Poster #134

Efgartigimod Demonstrates Consistent Improvements in Generalized Myasthenia Gravis Across Patient Subgroups, Including Early in Diagnosis

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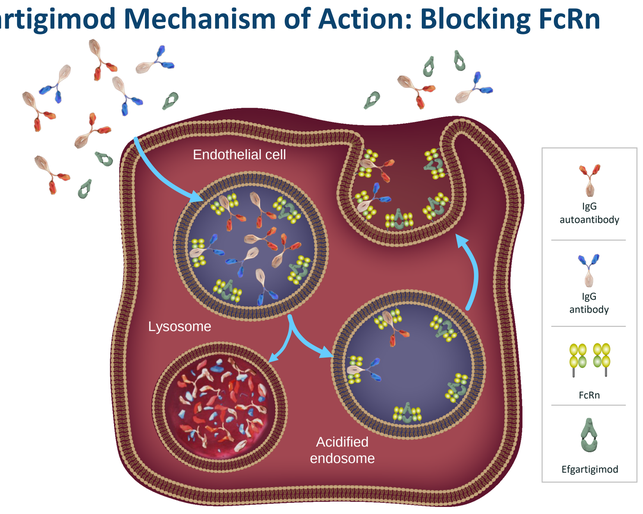
INTRODUCTION

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 IgM or IgA
  - No reduction in albumin levels
  - No increase in cholesterol

SUMMARY

- Efgartigimod demonstrates consistent improvements compared to placebo, regardless of disease duration, concomitant therapy, prior therapies (including thymectomy), or prior treatment failures
- These data suggest that efgartigimod is an effective treatment in a broad patient population, including early in disease, and early in the treatment journey of patients with gMG
- Efgartigimod was well tolerated, with most adverse events being mild or moderate in severity

METHODS

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

- A post hoc analysis of data collected from AChR-Ab+ patients in ADAPT was performed in subgroups based on baseline disease factors and concomitant gMG therapies

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]

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

Efgartigimod n=84
1:1
Placebo n=83

26 weeks (≤3 cycles[b])

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

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 Secondary Endpoint
- Percentage of AChR-Ab+ patients who were **QMG responders** after cycle 1, **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

N=151 → ADAPT+ (Open-Label Extension)

Note: Beige rectangles within arrow indicates day of efgartigimod infusion. AChR-Ab, acetylcholine receptor antibody; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; QMG, Quantitative Myasthenia Gravis. [a]Acetylcholinesterase inhibitor, steroid +/or nonsteroidal immunosuppressive therapy. Patients could not change concomitant therapies in ADAPT. [b]≤3 cycles dosed at ≥8 weeks after initial cycle. [c]With >50% from nonocular items.

RESULTS

Table 1. Baseline Characteristics
AChR-Ab+ Patients

	Efgartigimod (n=65)	Placebo (n=64)
Age, mean, y (SD)	44.7 (15.0)	49.2 (15.5)
Sex, female, n (%)	46 (70.8)	40 (62.5)
Time since diagnosis, mean, y (SD)	9.68 (8.3)	8.93 (8.2)
MG-ADL score, mean (SD)	9.0 (2.5)	8.6 (2.1)
QMG score, mean (SD)	16.0 (5.1)	15.2 (4.4)
MGFA class at screening, n (%)		
Class II	28 (43.1)	25 (39.1)
Class III	35 (53.8)	36 (56.3)
Class IV	2 (3.1)	3 (4.7)
Prior treatment with NSIST, n (%)	47 (72.3)	43 (67.2)
MG therapies at baseline, n (%)		
Any NSIST	40 (61.5)	37 (57.8)
Any steroid	46 (70.8)	51 (79.7)
Steroid and NSIST	34 (52.3)	31 (48.4)
AChEI only	13 (20.0)	6 (9.4)

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. Proportion of MG-ADL and QMG Responders by Disease Duration
AChR-Ab+ Patients, Cycle 1

