

Teclistamab Improves Patient-Reported Symptoms and Health-Related Quality of Life in Relapsed or Refractory Multiple Myeloma: Results From the Phase II MajesTEC-1 Study

Thomas G. Martin,¹ Philippe Moreau,² Saad Z. Usmani,³ Alfred Garfall,⁴ María-Victoria Mateos,⁵ Jesús F. San-Miguel,⁶ Albert Oriol,⁷ Ajay K. Nooka,⁸ Laura Rosinol,⁹ Ajai Chari,¹⁰ Lionel Karlin,¹¹ Amrita Krishnan,¹² Nizar Bahlis,¹³ Rakesh Popat,¹⁴ Britta Besemer,¹⁵ Joaquín Martínez-López,¹⁶ Michel Delforge,¹⁷ Danielle Trancucci,¹⁸ Lixia Pei,¹⁸ Rachel Kobos,¹⁸ John Fastenau,¹⁸ Katharine S. Gries,¹⁸ Niels W.C.J. van de Donk¹⁹

Abstract

Patients with relapsed/refractory multiple myeloma (RRMM) typically report poor health-related quality of life (HRQoL), which deteriorates as they progress through multiple lines of therapy. This study provides HRQoL data in patients with RRMM who received teclistamab in MajesTEC-1, including improvements in pain, global health status, and emotional functioning. These results support teclistamab as a promising treatment option in this population.

Introduction: Patients with relapsed or refractory multiple myeloma (RRMM) report significantly lower HRQoL compared with patients with newly diagnosed MM and experience further deterioration in HRQoL with each relapse and subsequent treatment. Therefore, consideration of the impact of treatment on HRQoL in addition to clinical outcomes is vital. **Patients and Methods:** In the phase I/II MajesTEC-1 (NCT03145181, NCT04557098) study, patients with RRMM who received teclistamab, an off-the-shelf, T-cell redirecting BCMA × CD3 bispecific antibody, had deep and durable responses with manageable safety. HRQoL was assessed using the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30-item and the EuroQol 5 Dimension 5 Level descriptive questionnaire. Changes over time from baseline were measured with a repeated measures mixed-effects model. Proportions of patients with clinically meaningful improvement after starting treatment and time to clinically meaningful worsening were assessed. **Results:** Compliance was maintained throughout the study. Compared with baseline, positive changes were observed for pain, global health status, and emotional functioning with treatment; other assessments were largely unchanged from baseline. Post hoc analysis showed patients with deeper clinical response generally reported improved

¹University of California San Francisco, San Francisco, CA

²Hematology Clinic, University Hospital Hôtel-Dieu, Nantes, France

³Levine Cancer Institute/Atrium Health, Charlotte, NC

⁴Abramson Cancer Center, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

⁵University Hospital of Salamanca/IBSAL/CIC/CIBERONC, Salamanca, Spain

⁶Clínica Universidad de Navarra (CCUN), CIMA, CIBERONC, IDISNA, Pamplona, Spain

⁷Institut Català d'Oncologia and Institut Josep Carreras, Hospital Germans Trias i Pujol, Badalona, Barcelona, Spain

⁸Winship Cancer Institute, Emory University, Atlanta, GA

⁹Hospital Clínic, IDIBAPS, University of Barcelona, Barcelona, Spain

¹⁰Mount Sinai School of Medicine, New York, NY

¹¹Service d'Hématologie Clinique, Centre Hospitalier Lyon Sud, Pierre-Bénite, France

¹²City of Hope Comprehensive Cancer Center, Duarte, CA

¹³Arnie Charbonneau Cancer Institute, University of Calgary, Calgary, AB, Canada

¹⁴University College London Hospitals, NHS Foundation Trust, London, UK

¹⁵University of Tuebingen, Tuebingen, Germany

¹⁶Haematological Malignancies Clinical Research Unit, Hospital 12 de Octubre Universidad Complutense, CNIO, CIBERONC, Madrid, Spain

¹⁷Universitaire Ziekenhuizen Leuven, Leuven, Belgium

¹⁸Janssen Research & Development, Raritan, NJ

¹⁹Amsterdam University Medical Center, Vrije Universiteit Amsterdam, Amsterdam, The Netherlands

Submitted: Sep 1, 2023; Accepted: Nov 9, 2023; Epub: 14 November 2023

Address for correspondence: Thomas G. Martin, MD, Division of Hematology/Oncology, 400 Parnassus Ave, 4th Floor, San Francisco, CA 94143
E-mail contact: Tom.Martin@ucsf.edu

2152-2650/\$ - see front matter © 2024 The Authors. Published by Elsevier Inc.

This is an open access article under the CC BY license

(<http://creativecommons.org/licenses/by/4.0/>)

<https://doi.org/10.1016/j.clml.2023.11.001>

HRQoL outcomes. Following an initial decline in HRQoL in some scales, the proportion of patients reporting clinically meaningful improvements increased, while the proportion reporting clinically meaningful worsening decreased over time. Clinically meaningful improvements in pain were reported in $\geq 40\%$ of patients at most assessment time points.

Conclusions: These results complement previously reported clinical benefits and support teclistamab as a promising therapeutic option for patients with RRMM.

Clinical Lymphoma, Myeloma and Leukemia, Vol. 24, No. 3, 194–202 © 2024 The Authors. Published by Elsevier Inc.

