

MagnetisMM-1: A Study of Elranatamab (PF-06863135), a B-Cell Maturation Antigen Targeted CD3-Engaging Bispecific Antibody, for Patients With Relapsed or Refractory Multiple Myeloma

Objective



- To evaluate the safety, PK, pharmacodynamics, and efficacy of elranatamab for patients with RRMM.

Conclusions



- Elranatamab at doses up to 1000 µg/kg SC weekly had a manageable safety profile.
- At doses ≥215 µg/kg/wk, elranatamab demonstrated confirmed ORR of 70.0% and sCR/CR rate of 30.0%.
- At RP2D of 1000 µg/kg/wk, confirmed ORR was 83.3% (5/6).
- 3 of 4 patients with prior BCMA-directed therapy achieved response (1 sCR and 2 VGPR).
- Elranatamab as a single agent achieves deep clinical and molecular responses as indicated by MRD negativity.
- These results support continued development of elranatamab for patients with multiple myeloma.



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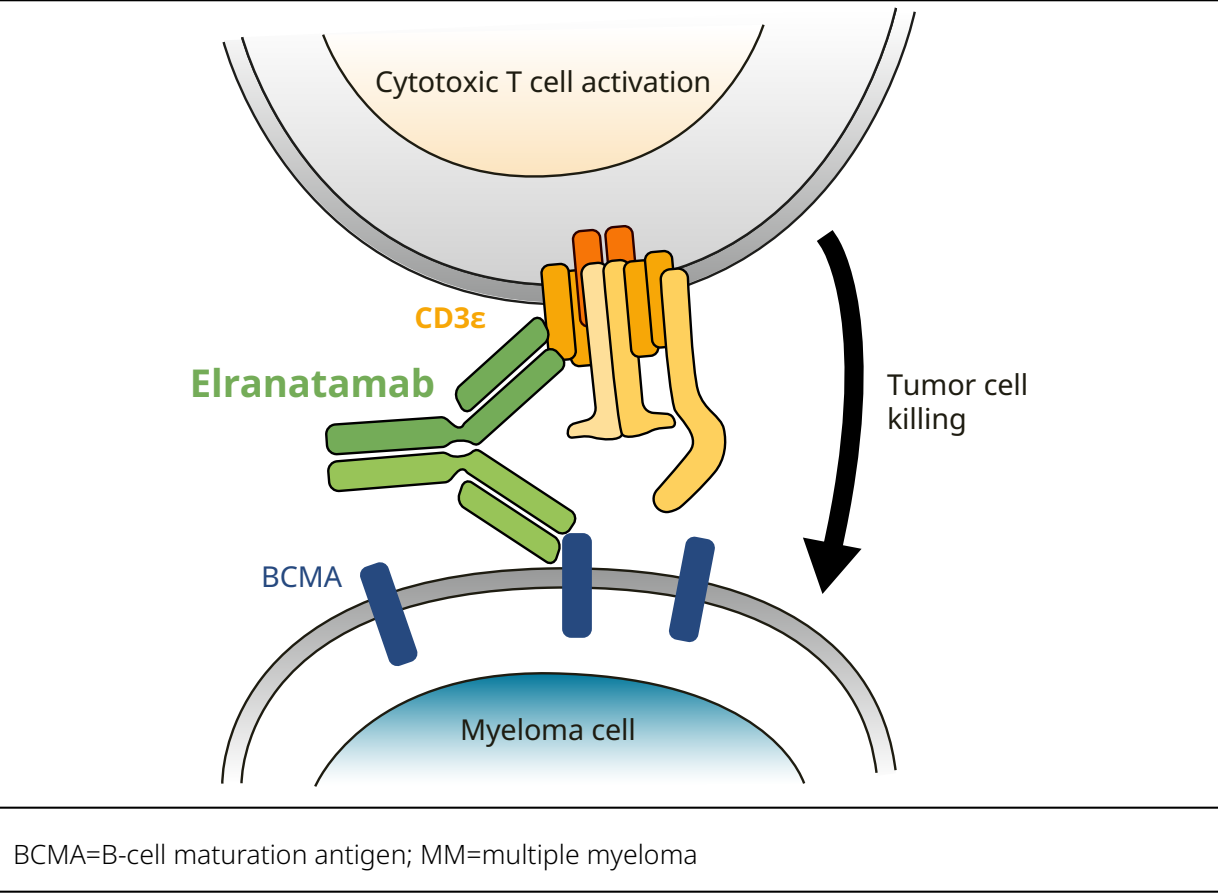
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Background

