FUTURE ONCOLOGY
2025, VOL. 21, NO. 7, 853–865
https://doi.org/10.1080/14796694.2025.2461430

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RESEARCH ARTICLE

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# Patient preferences for triple-class–exposed relapsed or refractory multiple myeloma treatment: a discrete-choice study

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**ABSTRACT**

**Aims:** To quantify patient preferences for attributes of novel treatments for triple-class–exposed (TCE) relapsed and/or refractory multiple myeloma (RRMM).

**Methods:** Using a discrete-choice experiment, we elicited preferences for 7 attributes: objective response rate (ORR), overall survival (OS), all-grade cytokine release syndrome risk, all-grade immune effector cell–associated neurotoxicity syndrome risk, serious infection risk (grade 3+), treatment administration, and initial hospitalization requirements.

**Results:** OS was the most important attribute (conditional relative importance [CRI] 32.0% for a 24-month increase), followed by serious infection risk (CRI 17.3% for avoiding a 60% risk), initial hospitalization requirements (CRI 15.0% for avoiding 14 days of initial hospitalization), and ORR (CRI 13.7% for a 38% increase). Based on differences between relative preference weights, fewer initial hospitalization days when starting treatment and off-the-shelf (vs. chimeric antigen receptor T [CAR T] cell–like) options were significantly preferred.

**Conclusions:** Therapy decisions for patients with TCE RRMM should consider tradeoffs between efficacy, safety, and attributes related to treatment process and initial monitoring.

**ARTICLE HISTORY**
Received 21 November 2024
Accepted 29 January 2025

**KEYWORDS**
BCMA bispecific antibody; BCMA-directed immunotherapy; CAR T cell therapy; conjoint analysis; discrete-choice experiment; patient preference; triple-class exposed relapsed/refractory multiple myeloma

## 1. Introduction

Multiple myeloma (MM), characterized by the proliferation of malignant plasma cells in the bone marrow, is the second most common hematological cancer and accounts for approximately 10% of all hematologic malignancies [1,2]. Recent treatment advancements are improving patient survival and duration of responses [3,4], resulting in long-term disease management where patients are often exposed to several therapy combinations and extended treatment periods [4,5]. These treatments carry both health benefits and negative effects, including drug toxicities, financial burden, and logistical impacts (e.g., frequent hospital visits) [5,6].

Patients with MM are treated with various standard-of-care treatments across lines of therapy, including proteasome inhibitors, immunomodulatory drugs (IMiDs), and anti-CD38 monoclonal antibodies [7]. Patients with relapsed and/or refractory multiple myeloma (RRMM) who have been treated previously with proteasome inhibitors, an IMiD, and an anti-CD38 monoclonal antibody (i.e., triple-class–exposed [TCE] RRMM) have experienced poor survival outcomes [8]. Traditional treatments for TCE RRMM—including conventional chemotherapy, salvage autologous stem cell transplant, and rechallenge with previously prescribed regimens—vary in efficacy and safety [8]. Immunotherapies that target B-cell maturation antigen (BCMA), such as chimeric antigen receptor T (CAR T) cell therapy and BCMA bispecific antibodies (bsAbs), have been approved in recent years and have offered efficacious, novel treatment options for patients with TCE RRMM. These treatments, while efficacious, may be associated with adverse events (AEs), including cytokine release syndrome (CRS), immune effector cell–associated neurotoxicity syndrome (ICANS), and infections [8,9]. They may also have different treatment processes and initial monitoring requirements, thereby impacting treatment decision-making [10].

While the TCE RRMM treatment landscape is evolving, current treatment options may be associated with potential side effects and burdensome treatment processes, and there is no consensus on a single standard of care for patients with TCE RRMM [8–10]. As such, healthcare providers and their patients are often confronted with complex trade-off scenarios where they must weigh the benefits and risks of treatment. Little information is available about patient preferences for novel bispecific treatments in the TCE RRMM setting. Increasing our understanding of patient preferences may inform the treatment landscape, enhance patient-centered care, and improve patient outcomes. Therefore, the aim of this study was to elicit patients' benefit-risk preferences for the attributes of novel BCMA-directed immunotherapies, including BCMA bsAbs and CAR T cell therapy, for patients with TCE RRMM, using a discrete-choice experiment (DCE).

## 2. Materials and methods

### 2.1. Study design

This cross-sectional online survey, conducted from 28 July 2023 through 25 September 2023, included a DCE designed to evaluate

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Supplemental data for this article can be accessed online at https://doi.org/10.1080/14796694.2025.2461430

**Article Highlights**

- B-cell maturation antigen (BCMA)–directed immunotherapies for the treatment of triple-class–exposed relapsed and/or refractory multiple myeloma (TCE RRMM) have varying efficacy, administration processes, and adverse events.
- A US discrete-choice experiment (DCE) designed to evaluate preferences and tradeoffs for attributes of novel BCMA-directed immunotherapies among 200 patients with TCE RRMM revealed overall survival to be the most important of the attributes evaluated; risk of serious infection, initial hospitalization requirements, and objective response rate were also important attributes.
- Parenteral administration of a treatment starting immediately and on a recurring schedule was preferred over a hypothetical treatment with an administration process like that of a chimeric antigen receptor T (CAR T) cell therapy.
- Respondents were willing to accept higher risks of cytokine release syndrome and immune effector cell–associated neurotoxicity syndrome to gain improvements in overall survival and objective response rate. Although they were more sensitive to higher risks of serious infections (grade 3+), respondents were willing to trade off serious infection risks for gains in overall survival.
- Preference weights based on the DCE data predicted that a profile similar to published data for linvoseltamab would be preferred over profiles similar to publicly available data for elranatamab and teclistamab. Respondents' predicted preferences for linvoseltamab versus CAR T cell therapy profiles depended on the efficacy profile.
- These results may support shared decision-making as patients with TCE RRMM and their care teams navigate the evolving multiple myeloma treatment landscape.

the preferences of patients with TCE RRMM using attributes that are relevant to and differentiate novel bispecific therapies for RRMM. The primary objective was to quantify preferences of patients with TCE RRMM for a key set of treatment features that may differentiate emerging BCMA bsAb treatments and CAR T cell treatments. The secondary objectives were to estimate from the preference weights the conditional relative importance (CRI) of each attribute, respondents' tolerance for treatment-related risks, and the minimum benefit that respondents would determine to be worth the risks of treatment. As an additional secondary objective, we calculated from the DCE data the predicted probability that an average respondent would select a particular bsAb or CAR T cell profile over another profile in a series of comparisons. Lastly, an exploratory objective was included to assess the extent to which respondents' demographic and clinical characteristics affected the likelihood of them selecting certain treatment profiles. The study was reviewed by the RTI International institutional review board and determined to be exempt from full review.

