

MagnetisMM-9: Efficacy and Safety of Step-Up Priming Doses and Longer Dosing Intervals of Elranatamab in Patients With Relapsed or Refractory Multiple Myeloma

Objective

To report updated safety and efficacy results in the MagnetisMM-9 study

Conclusions

- The alternative step-up priming regimen (4/20 mg) and alternative dosing schedules resulted in similar efficacy and safety vs the regimen used in the registrational MagnetisMM-3 (12/32-mg step-up) study
 - Responses were durable with encouraging DOR and PFS with the alternative step-up and longer dosing schedule
 - The lower priming doses produced an overall CRS rate similar to that of MagnetisMM-3, but the profile differed, with more CRS events occurring after doses 2, 3, or 4+ and a higher prevalence of recurrent CRS
- Therefore, the optimal elranatamab step-up regimen remains 12/32 mg from the original regimen in the MagnetisMM-3 study
- These results suggest that reducing the dose frequency of elranatamab does not compromise efficacy
- Future analyses of ongoing studies will be used to confirm these results



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Supplementary Materials

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References: 1. Elexio (elranatamab-bcmm). Prescribing information. Pfizer; 2023. 2. Lesokhin AM, et al. Nat Med 2023;29:2259-2267. 3. Tomasson MH, et al. Hemasphere 2024;8:e136.

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Background

- Elranatamab, a B-cell maturation antigen (BCMA) x CD3-directed bispecific monoclonal antibody, is approved as a monotherapy for the treatment of adult patients with relapsed or refractory multiple myeloma (RRMM) who received ≥3 prior therapies, including an immunomodulatory agent (IMiD), a proteasome inhibitor (PI), and an anti-CD38 monoclonal antibody, and who experienced disease progression during the last therapy¹
- In the phase 2 registrational MagnetisMM-3 trial, subcutaneous elranatamab was given as 2 step-up priming doses (12 and 32 mg on days 1 and 4 of cycle 1, respectively) followed by 76 mg once weekly (QW) in patients with RRMM naive to BCMA-directed therapy²
 - 56.3% of patients had cytokine release syndrome (CRS; grade 2, 14.3%; grade ≥3, 0%)²
 - Most events occurred after doses 1 (44.5%), 2 (20.2%), and 3 (5.9%)
 - Recurrent CRS (patients with >1 event) occurred in 15.1% of patients²
 - At a median follow-up of 28.4 months by reverse Kaplan-Meier (data cutoff: March 26, 2024), overall response rate (ORR) was 61.0% (37.4% with complete response or better)³
 - Median duration of response (DOR), progression-free survival (PFS), and overall survival (OS) were not reached (24-month rate, 66.9%), 17.2 months, and 24.6 months, respectively³

Results

PATIENTS AND TREATMENT

- A total of 85 patients were treated (Table 1)
- At data cutoff, the median treatment duration was 8.6 (range, 0.49-31.34), 2.9 (range, 0.30-20.34), 1.4 (range, 0.03-21.26), 3.3 (range, 0.13-16.66), and 3.8 (range, 0.03-31.34) months for patients in Part 1, Part 2A DL1, Part 2A DL2, Part 2B, and overall, respectively