- B-cell maturation antigen (BCMA) is a member of the tumor necrosis factor receptor superfamily universally expressed in multiple myeloma (MM).¹
- Elranatamab (PF-06863135), a humanized heterodimeric bispecific molecule, targets BCMA on MM cells and CD3 on T cells (**Figure 1**).²
- MagnetisMM-1 (NCT03269136) is a multipart phase 1 study designed to evaluate the safety, pharmacokinetics (PK), pharmacodynamics, and efficacy of elranatamab for patients with relapsed/refractory MM (RRMM).
- Here, we report results for subcutaneous (SC) dosing of elranatamab (data cutoff June 7, 2021).

Figure 1: Elranatamab targets BCMA on MM cells and CD3 on T cells



Methods

- Patients with RRMM received:
 - Monotherapy: Elranatamab 80, 130, 215, 360, 600, or 1000 µg/kg/wk; or
 - Combination therapy: Elranatamab 32 mg priming dose on Cycle 0 Day 1 (C0D1), followed 1 wk later by 44 mg/wk beginning C1D1 + pomalidomide (POM) 4 mg/d orally on D1–21 of a 28-day cycle, beginning with C1.
- Treatment-emergent adverse events (TEAEs) were graded by CTCAE v4.03, and cytokine release syndrome (CRS) by ASTCT criteria.³
 - Dose-limiting toxicity (DLT) was monitored to the end of C1.
- PK, pharmacodynamics, and immunogenicity were evaluated.
- Response was assessed by International Myeloma Working Group (IMWG) criteria.⁴
- Minimal residual disease was assessed by next-generation sequencing at a sensitivity of 1×10⁻⁵, in accordance with IMWG criteria.

Results – Monotherapy

DOSING GROUPS, PATIENT AND DISEASE CHARACTERISTICS, AND PRIOR TREATMENTS

- 30 patients had received elranatamab SC by the data cutoff.
 - 80 (n=6), 130 (n=4), 215 (n=4), 360 (n=4), 600 (n=6), and 1000 (n=6) µg/kg/wk.

- Patient characteristics, including prior treatments, are shown in **Table 1**.
 - Median age was 63 y, and 56.7% were female.
 - Patients received a median (range) of 8.0 (2–15) prior treatments, 86.7% were triple-class refractory, and 23.3% received prior BCMA-targeted therapy.

Table 1: Patient and disease characteristics and prior treatments in the full cohort (N=30)	
	SC dosing total
Female, n (%)	17 (56.7)
Median age, y (range)	63 (46–80)
≥65 y, n (%)	12 (40.0)
Cytogenetic risk	
High ^a	7 (23.3)
Standard	19 (63.3)
Unknown	4 (13.3)
Treatment	
Prior anti-myeloma therapies, median (range)	8.0 (2–15)
Triple-class refractory disease, n (%) ^b	26 (86.7)
Prior PIs, n (%)	30 (100.0)
Bortezomib	27 (90.0)
Carfilzomib	26 (86.7)
Ixazomib	8 (26.7)
Prior IMiDs, n (%)	30 (100.0)
Lenalidomide	29 (96.7)
Pomalidomide	27 (90.0)
Thalidomide	8 (26.7)
Prior anti-CD38 therapy, n (%)	29 (96.7)
Daratumumab	28 (93.3)
Isatuximab	4 (13.3)
Other ^c	2 (6.7)
Prior BCMA-targeted therapy, n (%)	7 (23.3)
Anti-BCMA ADC	6 (20.0)
CAR-T	3 (10.0)
Patients may have received more than 1 treatment within a given therapy class. ^a Definition of high cytogenetic risk includes t(4;14), t(14;16), del(17p), and del(13q). ^b Triple-class refractory disease is refractory to at least 1 PI, 1 IMiD, and 1 anti-CD38 therapy. ^c 2 patients treated at 80 and 360 µg/kg received prior anti-myeloma therapy with a CD38 × CD3 bispecific molecule. ADC=antibody drug conjugate; BCMA=B-cell maturation antigen; CAR-T=chimeric antigen receptor T-cell therapy; IMiD=immunomodulatory drug; PI=proteasome inhibitor; SC=subcutaneous	

SAFETY

- No DLT was observed.
- The most common TEAEs in the full cohort are listed in **Table 2**.

