MagnetisMM-3: Long-Term Update of Efficacy and Safety of Less Frequent Dosing of Elranatamab in Patients with Relapsed or Refractory Multiple Myeloma

Prince HM et al.

Poster Presentation at ASH 2024 (Abstract 4738)

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Pfizer-Sponsored Study

MagnetisMM-3: Long-Term Update of Efficacy and Safety of Less Frequent Dosing of Elranatamab in Patients with Relapsed or Refractory Multiple Myeloma (1/6)

Background

- In MagnetisMM-3 (NCT04649359), a multicenter, open-label, nonrandomized, Phase 2 registrational study, elranatamab monotherapy induced deep and durable responses in patients with BCMA-naïve RRMM (N=123)[1,2]
- This presentation reports results obtained ~32 months after the last patient initiated treatment, including the switch to Q4W dosing

Objective

- To report the long-term efficacy and safety of elranatamab in BCMA-naïve patients ~32 months after the last patient initiated treatment in MagnetisMM-3, including results after the switch to Q4W dosing

Methods

- Eligible patients with RRMM were disease refractory to ≥1 IMiD, ≥1 PI, and ≥1 anti-CD38 antibody
- Patients received SC elranatamab as step-up priming doses followed by elranatamab 76 mg QW for 6 cycles
- Patients treated with elranatamab QW for ≥6 cycles who achieved ≥PR lasting ≥2 months were transitioned to Q2W dosing and to Q4W after ≥6 cycles of Q2W dosing
- **Primary endpoint:** ORR by BICR per IMWG criteria
- Outcomes in patients who switched to Q4W dosing were assessed in a post-hoc analysis
- Efficacy impact of Q4W dosing was assessed by evaluating maintenance of response ≥6 months after the switch to Q4W
  - Patients were counted as responders if they had an assessment demonstrating response ≥6 months after the switch
- Safety impact of Q4W dosing was assessed by comparing TEAE incidence before and after the dose switch*
  - New-onset AEs for each participant were included for an equal time period before and after the switch (based on individual follow-up times after the switch), with a maximum time period of up to 6 months
- Data cutoff date: September 10, 2024; median follow-up by reverse Kaplan–Meier: 33.9 months (95% CI 33.4–34.6)

1. Lesokhin AM et al. *Nat Med.* 2023;29:2259-2267;
2. Elranatamab-bcmm. Prescribing information. Pfizer; 2023.
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Please see slide notes for footnotes and abbreviations.

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Patients and Treatment

- Overall, 123 BCMA-naïve patients were treated with elranatamab
  - Median age 68.0 years, 55.3% male
  - Race: 7.3% African American or Black, 13.0% Asian, 58.5% White
  - Patients were heavily pretreated: median 5 prior lines of therapy and 96.7% with triple-class refractory disease
- At data cutoff, 20 (16.3%) patients were still receiving treatment
- In patients without progressive disease by BICR and still on treatment at the start of cycle 7 (n=64), 90.6% fulfilled the protocol criteria to switch to Q2W dosing at C7D1
- 58 patients switched to Q2W dosing; median duration of Q2W dosing was 13.4 (range, 0.03–25.89) months
- Of 43 responding patients who completed ≥6 cycles of Q2W dosing, 28 patients switched to Q4W dosing;* median duration of Q4W dosing was 12.0 (range, 1.87–14.29) months

*Among the remaining 15 patients, reasons for not switching were: timing of the protocol amendment that enabled Q4W dosing (n=10), treatment hold (n=2), or unknown (n=3).
BCMA = B-cell maturation antigen; BICR = blinded-independent central review; C = cycle; D = day; Q2W = once every 2 weeks; Q4W = once every 4 weeks.

