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Preferences Among Patients With Triple Class–Exposed Relapsed/Refractory Multiple Myeloma in the Era of B-cell Maturation Antigen–Directed T-cell–Engaging Therapies

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INTRODUCTION

- Multiple myeloma (MM), a cancer characterized by the proliferation of malignant plasma cells in the bone marrow, is the second-most common hematological cancer.
- Patients who become refractory to or relapse on proteasome inhibitors, an immunomodulatory drug, and an anti-CD38 monoclonal antibody (i.e., experience triple class–exposed [TCE] relapsed/refractory MM [RRMM]) have limited treatment options and often experience poor survival outcomes.[1]
- Novel B-cell maturation antigen (BCMA)-directed immunotherapies, such as chimeric antigen receptor T (CAR-T) cell therapy and BCMA bispecific antibodies (BCMA bsAbs), are efficacious but may be associated with adverse events, including cytokine release syndrome (CRS), immune effector cell–associated neurotoxicity syndrome (ICANS), and infections.[1,2] Such treatments can require hospitalization or different routes of administration, thereby impacting treatment decision-making.
- There is no consensus on the standard of care for TCE RRMM, leaving healthcare providers and their patients to weigh the benefits and risks of these novel treatments.

OBJECTIVE

- To quantify patient preferences for the attributes of novel BCMA-directed immunotherapies, including CAR-T cell therapy and BCMA bsAbs for patients with TCE RRMM.

METHODS

- A discrete-choice experiment (DCE) was designed to elicit preference weights for 7 key attributes that differentiated novel therapies for RRMM (Table 1). Attributes were based on product labels, clinical data, and review by a clinician who treats patients with MM. The DCE was designed following recommended good research practices from ISPOR and IMI PREFER.[3,4] Attribute selection also was informed or validated by a literature review of DCE studies on MM treatment.[5–11] Attribute levels were informed by available clinical data and prescribing information.
- In an online survey, respondents answered 10 experimentally designed DCE questions, each offering a choice between 2 hypothetical treatment profiles defined by the 7 attributes. Figure 1 presents an example choice question.
- Preference weights were estimated using a random-parameters logit model[3] and were used to calculate (1) conditional relative importance (CRI) (i.e., the percentage of total utility change accounted for by the attribute) and (2) minimum acceptable benefit (MAB) and maximum acceptable risk (MAR) to estimate tradeoffs between efficacy and safety attributes.
- Additionally, respondent-level preference estimates were used to predict the probability of an average respondent selecting one treatment profile over another. Profiles were developed using the most recent publicly available clinical data for 3 BCMA bsAbs (linvoseltamab,[12] teclistamab,[13,14] elranatamab[15,16]), ide-cel and cilta-cel,[17-20] and the range of attributes and levels included in the DCE (Table 1). Probability of choice was calculated using the preference weights estimated in the random-parameters logit model and not by directly eliciting preferences for treatment-specific profiles.

Table 1. Final Treatment Attributes

Attributes and patient-friendly label	Patient-friendly attribute levels
Overall response rate	60 out of 100 people (60%)
"Likelihood of responding to treatment"	75 out of 100 people (75%)
	80 out of 100 people (80%)
	98 out of 100 people (98%)
Overall survival	12 months
"Amount of time you can expect to live after starting the treatment"	20 months
	24 months
	36 months
Treatment process and dosing frequency	• Possible waitlist for treatment (ranging from 2-8 months)
"How and how frequently you take the treatment"	• 4 or more weeks to create treatment after drawing blood
	• Pretreatment chemotherapy for 3 days
	• One IV infusion treatment until progression
	• Monitoring after treatment (up to 4 additional weeks); may require travel and caregiver support
	Starting immediately, IV or injection every week until progression
	Starting immediately, IV or injection every 2 weeks until progression
	Starting immediately, IV or injection every 4 weeks until progression
Total hospitalization requirement	14 days
"Days of hospitalization when starting treatment"	7 days
	2 days
	No hospitalization
Cytokine release syndrome all grade	95 out of 100 people (95%)
"Risk of cytokine release syndrome (CRS)	70 out of 100 people (70%)
Mild, moderate, or serious"	40 out of 100 people (40%)
ICANS all grade	20 out of 100 people (20%)
"Risk of ICANS (neurological impacts)	10 out of 100 people (10%)
Mild, moderate, or serious"	3 out of 100 people (3%)
Infection grade 3+	60 out of 100 people (60%)
"Risk of developing serious infection"	45 out of 100 people (45%)
	20 out of 100 people (20%)

