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Efgartigimod Improved Qualify of Life in gMG: A Randomized, Double-Blinded, Placebo-Controlled, Phase 3 Trial (ADAPT)

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Introduction

- Generalized myasthenia gravis (gMG) is associated with reduced health-related quality of life (HRQOL)[1,2]
- The lowest HRQOL levels are reported in patients with:
  - Disease symptoms that are not controlled adequately with therapy[3,4]
  - High treatment side-effect burden[3]
- The phase 3 ADAPT trial (NCT03669588) investigated efficacy, safety, tolerability, impact on normal daily activities, and HRQOL in patients with gMG treated with efgartigimod[5]
- The ADAPT trial demonstrated statistically significant efficacy and tolerability of efgartigimod in treated patients with gMG, and supported US Food and Drug Administration approval[6]
- In this analysis, we describe 2 important HRQOL outcomes in ADAPT:
  - Myasthenia Gravis Quality of Life 15-item scale, revised (MG-QOL15r)[7]
  - EuroQoL 5-dimension 5-level questionnaire (EQ-5D-5L), including visual analog scale (VAS), as generic health status measures[8]

MG-QOL15r[7]
- Patient-reported disease-specific measure
- Assesses patients' perception of disease and emotional/psychological burden
- Items rated on a 3-point Likert scale
- Higher scores indicate worse QOL

EQ-5D-5L[8]
- Patient-reported standardized QOL instrument used for clinical and economic appraisal across diseases
- Higher scores on dimensions and utility indicate worse QOL
- Higher score on VAS indicates better QOL

EQ-5D-5L, EuroQoL 5-dimension 5-level questionnaire; MG-QOL15r, Myasthenia Gravis Quality of Life 15-item scale, revised; QOL, quality of life; VAS, visual analog scale.

Methods

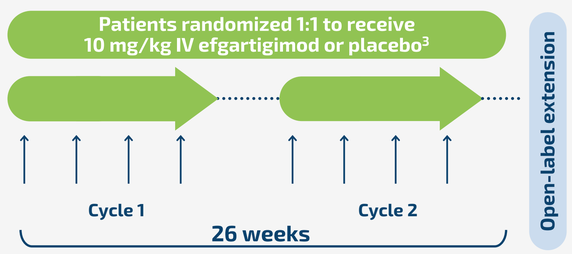
- MG-QoL15r and EQ-5D-5L scores were analyzed in patients with acetylcholine receptor antibody–positive (AChR-Ab+) gMG in the modified intention-to-treat population (patients with baseline and ≥1 post-baseline MG-ADL scores: n=65, efgartigimod; n=64, placebo) from baseline through Week 8 of cycle 1
- Mixed model for repeated measures were fitted for change from baseline
  - Least squares mean difference and *P* values were calculated at each visit

Figure 1. Study Design

adapt myasthenia gravis study

Inclusion Criteria
- MGFA class II, III, or IV
- AChR-Ab+/–
- MG-ADL score ≥5 (>50% nonocular)
- On ≥1 stable gMG treatment*

Retreatment Criteria
- ≥8 weeks since initiation of previous cycle
- Total MG-ADL score ≥5 (>50% nonocular)
- For MG-ADL responders, no CMI† in MG-ADL score



Treatment cycles of 4 weekly 1-hour IV infusions
All patients received initial cycle

Individualized treatment cycles (*≤3 cycles in 26 weeks*)
Time between cycles determined by duration of CMI† in MG-ADL

Primary Endpoint
- Percentage of AChR-Ab+ patients who were MG-ADL responders after cycle 1, defined by a ≥2-point reduction from cycle 1 baseline score for ≥4 consecutive weeks, with the first decrease occurring ≤1 week after last study drug infusion

Key Exploratory Endpoint
- Proportion of patients achieving MSE anytime during cycle 1

*Limited to acetylcholinesterase inhibitors, steroids, and/or NSIST.
†Defined as a ≥2-point improvement.
AChR-Ab+/–, acetylcholine receptor antibody positive or negative; CMI, clinically meaningful improvement; gMG, generalized myasthenia gravis; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MSE, minimal symptom expression; NSIST, nonsteroidal immunosuppressive therapy.

