2401

An Indirect Comparison of Elranatamab's Progression-Free Survival, Duration of Response, and Overall Survival From MagnetisMM-3 vs Real-World External Control Arms in Triple-Class Refractory Multiple Myeloma

Luciano J. Costa,[1] Thomas W. LeBlanc,[2] Hans Tesch,[3] Pieter Sonneveld,[4] Sarasa M.A. Johnson,[5] Francis Vekeman,[5] Patrick Hlavacek,[6] Aster Meche,[6] Paul Cislo,[7] David Hughes,[8] Guido Nador,[9] Marco DiBonaventura[6]

[1]University of Alabama at Birmingham, Birmingham, AL, USA; [2]Duke University School of Medicine, Durham, NC, USA; [3]Bethanien Hospital, Frankfurt, Germany; [4]Department of Hematology, Erasmus MC Cancer Institute, Rotterdam, the Netherlands; [5]Statlog, Montreal, QC, Canada; [6]Pfizer Inc, New York, NY, USA; [7]Pfizer Inc, Groton, CT, USA; [8]Pfizer Inc, Cambridge, MA, USA; [9]Pfizer Ltd, Surrey, UK

Objective

To contextualize the efficacy from the 28.4-month follow-up of the single-arm, phase 2 MagnetisMM-3 trial with that of an external RW control arm generated using the COTA database

Conclusions

Among BCMA-naive patients with RRMM who have similar demographics and disease characteristics, those treated with elranatamab in the MagnetisMM3 trial exhibited significantly longer PFS, DOR, and OS compared with those who were treated with regimens currently used in RW clinical practice

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References: **1**. Elrexfio (elranatamab-bcmm). Prescribing information. Pfizer; 2023. **2.** Elrexfio (elranatamab-bcmm). Summary of product characteristics. Pfizer; 2024. **3.** Costa LJ, et al. Future Oncol 2024;20:1175-1189. **4**. Mol I, et al. Curr Med Res Opin 2024;40:199-207. **5**. Mol I, et al. Leuk Lymphoma 2024;65:660-668.

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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) in the United States, Europe, and several additional countries, based on results of the registrational phase 2 MagnetisMM-3 study (NCT04649359)[1,2]
- The efficacy of elranatamab monotherapy in the MagnetisMM-3 trial was previously contextualized with real-world (RW) data in prior publications[3-5]
  - However, these studies relied upon ≈15 months of follow-up data from MagnetisMM-3, and the core endpoints of duration of response (DOR) and overall survival (OS) were not yet mature[3-5]
- Here, we provide the results of an updated RW comparison using extended follow-up clinical data of >2 years from MagnetisMM-3

Methods

- This retrospective cohort study indirectly compared the efficacy of elranatamab observed in MagnetisMM-3 Cohort A (BCMA naive; N=123) from the March 26, 2024 data cut (representing approximately 28 months of follow-up) with physicians' choice of treatment in COTA, a US-based oncology electronic health record database, as an external control
- MagnetisMM-3 eligibility criteria were applied to the COTA database to obtain a comparable population (**Table 1**), as previously described[3]
- Progression-free survival (PFS), DOR, and OS were compared using unweighted and inverse probability of treatment (IPT)–weighted Cox proportional hazard models. The latter was used to account for imbalances across cohorts on the following confounding variables:
  - Age, sex, race, comorbidities, Eastern Cooperative Oncology Group performance status, International Staging System, number of prior lines of therapy, penta-drug refractory status, cytogenetic risk, extramedullary disease, laboratory values, time since MM diagnosis, presence of bone lesions, and stem cell transplant
- Analyses incorporated multiple imputation (ie, multiple imputation through chained equations [MICE]) to address missing data

Table 1. MagnetisMM-3 eligibility criteria applied to the COTA database

Inclusion criteria	Exclusion criteria
• Aged ≥18 years	• Plasma cell leukemia, smoldering MM, or amyloidosis
• Prior MM diagnosis with measurable disease	• Prior SCT ≤12 weeks prior to index
• ECOG PS ≤2	• Active infection
• Refractoriness to ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38 antibody	• Prior investigational therapy during or ≤30 days prior to index LOT
	• Prior malignancy ≤3 years before index (except skin cancer)
	• Peripheral sensory or motor neuropathy

ECOG PS=Eastern Cooperative Oncology Group performance status; IMiD=immunomodulatory drug; LOT=line of therapy; MM=multiple myeloma; PI=proteasome inhibitor; SCT=stem cell transplant

