Elranatamab in Combination With Daratumumab and Lenalidomide in Patients With Newly Diagnosed Multiple Myeloma Not Eligible for Transplant: Initial Results From MagnetisMM-6 Part 1

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Objectives

- Evaluate the efficacy and safety of elranatamab + lenalidomide ± daratumumab (EDR or ER) vs daratumumab + lenalidomide + dexamethasone (DRd) in patients with transplant-ineligible NDMM
- Part 1 of the study evaluates the optimal dose of EDR or ER in patients with RRMM or NDMM to determine the recommended phase 3 dose for Part 2
- Initial results from part 1 dose level G (DLG) are presented

Conclusions

- Initial data from MagnetisMM-6 Part 1 dose level G demonstrate that the combination of elranatamab (76 mg Q4W) + daratumumab + lenalidomide is effective and manageable in transplant-ineligible patients with NDMM
  - Safety profile was predictable and consistent with known toxicities of the components; most frequent (≥50%) TEAEs were hematologic AEs, infections, and CRS
  - EDR showed early and promising efficacy with responses expected to deepen further with longer follow-up
- Phase 3 MagnetisMM-6 Part 2 (opening soon) will evaluate EDR (elranatamab 76 mg SC Q4W + daratumumab + lenalidomide) versus DRd (daratumumab + lenalidomide + dexamethasone) in transplant-ineligible and -deferred NDMM

Background

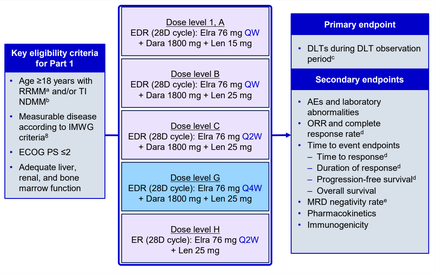
- Elranatamab is a BCMA-CD3 bispecific antibody approved as a monotherapy for patients with relapsed/refractory multiple myeloma who have received ≥1 immunomodulatory drug (IMiD), ≥1 proteasome inhibitor (PI), and ≥1 anti-CD38 monoclonal antibody (mAb)[1,2]
  - Based on MagnetisMM-3 (NCT04649359), the objective response rate (ORR) was 61.0%, median progression-free survival was 17.2 months, and median overall survival was 24.6 months[3,4]
- Combining elranatamab with lenalidomide and daratumumab may enhance immune cell–mediated myeloma cell death as:
  - Lenalidomide stimulates the activation of CD4+ and CD8+ T cells and NK cells[5]
  - Daratumumab has immunomodulatory effects and multiple actions (ie, antibody-dependent cell-mediated cytotoxicity, complement-dependent cytotoxicity, and antibody-dependent cellular phagocytosis) against CD38-expressing myeloma[6,7]
- MagnetisMM-6 (NCT05623020) is a phase 3, open-label, randomized study evaluating the efficacy and safety of elranatamab combined with lenalidomide (R) ± daratumumab (DARA) (EDR or ER) vs DARA + R + dexamethasone (DRd) in patients with transplant-ineligible (TI) newly diagnosed multiple myeloma (NDMM) (**Figure 1**)

Methods

STUDY DESIGN

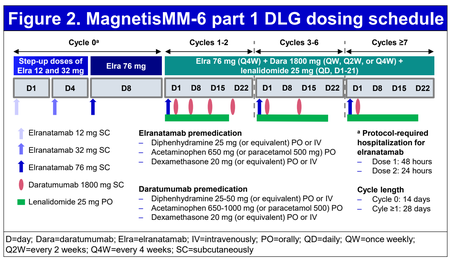
- MagnetisMM-6 Part 1 DLG is evaluating the combination of elranatamab 76 mg subcutaneous (SC) every 4 weeks (Q4W), daratumumab 1800 mg SC, and lenalidomide 25 mg orally in patients with TI NDMM
- DLG dosing schedule is shown in **Figure 2**
- Data cutoff was April 1, 2025

