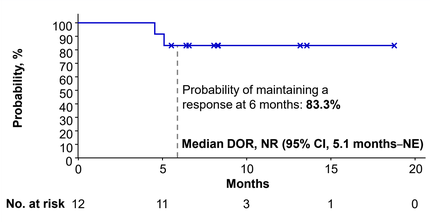
- The confirmed objective response rate (ORR) by investigator was 100%; the complete response or better rate was 75.0% (95% CI, 42.8-94.5) (**Figure 1**)
- Median time-to-response was 1.5 months (range, 0.5-3.4)
- At a median follow-up of 8.9 months (95% CI, 7.9-13.7), the median duration of response (DOR) was not reached (95% CI, 5.1-not estimable); the probability of maintaining a response at 6 months was 83.3% (**Figure 2**)
- Responses deepened over time; some responses persisted after treatment discontinuation (**Figure 3**)

Figure 1. Objective response rate



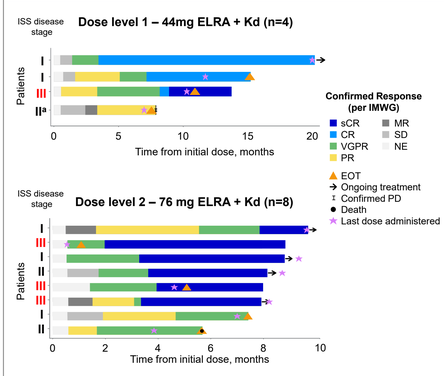
CR=complete response; ORR=objective response rate; PR=partial response; sCR=stringent CR; VGPR=very good PR

Figure 2. Duration of response



DOR=duration of response; NE=not estimable; NR=not reached

Figure 3. Swimmer plots for response by investigator



[a] Investigator derived
CR=complete response; ELRA=elranatamab; EOT=end of treatment; IMWG=International Myeloma Working Group; ISS=International Staging System; MR=minimal response; Kd=carfilzomib and dexamethasone; NE=not evaluable; sCR=stringent CR; SD=stable disease; VGPR=very good PR; PR=partial response

SAFETY

- No dose-limiting toxicities were observed at either DL (n=10)
- Frequent treatment-emergent adverse events (any-grade >25%; grade 3/4 ≥10%) are shown in **Table 2**
- Infections occurred in 11 patients (91.7%); 2 patients (16.7%) with grade 3/4
- All CRS events were grade ≤2; no ICANS was reported

Table 2. Treatment-emergent adverse events

TEAE, n (%)[a]	Any grade	Grade 3/4
Any	12 (100)	11 (91.7)
Haematologic		
Neutropenia	9 (75.0)	9 (75.0)
Thrombocytopenia	9 (75.0)	5 (41.7)
Leukopenia	8 (66.7)	4 (33.3)
Anaemia	8 (66.7)	4 (33.3)
Nonhaematologic		
Fatigue	10 (83.3)	2 (16.7)
CRS	9 (75.0)	0
Cough	7 (58.3)	0
Diarrhoea	6 (50.0)	1 (8.3)
CMV infection reactivation	6 (50.0)	1 (8.3)
Injection site reaction	6 (50.0)	0
Chills	5 (41.7)	0
Skin exfoliation	5 (41.7)	0
Nausea	5 (41.7)	0
Dizziness	5 (41.7)	0
Dry skin	5 (41.7)	0
Peripheral oedema	4 (33.3)	2 (16.7)
Vomiting	4 (33.3)	0
Hypophosphatemia	4 (33.3)	0
Headache	4 (33.3)	0
Blood alkaline phosphatase increase	3 (25.0)	2 (16.7)
Pulmonary embolism	2 (16.7)	2 (16.7)

[a] Any-grade TEAE reported in >25% of patients; grade 3/4 TEAE reported in ≥10% of patients; severity of CRS and ICANS was assessed according to the American Society for Transplantation and Cellular Therapy criteria
CMV=cytomegalovirus; CRS=cytokine release syndrome; TEAE=treatment-emergent adverse event

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.** Yee AJ, et al. Ther Adv Hematol 2021;12:1-13. **5.** He S, et al. Transl Cancer Res 2022;11:206-216.

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Contact: Karthik Ramasamy, karthik.ramasamy@ndorms.ox.ac.uk

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