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Long-Term Safety, Tolerability, and Efficacy of Efgartigimod in Participants With Generalized Myasthenia Gravis: Concluding Analyses From ADAPT+

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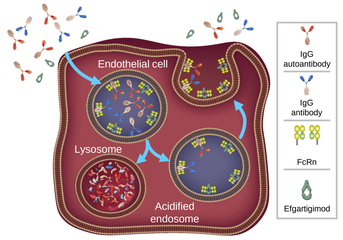
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have increased affinity for FcRn and outcompete endogenous IgG[2,3]
- Efgartigimod binding to FcRn prevents IgG recycling and promotes its lysosomal degradation, thus reducing IgG levels without directly impacting IgG production[2-5]
  - Targeted reduction of all IgG subtypes[2,4]
  - No impact on levels of IgM, IgA, IgE, or IgD[2,5]
  - No reduction in albumin or increase in cholesterol levels[4-6]

METHODS

ADAPT was a 26-week, global, multicenter, randomized, double-blind, placebo-controlled, phase 3 trial evaluating efgartigimod in participants with gMG. Participants who completed ADAPT were eligible to be rolled over to ADAPT+[4,a]

ADAPT
Placebo-Controlled, Randomized, Phase 3 Trial
(26 weeks total; ≤3 cycles)[a-c]

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

Cycles of 4 once-weekly infusions[d]

N=167 → 1:1 → Efgartigimod IV (10 mg/kg) n=84 / Placebo n=83 → N=151

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

ADAPT+
Long-Term, Open-Label Extension Study
(≤3 total years; ≤19 cycles)[b]

Year 1[d]

Initiation of new treatment cycle
- ≥4 weeks between cycles
- MG-ADL score ≥5[f]
- MG-ADL score within 2 points of baseline

Years 2 and 3[d]

Initiation of new treatment cycle
- ≥4 weeks between cycles
- Per investigator discretion

[a]Participants who required subsequent treatment cycles but were unable to complete a treatment cycle within the time frame of ADAPT were also eligible to be rolled over to ADAPT+. [b]Participants requiring rescue therapy in ADAPT and ADAPT+ Year 1 discontinued the study if they required rescue therapy; however, participants in ADAPT+ Years 2 and 3 did not. [c]≤3 cycles dosed at ≥8 weeks after initial cycle. [d]Arrows indicate efgartigimod administration. [e]AChEI, steroid +/or NSIST. Participants could not change concomitant therapies in ADAPT. Physicians could change concomitant therapies between doses in Year 1 and at any time in Years 2 and 3 of ADAPT+. [f]With >50% from nonocular items.

SUMMARY

- **Efgartigimod was well tolerated throughout the course of ADAPT+, with no increase in TEAEs, serious TEAEs, or infections observed with long-term treatment**
- **In AChR-Ab+ participants, efgartigimod treatment resulted in consistent and repeatable improvements in MG-ADL and QMG scores**
- **In AChR-Ab+ participants, efgartigimod treatment resulted in consistent and repeatable CMI in MG-ADL and QMG scores across increasing MG-ADL and QMG thresholds over multiple cycles in ADAPT+**
- **AChR-Ab+ participants with >350 days of follow-up across ADAPT/ADAPT+ showed varying intertreatment periods, which supports an individualized treatment approach**
- **These analyses suggest that long-term efgartigimod treatment is well tolerated and efficacious in participants with gMG**

RESULTS

Table 1. ADAPT+ Baseline Demographics and Disease Characteristics
Overall Population

Characteristics	Efgartigimod (n=145)
Age, y (SD)	47.0 (14.8)
Sex, n (%)	
Female	103 (71)
Male	42 (29)
Race, n (%)	
Asian	11 (7.6)
Black/African American	5 (3.4)
White	126 (86.9)
Time since gMG diagnosis, y (SD)	9.7 (8.2)
MGFA class at screening, n (%)	
II	55 (37.9)
III	86 (59.3)
IV	4 (2.8)
AChR-Ab+, n (%)	111 (76.6)
Total MG-ADL score, mean (SD)	9.8 (3.2)
Total QMG score, mean (SD)	15.4 (5.7)
Standard of care, n (%)	
NSIST	89 (61.4)
No NSIST	56 (38.6)
Steroid	111 (76.6)
No steroid	34 (23.4)

