An Indirect Comparison of Elranatamab's Progression-Free Survival and Overall Survival From MagnetisMM-3 vs Country-Specific Treatment Regimens From Real-World Data Sources

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Objectives

To contextualize the efficacy from the ongoing, single-arm, phase 2 MagnetisMM-3 trial with country-specific external control arms generated using RW data sources

Conclusions

Among BCMA–naive patients who have characteristics similar to those enrolled in the MagnetisMM-3 trial, those treated with elranatamab demonstrated significantly longer PFS and OS compared with those treated with currently available regimens for patients with triple-class exposed multiple myeloma in Finland, France, Italy, the Netherlands, and Sweden

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Background

- Elranatamab is a B-cell maturation (BCMA) × CD3 bispecific antibody approved for the treatment of relapsed/refractory multiple myeloma (RRMM), based on results of the registrational phase 2 MagnetisMM-3 study (NCT04649359)[1,2]
  - In MagnetisMM-3, elranatamab monotherapy induced deep and durable responses in patients with RRMM who had not received prior BCMA-directed therapy (ie, BCMA naive; Cohort A; N=123)[3]
- However, due to the lack of a control arm, it is difficult to contextualize the efficacy of elranatamab with that of other therapies routinely used in clinical practice across Europe

Methods

- This retrospective cohort study indirectly compared the efficacy observed in BCMA-naive patients treated with elranatamab in MagnetisMM-3 (Cohort A; N=123) from the March 2023 data cut (≈15 months of follow-up) with that of the COTA and Flatiron Health (FH) electronic health record databases as real-world (RW) external controls (from November 2015 to August 2021 [FH]/June 2022 [COTA]; median follow-up was 8 and 9 months, respectively)
- MagnetisMM-3 eligibility criteria were applied to the COTA and FH databases to obtain comparable populations (**Table 1**), as previously described[4]
- 5 country-specific (Finland, France, Italy, the Netherlands, and Sweden) external control arms were developed from 2 RW data sources, based on the regimens used in clinical practice in the respective countries
- Progression-free survival (PFS), and overall survival (OS) were compared using unweighted and inverse probability of treatment (IPT)–weighted Cox proportional hazard models
- Analyses were adjusted to account for imbalances across cohorts on the following confounding variables
  - Age, comorbidities, Eastern Cooperative Oncology Group performance status, International Staging System, prior lines/refractoriness, cytogenetic risk, extramedullary disease (COTA only), and laboratory values

Table 1. MagnetisMM-3 eligibility criteria applied to each RW database

Inclusion criteria	Exclusion criteria
• Prior MM diagnosis, ECOG PS ≤2, refractoriness to ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody, measurable disease, age ≥18 years, no other malignancy	• Plasma cell leukemia, smoldering MM, amyloidosis, prior SCT, active GVHD, active infection, prior investigational therapy ≤30 days before, or in index LOT

ECOG PS=Eastern Cooperative Oncology Group performance status; GVHD=graft vs host disease; IMiD=immunomodulatory drug; LOT=line of therapy; MM=multiple myeloma; PI=proteasome inhibitor; RW=real world; SCT=stem cell transplant

Results

PATIENTS AND TREATMENT

- 123 patients from MagnetisMM-3 Cohort A were compared with RW country-specific groups from the COTA and FH databases (**Table 2**)
- After weighting, the standardized mean differences between baseline demographics and disease characteristics in MagnetisMM-3 and the country-specific subgroups were mostly <0.2

