009

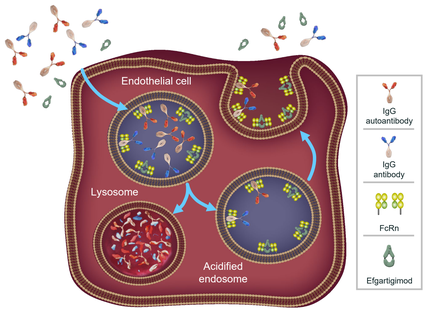
Achievement of Minimal Symptom Expression and Effect on Disease-Specific Measures in Acetylcholine Receptor Antibody-Positive Participants With Generalized Myasthenia Gravis Treated With Efgartigimod in ADAPT/ADAPT+

Srikanth Muppidi,[1] James F. Howard Jr,[2] Hiroyuki Murai,[3] Glenn Phillips,[4] Cynthia Qi,[4] Deborah Gelinas,[4] Edward Brauer,[4] Sihui Zhao,[4] Vera Bril,[5,6] John Vissing,[7] and the ADAPT Study Group

[1]Stanford Healthcare, Palo Alto, California, USA; [2]Department of Neurology, The University of North Carolina, Chapel Hill, North Carolina, USA; [3]Department of Neurology, School of Medicine, International University of Health and Welfare, Tokyo, Japan; [4]argenx, Ghent, Belgium; [5]Ellen & Martin Prosserman Centre for Neuromuscular Diseases, University Health Network, Toronto, Ontario, Canada; [6]University of Toronto, Toronto, Ontario, Canada; [7]Copenhagen Neuromuscular Center, Rigshospitalet, University of Copenhagen, Denmark

INTRODUCTION

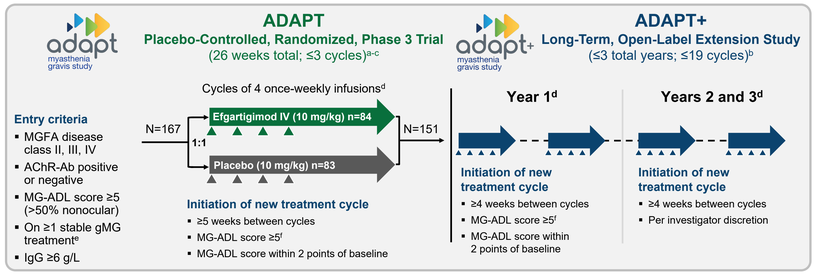
Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
  - FcRn is additionally involved in other cellular processes such as albumin recycling, as well as IgG-dependent phagocytosis and antigen presentation[2]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have increased affinity for FcRn and outcompete endogenous IgG[3,4]
- Efgartigimod binding to FcRn prevents IgG recycling and promotes its lysosomal degradation, reducing IgG levels without impacting IgG production[3-6]
  - Targeted reduction of all IgG subtypes[3,5]
  - No impact on levels of IgM, IgA, IgE, or IgD[3,6]
  - No reduction in albumin or increase in cholesterol levels[5-7]

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]



[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 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

In ADAPT, participants who achieved MSE had similar baseline disease severity and symptom burden to those who did not achieve MSE

Participants who achieved MSE also improved across multiple disease-specific measures and experienced QoL comparable to the healthy population

MSE rate in ADAPT+ was comparable to the MSE rate seen in ADAPT

Efgartigimod was well tolerated; AEs, were predominantly mild to moderate and did not increase in frequency during long-term treatment in ADAPT+

RESULTS

Table 1. ADAPT Baseline Demographics and Disease Characteristics By Achievement of MSE[a]