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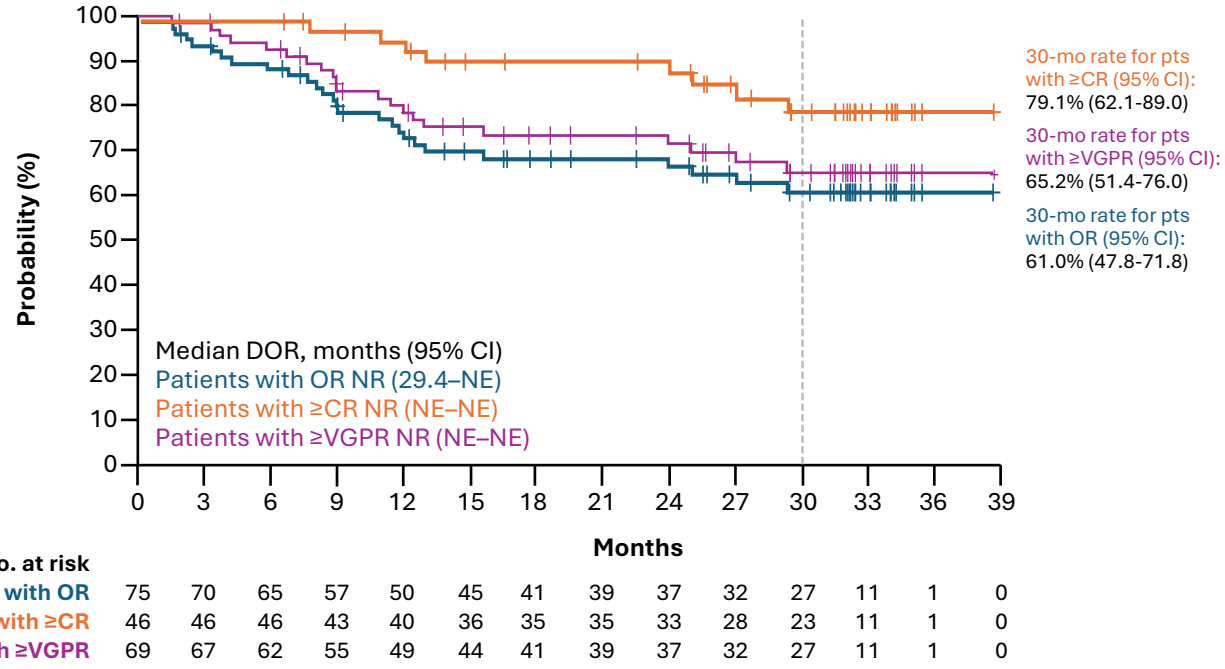
Efficacy: ORR, MRD-Negativity, and DOR

- With extended follow-up, ORR per BICR was 61.0% (≥CR rate 37.4%)
  - sCR, 16.3%; CR, 21.1%; VGPR, 18.7%; PR, 4.9%
  - MRD negativity (10^{-5}) rate was 90.3% in patients with ≥CR who were evaluable for MRD (n=31)
- Median DOR was NR (95% CI 29.4–NE) (**Figure**)
- Among responders per BICR who switched to Q4W dosing ≥6 months before the data cutoff (n=27), 92.6% maintained their response ≥6 months after the switch, including 88.0% who maintained ≥CR
- 1 (3.7%) patient had PD* and 1 (3.7%) patient permanently discontinued elranatamab 6 months after the switch to Q4W

Figure. DOR



No. at risk													
Pts with OR	75	70	65	57	50	45	41	39	37	32	27	11	1	0
Pts with ≥CR	46	46	46	43	40	36	35	35	33	28	23	11	1	0
Pts with ≥VGPR	69	67	62	55	49	44	41	39	37	32	27	11	1	0

*Per IMWG criteria in ≥1 assessment.
BICR = blinded-independent central review; CI = confidence interval; CR = complete response; DOR = duration of response; IMWG = International Myeloma Working Group; MRD = minimal residual disease; NE = not evaluable; NR = not reached; OR = objective response; ORR = objective response rate; PD = progressive disease; PR = partial response; Q4W = once every 4 weeks; sCR = stringent complete response; VGPR = very good partial response.

