Patient Preference and Adherence

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ORIGINAL RESEARCH

Perspectives of Healthcare Providers and Patients with Relapsed/Refractory Multiple Myeloma on Treatment Priorities and Novel Therapies

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Purpose: With novel therapies including chimeric antigen receptor T-cell (CAR-T) therapy and bispecific antibodies (BsAbs), healthcare providers (HCPs) face complexities managing treatment for patients with relapsed/refractory multiple myeloma (RRMM). This study, among the largest surveys on RRMM, examined unmet needs in care access, barriers to novel therapy use, and treatment decision-making.

Methods: This survey-based study (March-June 2024) enrolled 2284 participants (patients: 1301; HCPs: 983) across 7 countries. Patients with >1 relapse/progression and HCPs managing ≥3 patients were included. Data were analyzed using descriptive statistics and X^2 tests.

Results: For patients, treatment priorities included slowing disease progression (second line [2L], 47%; third or later line [≥3L], 49%), minimizing adverse events (AEs; 2L, 43%; ≥3L, 49%), and extending life (2L, 39%; ≥3L, 38%). HCPs prioritized prolonging survival and controlling disease. Younger patients (<65 vs ≥65 years) prioritized convenience (40% vs 24%; $P<0.01$) and avoiding referrals to new institutions for therapies (32% vs 20%; $P<0.01$). Across geographies, HCPs reported logistical challenges as key reasons that CAR-T (38%) or BsAb (34%) therapy was not offered. Novel therapies were offered to patients more frequently in the US vs EU (CAR-T, 84% vs 77%, $P=0.023$; BsAbs, 84% vs 76%, $P=0.011$), with a similar trend in the US vs Japan for CAR-T; however, across all geographies, few patients recalled being offered CAR-T (17%) or BsAbs (13%). Patients receiving BsAbs prioritized efficacy-related reasons (25–35%) and nonclinical factors like less time and financial impact (27–29%), whereas those who received CAR-T prioritized patient success stories (50%), efficacy-related factors (48–50%), and minimal financial burden (43%).

Conclusion: This study revealed gaps in treatment priorities; patients valued quality of life and AE management, while HCPs focused on efficacy and delaying progression. There is a significant need to educate HCPs and patients on the impact of shared decision-making when considering novel treatments for RRMM.

Keywords: bispecific antibodies, CAR-T therapy, patient perspectives, surveys

Introduction

Multiple myeloma (MM) is the second most common hematologic malignancy in high-income countries and is associated with significant morbidity and mortality.[1,2] The global treatment landscape for relapsed/refractory MM (RRMM) has become increasingly complex and difficult to navigate, with recent approvals of antimyeloma drugs and evolving management strategies including autologous stem cell transplants and biologics, leading to challenging

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decisions for healthcare providers (HCPs) and their patients.[3–5] Multirefractory MM represents an unmet medical need and has raised key questions about how treatments should be sequenced and/or combined after first-line (1L) treatment failure, especially as simultaneous quadruplet therapy (consisting of a proteasome inhibitor, an immunomodulatory drug [IMiD], an anti-CD38 antibody, and dexamethasone) is currently used in 1L treatment.[6] HCPs need to consider several factors, including their patients' preferences, when selecting the next treatment. HCPs should consider efficacy (eg, autologous stem cell transplant, chimeric antigen receptor T-cell [CAR-T] therapy, or a bridge/salvage regimen to a more curative option), tolerability of potential side effects associated with next-line therapy (eg, CAR-T, bispecific antibodies [BsAbs], proteasome inhibitors, and IMiDs have well-characterized adverse event [AE] profiles), and finally there is an increasing financial and logistical burden for some countries (especially associated with treatments such as CAR-T and other biological therapies that countries may need to support).[7]

Patient preferences have become an integral part of the decision-making process regarding their treatment care plan, especially when new treatment options for MM are chosen. Treatment decision-making based on the understanding of all treatment options (available or not) and patient treatment goals and care experience is critical for the development of a trusted relationship between the patient and HCP.[8] Healthcare organizations engaging with patients early and supporting HCPs to align with their patients' preferences could ultimately lead to improved adherence and treatment outcomes.[9] However, HCPs are often unaware of individual patient preferences[10] and can underestimate patient pain and quality of life (QoL).[11] In contrast to patients, HCPs focus on clinical indicators of disease, outcome, and prognosis, which might not be the only indicators considered by patients when evaluating treatments. For example, a recent qualitative survey among patients with MM highlighted concerns about life-threatening side effects that could cause permanent organ damage and negatively impact daily activities.[12]

Although numerous studies have explored how HCPs approach treatment decisions for patients with RRMM, there is a notable scarcity of studies directly comparing the viewpoints of patients and HCPs.[9] Among the few studies that do exist, HCP and patient cohorts were restricted by region, line of treatment, or age.[13] Additionally, treatment decisions based on clinical trial findings are not always generalizable to specific patient populations. There also appears to be a disconnect between HCPs and patients regarding expectations for treatment outcomes. In a recent study, patients placed health-related QoL as the most important benefit across all lines of treatment.[13,14] Conversely, health-related QoL was only a top-5 consideration in fourth-line therapy for HCPs.[13,14] Furthermore, some indications suggest that differences among care settings impact HCP decision-making; however, more research is needed. In a 2023 study by Vardell et al,[15] the authors highlighted that the proportion of patients receiving MM-directed therapy was significantly higher in academic centers compared with nonacademic centers, where treatment options are more limited. A notable improvement in overall survival was observed in patients who received therapy in an academic center compared with those from a nonacademic center, suggesting that treatment decision-making is dependent on treatment access at centers.[15]

A review of the literature has determined that HCPs make generalized assumptions about the needs of their patients when selecting appropriate MM-directed treatments.[9,11,14] In this study, we report the findings of a multicountry survey collaboratively developed by a multidisciplinary group of stakeholders including myeloma HCPs and patients. The survey was designed to engage patients with RRMM and HCPs to identify care and treatment gaps based on factors such as demographics, patient medical history, socioeconomic status, and treatment availability. The study objectives included identifying similarities and differences between HCP and patient treatment preferences and evaluating whether these findings were consistent across different countries and practice settings. The study also aimed to determine the settings (center of excellence [CoE]/academic vs non-CoE/community) and patient populations in which the use of novel treatment options such as BsAbs and CAR-T is lower and to understand the relative drivers and barriers for their adoption. Based on these findings, the study aimed to uncover opportunities to improve HCP-patient/caregiver dialogue and decision-making when discussing multiple treatment options.

