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Psychometric Evaluation of the Myasthenia Gravis Impairment Index (MGII) Patient-Reported Outcome (PRO) Ocular score in Ocular Myasthenia Gravis Using Data from a Phase 3 Clinical Trial in Ocular Myasthenia Gravis

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KEY TAKEAWAYS



The MGII (PRO) Ocular Score showed robust psychometric properties in oMG and served as the primary endpoint in ADAPT OCULUS, the first pivotal trial in oMG.



The MGII (PRO) Ocular Score psychometric properties support its interpretability and suitability as a clinical trial endpoint for detecting treatment benefit in oMG.



A MWPC 3-point improvement in the MGII (PRO) Ocular Score represents meaningful improvement from the patient perspective and can support interpretation of treatment benefit in future oMG trials.

BACKGROUND | METHODS

Ocular Myasthenia Gravis

- Ocular myasthenia gravis (oMG), defined as Myasthenia Gravis Foundation of America (MGFA) class I disease, is a rare, chronic, and debilitating neuromuscular condition mediated by pathogenic IgG autoantibodies that disrupt neuromuscular transmission in the extraocular and eyelid muscles.¹⁻³
- oMG is a condition primarily characterized by fluctuating diplopia and ptosis.^{2,3}
- oMG is associated with considerable functional and psychosocial burden as it can significantly interfere with daily activities and work capacity, resulting in substantial psychosocial difficulties.^{4,5}

Myasthenia Gravis Impairment Index (MGII) Patient-Reported Outcome (PRO) Ocular Score

- The MGII is a 28-item disease severity measure validated in MG⁶, comprising 22 PRO items and 6 physical examination (PE) items. Higher total scores indicate greater impairment.
- The MGII (PRO) Ocular Score is a 6-item subscale assessing ptosis and diplopia. The score has not been formally validated specifically in oMG, including evaluation of its reliability, validity, responsiveness, and interpretation of meaningful change.
- Validation of an ocular symptom-focused outcome measure in oMG is important to support disease-relevant assessment and interpretation of treatment benefit in clinical trials.

OBJECTIVE

- To evaluate the psychometric properties of the MGII (PRO) Ocular Score in oMG, including item and scale performance, reliability, validity, responsiveness, and thresholds for meaningful within-patient change (MWPC) and between-group (MBGD) differences using data from the Phase 3 ADAPT OCULUS trial (NCT06558279).

METHODS

- Data source:** Phase 3 registrational ADAPT OCULUS trial (NCT06558279), a randomized, double-blind, placebo-controlled study in adults with oMG. Analyses used Part A Baseline and Week 4 data.
- Participants:** 141 adults with oMG, defined as MGFA Class I.
- Analyses:**
 - Item and scale performance:** Completion rate and score distributions.
 - Reliability:** Test-retest reliability (Intraclass Correlation Coefficient [ICC]).
 - Validity:** Convergent, divergent and known-groups validity. Correlations was assessed with MG-ADL Ocular and Total score, a vision-specific measure (NEI VFQ-25), and broader QoL measures (MG-QoL15r, Neuro-QoL SF-Fatigue).
 - Responsiveness:** Associations between changes in MGII (PRO) Ocular Score and reference measures (MG-ADL Ocular Score, PGI-S and PGI-C Ocular Scores)
 - Interpretability:** MWPC and MBGD estimated using anchor- and distribution-based methods.
- Analyses presented focused on the assessment of the psychometric performance of the MGII (PRO) Ocular Score using blinded data, i.e., in a treatment-agnostic manner.
- Methods align with the United States (US) Food and Drug Administration (FDA) guidance for Clinical Outcome Assessment (COA) evaluation.⁷⁻⁹

RESULTS

Sample

- Participant demographic characteristics and health information are summarised in **Table 1**.

