Poster #015

Efgartigimod Demonstrates Consistent Improvements in Patients With Generalized Myasthenia Gravis Regardless of Disease Duration

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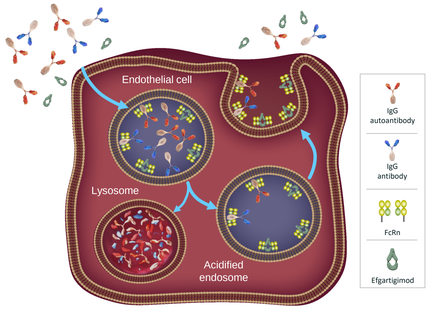
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG, extending its half-life and maintaining serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn[2,3]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting IgG lysosomal degradation without directly impacting its production[2-6]
  - Targeted reduction of all IgG subtypes
  - No impact on other immunoglobulins (ie, IgM, IgA, IgE, IgD)
  - No reduction in albumin levels
  - No increase in cholesterol

METHODS

ADAPT was a 26-week, global, randomized, double-blind, placebo-controlled, phase 3 trial evaluating the efficacy and safety of efgartigimod in patients with gMG[4]

- In this post hoc study, data collected from AChR-Ab+ patients in ADAPT were analyzed in subgroups based on disease duration (<3, 3–<6, and ≥6 years since gMG diagnosis)

adapt myasthenia gravis study

ADAPT
Patients randomized 1:1 to receive cycles of 4 infusions at weekly intervals of 10 mg/kg IV efgartigimod or placebo[4,a]

Entry criteria
- MGFA Disease Class II, III, IV
- AChR-Ab positive or negative
- MG-ADL score ≥5 (>50% nonocular)
- On ≥1 stable gMG treatment[b]
- IgG ≥6 g/L

Efgartigimod n=84 — 1:1 — Placebo n=83

26 weeks (≤3 cycles[c])

Initiation of new treatment cycle:
- ≥5 weeks between cycles
- MG-ADL score ≥5[d]
- MG-ADL score within 2 points of baseline

Primary Endpoint:
- Percentage of AChR-Ab+ patients who were **MG-ADL responders** after cycle 1[a]

Secondary Endpoints
- Percentage of AChR-Ab+ patients who were **QMG responders** after cycle 1[a]

Key Exploratory Endpoints
- Change from baseline in **MG-ADL** score
- Change from baseline in **QMG** score

Key Tertiary Endpoint
- Change from baseline in total **MG-QOL15r** score

N=151 → ADAPT+ (Open-Label Extension)

Note: Beige rectangles within arrow indicates day of efgartigimod infusion.
[a]MG-ADL responders were 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. QMG responders were defined by a ≥3-point reduction from cycle 1 baseline score for ≥4 consecutive weeks, with the first decrease occurring ≤1 week after last study drug infusion. [b]AChEI, steroid +/or NSIST. Patients could not change concomitant therapies in ADAPT. [c]≤3 cycles dosed at ≥8 weeks after initial cycle. [d]With >50% from nonocular items.

SUMMARY

Efgartigimod demonstrated improvements in MG-ADL, QMG, and MG-QOL15r scores compared to placebo, regardless of disease duration

Efgartigimod was well tolerated, with most AEs being mild or moderate in severity

These data suggest that efgartigimod is an effective treatment in patients with any duration of disease, including those with shorter disease duration (<3 years)

RESULTS

Table 1. Baseline Characteristics
AChR-Ab+ Population

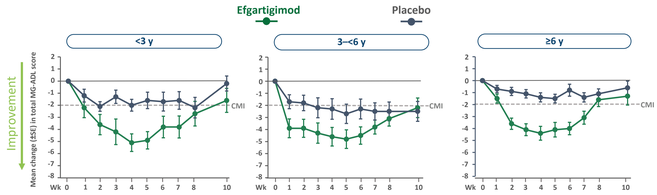
	Disease Duration <3 y		3–<6 y		≥6 y	
	Efgartigimod (n=14)	Placebo (n=17)	Efgartigimod (n=14)	Placebo (n=15)	Efgartigimod (n=37)	Placebo (n=32)
Age, mean, y (SD)	45.6 (19.2)	52.9 (16.0)	49.9 (18.5)	43.9 (18.0)	42.4 (11.3)	49.6 (13.8)
Sex, female, n (%)	8 (57.1)	10 (58.8)	8 (57.1)	9 (60.0)	30 (81.0)	21 (65.6)
Time since diagnosis, mean, y (SD)	2 (0.6)	1.7 (0.9)	4 (0.9)	4.6 (1.0)	14.7 (7.7)	14.8 (7.9)
MG-ADL score, mean (SD)	9.4 (2.3)	8.9 (2.4)	9.2 (2.2)	7.8 (1.7)	8.8 (2.7)	8.8 (2.1)
QMG score, mean (SD)	16.6 (7.2)	15.3 (3.9)	14.9 (5.2)	14.5 (5.0)	16.3 (4.2)	15.6 (4.4)
MG-QOL15r score, mean (SD)	17.6 (5.8)	15.6 (5.7)	16.6 (6.3)	15.6 (5.8)	14.6 (6.4)	17.6 (5.1)
EQ-5D-5L VAS score, mean (SD)	53.9 (14.2)	56.8 (20.8)	59.5 (25.3)	61.7 (11.6)	59.3 (15.0)	54.4 (17.2)
MGFA Disease Class at screening, n (%)						
Class II	8 (57.1)	5 (29.4)	6 (42.9)	6 (40.0)	14 (37.8)	14 (43.8)
Class III	4 (28.6)	11 (64.7)	8 (57.1)	8 (53.3)	23 (62.2)	17 (53.1)
Class IV	2 (14.3)	1 (5.9)	0 (0)	1 (6.7)	0 (0)	1 (3.1)

