Psychometric Evaluation of Multiple Sclerosis Impact Scale 29 Version 2 in Adults with Relapsing Multiple Sclerosis Participating in a Phase 2 Trial of Frexalimab

PCR122

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BACKGROUND

- Multiple sclerosis (MS) is a chronic immune-mediated disease affecting the central nervous system.
  - Relapsing multiple sclerosis (RMS) is the most common form of MS, representing around 85% of the total MS cases.[1]
  - People with MS experience disabilities that negatively impact their functional ability and mental health.[2]
- Multiple Sclerosis Impact Scale-29 (MSIS-29) is a 29-item patient-reported questionnaire measuring the perceived impact of disability on activities of daily living and well-being.[3]
- At present, there are limited psychometric studies done using version 2 of the MSIS-29 (MSIS-29v2) questionnaire.
- Frexalimab demonstrated efficacy and safety with high-dose treatment in a phase 2 trial (NCT04879628).[4,5]

OBJECTIVE

- This study aimed to validate the psychometric properties of MSIS-29v2 questionnaire in adults with RMS using data from a frexalimab phase 2 trial.

METHODS

- Two scores were derived from MSIS-29v2: the physical impact (20 items) and psychological impact (9 items) subscale scores, both ranging from 0 to 100, with higher score indicating worse disability. Item answer options on this version 2 range from 1 to 4 (eliminating Level 5 'Quite a bit' included in version 1).
- Psychometric properties of MSIS-29v2 were assessed using data from the 12-week, double-blind, randomised, placebo-controlled part of the frexalimab phase 2 trial in adult RMS participants (NCT04879628).
  - Participants aged 18-55 years diagnosed with RMS according to the 2017 revised McDonald criteria with ≥1 relapse within the previous year, or ≥2 relapses within 2 years, or ≥1 gadolinium-enhancing T1 lesion within 6 months were included.
- Analyses were performed in the intention-to-treat population using baseline and Week 12 data from pooled treatment arms.
- Item-to-item correlations, item-total correlations, internal consistency, test-retest reliability, construct validity and sensitivity to change were assessed.

RESULTS

Study population

- Overall, 129 participants with RMS were included in the psychometric analysis: mean (standard deviation [SD]) age 36.6 (9.4) years, 65.9% female, and mean (SD) time since symptom onset 7.7 (7.2) years.

Item-to-item correlations

- Item-to-item correlations were acceptable (i.e. between 0.4 and 0.9) for most items in each subscale at both visits.

Internal consistency

- Excellent internal consistency was observed for both domains (Cronbach's alpha between 0.91 and 0.96 at both visits).

Test-retest reliability

- Adequate test-retest reliability (ICC ≥0.78 for the physical domain and ≥0.66 for the psychological domain) was observed (**Table 1**).

Table 1. Test-retest reliability of MSIS-29v2 between baseline and Week 12

Domain (*N* = 48)	**ICC using PGIC-Fatigue (no change) — Week 12 (95% CI)**
MSIS-29v2 Physical impact score	0.78 (0.65; 0.87)
MSIS-29v2 Psychological impact score	0.74 (0.59; 0.85)
Domain (*N* = 59)	**ICC using PGIS-Fatigue (stable) — baseline and Week 12 (95% CI)**
MSIS-29v2 Physical impact score	0.80 (0.69; 0.88)
MSIS-29v2 Psychological impact score	0.66 (0.48; 0.78)

Reliability was defined as — low: intraclass correlation coefficient (ICC) < 0.50; moderate: 0.50 ≤ ICC ≤ 0.70; adequate: ICC ≥ 0.70.
CI, confidence interval; ICC, intraclass correlation coefficient; MSIS-29v2, Multiple Sclerosis Impact Scale-29 version 2; PGIC, Patient Global Impression of Change; PGIS, Patient Global Impression of Severity.

Construct validity

- Convergent validity was supported by high correlations ($r > 0.50$) with Patient-Reported Outcome Measurement Information System-Fatigue (PROMIS-Fatigue MS-8a) T-score and Patient Global Impression of Severity-Fatigue (PGIS-Fatigue) for both domains at baseline and Week 12 (**Table 2**).