Materials and Methods

Study Design

The study used a 30-minute, web-based quantitative survey sent between March and June 2024 to 1301 patients with RRMM and 983 oncologists across 7 countries (US, UK, France, Germany, Italy, Spain, and Japan). Written informed

consent was obtained from all participants included in the study. A steering committee was assembled comprising 2 patients with MM, 2 patient advocacy group representatives, 3 nurses/nurse practitioners, 1 pharmacist, and 7 specialists in hematology/oncology with varying perspectives based on geography, practice setting, and clinical vs research focus and representing 6 of the 7 countries studied in this research. The steering committee provided insights and feedback during survey and protocol development, tested the surveys after they were programmed online, and supported the interpretation of results. The study was reviewed and granted exemption from oversight (per the Department of Health and Human Services regulations 45 CFR 46.104(d)(2)) by the Advarra Institutional Review Board (Detroit, MI, USA) and conducted in line with the principles of the Declaration of Helsinki and local legal obligations.

Survey Participants

The target population included oncologists and patients with RRMM. Recruitment was monitored to understand the breakdown of participants based on race, ethnicity, age, gender, education, and other demographics with best efforts to ensure a suitable representation of the population of the MM community.

The study population was selected through screening criteria applied to both HCPs and patient participants identified through existing participant registries or patient advocacy groups in the included countries. Patients with MM aged ≥18 years who had experienced progression or relapse ≥1 time were included in this study. Additionally, care partners were permitted to participate if they responded to the survey from the perspective of a patient meeting these criteria. The inclusion criteria for HCPs included specialty in medical oncology, hematology/oncology, hematology (only in US), transplantation, or internal medicine with a subspecialty identified as medical oncology or hematology; active, full-time practice; and management of ≥3 patients with MM receiving second-line (2L) or later treatment within the last 12 months. HCPs were excluded from the study if they had <4 years or >35 years in practice since their training completion and spent <50% of their time treating patients. Respondents to the survey received honoraria for participating in the research; the amounts were in line with local fair market value.

Survey Development

The survey questionnaire was developed by identifying key research objectives through primary and secondary research. In addition, a subgroup of steering committee members contributed their expertise through concept-elicitation interviews and actively engaged in survey development and design. A second and nonoverlapping subgroup of steering committee members participated in the survey pilot. The survey was refined through multiple cycles of feedback from a range of contributors. The survey questions received feedback from 2 patient organizations to ensure patient-centricity. The questions were subsequently professionally translated into 6 languages for the 7 participating countries, and the translations were verified for accuracy by multiple myeloma experts who were native speakers in each country.

Initial questions in the survey explored general topics about RRMM, and later questions focused more specifically on the use of novel therapies, including CAR-T therapy and BsAbs. Certain survey questions were curated to be comparable across both patient and HCP surveys. Other questions were tailored specifically to the unique viewpoints of each participant group. Questions were presented in a range of formats, including multiple choice (single or multiple selection) and prioritization (ranking and rating). The question formats were tailored to gather comprehensive and nuanced insights. All questions in the survey were close-ended questions.

The survey was disseminated online and hosted on a secure platform programmed by OWL Programming (Rochester, NY, USA). Participants accessed the survey through a web link or Email invitation. While they provided personally identifiable information for recruitment, these data were kept confidential and not shared with the sponsor or its affiliates. Data collection occurred over a 12-week survey fielding period, with reminders sent to nonresponders to enhance the response rate.

This was a quantitative online survey that asked questions to understand participant experiences. The outcome variables included, but were not limited to, satisfaction related to RRMM treatment (efficacy, side effects, cost, logistics, and impacts on mental health and family) and gaps in access to the preferred care model (preferred role in treatment decision-making, communication with care providers about the disease, treatment options, and support services).

Data Analysis

The collected survey data were analyzed using descriptive statistics, X^2 tests, and stratified X^2 tests, conducted at the country level for directional insights and results. Participant characteristics were described with standard descriptive statistics appropriate to the variable type (ie, absolute counts and percentages for categorical variables and means, as well as standard deviations, medians, and ranges for continuous variables). Statistical analyses were conducted, with *P* values ≤.05 considered statistically significant.

Results

Patient Demographic Characteristics

Patients with MM mostly had comparable demographic characteristics across different regions, with a median age of 67 years (range, 20–86 years). Approximately two-thirds of patients were age 60–74 years, 64% of patients were male, and >80% of patients resided in cities and had attained a bachelor's degree or higher (Table 1). The majority of patients were receiving 2L or third-line (3L) treatment (≈80%), except for patients in the UK, where a higher proportion of patients were receiving >3 lines of therapy (86%). More than half of the patients from each country surveyed had been diagnosed >3 years ago, except for those in France and Italy. Almost two-thirds of patients were not in remission at the time of completing the survey, except in Spain,

Table 1 Patient Demographics

Category	US (n=305)	Europe (n=870)	Japan (n=126)	Global (N=1301)
Male, %	67	62	70	64
Age				
Median, years	66	67	70	67
Min-max, years	26–81	20–86	40–78	20–86
<45 years, %	20	10	2	12
45–59 years, %	14	19	7	17
60–74 years, %	60	67	75	66
≥75 years, %	5	3	17	5
Location, %				
Large city	39	45	48	44
Mid-sized/small city	43	37	44	39
Town/rural	18	18	9	17
Education, %				
Less than bachelor's degree	24	18	21	19
Bachelor's degree	48	47	48	47
Postgraduate	29	35	31	33
Most recent line of therapy, %				
2L	45	42	39	43
3L	35	37	40	37
≥4L	21	21	21	21

(*Continued*)

Table 1 (Continued).

Category	US (n=305)	Europe (n=870)	Japan (n=126)	Global (N=1301)
No. of years since MM diagnosis, %				
<3 years	43	50	39	47
≥3 years	54	50	61	52
Do not remember	3	0	0	1
MM currently in remission, %				
Yes	44	34	40	37
No	54	66	60	63
Other*	2	0	0	0
Received novel therapy for MM, %†				
CAR-T	8	8	4	8
BsAb††	12	9	N/A	10
Have received or currently receiving MM treatment through clinical trial, %	6	6	17	6

Notes: *Includes respondents who indicated they preferred not to say or who did not know their remission status. †CAR-T does not include patients from Spain or the UK, and BsAb does not include patients from Spain, the UK, or Japan. †† Includes BCMA or GPRC5D BsAb therapy. **Abbreviations**: 2L, second line; 3L, third line; 4L, fourth line; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T cell; GPRC5D, G protein-coupled receptor family C group 5 member D; MM, multiple myeloma.

where 90% of patients were not in remission (Supplementary Table 1). Less than 10% of patients had received CAR-T therapy, while a slightly larger proportion had received BsAbs (Table 1).

HCP Characteristics

Similarly to patients, HCP characteristics were broadly similar across countries, with approximately 60% of HCPs practicing at academic or CoE institutions and most having ≥15 years of practice experience (Table 2 and Supplementary Table 2). Most patients who were under the HCP respondents' care were receiving 1L treatment, with fewer patients receiving each subsequent line of treatment. Academic or CoE institutions were far better equipped to treat patients with CAR-T therapy and BsAbs than community or non-CoE hospitals (CAR-T, 61% vs 25%; BsAbs, 80% vs 56%, respectively; Table 2).