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PFS and OS

- Median PFS was 17.2 (95% CI 9.8–NE) months (**Figure 1**)
- Median OS was 24.6 (95% CI 13.4–NE) months (**Figure 2**)

Figure 1. PFS

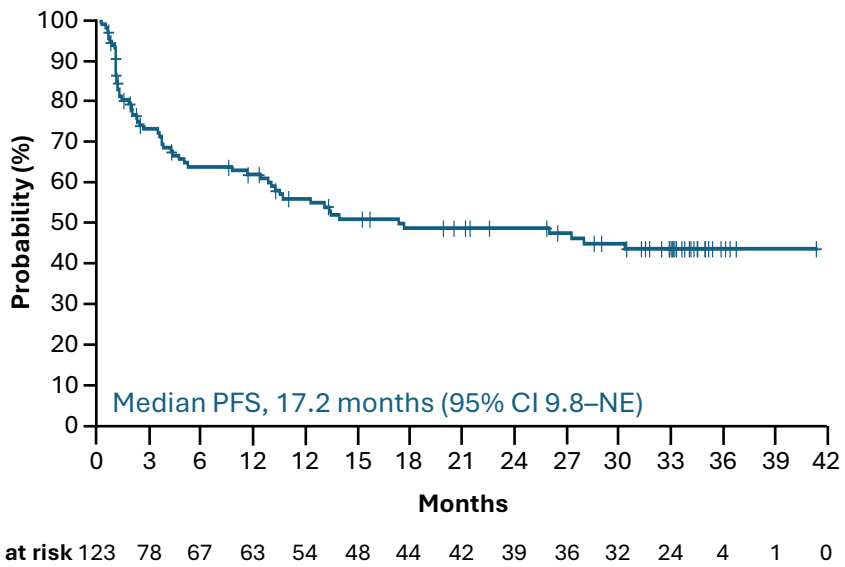
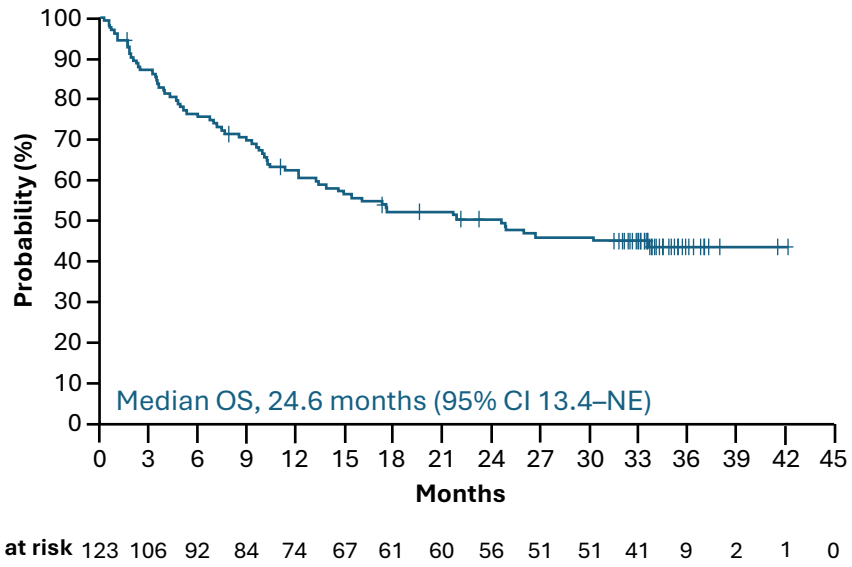


Figure 2. OS



CI = confidence interval; NE = not evaluable; OS = overall survival; PFS = progression-free survival.

