MM-374

Efficacy and Safety of Elranatamab in Patients With Relapsed/Refractory Multiple Myeloma (RRMM) and Prior B-cell Maturation Antigen (BCMA)-Directed Therapies: A Pooled Analysis From MagnetisMM Studies

Ajay K. Nooka, MD[1], Alexander M. Lesokhin, MD[2], Mohamad Mohty, MD[3], Ruben Niesvizky, MD[4], Christopher Maisel, MD[5], Bertrand Arnulf, MD[6], Sarah M. Larson, MD[7], Asya Nina Varshavsky-Yanovsky, MD, PhD[8], Xavier Leleu, MD[9], Lionel Karlin, MD[10], David H. Vesole, MD, PhD[11], Nizar J. Bahlis, MD[12], Carlos Fernandez de Larrea, MD[13], Noopur Raje, MD[14], Eric Leip, PhD[15], Umberto Conte, PharmD[16], Mohamed Elmeliegy, PhD[17], Andrea Viqueira, MD[18], Salomon Manier, MD[19]

[1]Winship Cancer Institute, Atlanta, GA, USA; [2]Division of Hematology and Oncology, Memorial Sloan Kettering Cancer Center/Weill Cornell Medical College, New York, NY, USA; [3]Sorbonne University, Hôpital Saint-Antoine, and INSERM UMRs938, Paris, France; [4]Weill Cornell Medical College - New York Presbyterian Hospital, New York, NY, USA; [5]Baylor University Medical Center, Dallas, Tx, USA; [6]Hôpital Saint-Louis, Paris, France; [7]University of California Los Angeles Medical Center, Los Angeles, CA, USA; [8]Fox Chase Cancer Center, Philadelphia, PA, USA; [9]Centre Hospitalier Universitaire de Poitiers, Poitiers, France; [10]Centre Hospitalier Lyon, Lyon, France; [11]John Theurer Cancer Center at Hackensack University Medical Center, Hackensack, NJ, USA; [12]Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, AB, Canada; [13]Hospital Clinic de Barcelona, Barcelona, Spain; [14]Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA; [15]Pfizer Inc, Cambridge, MA, USA; [16]Pfizer Inc, New York, NY, USA; [17]Pfizer Inc, San Diego, CA, USA; [18]Pfizer SLU, Madrid, Spain; [19]Lille University Hospital, Lille, France

Objective

- To evaluate the efficacy and safety of elranatamab monotherapy in patients with RRMM and prior exposure to BCMA-directed therapy in a pooled analysis

Conclusions

- Elranatamab monotherapy is efficacious in patients with RRMM and prior exposure of BCMA-directed therapy (ADC and/or CAR-T)
  - ORR 46.0%, with early, deep, and durable responses (median DOR, 17.1 mo)
  - Among patients with prior BCMA-directed CAR-T treatment, ORR was 52.8%; median DOR was not reached
  - Among patients with prior BCMA-directed ADC treatment, ORR was 42.4%; median DOR was 13.6 mo
- With a median follow-up of 11.3 mo, median PFS was 5.5 mo and median OS was 12.1 mo
  - Among patients with prior BCMA-directed CAR-T treatment, median PFS was 10.0 mo; median OS was 12.1 mo
  - Among patients with prior BCMA-directed ADC treatment, median PFS was 3.9 mo; median OS was 12.1 mo
- Elranatamab toxicities were manageable, with no new safety signals observed vs the BCMA-naïve population[1]
- The 2-step-up priming regimen of 12/32 mg successfully mitigated the rate and severity of CRS. Prior exposure to BCMA-directed therapy does not impact the CRS profile, which is similar to that in the BCMA-naive population[1]
- These results support elranatamab monotherapy as a treatment option for patients with RRMM post BCMA-directed therapy