Table 1. Demographics and baseline characteristics

	Part 1 76 mg ELRA (n=33)	Part 2A DL1 116 mg ELRA (n=12)	Part 2A DL2 152 mg ELRA (n=11)	Part 2B 152 mg ELRA (n=29)	Total (N=85)
Age, median (range), years	63.0 (36-79)	66.0 (49-78)	68.0 (48-86)	64.0 (49-77)	64.0 (36-86)
Male, n (%)	14 (42.4)	8 (66.7)	6 (54.5)	14 (48.3)	42 (49.4)
Race, n (%)					
African American or Black	2 (6.1)	0	1 (9.1)	1 (3.4)	4 (4.7)
Asian	19 (57.6)	5 (41.7)	3 (27.3)	8 (27.6)	35 (41.2)
White	11 (33.3)	6 (50.0)	7 (63.6)	17 (58.6)	41 (48.2)
Unknown	0	1 (8.3)	0	2 (6.9)	3 (3.5)
Not reported ^a	1 (3.0)	0	0	1 (3.4)	2 (2.4)
ECOG PS, n (%)					
0	19 (57.6)	5 (41.7)	7 (63.6)	14 (48.3)	45 (52.9)
1	14 (42.4)	7 (58.3)	4 (36.4)	15 (51.7)	40 (47.1)
Derived ISS disease stage, n (%)					
I	16 (48.5)	6 (50.0)	4 (36.4)	11 (37.9)	37 (43.5)
II	11 (33.3)	5 (41.7)	3 (27.3)	8 (27.6)	27 (31.8)
III	5 (15.2)	1 (8.3)	4 (36.4)	8 (27.6)	18 (21.2)
Missing	1 (3.0)	0	0	2 (6.9)	3 (3.5)
Cytogenetic risk, n (%)					
Standard	23 (69.7)	6 (50.0)	9 (81.8)	19 (65.5)	57 (67.1)
High ^b	10 (30.3)	6 (50.0)	2 (18.2)	9 (31.0)	27 (31.8)
Missing	0	0	0	1 (3.4)	1 (1.2)
Extramedullary disease, n (%) ^c					
Yes	8 (24.2)	3 (25.0)	4 (36.4)	5 (17.2)	20 (23.5)
No	25 (75.8)	9 (75.0)	7 (63.6)	24 (82.8)	65 (76.5)
Bone marrow plasma cells, n (%)					
<50%	27 (81.8)	11 (91.7)	9 (81.8)	20 (69.0)	67 (78.8)
≥50%	6 (18.2)	1 (8.3)	2 (18.2)	9 (31.0)	18 (21.2)
Prior lines of therapy, median (range), no.	5.0 (3-11)	4.5 (2-12)	5.0 (3-9)	5.0 (1-10)	5.0 (1-12)
Prior stem cell transplant, n (%)	28 (84.8)	10 (83.3)	9 (81.8)	23 (79.3)	70 (82.4)
Exposure status, n (%)					
Triple-class ^d	33 (100.0)	12 (100.0)	11 (100.0)	29 (100.0)	85 (100.0)
Penta-drug ^e	20 (60.6)	7 (58.3)	6 (54.5)	20 (69.0)	53 (62.4)
Refractory status, n (%)					
Triple-class ^d	31 (93.9)	11 (91.7)	8 (72.7)	23 (79.3)	73 (85.9)
Penta-drug ^e	12 (36.4)	4 (33.3)	2 (18.2)	10 (34.5)	28 (32.9)
Refractory to last line of therapy, n (%)	29 (87.9)	11 (91.7)	11 (100.0)	23 (79.3)	74 (87.1)
Prior BCMA-targeted therapy, n (%)	9 (27.3)	2 (16.7)	3 (27.3)	2 (6.9)	16 (18.8)

^a Includes patients recruited in countries where the collection of race is prohibited; ^b Includes t(4;14), t(14;16), and del(17p) chromosomal abnormalities; ^c Extramedullary disease was defined as any plasmacytoma not associated with bone; ^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

BCMA=B-cell maturation antigen; DL=dose level; EOC PS=Eastern Cooperative Oncology Group performance status; ELRA=elranatamab; ISS=International Staging System

