

Interpreting Clinically Meaningful Improvement on the Myasthenia Gravis Impairment Index (MGII) Patient Reported Outcome (PRO) Ocular Score: Responder Analyses from a Phase 3 Clinical Trial in Ocular MG

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Disclosures and Acknowledgments

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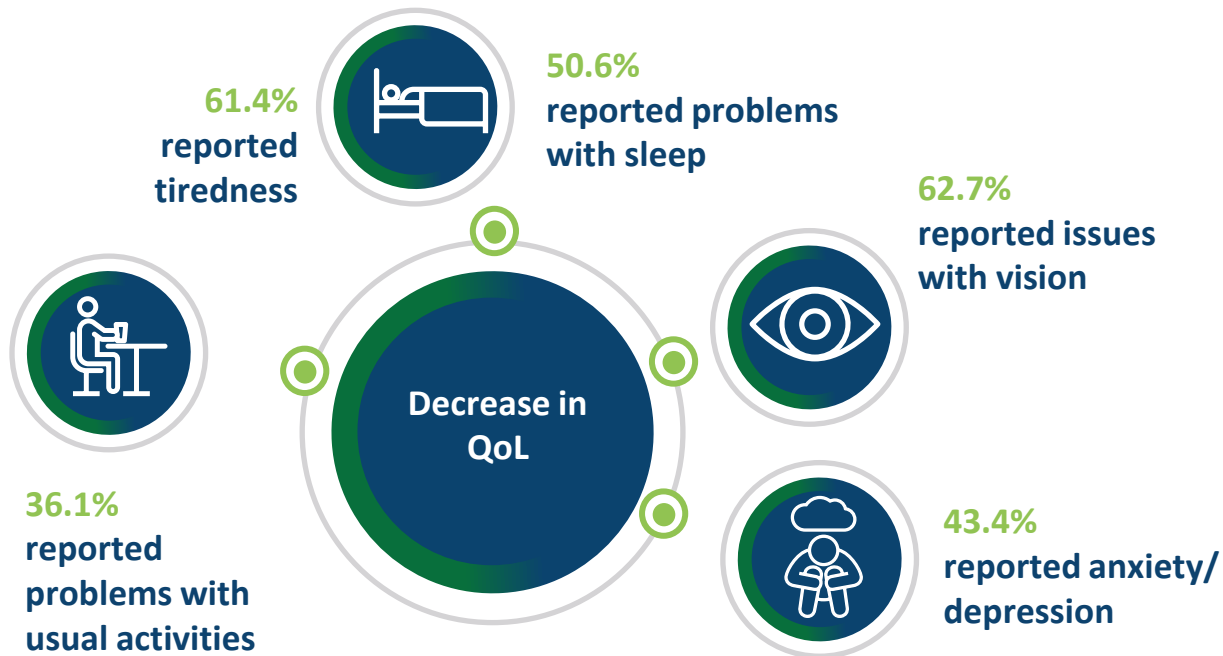
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Why a Patient-Reported Ocular Endpoint Matters in oMG

In a real-world study^a of 83 patients diagnosed with MG with MGFA Class I (ocular) symptoms^{1,a-d}:



Existing MG measures have limitations in oMG

- Broader MG measures may not optimally reflect ocular symptom change
 - MG-ADL has 2 items related to ocular symptoms, but these only capture frequency, not severity or impact
- A valid and reliable **ocular-specific PRO endpoint** is critical for capturing the patient experience and response to treatment
- According to **FDA**, “Patient-reported outcomes capture aspects of disease experience that are best known by patients themselves, including symptom **frequency, severity, and impact on functioning**”

An ocular-specific patient-reported outcome is needed to capture symptom frequency, severity, and impact from the patient perspective