Background

- Elranatamab is a humanized bispecific antibody that targets both B-cell maturation antigen (BCMA)-expressing multiple myeloma (MM) cells and CD3-expressing T cells[2]
- Data from the ongoing phase 2 MagnetisMM-3 study demonstrated the efficacy and safety of elranatamab monotherapy in BCMA-naïve patients with relapsed/refractory MM (RRMM)[1]
  - At data cut-off, median follow-up was 14.7 (range, 0.2–25.1) mo
  - Objective response rate per blinded independent central review was 61.0% (95% CI 51.8–69.6)
  - Median duration of response (DOR) has not been reached (95% CI, NE–NE)
  - Median progression free-survival (PFS) has not been reached (95% CI, 9.9 mo-NE)
- Here, the efficacy and safety of elranatamab monotherapy in patients with RRMM and prior exposure to BCMA-directed therapy (chimeric antigen receptor T-cell [CAR-T] and/or antibody drug conjugate [ADC]) was evaluated in a pooled analysis of 4 MagnetisMM studies

Methods

- Eligible patients with RRMM received at least 1 proteasome inhibitor, 1 immunomodulatory drug, 1 anti-CD38 antibody, and 1 BCMA-directed therapy (ADC and/or CAR-T cells)
- Pooled analysis of 4 MagnetisMM studies (**Table 1**)
- Efficacy endpoints were assessed by investigator per IMWG criteria[3]
- Safety assessments
  - Treatment-emergent adverse events (TEAEs) were graded by Common Terminology Criteria for Adverse Events (MM-1, v4.03; MM2, MM-3, & MM-9, v5.0)
  - Cytokine release syndrome (CRS) and immune cell-associated neurotoxicity (ICANS) were graded by American Society for Transplant and Cellular Therapy criteria[4]
- Data cutoff ~12 mo after initial dose of the last enrolled patient

Table 1: MagnetisMM studies included in the analysis

	MagnetisMM-1 (NCT03269136)	MagnetisMM-2 (NCT04798586)	MagnetisMM-3 (NCT04649359)	MagnetisMM-9 (NCT05014412)
Study Phase	1	1	2	1/2
Elranatamab monotherapy	215–1000 µg/kg SC, QW or Q2W[a]	1000 µg/kg SC, QW with a step-up dose of 600 µg/kg	76 mg SC, QW with 2-step-up doses of 12 mg and 32 mg	76 mg SC, QW with 2-step-up doses of 4 mg and 20 mg
n	13[a]	1	64	9

[a] Includes patients who received elranatamab within the efficacious dose range in the MagnetisMM-1 study[2]
QW=once weekly; Q2W=once every 2 weeks; SC=subcutaneous

Results

PATIENTS AND TREATMENT

- Patient demographics and characteristics are shown in **Table 2**
  - In the prior ADC vs CAR-T subgroups, a higher proportion of patients were aged ≥75 y (20.3% vs 2.8%), had a disease stage of III (27.1% vs 13.9%), and were refractory to prior BCMA-directed therapy (81.4% vs 36.1%). Patients with prior BCMA-directed ADC therapy had a higher number of prior lines of therapy (8.0 vs 7.0)
- Median duration of treatment was 3.5 (range, 0.03–30.9) mo
  - 39.1% of patients had been treated for >6 mo
- At the data cut-off, 23.0% of patients were still receiving elranatamab
- Most common primary reasons for permanent treatment discontinuation were progressive disease (46.0%) and adverse events (11.5%)

EFFICACY

- After a median follow-up of 11.3 (range, 0.3–32.3) mo, ORR was 46.0% (95% CI, 35.2–57.0) (**Figure 1A**)
  - Prior CAR-T treatment: 52.8%
  - Prior ADC treatment: 42.4%
- Among patients who achieved an objective response (n=40), median time to response was 1.7 (range, 0.3–9.3) mo
- Median DOR was 17.1 (95% CI, 9.8–NE) mo, although not yet mature after censoring data for 23 (57.5%) patients (**Figure 1B**)
- Median PFS and median overall survival were 5.5 (95% CI, 2.2–10.0) mo and 12.1 (7.5–NE) mo, respectively (**Figure 2**)

