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Psychometric Properties of the Multiple Myeloma Symptom and Impact Questionnaire in Patients With Relapsed/Refractory Multiple Myeloma: Analysis of Phase 2 CARTITUDE-2 Study Cohorts A, B, and C

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Key Takeaway

The MySIm-Q symptom score is reliable, valid, and responsive to change based on preliminary analyses from CARTITUDE-2 Cohorts A, B, and C, supporting its use as a fit-for-purpose PRO instrument in MM studies

Conclusions

- MySIm-Q symptom score internal consistency (Cronbach's α-coefficient, 0.89) and test-retest reliability (ICC[2,1], 0.81), 2 indicators of reliability, showed evidence of reproducibility
- Concurrent validity supported that the MySIm-Q symptom score evaluated similar constructs to existing PRO measures, and known-groups validity showed that the MySIm-Q symptom score differentiated between disease severity states
- Anchor- and distribution-based MWPC analyses demonstrate that the MySIm-Q symptom score is responsive to change and is capable of discriminating between patients maintaining improvement or declining in their condition or health state
- More extensive analysis of MySIm-Q symptom and impact measurement properties using data from the phase 3 CARTITUDE-4 study are forthcoming

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Disclosures

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Introduction

- Multiple myeloma (MM) is an incurable hematologic malignancy characterized by symptoms of bone pain, fatigue, and reduced physical and cognitive functioning that impact patient health-related quality of life (HRQoL)[1-3]
- Patient-reported outcome (PRO) instruments used in clinical practice were developed and validated prior to recent therapeutic advances (eg, chimeric antigen receptor [CAR] T-cell therapy); therefore, they may not reflect the disease experience of MM patient populations undergoing treatment with newer therapies
- The Multiple Myeloma Symptom and Impact Questionnaire (MySIm-Q) is a newly developed and validated MM-specific PRO instrument designed to account for the changing treatment landscape in MM[4]
  - MySIm-Q measures disease-related symptoms and impacts due to treatment modalities with differing mechanisms of action available in clinical practice today
  - It can be collected alongside other PRO instruments to measure and complement core PRO-based efficacy and tolerability endpoints in cancer clinical trials
- Here, we describe measurement properties of the MySIm-Q symptom score using data from the phase 2, multicohort, open-label, multicenter CARTITUDE-2 study

Methods

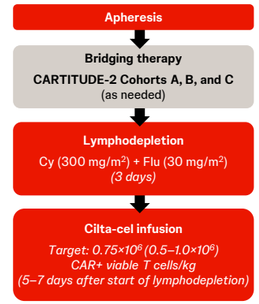
Key eligibility criteria and study design (Figure 1)

- Measurement properties of the MySIm-Q symptom score were assessed using data from Cohorts A, B, and C of CARTITUDE-2
  - **Cohort A**: comprised patients with lenalidomide-refractory MM and 1–3 prior lines of therapy (LOT), including a proteasome inhibitor (PI) and immunomodulatory drug (IMiD)[5]
  - **Cohort B**: comprised patients with 1 prior LOT, including a PI and IMiD, and disease progression ≤12 months after autologous stem cell transplant (ASCT) or frontline antimyeloma therapy for patients without ASCT[5]
  - **Cohort C**: comprised patients previously treated with a PI, IMiD, anti-CD38 antibody, and noncellular B-cell maturation antigen–directed therapy (eg, antibody-drug conjugate and bispecific T-cell engager)[6]

Assessments and statistical analysis

- **Internal consistency** was assessed at screening using Cronbach's α-coefficient; a threshold of >0.70 was selected as acceptable internal consistency[7]
- **Test-retest reliability** was assessed using a 2-way random intraclass correlation coefficient (ICC[2,1]),[8] with values ≥0.70 considered acceptable test-retest reliability

Figure 1: CARTITUDE-2 study design



Cy, cyclophosphamide; Flu, fludarabine.

