Efficacy and Safety of Less Frequent Dosing With Elranatamab in Patients With Relapsed or Refractory Multiple Myeloma: A US Subgroup Analysis From MagnetisMM-3

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Objectives

To report long-term efficacy and safety results of elranatamab approximately 38 months after the last patient's first dose in the subgroup of BCMA-naive patients enrolled in the US

Conclusions

- Consistent with overall Cohort A data, elranatamab was associated with deep, durable responses in the heavily-pretreated US subgroup
- With a median follow-up of 39.6 months:
  - ORR was 66.0%
  - Median DOR was 40.8 months but may not yet be mature
  - Median PFS was 27.3 months
  - Median OS was 43.6 months but may not yet be mature
- Overall, the safety profile, including infections, was consistent with that of the total study population
  - CRS and ICANS were grade 1 or grade 2 only
  - Infection prophylaxis including immunoglobulin replacement is recommended

Background

- Elranatamab is a humanized bispecific antibody that targets B-cell maturation antigen (BCMA) on myeloma cells and CD3 on T cells[1]
- The ongoing phase 2 MagnetisMM-3 (NCT04649359) study demonstrated the efficacy and safety of elranatamab monotherapy in patients with relapsed or refractory multiple myeloma (RRMM) and no prior BCMA-directed therapy (Cohort A)[1]
  - As of the September 10, 2024, data cutoff (median follow-up of 33.9 months in Cohort A), the overall response rate (ORR) was 61.0%, median progression-free survival (PFS) was 17.2 months, and median overall survival (OS) was 24.6 months[2]
- Here we report results for the subgroup of patients enrolled in MagnetisMM-3 (Cohort A) in the US

Methods

- Eligible patients had RRMM with disease refractory to ≥1 immunomodulatory drug, ≥1 proteasome inhibitor, and ≥1 anti-CD38 antibody
- Patients were given subcutaneous elranatamab as step-up priming doses followed by 76 mg once weekly (QW) for 6 cycles
- Patients treated with elranatamab QW for ≥6 cycles who achieved partial response or better lasting ≥2 months were transitioned to a dosing schedule of once every 2 weeks (Q2W), then to once every 4 weeks (Q4W) after ≥6 cycles of Q2W dosing
- The primary endpoint was ORR, assessed by blinded-independent central review (BICR) per International Myeloma Working Group (IMWG) criteria
- Secondary endpoints included duration of response (DOR) and PFS by BICR, OS, and safety
- Adverse events (AEs) were graded using the National Cancer Institute Common Terminology Criteria for AEs (version 5.0)
- Outcomes in patients who switched to Q4W dosing were assessed in a post hoc analysis
- The data cutoff date was March 10, 2025, approximately 38 months after the last patient's first dose
  - Median follow-up by reverse Kaplan-Meier was 39.6 (95% CI, 38.7-41.5) months

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References: 1. Lesokhin AM, et al. Nat Med 2023;29:2259-2267. **2.** Prince M, et al. Poster 4738 presented at: American Society of Hematology Annual Meeting and Exposition; December 7-10, 2024; San Diego, CA, USA.
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Results

PATIENTS AND TREATMENT

- Among the 123 BCMA-naive patients in Cohort A, 47 were enrolled in the US (**Table 1**)
- 22 (47%) patients switched from QW to Q2W; the median duration of Q2W dosing was 11.1 (range, 0.03-25.9) months
- Of the 17 patients who completed ≥6 cycles of Q2W dosing, 8 (17%) patients switched to Q4W dosing; the median duration of Q4W dosing was 15.0 (range, 6.5-20.7) months
  - Among the 9 remaining patients, 5 did not switch because they had ended therapy or had their last dose before the date of Q4W amendment, 3 were on a dose hold at the time of the Q4W amendment approval at each respective site and did not resume dosing as of the cutoff date, and the reason was unknown for 1 patient
- At data cutoff, 5 (10.6%) patients were still receiving treatment

Table 1. Demographics and baseline characteristics

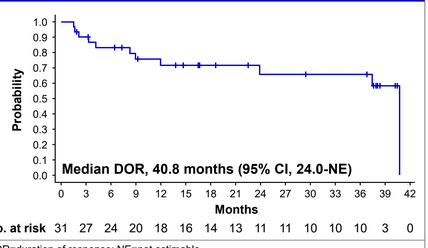
	N=47
Age, median (range), years	68.0 (36.0-89.0)
Male, n (%)	24 (51.1)
Race, n (%)	
African American or Black	8 (17.0)
Asian	3 (6.4)
White	34 (72.3)
Unknown	1 (2.1)
Not reported	1 (2.1)
ECOG PS, n (%)	
0	15 (31.9)
1	28 (59.6)
2	4 (8.5)
R-ISS disease stage, n (%)	
I	14 (29.8)
II	24 (51.1)
III	7 (14.9)
Unknown	2 (4.3)
Cytogenetic risk, n (%)	
Standard	32 (68.1)
High[a]	13 (27.7)
Missing	2 (4.3)
Extramedullary disease by BICR, n (%)[b]	
Yes	15 (31.9)
No	32 (68.1)
Patients with ≥1 poor prognosis feature[c]	32 (68.1)
Prior lines of therapy, median (range)	5.0 (2.0-22.0)
Prior stem cell transplant, n (%)	35 (74.5)
Exposure status, n (%)	
Triple-class[d]	47 (100)
Penta-drug[e]	37 (78.7)
Refractory status, n (%)	
Triple-class[d]	44 (93.6)
Penta-drug[e]	22 (46.8)
Refractory to last line of therapy, n (%)	46 (97.9)