SAFETY

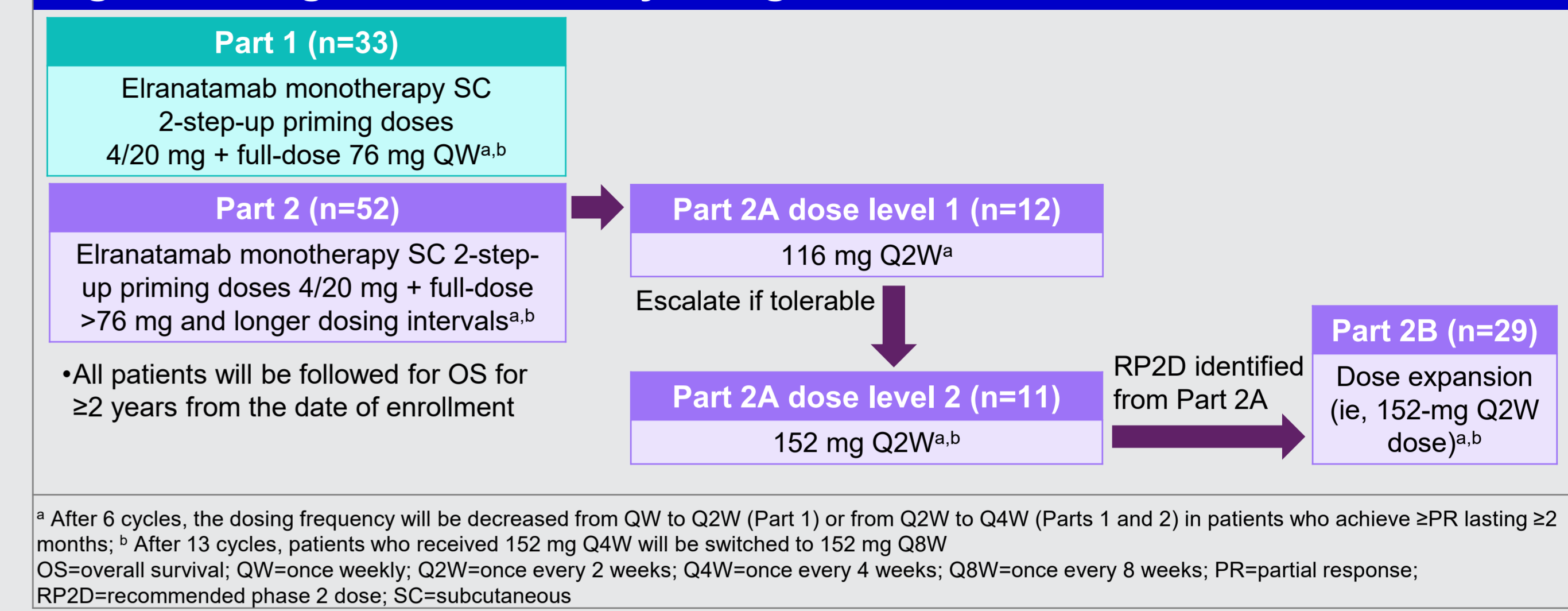
- TREATMENT-EMERGENT ADVERSE EVENTS
 - Common treatment-emergent events (TEAEs; ≥30%) are shown in Table 2
 - The most common TEAEs overall included infections (any grade, 72.9%; grade 3/4, 45.9%) and cytokine release syndrome (any grade, 63.5%; grade 3/4, 1.2%)
 - Immune effector cell-associated syndrome was reported in 4.7% (no grade 3/4) of patients overall
 - Overall, 16 (18.8%) patients had a grade 5 TEAE, including 9 (10.6%) due to disease progression and 4 (4.7%) from infections and 1 (1.2%) each due to fall, subdural hematoma, and food poisoning
 - CYTOKINE RELEASE SYNDROME (CRS)
 - Characteristics of CRS per cohort are reported in Table 3

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Methods

- MagnetisMM-9 (NCT05104412) is a phase 1/2, open-label, nonrandomized study of elranatamab examining an alternative 2-dose step-up priming regimen (4 and 20 mg on days 1 and 4 of cycle 1, respectively)
- Eligible patients had RRMM and were refractory to ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody
- After the priming doses, elranatamab 76 mg was given QW for 6 cycles (Part 1) or for 1 cycle followed by 116 (dose level 1; [DL1]) or 152 mg (DL2) once every 2 weeks (Q2W) for the next 5 cycles (Part 2A; Figure 1)
- The recommended phase 2 dose from Part 2A (152 mg Q2W) was evaluated in Part 2B (dose expansion)
- The grade ≥2 CRS rate during cycle 1 per American Society for Transplantation and Cellular Therapy criteria is the primary endpoint for both parts
- Secondary endpoints include evaluation of adverse events, pharmacokinetics, and efficacy
- Data cutoff date was August 19, 2024. The median durations of follow-up for patients in Part 1, Part 2A DL1, Part 2A DL2, Part 2B, and overall were 29.4 (range, 1.18-32.62), 17.5 (range, 1.48-27.86), 19.9 (range, 0.85-23.49), 15.5 (range, 1.05-17.94), and 16.2 (range, 0.85-32.62) months, respectively