## 2.2. Study population

Adults (aged ≥18 years) living in the United States (US) with a physician-confirmed diagnosis of TCE RRMM were recruited through physician referrals. Before completing the survey, eligible individuals provided informed consent. Individuals were excluded if they were currently using any investigational drug as part of a clinical trial to treat MM or had previously received treatment with ciltacabtagene autoleucel (cilta-cel), idecabtagene vicleucel (ide-cel), or a BCMA bsAb.

To estimate preference weights with acceptable precision for each attribute level and on the basis of precedents from previous studies [11,12], the target sample size was set at 200 respondents. Few DCE studies prospectively calculate minimum sample size because sample size estimation represents a challenge in this context. While many published studies have a sample size of between 100 and 300 respondents [12], minimum sample size depends on certain criteria, including the question format, complexity of the choice task, the desired precision of results, and the need to conduct subgroup analyses [11,13]. Therefore, the study team determined that a sample of 200 respondents was sufficient to estimate preference weights for each attribute level included in the study. Respondents were included in the final analysis sample if they answered ≥ 2 choice trade-off questions, varied their answers for the choice questions (i.e., did not select only Treatment A or only Treatment B), and completed the survey in ≥ 6 minutes (no upper limit was defined).

## 2.3. Survey design

### 2.3.1. Attribute selection

The primary purpose of this study was to understand preferences for the attributes of a set of novel BCMA-targeted therapies, including bispecific and CAR T cell therapies. To compare preferences for existing treatments, a top-down approach was used for selecting the attributes, as recommended by PREFER [14].

A targeted literature review was conducted to identify DCE studies that evaluated preferences for features of MM treatments. The literature review identified 9 studies exploring preferences in 5 patient samples, 4 physician samples, 2 caregiver samples, and 1 sample of nurses [10,15–22]. Across the studies, 42 unique attributes were categorized into 6 categories: efficacy, safety, treatment process, cost, quality of life, and flexibility. The attributes appearing most often in the patient preference literature were overall survival (OS), progression-free survival, treatment process (mode and/or frequency of administration), vision damage, and nerve damage.

Key attributes that may differentiate BCMA-directed immunotherapies and that reflected differences in efficacy, safety, treatment process (mode and/or frequency of administration), and initial monitoring (i.e., initial hospitalization) were evaluated on the basis of the criteria described in Appendix A. The selection was informed by the prescribing information and clinical data for BCMA-targeted CAR T cell treatments, cilta-cel and ide-cel; 2 approved BCMA bsAb treatments, teclistamab and elranatamab; and 1 BCMA bsAb treatment under investigation, linvoseltamab. Attributes and levels were then reviewed by a clinician who treats patients with MM to ensure that they reflected real-life treatment processes and AE management.

Ultimately, 7 attributes with varying levels were selected: 2 efficacy attributes (objective response rate [ORR]; OS), 3 safety attributes (all-grade CRS; all-grade ICANS; serious infections [grade 3+]), and 1 attribute each related to treatment process and initial monitoring (1 for treatment mode and dosing frequency; and 1 for initial hospitalization requirements) (Table 1). The levels were based on a range of clinical data available at the time the survey was developed. Efficacy attributes ORR and OS were selected on the basis of their importance in previous oncology preference studies and as attributes that differentiate the comparators of interest. A number of AE risks are associated with the treatments of interest. The CAR T cell therapies cilta-cel and

Table 1. Final treatment attributes.

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

CRS = cytokine release syndrome; ICANS = immune effector cell–associated neurotoxicity syndrome; IV = intravenous.

ide-cel include black box warnings for the following AEs: CRS, ICANS, neurologic toxicities, macrophage activation syndrome and hemophagocytic lymphohistiocytosis, prolonged and/or recurrent cytopenia, and secondary hematologic malignancies [23,24]. BCMA bsAb therapies are associated with risks of infection, including grade 3 and higher infection, as well as with risks of CRS and ICANS, and the approved therapies teclistamab and elranatamab include black box warnings for CRS and ICANS [25]. The risks of all-grade CRS and ICANS were selected for inclusion in the study on the basis of their seriousness and as AEs that differentiate CAR T cell and bispecific treatments. Even mild cases of CRS and ICANS may require additional close monitoring, including inpatient monitoring and/or additional therapeutic interventions. Infection risk is a well-known AE. While minor infections can be treated at home, serious infections may require hospitalization. In the survey, the attribute focuses on the risk of serious infections that require hospitalization and may result in long-term complications as a result of the treatment.

The process of administering the treatments (e.g., mode, frequency) differs significantly among BCMA bsAb and BCMA CAR T cell therapy, including the CAR T process (apheresis, manufacturing, and lymphodepletion prior to administration), the number and timing of the infusions or injections, and initial monitoring requirements (e.g., initial hospitalization). In addition, unlike with BCMA bispecific therapies, patients may have to wait to start CAR T cell treatment based on slot availability and manufacturing times [26].