This is an open access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>)

Keywords: B-cell maturation antigen, Bispecific antibody, EORTC QLQ-C30, EQ-5D-5L, Patient-reported outcomes

Introduction

Multiple myeloma (MM), a plasma cell cancer in the bone marrow, is associated with burdensome symptoms (eg, pain and fatigue) that diminish patients' ability to function and adversely impact their overall health-related quality of life (HRQoL).¹⁻³ Despite recent advances in the treatment of MM with proteasome inhibitors (PIs), immunomodulatory drugs (IMiDs), and monoclonal antibodies (mAbs),^{4,5} patients eventually relapse and often develop disease that is resistant to these agents.⁶⁻⁸ Patients who are refractory to multiple lines of therapy have limited treatment options and poor prognoses,^{6,9} and they experience further deterioration in HRQoL with each additional line of therapy.¹⁰ Patients with relapsed or refractory MM (RRMM) tend to report significantly lower HRQoL scores and report poorer appetite and more severe fatigue when compared with patients who have not yet developed RRMM.¹¹ Evidence has shown that most treatment options for patients with RRMM at best maintain, rather than improve, HRQoL and delay, rather than eliminate, symptom deterioration in this population.¹² Thus, as novel therapies are developed for patients with RRMM, it is important to consider treatment effects on patient-reported outcomes (PROs), in addition to standard clinical efficacy measures.

Teclistamab is the only approved B-cell maturation antigen (BCMA) \times CD3 bispecific antibody with a personalized, weight-based dosing schedule for the treatment of triple-class-exposed RRMM.¹³ In the first-in-human, phase I/II, single-arm MajesTEC-1 study, teclistamab was clinically manageable with substantial efficacy in patients with RRMM previously treated with at least 3 lines of therapy (including a PI, an IMiD, and an anti-CD38 mAb).^{14,15} Among 165 patients treated with the recommended phase II dose (RP2D) of teclistamab 1.5 mg/kg in phase I and phase II at a median follow-up of 14.1 months, the overall response rate (ORR) was 63%, median duration of response was 18.4 months, and median progression-free survival was 11.3 months.¹⁵ Based on these results, teclistamab was approved for the treatment of patients with RRMM by the European Medicines Agency as monotherapy for those who have received ≥ 3 prior therapies and who progressed on the last therapy,¹⁶ and it was approved by the U.S. Food and Drug Administration for treatment in patients with RRMM who have received 4 prior lines of therapy.¹⁷ Under both approvals, patients must have been treated previously with a PI, an IMiD, and an anti-CD38 mAb. Here, we report the on-treatment PROs from the MajesTEC-1 study in patients with RRMM treated with teclistamab at the RP2D.

Patients and Methods

Study Design and Patients

The study design and methods of the MajesTEC-1 study have been published.¹⁴ Briefly, this was an open-label, multicenter, phase I (NCT03145181) and phase II (NCT04557098) study in patients with RRMM. In phase II, patients received the RP2D of teclistamab (weekly subcutaneous dose of 1.5 mg/kg preceded by step-up doses of 0.06 and 0.3 mg/kg). Eligible patients were adults with a diagnosis of RRMM; progressive, measurable disease per International Myeloma Working Group (IMWG) criteria¹⁸; and an Eastern Cooperative Oncology Group performance status of 0 or 1. Patients must have also received ≥ 3 prior lines of therapy, including a PI, an IMiD, and an anti-CD38 mAb. Patients who had received prior BCMA-targeted therapy were not eligible. The study was conducted in accordance with the Declaration of Helsinki and Good Clinical Practice guidelines. The protocol and other relevant documents were approved by the institutional review boards of all participating institutions. All patients provided written informed consent.

Assessment of Patient-Reported Outcomes

PRO instruments included the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30 item (EORTC QLQ-C30) and the EuroQol 5 Dimension 5 Level (EQ-5D-5L) questionnaire.

The EORTC QLQ-C30 is a cancer-specific questionnaire with a 1-week recall period that consists of 30 items across 5 functional scales (physical, role, emotional, cognitive, and social), 1 global health status (GHS) scale, and several single items (eg, fatigue, nausea and vomiting, pain, appetite loss, constipation, and diarrhea).¹⁹ All scale and item scores were linearly transformed to a 0 to 100 scale according to the algorithm in the EORTC QLQ-C30 scoring manual version 3.0.²⁰ For symptom-oriented scales, higher scores correspond with worse symptom severity. Conversely, for the GHS and functional scales, higher scores represent better GHS and level of functioning. The reliability, validity, and clinically meaningful change threshold (≥ 10 points) for the EORTC QLQ-C30 have been demonstrated in patients with MM.²¹⁻²³ The EQ-5D-5L assesses generic health status on 5 dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and includes a visual analogue scale (VAS) wherein respondents rate their overall health on that day on a scale of 0 to 100, with scores ranging from 0 (worst imaginable health state) to 100 (best imaginable health state).²⁴

Results From the Phase II MajesTEC-1 Study

Patients within the all-treated population and who were enrolled in phase II of the study were analyzed for PRO compliance and assessments, provided they had available PRO data. Patients completed both PRO assessments during site visits through use of on-site tablets at screening and on day 1 of every other treatment cycle (28 days/cycle) while on treatment. PROs were not collected from patients enrolled in phase I of the study.

Statistical Analyses

The primary endpoint (ORR per IMWG criteria^{18,25}) was analyzed in all patients who had received at least 1 dose of teclistamab at the RP2D in phase I or phase II as of September 7, 2021. Compliance rates for PRO assessments, descriptive mean values at each time point, and time-to-event analyses were calculated using the efficacy analysis population, which was predefined to include all patients enrolled in phase II who had received their first dose of teclistamab on or before March 18, 2021. Analyses of longitudinal change and regression models for PROs was performed on the all-treated population and included all patients with a baseline PRO assessment and who had received 1 postbaseline assessment. These analyses were based on a clinical cut-off date of March 16, 2022.

Change from baseline in patient-reported overall symptoms, functioning, and HRQoL were secondary endpoints of the phase II part of the study. There was no imputation of missing data. No adjustments for multiplicity were made, as these analyses were not part of the statistical hierarchy, and no *P*-values are presented. Descriptive statistics were used as appropriate: number and percentage were used to report categorical variables, with means, medians, and ranges used to report continuous variables. Compliance rates for completion of PROs were calculated as the number of assessments received divided by the number of assessments expected (number of patients on treatment) at each time point. Changes from baseline in the EORTC QLQ-C30 scales and the EQ-5D-5L VAS were fitted to a mixed-effects repeated measures model that included patient as a random effect, and baseline PRO value and time as fixed effects. Post hoc analyses based on depth of patient response to teclistamab (complete response or better [\geq CR], very good partial response [VGPR], and partial response [PR]) were also conducted. Results are presented as least-squares (LS) means with 95% CIs.