Table 2 HCP Characteristics

	US (n=251)	Europe (n=580)	Japan (n=152)	Global (N=983)
Care setting, %				
Academic/CoE	47	64	60	59
Nonacademic	53	36	40	41
Years in practice, %				
<15 years	45	39	30	39
≥15 years	55	61	70	61

(*Continued*)

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Table 2 (Continued).

Average no. of patients managed in past year per line of therapy per HCP, %	Academic/ CoE	Nonacademic	Academic/ CoE	Nonacademic	Academic/ CoE	Nonacademic	Academic/ CoE	Nonacademic
1L	43	30	35	26	12	8	33	24
2L	33	23	26	18	10	5	25	18
3L	25	18	19	13	9	4	19	13
≥4L	19	12	15	9	6	3	14	9
Able to administer novel therapy, %*								
CAR-T	76	43	61	19	43	5	61	25
BsAb†	75	49	82	62	N/A	N/A	80	56

Notes: *CAR-T does not include HCPs from UK, and BsAb does not include HCPs from Japan. †Includes BCMA or GPRC5D BsAb therapy.
Abbreviations: 1L, first line; 2L second line; 3L, third line; 4L, fourth line; BCMA, B-cell maturation antigen; BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T cell; CoE, center of excellence; GPRC5D, G protein-coupled receptor family C group 5 member D; HCP, healthcare provider.

Treatment Decisions and Preferences Among Patients and HCPs

Considerations for Initiating Treatment

The top 3 priorities for patients in their choice to initiate a new treatment were consistent between lines of therapy and included (1) does the treatment slow down MM progression (47% and 49% in 2L and ≥3L, respectively), (2) does the treatment have side effects (43% and 49%), and (3) will it help me live longer (39% and 38%; Figure 1). Older patients (≥65 years) prioritized slowing down MM progression and limiting side effects (both $P<0.01$), whereas younger patients (<65 years) were more concerned with the convenience of treatment (route of treatment administration or time required)

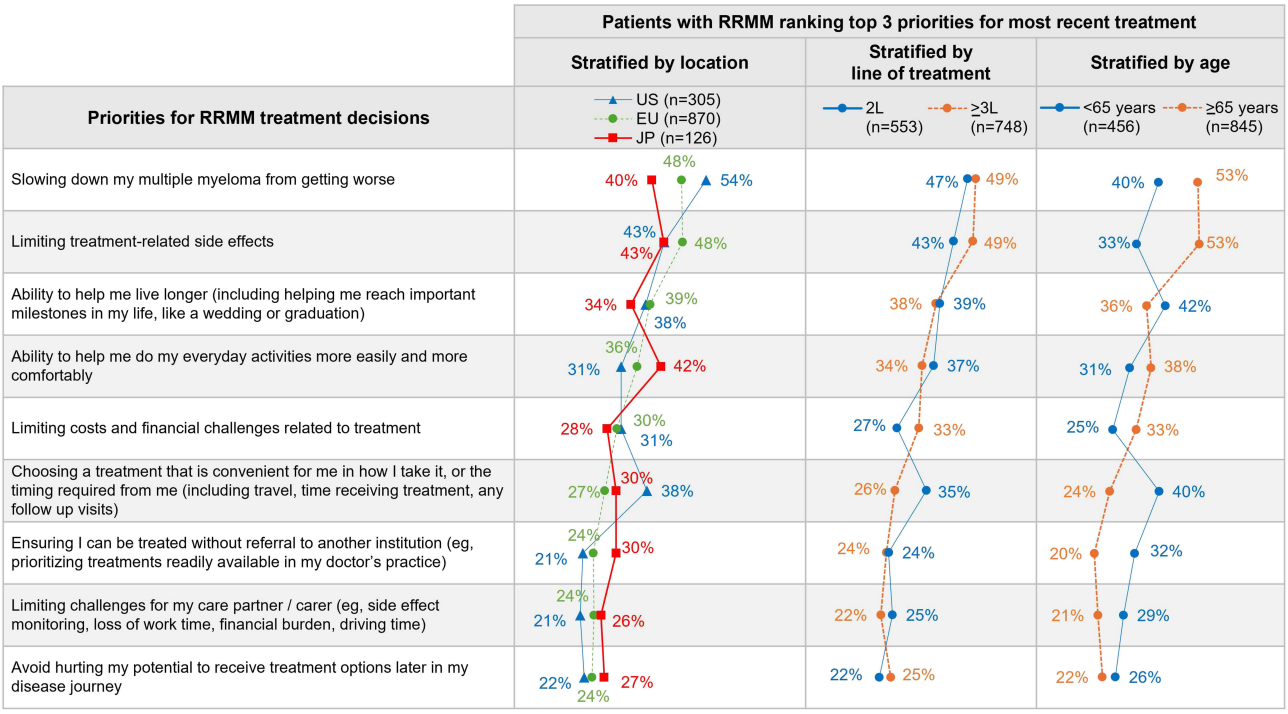

Figure 1 Patient priorities for treatment decisions. All values are expressed as percentages. EU includes France, Germany, Italy, Spain, and the UK.
Abbreviations: 2L, second line; 3L, third line; EU, Europe; JP, Japan; RRMM, relapsed/refractory multiple myeloma.

and avoiding referrals (P<0.01). Similar trends were observed when the different regions were considered (namely the US, Europe, and Japan; Figure 1). Treatments that improved patient ability to complete everyday activities and that limited the financial burden were also of importance to patients across all subgroups.

In contrast to patients, HCPs did not consider limiting AEs (<42%) and treatment costs (<15%) as high priority. HCP priorities for patients who were receiving 2L or ≥3L treatment were focused more on treatment efficacy, in terms of prolonging survival (71% and 64%, respectively), controlling disease (64% and 61%, respectively), and maintaining QoL (defined as maintaining the ability to do everyday activities more easily and more comfortably and maintain appearance; 57% and 62%, respectively; Figure 2). The majority of patients with RRMM (87%) shared a preference to be involved in treatment decisions, regardless of region, age, or line of therapy, with only 13% of patients preferring that an HCP recommends treatment independent of considering patient treatment goals or preferences.

Understanding Treatment Experience and Side Effects

Patients were asked about their MM treatment and care in general; 46% of patients across geographies reported experiencing "worse" or "slightly worse" than expected outcomes in managing side effects. Interestingly, there was a statistically significant difference across all categories comparing by line of therapy (2L vs ≥3L) and age (<65 years vs ≥65 years), with later-line (≥3L) and older (≥65 years) patients reporting worse care relative to expectations than their counterparts (2L and <65 years, respectively; Supplementary Figure 1).