### 2.3.2. Survey instrument

The online survey instrument included screening questions; demographic and socioeconomic questions; informed consent; and questions related to MM disease history, treatment history, and AEs. Patient-friendly descriptions of all attributes and practice DCE questions were provided, as were questions to assess respondents' comprehension of the material included in the survey. Respondents were presented with a series of DCE choice questions with graphics (exemplified in Figure 1). In each choice question, respondents were asked to choose between 2 experimentally designed, hypothetical MM treatment profiles; these profiles, defined by the selected attributes, were determined by an experimental design that varied the levels to create tradeoffs among attributes. The experimental design was developed using SAS statistical software, version 9 or higher (SAS Institute, Inc.; Cary, North Carolina). A commonly used D-optimal algorithm in SAS was used to construct a fractional factorial experimental design [27,28]. D-efficiency is a measure of the independence and balance of the tradeoffs included in the choice tasks. The final experimental design was evaluated for correlation and balance in attribute levels.

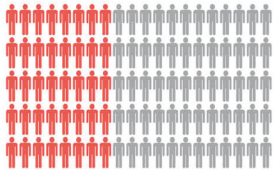
| Treatment Feature | Treatment A | Treatment B |
|---|---|---|
| The likelihood of responding to treatment |  80 out of 100 people (80%) |  75 out of 100 people (75%) |
| Amount of time you can expect to live after starting the treatment | 12 months | 24 months |
| How and how frequently you take the treatment | • Possible waitlist for treatment (ranging from **2-8 months**)<br>• **4 or more weeks** to create treatment after drawing blood<br>• Pre-treatment chemotherapy for **3 days**<br>• One IV infusion treatment until progression<br>• 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?** |  |  |

Figure 1. Example discrete-choice experiment question.

ICANS = immune effector cell–associated neurotoxicity syndrome; IV = intravenous.

Attribute levels seen by the participant would vary.

To avoid presenting more choice tasks than respondents could feasibly answer in a DCE survey instrument, the experimental design for the survey was split into 6 blocks. Each block had 10 choice tasks, and respondents saw only 1 block when completing the DCE survey instrument. To ensure the blocks were evenly distributed across the sample, respondents were randomly assigned to a block (the other sections of the survey were presented in full to all respondents). The order of the choice questions in each block was randomized across respondents. The survey instrument and experimental design were developed according to good research practice guidelines [29–31].

To explore the impact of reducing wait times for CAR T cell therapy while fixing the other attributes, the survey also included a direct-elicitation question that presented participants with 2 fixed options using the attributes from the DCE questions (Figure 2): (1) a treatment profile resembling a CAR T cell treatment or (2) a treatment profile resembling a BCMA

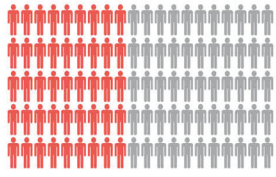
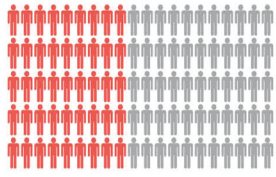
| Treatment Feature | Treatment A | Treatment B |
|---|---|---|
| The likelihood of responding to treatment |  98 out of 100 people (98%) |  71 out of 100 people (71%) |
| Amount of time you can expect to live after starting the treatment | 36 months | 20 months |
| How and how frequently you take the treatment | • 8 months waiting time before start treatment process<br>• 4 or more weeks to create treatment after drawing blood<br>• Pre-treatment chemotherapy for 3 days<br>• One IV infusion treatment until progression<br>• Monitoring after treatment (up to 4 additional weeks); May require travel and caregiver support | Starting immediately, injection or IV infusion every **2 weeks** until multiple myeloma progression |
| Days of hospitalization when starting treatment | 10 days | 2 days |
| Risk of cytokine release syndrome (CRS) **Mild, moderate, or serious** |  95 out of 100 people (95%) |  45 out of 100 people (45%) |
| Risk of ICANS (neurological impacts) **Mild, moderate, or serious** |  23 out of 100 people (23%) |  6 out of 100 people (6%) |
| Risk of developing serious infection |  23 out of 100 people (23%) |  45 out of 100 people (45%) |
| **Which would you choose?** | | |

Figure 2. Example direct-elicitation choice question.

ICANS = immune effector cell–associated neurotoxicity syndrome; IV = intravenous.

bsAb treatment. The direct-elicitation question resembled the DCE questions (Figure 1); however, unlike in the DCE questions, in which wait time was embedded in the description of the general CAR T cell process, the wait time was set to 8 months for the CAR T cell treatment profile in the direct-elicitation question. Data used in the profiles for these treatments were based on a hypothetical CAR T cell treatment with high efficacy and a BCMA bsAb profile consistent within the range of data from commercially available therapies or therapies in late clinical development. Following the direct-elicitation question, a series of follow-up questions that varied the wait time (i.e., 6 months, 2 months, 1 month) of the CAR T cell treatment profile was used to evaluate the sensitivity of treatment choice to wait times. Finally, respondents answered a series of questions focused on the treatment process, assuming the benefits and risks of the treatments were equal, and were asked in a series of pairwise comparisons to choose their preferred mode of administration.

#### 2.3.3. Survey pretesting

The survey was pretested via individual, 1-hour, semistructured teleconference or video-conference interviews with a convenience sample of 14 US adults who had self-reported MM, with a mixture of patients who were TCE and those who had received at least 1 prior MM treatment. Patients who reported using any investigational drug as part of a clinical trial for MM were excluded. Participants were recruited by Global Perspectives and provided informed consent to complete the pretest interview. During the pretest interviews, participants were asked to read the draft survey either out loud or to themselves and to think out loud as they completed each survey item. Participants were asked a series of debriefing questions to determine whether they understood the descriptions, definitions, and instructions; accepted the hypothetical context of the survey; and successfully completed the choice questions in the survey instrument as intended. Pretesting confirmed the relevance and importance of all hypothetical treatment profiles (i.e., attributes and levels) from the patient perspective. On the basis of observations and findings from the pretesting, the survey was revised to improve readability and flow and to address any potential sources of confusion and bias.