SAFETY

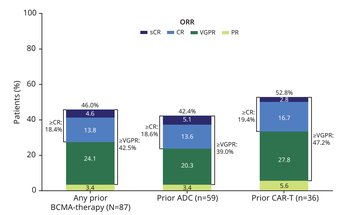
- TEAEs were reported in all 87 patients treated with elranatamab, with grade 3/4 events reported in 65.5% of patients
  - Most commonly reported TEAEs are shown in **Table 3**
- CRS and ICANS, respectively, were reported in 65.5% (grade 3/4, 2.3%) and 5.7% (grade 3/4, 2.3%) of patients (**Table 4**)
  - Among patients who received the 2-step-up priming regimen of 12/32 mg (n=64), CRS was reported in 60.9% (grade 3/4, 1.6%) patients
  - Permanent treatment discontinuation due to CRS and ICANS was reported in 1 (1.1%) and 2 (2.3%) patients, respectively
- The 2-step-up priming regimen of 12/32 mg with premedication successfully mitigated the rate and severity of CRS (**Figure S1**)[1]
  - The CRS profile was predictable with the majority of events occurring with the first 2 doses (82.2%) and first 3 doses (95.6%)
- Infections were reported in 73.6% (grade 3/4, 26.4%; grade 5, 9.2%) of patients (**Table 5**)
  - Most frequently reported were COVID-19–related TEAEs (25.3%)
- Infections led to permanent discontinuation of elranatamab in 6.9% of patients
  - Infection TEAEs leading to discontinuation were COVID-19 (4.6%) and sepsis (2.3%)
- TEAEs led to death in 23 patients:
  - 11 due to progressive disease
  - 8 due to infections: COVID-19 (n=3), COVID-19 pneumonia (n=2), septic shock (n=2), and sepsis (n=1)
  - 2 were considered treatment-related by investigator: cardiac arrest (n=1) and septic shock (n=1)

Table 2: Demographics and baseline characteristics

	Any prior BCMA therapy (n=87)	Any prior ADC (n=59)	Any prior CAR-T (n=36)
Age			
Median (range), y	66.0 (40–84)	66.0 (41–84)	62.5 (40–79)
≥75 y, n (%)	13 (14.9)	12 (20.3)	1 (2.8)
Male, n (%)	41 (47.1)	23 (39.0)	20 (55.6)
Race, n (%)			
White	56 (64.4)	34 (57.6)	26 (72.2)
Black or African American	7 (8.0)	5 (8.5)	4 (11.1)
Asian	5 (5.7)	4 (6.8)	2 (5.6)
Not reported[a]	19 (21.8)	16 (27.1)	4 (11.1)
ECOG performance status, n (%)			
0	26 (29.9)	15 (25.4)	14 (38.9)
1	57 (65.5)	40 (67.8)	22 (61.1)
2	4 (4.6)	4 (6.8)	0
R-ISS disease stage, n (%)			
I	18 (20.7)	11 (18.6)	9 (25.0)
II	44 (50.6)	30 (50.8)	19 (52.8)
III	20 (23.0)	16 (27.1)	5 (13.9)
Unknown/missing	5 (5.7)	2 (3.9)	3 (8.3)
Cytogenetic risk, n (%)			
Standard	57 (65.5)	39 (66.1)	23 (63.9)
High[b]	21 (24.1)	13 (22.0)	11 (30.6)
Missing	9 (10.3)	7 (11.9)	2 (5.6)
Extramedullary disease, n (%)[c]			
Yes	47 (54.0)	33 (55.9)	17 (47.2)
No	37 (42.5)	25 (42.4)	16 (44.4)
Missing	3 (3.4)	1 (1.7)	3 (8.3)
Bone marrow plasma cells, n (%)			
<50%	61 (70.1)	42 (71.2)	24 (66.7)
≥50%	16 (18.4)	10 (16.9)	7 (19.4)
Missing	10 (11.5)	7 (11.9)	5 (13.9)
Prior lines of therapy, median (range)	7.0 (3–19)	8.0 (3–19)	7.0 (3–14)
Prior stem cell transplant, n (%)	71 (81.6)	51 (86.4)	28 (77.8)
Prior BCMA-targeted therapy, n (%)			
ADC	59 (67.8)	59 (100)	8 (22.2)
CAR-T	36 (41.4)	8 (13.6)	36 (100)
ADC and CAR-T	8 (9.2)	8 (13.6)	8 (22.2)
Exposure status, n (%)			
Triple-class[d]	87 (100)	59 (100)	36 (100)
Penta-drug[e]	74 (85.1)	49 (83.1)	33 (91.7)
Refractory status, n (%)			
Triple-class[d]	84 (96.6)	57 (96.6)	35 (97.2)
Penta-drug[e]	48 (55.2)	32 (54.2)	23 (63.9)
Refractory to prior BCMA therapy, n (%)	54 (62.1)	48 (81.4)	13 (36.1)
ADC	47 (54.0)	47 (79.7)	6 (16.7)
CAR-T	10 (11.5)	4 (6.8)	10 (27.8)
Refractory to last line of therapy, n (%)	74 (85.1)	54 (91.5)	28 (77.8)

