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Updated results of a matching-adjusted indirect comparison of elranatamab versus teclistamab in patients with triple-class exposed/refractory multiple myeloma

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Objectives

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

Conclusions

- Elranatamab demonstrated significantly longer overall survival (OS) and progression-free survival (PFS) than teclistamab, and numerically longer duration of response (DoR).
- Among patients who achieved complete response (CR) or higher, elranatamab showed significantly longer PFS and DoR.

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Disclosures:

Contact:

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Background

- Elranatamab and teclistamab are two BCMA-directed bispecific antibodies with conditional marketing authorization by the European Medicines Agency (EMA)[5,6] for the treatment of adult patients with relapsed/refractory MM (RRMM) who have received at least three prior therapies, including a proteasome inhibitor (PI), an immunomodulatory agent (IMiD) and an anti-CD38 monoclonal antibody (mAb) (i.e., TCEMM).
- In the absence of head-to-head trials between elranatamab and teclistamab, an unanchored matching-adjusted indirect comparison (MAIC) was previously conducted to assess their relative efficacy.[2]
- New data of elranatamab based on a longer follow-up has recently been published.[2]
- This study aims to update the results based on the longer follow-up for elranatamab.

Methods

- The inclusion and exclusion criteria were comparable between the MagnetisMM-3 and MajesTEC-1 trials.
- To adjust for cross-trial differences, patients naïve to prior BCMA-directed therapy from Cohort A of MagnetisMM-3 were reweighted to match the baseline characteristics of patients from MajesTEC-1.
  - Weights were determined using a propensity score-type logistic regression via the method of moments[7] based on age, median time since diagnosis, International Staging System (ISS) disease stage, high-risk cytogenetics, extramedullary disease, number of prior lines of therapy, Eastern Cooperative Oncology Group performance status (ECOG PS), and penta-class exposed and refractory status; sex was also included in the analysis for the OS endpoint.
- The adjusted variables were the same as the previous MAIC study, which were obtained based on Cox regressions using MagnetisMM-3 individual patient-level data, a systematic literature review of the prognostic variables and effect modifiers in relapsed or refractory MM, a review of the prognostic variables identified in clinical studies for TCEMM, and a review of the recent relevant indirect comparisons. The variables were confirmed by clinical experts.
- Outcomes included DoR, PFS, OS among all patients, and DoR, PFS, and OS among patients who achieved a CR or higher.
- Results were reported as hazard ratios (HRs) with 95% confidence intervals (CIs).
- 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 (version 2023.06.2) following the code provided in the National Institute for Health and Care Excellence Decision Support Unit 18.[8]

Results

COMPATIBILITY ASSESSMENT

- Patient baseline characteristics from MajesTEC-1 and unweighted baseline characteristics of patients in MagnetisMM-3 are presented in **Table 1.**
- Eligibility criteria were similar, with two exceptions:
  - MagnetisMM-3 primarily enrolled patients with triple-class refractory disease, while MajesTEC-1 included patients with triple-class exposed disease;
  - MajesTEC-1 excluded patients with an ECOG PS of >1, whereas MagnetisMM-3 allowed enrollment of patients with an ECOG PS of 2. Patients with an ECOG PS of 2 in the MagnetisMM-3 trial were therefore excluded from the analysis (resulting in 116 patients).

Table 1: Patient demographics and baseline characteristics[a]

	MagnetisMM-3 (cohort A; n = 116)	MajesTEC-1 (n = 165)
Age, median, years	68	64
≥75, %	18%	15%
Male, %	55%	58%
Time since diagnosis, median, years	6.2	6.0
High-risk cytogenetics %	27%	23%
ISS disease stage %		
I	30%	52%
II	37%	35%
III	20%	12%
ECOG PS, %		
0	39%	33%
1	61%	67%
Extramedullary disease, %[b]	28%	17%
Number of prior lines, median	5	5
>3 lines of therapy, %	79%	74%
Refractory/exposure status, %		
Triple-class refractory[c]	97%	78%
Penta-drug refractory	41%	30%
Penta-drug exposed	71%	70%

[a] The reported percentages for baseline characteristics are based on the total number of patients in both MagnetisMM-3 and MajesTEC-1; [b] Extramedullary disease was defined as the presence of ≥1 extramedullary soft tissue lesion in MajesTEC-1. An additional variable was created in the patient-level data of MagnetisMM-3 to match this definition. [c] Triple-class refractory status was not adjusted in the MAIC due to the resulting small ESS.

ECOG PS = Eastern Cooperative Oncology Group performance status; ESS = effective sample size; ISS: International Staging System

RESULTS AMONG ALL PATIENTS

- Patients treated with elranatamab had numerically better DoR in both the base case (HR: 0.57; 95% confidence interval (CI) [0.30, 1.05]) and the sensitivity analysis (HR: 0.62; 95% CI [0.35, 1.10]) (**Table 2**).
- For PFS, the post-matching ESS for elranatamab was 75 in the base case and 89 in the sensitivity analysis (**Table 2**). In both the base case and sensitivity analysis, elranatamab was associated with significantly longer PFS than teclistamab (HR: 0.55; 95% CI [0.37, 0.83]; HR: 0.59; 95% CI [0.40, 0.86]).
- For OS, the ESS was 73 in the base case and 87 in the sensitivity analyses (**Table 2**). Elranatamab was associated with a significantly longer OS compared with teclistamab in the base case (HR: 0.62; 95% CI [0.40, 0.95]).

