MM-378

Efficacy and Safety of Elranatamab by Age and Frailty in Patients With Relapsed/Refractory Multiple Myeloma (RRMM): A Subgroup Analysis From MagnetisMM-3

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Objective

- To report the efficacy and safety of elranatamab in subgroups of patients by age and frailty in the ongoing phase 2 MagnetisMM-3 study

Conclusions

- Elranatamab maintained efficacy across subgroups of age and frailty after ~15 mo of follow up, with objective response rates of 56.4–63.1% and probabilities of maintaining response at 15 mo of 68.5–74.4%
- The safety profile of elranatamab was generally consistent across subgroups
  - The majority of TEAEs were ≤ Grade 2
  - The most common Grade 3/4 TEAEs were hematologic
  - The incidence and severity of infections was similar across subgroups
- These results demonstrate that elranatamab is efficacious and has a manageable safety profile in elderly or frail patients with RRMM and may be a treatment option for those ineligible for more intensive myeloma therapies

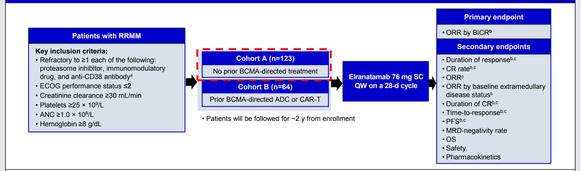
Background

- Multiple myeloma (MM) is a B-cell malignancy that results in bone destruction and marrow failure[1]
  - MM is predominantly a disease of elderly and frail patients, who are often ineligible for intensive therapies[2]
- B-cell maturation antigen (BCMA) is a member of the tumor necrosis factor receptor superfamily universally expressed on MM cells[3]
- Elranatamab is a humanized bispecific antibody that targets both BCMA-expressing MM cells and CD3-expressing T cells[3]
- Data from the ongoing phase 2 MagnetisMM 3 study (NCT04649359) demonstrated the safety and efficacy of elranatamab in patients with RRMM and no prior BCMA-directed therapy (Cohort A)[4]
- Results by age and frailty subgroups in BCMA-naïve patients from MagnetisMM-3 are presented

Methods

- MagnetisMM-3 (NCT04649359) is an open-label, multicenter, non-randomized, phase 2 study to evaluate the safety and efficacy of elranatamab monotherapy in patients with relapsed/refractory MM (RRMM) (**Figure 1**)
  - Cohort A of the study enrolled patients naïve to BCMA-directed therapies (n=123)
- Patients received subcutaneous elranatamab 76 mg once weekly (QW) on a 28-day cycle with a 2-step-up priming dose regimen of 12 mg on day 1 and 32 mg on day 4 during the first wk
- This analysis reports results in subgroups of patients by age: <65 (n=43) vs ≥65 y (n=80), and frailty: non-frail (n=84) vs frail (n=39) in BCMA-naïve patients
- A simplified frailty scale that scored patients based on age (≤75, 76–80, and >80 y), Charlson Comorbidity Index (≤1, >1), and Eastern Cooperative Oncology Group (ECOG) performance status (0, 1, and ≥2) was used to define patient subgroups[5]
- Results include data through ~15 mo after last patient initial dose
- Analyses are based on a data cutoff date of March 14, 2023, except for analyses of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) which are based on a cutoff date of January 12, 2023

Figure 1: MagnetisMM-3 study design



[a] Refractory was defined as having disease progression while on therapy or within 60 d of last dose in any line, regardless of response; [b] By BICR assessment per IMWG response criteria[c]; [c] By investigator assessment per IMWG response criteria
ADC=antibody drug conjugate; ANC=absolute neutrophil count; BCMA=B-cell maturation antigen; BICR=blinded independent central review; CAR-T=chimeric antigen receptor T-cell; CR=complete response; ECOG=Eastern Cooperative Oncology Group; IMWG=International Myeloma Working Group; MRD=minimal residual disease; ORR=objective response rate; OS=overall survival; PFS=progression-free survival; QW=once weekly; SC=subcutaneous