Results

PATIENTS AND TREATMENT

- 123 BCMA-naive patients from MagnetisMM-3 were compared with 577 patients treated with RW physicians' choice of therapy from the COTA database (**Table 2**)
  - The most common regimens were daratumumab + pomalidomide + dexamethasone (7.3%), elotuzumab + pomalidomide + dexamethasone (5.4%), carfilzomib + dexamethasone + cyclophosphamide (4.9%), carfilzomib + dexamethasone (4.9%), and carfilzomib + pomalidomide + dexamethasone (4.9%)

Table 2. Baseline demographics and disease characteristics

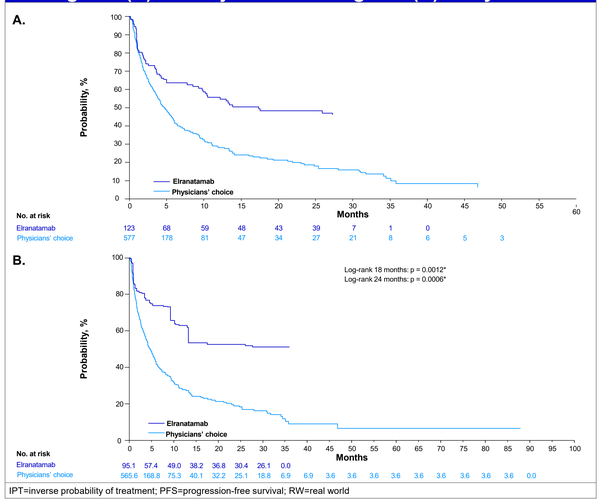
	MagnetisMM-3 (N=123)	COTA (N=577)	*P* value	Unweighted SMD[a]	IPT-weightedSMD[a]
Age at index, mean (SD), years	67.1 (9.4)	67.2 (10.0)	.907	0.011	0.218
Female, n (%)	55 (44.7)	266 (46.1)	.780	0.028	0.041
White, n (%)	72 (58.5)	415 (71.9)	.003	0.284	0.047
ISS disease stage, n (%)					
I	36 (29.3)	58 (10.1)	.000	1.350	0.115
II	46 (37.4)	70 (12.1)			
III	24 (19.5)	51 (8.8)			
Unknown/missing	17 (13.8)	398 (69.0)			
ECOG PS, n (%)					
0	45 (36.6)	181 (31.4)	.095	0.290	0.128
1	71 (57.7)	326 (56.5)			
2	7 (5.7)	70 (12.1)			
CCI score, n (%)					
2	83 (67.5)	432 (74.9)	.328	0.221	0.289
3	21 (17.1)	83 (14.4)			
4	11 (8.9)	44 (7.6)			
5	6 (4.9)	13 (2.3)			
≥6	2 (1.6)	5 (0.9)			
Time from initial MM diagnosis, mean (SD), years	6.6 (3.8)	5.6 (4.0)	.013	0.247	0.100
No. of prior LOTs, mean (SD)	5.2 (2.6)	4.8 (2.3)	.090	0.175	0.049
Penta-drug refractory disease, n (%)[b]	51 (41.5)	99 (17.2)	.000	0.554	0.247
High-risk cytogenetics, n (%)[c]	31 (25.2)	165 (28.6)	.447	0.077	0.224
Bone lesions, n (%)[d]	35 (28.5)	267 (46.3)	.000	0.375	0.077
Extramedullary disease, n (%)	38 (30.9)	97 (16.8)	.000	0.335	0.391
SCT, n (%)[d]	87 (70.7)	369 (64.0)	.152	0.145	0.021
AST, mean (SD), µkat/L	0.4 (0.2)	0.4 (0.3)	.380	0.085	0.075
ALT, mean (SD), µkat/L	0.3 (0.2)	0.4 (0.4)	.008	0.228	0.058
Hemoglobin, mean (SD), g/L	110.3 (18.6)	106.5 (20.3)	.047	0.199	0.040
Creatinine clearance, mean (SD), mL/min	75.3 (29.9)	68.7 (32.0)	.042	0.222	0.043
Calcium in serum or plasma, mean (SD), mmol/L	2.3 (0.2)	2.3 (0.2)	.007	0.222	0.148
Bilirubin, mean (SD), mmol/L	9.5 (5.0)	9.0 (10.7)	.451	0.053	0.135
Serum albumin, mean (SD), g/L	3.8 (0.6)	3.4 (0.6)	.000	0.597	0.211