AChR-Ab+ Population

	Placebo		Efgartigimod	
Characteristics	**MSE (n=7)**	**Non-MSE (n=57)**	**MSE (n=29)**	**Non-MSE (n=36)**
Age, years, mean (SD)	48.7 (16.2)	49.2 (15.6)	42.4 (15.5)	46.5 (14.5)
Sex, n (%)				
Female	3 (42.9)	37 (64.9)	21 (72.4)	25 (69.4)
Male	4 (57.1)	20 (35.1)	8 (27.6)	11 (30.6)
BMI, kg/m^2 (SD)	28.9 (4.6)	28.0 (6.2)	26.3 (5.0)	29.6 (9.7)
Time since gMG diagnosis, y, mean (SD)	6.3 (3.4)	9.3 (8.6)	9.0 (6.8)	10.2 (9.3)
MGFA class at screening, n (%)				
II	5 (71.4)	20 (35.1)	11 (37.9)	17 (47.2)
III	1 (14.3)	35 (61.4)	18 (62.1)	17 (47.2)
IV	1 (14.3)	2 (3.5)	0	2 (5.6)
Previous thymectomy, n (%)	2 (28.6)	28 (49.1)	22 (75.9)	23 (63.9)
Total MG-ADL score, mean (SD)	7.0 (1.7)	8.8 (2.1)	8.2 (1.8)	9.7 (2.7)
Total QMG score, mean (SD)	8.2 (1.9)	16.0 (3.9)	15.8 (4.9)	16.2 (5.4)
Total MG-QoL15r score, mean (SD)	14.6 (6.8)	16.9 (5.3)	14.8 (5.8)	16.4 (6.6)
Total MGC score, mean (SD)	16.0 (7.1)	18.4 (4.9)	18.2 (5.7)	18.9 (6.4)
Commonly prescribed therapies, n (%)				
NSIST	4 (57.1)	33 (57.9)	19 (65.5)	21 (58.3)
Steroid	3 (42.9)	48 (84.2)	21 (72.4)	25 (69.4)
NSIST and/or steroid	6 (85.7)	51 (89.5)	24 (82.8)	28 (77.8)

[a]MSE is defined as MG-ADL score of 0 or 1.

- Those who achieved MSE in the placebo group had a significantly lower mean MG-ADL score (*P*=.0379), mean QMG score (*P*<.0001), and higher rates of MGFA class II at screening (*P*=.0301)
- Among those treated with efgartigimod, the only significant difference in baseline characteristics was a mean MG-ADL score 1.5 points lower among those who achieved MSE (*P*=.0084)

Table 2. Summary of TEAEs

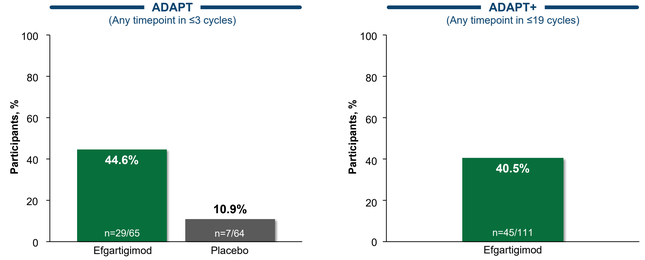
Overall Population

	ADAPT				ADAPT+	
	Placebo (n=83) [34.5 PY]		Efgartigimod (n=84) [34.9 PY]		Efgartigimod (n=145) [229.0 PY]	
	ER[a]	n (%)	ER[a]	n (%)	ER[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]
Discontinued due to TEAEs	0.09	3 (4)	0.20	3 (4)	0.06	12 (8)

[a]ER 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.

Figure 1. Proportion of Participants With MSE in ADAPT/ADAPT+

AChR-Ab+ Population

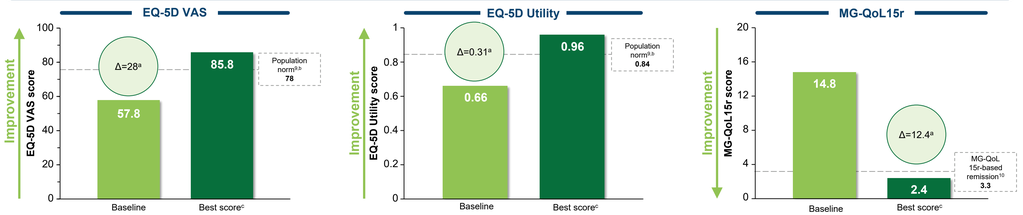


- **21 of 26[a] participants (81%) from the efgartigimod arm who achieved MSE during ADAPT also achieved MSE during ADAPT+**
- **8 of 35[a] participants (23%) from the efgartigimod arm who did not achieve MSE in ADAPT achieved MSE during ADAPT+**

[a]61 of the 65 AChR-Ab+ participants treated with efgartigimod in ADAPT rolled over into ADAPT+.

Figure 2. Change in HRQoL Outcomes Among Participants Who Achieved MSE in ADAPT (n=29)

AChR-Ab+ Population



[a]Change (Δ) reported is maximum change from study baseline across postbaseline visits of any treatment cycle of ADAPT. [b]Population normal values were derived from an age-matched cohort with individuals aged 35 to 44 years. [c]Best score is reported as maximal score/change from study baseline across postbaseline visits at any cycle.