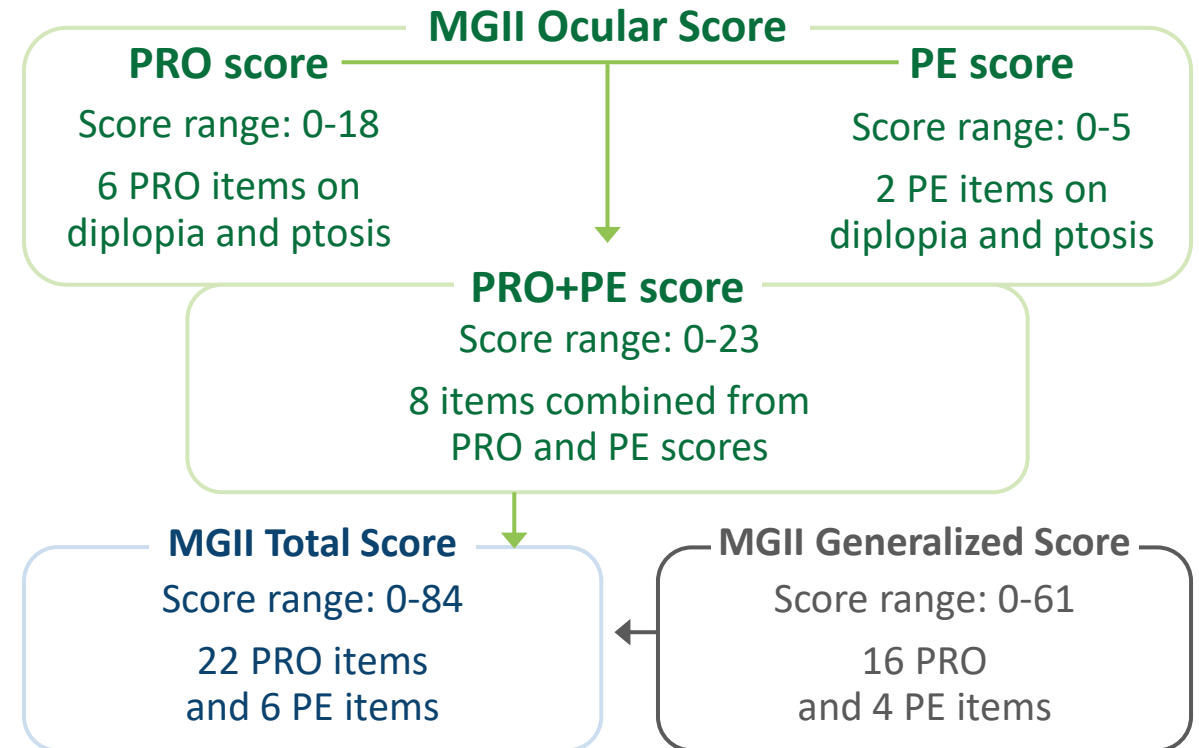
MGFA, Myasthenia Gravis Foundation of America; **MG**, myasthenia gravis; **oMG**, ocular myasthenia gravis; **PRO**, patient-reported outcome.

^aData from the MyRealWorld-MG (MRW-MG) study, an international, prospective, observational, longitudinal study of patients diagnosed with MG. ^bPatients from the US, Canada, UK, Spain, Germany, Italy, and Japan used a mobile application, MyRealWorld-MG, to answer questions related to their QoL with MG. ^c83 of 834 patients (14%) were classified as MGFA class I, defined as exclusive experience of ocular symptoms. ^dPercentages reflect patients who reported mild, moderate, severe, and extreme problems in each symptom category.¹

1. Dewilde S, et al. *BMJ Open*. 2023;13(1):e066445.

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

- The MGII is a 28-item disease severity measure validated in MG,^{1,2} with 22 PRO items and 6 physical examination (PE) items.
- **MGII (PRO) Ocular Score**, consist of 6 PRO items specifically designed around the 2 core symptoms - **Diplopia & Ptosis**.
- MGII (PRO) Ocular Score capture **Frequency, Severity, and Impact** of Diplopia and Ptosis.
- The score produces a **more comprehensive, patient-centric** evaluation of oMG symptoms and their **impact** than general MG measures.
- **MGII (PRO) Ocular Score change from baseline to Week 4** is the **primary endpoint** in the Phase 3 ADAPT OCULUS clinical trial in oMG (NCT06558279).



The MGII (PRO) Ocular Score was used to assess ocular impairment from the patient perspective, while the MGII (PRO+PE) Ocular Score provides a complementary assessment incorporating both patient-reported and clinician-assessed ocular impairment.

What Change in MGII (PRO) Ocular Score Is Clinically Meaningful? How Many Patients Achieve It?

How to Define Clinically Meaningful Change?

Meaningful Within-Patient Change (MWPC): How much does an individual patient need to improve for that improvement to be considered meaningful?

The smallest improvement that an individual patient would perceive as meaningful.

MGII Score	MWPC	
	Main Estimate	Range
MGII (PRO) Ocular Score	3	3 to 4
MGII (PRO+PE) Ocular Score	4	4 to 5

Responder Analysis

Compare the proportion of participants who achieved meaningful improvement with efgartigimod PH20 SC versus placebo.