TABLE 1 Demographic and Clinical Characteristics

Characteristic	Sample (N=141)	Characteristic	Sample (N=141)
Age, n (%)		Ethnicity, n (%)	
18 to <65 years	96 (68.1%)	Hispanic or Latino	5 (3.6%)
≥65 years	45 (31.9%)	Not Hispanic or Latino	131 (93.6%)
Males, n (%)	93 (66.0%)	Unknown	3 (2.1%)
Race, n (%)		Not reported	1 (0.7%)
White	95 (67.9%)	Missing	1
Black/African American	4 (2.9%)	Years since diagnosis, Mean (SD)	5.17 (7.5)
Asian	38 (27.1%)	AChR-Ab Seropositivity, n (%)	
Other	2 (1.4%)	AChR-Ab Seropositive	113 (80.1%)
Not reported	2 (0.7%)	AChR-Ab Seronegative	28 (19.9%)
Missing	1		

Item and scale performance

- 100% completion rate was observed for all MGII (PRO) Ocular Score items.
- No floor or ceiling effects were observed at either Baseline or Week 4, indicating no substantial clustering of scores at either extreme of the scale.
- At Baseline, no participants scored at ceiling, rising to 11.0% by Week 4, a shift consistent with improvement in ocular symptoms over time and demonstrating the score’s ability to capture improvement (**Table 2**).

TABLE 2 MGII (PRO) Ocular Score Scale Distribution at Baseline and Week 4

Statistic	Baseline (N = 141)	Week 4 (N = 136)
SD	3.40	5.29
Best Possible Score (Ceiling), n (%)	0 (0.0%)	15 (11.0%)
Within 0.5 SD of Ceiling, n (%)	0 (0.0%)	16 (11.8%)
Worst Possible Score (Floor), n (%)	8 (5.7%)	6 (4.4%)
Within 0.5 SD of Floor, n (%)	16 (11.3%)	17 (12.5%)

Notes: A floor or ceiling effect is present if ≥ 15% of participants score within 0.5 SD of the worst possible score (floor) or best possible score (ceiling).

Reliability

- The MGII (PRO) Ocular Score showed good test-retest reliability (ICC >0.70) among participants with stable ocular symptoms between visits (no change on ocular anchor measures), confirming reproducible scores when symptoms are unchanged.

Validity

- Convergent validity was supported by strong correlations with the MG-ADL Ocular and Total scores, strongest for the same-construct ocular score, confirming good conceptual alignment. Divergent validity was supported by weak correlations with measures of different constructs (MG-QoL15r total score and Neuro-QoL SF-Fatigue), consistent with the minimal expected overlap with generalized quality-of-life and fatigue measures (**Table 3**).

TABLE 3 Correlations Between the MGII (PRO) Ocular Score and Reference Measures at Baseline

MGII Score	Reference Measure	Strength of Correlation (r)		
		Expected	Observed	r
MGII (PRO) Ocular Score	MG-ADL Ocular Score	+++	+++	0.725
	MG-ADL Total Score	++	+++	0.632
	NEI VFQ-25 Total Score	+++	+	-0.171
	MG-QoL15r Total Score	+	+	0.120
	Neuro-QoL SF-Fatigue	+	+	0.065

Notes: Expected correlation strength was defined a priori based on the degree of conceptual overlap with the MGII (PRO) Ocular Score. Expected correlations: + = small correlations (<|0.3|); ++ = moderate correlations (≥|0.3| to <|0.5|); +++ = large correlations (≥|0.5|). Major discrepancies between expected and observed strength of correlations are indicated in bold.

DISCLOSURES AND ACKNOWLEDGMENTS

MO, RHJ, WYH, MM, FMV, FG, CB and JG are employees of argenx and own company shares. RC and JB were hired as consultants to argenx through Clinical Outcomes Solutions in connection with this study. CBT has served as member of the advisory board for argenx, Alexion, UCB, and Janssen, has been a consultant for argenx, Janssen, and UCB, has received research support from the US Department of Defense, Muscular Dystrophy Canada and MGNet, Grifols, and Octapharma, and is the primary developer of the MGII and may receive royalties GS has no conflicts of interest.