Treatment side effects considered to be "extremely challenging" to HCPs did not always match the perceptions of patients who had experienced them. While there was agreement on the most challenging AEs for patients with RRMM, leukemia (patient 69% vs HCP 62%) and serious infections (65% vs 64%, respectively), perceptions did not align for bone-related side effects (64% vs 39%; P<0.01; this gap was larger in Europe and Japan vs US; P<0.01), thrombocytopenia (64% vs 43%; P<0.01), and neutropenia (61% vs 41%; P<0.01; Figure 3). In Europe and Japan, there was a higher magnitude of difference between patient and HCP perceptions about the side effects of thrombocytopenia (patient 69% vs HCP 42%; P<0.01). HCPs were also more concerned than their patients about immune cell–associated

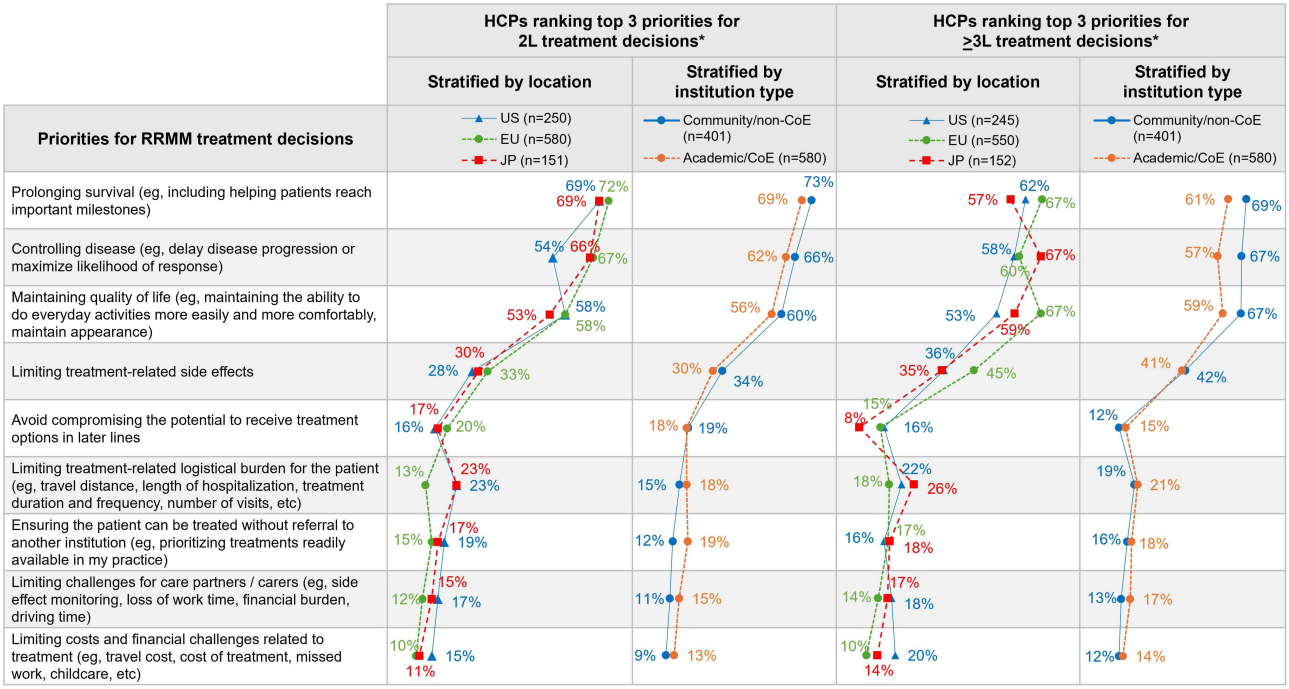

Figure 2 HCP priorities for treatment decisions. All values expressed as a percentage. EU includes France, Germany, Italy, Spain, and the UK.
Notes: * HCPs were asked about treatment priorities for 2L and ≥3L patients with MM only if they managed at least one 2L and ≥3L patient with MM.
Abbreviations: 2L, second line; 3L, third line; CoE, center of excellence; EU, Europe; HCP, healthcare provider; JP, Japan; RRMM, relapsed/refractory multiple myeloma.

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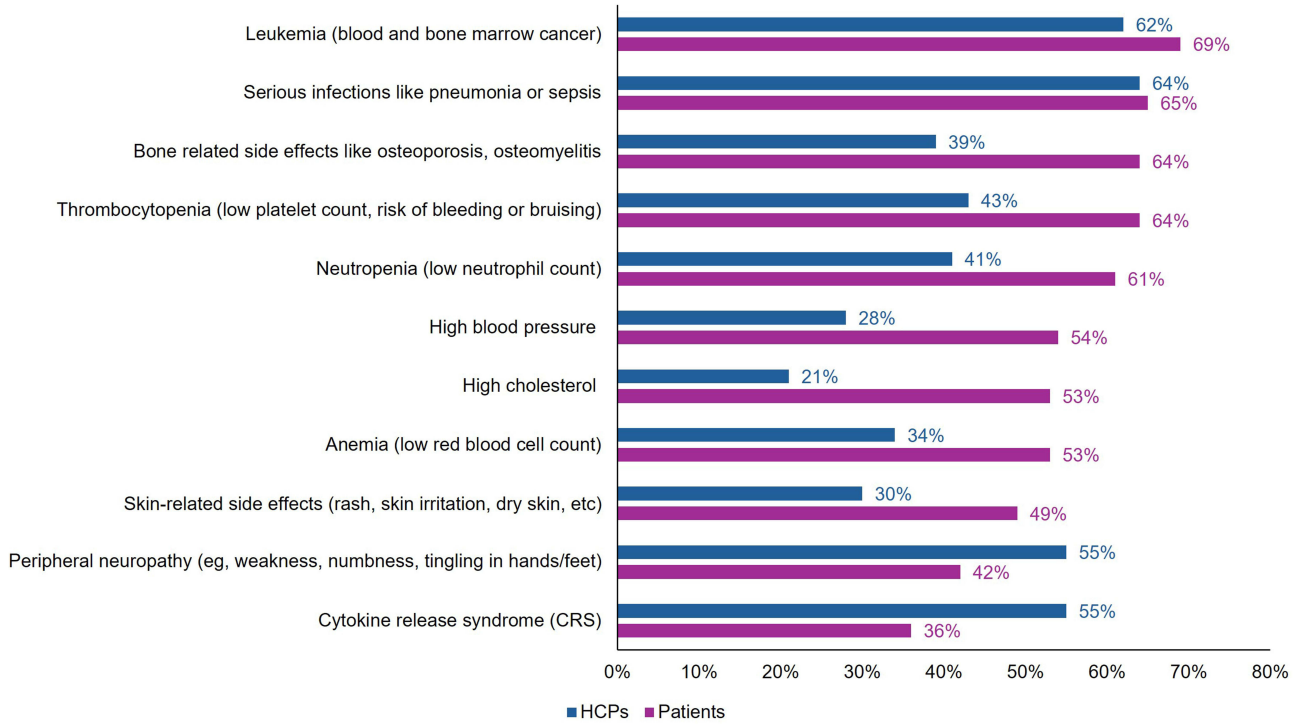

Figure 3 Challenging AEs for patients with RRMM according to HCPs and patients with RRMM who had experienced these treatment-related AEs.
Abbreviations: AE, adverse event; HCP, healthcare provider; RRMM, relapsed/refractory multiple myeloma.

neurotoxicity syndrome (50% vs 61%; $P<0.01$), neuropathy (patient 42% vs HCP 55%; $P=0.024$), and cytokine release syndrome (36% vs 55%; $P<0.01$; Figure 3).