Table 2. Baseline demographics and disease characteristics

	MagnetisMM-3	Finland		France		Italy		The Netherlands		Sweden	
	Cohort A N=123	COTA n=190	FH n=143	COTA n=84	FH n=63	COTA n=192	FH n=124	COTA n=221	FH n=147	COTA n=32	FH n=38
Age, mean (SD), years	67.1 (9.4)	68.0 (9.5)	69.9 (10.1)	69.1 (9.0)	70.0 (9.6)	68.5 (9.4)	70.0 (10.2)	68.0 (9.4)	69.6 (10.1)	69.9 (8.8)	70.2 (9.8)
Female, n (%)	55 (44.7)	83 (43.7)	66 (46.2)	38 (45.2)	30 (47.6)	91 (47.4)	55 (44.4)	102 (46.2)	69 (46.9)	16 (50.0)	19 (50.0)
BMI, mean (SD), kg/m²	26.6 (5.4)	28.8 (6.2)	27.3 (5.6)	29.2 (6.3)	27.1 (5.5)	29.3 (6.4)	27.5 (5.6)	29.1 (6.2)	27.3 (5.6)	30.7 (5.6)	27.2 (5.4)
Race, n (%)											
White	72 (58.5)	142 (74.7)	95 (66.4)	53 (63.1)	50 (79.4)	140 (72.9)	82 (66.1)	164 (74.2)	98 (66.7)	22 (68.8)	29 (76.3)
Non-White	51 (41.5)	48 (25.3)	48 (33.6)	31 (36.9)	13 (20.6)	52 (27.1)	42 (33.9)	57 (25.8)	49 (33.3)	10 (31.3)	9 (23.7)
ISS disease stage, n (%)[a]											
I	35 (28.5)	24 (12.6)	10 (7.0)	12 (14.3)	4 (6.3)	22 (11.5)	9 (7.3)	30 (13.6)	10 (6.8)	4 (12.5)	2 (5.3)
II	45 (36.6)	21 (11.1)	17 (11.9)	7 (8.3)	5 (7.9)	20 (10.4)	14 (11.3)	24 (10.9)	17 (11.6)	3 (9.4)	3 (7.9)
III	25 (20.3)	17 (8.9)	18 (12.6)	5 (6.0)	9 (14.3)	18 (9.4)	18 (14.5)	20 (9.0)	18 (12.2)	1 (3.1)	5 (13.2)
Unknown/missing	18 (14.6)	128 (67.4)	98 (68.5)	60 (71.4)	45 (71.4)	132 (68.8)	83 (66.9)	147 (66.5)	102 (69.4)	24 (75.0)	28 (73.7)
ECOG PS, n (%)[a]											
0/1	116 (94.3)	165 (86.8)	119 (83.2)	77 (91.7)	50 (79.4)	165 (85.9)	103 (83.1)	188 (85.1)	123 (83.7)	27 (84.4)	31 (81.6)
2	7 (5.7)	25 (13.2)	24 (16.8)	7 (8.3)	13 (20.6)	27 (14.1)	21 (16.9)	33 (14.9)	24 (16.3)	5 (15.6)	7 (18.4)
CCI score, n (%)[b]											
2	83 (67.5)	160 (84.2)	114 (79.7)	66 (78.6)	49 (77.8)	157 (81.8)	98 (79.0)	184 (83.3)	117 (79.6)	27 (84.4)	29 (76.3)
3	21 (17.1)	17 (8.9)	13 (9.1)	11 (13.1)	4 (6.3)	21 (10.9)	11 (8.9)	21 (9.5)	14 (9.5)	4 (12.5)	3 (7.9)
4	11 (8.9)	9 (4.7)	10 (7.0)	4 (4.8)	5 (7.9)	9 (4.7)	9 (7.3)	10 (4.5)	10 (6.8)	1 (3.1)	4 (10.5)
5	6 (4.9)	2 (1.1)	3 (2.1)	1 (1.2)	2 (3.2)	3 (1.6)	3 (2.4)	4 (1.8)	3 (2.0)	NA	1 (2.6)
6	2 (1.6)	2 (1.1)	3 (2.1)	2 (2.4)	3 (4.8)	2 (1.0)	3 (2.4)	2 (0.9)	3 (2.0)	NA	NA
Time from initial MM diagnosis, mean (SD), years	6.6 (3.8)	5.1 (3.9)	4.0 (2.3)	5.5 (4.1)	3.8 (2.2)	5.2 (4.0)	4.0 (2.3)	5.4 (4.4)	4.0 (2.3)	5.4 (4.4)	3.5 (1.9)
Penta-drug refractory disease, n (%)[c]	52 (42.3)	33 (17.4)	19 (13.3)	17 (20.2)	4 (6.3)	35 (18.2)	17 (13.7)	43 (19.5)	20 (13.6)	4 (12.5)	1 (2.6)
High-risk cytogenetics, n (%)[d]	31 (25.2)	37 (19.5)	34 (23.8)	23 (27.4)	17 (27.0)	40 (20.8)	31 (25.0)	42 (19.0)	36 (24.5)	3 (9.4)	9 (23.7)
Extramedullary disease, n (%)	38 (30.9)	25 (13.2)	NR	6 (7.1)	NR	25 (13.0)	NR	29 (13.1)	NR	3 (9.4)	NR
No. of prior LOTs, mean (SD)[e]	5.2 (2.6)	4.6 (2.3)	4.0 (1.7)	4.8 (2.5)	3.8 (1.5)	4.7 (2.3)	4.1 (1.7)	5.0 (2.5)	4.0 (1.7)	4.2 (2.2)	3.7 (1.5)
SCT, n (%)[f]	87 (70.7)	106 (55.8)	51 (35.7)	52 (61.9)	20 (31.7)	109 (56.8)	45 (36.3)	127 (57.5)	53 (36.1)	19 (59.4)	13 (34.2)