### 2.4. Statistical analysis

The analyses of deidentified data were performed with STATA 17 (StataCorp, College Station, Texas). To avoid estimation bias, a random-parameters logit (RPL) regression model was used to analyze the choice data collected in this DCE and to estimate attribute-level preference weights. Using the RPL model estimates, calculations were made for the following items as well: (1) the CRI of each attribute; (2) the mean maximum acceptable risks (MARs) of treatment-related AEs tolerated in exchange for specific improvements in treatment benefit or treatment-related processes; (3) the mean minimum acceptable benefits (MABs) required in exchange for specific risks of treatment-related AEs; and (4) the predicted choice probabilities, which represent the probability of an average respondent selecting one treatment profile with specified attribute levels over another. Probability of choice of treatment-specific profiles was not elicited directly but rather was estimated from the analysis of the DCE data, which were applied to profiles developed from the most recently available clinical data for 3 BCMA bsAb treatments (linvoseltamab [32], teclistamab [25,33], elranatamab [34,35]), ide-cel and ciltacel [23,24,36,37], and the range of attributes and levels included in the DCE. Specific details on the data sources for the inputs used for these profiles are provided in the Supplementary Appendix (Appendix A).

Preference heterogeneity was explored by testing for differences in preferences by 4 pairs of mutually exclusive subgroups defined by age (< 65 years vs. ≥ 65 years), location (rural vs. urban and suburban), ethnicity (White vs. other race and ethnicity), and experience with stem cell treatment (prior experience vs. no experience). To further explore preference heterogeneity, the responses to the fixed direct-elicitation question were evaluated in a multivariable logit regression model. Responses to the fixed-choice question and follow-up questions were analyzed descriptively.

## 3. Results

### 3.1. Respondent characteristics

A total of 201 physician-referred individuals were contacted to participate in the survey and accessed the survey link. One individual was ineligible to participate, leaving 200 respondents who completed the survey. Among the final sample, the average age was 61 years (range, 40–75 years) (Table S1, Appendix B). Though all respondents had physician-confirmed TCE RRMM, there were 197 individuals who self-reported a response to prior treatment, of whom 195 had relapsed or become refractory. Of the overall respondent sample, 48% identified as male, 43% as female, and 2% as nonbinary, while 8% preferred not to report their gender; 46% identified as White with no other race or ethnicity, and approximately one-third of respondents had a 4-year college degree or higher. Additionally, 15% of respondents reported having to retire early due to MM, and 3% of respondents reported not working due to MM. Over 94% of respondents answered each of the survey comprehension questions correctly.

### 3.2. Attribute importance

Overall, the estimated preference weights for all the attributes were consistent with the natural ordering of the levels—that is, better outcomes or features were preferred to worse outcomes or features (Figure 3; Table S2, Appendix C). For OS, preference weights were significantly different between each consecutive level, including a 4-month improvement in survival (going from 20 to 24 months). While preference weights between an ORR of 60% and 75% were not statistically significantly different (holding other tested attributes equal), those for ORR at higher levels (i.e., between an ORR of 75% to 80% and 80% to 98%) were significantly different. Respondents placed relatively little weight on the incidence of CRS or ICANS over the range of levels presented in the survey (see Table 1). For serious infections, preference weights were significantly different between each consecutive level (60% to 45% risk and 45% to 20% risk). While initial hospitalization requirements were of moderate importance, treatment process (mode and frequency of administration) did not contribute as highly to respondents' choices. However, parenteral administration of a treatment starting immediately and on a recurring schedule was preferred over a CAR T cell–like treatment with a waiting period.

Given the levels chosen for the attributes in the study, OS was the most important attribute overall (Figure 4). An increase in OS from 12 months to 36 months accounted for 32% of the total possible change in utility. The next most influential attributes, all with similar levels of influence on treatment choices, were avoiding a 60% risk of serious infection (CRI = 17.3%), avoiding a 14-day initial hospitalization requirement when starting the treatment (CRI = 15.0%), and having a 38-percentage-point increase in the likelihood of responding to treatment (CRI = 13.7%). The following attributes, all with similar levels of influence, were less influential than the other attributes: a reduction in the risk of any-grade ICANS from 20% to 3% (CRI = 7.8%), parenteral administration