- **Concurrent validity** (convergent validity) was considered supportive if Spearman correlations with the European Organisation for Research and Treatment of Cancer quality of life questionnaire core 30 (EORTC QLQ-C30) domain and items scores at screening were ≥0.4[9]
- **Known-groups validity** (discriminant validity) was determined at screening; Patient Global Impression of Severity (PGIS) and EORTC QLQ-C30 Global Health Status (GHS)/QoL domain items 29 and 30 were used as known-group validators
  - Differences calculated using a t-test, the mean differences and corresponding 95% confidence intervals (CIs), *P* values, and semi-partial ω^2 effect-size estimates
- **Meaningful within-patient change (MWPC)** estimates were calculated using an anchor-based approach and supplemented with an estimate derived from a distribution-based approach
  - Anchor: Patient Global Impression of Change (PGIC) at day 100
    - Median change scores were stratified by anchor groups of "minimal improvement," "no change," and "minimal deterioration"
    - Anchor analyses were further supported visually by empirical cumulative distribution functions (eCDFs) and empirical probability density functions (ePDFs)

Results

Study population

- A total of 82 patients completed MySIm-Q assessments (cohort A, n=43; cohort B, n=19; cohort C, n=20)

Measurement properties

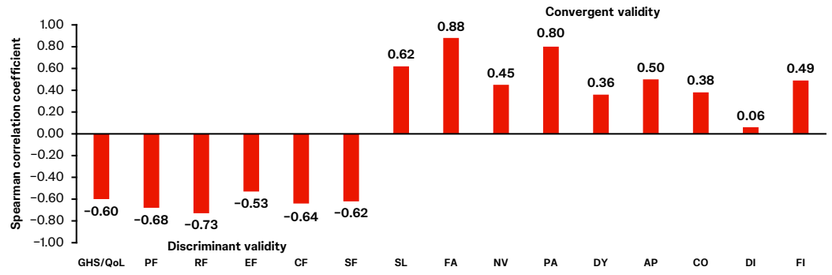
- Internal consistency was acceptable; Cronbach's α-coefficient was 0.89 for MySIm-Q symptom score
  - Item to MySIm-Q symptom score correlations ranged from 0.35–0.84 (**Table 1**)

Table 1: Internal consistency for the MySIm-Q symptom score

	Item to MySIm-Q symptom score correlation
Worst pain back	0.60
Worst pain leg	0.70
Worst pain other area	0.49
Worst numbness/tingling in hands and feet	0.35
Low energy	0.84
Tire easily	0.80
Muscle weakness	0.74
Trouble with sleep	0.55
Poor appetite	0.55
Difficulty with memory	0.50
Difficulty concentrating	0.62

- Test-retest reliability for the MySIm-Q symptom score was adequate; the ICC(2,1) was 0.81, exceeding the minimally acceptable value of 0.70
- MySIm-Q symptom score demonstrated acceptable concurrent validity with existing symptom and impact measures from the EORTC QLQ-C30 (**Figure 2**)
  - All correlations except the diarrhea domain met or exceeded the minimum correlation requirement of |r| ≥0.4, or were within rounding error of this criterion, with a high proportion exceeding | 0.60 |

Figure 2: Concurrent validity for the MySIm-Q symptom score



AP, appetite loss; CF, cognitive functioning; CO, constipation; DI, diarrhea; DY, dyspnea; EF, emotional functioning; FA, fatigue; FI, financial difficulties; NV, nausea and vomiting; PA, pain; PF, physical functioning; RF, role functioning; SF, social functioning; SL, insomnia.

- Known-groups validity for the MySIm-Q symptom score was supported
  - Discrimination across disease severity groups based on PGIS was shown for every category, with each PGIS category exhibiting incrementally larger differences from the "never" (reference) category (**Table 2**)
    - The "very severe" category was the exception; however, the sample size comprised 3 patients and estimates were unstable
- Discrimination evidence across disease severity groups based on EORTC QLQ-C30 GHS/QoL domain items were generally supportive