Figure 1. MagnetisMM-9 study design



^a After 6 cycles, the dosing frequency will be decreased from QW to Q2W (Part 1) or from Q2W to Q4W (Parts 1 and 2) in patients who achieve ≥PR lasting ≥2 months; ^b After 13 cycles, patients who received 152 mg Q4W will be switched to 152 mg Q8W

OS=overall survival; QW=once weekly; Q2W=once every 2 weeks; Q4W=once every 4 weeks; Q8W=once every 8 weeks; PR=partial response; RPD2=recommended phase 2 dose; SC=subcutaneous

Table 2. Most common (≥30%) TEAEs

	Part 1 76 mg ELRA (n=33)	Part 2A DL1 116 mg ELRA (n=12)	Part 2A DL2 152 mg ELRA (n=11)	Part 2B 152 mg ELRA (n=29)	Total (N=85)	
TEAE, n (%) ^a	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Any	33 (100.0)	26 (78.8)	12 (100.0)	9 (75.0)	11 (100.0)	6 (54.5)
Hematologic						
Neutropenia	19 (57.6)	19 (57.6)	7 (58.3)	7 (58.3)	6 (54.5)	6 (54.5)
Anemia	15 (45.5)	11 (33.3)	6 (50.0)	6 (50.0)	5 (45.5)	3 (27.3)
Leukopenia	10 (30.3)	8 (24.2)	4 (33.3)	4 (36.4)	4 (36.4)	8 (27.6)
Thrombocytopenia	7 (21.2)	5 (15.2)	6 (50.0)	5 (41.7)	4 (36.4)	3 (27.3)
Lymphopenia	2 (6.1)	2 (6.1)	2 (16.7)	2 (16.7)	3 (27.3)	2 (18.2)
Nonhematologic						
Infections ^b	26 (78.8)	15 (45.5)	10 (83.3)	7 (58.3)	8 (72.7)	5 (45.5)
CRS	20 (60.6)	0	10 (83.3)	0	10 (90.9)	1 (9.1)
Diarrhea	17 (51.5)	3 (9.1)	6 (50.0)	0	2 (18.2)	0
Pyrexia	14 (42.4)	0	4 (33.3)	0	0	7 (24.1)
Fatigue	13 (39.4)	1 (3.0)	7 (58.3)	2 (16.7)	6 (54.5)	0
Decreased appetite	13 (39.4)	0	7 (58.3)	0	3 (27.3)	2 (18.2)
Hypogammaglobulinemia	12 (36.4)	1 (3.0)	1 (8.3)	1 (8.3)	1 (9.1)	0
Injection site reaction	10 (30.3)	0	7 (58.3)	0	3 (27.3)	0
Headache	10 (30.3)	0	0	2 (16.7)	0	5 (17.2)
Nausea	9 (27.3)	0	4 (33.3)	0	2 (18.2)	0
Dry skin	6 (18.2)	0	2 (16.7)	0	4 (36.4)	0
Back pain	7 (21.2)	0	5 (41.7)	2 (16.7)	1 (9.1)	0
Pain in extremity	4 (12.1)	0	4 (33.3)	0	1 (9.1)	0
Blood creatine increased	2 (6.1)	0	2 (16.7)	0	4 (36.4)	1 (9.1)
Arthralgia	2 (6.1)	0	4 (33.3)	0	2 (18.2)	0