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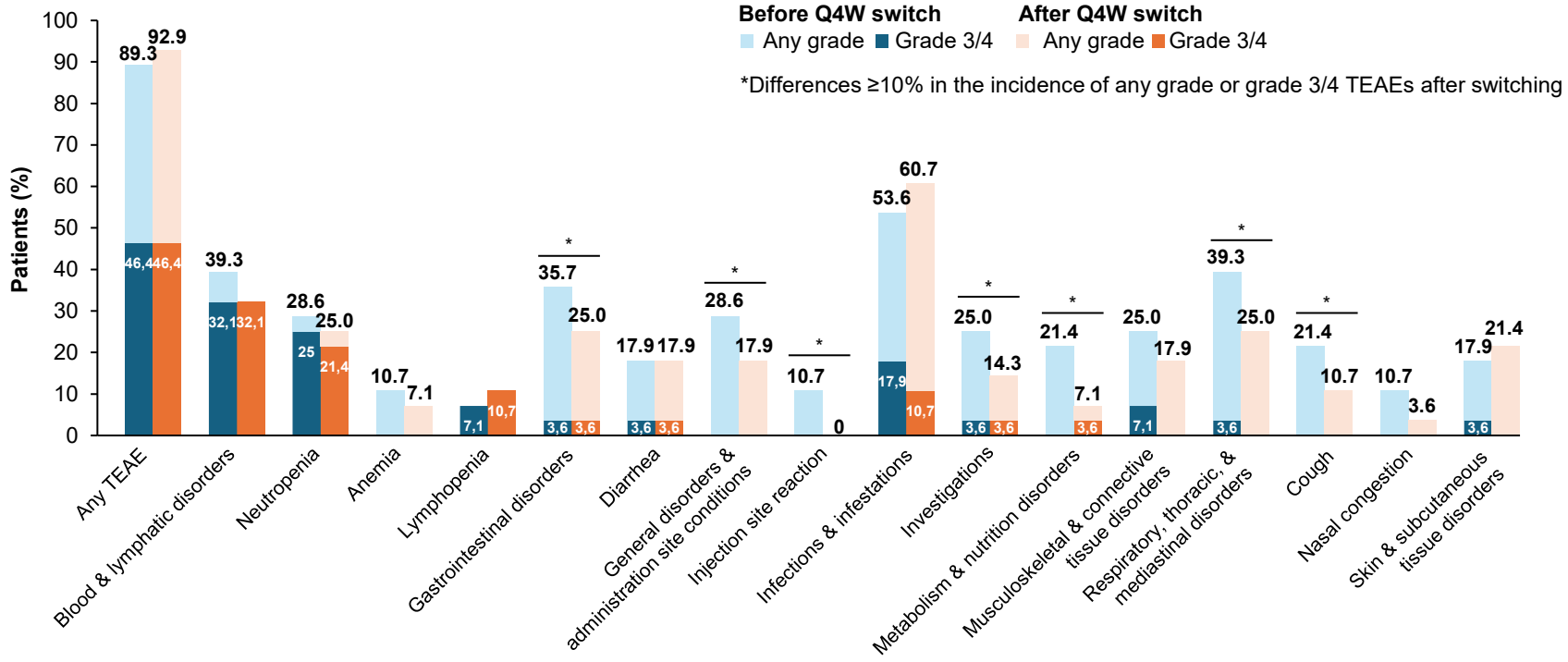
Safety

- No new safety signals were observed with extended follow-up
  - Infections: any grade, 70.7%; grade 3/4, 41.5%; grade 5, 7.3%
  - CRS: 57.7%
  - ICANS: 4.9%
- There were 3 new deaths with an additional ~6 months of follow-up since the last report,[1] with 1 each due to PD, treatment toxicity, and unknown reason
- The incidence and severity TEAEs up to 6 months before and after switching to Q4W dosing are presented in the **Figure**

Figure. Most Common TEAEs Before and After Switch to Q4W Dosing†



†TEAEs occurring in ≥20% of patients at the level of SOC and in ≥10% of patients at the level of PT up to 6 months before or after switching to Q2W.
CRS = cytokine release syndrome; ICANS = immune effector cell-associated neurotoxicity syndrome; PD = progressive disease; PT = preferred term; Q4W = once every 4 weeks; SOC = system organ class; TEAE = treatment-emergent adverse event.

1. Mohty M et al. Presentation at EHA 2024 (Poster P932).
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Authors' Conclusions

- For patients in MagnetisMM-3, the median DOR has still not been reached after a median follow-up of 33.9 months (by reverse Kaplan–Meier)
- For patients with ≥CR, the probability of maintaining a response at 30 months was 79.1%
- The MRD negativity rate was 90.3%
- Following the switch from Q2W to Q4W dosing, 92.6% of patients maintained their response ≥6 months after the switch
- Of all 28 patients who switched to Q4W dosing, the incidence of grade 3/4 infections decreased from 17.9% to 10.7%
- These data demonstrate that reducing the dosing frequency of elranatamab to Q4W may improve safety without compromising efficacy

CR = complete response; DOR = duration of response; Q2W = once every 2 weeks ; Q4W = once every 4 weeks; RRMM = relapsed or refractory multiple myeloma.

1. Mohty M et al. Poster presentation at EHA 2024 (Poster P932).

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