While limiting treatment-related side effects was generally a priority among patients, it was particularly important for patients aged ≥65 years (53% vs 33% for <65 years; $P<0.01$; Figure 1) and those with comorbidities (52% vs 32%; $P=0.055$). In the US, patients had a greater focus on fatigue compared with European and Japanese patients (US 55% vs EU/Japan 38%; $P<0.01$), whereas European and Japanese patients placed a stronger emphasis on bone-related AEs than patients in the US (EU/Japan 70% vs US 54%; $P=0.041$). Although it is possible that cultural differences may play a role in these variances, the survey was not designed to specifically determine patient experience in relation to culture. The trends for other AEs were consistent globally, and patterns were similar between academic and community settings for all key AEs mentioned.

Treatment-Related Logistical Burden on Patients

When HCPs were asked to consider the logistical burden for their patients with RRMM in later lines of treatment, only a small percentage prioritized limiting this burden for 2L (17%) or ≥3L (20%) patients. In contrast, managing the logistical burden was a higher priority for patients, with 35% of 2L patients and 26% of ≥3L patients emphasizing its importance (Figure 2). Interestingly, 2L patients with RRMM prioritized minimizing logistical burden more than ≥3L patients, and the discrepancy between 2L patient and HCP emphasis on this factor was stronger in the US and Japan compared with Europe ($P<0.01$). Compared with the US and Japan, there was a greater discrepancy between 2L patient and HCP emphasis on limiting the burden to carers/care partners ($P<0.01$) in Europe. Furthermore, younger patients (<65 years) placed a higher priority on treatment convenience (40% vs 24%; $P<0.01$) and avoiding referrals to other institutions (32% vs 20%; $P<0.01$) across all lines of RRMM therapy compared with older patients (Figure 1). This trend was particularly pronounced in the US and EU ($P<0.01$).

Patient and HCP Perspectives and Considerations on Novel Therapies

Novel Therapy Awareness

When considering novel therapies, more patients across countries surveyed had heard of CAR-T therapy compared with BsAbs, with almost half of US patients (48%) knowing something about CAR-T compared with 40% for BsAbs (P=0.05; Figure 4A). HCPs identified that approximately 37% of their patients were eligible for CAR-T therapy, and 43% were eligible for BsAb therapy (Figure 4B). In the US, both CAR-T and BsAb therapies were more commonly offered by HCPs to their patients compared with those in the EU (CAR-T: 84% in US vs 77% in EU, P=0.023; BsAbs: 84% in US vs 76% in EU, P=0.011). While differences in healthcare insurance coverage across countries may influence access to these therapies, the survey was not designed for this analysis. Only a small proportion of patients from all locations recalled their HCP offering these novel therapies as options (CAR-T: 17%; BsAbs: 13%). Of these patients, approximately 76% reported that they received CAR-T therapy, and 57% received BsAbs (with 31% still considering BsAbs). Overall, 55% of HCPs reported feeling "very" or "extremely confident" in determining patient eligibility for CAR-T therapies, compared with a higher confidence level of 64% for BsAb therapies (P<0.01; Figure 4C). Also, HCPs in CoE/academic settings felt more confident determining patient eligibility for these novel therapies than HCPs in non-CoE /community settings, and this was true for both CAR-T (62% vs 45%; P<0.01) and BsAbs (68% vs 58%; P<0.01) therapies) (Figure 4C).

In the US, non-White patients were more likely than White patients to be unaware of novel therapies (never heard of CAR-T: 33% vs 19%, P<0.01; never heard of BsAbs: 51% vs 23%, P<0.01; Supplementary Table 3). There was a significant trend for White patients to be more readily offered CAR-T than their non-White counterparts (offered CAR-T: 29% vs 6%; P<0.01), with BsAbs also more likely offered to White patients (offered BsAbs: 21% vs 8%; P=0.096). Socioeconomic status may play a role, with 47% of non-White patients reporting difficulty affording healthcare, education, and housing vs 26% of White patients (P<0.01); White patients were also more likely to visit a physician specializing in MM compared with non-White patients (59% vs 41%, respectively; P<0.01).

BsAb Treatment Considerations

Patients who decided to receive BsAbs often mentioned that the efficacy benefits of BsAbs (eg, remission [35%], symptom relief [29%], opportunity for improved survival [25%]), as well as nonclinical factors (eg, treatment taking up less time [29%], treatment less likely to impact finances [27%]), were important in the treatment decision-making process (Figure 5A). In terms of efficacy, there were nonsignificant trends in the comparison of US and European patients: US patients focused more on achieving remission (P=0.546), and patients in Europe prioritized relieving symptoms (P=0.333) and limiting time commitment (P=0.155). The main reasons for patients declining BsAb therapy included being overwhelmed by the amount of education required before committing to the treatment (55%), BsAb therapy requiring hospitalization or time at a specialist treatment center (55%), and personal preference for another treatment as a better option (55%) (Supplementary Table 4).

CAR-T Treatment Considerations

Similarly to BsAbs, patients decided to initiate CAR-T therapy predominantly due to hearing about successful CAR-T treatments in other patients (50%); however, the efficacy benefits of CAR-T therapies (eg, improved chance of survival [50%], remission [48%], improved QoL [48%]), and minimal impact on patient finances [43%]) also played a role (Figure 6A). In contrast to BsAbs, European patient focus for CAR-T therapy was directed toward achieving remission and maintaining QoL, whereas US patients reported that impact on their time and finances were major considerations for choosing CAR-T therapy. Reasons for declining CAR-T therapy included concern about the long-term safety (64%), uncertainly how well the treatment would work (55%) and concern about the short-term side effects (55%) (Supplementary Table 5).

HCP Experience With Novel Therapies

HCPs reported that the key reason why eligible patients were not offered CAR-T therapy or BsAbs as treatment options was the logistical challenges involved for patients (eg, patients live too far from the administering center, dosing schedule