[a] Within 90 days prior to or on the index date; [b] During the year before or on the index date; [c] At the time of TCR eligibility. Refers to disease refractory to at least 2 proteasome inhibitors, 2 immunomodulatory drugs, and 1 anti-CD38 antibody; [d] Includes t(4;14), t(14;16) or del(17p) chromosomal abnormalities; [e] Prior to the index date; [f] During the baseline period.
BMI=body mass index; CCI=Charlson Comorbidity Index; ECOG PS=Eastern Cooperative Oncology Group performance status; FH=Flatiron Health; ISS=International Staging System; LOT=line of therapy; MM=multiple myeloma; NA=not applicable; NR=not reported; SCT=stem cell transplant

EFFICACY

- The median PFS and OS of patients with RRMM treated with elranatamab could not be determined because more than half of the patients did not have disease progression and were still alive at the time of data collection (**Table 3**)
  - At the time of this analysis, patients had been treated with elranatamab for a median of 5.6 months
- However, the median PFS of patients treated with country-specific regimens in COTA and FH ranged from 2.6 to 7.2 months
- The median OS of patients treated with country-specific regiments in COTA and FH ranged from 6.3 to 15.1 months
  - IPT-weighted analysis of PFS and OS for Sweden-specific regimens could not be performed due to limited sample sizes

Table 3. Median PFS and OS of elranatamab vs RW country-specific treatments in unweighted and IPT-weighted analyses

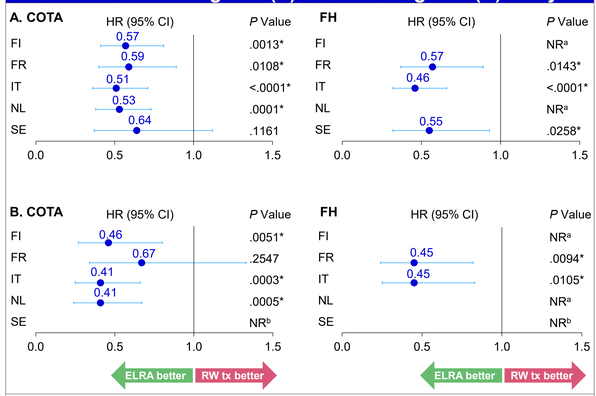
	MagnetisMM-3	Finland		France		Italy		The Netherlands		Sweden	
	Cohort A N=123	COTA n=190	FH n=143	COTA n=84	FH n=63	COTA n=192	FH n=124	COTA n=221	FH n=147	COTA n=32	FH n=38
Median PFS (95% CI), months											
Unweighted	NE[a]	5.4 (3.3-7.1)	4.4 (3.2-7.2)	5.7 (3.5-11.1)	5.9 (3.1-8.8)	4.8 (3.1-6.3)	3.7 (2.7-7.0)	4.8 (3.1-6.0)	5.1 (3.2-7.2)	4.7 (2.9-14.1)	7.2 (2.0-11.1)
IPT weighted	NE[a]	5.7 (3.5-8.5)	3.7 (2.5-7.2)	7.2 (0.1-NR)	2.6 (0.03-7.1)	5.6 (3.3-7.2)	2.7 (1.9-5.1)	5.3 (3.3-6.3)	3.7 (2.1-7.2)	NR[b]	NR[b]
Median OS (95% CI), months											
Unweighted	NE[a]	12.7 (9.8-16.3)	11.4 (7.8-13.3)	15.1 (9.8-17.5)	9.0 (5.9-11.8)	11.2 (9.0-15.0)	9.4 (6.9-11.8)	11.2 (9.4-15.0)	11.2 (7.8-13.2)	15.1 (8.3-19.2)	9.5 (3.2-14.2)
IPT weighted	NE[a]	13.4 (9.2-15.5)	11.6 (6.5-18.7)	15.1 (5.8-17.5)	6.3 (0.1-11.2)	11.6 (8.3-15.1)	11.2 (5.2-15.2)	11.2 (8.5-14.8)	11.8 (7.6-18.7)	NR[b]	NR[b]