Table 2. Safety Data
Overall Population

	Efgartigimod (n=84)	Placebo (n=83)
AEs,[a] n (%)	65 (77.4)	70 (84.3)
SAEs, n (%)	4 (4.8)	7 (8.4)
Discontinued due to AEs,[b] n (%)	3 (3.6)	3 (3.6)

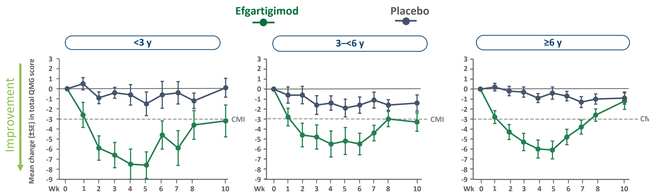
[a]Most AEs were mild to moderate in severity. [b]Patients treated with efgartigimod: gMG worsening, rectal adenocarcinoma, thrombocytosis (determined to be unlikely related to efgartigimod by the investigator); patients treated with placebo: myocardial ischemia, atrial fibrillation, spinal ligament ossification.

Figure 1. MG-ADL Total Score by Disease Duration
Mean Change From Cycle Baseline in Cycle 1
AChR-Ab+ Population



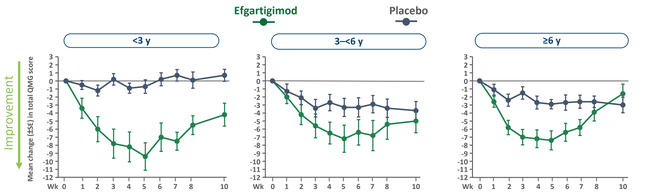
Sample Size, Wk 0 — EFG n=14 PBO n=17 | EFG n=14 PBO n=15 | EFG n=37 PBO n=32

Figure 2. QMG Total Score by Disease Duration
Mean Change From Cycle Baseline in Cycle 1
AChR-Ab+ Population



Sample Size, Wk 0 — EFG n=14 PBO n=16 | EFG n=14 PBO n=15 | EFG n=37 PBO n=31

Figure 3. MG-QOL15r Total Score by Disease Duration
Mean Change From Cycle Baseline in Cycle 1
AChR-Ab+ Population



Sample Size, Wk 0 — EFG n=14 PBO n=17 | EFG n=14 PBO n=15 | EFG n=37 PBO n=32

Figure 4. Change in MG-ADL at Week 4 of Cycle 1 by Disease Duration
AChR-Ab+ Population

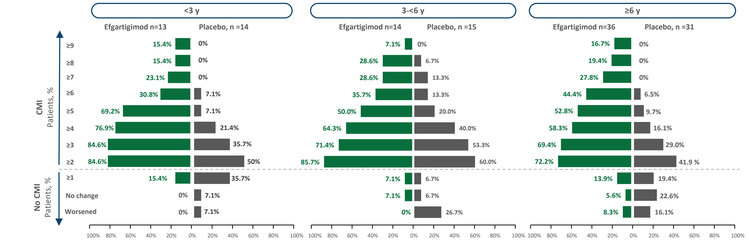


Figure 5. Change in QMG at Week 4 of Cycle 1 by Disease Duration
AChR-Ab+ Population

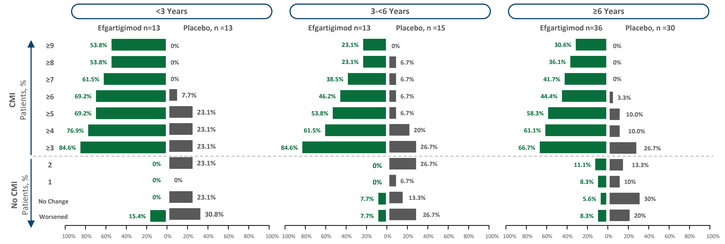
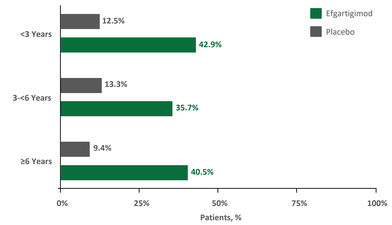


Figure 6. Minimal Symptom Expression at Anytime in Cycle 1 by Disease Duration
AChR-Ab+ Population



ABBREVIATIONS
AChEI, acetylcholinesterase inhibitor; AChR-Ab+, acetylcholine receptor antibody seropositive; AE, adverse event; CMI, clinically meaningful improvement; FcRn, neonatal Fc receptor; EQ-5D-5L VAS, EuroQol 5-Dimension, 5-Level Visual Analogue Scale; Fc, fragment crystallizable region; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MG-QOL15r, 15-item Quality of life scale for Myasthenia Gravis, Revised; MSE, minimal symptom expression; NSIST, nonsteroidal immunosuppressive therapy; QMG, Quantitative Myasthenia Gravis; SAE, serious adverse event.

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1. Sesarman A, et al. *Cell Mol Life Sci.* 2010;67(15):2533-2550. **2.** Ulrichts P, et al. *J Clin Invest.* 2018;128(10):4372-4386. **3.** Vaccaro C, et al. *Nat Biotech.* 2005;23(10):1283-1288. **4.** Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526-536. **5.** Nixon AE, et al. *Front Immunol.* 2015;6:176. **6.** Ward ES, et al. *Front Immunol.* 2022;13:892534.

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