[a] Includes t(4;14), t(14;16), del(17p) chromosomal abnormalities; [b] Extramedullary disease was defined as any plasmacytoma (extramedullary and/or paramedullary with a soft-tissue component); [c] Poor prognosis feature refers to ≥1 of the following: ECOG PS of 2, R-ISS stage III, EMD at baseline by BICR, high cytogenetic risk, BMPCs ≥50%; [d] Triple-class refers to ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 antibody; [e] Penta-drug refers to ≥2 proteasome inhibitors, ≥2 immunomodulatory drugs, and ≥1 anti-CD38 antibody
BICR=blinded independent central review; BMPC=bone marrow plasma cell; ECOG PS=Eastern Cooperative Oncology Group performance status; EMD=extramedullary disease; R-ISS=Revised Multiple Myeloma International Staging System

EFFICACY

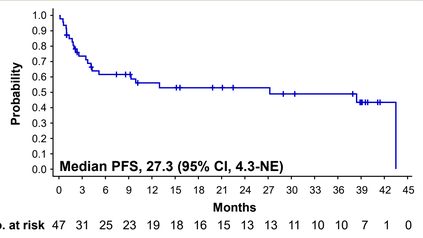
- ORR by BICR was 66.0% (95% CI, 50.7-79.1)
  - sCR, 27.7%; CR, 14.9%; VGPR, 17.0%; PR, 6.4%
  - Median time to response was 1.1 (range, 1.0-7.4) months
  - Median time to CR or better was 4.76 (range, 1.2-12.8) months
- Median DOR was 40.8 (95% CI, 24.0-not estimable [NE]) months (**Figure 1**)
- Median PFS was 27.3 (95% CI, 4.3-NE) months (**Figure 2**)
- Median OS was 43.6 (95% CI, 14.9-NE) months (**Figure 3**)
- DOR and OS data may not be mature as the median values are longer than the 38-month duration from the last patient's first dose to data cutoff
- Among 18 responders who switched to Q2W, 14 (77.8%) maintained or improved their response ≥6 months after the switch
- Among 8 responders who switched to Q4W, 7 (87.5%) maintained their response ≥6 months after the switch

Figure 1. Duration of response



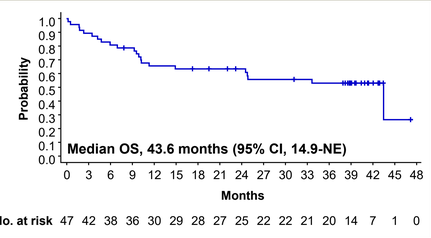
DOR=duration of response; NE=not estimable

Figure 2. Progression-free survival



NE=not estimable; PFS=progression-free survival

Figure 3. Overall survival



NE=not estimable; OS=overall survival

SAFETY

- Safety is consistent with that of the overall study population; no new safety signals were observed with longer follow-up
- The most common treatment-emergent adverse events (TEAEs; ≥25%) are listed in **Table 2**
  - Cytokine release syndrome (CRS) was reported in 61.7% of patients (all grade 1 [34.0%] or grade 2 [27.7%])
  - Immune effector cell-associated neurotoxicity syndrome (ICANS) was reported in 8.5% of patients (grade 1 [4.3%], grade 2 [4.3%])
  - Infections were reported in 70.2% of patients, consistent with the rate observed in the overall population
- Overall, 5 patients (10.6%) died due to TEAEs
  - 3 patients (6.4%) died due to disease progression
  - 2 patients (4.3%) died due to a TEAE other than disease progression; none died due to infections

Table 2. Most common (≥25%) TEAEs

	N=47	
TEAE, n (%)[a]	**Any grade**	**Grade 3/4**
Any	47 (100)	37 (78.7)
Hematologic		
Anemia	21 (44.7)	16 (34.0)
Neutropenia	20 (42.6)	20 (42.6)
Non-hematologic		
Infections[b,c]	33 (70.2)	20 (42.6)
Fatigue	29 (61.7)	4 (8.5)
Cytokine release syndrome	29 (61.7)	0
Diarrhea	27 (57.4)	3 (6.4)
Decreased appetite	27 (57.4)	1 (2.1)
Injection site reaction	18 (38.3)	0
Headache	18 (38.3)	0
Nausea	16 (34.0)	0
Dry skin	16 (34.0)	0
Pyrexia	15 (31.9)	2 (4.3)
Hypokalemia	14 (29.8)	7 (14.9)
Aspartate aminotransferase increased	13 (27.7)	2 (4.3)
Nasal congestion	13 (27.7)	0
SARS-CoV-2 test positive	12 (25.5)	3 (6.4)
Arthralgia	12 (25.5)	1 (2.1)
Insomnia	12 (25.5)	0

[a] TEAEs according to the Medical Dictionary of Regulatory Activities v 27.0 and Common Criteria for Adverse Events v5; severity of CRS assessed according to the American Society for Transplantation and Cellular Therapy criteria; [b] Infections include preferred terms in the system organ class of infections and infestations; [c] No grade 5 infections were reported
TEAE=treatment-emergent adverse event