IV = intravenous.

Figure 1. Example DCE Choice Question

Treatment Feature	Treatment A	Treatment B
The likelihood of responding to treatment	80 out of 100 people (80%)	75 out of 100 people (75%)
Amount of time you can expect to live after starting the treatment	12 months	24 months
How and how frequently you take the treatment	• Possible waitlist for treatment (ranging from **2-8 months**) • **4 or more weeks** to create treatment after drawing blood • Pre-treatment chemotherapy for **3 days** • One IV infusion treatment until progression • Monitoring after treatment (**up to 4 additional weeks**); May require travel and caregiver support	Starting immediately, injection or IV infusion **every 2 weeks** until progression
Days of hospitalization when starting treatment	2 days	7 days
Risk of cytokine release syndrome (CRS) **Mild, moderate, or serious**	40 out of 100 people (40%)	70 out of 100 people (70%)
Risk of ICANS (neurological impacts) **Mild, moderate, or serious**	10 out of 100 people (10%)	3 out of 100 people (3%)
Risk of developing **serious** infection	20 out of 100 people (20%)	60 out of 100 people (60%)
Which would you choose?	○	○

[a]Attribute levels seen by the survey participant would vary.

RESULTS

Respondent Characteristics

- The sample included 200 respondents in the United States (US) with a physician-confirmed diagnosis of TCE RRMM. Average participant age was 61 years; 43% of the sample identified as female and 48% as male; 46% identified as White and no other race or ethnicity; 36% had a 4-year college degree or higher. Average time since diagnosis with MM was 4.2 years; 57% of respondents are currently receiving treatment, and 31% had received a stem-cell transplant.

Preference Weights and CRI

- On average, respondents' preferences were ordered as expected, with better outcomes preferred to worse outcomes. Figure 2 presents the preference weights and Figure 3 presents CRIs.
  - Overall survival (OS) was the most important attribute, with a CRI of 32.0% for a 24-month increase; preference weights were statistically significant between each consecutive level of OS, including a 4-month improvement in survival (20 to 24 months).
  - The next-most important attributes were rates of serious infection (CRI = 17.3% for a 60% lower risk), hospitalization requirements (CRI = 15.0% for avoiding 14 days of hospitalization), and overall response rate (ORR) (CRI = 13.7% for a 38% increase). Off-the-shelf options (vs. CAR-T–like manufacturing and administration process) were significantly preferred.
  - Given the attribute levels presented in the survey, risk of all-grade ICANS, mode and frequency of treatment, and risk of all-grade CRS all had similar influence on treatment choices but were less influential than the other attributes.

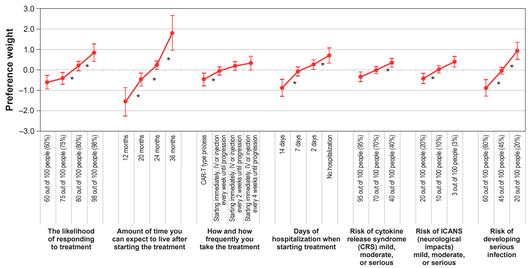
Minimum Acceptable Benefit and Maximum Acceptable Risk

