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653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

An Indirect Comparison of Elranatamab's Progression-Free Survival and Overall Survival from Magnetismm-3 Versus Real-World External Control Arms in Triple-Class Refractory Multiple Myeloma

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BACKGROUND
Elranatamab(ELRA) is a BCMAxCD3 bispecific antibody being investigated for the treatment of relapsed/refractory multiple myeloma (MM). The phase 2 MagnetisMM-3 (MM-3; NCT04649359) trial was single-armed; the aim of this study was to contextualize the efficacy data from MM-3 with two real-world (RW) external control arms.

METHODS
We conducteda retrospective cohort study to indirectly compare the efficacy observed in MM-3 Cohort A (BCMA-naïve; N=123) from the March 2023 data cut (approximately 15 months of follow-up) with two US-based oncology electronic health record databases, COTA and Flatiron Health (FH), as external controls. MM-3 inclusion (eg, prior MM diagnosis, ECOG≤2, refractory to ≥1 PI, ≥1 IMiD, and ≥1 anti-CD38) and exclusion (I/E) criteria (eg, plasma cell leukemia, smoldering MM) were applied to each RW database to obtain comparable patient populations across sources. After imposing MM-3 I/E criteria, we conducted comparisons between data sources on progression-free survival (PFS) and overall survival (OS) using Kaplan-Meier estimators or Cox proportional hazard models ("unweighted analyses") and restricted mean survival time (RMST) analyses in instances where the proportional hazards assumption was violated. We used additional Cox proportional hazard models, Kaplan-Meier estimators, or semi-parametric models implementing inverse probability of treatment weighting (IPTW), doubly robust, and propensity score (PS) matching analyses to adjust for any remaining imbalances across cohorts on confounding variables (eg, age, comorbidities, Eastern Cooperative Oncology Group (ECOG) score, International Staging System (ISS), prior lines/refractoriness, cytogenetic risk, extramedullary disease [COTA only], lab values).

RESULTS
N=123 patients from MM-3 Cohort A were compared with the 239 and 152 patients identified from the COTA and FH databases, respectively. Treatment regimens in the RWD sources included various combinations of PIs (carfilzomib- and bortezomib-based regimens were each used by 43% and 15% of patients, respectively), IMiDs (lenalidomide- and pomalidomide-based regimens were used by 9% and 41% of patients, respectively), and mAbs (daratumumab- and isatuximab-based regimens were used by 32% and 1% of patients, respectively), among other agents (eg, selinexor-based regimens were used by 5% of patients). Across unweighted, IPTW, doubly robust, and PS matching analyses, ELRA was associated with significantly longer PFS than RW physicians' choice of treatment from both COTA and FH (hazard ratios [HRs] ranged from 0.37 to 0.57; see **Table 1**). Similarly, across unweighted, IPTW, doubly robust, and PS matching analyses, ELRA was associated with significantly longer OS than RW physicians' choice from COTA (HRs ranging from 0.46 to 0.65) and longer OS across unweighted (RMST difference at 15 months = 1.70) and PS matching analyses (HR = 0.60) than RW physicians'

choice from FH. IPTW and doubly robust methods indicated only directionally longer OS for ELRA than RW physician's choice from FH (RMST difference at 15 months = 0.72 and HR = 0.66, respectively).

CONCLUSIONS

Among BCMA-naïve patients who resemble those enrolled in the MM-3 trial, those treated with ELRA exhibit significantly longer PFS and OS compared with real-world treatments.

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Table. PFS and OS Differences Between ELRA and Real-World Physicians' Choice of Treatment from the COTA and FH Databases

	PFS		OS	
	ELRA vs physicians' choice (COTA)	ELRA vs physicians' choice (FH)	ELRA vs physicians'choice (COTA)	ELRA vs physicians'choice (FH)
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
Unweighted	0.51 (0.37-0.71) *P*<.0001	NE[a]	0.65 (0.47-0.88) *P*=.0062	NE[a]
IPTW	0.37 (0.22-0.64) *P*=.0003	NE[a]	0.46 (0.27-0.77) *P*=.0032	NE[a]
Doubly robust	0.53 (0.32-0.86) *P*=.0113	0.53 (0.30-0.91) *P*=.0213	0.55 (0.34-0.88) *P*=.0119	0.66 (0.37-1.17) *P*=.16
PSM	0.57 (0.37-0.87) *P*=.0101	0.41 (0.27-0.62) *P*<.0001	0.53 (0.35-0.81) *P*=.0032	0.60 (0.37-0.97) *P*=.0380

CI, confidence interval; ELRA, elranatamab; FH, Flatiron Health; HR, hazard ratio; IPTW, inverse probability of treatment weighting; NE, not evaluable; OS, overall survival; PFS, progression free-survival; PSM, propensity score matching.

[a] Due to violations of the proportional hazards assumption, HRs were not produced. Instead, restricted mean survival time (RMST) analyses were conducted. At 15 months, the RMST difference in PFS between ELRA and physicians' choice from FH was 3.55 months (95% CI, 2.02 to 5.08; *P*<.0001) and 3.58 months (1.31 to 5.85; *P*=.002) for unweighted and IPTW analyses, respectively. Similarly, at 15 months, the RMST difference in OS between ELRA and physicians' choice from FH was 1.70 months (0.41 to 2.99; *P*=.010) and 0.72 months (−1.41 to 2.85; *P*=.51) for unweighted and IPTW analyses, respectively.

Figure 1

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