Results

Table 1. Patient Baseline Characteristics (AChR-Ab+ Patients)

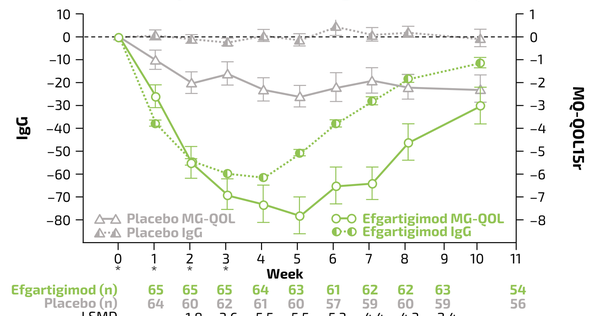
	AChR-Ab+ Patients (mITT Population)		
	Efgartigimod (n=65)	Placebo (n=64)	Total (n=129)
Age, years, mean (SD)	44.7 (14.97)	49.2 (15.54)	46.9 (15.36)
18 to <65, n	57	51	108
≥65, n	8	13	21
Sex at birth			
Female, n	46	40	86
Male, n	19	24	43
Time since diagnosis, years, mean (SD)	9.68 (8.25)	8.93 (8.21)	9.30 (8.21)
MG-ADL total score, mean (SD)	9.0 (2.48)	8.6 (2.14)	8.8 (2.32)
QMG total score, mean (SD)	16.0 (5.14)	15.2 (4.39)	15.6 (4.78)
MG-QOL15r score, mean (SD)	15.7 (6.3)	16.6 (5.5)	16.2 (5.87)
Concomitant gMG treatment			
NSISTs, n	40	37	77
No NSISTs, n	25	27	52
Steroids, n	46	51	97
AChE inhibitors, n	57	57	114

Note: Ranges for the clinical outcome assessments are as follows: MG-ADL total score, 0 to 24; QMG score 0 to 39; and MG-QOL15r, 0 to 30. For each instrument, higher scores indicate more severe disease.
AChE, acetylcholinesterase; AChR-Ab+, acetylcholine receptor antibody positive; gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; mITT, modified intention to treat; MG-QOL15r, Myasthenia Gravis Quality of Life 15-item scale, revised; NSIST, nonsteroidal immunosuppressive therapy; QMG, Quantitative Myasthenia Gravis.

Results

- Significant improvements in MG-QOL15r scores were seen with efgartigimod compared with placebo at Weeks 1–8 (**Figure 2**)
  - Maximum improvement in HRQOL was observed at Week 4 or 5, which corresponds with time points showing greatest change in immunoglobulin G (IgG) level
  - Similar to trends seen in other HRQOL measures in the study
- EuroQol-visual analog scale change from baseline showed significant improvements at Weeks 1–6 (**Figure 3**)
- Improvements were also observed across all 5 EQ-5D-5L domains with efgartigimod (**Figure 4**)

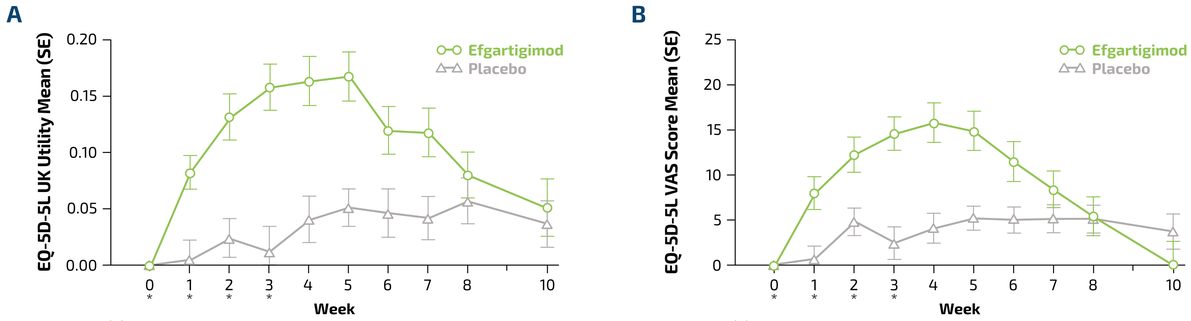
Figure 2. Mean Changes (±SE) From Baseline for Treatment Cycle 1 in Total IgG and MG-QOL15r



Week	0*	1*	2*	3*	4	5	6	7	8	9	10	11
Efgartigimod (n)	65	65	65	64	63	61	62	62	63			54
Placebo (n)	64	60	62	61	60	57	59	60	59			56
LSMD		−1.8	−3.6	−5.5	−5.5	−5.3	−4.4	−4.3	−2.4			
P value		.0062	<.0001	<.0001	<.0001	<.0001	<.0001	<.0001	.0123			

*Treatment time point.
IgG, immunoglobulin G; LSMD, least squares mean difference; MG-QOL15r, Myasthenia Gravis Quality of Life 15-item scale, revised; SE, standard error.