- Figure 4 displays the minimum acceptable increase in OS that respondents would require to tolerate treatment-related adverse events, all else being equal. On average, respondents wanted 24.2 total months of OS for an increase in the risk of serious infection from 20% to 60%, 17.1 total months of OS for an increase in risk of CRS from 40% to 95%, and 18.0 total months of OS for an increase in risk of ICANS from 3% to 20%.
- Table 2 shows the estimated maximum level of risk that respondents would be willing to accept to gain selected OS improvements, all else being equal. For an increase in OS from 12 to 36 months, respondents were willing to accept an estimated > 60% risk of serious infections, > 95% risk of CRS, and > 20% risk of ICANS.

Predicted Preference Shares

- Figure 5 displays the predicted preference shares for select treatment profiles using publicly available clinical data from bispecific and CAR-T treatments with varying safety and efficacy profiles.
- On average, respondents were more likely to select the profile based on data for linvoseltamab compared with profiles based on data for teclistamab (81% vs. 19%) and elranatamab (66% vs. 34%), driven primarily by differences in efficacy inputs, based on the most recent publicly available data.
- When compared with profiles based on data for 2 CAR-T treatments, the profile based on data for linvoseltamab had a higher probability of selection than did a CAR-T profile with lower efficacy (81% vs. 19%), but a lower probability of selection than the CAR-T profile with higher efficacy (36% vs. 64%), thus underscoring the relative importance of treatment efficacy in terms of both OS and ORR.
- When assuming 0 hospitalization days across all profiles, predicted preference shares were not significantly altered.

Figure 2. Relative Preference Weights for DCE Treatment Attributes



CI = confidence interval.

Note: The preference weights measure the relative impact each attribute level has on the average respondent's treatment choice. The vertical bars surrounding each mean preference weight denote the 95% CI (computed by the delta method). Asterisks placed above line segments denote attribute level changes that are statistically different from 0 at the 95% CI.

Figure 3. Conditional Relative Attribute Importance of DCE Attributes

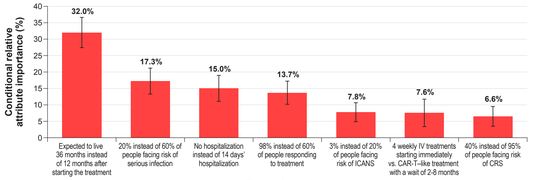
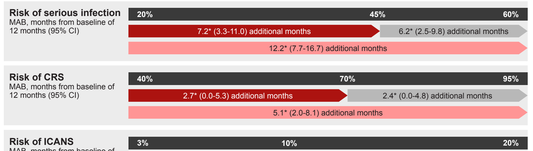


Figure 4. MAB Measures in Terms of Improvement in OS



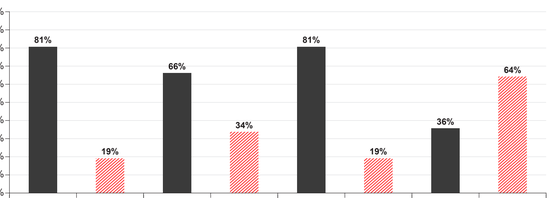
Note: The asterisks indicate statistically significant estimates at the 95% level. For each MAB calculation, all other attributes are held constant.

Table 2. MAR of Treatment-Related Adverse Events for Improvements in OS

Change in OS		Mean MAR (95% CI)		
From level	To level	Serious infection	CRS	ICANS
12 months	20 months	47.0 (37.1-56.9)	> 95	> 20
12 months	24 months	59.5 (49.0-70.1)	> 95	> 20
12 months	36 months	> 60	> 95	> 20
20 months	24 months	37.9 (27.2-48.7)	> 95	17.3 (6.7-28.0)
20 months	36 months	> 60	> 95	> 20
24 months	36 months	55.8 (45.4-66.2)	> 95	> 20

Note: It is possible to estimate a specific value for the MAR outside the range of levels included in the study only by making the strong assumption that the disutility of each unit increase in risk remains constant beyond the greatest level of risk. Mean MAR values estimated outside the range of levels are displayed as greater than the maximum risk presented in the survey (i.e., > 60; > 95; and > 20). For each MAR calculation, all other attributes are held constant.

