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The Migraine-Specific Quality of Life Questionnaire, Role Function Restrictive Domain: Defining Clinically Meaningful Categories of Functional Impairment Severity

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BACKGROUND AND OBJECTIVE

Background

- Improving and restoring the ability to perform day-to-day activities are established treatment goals for preventive and acute migraine treatment[1]
- The Migraine-Specific Quality of Life Questionnaire (MSQ v2.1) is a patient-reported outcome (PRO) instrument recommended for measuring meaningful change in this area[1]
- Like many PROs, the MSQ v2.1, Role Function-Restrictive Domain (RFR) is scored on a continuous scale[2]
- Meaningful ordered categories of the continuous scale would facilitate clinical interpretation of results which would be of benefit to researchers and clinicians

Objective

- The objective of this work was to determine score categories of the MSQ v2.1 RFR domain that would represent meaningful degrees of migraine disease severity and functional impairment
- This objective was motivated by the desire to improve the understanding, meaningfulness, and utility of MSQ v2.1 RFR scores for researchers, clinicians, and patients

KEY RESULTS

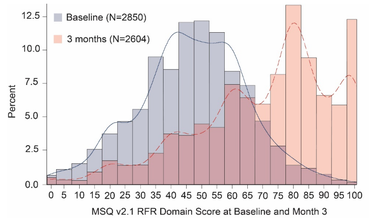
MSQ v2.1 RFR Domain Score Categories of Patients by PGI-S Groups at Baseline and Month 3

MSQ v2.1 RFR Domain Score Categories		PGI-S Groups						
	Time point	Normal, not at all ill, %	Borderline ill, %	Mildly ill, %	Moderately ill, %	Markedly ill, %	Severely ill, %	Extremely ill, %
85-100 Not/minimally impaired	Baseline (n=45)	37.8	6.7	13.3	33.3	6.7	2.2	0
	Month 3 (n=738)	28.9	22.1	23.6	17.5	5.3	2.3	0.4
75-84 Mildly impaired	Baseline (n=84)	9.5	13.1	25.0	47.6	4.8	0	0
	Month 3 (n=613)	6.5	18.6	36.9	27.1	7.0	3.1	0.8
55-74 Moderately impaired	Baseline (n=781)	3.6	6.1	19.3	46.5	19.6	4.6	0.3
	Month 3 (n=681)	3.2	5.1	27.6	42.3	15.4	5.6	0.7
40-54 Severely impaired	Baseline (n=1105)	2.4	1.5	6.5	34.9	41.4	12.1	1.1
	Month 3 (n=351)	0.6	1.1	7.4	35.6	39.9	13.4	2.0
<40 Extremely impaired	Baseline (n=835)	1.2	1.1	1.9	13.3	38.1	35.3	9.1
	Month 3 (n=221)	0	0.9	0.9	9.5	42.5	35.7	10.4

MSQ=Migraine-Specific Quality of Life questionnaire; PGI-S=Patient Global Impression of Severity; RFR=Role Function-Restrictive domain.

- The largest proportion of patients were within the corresponding PGI-S category level across each of the MSQ RFR categories of 85-100, 75-84, 55-74, 40-54, and <40

Histogram of the MSQ v2.1 RFR Domain Scores at Baseline and Month 3

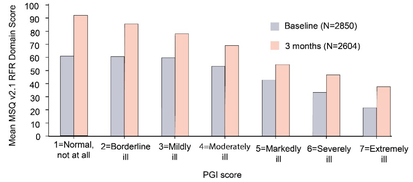


- Moderate to large correlations were observed at Baseline with RFR domain scores and the other PROs

MSQ RFR Correlations

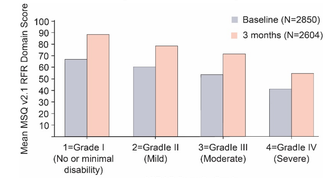
Time Point	PGI-S	MIDAS	Migraine headache days
Baseline	-0.55	-0.60	-0.43
Month 3 Change	-0.43	-0.46	-0.50

Mean MSQ v2.1 RFR Domain Score at Baseline and Month 3 by PGI-S Level



- Mean RFR domain scores by PGI-S category levels at Baseline and Month 3 demonstrated responsiveness, or ability of the RFR to distinguish clinically important change over time

Mean MSQ v2.1 RFR Domain Score at Baseline and Month 3 by MIDAS Severity Grade



- Mean RFR domain scores by MIDAS Severity Grades at Baseline and Month 3 demonstrated responsiveness, or ability of the RFR to distinguish clinically important change over time

MIDAS=Migraine Disability Assessment; MSQ=Migraine-Specific Quality of Life questionnaire; PGI-S=Patient Global Impression of Severity; RFR=Role Function-Restrictive domain.

CONCLUSION

- PGI-S was the selected anchor, because it correlates well with the RFR domain and is a direct self-reported measure of the overall severity of migraine as a chronic condition
- The proposed MSQ v2.1 RFR score categories provide clear cut-offs to define a range of functional impairment from “not/minimally impaired,” to “extremely impaired”
- This study enables additional evaluation and interpretation of functional impairment due to migraine, and changes with treatment, that are meaningful to patients, practitioners, and researchers

Methods

Study Design

- Pooled data from two episodic migraine (EM) and one chronic migraine (CM) phase III clinical trials was analyzed
- Two migraine clinician experts were consulted about the design, analytical methods, results, and recommendations for the present study
- Anchor variables included the Patient Global Impression of Severity (PGI-S) and Migraine Disability Assessment (MIDAS)
- Following review of the descriptive and responsiveness results, RFR score categories were proposed by the investigators and vetted with the clinician experts