Results

PATIENTS AND TREATMENT

- Patient demographics, characteristics, and prior treatments are presented in **Table 1**

Table 1: Baseline demographics and characteristics and prior treatments

	<65 y n=43	≥65 y n=80	Non-frail n=84	Frail n=39
Age, median (range), y	58.0 (36–64)	71.0 (65–89)	65.0 (36–79)	75.0 (47–89)
Male, n (%)	26 (60.5)	42 (52.5)	44 (52.4)	24 (61.5)
Race				
White	25 (58.1)	47 (58.8)	49 (58.3)	23 (59.0)
Asian	7 (16.3)	9 (11.3)	15 (17.9)	1 (2.6)
Black or African American	5 (11.6)	4 (5.0)	5 (6.0)	4 (10.3)
Not reported or unknown	6 (14.0)	20 (25.0)	15 (17.9)	11 (28.2)
ECOG performance status, n (%)				
0	23 (53.5)	22 (27.5)	41 (48.8)	4 (10.3)
1	19 (44.2)	52 (65.0)	43 (51.2)	28 (71.8)
2	1 (2.3)	6 (7.5)	0	7 (17.9)
R-ISS disease stage, n (%)				
I	11 (25.6)	17 (21.3)	24 (28.6)	4 (10.3)
II	24 (55.8)	44 (55.0)	47 (56.0)	21 (53.8)
III	6 (14.0)	13 (16.3)	8 (9.5)	11 (28.2)
Unknown	2 (4.7)	6 (7.5)	5 (6.0)	3 (7.7)
Extramedullary disease by BICR, n (%)[a]	14 (32.6)	25 (31.3)	26 (31.0)	13 (33.3)
Bone marrow plasma cells, n (%)				
<50%	30 (69.8)	59 (73.8)	60 (71.4)	29 (74.4)
≥50%	9 (20.9)	17 (21.3)	18 (21.4)	8 (20.5)
Missing	4 (9.3)	4 (5.0)	6 (7.1)	2 (5.1)
Prior lines of anti-myeloma therapy, median (range)	5.0 (2–22)	5.0 (2–12)	5.0 (2–22)	5.0 (2–12)
Refractory status, n (%)				
Triple-class[b]	41 (95.3)	78 (97.5)	84 (100.0)	35 (89.7)
Penta-drug[c]	19 (44.2)	33 (41.3)	38 (45.2)	14 (35.9)
Refractory to last line of therapy	43 (100.0)	75 (93.8)	80 (95.2)	38 (97.4)

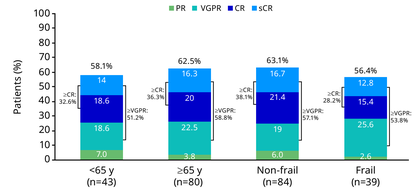
[a] Extramedullary disease was defined as presence of any plasmacytoma (extramedullary and/or paramedullary) with a soft tissue component; [b] Triple-class refers to at least 1 proteasome inhibitor, 1 immunomodulatory drug, and 1 anti-CD38 antibody; [c] Penta-drug refers to at least 2 proteasome inhibitors, 2 immunomodulatory drugs, and 1 anti-CD38 antibody
BICR=blinded independent central review; ECOG=Eastern Cooperative Oncology Group; R-ISS=Revised Multiple Myeloma International Staging System

- The median treatment duration was 8.2 vs 5.5 mo in the <65 vs ≥65 y, and 6.4 vs 5.6 mo in the non-frail and frail subgroups, respectively (**Table 2**)
- At the data cut off, 34.9%, 32.5%, 35.7%, and 28.2% of patients were still receiving treatment in the <65, ≥65 y, non-frail, and frail subgroups, respectively
- Discontinuation occurred in 65.1% vs 67.5% of patients aged <65 vs ≥65 y and in 64.3% vs 71.8% of the non-frail vs frail groups, respectively (**Table 2**)
  - The most common reason for discontinuation in all subgroups was progressive disease

