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POSTER ABSTRACTS

653.MULTIPLE MYELOMA: PROSPECTIVE THERAPEUTIC TRIALS

A Matching-Adjusted Indirect Comparison of the Efficacy of Elranatamab and Teclistamab in Patients with Triple-Class Exposed/Refractory Multiple Myeloma

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BACKGROUND
Elranatamab, a novel B-cell maturation antigen (BCMA)- and CD3-directed bispecific antibody, recently demonstrated efficacy and safety in patients with triple-class exposed/refractory multiple myeloma (TCE/R MM) in the phase 2, single-arm MagnetisMM-3 trial (NCT04649359). Teclistamab (TEC) is a BCMA-CD3 directed bispecific antibody which was recently approved in the US for patients with TCE/R MM who received 4+ prior lines of treatment, based on response rates in the MajecTEC-1 trial (NCT04557098). In the absence of comparative trials of elranatamab and TEC, an unanchored matching-adjusted indirect comparison (MAIC) was conducted to assess their relative efficacy.
METHODS
Individual patient data (IPD) from the 14.7 month follow- up of MagnetisMM-3 Cohort A (BCMA-naïve, N = 123), were reweighted to match published summary data from ~23 month follow-up in MajesTEC-1 (N=165) in Sidana et al (2023). Overall, the inclusion and exclusion criteria of the trials were similar; however, MajesTEC-1 excluded patients with Eastern Cooperative Oncology Group (ECOG) performance status >1; therefore, patients with ECOG 2 in the MagnetisMM-3 trial were removed from the analysis (resulting N=116). To adjust for cross-trial differences, patients from MagnetisMM-3 were reweighted to match the baseline characteristics of the TEC trial patients. Weights were determined using a propensity score-type logistic regression via the method of moments (Signorovitch et al. 2012) based on age, median time since diagnosis, International Staging System disease stage, high-risk cytogenetics, extramedullary disease, number of prior lines of therapy, ECOG performance status, and penta-exposed and penta-refractory status. In the analysis for the overall survival (OS) endpoint, sex was also included. The adjusted variables were obtained based on univariate Cox regressions using the MagnetisMM-3 IPD, a systematic literature review of prognostic variables and effect modifiers in relapsed or refractory MM, a review of the prognostic variables identified in clinical studies for TCE/R MM, and a review of the recent relevant indirect comparisons, and were confirmed by clinical experts. A sensitivity analysis was conducted in which missing values of the adjusted baseline characteristics for elranatamab were imputed by a random sample of the observations in MagnetisMM-3 to potentially increase the effective sample size (ESS). Unanchored MAIC analyses were conducted in R studio following the code provided in the National Institute for Health and Care Excellence (NICE) Decision Support Unit (DSU) 18 by Phillippo et al (2016). The efficacy outcomes included objective response rate (ORR), duration of response (DoR), progression-free survival (PFS), and OS. Kaplan-Meier curves of DoR, PFS, and OS from MajesTEC-1 were digitized according to Guyot et al (2012). Results were reported as rate difference (i.e., the difference between the ORR of elranatamab and TEC) and odds ratios (ORs) for binary endpoints or hazard ratios (HRs) for time-to-event endpoints, with 95% confidence intervals (CIs).
RESULTS
After adjustment in the MAIC, the selected key baseline characteristics were comparable between elranatamab and TEC. For all endpoints except OS, the post-matching ESS for elranatamab was 75 in the base case and 89 in the sensitivity analysis. For OS, the ESSs were 73 and 87 for the base case and scenario analyses, respectively. Compared with TEC, elranatamab was associated with significantly better ORR (rate difference: 12.30; 95% CI: 0.70-23.90; OR: 1.79; 95% CI: 1.01-3.19) and PFS (HR 0.59; 95% CI 0.39-0.89). Patients treated with elranatamab had numerically better DoR (HR: 0.64; 95% CI: 0.33-1.23) and

OS (HR: 0.66; 95% CI: 0.42-1.03) compared to those who received TEC (Table 1 and 2). Results in the sensitivity analysis were consistent with the base case.