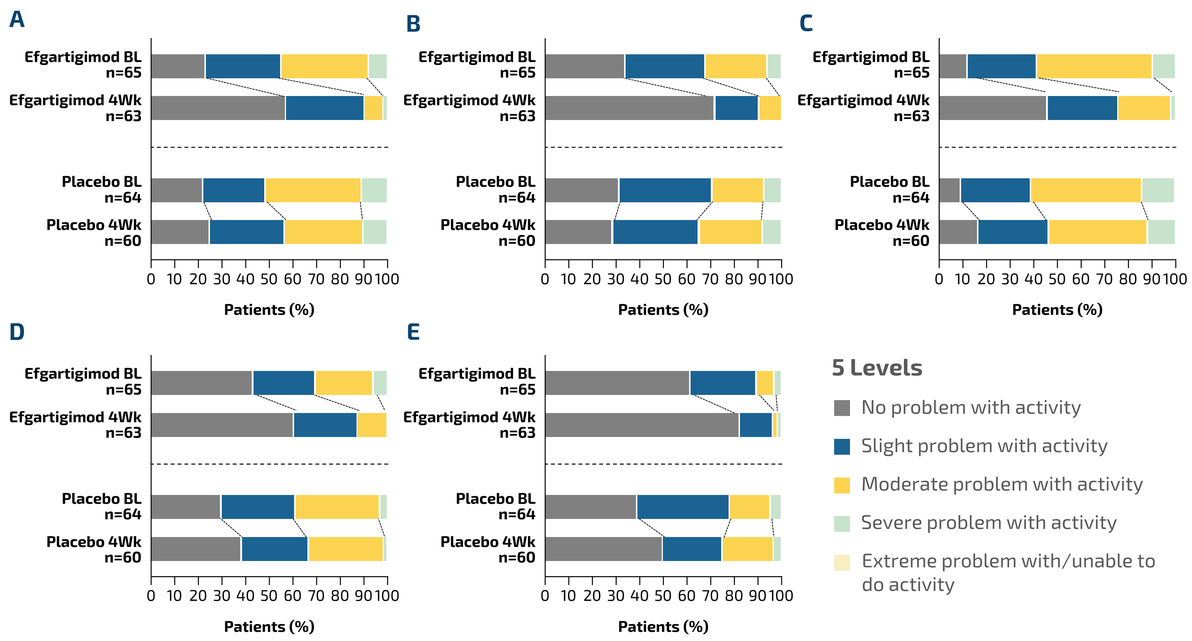
Figure 3. Mean Changes in Treatment Cycle 1 From Baseline in (A) UK Utility Scores and (B) VAS Scores



Week	0*	1*	2*	3*	4	5	6	7	8	10
A										
Efgartigimod (n)	65	64	65	64	63	61	63	62	63	54
Placebo (n)	64	60	62	61	60	58	60	60	59	56
LSMD		0.10	0.13	0.17	0.15	0.14	0.10	0.10	0.05	
P value		<.0001	<.0001	<.0001	<.0001	<.0001	.0007	.0002	.0442	
B										
Efgartigimod (n)	65	64	65	64	63	61	63	62	63	54
Placebo (n)	64	60	62	61	60	58	60	60	59	56
LSMD		8.0	7.8	12.9	13.3	10.4	6.9	3.6	0.6	
P value		.0004	.0004	<.0001	<.0001	<.0001	.0058	.1306	.7784	

*Treatment time point.
EQ-5D-5L, EuroQoL 5-dimension 5-level questionnaire; LSMD, least squares mean difference; SE, standard error; VAS, visual analogue scale.

Figure 4. Improvements With Efgartigimod in Treatment Cycle 1 From Baseline According to EQ-5D-5L Score for (A) Mobility, (B) Self Care, (C) Usual Activities, (D) Pain/Discomfort, and (E) Anxiety and Depression



4Wk, Week 4; BL, baseline; EQ-5D-5L, EuroQoL 5-dimension 5-level questionnaire.

Summary

Treatment with efgartigimod resulted in substantial and rapid HRQOL improvements for up to 8 weeks after the first infusion

Statistically significant improvements were seen across multiple measures and corresponded with reductions in total IgG

The substantial and durable improvements in HRQOL endpoints in this trial demonstrate the broader benefit of treatment with efgartigimod beyond relief of immediate signs and symptoms of gMG

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