Table 2: Patient disposition

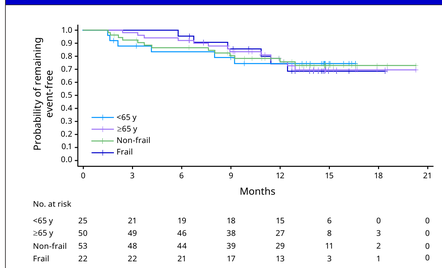
	<65 y n=43	≥65 y n=80	Non-frail n=84	Frail n=39
Duration of treatment, median (range), mo	8.2 (0.1–19.4)	5.5 (0.0–24.4)	6.4 (0.0–23.5)	5.6 (0.1–24.4)
Discontinued	28 (65.1)	54 (67.5)	54 (64.3)	28 (71.8)
Adverse event	4 (9.3)	13 (16.3)	10 (11.9)	7 (17.9)
Death	1 (2.3)	8 (10.0)	5 (6.0)	4 (10.3)
Lack of efficacy	0	3 (3.8)	1 (1.2)	2 (5.1)
Progressive disease	22 (51.2)	26 (32.5)	36 (42.9)	12 (30.8)
Withdrawal by subject	0	4 (5.0)	1 (1.2)	3 (7.7)
Global deterioration of health status	1 (2.3)	0	1 (1.2)	0
Ongoing	15 (34.9)	26 (32.5)	30 (35.7)	11 (28.2)

Figure 2: Best overall response and objective response rate



Objective response defined as sCR+CR+VGPR+PR
CR=complete response; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

Figure 3: Duration of response



The probability of remaining event-free for patients in each subgroup is plotted over time

EFFICACY

- The best overall response and overall response rate by blinded independent central review after a median follow-up of 14.7 (range, 0.2–25.1) mo is presented in **Figure 2**
- Median duration of response was not reached in any patient subgroup. The probability of maintaining response (95% CI) at 15 mo was 74.4% (51.5–87.6%) vs 69.5% (52.7–81.3%) for patients aged <65 vs ≥65 y and 72.9% (57.6–83.4%) vs 68.5% (42.6–84.6%) for non-frail vs frail patients (**Figure 3**)

SAFETY

- Any Grade treatment-emergent adverse events (TEAEs) were reported in 100% of patients in the study
- Grade 3/4 TEAEs were reported in 74.4%, 68.8%, 73.8%, and 64.1% of patients in <65 y, ≥65 y, non-frail, and frail subgroups, respectively (**Table 3**)
- The most common TEAEs reported in at least 20% of patients in any subgroup are reported in **Table 3**
- The majority of TEAEs were ≤ Grade 2
- The most common Grade 3/4 TEAEs were hematologic
- The incidences of TEAEs of special interest (infections, CRS, and ICANS) were consistent across subgroups (**Table 4**)
- TEAEs led to death in 7 (16.3%) and 18 (22.5%) patients aged <65 vs ≥65, respectively (5 and 6, respectively, due to progressive disease)
- TEAEs led to death in 14 (16.7%) and 11 (28.2%) patients in non-frail vs frail subgroups, respectively (7 and 4, respectively, due to progressive disease)