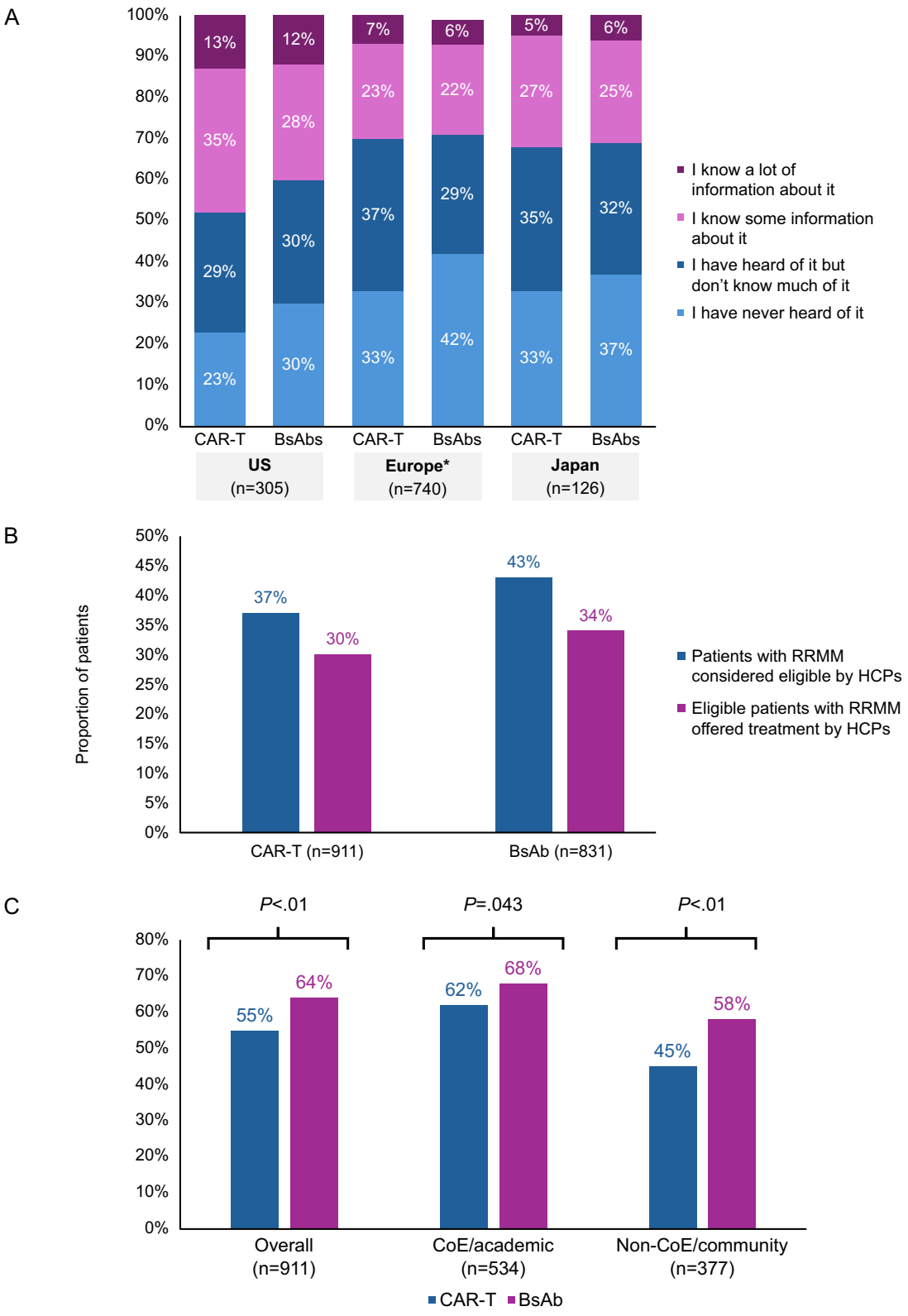

Figure 4 (**A**) Patient awareness of novel therapies. (**B**) Patients eligible and offered novel therapies. (**C**) HCP confidence in determining RRMM patient eligibility for novel therapies.

Notes: *Europe includes France, Germany, Italy, Spain, and the UK.

Abbreviations: BsAb, bispecific antibody; CAR-T, chimeric antigen receptor T cell; CoE, center of excellence; HCP, healthcare provider; RRMM, relapsed/refractory multiple myeloma.

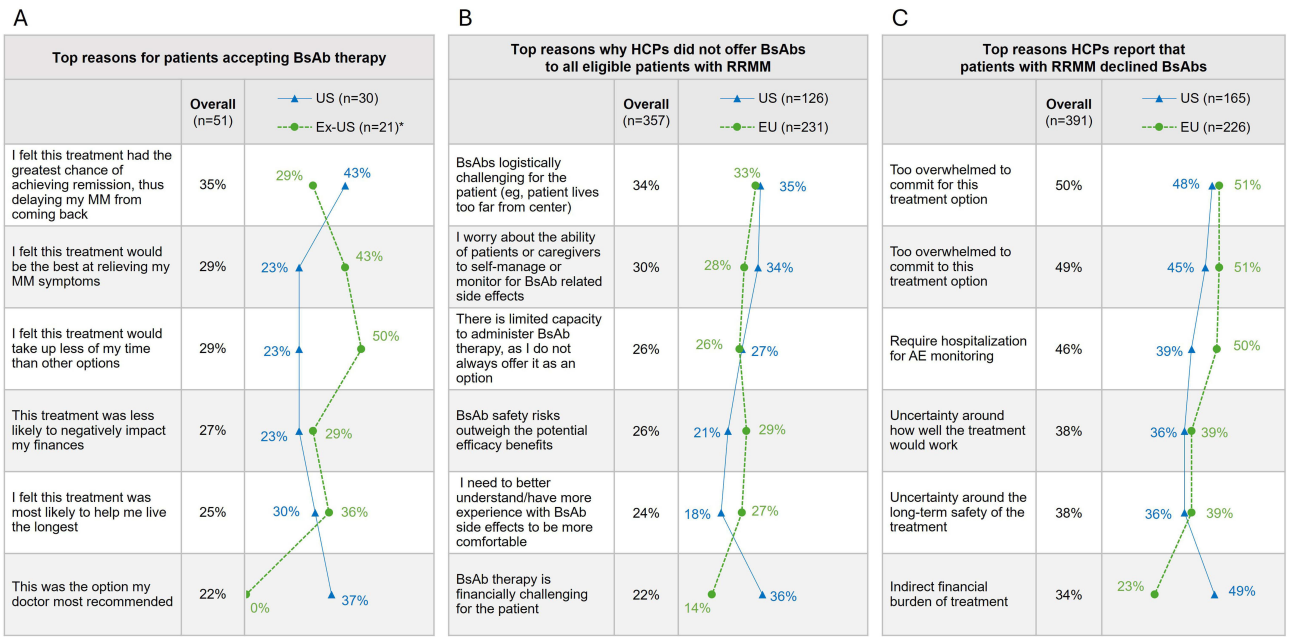

Figure 5 (**A**) Reasons why patients accepted BsAb therapy. (**B**) Reasons why HCPs did not offer BsAbs to all eligible patients with RRMM. (**C**) Reasons why patients declined BsAb therapy.
Notes: *Ex-US includes patients from Japan (n=7) and Europe (n=14); EU includes France, Germany, Italy, Spain, and the UK.
Abbreviations: AE, adverse event; BsAb, bispecific antibody; EU, Europe; HCP, healthcare provider; RRMM, relapsed/refractory multiple myeloma.