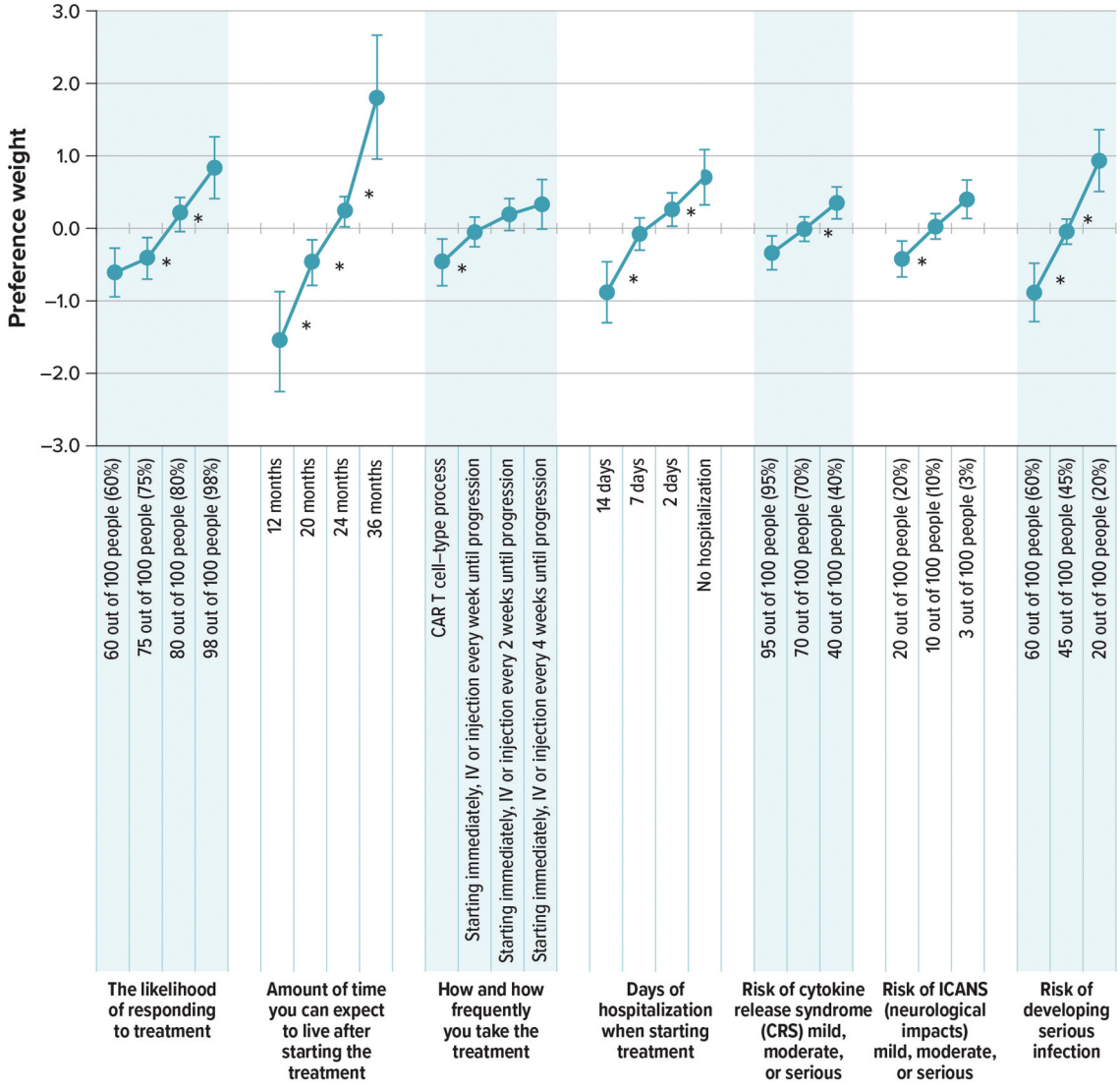



Figure 3. Relative preference weights for treatment attributes.

CAR T = chimeric antigen receptor T; CI = confidence interval; ICANS = immune effector cell–associated neurotoxicity syndrome; IV = intravenous.

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.

of a treatment starting immediately and occurring every 4 weeks versus a CAR T cell–like treatment with a waiting period (CRI = 7.6%), and a reduction in the risk of any-grade CRS from 95% to 40% (CRI = 6.6%). No significant, systematic differences in preferences were found for the subgroups tested (Table S3, Appendix C).

### 3.3. Maximum acceptable risks and minimum acceptable benefits

The MARs of CRS, ICANS, and serious infections and the corresponding 95% confidence intervals (CIs) were calculated for all possible changes between levels of efficacy. The MARs reflect the estimated maximum level of risk that respondents would be willing to accept to gain selected improvements in efficacy, all else being equal. When OS was increased from 12 to 36 months, the estimated MARs for CRS, ICANS, and serious infections were > 95%, > 20%, and > 60%, respectively. When ORR was increased from 60% to 98%, the estimated MARs for CRS, ICANS, and serious infections were > 95%, > 20%, and 53.4%, respectively. See Table S4 through Table S6 (Appendix D) for MARs for changes in efficacy, treatment process, and initial monitoring attributes.

The MABs and the corresponding 95% CIs were calculated for all changes in risks of AEs. The MABs reflect the minimum acceptable increases in survival and treatment response rate that respondents would require to tolerate treatment-related AEs, all else being equal. The MABs for OS when the risk of CRS was increased from 40% to 95%, the risk of ICANS was increased from 3% to 20%, and the risk of serious infection was increased from 20% to 60% were 17.1 months, 18.0 months, and 24.2 months, respectively. The MABs for ORR when the risk of CRS was increased from 40% to 95%, the risk of ICANS was increased

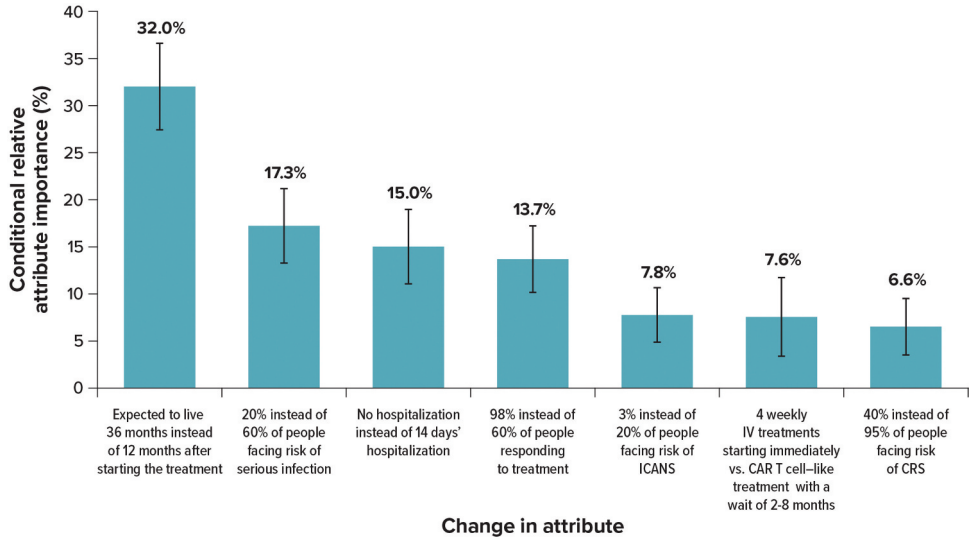



Figure 4. Conditional relative attribute importance.

CAR T = chimeric antigen receptor T; CRS = cytokine release syndrome; ICANS = immune effector cell–associated neurotoxicity syndrome; IV = intravenous.

from 3% to 20%, and the risk of serious infection was increased from 20% to 60% were 79.1%, 80.6%, and > 98%, respectively. See Table S7 and Table S8 (Appendix D) for MABs for changes in risks of AEs, treatment process, and initial monitoring attributes.

