Abstract: P1977

Title: UPDATED RESULTS OF A MATCHING-ADJUSTED INDIRECT COMPARISON OF ELRANATAMAB VERSUS TECLISTAMAB IN PATIENTS WITH TRIPLE-CLASS EXPOSED/REFRACTORY MULTIPLE MYELOMA

Abstract Type: e-Poster Presentation

Topic: Myeloma and other monoclonal gammopathies - Clinical

Background:

Elranatamab (ELRA) is a BCMAxCD3 bispecific antibody approved for the treatment of triple-class exposed multiple myeloma (TCE MM) (MM-3; NCT04649359). Long-term efficacy and safety data based on a median follow-up of 17.6 months has recently been published in Tomasson et al (2023). Teclistamab (TEC) is BCMA-CD3 directed bispecific antibody which is also approved for the treatment of TCE MM (MajesTEC-1; NCT04557098).

Aims:

In the absence of head-to-head trials between ELRA and TEC, an unanchored matching-adjusted indirect comparison (MAIC) was previously conducted to assess their relative efficacy (Mol et al, 2024). This study aims to update the results based on a longer follow-up for ELRA.

Methods:

Individual patient data (IPD) from MM-3 (17.6-month follow-up; BCMA naive, N=123) were reweighted to match published summary data from MajesTEC-1 (≈23-month follow-up; N=165). Eligibility criteria were similar, with two exceptions: MM-3 inclusion criteria specified enrollment for patients who were triple-class refractory (TCR). In contrast, MajesTEC-1 inclusion criteria enrolled a broader set of patients who were TCE. Additionally, MajesTEC-1 excluded patients with ECOG PS >1; therefore, patients with ECOG PS 2 in MM-3 were removed from the analysis (n=7).

To adjust for cross-trial differences, MM-3 patients were reweighted to match baseline summary characteristics of MajesTEC-1 patients. The same list of variables as used in the previous MAIC publication were adjusted, including age, sex (overall survival only), median time since diagnosis, International Staging System disease stage, high-risk cytogenetics, extramedullary disease, number of prior lines of therapy, Eastern Cooperative Oncology Group scale, and penta-exposed/refractory status. A sensitivity analysis was conducted in which a random sample of the observations in MM-3 imputed missing values of the adjusted baseline characteristics for ELRA.

Unanchored MAIC analyses were conducted following the code provided in the National Institute for Health and Care Excellence Decision Support Unit 18 by Phillippo et al (2016). Efficacy outcomes included duration of response (DoR), progression-free survival (PFS), and overall survival (OS). Additionally, efficacy outcomes among patients who achieved at least a complete response (CR) or higher were also included in the analyses. Results were presented in hazard ratios (HR) with 95% confidence intervals (CIs).

Results:

After adjustment in the MAIC, the selected key baseline characteristics were matched between ELRA and TEC. For all endpoints except OS, the post-matching effective sample size (ESS) for ELRA was 75 in the base case and 89 in the sensitivity analysis. For OS, the ESSs were 73 and 87, respectively. Compared with TEC, ELRA was associated with a significantly longer PFS (HR=0.55 [95% CI 0.37, 0.83], p<.01) and OS (HR=0.62 [0.40, 0.95], p=.03). Patients treated with ELRA had a numerically longer DoR (HR=0.57 [0.30, 1.05], p=.07) compared to those who received TEC (Table 1). Among patients who achieved ≥CR, ELRA was associated with a significantly longer PFS (HR=0.16 [0.05, 0.53], p<.01), and DoR (HR=0.16 [0.05, 0.51], p<.01) and a numerically longer OS

(HR=0.41 [0.13, 1.29], p=.13) compared with TEC (Table 1).

Table 1. Comparison of ELRA vs TEC for time-to-event endpoints for all BCMA-naïve patients and among those who achieved ≥CR.

		All BCMA-naïve patients			BCMA-naïve patients who achieved ≥CR*		
	Outcome and analysis	**ESS**	**HR [95%CI]**	**P-value**	**ESS**	**HR [95%CI]**	**P-value**
PFS	Naïve comparison	116	0.78 [0.56, 1.09]	.14	45	0.26 [0.09, 0.75]	.01
	MAIC base case	75	0.55 [0.37, 0.83]	<.01	31	0.16 [0.05, 0.53]	<.01
	MAIC sensitivity	89	0.59 [0.40, 0.86]	.01	38	0.19 [0.06, 0.60]	.01
OS	Naïve comparison	116	0.98 [0.70, 1.38]	.91	45	0.68 [0.25, 1.85]	.45
	MAIC base case	73	0.62 [0.40, 0.95]	.03	30	0.41 [0.13, 1.29]	.13
	MAIC sensitivity	87	0.71 [0.48, 1.06]	.10	36	0.49 [0.17, 1.43]	.19
DoR	Naïve comparison	116	0.65 [0.39, 1.08]	.09	45	0.26 [0.09, 0.73]	.01
	MAIC base case	75	0.57 [0.30, 1.05]	.07	31	0.16 [0.05, 0.51]	<.01
	MAIC sensitivity	89	0.62 [0.35, 1.10]	.10	38	0.19 [0.06, 0.59]	<.01

Note: *Since the baseline variables among patients who achieved ≥CR for TEC were not available, the weights were always generated by matching the whole ELRA population to the whole TEC population. However, the ESS reported for patients who achieved CR was calculated among patients with a response ≥CR. It was calculated as the sum of the weights among patients with ≥CR squared, divided by the sum of the squared weights among the same group of patients with ≥CR.

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

Summary/Conclusion:

In this MAIC, ELRA demonstrated significantly longer OS and PFS than TEC, and numerically longer DoR. Among patients who achieved ≥CR, ELRA showed significantly longer PFS and DoR. These results suggest that ELRA continues to be an effective option for treating patients with TCE MM.

Keywords: B-cell maturation antigen, Multiple myeloma, Bispecific, Cancer immunotherapy