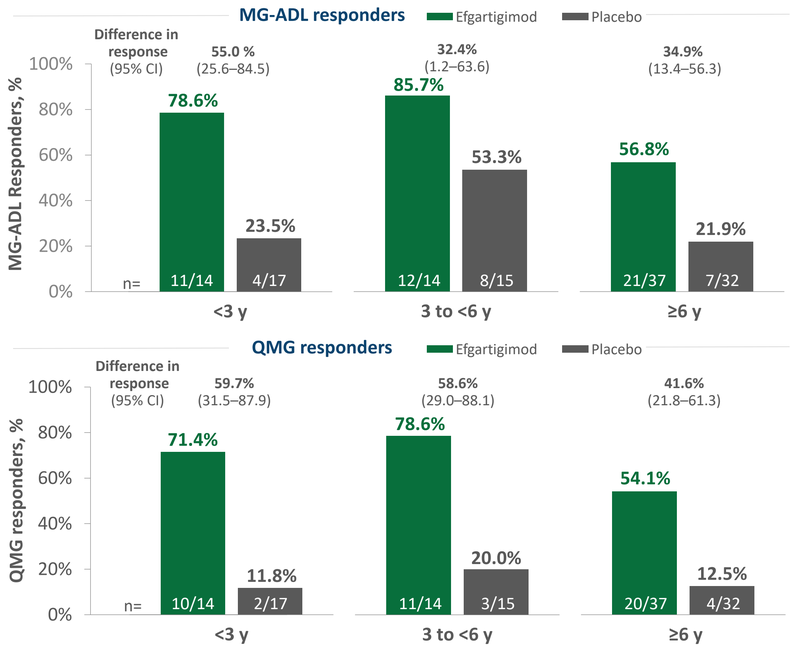


Figure 2. Proportion of MG-ADL and QMG Responders by Concomitant Therapies
AChR-Ab+ Patients, Cycle 1

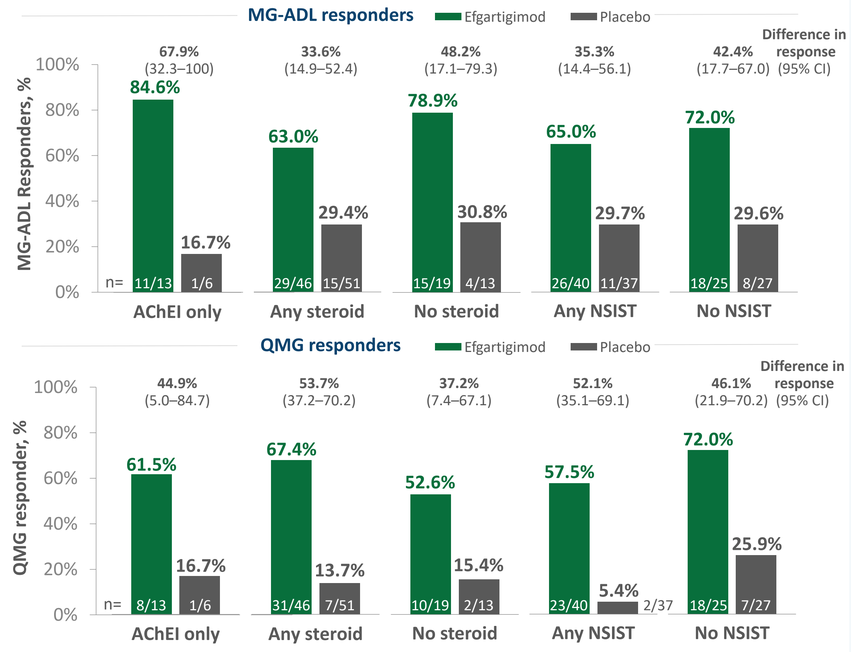


Figure 3. Proportion of MG-ADL and QMG Responders by Prior Therapies
AChR-Ab+ Patients, Cycle 1