### 3.4. Predicted choice probabilities

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

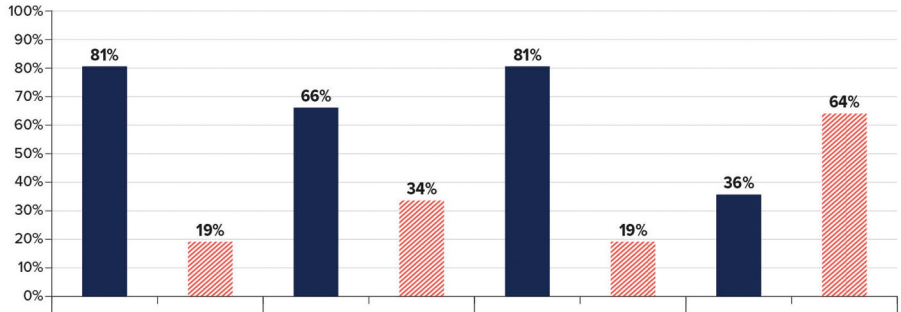
### 3.5. Direct-elicitation question

Treatment choice was influenced by the wait time required to start a hypothetical BCMA CAR T cell treatment (Table 2). As the wait time to receive the hypothetical BCMA CAR T cell treatment increased from 1 month to 8 months, the number of respondents who selected the hypothetical BCMA CAR T cell treatment profile over the hypothetical BCMA bsAb treatment profile decreased from 161 to 118. Overall, the likelihood of selecting the hypothetical BCMA bsAb treatment over the hypothetical BCMA CAR T cell treatment decreased as time since diagnosis increased (Table S9, Appendix E). Respondents who identified as female also had a lower likelihood of selecting the hypothetical BCMA bsAb treatment, and the likelihood of selecting the hypothetical BCMA bsAb treatment was higher if the respondent previously had a stem cell treatment. Similarly, the likelihood of selecting the hypothetical BCMA bsAb treatment was higher for those who had difficulty in staying at a hospital several hours from home.

## 4. Discussion

This patient preference study elicited the tradeoffs respondents with physician-confirmed TCE RRMM were willing to make among the benefits, risks, and treatment process and initial monitoring attributes associated with emerging BCMA bsAb and CAR T cell treatments for MM. Over the range of levels, all the attributes included in the study played some role in respondents' choices. Respondents, on average, placed the most value on OS (CRI of 32.0%), valuing improvements in OS as short as a 4-month increase (20–24 months). The next most influential attributes were the risk of serious infection, days of initial hospitalization when starting the treatment, and treatment response, all with CRIs similar to and not significantly different from one another (17.3%, 15.0%, and 13.7%, respectively). Improving the likelihood of treatment response from 60% to 75% did not influence respondents' choices, but respondents valued higher levels of improvements in likelihood of treatment response (i.e., from 75% to 80% and 80% to 98%).

Although they had a similar influence on treatment choices, an increase in the risk of ICANS from 3% to 20% and an increase in the risk of CRS from 40% to 95% had less impact on treatment choice than the other attributes, and these attributes' CRIs were not statistically different from each other. Respondents were willing to accept increased risk of either CRS or ICANS for




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

**Figure 5.** Predicted choice probabilities.

CAR T = chimeric antigen receptor T; CRS = cytokine release syndrome; ICANS = immune effector cell–associated neurotoxicity syndrome; QW = every week; Q2W = every 2 weeks; Q4W = every 4 weeks.

[a]Bumma et al. [32], Garfall et al. [33], Mohty et al. [35], Anderson et al. [36], Lin et al. [37].

[b]Bumma et al. [32], Garfall et al. [33], Mohty et al. [35], Anderson et al. [36], Lin et al. [37].

[c]Bumma et al. [32], Tecvayli PI [25], Elrexfio PI [34], Abecma PI [24], Carvykti PI [23].

[d]Bumma et al. [32], Tecvayli PI [25], Elrexfio PI [34], Abecma PI [24], Carvykti PI [23].

[e]Bumma et al. [32], Tecvayli PI [25], Elrexfio PI [34], Carvykti PI [23].

[f]Bumma et al. [32], Tecvayli PI [25], Elrexfio PI [34], Carvykti PI [23].

[g]Bumma et al. [32], Tecvayli PI [25], Elrexfio PI [34], Carvykti PI [23].

[h]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.

improvement in OS and ORR. Respondents were more sensitive to increases in the risk of serious infection across the range of levels included in the survey; still, they were willing to make tradeoffs between risk of serious infection and increasing OS and ORR benefits. It is possible that the results may be partly explained by patients' familiarity with serious infections and their consequences and by their lack of familiarity with CRS and ICANS (despite these being explained in the survey) as risks associated with novel therapies. The defined risk period, short duration, and usually low grade of CRS and ICANS also may have influenced the relative importance of these attributes.

Like CRS and ICANS, mode and frequency of treatment did not contribute as highly to respondents' choices. However, holding treatment benefits and risks constant, parenteral administration of a treatment starting immediately and on a recurring schedule was preferred over a hypothetical CAR T cell–like treatment with one-time administration after a waiting period. It is important to note that results for the hypothetical CAR T cell treatment were based on previously published wait times [26]. Therefore, as wait times (or other attributes) improve, results could change. Indeed, results from the direct-elicitation follow-up questions revealed that treatment choice was influenced by the wait time to start a hypothetical BCMA CAR T cell therapy, although these results were outside the DCE framework.