CONCLUSIONS

In this MAIC, elranatamab demonstrated significantly better ORR and PFS than TEC, and numerically better DOR and OS in both the base case and the sensitivity analysis. These results suggest that elranatamab is an effective option for treating patients with TCE/R MM.

Disclosures Mol: *Pfizer Inc:* Consultancy. **Hu:** *Pfizer Inc:* Consultancy. **LeBlanc:** *Agilix:* Consultancy, Honoraria; *Agios:* Consultancy, Honoraria, Speakers Bureau; *Astellas:* Consultancy, Honoraria, Speakers Bureau; *AstraZeneca:* Consultancy, Honoraria, Research Funding; *BeiGene:* Consultancy, Honoraria; *BlueNote:* Consultancy, Honoraria; *BMS/Celgene:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *CareVive:* Consultancy, Honoraria; *Flatiron:* Consultancy, Honoraria; *Genentech:* Consultancy, Honoraria; *GSK:* Consultancy, Honoraria, Research Funding; *Lilly:* Consultancy, Honoraria; *Meter Health:* Consultancy, Honoraria; *Novartis:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria; *Incyte:* Honoraria, Speakers Bureau; *Dosentrx:* Current equity holder in private company; *UpToDate:* Patents & Royalties; *American Cancer Society:* Research Funding; *Deverra Therapeutics:* Research Funding; *Duke University:* Research Funding; *Jazz Pharmaceuticals:* Research Funding; *Leukemia and Lymphoma Society:* Research Funding; *AbbVie:* Consultancy, Honoraria, Research Funding, Speakers Bureau; *National Institute of Nursing Research/National Institutes of Health:* Research Funding; *Seattle Genetics:* Research Funding; *Servier:* Consultancy, Honoraria. **Cappelleri:** *Pfizer Inc:* Current Employment, Current equity holder in publicly-traded company. **Chu:** *Pfizer Inc:* Current Employment, Current equity holder in publicly-traded company. **Nador:** *Pfizer Inc:* Current Employment, Current equity holder in publicly-traded company. **Aydin:** *Pfizer Inc:* Current Employment, Current equity holder in publicly-traded company. **Schepart:** *Pfizer Inc:* Current Employment, Current equity holder in publicly-traded company. **Hlavacek:** *Pfizer Inc:* Current Employment, Current equity holder in publicly-traded company.

Table 1. Comparison of elranatamab vs TEC for binary endpoints

	Outcome and analysis	Elranatamab (%)	TEC (%)	ESS	Rate difference [95% CI]	Odds ratio [95% CI]	P-value (Fisher test)
ORR	Naïve comparison	62%	63%	116	-0.96 [-12.5, 10.54]	0.96 [0.59, 1.57]	0.90
	Base case	75%	63%	75	12.30 [0.70, 23.90]	1.79 [1.01, 3.19]	0.05
	Sensitivity (imputation random)	75%	63%	89	12.44 [1.28, 23.60]	1.80 [1.04, 3.14]	0.04

Note: the rate difference here is calculated as the difference between the ORR rate of elranatamab and teclistamab.

CI, confidence interval; ESS, effective sample size; ORR, objective response rate; TEC, teclistamab

Table 2. Comparison of elranatamab vs TEC for time-to-event endpoints

	Outcome and analysis	ESS	HR [95%CI]	P-value
PFS	Naïve comparison	116	0.86 [0.61, 1.21]	0.37
	Base case	75	0.59 [0.39, 0.89]	0.01
	Sensitivity (imputation random)	89	0.65 [0.44, 0.95]	0.03
OS	Naïve comparison	116	1.05 [0.74, 1.50]	0.78
	Base case	73	0.66 [0.42, 1.03]	0.07
	Sensitivity (imputation random)	87	0.79 [0.52, 1.18]	0.25
DoR	Naïve comparison	116	0.78 [0.45, 1.36]	0.38
	Base case	75	0.64 [0.33, 1.23]	0.18
	Sensitivity (imputation random)	89	0.77 [0.42, 1.39]	0.38

Note: While DoR is only captured among patients with a response, the MAIC weighs all patients (regardless of response).

CI, confidence interval; DoR, duration of response, ESS, effective sample size; HR, hazard ratio; OS, overall survival; PFS, progression-free survival; TEC, teclistamab

Figure 1

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