Figure 1. MagnetisMM-6 part 1 study design



[a] Must have received 1 or 2 prior lines of MM therapy including ≥1 IMiD and ≥1 PI; [b] Defined as age ≥65 years or <65 years with comorbidities impacting the possibility of transplant; [c] DLTs will not be assessed in any DL that represents a lower dose than an already cleared DL, or where the initial DLT period is the same as an already cleared DL; [d] Per IMWG response criteria; [e] Per IMWG sequencing criteria
AE=adverse event; D=day; Dara=daratumumab; DL=dose level; DLT=dose-limiting toxicity; ECOG PS=Eastern Cooperative Oncology Group performance status; EDR=elranatamab + daratumumab + lenalidomide; Elra=elranatamab; ER=elranatamab + lenalidomide; IMiD=immunomodulatory drug; IMWG=International Myeloma Working Group; Len=lenalidomide; MRD=minimal residual disease; NDMM=newly diagnosed multiple myeloma; ORR=objective response rate; PI=proteasome inhibitor; PO=orally; QW=once weekly; Q2W=every 2 weeks; Q4W=every 4 weeks; RRMM=relapsed or refractory multiple myeloma; SC=subcutaneously; TI=transplant ineligible;

Figure 2. MagnetisMM-6 part 1 DLG dosing schedule



D=day; Dara=daratumumab; Elra=elranatamab; IV=intravenously; PO=orally; QD=daily; QW=once weekly; Q2W=every 2 weeks; Q4W=every 4 weeks; SC=subcutaneously

Results

BASELINE CHARACTERISTICS

- All patients (100%) had NDMM
- Baseline demographics and clinical characteristics are shown in **Table 1**

Table 1. Baseline demographics and clinical characteristics

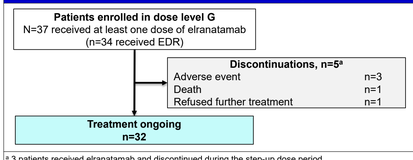
	N=37
Age, median (range), years	75.0 (67-83)
Female, n (%)	23 (62.2)
Race, n (%)	
Asian	5 (13.5)
White	32 (86.5)
ECOG PS, n (%)	
0	22 (59.5)
1	14 (37.8)
2	1 (2.7)
R-ISS disease stage by investigator, n (%)	
I	9 (24.3)
II	20 (54.1)
III	5 (13.5)
Unknown	3 (8.1)
Extramedullary disease by investigator, n (%)	
Yes	0
No	37 (100)
Baseline bone marrow plasma cells, n (%)	
<50%	28 (75.7)
≥50%	9 (24.3)
Frail status, n (%)[a]	
Yes	9 (24.3)
No	28 (75.7)

[a] According to the simplified IMWG scale using scores for ECOG PS, Charlson Comorbidity Index, and age
ECOG PS=Eastern Cooperative Oncology Group performance status; IMWG=International Myeloma Working Group; NDMM=newly diagnosed multiple myeloma; R-ISS=Revised International Staging System

PATIENT DISPOSITION

- 37 patients with TI NDMM enrolled and received ≥1 dose of elranatamab (**Figure 3**)
  - 34 patients received the EDR regimen
- As of the data cutoff, a median (range) follow-up was 7.9 (1.2-9.5) months
  - 32 (86.5%) patients were still on treatment

Figure 3. MagnetisMM-6 patient disposition



[a] 3 patients received elranatamab and discontinued during the step-up dose period
Data cutoff was April 1, 2025
EDR=elranatamab + daratumumab + lenalidomide; NDMM=newly diagnosed multiple myeloma; TI= transplant ineligible

SAFETY: TREATMENT-EMERGENT ADVERSE EVENTS (TEAEs)

- The most frequent (≥50%) TEAEs were hematologic (83.8%; grade 3/4 78.4%), infections (70.3%; grade 3/4 18.9%), and CRS (62.2%, grade 3/4 0%) (**Table 2**)
- All CRS events were grade ≤2
- One grade 2 ICANS event was reported

Table 2. TEAEs (≥15%)