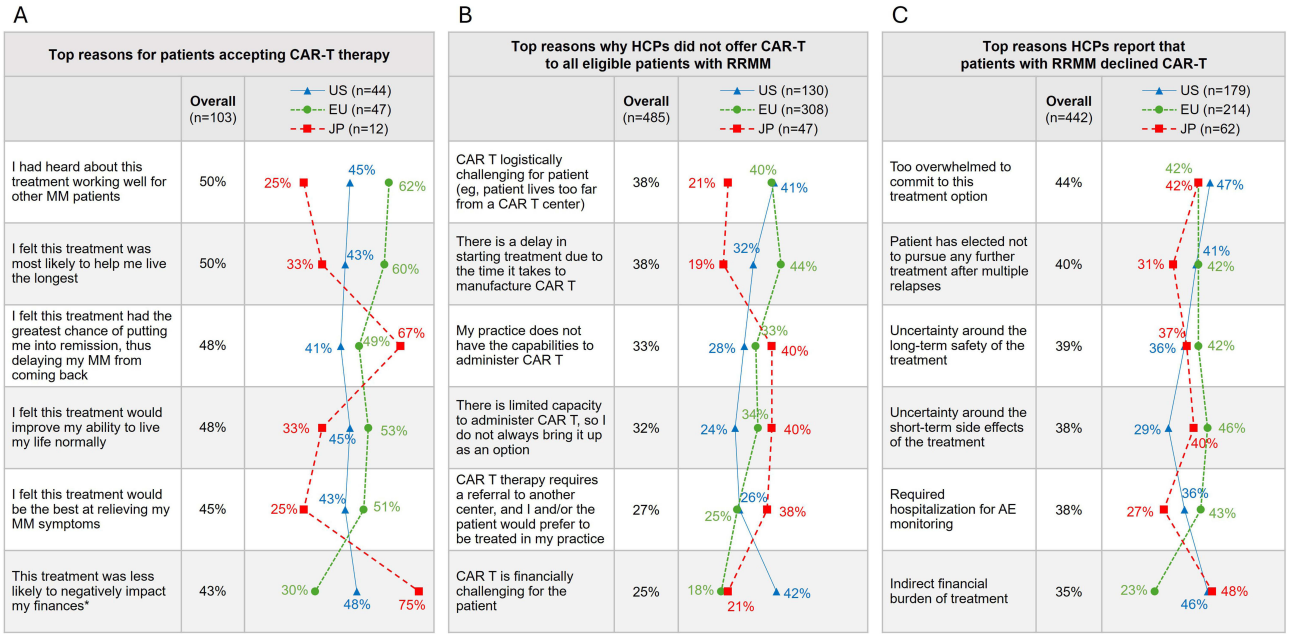

Figure 6 (**A**) Reasons why patients accepted CAR-T therapy. (**B**) Reasons why HCPs did not offer CAR-T therapy to all eligible patients with RRMM. (**C**) Reasons why patients declined CAR-T therapy.
Notes: *For example, due to the cost of treatment and medical care, travel, missed work, childcare, and hospitalization. EU includes France, Germany, Italy, Spain, and the UK.
Abbreviations: AE, adverse event; CAR-T, chimeric antigen receptor T cell; EU, Europe; HCP, healthcare provider; JP, Japan; RRMM, relapsed/refractory multiple myeloma.

presents challenges; BsAb: 34%, CAR-T: 38%). Other reasons specific to CAR-T therapy include the delay in starting treatment due to manufacturing (38%), their practice lacking the capability to administer (33%), and limited capacity to administer (32%; Figure 6B). Other common reasons not to offer BsAbs included worry about patient ability to monitor AEs (30%) and perceptions that safety risks outweigh potential benefits (26%; Figure 5B).

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When HCPs were asked what they thought the predominant reasons were for their patients declining novel treatments (CAR-T and BsAb), the survey reported the following: patients were too overwhelmed to commit to a new treatment (44% and 50%), patients elected not to pursue further treatment after multiple relapses (40% and 49%), patients were deterred by hospitalization requirements (38% and 46%), and patients felt uncertain about how effective treatment would be (33% and 38%; Figures 5C and 6C). While patients had similar reasons for declining treatment, they also stated that they were concerned about the long-term safety or cost of novel treatment or would prefer to wait for their HCP or other patients to have more experience with the treatment (Supplementary Tables 4 and 5).

Discussion

This is the first large-scale survey study that directly compared perspectives of RRMM-treating HCPs and patients with RRMM to understand their preferences on treatment priorities, decision-making, and attitudes toward novel therapies across different regions, age groups, ethnicities, and lines of treatment through 2 complementary surveys. Patients with RRMM and HCPs were seen to have disparate priorities when it came to their treatment decision-making processes. These findings are consistent with previous reports of patients placing greater importance on minimizing side effects, extending life, preventing disease progression, and maintaining QoL, compared with HCP priorities.[16–18] Similarly, in a previous discrete-choice and swing rating experiment study in Europe, QoL attributes affecting a patient's physical, mental, social and psychological health were considered very important, next to life expectancy.[19] Patients needed to consider the balance between a treatment extending life expectancy and maintaining QoL, and between their physical and mental well-being, with their priorities depending on multiple factors. Managing the financial burden associated with treatment cost and treatment logistics was also a key consideration for patients, reflecting findings from an earlier study.[17] In contrast, HCPs were more focused on efficacy outcomes, including prolonging survival and controlling disease, particularly in patients currently receiving 2L treatment since they are more likely to respond to treatment than patients receiving later lines of therapy.[20] HCPs also emphasized maintaining QoL for their patients. These findings are aligned with a discrete-choice experiment study in the US that explored hemato-oncologist treatment decisions and the trade-offs they make when selecting the next line of therapy.[9] Efficacy, particularly overall survival, and durability were key considerations across all lines of therapy in these studies; however, QoL was only regarded in the top 10 most frequent factors for the fourth line of treatment.[9]

In addition, a significant portion of patients with RRMM in this study (Supplementary Figure 1) reported that their treatment experience was worse than they had expected prior to initiation. Based on the study findings, over 80% of patients with RRMM (regardless of being treated in academic or community settings) want to be directly involved in the decision-making process when new treatment options are selected. The current findings generally point to a gap in patient-HCP communication and subsequent treatment execution, highlighting an area in which RRMM patient care and management could be improved. To address this, improving HCP awareness of patient preference and encouraging patients to be active participants in their care decisions will provide HCPs the information needed to guide treatment decisions based on patient preference. HCPs can address this in part by asking patients the right questions and providing them with relevant information in the form of leaflets and other educational resources so that they can make informed decisions. To help in the shared decision-making process, HCPs should engage with their patients to address their concerns about treatment, side effects, impact on QoL, and financial considerations. Through continued communication and engagement with their patients, HCPs will gain further insights into patient preference, fostering a stronger HCP-patient relationship and potentially leading to better outcomes. Developing expertise in non-CoE/community hospitals and partnering with patient advocacy groups will be the key to expanding and raising awareness of treatment options to patients who may be underserved by their local care setting. Potential strategies could include resident-in-training opportunities at academic centers or engaging with RRMM experts at society conferences or local meetings.