More Often Patients Treated with Efgartigimod PH20 SC Achieved Meaningful Improvement

- At Week 4, a **higher proportion** of participants achieved meaningful improvement with efgartigimod PH20 SC compared with placebo
- MGII (PRO) Ocular Score (MWPC threshold of 3):
 - 58.0% of efgartigimod PH20 SC achieved meaningful improvement** vs. 37.3% of placebo
- MGII (PRO+PE) Ocular Score (MWPC threshold of 4):
 - 52.2% of efgartigimod PH20 SC achieved meaningful improvement** vs. 38.8% of placebo

MGII (PRO) Ocular Score at Week 4				
MWPC	3 (main estimate)		4 (alternative estimate)	
	EFG PH20 SC (N=71)	Placebo (N=70)	EFG PH20 SC (N=71)	Placebo (N=70)
n non-missing	69	67	69	67
Improved	40 (58.0%)	25 (37.3%)	33 (47.8%)	22 (32.8%)
Stable	26 (37.7%)	38 (56.7%)	35 (50.7%)	44 (65.7%)
Worsened	3 (4.3%)	4 (6.0%)	1 (1.4%)	1 (1.5%)

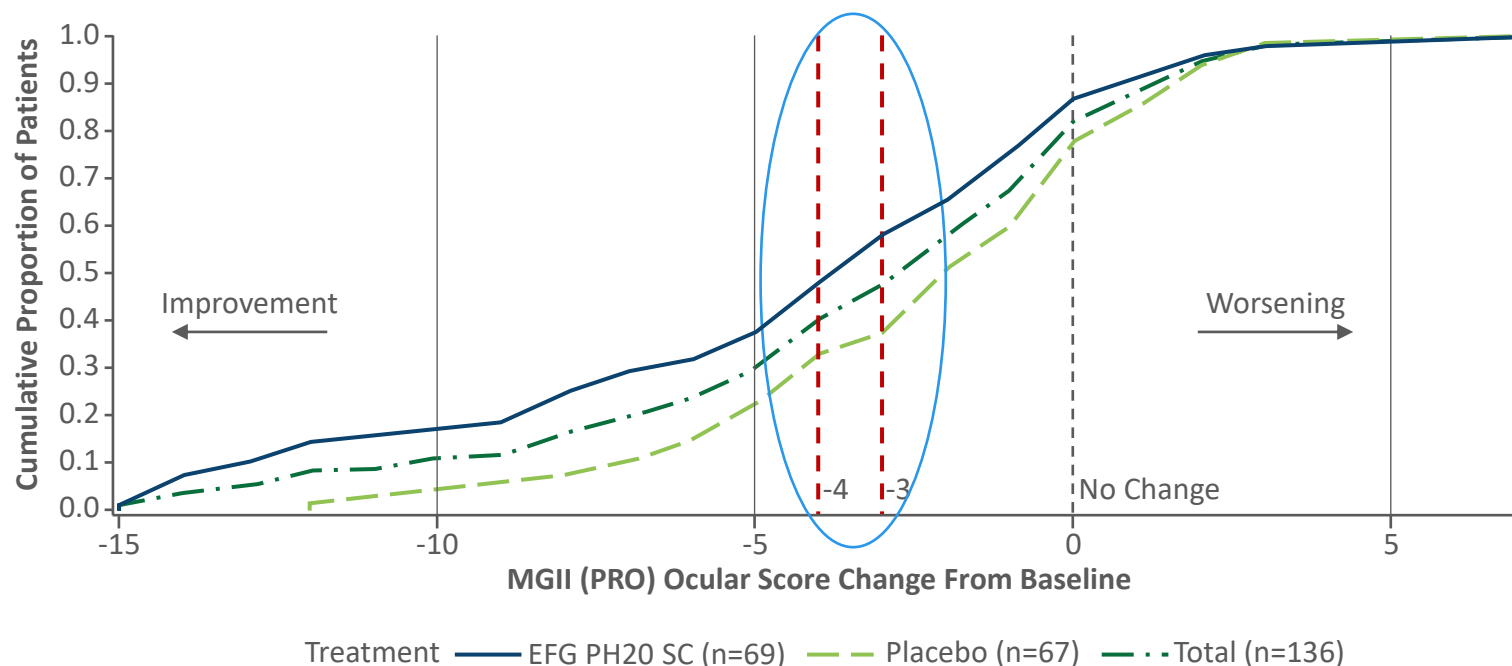
MGII (PRO+PE) Ocular Score at Week 4				
MWPC	4 (main estimate)		5 (alternative estimate)	
	EFG PH20 SC (N=71)	Placebo (N=70)	EFG PH20 SC (N=71)	Placebo (N=70)
n non-missing	69	67	69	67
Improved	36 (52.2%)	26 (38.8%)	34 (49.3%)	23 (34.3%)
Stable	32 (46.4%)	38 (56.7%)	34 (49.3%)	43 (64.2%)
Worsened	1 (1.4%)	3 (4.5%)	1 (1.4%)	1 (1.5%)

A higher proportion of participants achieved a meaningful improvement with efgartigimod PH20 SC compared with placebo across both MGII (PRO, PRO+PE) Ocular Scores