TEAE, n (%)[a]	Any grade (N=37)	Grade 3/4 (N=37)
Any	37 (100)	35 (94.6)
Hematologic		
Neutropenia[b]	28 (75.7)	27 (73.0)
Anemia[c]	13 (35.1)	7 (18.9)
Thrombocytopenia[d]	6 (16.2)	4 (10.8)
Nonhematologic		
CRS	23 (62.2)	0
Pyrexia	14 (37.8)	0
Cough	11 (29.7)	0
Injection site reaction	11 (29.7)	0
Nausea	11 (29.7)	0
Rash	11 (29.7)	3 (8.1)
Diarrhea	9 (24.3)	1 (2.7)
Hypogammaglobulinemia	9 (24.3)	1 (2.7)
Constipation	8 (21.6)	0
Decreased appetite	8 (21.6)	2 (5.4)
Fatigue	7 (18.9)	0
Peripheral sensory neuropathy	7 (18.9)	0
Asthenia	6 (16.2)	4 (10.8)
Cytomegalovirus test positive	6 (16.2)	0
Edema peripheral	6 (16.2)	0

[a] TEAEs according to the Medical Dictionary for Regulatory Activities v27.1 and Common Terminology Criteria for Adverse Events v5; severity of CRS and ICANS was assessed according to the American Society for Transplantation and Cellular Therapy criteria[b]; [b] Including neutrophil count decreased, neutrophil percentage decreased, cyclic neutropenia, agranulocytosis, granulocytopenia, and granulocyte count decreased; [c] Includes hemoglobin decreased, red blood cell count decreased, hematocrit decreased, normochromic anemia, normocytic anemia, and normochromic normocytic anemia; [d] Includes platelet count decreased
CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome; TEAE=treatment-emergent adverse event

SAFETY: INFECTIONS

- Frequent (any grade >10%) infections included upper respiratory tract infection and *Escherichia* urinary tract infection (**Table 3**)
  - One case of grade 5 Candida pneumonia was reported
- Anti-infective prophylaxis was given, and 34 patients (91.9%) received immunoglobulin replacement therapy

Table 3. Infections (≥5%)

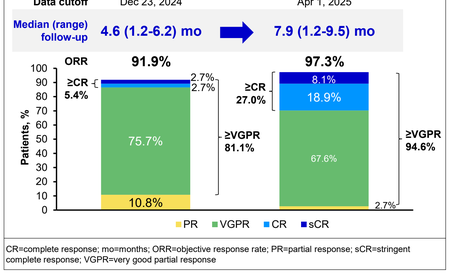
TEAE, n (%)[a]	Any grade (N=37)	Grade 3/4 (N=37)
Infections[b]	26 (70.3)	7 (18.9)
Upper respiratory tract infection	8 (21.6)	0
Escherichia urinary tract infection	4 (10.8)	1 (2.7)
Cytomegalovirus reactivation[c]	4 (10.8)	1 (2.7)
Bronchitis	3 (8.1)	0
Rhinitis	3 (8.1)	0
Viral upper respiratory tract infection	3 (8.1)	0
Pneumonia	2 (5.4)	1 (2.7)
Urinary tract infection	2 (5.4)	0

[a] TEAEs according to the Medical Dictionary for Regulatory Activities v27.1 and Common Terminology Criteria for Adverse Events v5; [b] Infections include preferred terms in the system organ class of infections and infestations; [c] 3 patients with cytomegalovirus infection reactivation, 1 patient with cytomegalovirus viremia and pneumonia cytomegaloviral (grade 3)
TEAE=treatment-emergent adverse event

EFFICACY: EARLY EMERGING RESPONSE DATA

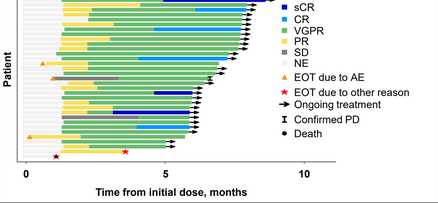
- Confirmed ORR by investigator was 97.3% (95% CI, 85.8-99.9) (**Figure 4**)
  - 94.6% had VGPR or better
  - 27.0% had CR or better
- Responses occurred early with a median (range) time to response of 1.5 (0.3-4.2) months (**Figure 5**)

Figure 4. Best overall response to EDR



CR=complete response; mo=months; ORR=objective response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

Figure 5. Duration of progression-free survival



AE=adverse event; CR=complete response; EOT=end of trial; IMWG=International Myeloma Working Group; NE=not evaluable; PD=progressive disease; PR=partial response; sCR=stringent complete response; SD=stable disease; VGPR=very good partial response

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