- In ADAPT+, 145 participants received ≥1 cycle over a median study duration of 651 days (minimum-maximum, 50-1074)
  - Participants in ADAPT+ received ≤19 treatment cycles
- Total follow-up since first treatment in study was 229 PY

Table 2. Summary of TEAEs
Overall Population

	ADAPT: Placebo (n=83) [34.5 PY]		ADAPT: Efgartigimod (n=84) [34.9 PY]		ADAPT+: Efgartigimod (n=145) [229.0 PY]	
	IR[a]	n (%)	IR[a]	n (%)	IR[a]	n (%)
TEAEs[b]	**7.83**	70 (84)	**7.23**	65 (77)	**3.53**	124 (86)
SAEs	**0.29**	7 (8)	**0.11**	4 (5)[c]	**0.24**	36 (25)[c]
≥1 Infusion-related reaction event	**0.26**	8 (10)	**0.09**	3 (4)	**0.09**	15 (10)
Infection TEAEs	**1.22**	31 (37)	**1.61**	39 (46)	**0.73**	80 (55)
Discontinued due to TEAEs	**0.09**	3 (4)	**0.20**	3 (4)	**0.06**	12 (8)
Severe TEAEs (grade ≥3)	**0.35**	8 (10)	**0.29**	9 (11)	**0.33**	40 (28)
Death[d]	-	0 (0)	-	0 (0)	**0.02**	5 (3)
Most frequent TEAEs						
Nasopharyngitis	**0.49**	15 (18)	**0.34**	10 (12)	**0.10**	20 (14)
Upper respiratory tract infection	**0.14**	4 (5)	**0.32**	9 (11)	**0.03**	6 (4)
Urinary tract infection	**0.12**	4 (5)	**0.26**	8 (10)	**0.08**	13 (9)
Headache	**1.13**	23 (28)	**1.15**	24 (29)	**0.45**	36 (25)
Nausea	**0.43**	9 (11)	**0.20**	7 (8)	**0.06**	9 (6)
Diarrhea	**0.41**	9 (11)	**0.17**	6 (7)	**0.08**	14 (10)
COVID-19[e]	-	0 (0)	-	0 (0)	**0.10**	23 (16)[f]

[a]IR was calculated as number of events per total PY of follow-up. [b]TEAEs were predominantly mild or moderate. [c]Only 1 SAE was considered treatment related per investigator. [d]None of the deaths in ADAPT+ were related to efgartigimod administration per the principal investigator. [e]Includes all preferred terms of COVID-19, COVID-19 pneumonia, coronavirus infection, exposure to SARS-CoV-2, and SARS-CoV-2 test positive. [f]Among participants reporting COVID-19 during ADAPT+, 83% had not received prior COVID-19 vaccination.

- No new safety signals were observed in ADAPT+, with the safety profile over time consistent with that in ADAPT
- TEAE IRs were similar between efgartigimod and placebo in ADAPT, and IRs of most TEAEs did not increase with long-term treatment in ADAPT+
- No reductions in albumin levels or increases in LDL levels were observed with efgartigimod in ADAPT or ADAPT+