The proportions of patients with clinically meaningful improvement or worsening at any time on study treatment were calculated using thresholds that were defined a priori and based on the published literature: change ≥ 10 points for the EORTC QLQ-C30 scales^{26,27} and ≥ 7 points for the EQ-5D-5L VAS.²⁸

The median time to meaningful worsening was calculated using the Kaplan-Meier method; for this analysis, worsening was defined using a distribution-based meaningful change threshold defined as at least one half of 1 standard deviation from baseline. Death due to disease progression was included as worsening. Patients who had not met the definition of worsening were censored at the last PRO assessment.

Results

Patient Characteristics and Compliance With PROs

In total, 165 patients were treated with teclistamab at the RP2D in phase I and phase II; all 125 patients enrolled in phase II provided

PRO data for analyses. Among all 165 patients, the median duration of treatment was 8.5 months (range, 0.2-24.4). The median age was 64 years (range, 33-83), and 56% of patients were male (Table 1). Patients had previously received a median of 5 prior lines of therapy (range, 2-14). Mean EORTC QLQ-C30 values at baseline reflected the poor overall GHS in this RRMM population, with the greatest impacts in role and physical functioning and symptoms of pain and fatigue (Table 1).

Compliance rates for all patients who provided PRO assessments ($n = 125$) were 83% at baseline for the EORTC QLQ-C30 and 77% for the EQ-5D-5L and were similar through cycle 8 ($\geq 77\%$). The most common specified reasons given for not completing the PRO instruments at baseline were technical failure ($n = 4$), questionnaire not returned ($n = 3$), no questionnaire translation ($n = 2$), and patient refusal to complete the questionnaire ($n = 2$), while none of the patients reported that they were too ill to complete the questionnaires.

Change in PROs During Treatment

Treatment with teclistamab was associated with a reduction in symptoms and a sustained improvement in overall HRQoL. Pain scores improved as early as cycle 2 and showed meaningful improvement (95% CIs for LS mean change did not include 0) at cycles 4 through 12 (Figure 1A). Fatigue initially worsened but returned to near-baseline levels for cycles 4, 6, and 8 before showing a trend toward improvement for cycles 10 and 12 (Figure 1B). Symptoms of nausea and vomiting worsened from baseline at cycle 2 but showed little change from baseline from cycle 4 onward (Figure 1C). Average EORTC QLQ-30 GHS scores improved from baseline at cycles 4, 6, 8, 10, and 12 (Figure 1D). LS mean change in EQ-5D-5L VAS showed improvement from cycle 4 through cycle 12 (Figure 1E). A post hoc subgroup analysis based on depth of patient response to teclistamab (\geq CR or VGPR and PR) was also conducted. Results from this analysis of patients with stable disease or minimal response are not shown due to low patient numbers beyond cycle 4 of treatment. The analysis of patients with \geq CR compared with VGPR and PR showed that patients with \geq CR generally reported improved HRQoL compared with those with VGPR and PR (Supplemental Figure 1A–1E).

Emotional functioning scores improved from baseline at all time points (Supplemental Figure 2A). Physical functioning scores initially worsened from baseline at the beginning of cycle 2 but showed a trend for improvement by cycle 8 (Supplemental Figure 2B). Role functioning scores initially worsened from baseline at cycle 2 but showed a trend toward improvement by cycle 6 (Supplemental Figure 2C). Cognitive and social functioning scores showed little change during the study (Supplemental Figure 2D and E). Similar trends were observed across subgroups with patients reaching \geq CR, VGPR, or PR, showing trend for improvement in emotional, physical, and role functioning (Supplemental Figure 3A–C), and little change from baseline in cognitive and social functioning (Supplemental Figure 3D and E).

A sensitivity analysis that included 8.7 additional months of follow-up revealed no change in the overall results in terms of changes from baseline during treatment (data not shown).

Table 1 Patient Characteristics and EORTC QLQ-C30 and EQ-5D-5L Scores at Baseline.

Characteristic	All Treated Population (N = 125)
Age, years	
Median (range)	64.0 (33-83)
≥ 75, n (%)	19 (15.2)
Male, n (%)	70 (56.0)
Race, n (%)	
White	100 (80.0)
Black or African American	20 (16.0)
Asian	3 (2.4)
Multiple or other	2 (1.6)
ECOG performance status, n (%)	
0	38 (30.4)
≥ 1 ^a	87 (69.6)
Years from MM diagnosis to first dose, median (range)	6.2 (0.9-22.7)
No. of prior lines of therapy for MM, median (range)	5.0 (2-14)
Triple-class ^b exposed, n (%)	125 (100)
Penta-drug ^c exposed, n (%)	90 (72.0)
Triple-class ^b refractory, n (%)	96 (76.8)
Penta-drug ^c refractory, n (%)	34 (27.2)
	Efficacy population (n = 125)
EORTC QLQ-C30 score, mean (SD) ^d	n = 104
GHS	58.3 (25.0)
Physical functioning	71.5 (20.9)
Role functioning	66.5 (29.6)
Emotional functioning	72.6 (20.3)
Cognitive functioning	84.5 (17.6)
Social functioning	74.2 (23.7)
Pain	43.3 (32.1)
Fatigue	39.9 (25.1)
Nausea and vomiting	4.3 (9.9)
Dyspnea	22.1 (24.8)
Sleep disturbance	30.1 (29.6)
Constipation	18.3 (27.0)
Appetite loss	16.7 (27.5)
Diarrhea	12.8 (21.9)
Financial difficulties	13.1 (25.2)
EQ-5D-5L score, mean (SD) ^e	n = 96
VAS	61.8 (23.0)

Abbreviations: ECOG = Eastern Cooperative Oncology Group; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30 item; EQ-5D-5L = EuroQol 5 Dimension 5 Level; GHS = global health status; IMiD = immunomodulatory drug; MM = multiple myeloma; PI = proteasome inhibitor; SD = standard deviation; VAS = visual analogue scale.