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TABLE 4 Responsiveness of the MGII (PRO) Ocular Score Relative to Change in Reference Measures from Baseline to Week 4

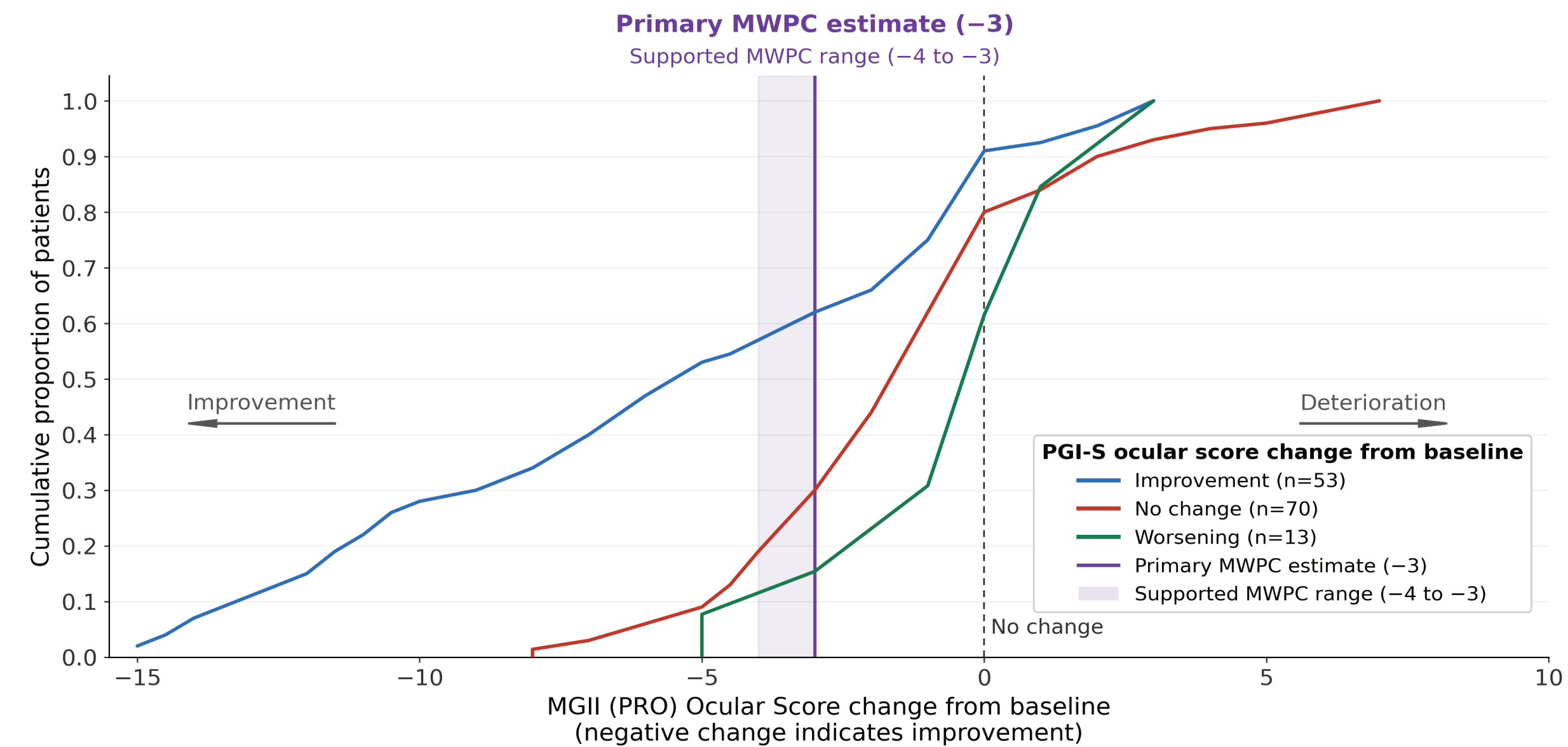
Correlation with reference measure	Change level	N	Mean change (SD)	Within-group SRM	Between-group SRM
MG-ADL Ocular Score <i>0.759</i>	Improved (<-1)	39	-8.1 (4.14)	-1.949***	—
	Stable (-1 to 1)	95	-1.2 (2.71)	-0.438***	-2.157***
	Worsened (>1)	2	1.5 (0.71)	2.121	—
PGI-S Ocular Score <i>0.579</i>	Improved (<0)	53	-5.8 (5.11)	-1.134***	—
	Stable (0)	70	-1.7 (3.05)	-0.543***	-1.017***
	Worsened (>0)	13	-0.2 (2.19)	-0.070	-0.511
PGI-C Ocular Score <i>0.592</i>	Much/Very Much Improved (≤2)	31	-7.5 (4.95)	-1.505***	—
	Improved (3)	39	-3.0 (3.34)	-0.892***	-1.085***
	No Change (4)	56	-1.4 (3.42)	-0.397**	-0.478*
	Worse (5)	7	-1.0 (2.52)	-0.397	-0.107
	Much/Very Much Worse (≥6)	3	1.7 (1.53)	1.091	—