MGII (PRO) Ocular Score Changes Favored Efgartigimod PH20 SC Across a Range of Improvement Thresholds

- At the 3 & 4 point MWCP thresholds, a **greater proportion of participants** treated with **efgartigimod PH20 SC** achieved meaningful improvement compared with placebo
- Across a broad range of improvement thresholds, a **greater proportion of participants** treated with **efgartigimod PH20 SC** experienced **improvement** compared with placebo
- Similar results were observed when plotting the MGII (PRO+PE) Ocular Score CDF curve

Cumulative Distribution Function (CDF) Curves for Change From Baseline in the MGII (PRO) Ocular Score at Week 4



The treatment effect consistently favored EFG PH20 SC across the distribution of MGII (PRO) Ocular Score changes.



Participants Receiving Efgartigimod PH20 SC Had Higher Estimated Odds of Achieving Meaningful Improvement

- Using the **main 3-point MGII (PRO) Ocular Score** MWPC estimate, participants receiving **efgartigimod PH20 SC** had **2.34-fold higher** estimated odds of **meaningful improvement** versus placebo
- For the **MGII (PRO+PE) Ocular Score**, estimated odds **avored efgartigimod PH20 SC** using both the main and alternative MWPC estimates

Logistic Regression Model Comparing Odds of Improvement on the MGII (PRO, PRO+PE) Ocular Scores at Week 4

	Odds Ratio for Achieving Meaningful Change ^a	95% CI	P-value
MGII (PRO) Ocular Score			
EFG PH20 SC (vs. Placebo): MWPC 3	2.342	1.052, 5.213	0.0370
EFG PH20 SC (vs. Placebo): MWPC 4	1.814	0.796, 4.135	0.1566
MGII (PRO+PE) Ocular Score			
EFG PH20 SC (vs. Placebo): MWPC 4	1.941	0.858, 4.391	0.1113
EFG PH20 SC (vs. Placebo): MWPC 5	2.325	1.016, 5.312	0.0458

Across both MGII Ocular Scores and all evaluated MWPC thresholds, the estimated odds of achieving meaningful improvement favored efgartigimod PH20 SC over placebo

^aOdds of achieving meaningful change versus stable/worsening; Odds Ratios greater than one reflect a higher odds of achieving meaningful change in the EFG PH20 SC group.
CI, confidence interval; EFG, efgartigimod; MGII, Myasthenia Gravis Impairment Index; MWPC, meaningful within-patient change; PE, physical examination; PRO, patient-reported outcomes; SC, subcutaneous.



The ADAPT OCULUS Treatment Effect Was Reflected in Meaningful Improvement in a Greater Proportion of Participants Receiving Efgartigimod PH20 SC Than Placebo

- Efgartigimod PH20 SC demonstrated significantly **greater mean improvement** than placebo in the **MGII (PRO) and MGII (PRO+PE) Ocular Scores** at Week 4
- A **higher proportion** of participants achieved a **meaningful improvement** with **efgartigimod PH20 SC** compared with placebo
- **Responder analyses** translate the **ADAPT OCULUS treatment effect** into an interpretable **patient-level benefit**

	Efgartigimod PH20 SC	Placebo PH20 SC	Efgartigimod PH20 SC vs Placebo PH20 SC	
	LS mean (95.5% CI ^a)	LS mean (95.5% CI ^a)	LS mean difference (95.5% CI ^a)	<i>P</i> value ^{a,b}
MGII (PRO) Ocular Score	-4.04 (-5.17; -2.92)	-1.99 (-3.11; -0.87)	-2.05 (-3.56; -0.55)	<i>0.012</i>
MGII (PRO+PE) Ocular Score	-5.02 (-6.36; -3.67)	-2.57 (-3.92; -1.23)	-2.44 (-4.25; -0.63)	<i>0.018</i>

Together, the analyses demonstrate a statistically significant group-level treatment effect and support its interpretation as meaningful improvement at the individual-participant level

KEY TAKEAWAYS



At Week 4, a **higher proportion** of participants of ADAPT OCULUS, the first pivotal Phase 3 oMG study, receiving efgartigimod PH20 SC achieved **meaningful improvement** versus placebo for **MGII (PRO)** and **MGII (PRO+PE) Ocular Scores**



Across the MGII (PRO) Ocular Score distribution, **efgartigimod PH20 SC** showed **greater improvements** compared to placebo



Together with statistically significant ADAPT OCULUS primary endpoint, these analyses supports a **clinically meaningful, patient-level treatment benefit of efgartigimod PH20 SC in adults with oMG**



These findings contribute to the **evolving evidence** base for **ocular-specific outcome measurement** and may help inform endpoint selection and interpretation in future oMG studies