^a One patient had ECOG performance status of 3 at screening.

^b Triple-class was defined as ≥ 1 PI, ≥ 1 ImiD, and 1 anti-CD38 antibody.

^c Penta-drug was defined as ≥ 2 Pis, ≥ 2 ImiDs, and 1 anti-CD38 antibody.

^d EORTC QLQ-C30 scores range from 0 to 100; higher scores indicate better health on the GHS, better function on the functional scales, and greater symptom severity on the symptom scales.

^e EQ-5D-5L scores range from 0 to 100; higher scores represent better patient-evaluated health status.

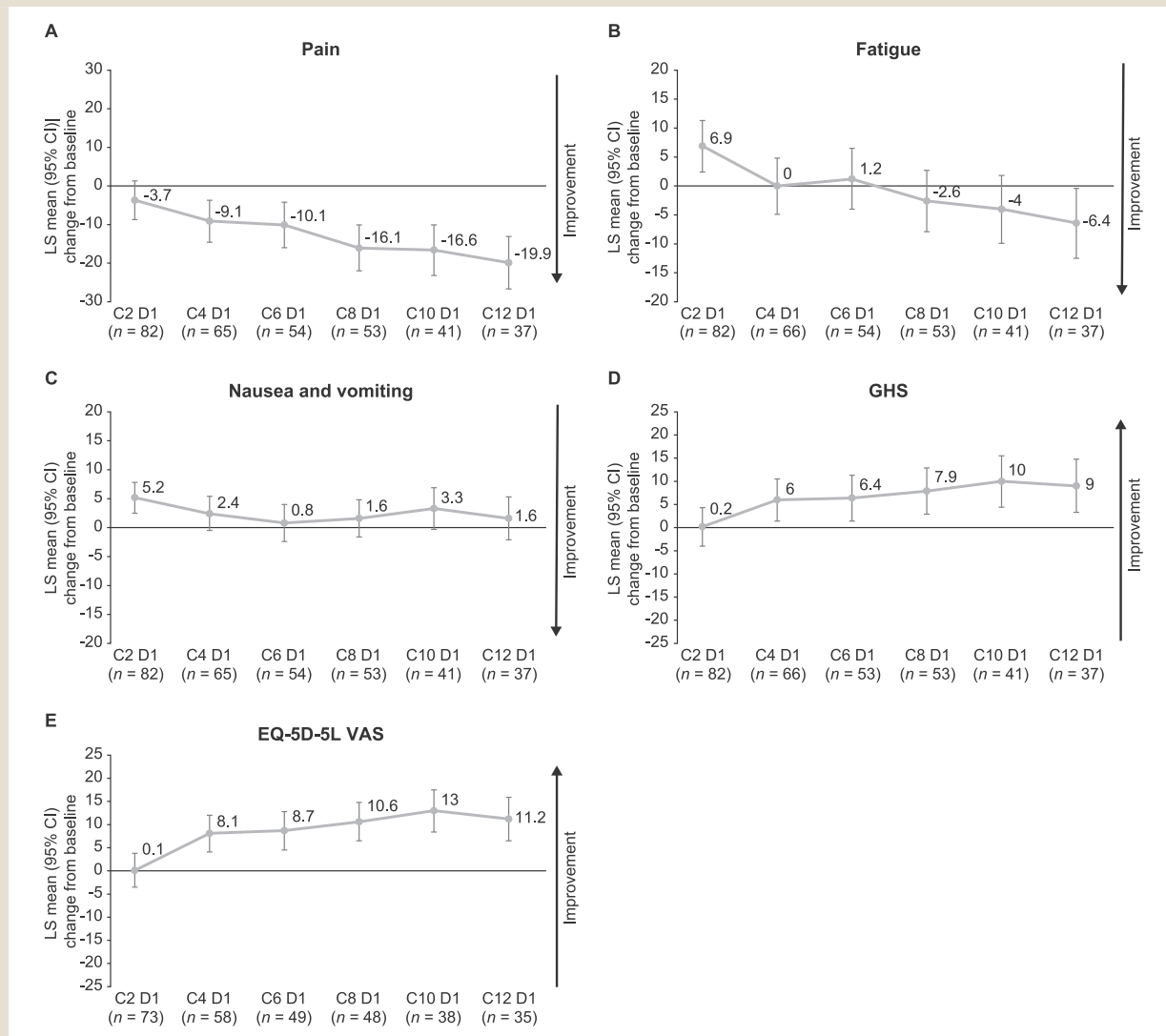
Proportion of Patients With Meaningful Changes From Baseline

The proportion of patients reporting clinically meaningful improvements generally increased over time for all scales of the EORTC QLQ-C30 and the EQ-5D-5L VAS scores (Figure 2).

Meaningful improvements in pain and fatigue were reported by more than a third of patients at cycles 4 through 12, with approximately 50% of patients reporting clinically meaningful improvement at cycle 12. Meaningful improvement in nausea and vomiting was reported by 8% of patients at cycle 12 (Figure 2A). The

Results From the Phase II MajesTEC-1 Study

Figure 1 Change from baseline in EORTC QLQ-C30 (A) pain, (B) fatigue, (C) nausea and vomiting, (D) GHS, and (E) EQ-5D-5L VAS scores. Values are LS mean changes from a mixed-effects model for repeated measures. C = cycle; D = day; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30 item; EQ-5D-5L VAS = EuroQol 5 Dimension 5 Level visual analogue scale; GHS = global health status; LS = least squares.



proportion of patients reporting meaningful improvement in GHS and functioning increased over time, with 49% of patients reporting meaningful improvement in GHS at cycle 12 (Figure 2B). Changes in the EQ-5D-5L VAS score showed improvement in general health at cycles 2 through 12, with more than 50% of patients reporting overall improvement from cycle 10 onward (Figure 2C).