^a TEAEs according to the Medical Dictionary for Regulatory Activities v27.0 and Common Terminology Criteria for Adverse Events v5. CRS was assessed according to ASTCT criteria. Any-grade TEAEs reported in ≥30% of patients, and grade 3/4 TEAEs reported in ≥10% of patients; ^b Infections include preferred terms in the system organ class of infections and infestations

ASTCT=American Society for Transplantation and Cellular Therapy; CRS=cytokine release syndrome; DL=dose level; ELRA=elranatamab; TEAE=treatment-emergent adverse event

Table 3. Characteristics of CRS

	Part 1 76 mg ELRA (n=33)	Part 2A DL1 116 mg ELRA (n=12)	Part 2A DL2 152 mg ELRA (n=11)	Part 2B 152 mg ELRA (n=29)	Total (N=85)
Patients with AE, n (%) ^a	20 (60.6)	10 (83.3)	10 (90.9)	14 (48.3)	54 (63.5)
Dose 1	10 (30.3)	4 (33.3)	4 (36.4)	7 (24.1)	25 (29.4)
Dose 2	9 (27.3)	3 (25.0)	4 (36.4)	7 (24.1)	23 (27.1)
Dose 3	5 (15.2)	4 (33.3)	3 (27.3)	6 (20.7)	18 (21.2)
Dose 4	2 (6.1)	1 (8.3)	0	1 (3.4)	4 (4.7)
Dose ≥5	2 (6.1)	2 (16.7)	1 (9.1)	0	5 (5.9)
Grade ≥2 CRS rate during Cycle 1, % (90% CI)	15.2 (6.2-29.3)	16.7 (3.1-43.8)	27.3 (7.9-56.4)	6.9 (1.2-20.2)	14.1 (8.4-21.9)
Patients with >1 event, n (%)	6 (18.2)	4 (33.3)	2 (18.2)	5 (17.2)	17 (20.0)
Time to onset, median (range), days	2.0 (1.0-7.0)	2.0 (2.0-5.0)	2.0 (1.0-7.0)	2.0 (2.0-4.0)	2.0 (1.0-7.0)
Time to resolution, median (range), days	2.0 (1.0-19.0)	2.0 (1.0-10.0)	1.5 (1.0-4.0)	2.0 (1.0-8.0)	2.0 (1.0-19.0)

