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Long-Term Survival After Elranatamab Monotherapy in Patients With Relapsed or Refractory Multiple Myeloma: MagnetisMM-3

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Objective

To report updated results in BCMA-naive patients >2 years after the last patient was initially dosed in MagnetisMM-3

Conclusions

Elranatamab continued to demonstrate deep and durable responses in heavily pretreated (median of 5 prior LOTs; 96.7%, triple-class refractory), BCMA-naive patients with RRMM

- MRD negativity rate was 90.3% in evaluable patients with CR or better
- Median DOR was still not reached (2-year rate, 66.9% [95% CI, 54.4-76.7])
- Median PFS was 17.2 (95% CI, 9.8-NE) months
- Median OS was 24.6 (95% CI, 13.4-NE) months

No new safety signals were observed. Although longer follow-up is needed, few SPMs were seen (<5%; all squamous cell carcinomas)

- No hematologic SPMs were reported

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References: 1. Lesokhin AM, et al. Nat Med 2023;29:2259-2267. **2.** Tomasson M, et al. Blood 2023;142(suppl 1):3385. **3.** ClinicalTrials.gov. https://clinicaltrials.gov/study/NCT04649359. Accessed April 26, 2024.

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Background

- Elranatamab is a humanized, bispecific antibody that targets B-cell maturation antigen (BCMA) on myeloma cells and CD3 on T cells
- In MagnetisMM-3 (NCT04649359), a multicenter, open-label, nonrandomized, phase 2 registrational study, elranatamab monotherapy induced deep and durable responses in patients with relapsed or refractory multiple myeloma (RRMM) who had not received prior BCMA-directed therapy (ie, BCMA-naive; N=123)[1,2]
  - At the last data cut (September 11, 2023), the overall survival (OS) data were not yet mature, with >50% of patients censored, after a median follow-up (by reverse Kaplan-Meier method) of 22.0 (95% CI, 21.6-22.6) months (originally reported by descriptive statistics at 17.6 [range 0.2-31.1] months)[2]
  - Here, we report the results observed >2 years after the last patient's initial dose on January 7, 2022

Methods

- Eligible patients had disease refractory to ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 antibody
- Patients received subcutaneous elranatamab as 2 step-up priming doses followed by 76 mg once weekly (QW)
- Patients who received ≥6 months of QW dosing and achieved a partial response or better for ≥2 months were transitioned to a once every 2 weeks (Q2W) dosing schedule and to a Q4W dosing schedule after ≥6 Q2W cycles
- **Primary endpoint**
  - Objective response rate (ORR), assessed by blinded-independent central review (BICR), per International Myeloma Working Group criteria[3]
- **Secondary endpoints**
  - Duration of response (DOR) and progression-free survival (PFS) by BICR
  - OS
  - Safety
- Secondary primary malignancies (SPMs) were determined by clinical review using the system organ class: Neoplasms benign, malignant, and unspecified (including cysts and polyps)
- The data cutoff date was March 26, 2024; median follow-up by reverse Kaplan-Meier method was 28.4 (95% CI, 28.0-29.0) months

Results

PATIENTS AND TREATMENT

- Overall, 123 BCMA-naive patients were treated with elranatamab (**Table 1**)

Table 1. Demographics and baseline characteristics

	N=123
Age, median (range), years	68.0 (36.0-89.0)
Male , n (%)	68 (55.3)
Race, n (%)	
African American or Black	9 (7.3)
Asian	16 (13.0)
White	72 (58.5)
Unknown	1 (0.8)
Not reported[a]	25 (20.3)
ECOG PS, n (%)	
0	45 (36.6)
1	71 (57.7)
2	7 (5.7)
R-ISS disease stage, n (%)	
I	28 (22.8)
II	68 (55.3)
III	19 (15.4)
Unknown/missing	8 (6.5)
Cytogenetic risk, n (%)	
Standard	83 (67.5)
High[b]	31 (25.2)
Missing	9 (7.3)
Extramedullary disease by BICR, n (%)[c]	
Yes	39 (31.7)
No	84 (68.3)
Bone marrow plasma cells, n (%)	
<50%	89 (72.4)
≥50%	26 (21.1)
Missing	8 (6.5)
Patients with ≥1 poor prognosis feature, n (%)[d]	94 (76.4)
Prior lines of therapy, median (range)	5.0 (2.0-22.0)
Prior stem cell transplant, n (%)	87 (70.7)
Exposure status, n (%)	
Triple-class[e]	123 (100)
Penta-drug[f]	87 (70.7)
Refractory status, n (%)	
Triple-class[e]	119 (96.7)
Penta-drug[f]	52 (42.3)
Refractory to last line of therapy, n (%)	118 (95.9)

[a] Includes patients recruited in countries where the collection of race is prohibited; [b] Includes t(4;14), t(14;16), del(17p) chromosomal abnormalities; [c] Extramedullary disease was defined as any plasmacytoma (extramedullary and/or paramedullary with a soft-tissue component); [d] Poor prognosis feature refers to at least one of the following: ECOG PS of 2, R-ISS stage III, EMD at baseline by BICR, high cytogenetic risk, BMPCs ≥50%, or penta-drug refractory disease; [e] Triple-class refers to ≥1 proteasome inhibitor, ≥1 immunomodulatory drug, and ≥1 anti-CD38 antibody; [f] 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.