Table 3: Common TEAEs reported by at least 20% of patients in any subgroup

	<65 y n=43		≥65 y n=80		Non-frail n=84		Frail n=39	
	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4	Any grade	Grade 3/4
Any TEAE	43 (100)	32 (74.4)	80 (100)	55 (68.8)	84 (100)	62 (73.8)	39 (100)	25 (64.1)
TEAEs in ≥20% of patients, n (%)								
Hematologic								
Neutropenia	22 (51.2)	22 (51.2)	38 (47.5)	38 (47.5)	43 (51.2)	43 (51.2)	17 (43.6)	17 (43.6)
Anemia	21 (48.8)	20 (46.5)	39 (48.8)	26 (32.5)	35 (41.7)	26 (31.0)	25 (64.1)	20 (51.3)
Thrombocytopenia	16 (37.2)	13 (30.2)	22 (27.5)	16 (20.0)	26 (31.0)	20 (23.8)	12 (30.8)	9 (23.1)
Lymphopenia	6 (14.0)	5 (11.6)	27 (33.8)	26 (32.5)	15 (17.9)	13 (15.5)	18 (46.2)	18 (46.2)
Non-hematologic								
CRS	25 (58.1)	0	46 (57.5)	0	48 (57.1)	0	23 (59.0)	0
Diarrhea	17 (39.5)	2 (4.7)	35 (43.8)	0	36 (42.9)	2 (2.4)	16 (41.0)	0
Headache	14 (32.6)	0	15 (18.8)	0	24 (28.6)	0	5 (12.8)	0
Pyrexia	13 (30.2)	2 (4.7)	24 (30.0)	3 (3.8)	30 (35.7)	3 (3.6)	7 (17.9)	2 (5.1)
Decreased appetite	13 (30.2)	0	28 (35.0)	1 (1.3)	25 (29.8)	1 (1.2)	16 (41.0)	0
Injection site reaction	14 (32.6)	0	19 (23.8)	0	24 (28.6)	0	9 (23.1)	0
Fatigue	12 (27.9)	2 (4.7)	33 (41.3)	2 (2.5)	29 (34.5)	2 (2.4)	16 (41.0)	2 (5.1)
Upper respiratory tract infection	9 (20.9)	0	11 (13.8)	0	17 (20.2)	0	3 (7.7)	0
Nausea	11 (25.6)	0	22 (27.5)	0	19 (22.6)	0	14 (35.9)	0
Cough	11 (25.6)	0	20 (25.0)	0	22 (26.2)	0	9 (23.1)	0
Back pain	11 (25.6)	3 (7.0)	7 (8.8)	0	13 (15.5)	1 (1.2)	5 (12.8)	2 (5.1)
Hypokalemia	10 (23.3)	4 (9.3)	22 (27.5)	9 (11.3)	23 (27.4)	9 (10.7)	9 (23.1)	4 (10.3)
Dry skin	9 (20.9)	0	12 (15.0)	0	14 (16.7)	0	7 (17.9)	0
Arthralgia	8 (18.6)	1 (2.3)	16 (20.0)	2 (2.5)	14 (16.7)	1 (1.2)	10 (25.6)	2 (5.1)
Asthenia	6 (14.0)	2 (4.7)	18 (22.5)	4 (5.0)	16 (19.0)	4 (4.8)	8 (20.5)	2 (5.1)
Vomiting	4 (9.3)	0	16 (20.0)	0	12 (14.3)	0	8 (20.5)	0

TEAEs according to MedDRA v25.1 and CTCAE V5 reported in ≥20% of patients in any subgroup are presented. Data are sorted by incidence of TEAEs in the <65 y subgroup
Severity of CRS was assessed according to the American Society for Transplantation and Cellular Therapy criteria 2019
CRS=cytokine release syndrome; CTCAE=Common Terminology Criteria for Adverse Events; MedDRA =Medical Dictionary for Regulatory Activities; TEAE=treatment-emergent adverse event

Table 4: TEAEs of special interest

	<65 y n=43			≥65 y n=80			Non-frail n=84			Frail n=39		
	Any grade	Grade 3/4	Grade 5	Any grade	Grade 3/4	Grade 5	Any grade	Grade 3/4	Grade 5	Any grade	Grade 3/4	Grade 5
Infections	31 (72.1)	16 (37.2)	2 (4.7)	55 (68.8)	33 (41.3)	6 (7.5)	59 (70.2)	35 (41.7)	4 (4.8)	27 (69.2)	14 (35.9)	4 (10.3)
CRS	25 (58.1)	0	0	46 (57.5)	0	0	48 (57.1)	0	0	23 (59.0)	0	0
ICANS	1 (2.3)	0	0	5 (6.3)	0	0	5 (6.0)	0	0	1 (2.6)	0	0

Severity of CRS and ICANS was assessed according to the American Society for Transplantation and Cellular Therapy criteria 2019
CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome; TEAE=treatment-emergent adverse event

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