Figure 1. TEAEs by Cycle
Overall Population

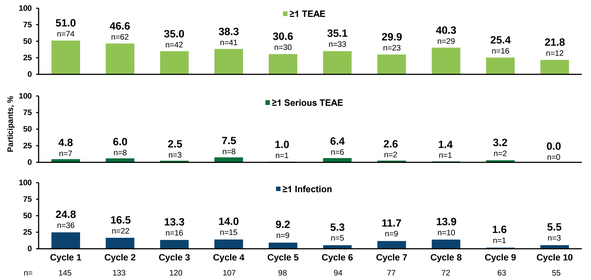
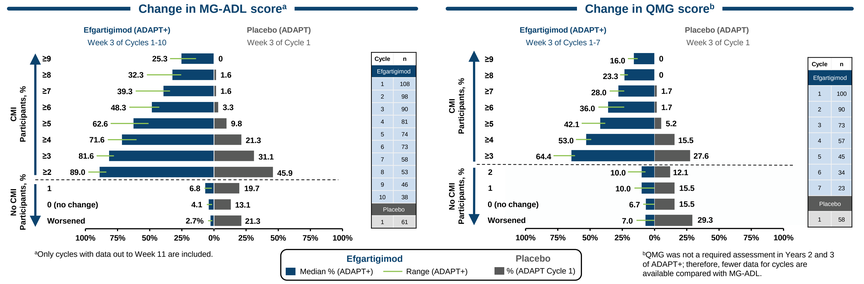
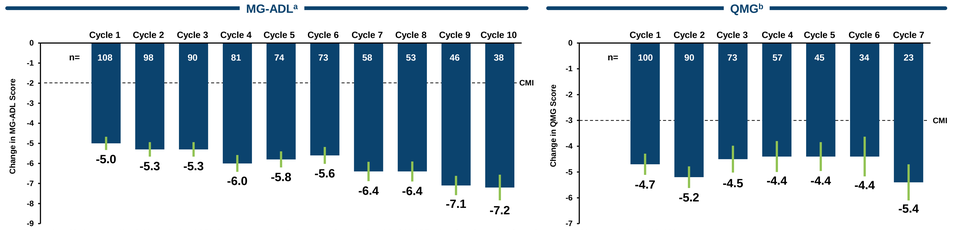


Figure 2. Proportion of Participants With Increasing MG-ADL or QMG Thresholds
AChR-Ab+ Population



[a]Only cycles with data out to Week 11 are included. [b]QMG was not a required assessment in Years 2 and 3 of ADAPT+; therefore, fewer data for cycles are available compared with MG-ADL.

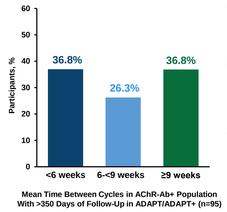
Figure 3. Mean Change in MG-ADL and QMG Scores From Cycle Baseline at Week 3
AChR-Ab+ Population



[a]Only cycles with data out to Week 11 are depicted. [b]QMG was not a required assessment in Years 2 and 3 of ADAPT+; therefore, fewer data for cycles are available compared with MG-ADL.

- Efgartigimod demonstrated consistent and repeatable improvement in both MG-ADL and QMG scores over multiple cycles in ADAPT+

Figure 4. Distribution of Time Between Cycles
AChR-Ab+ Population With >350 Days of Follow-Up in ADAPT/ADAPT+



- ***Time between cycles*** **is defined as the time from the last infusion of the previous treatment cycle to the first infusion of the subsequent treatment cycle**
- ADAPT+ demonstrated that individualization of cycle dosing allows for flexible or fixed time between cycles, and initiation of subsequent cycles is based on clinical evaluation and participant/health care professional goals
- Median number of cycles per year was 5.1 (minimum-maximum, 0.5-7.5; mean ± SD, 4.8 ± 1.9 cycles)

ABBREVIATIONS
AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor antibody; CMI, clinically meaningful improvement; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgA, immunoglobulin A; IgD, immunoglobulin D; IgE, immunoglobulin E; IgG, immunoglobulin G; IgM, immunoglobulin M; IR, incidence rate; IV, intravenously; LDL, low-density lipoprotein; LLN, lower limit of normal; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; PY, participant-years; QMG, Quantitative Myasthenia Gravis; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

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REFERENCES

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 Biotechnol.* 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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