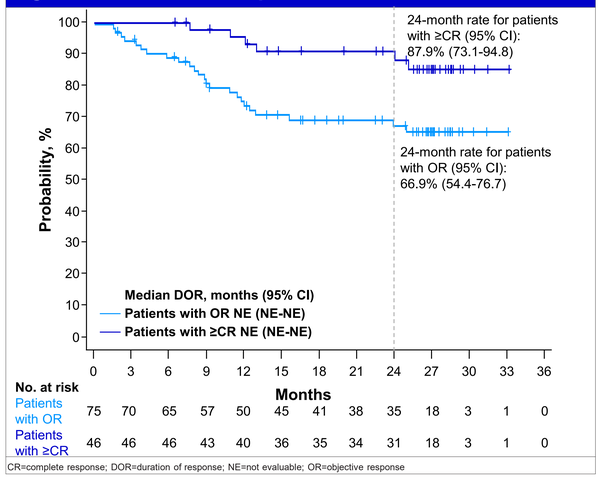
EFFICACY

- With extended follow-up, ORR per BICR remained at 61.0% (CR or better rate, 37.4%)
  - sCR, 16.3%; CR, 21.1%; VGPR, 18.7%, PR, 4.9%
  - Minimal residual disease (MRD) negativity rate was 90.3% in patients with CR or better who were evaluable for MRD (n=31) at the threshold of 10^{-5}
- Median DOR was not reached (NR); the probability of maintaining a response at 2 years was 66.9% (95% CI, 54.4-76.7) among all responders and was 87.9% (95% CI, 73.1-94.8) in patients with CR or better (**Figure 1**)
- Median PFS was 17.2 (95% CI, 9.8-not evaluable [NE]) months (**Figure 2**)
  - In patients with CR or better, median PFS was NR; the probability of being progression-free at 2 years was 90.6% (95% CI, 76.9-96.4)
- Median OS was 24.6 (95% CI, 13.4-NE) months(**Figure 3**)

SAFETY

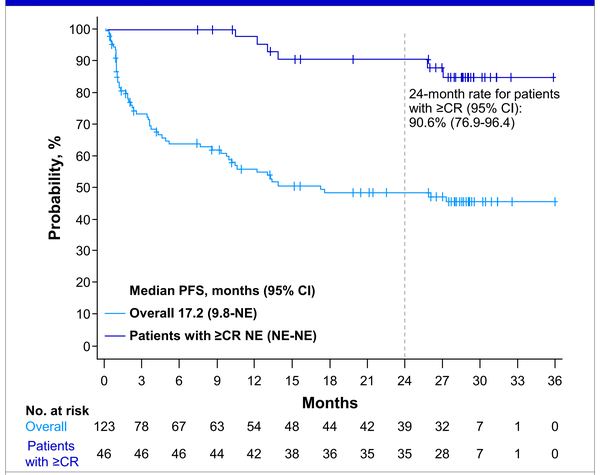
- No new safety signals were observed with extended follow-up
- With 6 more months of follow-up, 4 new deaths had occurred
  - 2 patients with disease under study and 1 patient each with unknown reason and septic shock
- 5 (4.1%) had SPMs, all of which were squamous cell carcinomas of the skin
  - No hematologic SPMs were observed
  - All 5 patients with an SPM had received prior lenalidomide and a stem cell transplant

Figure 1. Duration of response



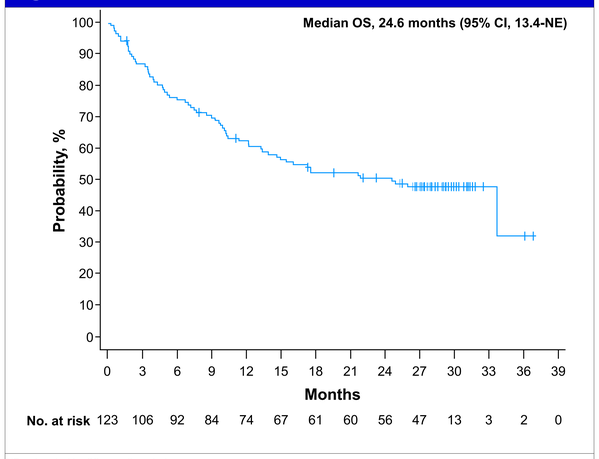
CR=complete response; DOR=duration of response; NE=not evaluable; OR=objective response

Figure 2. Progression-free survival



CR=complete response; NE=not evaluable; PFS=progression-free survival

Figure 3. Overall survival



NE=not evaluable; OS=overall survival