Table 2: TEAEs (all causality) occurring in >1/3 of patients in the full cohort (N=30)					
TEAE, n (%)	Grade 1	Grade 2	Grade 3	Grade 4	Total
Hematologic					
Lymphopenia	0	0	7 (23.3)	19 (63.3)	26 (86.7)
Anemia	1 (3.3)	4 (13.3)	18 (60.0)	0	23 (76.7)
Thrombocytopenia	4 (13.3)	2 (6.7)	5 (16.7)	6 (20.0)	17 (56.7)
Neutropenia	0	0	6 (20.0)	10 (33.3)	16 (53.3)
Leukopenia	1 (3.3)	3 (10.0)	7 (23.3)	1 (3.3)	12 (40.0)
Non-hematologic					
CRS	16 (53.3)	6 (20.0)	0	0	22 (73.3)
Injection site reaction	14 (46.7)	2 (6.7)	0	0	16 (53.3)
Nausea	4 (13.3)	6 (20.0)	2 (6.7)	0	12 (40.0)
CRS=cytokine release syndrome; TEAE=treatment-emergent adverse event					

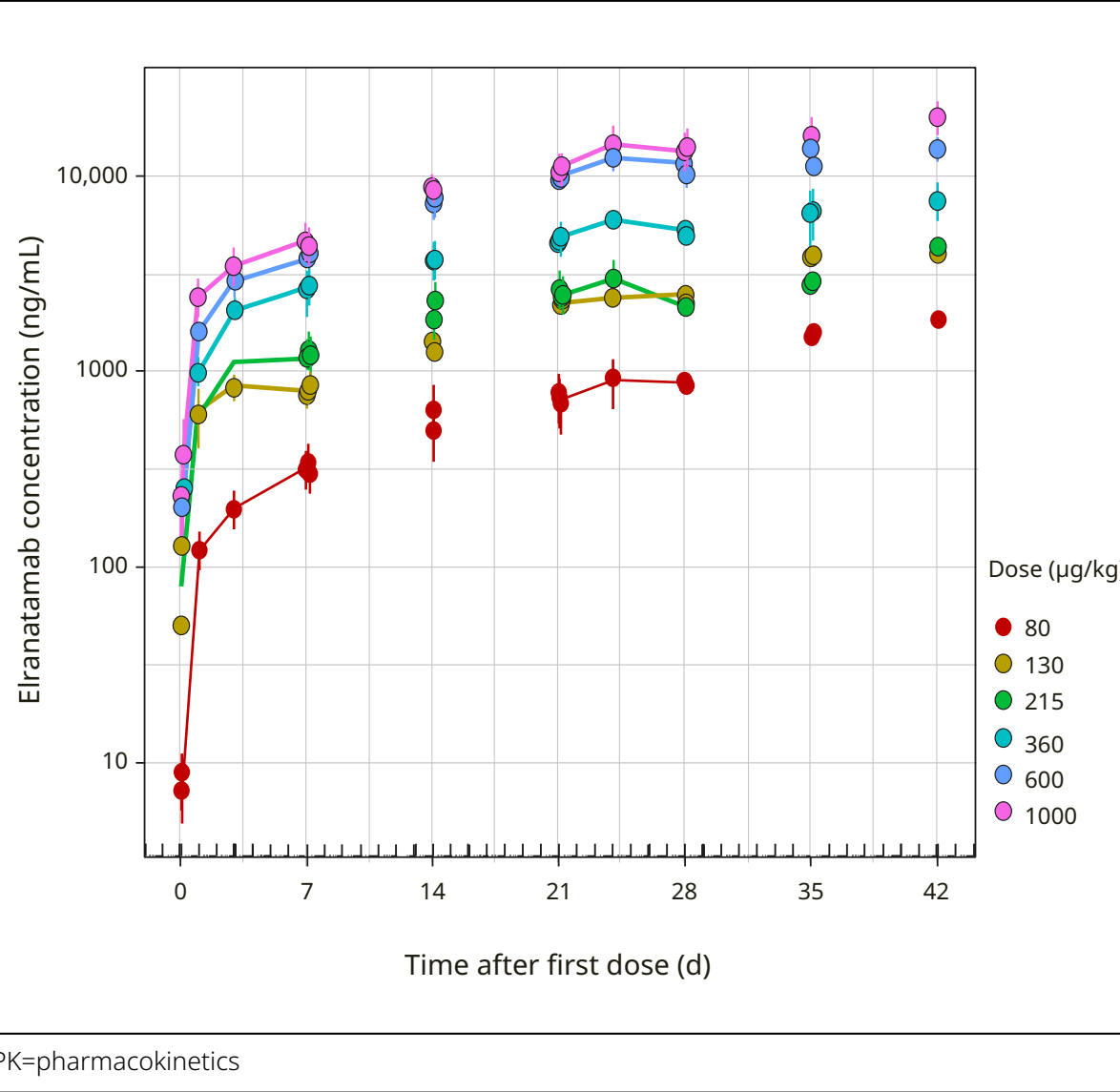
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- CRS was limited to G1 or G2, with no events >G2.
 - Median (range) time to onset was 1.0 (1–3) day and median (range) duration was 3.0 (1–10) days.
 - 9 (30.0%) patients received tocilizumab and 3 (10.0%) received steroid treatment for CRS.
 - No permanent treatment discontinuations, dosing interruptions, or dose reductions occurred due to CRS.