Participants

- Trials (I5Q-MC-CGAG [CGAG], I5Q-MC-CGAH [CGAH], and I5Q-MC-CGAI [CGAI]) were Phase 3, multi-site randomized, double-blind, placebo-controlled studies to compare the efficacy and safety of two dosing regimens of galcanezumab with placebo in preventing migraine headaches
- Studies CGAG (N=858 patients enrolled) and CGAH (N=915 patients enrolled) were in adult patients with episodic migraine, while study CGAI was in adult patients with chronic migraine (N=1090)
- The PRO population used in the present analyses includes only those trial participants with both Baseline and Month 3 PRO data

Measures

- **MSQ v2.1:** Instrument addressing physical and emotional impact on functioning over past 4 weeks (0-100 scale, where 100 indicates full functionality)[2,3]
- **MIDAS:** Scale quantifying headache-related disability over a 3-month period (0-270). Higher scores indicate more disability: 0–5, little/no disability; 6–10, mild disability; 11–20, moderate disability; >20, severe disability.[4]
- **PGI-S:** Measures a patient’s assessment of their level of illness for their current condition (i.e., migraine). The PGI-S is scored on a 7-point scale: 1 = “Normal, not at all ill,” to 7 = “Extremely ill.”[5]
- **Number of monthly migraine headache days:** Daily electronic diary captured migraine headache day information-and migraine headache days was provided for each of the 30-day periods

Statistical analyses

- Analyses were pre-specified in a secondary statistical analysis plan
- The relationship between the RFR domain with the PGI-S, MIDAS total score, and number of migraine headache days were examined using Pearson's product-moment and Spearman’s rank correlation coefficients at baseline and 3 months
- A coefficient of ≥0.30 is considered a moderate correlation, and a coefficient ≥0.5 is considered a large or strong correlation.[6] Histograms portraying the mean RFR domain by PGI-S and MIDAS severity grade were generated.
- The RFR between relevant change levels of the PGI-S and MIDAS were assessed descriptively
- The following multi-level change groups from Baseline to Month 3 were used:
  - **PGI-S Ratings:** Improvement -6 to -1 category levels; No Change; Worsening +1 to +6 category levels-
    (Normal, not at all ill; Borderline ill; Mildly ill; Moderately ill; Markedly ill; Severely ill; Extremely ill)
  - **MIDAS Grade Levels:** Improvement -3 to -1 grades; No change; Worsening +1 to +3 grades-
    (Little or No Disability (Grade I); Mild Disability (Grade II); Moderate Disability (Grade III); Severe Disability (Grade IV)

Results

Patient Demographic and Disease Characteristics, and MSQ v2.1 ePRO RFR Domain Scores at Baseline: PRO Population

Characteristics	CGAG[a] PRO Population (n=851)	CGAH[a] PRO Population (n=909)	CGAI[b] PRO Population (n=1090)
Age (years), mean (SD)	40.6 (11.6)	41.8 (11.1)	41.0 (12.1)
Women, %	83.7	85.4	85.2
Race, %			
White	80.3	70.2	79.2
Black or African American	11.0	6.9	6.3
Asian	2.8	11.2	4.9
American Indian or Alaska Native	0.4	4.5	0.6
Native Hawaiian or Other Pacific Islander	0.4	0.2	0.1
Multiple	5.2	6.9	8.9
Missing	0	0	0.1
Years since migraine diagnosis, mean (SD)	20.0 (12.4)	20.6 (12.4)	21.2 (12.8)
Number of migraine headache days, mean (SD)	9.1 (3.0)	9.1 (2.9)	19.4 (4.5)
Role Function-Restrictive Domain, mean (SD)	51.5 (16.0)	51.7 (15.6)	38.7 (17.2)
Floor, %[c]	0.5	0.2	1.0
Ceiling, %[c]	0	0.2	0

Max=maximum; Min=minimum; MSQ=Migraine-Specific Quality of Life questionnaire; n=number of patients within each specific category; PRO=Patient-reported outcome.
[a]Episodic migraine
[b]Chronic migraine
[c]For all values, the floor effect is assessed based on minimum value, and the ceiling effect is assessed based on the maximum value possible for the range.

- For the EM populations the mean number of monthly migraine headache days were similar
- The mean number of monthly migraine headache days was ~2x greater in the CM population
- For the EM populations the mean MSQ RFR scores were similar and ~ 13 points lower (worse) for the CM population
- No floor or ceiling effects for the domain (or any of the individual items) across both EM and CM

Limitations

- Clinical trial populations differ from real world patients, which would potentially compromise the generalizability of the RFR score categories
- Selection bias or lack of external validity is a common risk and constraint of randomized controlled trials[7]
- Patients in the three galcanezumab trials had to have a migraine diagnosis for at least one year and meet criteria for the frequency of migraine headache days per month (i.e., at least four in the episodic trials and diagnosis of chronic migraine in CGAI), the RFR categories may not apply to excluded subpopulations

References

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Disclosures

Ford J. and Ayer D. are employees and stockholders of Eli Lilly and company. Bushnell D. is an employee of Evidera, Bethesda, MD, USA. Speck R. was an employee of Evidera, Bethesda, MD, USA during the conduct of this research. Kudrow D. is a Neurologist and Headache Specialist with the following disclosures: Advisory Board Member: Amgen, Lundbeck, Biohaven, Allergan (AbbVie), Eli Lilly, Satsuma; Research support (Investigator): Eli Lilly, Amgen, Lundbeck, Teva, Biohaven, Allergan, Satsuma, Axsome; Speaker Bureau: Amgen, Ely Lilly, Lundbeck, Teva, Biohaven and Allergan. Christie S. is a Neurologist Headache Specialist with the following disclosures: Grants/Research Support from Abbvie.

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