The proportion of patients reporting clinically meaningful worsening generally decreased over time for all scales of the EORTC QLQ-C30 and the EQ-5D-5L VAS scores (data not shown). Less than 40% of patients reported clinically meaningful worsening in pain and nausea and vomiting at all assessment time points, and <50% in fatigue at cycles 4 through 12. At cycle 12, <25% of patients reported clinically meaningful worsening in pain, fatigue, and nausea and vomiting. Assessment of worsening change on the

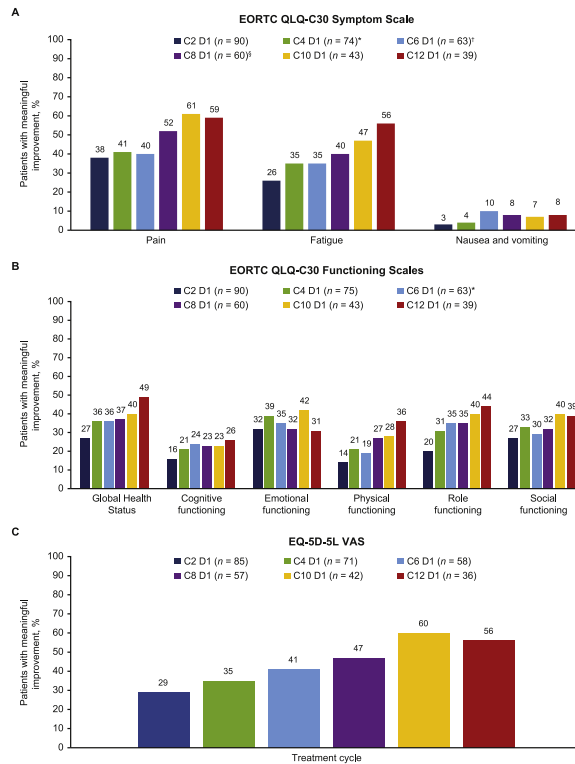
EORTC QLQ-C30 scale showed fewer patients reported worsening from cycles 2 to 12 across all items, except emotional functioning, which was reported in approximately 60% to 70% of patients at cycles 2 through 12. The proportion of patients who reported clinically meaningful worsening in EQ-5D-5L VAS score declined over time as patients remained on treatment.

Among patients reporting meaningful worsening at any time point, the median time to a first report of meaningful worsening ranged from 2.6 months (role functioning) to 13.1 months (emotional functioning) (Supplemental Table 1).

Discussion

As survival outcomes in patients with MM improve, it is increasingly important to evaluate the impact of treatment on

Figure 2 Percentage of patients who achieved meaningful improvement from baseline in EORTC QLQ-C30 (A) symptom, (B) functioning scales, and (C) EQ-5D-5L VAS based on a literature-defined threshold. Meaningful improvement was defined as a ≥ 10 -point decrease from baseline for symptom scales and ≥ 10 -point increase from baseline for functioning scales and ≥ 7 points for the EQ-5D-5L VAS. C = cycle; D = day; EORTC QLQ-C30 = European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire core 30 item; EQ-5D-5L VAS = EuroQol 5 Dimension 5 Level visual analogue scale. (A) ^an = 75 for fatigue. ^bn = 62 for pain. ^cn = 58 for pain. (B) ^an = 62 for global health status.



patients' symptom burden and HRQoL.²⁹⁻³¹ Patients enrolled in the MajesTEC-1 study with heavily pretreated RRMM experienced early and sustained clinically meaningful improvements in patient-reported overall symptoms, functioning, and HRQoL during teclistamab treatment, alongside early, deep, and durable clinical responses with an ORR of 63%. Patients had improvements in mean EORTC QLQ-C30 pain and GHS scores and in mean EQ-5D-5L VAS scores from baseline by the beginning of cycle 4 through cycle 12, with improvements seen over time, supporting the benefit of teclistamab in this patient population. Additionally, post hoc analyses of PROs based on depth of response showed patients in the \geq CR subgroup had better HRQoL outcomes, supporting the importance of achieving a deep clinical response with treatment. Importantly, in this population with severe disease and limited treatment options, approximately 59% of patients reported meaningful improvement in pain and 56% of patients reported meaningful improvement in fatigue by cycle 12. The observed reductions in pain with teclistamab may be particularly meaningful to patients with RRMM, as pain has a substantial impact on overall HRQoL, as

well as physical, social, emotional, and role functioning in patients with MM.^{32,33}

Although 60% to 70% of patients reported worsening in emotional functioning across all cycles, it is notable that 30% to 40% also reported improvement beginning at cycle 2, which was maintained at all later time points. More than 75% of patients with RRMM have reported emotional impacts of RRMM,³⁴ and emotional aspects of HRQoL, such as depression and anxiety, have been associated with increased MM symptom burden.³⁵ Although smaller proportions of patients reported meaningful improvement on functioning scales compared with improvement in symptoms, with 49% reporting meaningful improvement in GHS at cycle 12, improvement in functioning remains a distal concept compared with improvement in symptoms. Additional follow-up is needed to assess the full benefit of meaningful improvement in functional outcomes.

Scores for physical, role, cognitive, and social functioning scales were either largely unchanged from baseline or showed a decline in cycle 2 followed by a trend toward improvement from cycle 4

Results From the Phase II MajesTEC-1 Study

onward. In this heavily pretreated patient population, the observation even of maintenance of baseline HRQoL, without meaningful improvements, can still be viewed as clinically beneficial.