PK AND PHARMACODYNAMICS

- Exposure increased in an approximately dose-proportionate manner (**Figure 2**).
 - Time to maximum concentration was 3–7 days after a single dose.
 - Population PK analysis supports a fixed-dose approach for further development.
- Serum cytokine increases occurred predominantly following the first dose.

Figure 2: Elranatamab PK profile by dose



PK=pharmacokinetics

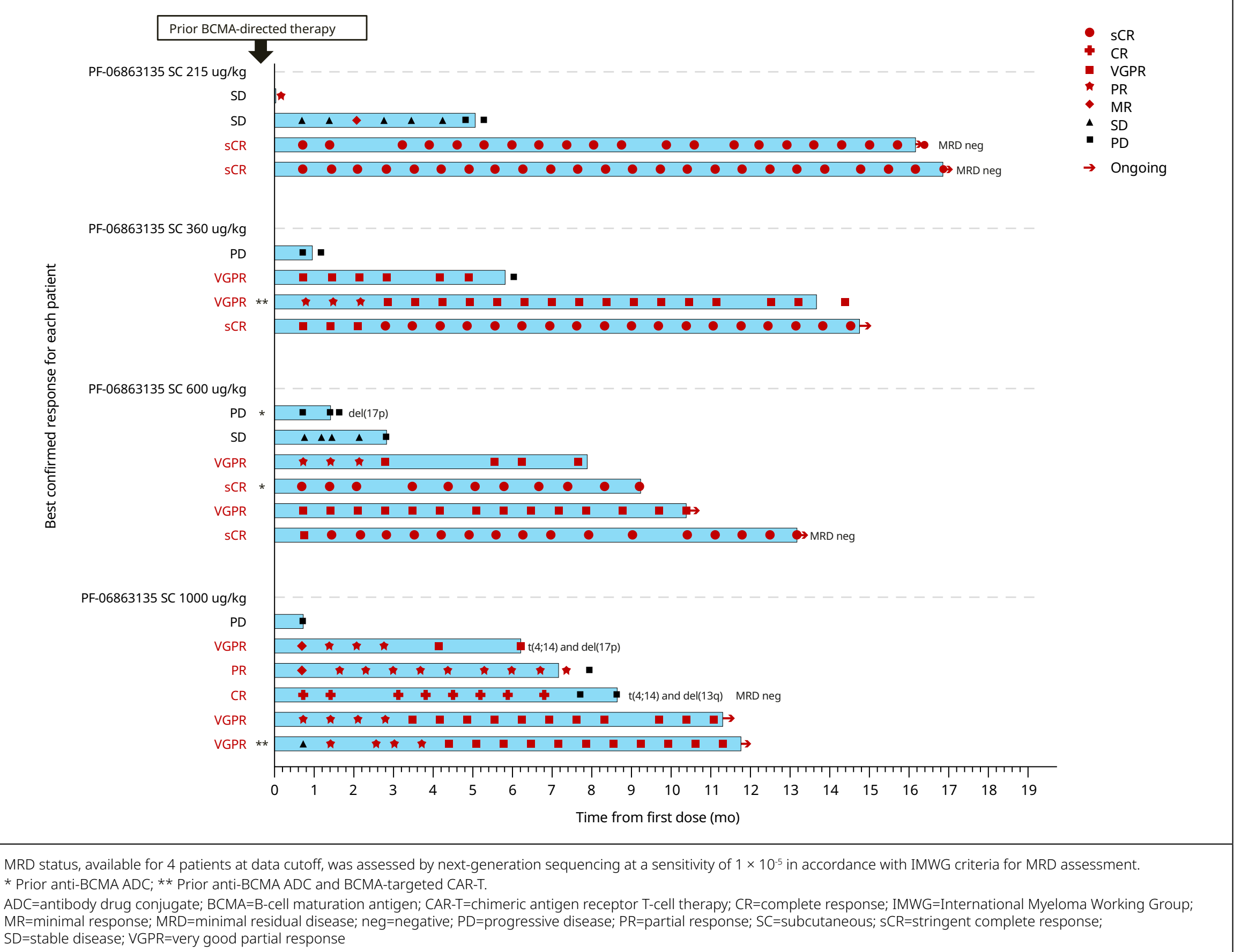
EFFICACY

- At doses ≥215 µg/kg (n=20), objective response rate (ORR) was 70.0% and stringent complete response/complete response (sCR/CR) rate was 30.0% (**Table 3**, **Figure 3**).
 - At the recommended phase 2 dose (RP2D) of 1000 µg/kg, confirmed ORR was 83.3% (5/6).
 - Median duration of follow-up was 10.9 months.
 - 3 of 4 patients with prior BCMA-directed therapy achieved response.
 - All 4 evaluable patients with CR or sCR achieved MRD negativity by IMWG criteria (1×10⁻⁵).
- Median (range) time to response in the 14 responders was 22.0 (21–50) days.
 - Median duration of response has not yet been reached.
 - Probability (95% CI) of responders being event free at 6 months was 92.3% (56.7–98.9).

Table 3: IMWG-confirmed responses by elranatamab dose

Response, n (%)	215 µg/kg (n=4)	360 µg/kg (n=4)	600 µg/kg (n=6)	1000 µg/kg (n=6)	Total ≥215 µg/kg (n=20)
sCR	2 (50.0)	1 (25.0)	2 (33.3)	0	5 (25.0)
CR	0	0	0	1 (16.7)	1 (5.0)
VGPR	0	2 (50.0)	2 (33.3)	3 (50.0)	7 (35.0)
PR	0	0	0	1 (16.7)	1 (5.0)
MR	0	0	0	0	0
SD	2 (50.0)	0	1 (16.7)	0	3 (15.0)
PD	0	1 (25.0)	1 (16.7)	1 (16.7)	3 (15.0)
ORR	2 (50.0)	3 (75.0)	4 (66.7)	5 (83.3)	14 (70.0)
CR=complete response; IMWG=International Myeloma Working Group; MR=minimal response; ORR=objective response rate; PD=progressive disease; PR=partial response; sCR=stringent complete response; SD=stable disease; VGPR=very good partial response					