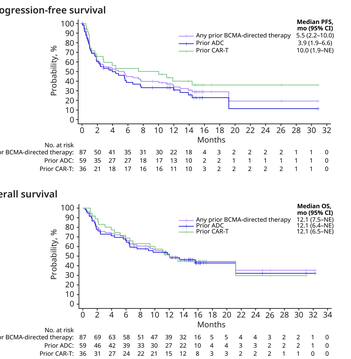
[a] Includes patients recruited in countries where the collection of race is prohibited. [b] Includes t(4;14), t(14;16), del(17p) chromosomal abnormalities; [c] Extramedullary disease was defined as presence of any plasmacytoma recorded as 'extramedullary' or 'other' including 'mass' or 'plasmacytoma' specified on the case report form in MM-1, and any plasmacytoma (extramedullary and/or paramedullary) with a soft-tissue component in MM-2, MM-3, and MM-9; [d] Triple-class refers to at least 1 proteasome inhibitor, 1 immunomodulatory drug, and 1 anti-CD38 antibody; [e] Penta-drug refers to at least 2 proteasome inhibitors, 2 immunomodulatory drugs, and 1 anti-CD38 antibody
ADC=antibody drug conjugate; CAR-T=chimeric antigen receptor-T cell; ECOG=Eastern Cooperative Oncology Group; R-ISS=Revised Multiple Myeloma International Staging System

Figure 1: Best overall response (A) and duration of response (B)



ADC=antibody drug conjugate; CAR-T=chimeric antigen receptor T-cell; CR=complete response; DOR=duration of response; ORR=objective response rate; PR=partial response; sCR=stringent complete response; VGPR=very good partial response

Figure 2: Progression-free and overall survival in patients with RRMM receiving elranatamab



ADC=antibody drug conjugate; CAR-T=chimeric antigen receptor T-cell; NE=not evaluable

Table 3: Most common TEAEs (any grade ≥20%)

Patients, n (%)	Any prior BCMA therapy (N=87)	
	Any grade	Grade 3/4
Hematologic		
Anemia	51 (58.6)	40 (46.0)
Neutropenia	39 (44.8)	36 (41.4)
Thrombocytopenia	35 (40.2)	25 (28.7)
Lymphopenia	28 (32.2)	26 (29.9)
Leukopenia	19 (21.8)	11 (12.6)
Non-hematologic		
CRS	57 (65.5)	2 (2.3)
Diarrhea	31 (35.6)	0
COVID-19–related[a]	22 (25.3)	8 (9.2)
Decreased appetite	20 (23.0)	1 (1.1)
Cough	19 (21.8)	1 (1.1)
Injection site reaction	18 (20.7)	0
Pyrexia	18 (20.7)	1 (1.1)

[a] Includes preferred terms in COVID-19 (narrow) standardized MedDRA queries
MedDRA=Medical Dictionary for Regulatory Activities; TEAE=treatment-emergent adverse event