Notes: For within groups, SRM is calculated by dividing the mean change score between Baseline and Week 4 by the SD of the change score. For between groups, the SRM is calculated by dividing the difference in change scores between consecutive groups by the pooled change SD. Based on Cohen’s recommendations¹⁰, the following values represent the magnitude of responsiveness: small change if around |0.2|, moderate change if around |0.5| and large change if around |0.8|. P values: * P < 0.05, ** P < 0.01, *** P <0.001.

Interpretability

- MWPC:** A ≥3-point decrease (range: 3–4 points) in the MGII (PRO) Ocular Score was identified as the primary threshold for meaningful improvement. This estimate was derived using PGI-S Ocular as the primary anchor and supported by PGI-C Ocular and the MG-ADL Ocular Domain (Figure 1).
- MBGD:** A 3-point between-group difference (range: 2–4 points) in the MGII (PRO) Ocular Score change from baseline at Week 4 was identified as the primary estimate of a meaningful difference between groups. Differences between the Improved and No Change groups were statistically significant across all anchors (MG-ADL Ocular, PGI-S Ocular and PGI-C Ocular) (P<0.0001).

FIGURE 1 eCDF of MGII (PRO) Ocular Score Change by PGI-S Ocular Anchor Category at Week 4



Notes: A leftward shift indicates greater improvement in MGII (PRO) Ocular Score. Participants reporting improvement on PGI-S Ocular showed greater score reductions than those reporting no change or worsening, supporting the selected 3-point decrease as the primary MWPC estimate

ABBREVIATIONS

AChR: acetylcholine receptor; ADLs: activities of daily living; COA: clinical outcome assessment; eCDF: empirical cumulative distribution function; FDA: Food and Drug Administration; gMG: generalized myasthenia gravis; ICC: intraclass correlation coefficient; MG: myasthenia gravis; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGFA: Myasthenia Gravis Foundation of America; MGII: Myasthenia Gravis Impairment Index; MG-QoL15r: Myasthenia Gravis Quality of Life 15-item Revised; MBGD: meaningful between-group difference; MWPC: meaningful within-patient change; NEI VFQ-25: National Eye Institute Visual Function Questionnaire-25; Neuro-QoL SF-Fatigue: Quality of Life in Neurological Disorders Short Form-Fatigue; oMG: ocular myasthenia gravis; PE: physical examination; PGI-C: Patient Global Impression of Change; PGI-S: Patient Global Impression of Severity; PRO: patient-reported outcome; SD: standard deviation; SRM: standardized response mean; US: United States.