Teclistamab treatment is associated with cytokine release syndrome (CRS), with most CRS events being grade 1 or 2 and occurring during initial step-up doses and the first treatment dose received at the RP2D.¹⁵ Due to this association, patients were hospitalized and monitored for onset of CRS during step-up doses. This hospitalization may have a negative impact on patients' HRQoL, and therefore, may account for the initial decline observed in PROs in some scales in this study. This is supported by the observation that HRQoL was largely stable or improved over the course of treatment following hospitalization.

As with all studies, there are some potential limitations, including that this is an on-treatment analysis with a decreasing patient sample size over time, and that as a single-arm trial, there is no active control arm for direct comparison. Although change from baseline in PROs was a secondary endpoint, statistical analyses were exploratory in nature. There also exists a potential for responder bias in these analyses. A post hoc analysis investigating compliance rates in patients reporting <VGPR or ≥VGPR was carried out; however, small patient numbers in cycles 4 through 12 in patients with <VGPR precluded definitive conclusions regarding responder bias. It is reasonable to assume that response to treatment and symptom resolution would be associated with improvement in HRQoL or that disease progression would be associated with worsening of some PROs.

This analysis also exhibited several strengths in that PROs were prespecified secondary endpoints and were evaluated frequently throughout the trial, and that consistent results were seen between the EORTC QLQ-C30 GHS scale and the EQ-5D-5L VAS scale.

Conclusions

Patients with triple-class exposed RRMM treated with teclistamab reported early and sustained clinically meaningful improvements in disease-related symptoms and HRQoL that were consistent with observed clinical outcomes in MajesTEC-1. In this population with severe disease and limited options, the majority of patients reported meaningful improvements in symptoms, especially pain, for which ≥63% reported meaningful improvements at all time points. These PRO results complement recent clinical data and support the use of teclistamab in patients with RRMM.

Clinical Practice Points

- Patients with relapsed/refractory multiple myeloma (RRMM) typically report poor health-related quality of life (HRQoL) that declines with each relapse and subsequent line of therapy. Treatment options in this heavily-pretreated population are limited and typically maintain rather than improve patients' HRQoL.
- Teclistamab is the only approved BCMA×CD3 bispecific antibody with a personalized weight-based dosing schedule for the treatment of triple-class exposed RRMM. In the phase I/II MajesTEC-1 study, teclistamab elicited deep and durable responses with a low rate of discontinuations due to adverse events.

- Patients' HRQoL was assessed in MajesTEC-1 using 2 validated questionnaires. Improvements from baseline were observed for pain, global health status, and emotional functioning, while other HRQoL domains were unchanged. Over time, the proportion of patients reporting meaningful improvements increased and the proportion reporting meaningful worsening decreased.
- These patient-reported outcomes add to the body of evidence supporting teclistamab as a promising therapy for patients with RRMM and ≥3 prior lines of therapy.

Ethics Statement

Each study site's local independent ethics committee or institutional review board approved the study protocol. The study was conducted in accordance with the principles of the Declaration of Helsinki and the International Conference on Harmonization Good Clinical Practice guidelines.

Patient Consent

All patients provided written informed consent.

Permission to Reproduce Material From Other Sources

Not applicable.

Clinical Trial Registration

ClinicalTrials.gov identifier:NCT03145181, NCT04557098

Data Availability Statement

The data sharing policy of Janssen Pharmaceutical Companies of Johnson & Johnson is available at <https://www.janssen.com/clinicaltrials/transparency>. As noted on this site, requests for access to the study data can be submitted through Yale Open Data Access (YODA) Project site at <http://yoda.yale.edu>.

Disclosure

TGM has served in a consulting/advisory role for Juno Therapeutics and GSK, and has received research funding from Sanofi, Amgen, and Janssen Oncology. PM has served in a consulting/advisory role for Celgene, Janssen, Amgen, GSK, Sanofi, AbbVie, and Oncopeptides, and received honoraria from Celgene, Janssen-Cilag, Amgen, GSK, AbbVie, Sanofi, and Oncopeptides. SZU has served in consulting/advisory role for Celgene, Amgen, Janssen, Seagen, Takeda, GSK, Karyopharm Therapeutics, AbbVie, SkylineDX, Merck, Oncopeptides, Genentech, Gilead Sciences, and BMS/Celgene, has served on speakers' bureaus for Takeda, Amgen, Janssen Oncology, Sanofi, BMS/Celgene, and received research funding from Celgene, Array BioPharma, Janssen Oncology, Pharmacyclics, Sanofi, BMS, Amgen, Seagen, Merck, Skyline Diagnostics, and GSK. AG has served in a consulting/advisory role for Janssen Oncology, GSK, BMS, and Amgen, has patent applications in the field of CAR-T therapy and has stock and other ownership interests in Cabaletta Bio, and has received research funding from Novartis, Tmunity Therapeutics, Inc., Janssen Oncology, and CRISPR Therapeutics. MVM has served in a consulting/advisory role for Takeda, Janssen-Cilag, Celgene, Amgen, AbbVie, GSK, Pfizer, Regeneron, Roche/Genentech, and received