Table 2. Convergent validity of MSIS-29v2 at baseline and Week 12

	Correlations, *r* (*N* = 128)	
MSIS-29v2 Physical impact score	**At baseline**	**Week 12**
PROMIS-Fatigue-MS-8 T-score[a]	0.81	0.82
PGIS-Fatigue score[b]	0.72	0.65
MSIS-29v2 Psychological impact score	**At baseline**	**Week 12**
PROMIS-Fatigue-MS-8 T-score[a]	0.76	0.83
PGIS-Fatigue score[b]	0.66	0.68

[a]Spearman correlation; [b]Polyserial correlation.
Correlations were defined as– low: $r < 0.30$; moderate: $0.30 \le r \le 0.50$ and high: $r > 0.50$.
MSIS-29v2, Multiple Sclerosis Impact Scale-29 version 2; PGIS, Patient Global Impression of Severity; PROMIS–Fatigue–MS; Patient-Reported Outcome Measurement Information System–Fatigue–Multiple Sclerosis.

- Construct validity was further supported by significant differences observed in both domain impact scores among groups defined by PGIS-Fatigue at baseline and Week 12 ($P < 0.001$)
- The groups defined by PGIS-Fatigue showed moderate ($r = 0.5$-0.8) and large ($r > 0.8$) effect sizes at both time periods (**Table 3**).

Sensitivity to change

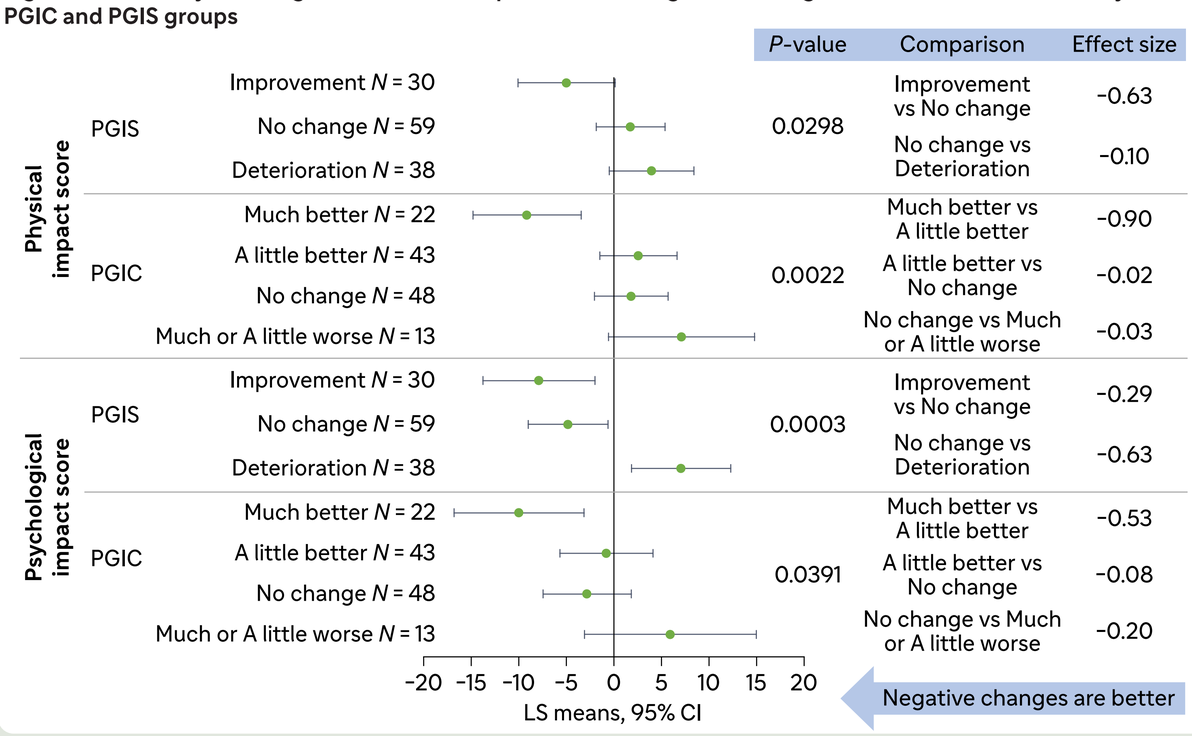
- Statistically significant differences in physical and psychological impact mean change from baseline were observed at Week 12 among groups defined by change in PGIS-Fatigue and by Patient Global Impression of Change-Fatigue (PGIC-Fatigue) level (**Figure 1**).
- Overall, moderate ($r = 0.5$-0.8) to large ($r > 0.8$) effect sizes between consecutive group mean changes were observed for improved vs stable participants.