[a] SMDs were calculated after MICE; [b] Refers to disease refractory to ≥2 proteasome inhibitors, 2 immunomodulatory drugs, and 1 anti-CD38 antibody; [c] Includes t(4;14), t(14;16), or del(17p) chromosomal abnormalities; [d] During the baseline period or on the index date.
ALT=alanine aminotransferase; AST=aspartate aminotransferase; CCI=Charlson Comorbidity Index; ECOG PS=Eastern Cooperative Oncology Group performance status; IPT=inverse probability of treatment; ISS=International Staging System; LOT=line of therapy; MICE=multiple imputation by chained equations; MM=multiple myeloma; SCT=stem cell transplant; SMD=standardized mean difference

EFFICACY

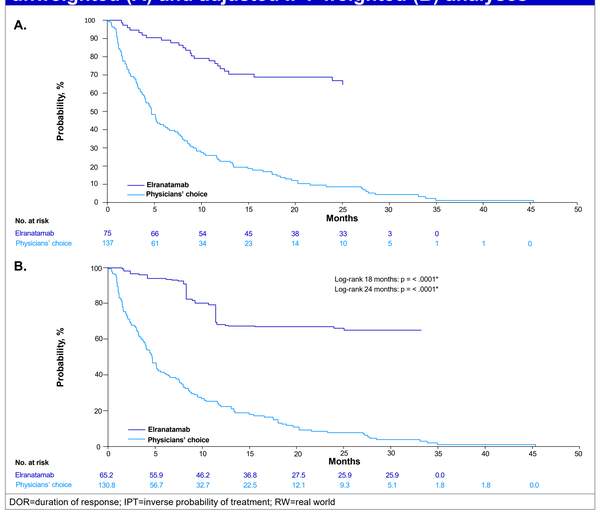
- PFS was significantly longer with elranatamab vs physicians' choice of treatment in the COTA database in both unweighted and adjusted IPT-weighted analyses (**Figure 1**), although this result may be limited by the length of follow-up
  - Unweighted median PFS: 17.2 vs 4.7 months; hazard ratio (HR), 0.5; *P*<.0001
  - Adjusted IPT-weighted median PFS: not reached (NR) vs 4.7 months; HR, 0.4; *P*=.0004
- DOR was also significantly longer with elranatamab vs physicians' choice of treatment in the COTA database in both unweighted and adjusted IPT-weighted analyses (**Figure 2**)
  - Unweighted median DOR: NR vs 4.7 months; HR, 0.2; *P*<.0001
  - Adjusted IPT-weighted median DOR: NR vs 4.7 months; HR, 0.2; *P*<.0001
- In addition, OS was significantly longer with elranatamab vs physicians' choice of treatment in the COTA database in both unweighted and adjusted, IPT-weighted analyses (**Figure 3**)
  - Unweighted median OS: 24.6 vs 12.8 months; HR, 0.6; *P*=.0008
  - Adjusted IPT-weighted median OS: 33.7 vs 12.8 months; HR, 0.6; *P*=.0355

Figure 1. PFS of elranatamab vs RW physicians' choice via unweighted (A) and adjusted IPT-weighted (B) analyses



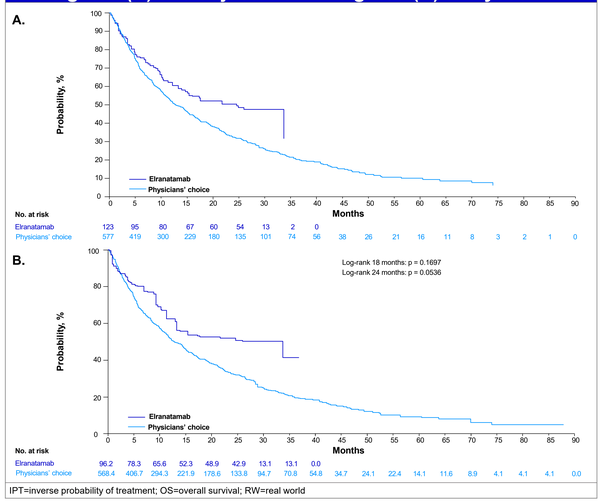
IPT=inverse probability of treatment; PFS=progression-free survival; RW=real world

Figure 2. DOR of elranatamab vs RW physicians' choice via unweighted (A) and adjusted IPT-weighted (B) analyses



DOR=duration of response; IPT=inverse probability of treatment; RW=real world

Figure 3. OS of elranatamab vs RW physicians' choice via unweighted (A) and adjusted IPT-weighted (B) analyses



IPT=inverse probability of treatment; OS=overall survival; RW=real world