Preference weights estimated from the DCE survey predicted that patients would prefer a profile similar to published data for linvoseltamab over profiles similar to publicly available data for elranatamab or teclistamab. These preferences were driven primarily by numerically higher efficacy data inputs that outweighed the different AE profiles and days of initial hospitalization when patients started treatment. When compared with profiles based on data for CAR T cell treatments, predicted preferences for the linvoseltamab-like treatment profile was more likely to be preferred than a CAR T cell profile with lower efficacy but less likely to be preferred over a CAR T cell profile with higher efficacy, thus underscoring the relative importance of treatment efficacy in terms of both OS and ORR. It is important to note that patients did not directly

Table 2. Direct-elicitation follow-up questions.

| Question | Respondents with multiple myeloma (N = 200) |
|---|---|
| If these are your only options, which would you choose? | |
| Treatment A (similar to a BCMA CAR T) | 118 (59.0%) |
| Treatment B (similar to a BCMA bispecific) | 82 (41.0%) |
| **Among those who chose Treatment B (similar to a BCMA bispecific) in the first direct elicitation** | |
| N | 82 |
| In the previous question, you selected Treatment B when the waitlist for Treatment A was 8 months. What if the waitlist for Treatment A was 6 months? Please look at the table below. If these are your only options, which would you choose? | |
| Treatment A (similar to a BCMA CAR T) | 19 (23.2%) |
| Treatment B (similar to a BCMA bispecific) | 63 (76.8%) |
| **Among those who chose Treatment B (similar to a BCMA bispecific) in the second direct elicitation** | |
| N | 63 |
| In the previous question, you selected Treatment B when the waitlist for Treatment A was 6 months. What if the waitlist for Treatment A was 2 months? Please look at the table below. If these are your only options, which would you choose? | |
| Treatment A (similar to a BCMA CAR T) | 21 (33.3%) |
| Treatment B (similar to a BCMA bispecific) | 42 (66.7%) |
| **Among those who chose Treatment B (similar to a BCMA bispecific) in the third direct elicitation** | |
| N | 42 |
| In the previous question, you selected Treatment B when the waitlist for Treatment A was 2 months. What if the waitlist for Treatment A was 1 month? Please look at the table below. If these are your only options, which would you choose? | |
| Treatment A (similar to a BCMA CAR T) | 3 (7.1%) |
| Treatment B (similar to a BCMA bispecific) | 39 (92.9%) |
| **Among those who chose Treatment A (similar to a BCMA CAR T) in any of the direct-elicitation questions** | |
| N | 161 |
| On a scale of 1 to 5, where 1 is not at all worried and 5 is very worried, how worried would you be if there was a 2 to 8-month waiting list for Treatment A? | |
| 1 Not at all worried | 20 (12.4%) |
| 2 | 40 (24.8%) |
| 3 | 40 (24.8%) |
| 4 | 44 (27.3%) |
| 5 Very worried | 17 (10.6%) |
| Mean (SD) | 3.5 (1.1) |
| **All participants** | |
| If all the benefits and risks were equal for both the treatments except for features listed in the table, which treatment would you choose? | |
| Treatment A (administration similar to a BCMA CAR T) | 43 (21.5%) |
| Treatment B (administration by injection or IV infusion every 2 weeks) | 157 (78.5%) |
| If all the benefits and risks were equal for both treatments except for features listed in the table, which treatment would you choose? | |
| Treatment A (administration similar to a BCMA CAR T) | 33 (16.5%) |
| Treatment B (administration by injection or IV infusion every 4 weeks) | 167 (83.5%) |
| If all the benefits and risks were equal for both the treatments except for features listed in the table, which treatment would you choose? | |
| Treatment A (administration by injection or IV infusion every 2 weeks) | 66 (33.0%) |
| Treatment B (administration by injection or IV infusion every 4 weeks) | 134 (67.0%) |

BCMA = B-cell maturation antigen; CAR T = chimeric antigen receptor T cell; IV = intravenous; SD = standard deviation.
See Figure 2 for product profiles, including overall survival ("How long the treatment can extend your life").

review or express preferences for any product profiles; the estimates for the predicted probability of selection were based on the results of the DCE analysis results.

Subgroup analysis results indicated that the preferences revealed in the DCE data did not vary systematically with age, race/ethnicity, location, and whether or not the respondent had stem cell treatment. In exploratory logit analyses conducted to further identify preference heterogeneity within the sample, identifying as female and an increase in the time since diagnosis were associated with a statistically significant lower likelihood of selecting the profile of the BCMA bsAb–like treatment over the CAR T cell–like treatment with an 8-month waitlist in the fixed-choice questions. Conversely, having had a stem cell treatment and reporting a difficulty staying at a hospital several hours away were associated with a statistically significant higher likelihood of selecting the BCMA bsAb–like treatment over a CAR T cell–like treatment.

Many new and effective treatments have been approved for MM in the last 15 years, and many more are under development [9]. Accordingly, the proportion of patients with MM receiving novel agents increased from 8.7% in 2000 to 61.3% in 2014 [38]. As treatment options expand, patients and their healthcare providers must collectively consider tradeoffs among clinical (e.g., efficacy, safety) and practical (e.g., mode and frequency of administration) attributes of potential MM therapies [10,15]. This process of shared decision-making may be particularly important for patients with TCE RRMM, who have historically had limited treatment options, no standard of care, and often poor prognoses [8–10]. Findings from this study suggest that patients with TCE RRMM will accept increased toxicities for improvements in OS and ORR. It could be speculated that patient preferences for improved OS may be even more pronounced earlier in the disease course, when multidrug regimens and autologous stem cell transplant are common, as well as later in the disease course, when prognosis is poor. In addition to patients' willingness to accept toxicities in exchange for survival benefits, findings from this study suggest that aspects of convenience also affect their decision-making, particularly when safety and efficacy are similar.

Although comparisons with previous preference studies must be undertaken with caution owing to differences in attributes and design, our findings are broadly similar with those from recent DCEs in MM that have found increased life expectancy to be a consistent priority for patients and physicians, while the relative importance of side-effect, administration, and symptom attributes tended to vary [18,22,39]. Despite the fact that patient preference information can help inform a product's benefit-risk assessment and support regulatory, treatment, and reimbursement decisions [14,40], there is a paucity of literature on this topic for patients with TCE RRMM [10,15,17]. Thus, understanding the preferences of patients with TCE RRMM informs shared decision-making, adds value to treatment development, and may improve treatment adherence and patient outcomes [10,15].