Figure 3: Duration of treatment and best overall response



MRD status, available for 4 patients at data cutoff, was assessed by next-generation sequencing at a sensitivity of 1 × 10⁻⁵ in accordance with IMWG criteria for MRD assessment.

* Prior anti-BCMA ADC; ** Prior anti-BCMA ADC and BCMA-targeted CAR-T.

ADC=antibody drug conjugate; BCMA=B-cell maturation antigen; CAR-T=chimeric antigen receptor T-cell therapy; CR=complete response; IMWG=International Myeloma Working Group; MR=minimal response; MRD=minimal residual disease; neg=negative; PD=progressive disease; PR=partial response; SC=subcutaneous; sCR=stringent complete response; SD=stable disease; VGPR=very good partial response

Results – Combination Therapy with Pomalidomide

- 9 patients were assigned to combination therapy, and all patients had MM that was relapsed/refractory to prior proteasome inhibitor, immunomodulatory drug, and anti-CD38 therapy.
- 8 patients received the combination with POM, and 1 patient received elranatamab monotherapy.
- The most common TEAEs (all causality) occurring in >1/3 of patients included CRS (78%; none >G2), fatigue (78%; 11% G3, 0% G4), neutropenia (78%; 22% G3, 56% G4), diarrhea (67%; none >G1), injection site reaction (67%; none >G1), pyrexia (56%; none >G2), hypokalemia (44%; 22% G3, 0% G4), and nausea (44%; none >G2).
- 2 patients with pre-existing peripheral neuropathy (PN) who received the combination with POM developed G3 PN which, following suspension of study treatment, improved to G2 for both patients.
- All patients in this cohort were transitioned to elranatamab monotherapy.
- No drug–drug interaction was observed in combination with POM.
- Confirmed ORR was 78% (7 of 9 patients) on an intent-to-treat basis, including 1 sCR, 2 VGPR, and 4 PR.