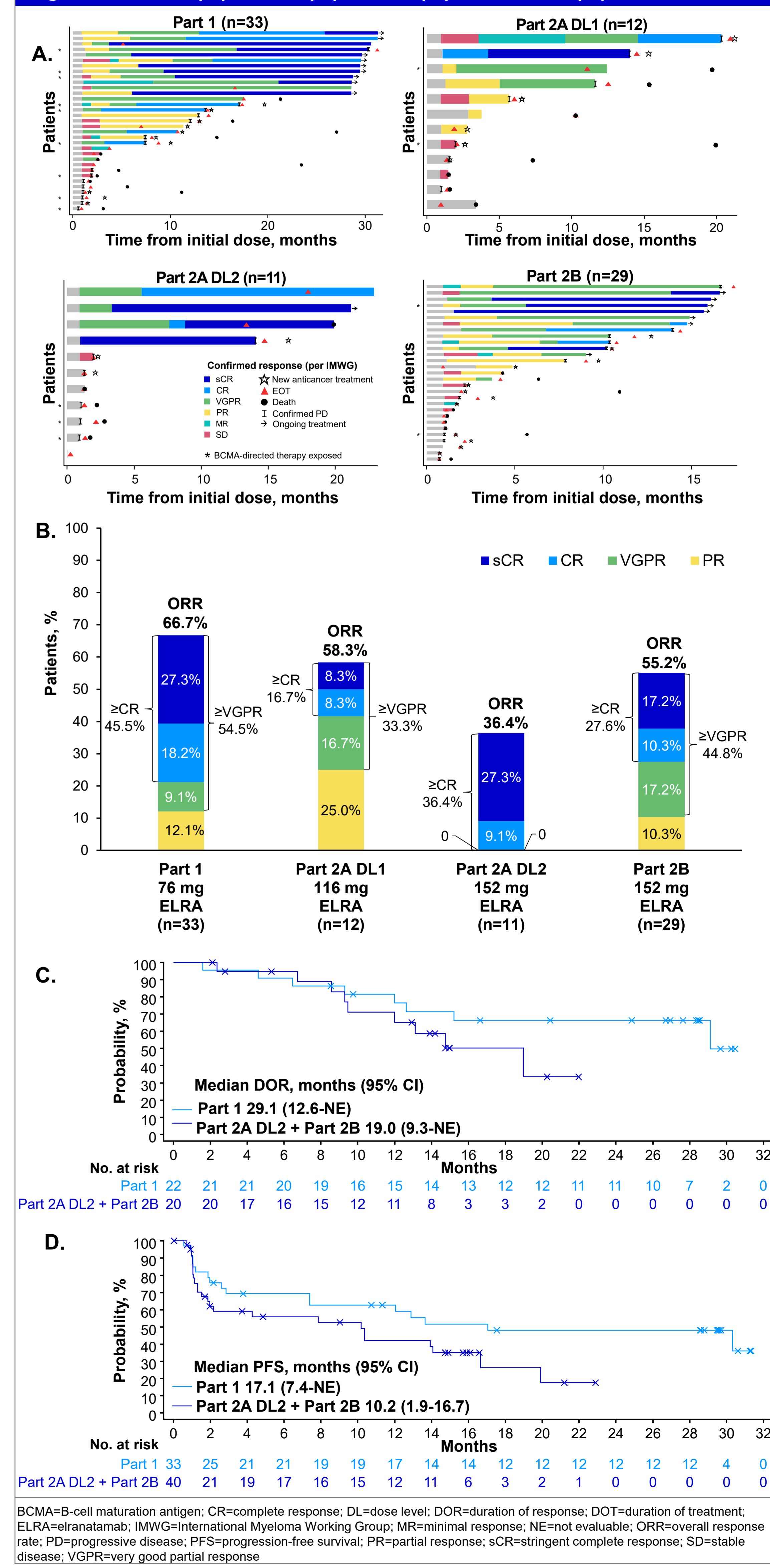
^a According to ASTCT criteria

AE=adverse event; ASTCT=American Society for Transplantation and Cellular Therapy; CRS=cytokine release syndrome; DL=dose level; ELRA=elranatamab

EFFICACY

- The duration of treatment swimmer plots, ORR, DOR, and PFS are shown in Figure 2A-D
- The ORR was 57.6% for patients overall
 - ORRs were 64.1% vs 33.3%, 35.0% vs 64.6%, 51.9% vs 61.4%, 50.0% vs 59.4% for patients with derived International Staging System stage I/II (n=64) vs stage III disease (n=18), with (n=20) vs without (n=65) baseline extramedullary disease, high-risk (n=27) vs standard-risk (n=57) cytogenetics, and prior (n=16) vs no prior (ie, naive; n=69) BCMA-targeted therapy, respectively
 - Minimal residual disease (MRD) negativity (10⁻⁵) rate was 78.9% in patients with complete response or better who were evaluable for MRD (n=19)
- As of the data cutoff date, 10 patients overall switched to 152-mg Q8W dosing and had ≥3 months of possible follow-up
 - Among these patients, 7 maintained and 1 improved their response; response was lost in 2 patients
- With a median follow-up of 29.4 (range, 1.2-32.6) months by reverse Kaplan-Meier, the data from Part 1 are the most mature data of all cohorts in MagnetisMM-9

Figure 2. DOT (A), ORR (B), DOR (C), and PFS (D)



BCMA=B-cell maturation antigen; CR=complete response; DL=dose level; DOR=duration of response; DOT=duration of treatment; ELRA=elranatamab; IMWG=International Myeloma Working Group; MR=minimal response; NE=not evaluable; ORR=overall response rate; PD=progressive disease; PFS=progression-free survival; PR=partial response; sCR=stringent complete response; SD=stable disease; VGPR=very good partial response