Table 3. Construct validity of MSIS-29v2 at baseline and Week 12

MSIS-29v2 Physical impact score							
Timepoint	**PGIS-Fatigue score**	***N***	**LS means**	**95% CI**	***P*-value**	**Effect size**	
Baseline	1. None	30	8.28	2.54; 14.02	<0.0001		
	2. Mild	49	15.44	10.95; 19.93		Mild vs None	0.63
	3. Moderate	34	39.02	33.63; 44.41		Moderate vs Mild	1.42
	4. Severe or Very severe	15	58.33	50.22; 66.45		Severe or Very severe vs Moderate	0.91
Week 12	1. None	34	8.38	1.95; 14.81	<0.0001		
	2. Mild	37	18.38	12.22; 24.54		Mild vs None	0.72
	3. Moderate	41	37.40	31.54; 43.25		Moderate vs Mild	0.94
	4. Severe or Very severe	16	50.63	41.25; 60.00		Severe or Very severe vs Moderate	0.56
MSIS-29v2 Psychological impact score							
Timepoint	**PGIS-Fatigue score**	***N***	**LS means**	**95% CI**	***P*-value**	**Effect size**	
Baseline	1. None	30	18.89	11.95; 25.82	<0.0001		
	2. Mild	49	25.93	20.50; 31.35		Mild vs None	0.44
	3. Moderate	34	46.73	40.22; 53.25		Moderate vs Mild	1.14
	4. Severe or Very severe	15	66.42	56.61; 76.23		Severe or Very severe vs Moderate	0.84
Week 12	1. None	34	10.89	4.66; 17.12	<0.0001		
	2. Mild	37	29.53	23.56; 35.50		Mild vs None	1.07
	3. Moderate	41	42.28	36.60; 47.95		Moderate vs Mild	0.62
	4. Severe or Very severe	16	58.33	49.25; 67.41		Severe or Very severe vs Moderate	0.83

Effect sizes were defined as — small: $r < 0.5$; moderate: $0.5 \le r \le 0.8$ and high: $r > 0.8$.
CI, confidence interval; LS, least square; MSIS-29v2, Multiple Sclerosis Impact Scale-29 version 2; PGIS, Patient Global Impression of Severity.

Figure 1. Sensitivity to change of MSIS-29v2 impact scores using mean change from baseline to Week 12 by PGIC and PGIS groups



P-value	Comparison	Effect size
0.0298	Improvement vs No change	-0.63
	No change vs Deterioration	-0.10
0.0022	Much better vs A little better	-0.90
	A little better vs No change	-0.02
	No change vs Much or A little worse	-0.03
0.0003	Improvement vs No change	-0.29
	No change vs Deterioration	-0.63
0.0391	Much better vs A little better	-0.53
	A little better vs No change	-0.08
	No change vs Much or A little worse	-0.20

Effect sizes were defined as - small: $r < 0.5$; moderate: $0.5 \le r \le 0.8$ and high: $r > 0.8$.
CI, confidence interval; LS, least square; MSIS-29v2, Multiple Sclerosis Impact Scale-29 version 2; PGIC, Patient Global Impression of Change; PGIS, Patient Global Impression of Severity.

CONCLUSIONS

- In this study, both physical and psychological subscales of MSIS-29v2 showed robust measurement properties in adults with RMS included in a phase 2 clinical trial.
- This indicates that the instrument can be a valuable outcome measure in evaluating physical and psychological impact in this population.

Disclosures

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