[a] More than half of the patients in MagnetisMM-3 Cohort A did not have disease progression and were still alive at the time of data collection; thus, median PFS and OS could not be determined; [b] Analysis could not be performed due to the limited sample size of the RW data
FH=Flatiron Health; IPT=inverse probability of treatment; NE=not evaluable; NR=not reported; OS=overall survival; PFS=progression-free survival; RW=real world

EFFICACY

- Elranatamab was associated with significantly longer PFS (P<.05) vs RW country-specific treatment regimens in both COTA and FH databases (**Figure 1**), except when compared with the Netherlands– and France-specific treatment regimens in COTA via unweighted and IPT-weighted analyses, respectively

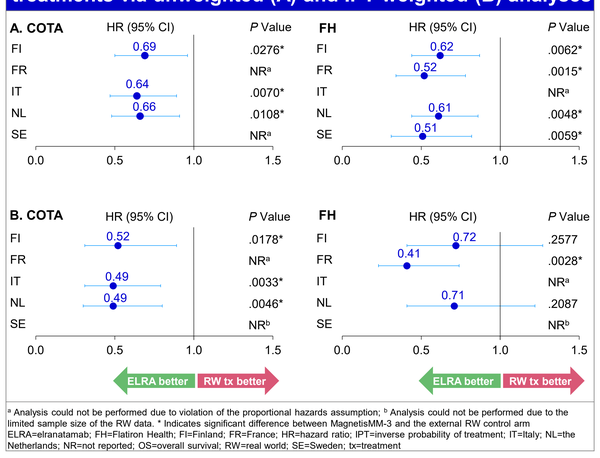
Figure 1. PFS of elranatamab vs RW country-specific treatments via unweighted (A) and IPT-weighted (B) analyses



[a] Analysis could not be performed due to violation of the proportional hazards assumption; [b] Analysis could not be performed due to the limited sample size of the RW data. * Indicates significant difference between MagnetisMM-3 and the external RW control arm
ELRA=elranatamab; FH=Flatiron Health; FI=Finland; FR=France; HR=hazard ratio; IPT=inverse probability of treatment; IT=Italy; NL=the Netherlands; NR=not reported; PFS=progression-free survival; RW=real world; SE=Sweden; tx=treatment

- Elranatamab was associated with significantly longer OS (P<.05) vs RW country-specific treatment regimens in both COTA and FH databases (**Figure 2**), except when compared with the Netherlands– and Finland-specific treatment regimens in FH via IPT-weighted analyses

Figure 2. OS of elranatamab vs RW country-specific treatments via unweighted (A) and IPT-weighted (B) analyses



[a] Analysis could not be performed due to violation of the proportional hazards assumption; [b] Analysis could not be performed due to the limited sample size of the RW data. * Indicates significant difference between MagnetisMM-3 and the external RW control arm
ELRA=elranatamab; FH=Flatiron Health; FI=Finland; FR=France; HR=hazard ratio; IPT=inverse probability of treatment; IT=Italy; NL=the Netherlands; NR=not reported; OS=overall survival; RW=real world; SE=Sweden; tx=treatment