Table 4: AEs of special interest: CRS and ICANS

TEAE of special interest	Any prior BCMA therapy (N=87)[a]	
	CRS	ICANS
Patients with TEAE, n (%)	57 (65.5)	5 (5.7)
Maximum grade 1	42 (48.3)	0
Maximum grade 2	13 (14.9)	3 (3.4)
Maximum grade 3	2 (2.3)	2 (2.3)
Maximum grade ≥4	0	0
Patients with >1 TEAE, n (%)	8 (9.2)	1 (1.1)
Median time to onset of TEAE, d (range)	2.0 (1.0–4.0)	2.0 (1.0–3.0)
Median time to resolution of TEAE, d (range)	2.0 (1.0–10.0)	2.0 (1.0–18.0)
Patients who received tocilizumab[b] or steroids for TEAE, n (%)		
Tocilizumab	19 (21.8)	2 (2.3)
Steroids	10 (11.5)	3 (3.4)
Permanent discontinuation due to AE, n (%)	1 (1.1)[c]	2 (2.3)[c]

[a] Includes patients enrolled in MagnetisMM studies with different priming regimens (**Table 1**). [b] Includes tocilizumab and siltuximab; [c] 1 patient discontinued due to concurrent Grade 2 CRS and Grade 3 ICANS
AE=adverse event; CRS=cytokine release syndrome; ICANS=immune effector cell-associated neurotoxicity syndrome; TEAE=treatment-emergent adverse event

Table 5: AEs of special interest: Infection

n (%)	Any prior BCMA therapy (N=87)		
	Any grade	Grade 3/4	Grade 5
Infection TEAEs in ≥5% of patients			
COVID-19–related[a]	22 (25.3)	8 (9.2)	5 (5.7)
Pneumonia	15 (17.2)	5 (5.7)	0
Upper respiratory tract infection	12 (13.8)	0	0
Sinusitis	9 (10.3)	1 (1.1)	0
Urinary tract infection	8 (9.2)	1 (1.1)	0
Rhinovirus infection	7 (8.0)	1 (1.1)	0
Bronchitis	6 (6.9)	2 (2.3)	0
Key infection TEAEs in <5% of patients[b]			
CMV infection reactivation	3 (3.4)	1 (1.1)	0
Pneumocystis jirovecii pneumonia	2 (2.3)	1 (1.1)	0
CMV infection	1 (1.1)	1 (1.1)	0

[a] Includes preferred terms in COVID-19 (narrow) standardized MedDRA queries; [b] Key infection TEAEs includes preferred terms: CMV infection reactivation, Pneumocystis jirovecii pneumonia, CMV infection, adenoviral hepatitis, adenovirus infection, hepatitis B reactivation, pneumonia adenoviral, pneumonia CMV, pneumonia pseudomonal
AE=adverse event; CMV=cytomegalovirus; TEAE=treatment-emergent adverse event

References: 1. Lesokhin AM, et al. Nat Med 2023. Published online 15 August 2023. https://doi.org/10.1038/s41591-023-02528-9 **2.** Shah N, et al. Leukemia 2020;34:985-1005. **3.** Kumar S, et al. Lancet Oncol 2016;17:e328-e46. **4.** Lee DW, et al. Biol Blood Marrow Transplant 2019;25:625-38. **5.** Raje N, et al. Blood 2022;140:388-90.

Disclosures: **AKN:** honoraria: Amgen, Adaptive, BeyondSpring BMS, GSK, Janssen, Karyopharma, Oncopeptides, Sanofi, SecureBio, Takeda; consulting and advisory: Adaptive, Amgen, BeyondSpring BMS, GSK, Janssen, Karyopharma, Oncopeptides, Sanofi, SecureBio, Takeda; research funding: Amgen, Janssen Oncology, Takeda.

Acknowledgments: We thank the MagnetisMM trial patients and their families, as well as the study investigators, nurses, and site staff. This study was sponsored by Pfizer. Medical writing support was provided by Gemma Shay-Lowell, PhD, CMPP, of Engage Scientific Solutions and was funded by Pfizer.

Contact: Ajay K. Nooka, anooka@emory.edu

Copyright © 2023

Presented at the Society of Hematologic Oncology (SOHO)
September 6–9, 2023, Houston, Texas