### 4.1. Strengths and limitations

This study has several strengths. The survey was carefully designed, was pretested using in-depth interviews with patients with a physician diagnosis of TCE RRMM, and used an experimental design developed using good research practices [31]; likewise, treatment profiles included in this study were modeled from published data on existing treatments for MM. In addition, the treatment-choice data were analyzed using advanced RPL methods to avoid estimation bias, both from unobserved variation in preferences across the sample and from within-sample correlation in the choice sequence for each respondent [30]. The survey was conducted with a sample of patients with physician-confirmed TCE RRMM.

In addition to these strengths, there are certain limitations that should be considered. First, respondents evaluated hypothetical treatments, and their choices may not have the same significance as choices involving actual treatment decisions. Second, the recruitment methods (i.e., convenience sample of patients recruited through physician referrals) and study design could introduce selection and information bias, making results less generalizable to the larger population of patients with TCE RRMM. The physicians providing the referrals may not be representative of physicians treating patients with TCE RRMM, and the sample of patients may not be representative. Third, the lack of statistically significant differences between subgroups could be a result of insufficient sample size in any subgroup rather than a true lack of difference in preferences between subgroups. Fourth, patient preferences for specific BCMA bsAb and CAR T cell treatment profiles were predicted from the DCE data based on the attributes included in the DCE, and preferences may differ based on treatment attributes not included in the DCE, patient-specific considerations, and consultation with healthcare providers. The product profiles presented were based on the most recent publicly available data for each product or class. Because no head-to-head clinical comparisons are available for the products represented, cross-trial differences in patient populations and study design may exist, and no adjustments were performed to account for those differences for purposes of the patient preference prediction analysis. Nevertheless, the predicted choice probabilities provide insight into how patients may weigh multiple treatment attributes simultaneously across published and publicly available data. Lastly, although this study included treatment characteristics that may be important to patient decision-making and reflected the clinical data that were available for BCMA-targeted therapies at the time the survey was designed (e.g., OS, ORR, and risks of AEs), the study did not include other measures of efficacy and safety, which could be explored in future research.

## 5. Conclusion

As newer treatments with different benefits, risks, treatment process, and initial monitoring requirements become available for patients with TCE RRMM, it is important to understand patients' preferences across the treatment landscape. In this study, on average, respondents valued OS and, to a lesser extent, ORR. Respondents were willing to accept higher risks of CRS and ICANS to gain any improvements in ORR or OS. Additionally, while respondents were more sensitive to higher risks of serious infections, they were willing to make tradeoffs for increasing OS. Days of initial hospitalization was also an important attribute, but mode and frequency of administration did not contribute substantially to respondents' choices; however, parenteral administration of a treatment starting immediately and on a recurring schedule was preferred over a hypothetical treatment with an administration process like that of a CAR T cell therapy. Although patients did not directly indicate preferences for any product profiles, preference weights based on the DCE data predicted that a profile similar to published data for linvoseltamab would be preferred over profiles similar to publicly available data for elranatamab and teclistamab; preferences for linvoseltamab versus CAR T cell profiles depended on the efficacy profile. These results may help inform treatment development, enhance shared decision-making as patients navigate the changing MM treatment landscape, and improve outcomes for patients with TCE RRMM. Future studies could explore patient preferences for additional efficacy and risk attributes as the treatment landscape continues to evolve.

## Acknowledgments

The authors thank the patients who participated in this study. Kimberly Moon of RTI Health Solutions provided overall project management support for this study. Part of this work was presented at the 12th annual meeting of the Society of Hematologic Oncology (SOHO); 4–7 September 2024; Houston, Texas, USA [41].

## Author contributions

SA, CM, TJI, LC, QM, JH, and KRL contributed to the conception or design of the study. CM, PC, and CB acquired and analyzed the data. SA, TI, GK, JH, CM, and KR helped interpret the data. All authors helped draft the manuscript or revised it critically for important intellectual content. Lastly, all authors approved the final version of the manuscript to be published and agreed to take responsibility for all aspects of the work.

## Disclosure statement

SA reports having received consultancy fees from GSK, Sanofi, BMS, Takeda, BeiGene, Pharmacyclics, Amgen, Janssen, Regeneron, Cellectar Biosciences, and Pfizer; and research funding paid to their institution from GSK, BMS, Pharmacyclics, Amgen, Janssen, Cellectar, AbbVie, and Ascentage Pharma. TJI, LC, JH, GK, KRL, and QM are employees of Regeneron Pharmaceuticals, Inc. and may hold shares and/or stock options in the company. JH holds stock in Pfizer Inc. CM, PC, and CB are full-time employees of RTI Health Solutions, an independent nonprofit research organization, which was retained by Regeneron Pharmaceuticals, Inc. to conduct the research that is the subject of this manuscript. This work was supported by Regeneron Pharmaceuticals, Inc. RTI Health Solutions, an independent nonprofit research organization, received funding under a research contract with Regeneron Pharmaceuticals, Inc. to conduct this study and provide publication support in the form of manuscript writing, styling, and submission. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.

Lacey Lopez and Madison Walker of RTI Health Solutions provided medical writing services, which were funded by Regeneron Pharmaceuticals, Inc.

## Ethical conduct of research

The RTI International Institutional Review Board reviewed the study protocol and deemed the study exempt from full review (STUDY00022243). All respondents provided informed consent electronically.

## Funding

This manuscript was funded by Regeneron Pharmaceuticals, Inc. Authors affiliated with Regeneron Pharmaceuticals had a role in study design, data collection and analysis, the decision to publish, and preparation of the manuscript.

## Data availability statement

The data that support the findings of this study are available from the corresponding author (Timothy J. Inocencio [timothy.inocencio@regeneron.com]), upon reasonable request.

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