honoraria from Janssen-Cilag, Celgene, Amgen, Takeda, GSK, AbbVie/Genentech, and Sanofi. JSM has served in a consulting/advisory role for Amgen, Celgene, Takeda, BMS, MSD, Novartis, Sanofi, Janssen, Roche, AbbVie, GSK, Karyopharm Therapeutics, Secura Bio, Regeneron, and Haemalogix. AO has served in a consulting/advisory role for Celgene, Janssen, Amgen, Sanofi, and GSK; and served on speakers' bureaus for Amgen and Celgene. AN has served in a consulting/advisory role for Amgen, Janssen Oncology, BMS, GSK, Takeda, Oncopeptides, Karyopharm Therapeutics, Adaptive Biotechnologies, Genzyme, BeyondSpring Pharmaceuticals, Secura Bio, has received travel, accommodations, expenses from GSK, Amgen, Janssen Oncology, BMS/Celgene, GSK, Takeda, Oncopeptides, Karyopharm Therapeutics, Adaptive Biotechnologies, Genzyme, BeyondSpring Pharmaceuticals, and Secura Bio; and has received research funding from Amgen, Janssen Oncology, Takeda, BMS/Celgene, Arch Oncology, and GSK. LR has served in a consulting/advisory role for Janssen-Cilag, Celgene, Amgen, and Sanofi, and has received honoraria from Janssen-Cilag, Celgene, Amgen, Takeda, GSK, and Sanofi. AC has served in a consulting/advisory role for Amgen, Janssen, Seagen, Karyopharm Therapeutics, Genzyme, Oncopeptides, Takeda, Antengene, GSK, Secura Bio, Shattuck Labs, Genentech, AbbVie, and BMS/Celgene, and has received research funding from Celgene, Janssen, Amgen, Seagen, Takeda, and Pharmacyclics. LK has received honoraria from and served in a consulting/advisory role for Amgen, Celgene-BMS, GSK, Janssen, Takeda, Sanofi, and AbbVie, reports employment with Aguetant (immediate family member), and has received travel, accommodations, expenses from Amgen, Takeda, Janssen, and Sanofi. AK reports leadership with Sutro scientific advisory board, has stock and other ownership interests in BMS; has served in a consulting/advisory role for Janssen, BMS, Sanofi, Regeneron, Pfizer, and GSK; has served on speakers' bureaus for Takeda, BMS, and GSK, and received research funding from Janssen. NB has served in a consulting/advisory role for Janssen, Celgene, Amgen, Sanofi, Takeda, Pfizer, and Karyopharm Therapeutics, and has received honoraria from Celgene, Janssen, AbbVie, Amgen, Sanofi, Takeda, Karyopharm Therapeutics, GSK, and Genentech/Roche, and research funding from Janssen and Celgene. RP has served in a consulting/advisory role for AbbVie, GSK, and Celgene, has received travel/accommodations/expenses from Janssen and Takeda, received honoraria from Janssen, Takeda, Celgene, GSK, and AbbVie, received research funding from GSK and reports being supported by the National Institute for Health and Care Research University College London Hospitals Biomedical Research Centre. BB has received travel/accommodations/expenses and honoraria from Janssen-Cilag, Amgen, Sanofi, and GSK. JML has served in a consulting/advisory role, served on speakers' bureau for, and received research funding from Janssen, BMS, and Novartis. MD has served in a consulting/advisory for and received honoraria from Amgen, Celgene, and Janssen. DT and RK are employees of Janssen. LP is an employee of Janssen, and reports equity ownership in Janssen. JF reports employment with Janssen, received travel/accommodations/expenses from Janssen, has stock and other ownership interests in Johnson & Johnson, and has received research funding from Janssen. KSG reports employment and stock or other ownership interests with Janssen. NWCJVDD has received research

support from Janssen Pharmaceuticals, Amgen, Celgene, Novartis, Cellectis and BMS, and serves in advisory boards for Janssen Pharmaceuticals, Amgen, Celgene, BMS, Takeda, Roche, Novartis, Bayer, Adaptive, and Servier.

Acknowledgments

The authors wish to thank all patients who volunteered to participate in this study, their families and caregivers, the staff members at the study sites who supported this study, the data and safety monitoring committee, and all staff involved in data collection and analysis. Editorial and medical writing support was provided by Rachael Smith, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

The MajesTEC-1 study was funded by Janssen Research & Development, LLC. Medical writing support was provided by Rachael Smith, PhD, of Eloquent Scientific Solutions, and funded by Janssen Global Services, LLC.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.clml.2023.11.001.

References

- Larsen RF, Jarden M, Minet LR, Frolund UC, Moller S, Abildgaard N. Physical function in patients newly diagnosed with multiple myeloma: a Danish cohort study. *BMC Cancer*. 2020;20(1):169.
- Johnsen AT, Tholstrup D, Petersen MA, Pedersen L, Groenvold M. Health related quality of life in a nationally representative sample of haematological patients. *Eur J Haematol*. 2009;83(2):139–148.
- Mols F, Oerlemans S, Vos AH, et al. Health-related quality of life and disease-specific complaints among multiple myeloma patients up to 10 yr after diagnosis: results from a population-based study using the PROFILES registry. *Eur J Haematol*. 2012;89(4):311–319.
- Dimopoulos MA, Moreau P, Terpos E, et al. Multiple myeloma: EHA-ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up(dagger). *Ann Oncol*. 2021;32(3):309–322.
- Mikhael J, Ismaila N, Cheung MC, et al. Treatment of multiple myeloma: ASCO and CCO Joint Clinical Practice Guideline. *J Clin Oncol*. 2019;37(14):1228–1263.
- Gandhi UH, Cornell RF, Lakshman A, et al. Outcomes of patients with multiple myeloma refractory to CD38-targeted monoclonal antibody therapy. *Leukemia*. 2019;33(9):2266–2275.
- Jagannath S, Rifkin RM, Gasparetto CJ, et al. Treatment journeys of patients with newly diagnosed multiple myeloma (NDMM): results from the Connect MM Registry. *Clin Lymphoma Myeloma Leuk*. 2020;20(5):272–276.
- Kumar SK, Lee JH, Lahuerta JJ, et al. Risk of progression and survival in multiple myeloma relapsing after therapy with IMiDs and bortezomib: a multicenter international myeloma working group study. *Leukemia*. 2012;26(1):149–157.
- Kumar SK, Dimopoulos MA, Kastritis E, et al. Natural history of relapsed myeloma, refractory to immunomodulatory drugs and proteasome inhibitors: a multicenter IMWG study. *Leukemia*. 2017;31(11):2443–2448.
- Engelhardt M, Ihorst G, Singh M, et al. Real-world evaluation of health-related quality of life in patients with multiple myeloma from Germany. *Clin Lymphoma Myeloma Leuk*. 2021;21(2):e160–e175.
- Kamal M, Wang XS, Shi Q, et al. Symptom burden and its functional impact in patients with "symptomatic" relapsed or refractory multiple myeloma. *Support Care Cancer*. 2021;29(1):467–475.
- Hungria V, Beksac M, Weisel KC, et al. Health-related quality of life maintained over time in patients with relapsed or refractory multiple myeloma treated with daratumumab in combination with bortezomib and dexamethasone: results from the phase III CASTOR trial. *Br J Haematol*. 2021;193(3):561–569.
- Pillarsetti K, Powers G, Luistro L, et al. Teclistamab is an active T cell-redirecting bispecific antibody against B-cell maturation antigen for multiple myeloma. *Blood Adv*. 2020;4(18):4538–4549.
- Usmani SZ, Garfall AL, van de Donk N, et al. Teclistamab, a B-cell maturation antigen × CD3 bispecific antibody, in patients with relapsed or refractory multiple myeloma (MajesTEC-1): a multicentre, open-label, single-arm, phase 1 study. *Lancet*. 2021;398(10301):665–674.
- Moreau P, Garfall AL, van de Donk N, et al. Teclistamab in relapsed or refractory multiple myeloma. *N Engl J Med*. 2022;387(6):495–505.
- TECVAYLI [summary of product characteristics]. Janssen Biologics BV; 2022. Available at: https://www.ema.europa.eu/en/documents/product-information/tecvayli-epar-product-information_en.pdf. Accessed: September 1, 2023.