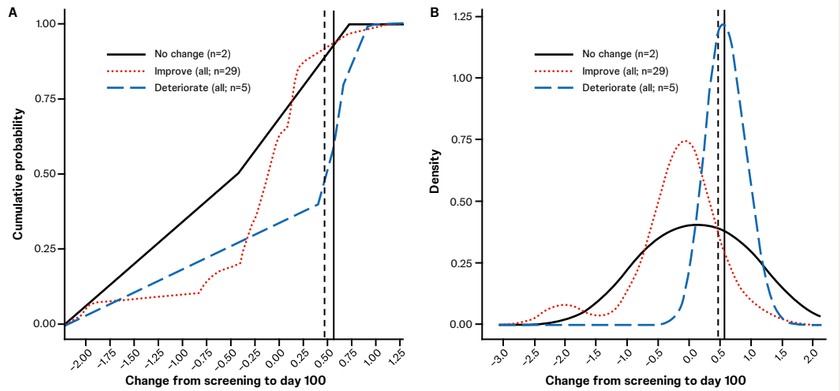
Table 2: Known-groups validity of MySIm-Q symptom score

Known-groups validator	Estimate (95% CI)	*P* value	ω^2
PGIS			0.946
Never vs mild	0.53 (0.23, 0.84)	0.0010	–
Never vs moderate	1.17 (0.83, 1.52)	<0.0001	–
Never vs severe	1.55 (1.12, 1.98)	<0.0001	–
Never vs very severe	1.41 (0.65, 2.18)	0.0005	–
EORTC GH29			0.921
Excellent vs very poor	1.34 (0.52, 2.17)	0.0018	–
Excellent vs GH29 2	1.41 (0.71, 2.11)	0.0002	–
Excellent vs GH29 3	1.06 (0.36, 1.76)	0.0035	–
Excellent vs GH29 4	1.15 (0.57, 1.73)	0.0002	–
Excellent vs GH29 5	0.95 (0.42, 1.48)	0.0007	–
EORTC GH30			0.939
Excellent vs very poor	−0.04 (−1.15, 1.06)	0.9378	–
Excellent vs GH30 2	1.48 (0.96, 2.00)	<0.0001	–
Excellent vs GH30 3	1.14 (0.62, 1.65)	<0.0001	–
Excellent vs GH30 4	1.45 (0.98, 1.92)	<0.0001	–
Excellent vs GH30 5	0.79 (0.37, 1.21)	0.0004	–
Excellent vs GH30 6	0.50 (0.09, 0.92)	0.0172	–

Reference groups for known validators were "never" for the PGIS severity group and "excellent" for the EORTC QLQ-C30 GHS/QoL items groups. EORTC GH29 and EORTC GH30 response options were rated using a 7-point scale ranging from very poor (1) to excellent (7).

- The PGIC anchor-based MWPC deterioration threshold and the average distribution-based clinical significance threshold triangulated well
  - The PGIC anchor-based threshold median estimate was 0.57 and the distribution-based clinical significance threshold mean estimate was 0.47, yielding an average of 0.52
  - Discrimination between "deterioration," "improvement," and "no change" based on the proposed deterioration threshold of 0.57 from the PGIC anchor was demonstrated by noticeable separation in eCDF and ePDF curves (**Figure 3A** and **B**)

Figure 3: eCDF (A) and ePDF (B) for the MySIm-Q symptom score



Total N is 36. Vertical reference lines are meaningful within-patient change; the solid line indicates anchor-based meaningful deterioration (0.57), while the dashed line is the average distribution-based threshold (0.47). 40.0% of the deterioration group met the threshold for meaningful deterioration, while 50.0% of the no change group did. 60.0% of the deterioration group met the distribution-based threshold, while 50.0% of the no change group did.

References

1. Jordan K, et al. *Support Care Cancer* 2014;22:417-26. 2. Ramsenthaler C, et al. *Eur J Haematol* 2016;97:416-29. 3. Mols F, et al. *Eur J Haematol* 2012;89:311-9. 4. Gries KS, et al. *Value Health* 2021;24:1807-19. 5. Hillengass J, et al. *Blood* 2023;142(suppl 1):1021. 6. Cohen AD, et al. *Blood* 2023;141:219-30. 7. Cronbach LJ. *Psychometrika* 1951;16:297-334. 8. Shrout PE, Fleiss JL. *Psychol Bull* 1979;86:420-8. 9. Campbell DT, Fiske DW. *Psychol Bull* 1959;56:81-105.

Multiple Myeloma

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