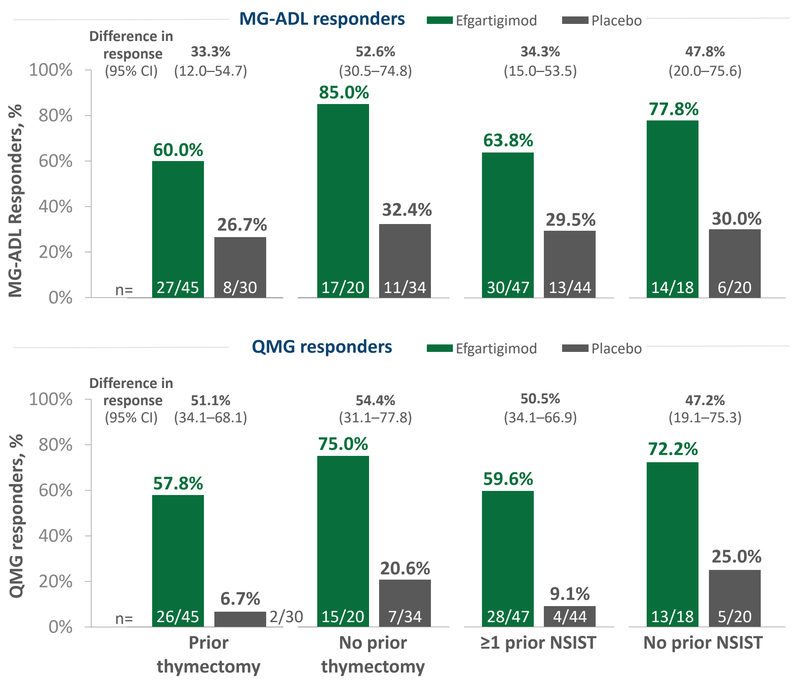
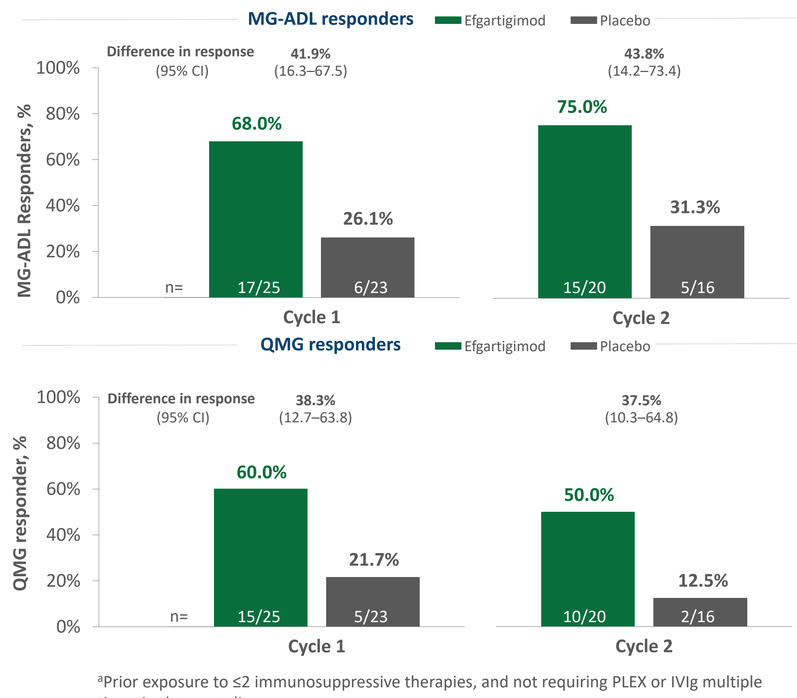


Figure 4. Proportion of MG-ADL and QMG Responders Among Patients Without Prior Treatment Failures[a]
AChR-Ab+, Cycles 1 and 2



[a]Prior exposure to ≤2 immunosuppressive therapies, and not requiring PLEX or IVIg multiple times in the preceding year.

ABBREVIATIONS

AChEI, acetylcholinesterase inhibitor; AChR-Ab+, acetylcholine receptor antibody seropositive; AE, adverse event; FcRn, neonatal Fc receptor; Ig, immunoglobulin; IVIg, intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living; NSIST, nonsteroidal immunosuppressive therapy; PLEX, plasma exchange; QMG, Quantitative Myasthenia Gravis; SAE, serious adverse event.

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