Perspective on Managing AEs

Despite clear differences in treatment decision-making priorities, HCPs and patients agreed on the importance of limiting treatment-related side effects, a view that was upheld across all regions and patient segments. However, there was a divergence on the most challenging side effects. Patients were more concerned about bone-related side effects,

thrombocytopenia, and neutropenia. In contrast, HCPs viewed neuropathy and cytokine release syndrome as more challenging than patients did. Literature also highlights these differing concerns, with patients also worrying about kidney effects, while HCPs were additionally concerned about low white blood cell counts indicative of leukemia.[16,17,21] Furthermore, patients often perceived side effects as more severe than their treating HCPs did, as reflected by higher reporting rates among patients. This highlights the difficulty in quantifying the impact of AEs where there may be a disconnect between HCPs and patient perception of subjective symptoms.

There may be technological solutions that can improve the quality of care that patients with RRMM receive, especially related to AE communications and management, as well as part of the treatment decision-making process. Advancements in mobile and AI platforms can allow for easier communications between HCPs, patients, and caregiver/family members to report AEs, access clinical care, and support HCP-patient knowledge sharing.[22]

Novel Therapy Summary

There is potential for BsAbs and CAR-T therapies to be appealing treatment options for ≥3L patients with RRMM,[23,24] but generally patient awareness of these therapies remains limited, with US patients being the most informed compared with those in Europe and Japan. This discrepancy predominantly occurred among HCPs in community settings, who were not always confident in identifying eligible patients with RRMM or were unfamiliar with CAR-T therapy or BsAbs compared with HCPs at academic centers. However, we expect this trend to change in time as HCPs become more experienced using these novel therapies. A recent study reported similar findings between community and academic centers, identifying community HCP lack of experience and limited access to treatment as 2 of the biggest barriers to patient treatment with these novel therapies.[25] Consequently, the number of community HCPs offering novel therapies was low across all regions and lines of therapy. In contrast to a recent study by Hydren et al,[26] the overall familiarity with BsAbs among patients was seen to lag behind that of CAR-T. However, HCPs reported being equally confident in managing both BsAbs and CAR-T therapy. This educational gap between centers underscores the need for improved education for both patients and HCPs regarding available therapies and improved communication from community HCPs to fully understand patient concerns and ability to manage the burden of novel treatments. Additionally, greater involvement of community centers in clinical trials and a better understanding of inclusion criteria are crucial to addressing the enrollment disparities observed between community and academic centers.[27] Globally, patients were more likely to request CAR-T therapy than BsAbs when discussing treatment options with HCPs, with greater awareness observed in the US. Similar to other studies, when CAR-T therapy was offered to patients, approximately 75% of those eligible ultimately received the treatment.[26] In contrast, BsAbs lag behind, with only 50-60% of patients offered BsAb therapy eventually receiving it. Possible reasons underlying this could include lack of access (including resourcing restrictions [limited infusion capacity], administration issues, and therapy approvals).[25] In addition, a survey of blinatumomab use cited lack of therapy familiarity, transitioning patients from in- to outpatient care, cost, and managing AEs as barriers to uptake of this early BsAb.[28] In the US, non-White patients were less likely to be offered BsAbs or CAR-T therapy compared with their White counterparts. This disparity may be partially explained by the statistically lower socioeconomic status of non-White patients, their limited ability to afford healthcare, and reduced access to MM specialists, as observed in the current study.

Additionally, as noted in other studies, factors contributing to the lower uptake of CAR-T therapy include the financial burden on patients and the need for clear guidance on the treatment pathway for ≥3L patients.[29] To reduce the logistical burden on patients considering these novel therapies, support programs should consider offering transportation, streamlining outpatient or hospital visits, and providing training, support, and patient-friendly equipment to allow patients to adopt remote monitoring. The requirements for novel therapies such as BsAbs and CAR-T therapy pose significant challenges and often deter some HCPs from pursuing these treatments. The main reasons why HCPs did not offer BsAb treatment included logistical challenges (including distance from administering center and dosing schedule), lack of monitoring for AEs, and insufficient experience in managing these AEs. HCPs not offering treatments based on a patient's ability to monitor AEs without first discussing a monitoring plan could be considered biased. Such a bias may need to be addressed if patients are to receive optimal care. CAR-T therapy uptake faces similar challenges as BsAbs among patients and HCPs but also involves additional complexities, such as the logistics of manufacturing and the need

for referrals to other institutions. Patients often declined CAR-T treatment primarily due to long-term safety concerns, logistical challenges, cost, and HCP experience managing therapy.[29] These points highlight educational and logistical gaps that can be addressed through adequate patient and HCP education/training on the safe administration and use of these therapies and through adoption of these therapies by community hospitals to improve patient access.[30]

Strengths and Limitations

Strengths of this study include its global reach and relatively large sample size, which enhance the generalizability of the findings. Compared with other data collection methods, such as clinical trials, the survey method facilitated a much faster turnaround time, thereby reducing the lag between data collection and the implementation of potential resulting actions. The web-based quantitative survey approach provided a standardized method of data collection, ensuring consistency in both the questions posed and the responses received, without the need for human facilitation. Additionally, the anonymity offered by the survey encouraged candid responses to potentially sensitive topics.

Some limitations to this study exist. Convenience sampling may have introduced selection bias, favoring participants who were already part of study panels or more actively involved in the MM community, thereby influencing the findings. To mitigate these limitations, future recruitment through MM doctors to their patient populations could help reach a broader set of patients with MM. Additionally, survey responses may be subject to various biases, such as recall bias, nonresponse bias, and technological literacy bias. Furthermore, as this was a noninterventional study, there was no experimental control group or randomization of patients to HCPs, limiting the ability to establish causal links. Finally, the survey was not designed to determine patient experience in relation to cultural differences.

Conclusions

This study has highlighted a significant disparity in HCP and patient preferences related to RRMM treatment decision-making, with patients valuing QoL and AE management and HCPs prioritizing treatment efficacy and delaying progression to the next treatment. There is a sizable educational gap with respect to novel treatments between HCPs and patients and within regions and age groups. For optimal use of these therapies, there is a need to train HCPs in shared decision-making, which includes actively listening to patients and asking the right questions to provide the necessary information for informed decisions. There is also a need to train HCPs in the community setting on the eligibility of patients for novel treatments, as well as how to initiate, monitor, and manage these therapies in patients with RRMM, through traditional educational means, preceptorships, and expert meetings. Additionally, there is a need for HCPs and patient advocacy groups to educate patients and present them with all the treatment options available in their region. Fostering a more cohesive dialogue with patients about their priorities can increase the likelihood of informed personalized decision-making on conventional and novel treatment options, improving patient compliance, outcomes, and expectations of care.

Data Sharing Statement

Upon request, and subject to review, Pfizer will provide the data that support the findings of this study. Subject to certain criteria, conditions, and exceptions, Pfizer may also provide access to the related individual de-identified patient data. See https://www.pfizer.com/science/clinical-trials/trial-data-and-results for more information.

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