Table 2. Comparison of elranatamab versus teclistamab for all BCMA-naïve patients

Analysis	ESS	HR [95% CI][a]	P-value
DoR[b]			
Naïve comparison	116	0.65 [0.39, 1.08]	0.09
Base-case adjusted	75	0.57 [0.30, 1.05]	0.07
Sensitivity analysis	89	0.62 [0.35, 1.10]	0.10
PFS			
Naïve comparison	116	0.78 [0.56, 1.09]	0.14
Base-case adjusted	**75**	**0.55 [0.37, 0.83]**	**<0.01**
Sensitivity analysis	**89**	**0.59 [0.40, 0.86]**	**0.01**
OS			
Naïve comparison	116	0.98 [0.70, 1.38]	0.91
Base-case adjusted	**73**	**0.62 [0.40, 0.95]**	**0.03**
Sensitivity analysis	87	0.71 [0.48, 1.06]	0.10

[a] Bold denotes statistical significance at p<=0.05; [b] 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

RESULTS AMONG PATIENTS WHO ACHIEVED A COMPLETE RESPONSE OR HIGHER

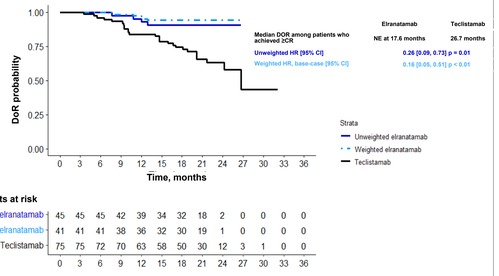
- Among patients who achieved a CR or higher, elranatamab was associated with a statistically significantly longer DoR compared teclistamab both in the base case (HR: 0.16; 95% CI [0.05, 0.51]) and sensitivity analysis (HR: 0.19; 95% CI [0.06, 0.59]) (**Table 3; Figure 1).**
- Elranatamab also showed a significantly longer PFS compared with teclistamab among patients who achieved ≥CR, in both the base case (HR: 0.16; 95% CI [0.05, 0.53]) and sensitivity analysis (HR: 0.19; 95% CI [0.06 , 0.60]) (**Table 3; Figure 2).**
- Elranatamab was associated with a numerically longer OS compared with teclistamab for patients who achieved a ≥CR (base case HR: 0.41; 95% CI [0.13,1.29]) (**Table 3; Figure 3).**

Table 3. Comparison of elranatamab versus teclistamab among patients who achieved ≥ CR

Analysis	ESS[a]	HR [95% CI][b]	P-value
DoR[c]			
Naïve comparison	45	**0.26 [0.09, 0.73]**	**0.01**
Base-case adjusted	31	**0.16 [0.05, 0.51]**	**<0.01**
Sensitivity analysis	38	**0.19 [0.06, 0.59]**	**<0.01**
PFS			
Naïve comparison	45	**0.26 [0.09, 0.75]**	**0.01**
Base-case adjusted	31	**0.16 [0.05, 0.53]**	**<0.01**
Sensitivity analysis	38	**0.19 [0.06, 0.60]**	**0.01**
OS			
Naïve comparison	45	0.68 [0.25, 1.85]	0.45
Base-case adjusted	30	0.41 [0.13, 1.29]	0.13
Sensitivity analysis	36	0.49 [0.17, 1.43]	0.19

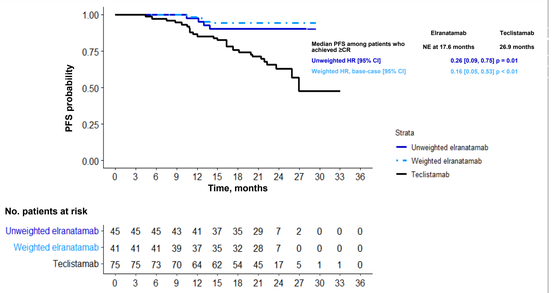
[a] The ESS reported for patients who achieved CR was calculated among patients with a response ≥CR. It was calculated as the sum of the weights among patients with ≥CR squared, divided by the sum of the squared weights among the same group of patients with ≥CR.[b] Bold denotes statistical significance; [c] 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

Figure 1. DoR results for elranatamab in MagnetisMM-3 versus teclistamab in MajesTEC-1 among those who achieved ≥ CR



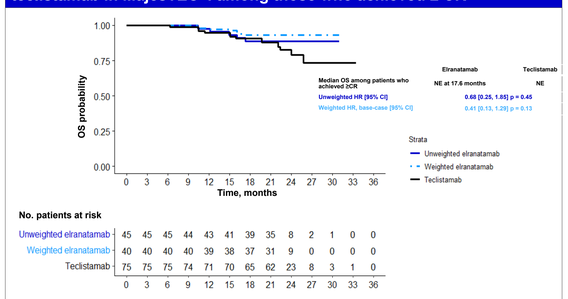
CI = confidence interval; CR = complete response; DoR = Duration of response; HR = hazard ratio; NE = not evaluable;

Figure 2. PFS results for elranatamab in MagnetisMM-3 versus teclistamab in MajesTEC-1 among those who achieved ≥ CR



CI = confidence interval; CR = complete response; HR = hazard ratio; NE = not evaluable; PFS = progression-free survival

Figure 3. OS results for elranatamab in MagnetisMM-3 versus teclistamab in MajesTEC-1 among those who achieved ≥ CR



CI = confidence interval; CR = complete response; HR = hazard ratio; NE = not evaluable; OS = overall survival