Results From the Phase II MajesTEC-1 Study

- TECVAYLI [prescribing information]. Janssen Biotech, Inc; 2022. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/761291s000lbl.pdf. Accessed: September 1, 2023.
- Rajkumar SV, Harousseau JL, Durie B, et al. Consensus recommendations for the uniform reporting of clinical trials: report of the International Myeloma Workshop Consensus Panel 1. *Blood*. 2011;117(18):4691–4695.
- Aaronson NK, Ahmedzai S, Bergman B, et al. The European Organization for Research and Treatment of Cancer QLQ-C30: a quality-of-life instrument for use in international clinical trials in oncology. *J Natl Cancer Inst*. 1993;85(5):365–376.
- Fayers P, Aaronson NK, Bjordal K, Groenvold M, Curran D, Bottomley A. *EORTC QLQ-C30 Scoring Manual (3rd edition)*. Brussels, Belgium: European Organisation for Research and Treatment of Cancer; 2001.
- Wisloff F, Eika S, Hippe E, et al. Measurement of health-related quality of life in multiple myeloma. Nordic Myeloma Study Group. *Br J Haematol*. 1996;92(3):604–613.
- Dimopoulos MA, Delforge M, Hajek R, et al. Lenalidomide, melphalan, and prednisone, followed by lenalidomide maintenance, improves health-related quality of life in newly diagnosed multiple myeloma patients aged 65 years or older: results of a randomized phase III trial. *Haematologica*. 2013;98(5):784–788.
- Cella D, McKendrick J, Kudlac A, et al. Impact of elotuzumab treatment on pain and health-related quality of life in patients with relapsed or refractory multiple myeloma: results from the ELOQUENT-2 study. *Ann Hematol*. 2018;97(12):2455–2463.
- Herdman M, Gudex C, Lloyd A, et al. Development and preliminary testing of the new five-level version of EQ-5D (EQ-5D-5L). *Qual Life Res*. 2011;20(10):1727–1736.
- Kumar S, Paiva B, Anderson KC, et al. International Myeloma Working Group consensus criteria for response and minimal residual disease assessment in multiple myeloma. *Lancet Oncol*. 2016;17(8):e328–e346.
- Cocks K, King MT, Velikova G, Fayers PM, Brown JM. Quality, interpretation and presentation of European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30 data in randomised controlled trials. *Eur J Cancer*. 2008;44(13):1793–1798.
- Osoba D. Health-related quality of life and cancer clinical trials. *Ther Adv Med Oncol*. 2011;3(2):57–71.
- Pickard AS, Neary MP, Cella D. Estimation of minimally important differences in EQ-5D utility and VAS scores in cancer. *Health Qual Life Outcomes*. 2007;5:70.
- Tremblay G, Daniele P, Breeze J, et al. Quality of life analyses in patients with multiple myeloma: results from the Selinexor (KPT-330) Treatment of Refractory Myeloma (STORM) phase 2b study. *BMC Cancer*. 2021;21(1):993.
- Delforge M, Shah N, Miguel JSF, et al. Health-related quality of life with idecabtagene vicleucel in relapsed and refractory multiple myeloma. *Blood Adv*. 2022;6(4):1309–1318.
- Larocca A, Leleu X, Touzeau C, et al. Patient-reported outcomes in relapsed/refractory multiple myeloma treated with melflufen plus dexamethasone: analyses from the Phase II HORIZON study. *Br J Haematol*. 2022;196(3):639–648.
- Jordan K, Proskorovsky I, Lewis P, et al. Effect of general symptom level, specific adverse events, treatment patterns, and patient characteristics on health-related quality of life in patients with multiple myeloma: results of a European, multi-center cohort study. *Support Care Cancer*. 2014;22(2):417–426.
- Ludwig H, Bailey AL, Marongiu A, et al. Patient-reported pain severity and health-related quality of life in patients with multiple myeloma in real world clinical practice. *Cancer Rep (Hoboken)*. 2022;5(1):e1429.
- Nathwani N, Bell J, Cherepanov D, et al. Patient perspectives on symptoms, health-related quality of life, and treatment experience associated with relapsed/refractory multiple myeloma. *Support Care Cancer*. 2022;30(7):5859–5869.
- Zaleta AK, Miller MF, Olson JS, et al. Symptom burden, perceived control, and quality of life among patients living with multiple myeloma. *J Natl Compr Canc Netw*. 2020;18(8):1087–1095.