Figure 5. Predicted Preference Shares



	Profile with data based on linvoseltamab vs. teclistamab		Profile with data based on linvoseltamab vs. elranatamab		Profile with data based on linvoseltamab vs. CAR-T profile with lower efficacy		Profile with data based on linvoseltamab vs. CAR-T profile with higher efficacy	
The likelihood of responding to treatment[12,13,15,17,20]	71%	63%	71%	61%	71%	73%	71%	98%
Amount of time you can expect to live after starting the treatment[12,13,15,17,20]	31 months	22 months	31 months	25 months	31 months	25 months	31 months	36 months
How and how frequently you take the treatment[12,14,16,18,19]	QW*/Q2W/ Q4W	QW*/Q2W	QW*/Q2W/ Q4W	QW*/Q2W	QW*/Q2W/ Q4W	CAR-T process	QW*/Q2W/ Q4W	CAR-T process
Days of hospitalization when starting treatment[12,14,16,18,19]	2	6	2	3	2	7	2	7
Risk of CRS (mild, moderate, or serious)[12,14,16,19]	46%	72%	46%	58%	46%	84%	46%	84%
Risk of neurological impacts (ICANS) (mild, moderate, or serious)[12,14,16,19]	8%	6%	8%	3%	8%	20%	8%	20%
Risk of developing serious infection[12,14,16,19]	40%	39%	40%	38%	40%	24%	40%	24%

* Predicted preference shares were calculated accounting for administration of linvoseltamab once weekly, once biweekly, and once every 4 weeks. The displayed predicted preference shares show only the results assuming the dosing frequency upon treatment initiation (once weekly) given that the dosing frequency may change over time.

QW = once weekly; Q2W = every 2 weeks; Q4W = every 4 weeks.

Note: Hospitalization requirements for investigational linvoseltamab were based on the clinical trial protocol. Requirements for elranatamab and teclistamab were based on US prescribing information. 7 days for CAR-T were assumed as a conservative assumption because US prescribing information recommends daily monitoring for 7-10 days after CAR-T infusion.[18,19]

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CONCLUSIONS

- All attributes included in the study played some role in respondents' choices, given the attributes and range of levels included in the survey.
- On average, respondents placed the most value on improvements in OS, including improvements in OS that are as short as 4 months and, to a lesser extent, ORR. Respondents were willing to accept higher rates of CRS, ICANS, and serious infections to gain improvements in ORR or OS, but they were more sensitive to higher risks of serious infections than other risks, given the range of risks presented in the survey.
- Respondents also valued fewer hospitalization days when starting treatment about as much as improving ORR and reducing the risk of serious infection. Furthermore, respondents preferred to have off-the-shelf treatments rather than CAR-T–like manufacturing and administration processes.
- Preference weights based on DCE questionnaire results predicted patients would prefer a profile similar to published data for linvoseltamab over profiles similar to publicly available data for elranatamab and teclistamab, but predicted preferences for CAR-T versus linvoseltamab depended on the efficacy profile. Patients did not directly review or express preferences for any product profiles.
- Limitations include: Patient preferences for treatment options were predicted on DCE choice questions. Preferences may differ based on patient-specific considerations and consultation with their healthcare provider. Product profiles presented are based on the most recent publicly available data for each product or class. Cross-trial differences in patient populations and study design may exist and no adjustments have been performed to account for those differences for purposes of this patient preference prediction analysis.
- This study demonstrates that OS, infections, hospitalization, and off-the-shelf availability are important to patients with RRMM.
- When considering treatment options for RRMM, patients and healthcare providers should consider tradeoffs among these attributes to determine the best course of action.

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