Table 3. Sustained Benefit Disease-Specific and QoL Measures in Participants Who Achieved MSE in ADAPT (n=29)

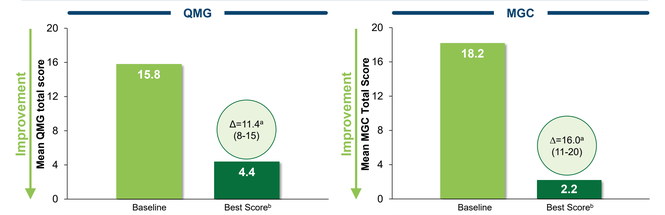
AChR-Ab+ Population

	Efgartigimod Patients With MSE
Change in QMG from baseline	
% visits with improvement in QMG ≥3	77.1% ± 5.07%
% visits with improvement in QMG ≥5	64.7% ± 5.49%
Change in MGC from baseline	
% visits with improvement in MGC ≥3	84.8% ± 3.10%
% visits with improvement in MGC ≥5	75.2% ± 4.46%
Absolute QoL benefit[a]	
% visits with MG-QoL15r ≤8	63.4% ± 5.80%
% visits with EQ-5D utility ≥0.84	61.7% ± 6.28%
% visits with EQ-5D VAS ≥78	39.5% ± 5.28%

[a]MG-QoL15r threshold of ≤8 is based upon the PASS threshold for MG-QoL15 in Mendoza 2020.[9] EQ-5D Utility and EQ-5D VAS thresholds based on population normal values for individuals aged 35 to 44 years.[9]

Figure 3. Change in QMG and MGC Among Participants Who Achieved MSE in ADAPT (n=29)

AChR-Ab+ Population



[a]Change (Δ) reported is maximum change from study baseline across postbaseline visits of any treatment cycle of ADAPT. [b]Best score is reported as the minimal score/maximal reduction from study baseline across postbaseline visits at any cycle.

ABBREVIATIONS

AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor antibody; BMI, body mass index; EQ-5D VAS, EuroQol 5-Dimension, 5-Level Visual Analog Scale; ER, event rate; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; HRQoL, health-related quality of life; IgA, immunoglobulin A; IgD, immunoglobulin D; IgE, immunoglobulin E; IgG, immunoglobulin G; IgM, immunoglobulin M; IV, intravenously; MCID, minimal clinically important difference; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGC, Myasthenia Gravis Composite; MGFA, Myasthenia Gravis Foundation of America; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; MSE, minimal symptom expression; NSIST, nonsteroidal immunosuppressive therapy; PASS, patient-acceptable symptom states; PY, participant-year; QoL, quality of life; QMG, Quantitative Myasthenia Gravis; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

REFERENCES

1. Sesarman A, et al. *Cell Mol Life Sci.* 2010;67(15):2533-2550. **2.** Pyzik M, et al. *Nat Rev Immunol.* 2023;23(7):415-432. **3.** Ulrichts P, et al. *J Clin Invest.* 2018;128(10):4372-4386. **4.** Vaccaro C, et al. *Nat Biotechnol.* 2005;23(10):1283-1288. **5.** Howard JF Jr, et al. *Lancet Neurol.* 2021;20(7):526-536. **6.** Nixon AE, et al. *Front Immunol.* 2015;6:176. **7.** Ward ES, et al. *Front Immunol.* 2022;13:892534. **8.** Mendoza M, et al. *Neurology.* 2020;95(12):e1617-e1628. **9.** Jiang R, et al. *Qual Life Res.* 2021;30(3):803-816. **10.** Burns TM, et al. *Muscle Nerve.* 2010;41(2):219-226. **11.** Thomsen JLS, Andersen H. *Front Neurol.* 2020;11:596382.

ACKNOWLEDGMENTS AND DISCLOSURES: The authors gratefully acknowledge the ADAPT trial participants and investigators.

SM: Alexion, argenx, UCB/Ra, and Horizon. **JFH:** Alexion AstraZeneca Rare Disease, argenx, Cartesian, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, Ra Pharmaceuticals/UCB Bioscience, Takeda, AcademicCME, Biologix, F. Hoffmann-LaRoche, Horizon Therapeutics, Medscape, Merck EMB Serono, NMD Pharma, Novartis, PeerView, PlatformQ, Regeneron, Sanofi, Zai Labs, and Toleranzia AB. **HM:** Alexion, AstraZeneca Rare Disease, argenx, UCB, Roche, Japan Blood Products Organization, Chugai, and Japan's Ministry of Health, Labour and Welfare. **GP, CQ, DG, EB,** and **SZ:** argenx. **VB:** Alexion, Grifols, CSL, UCB, argenx, Takeda, Octapharma, Akcea, Momenta (J&J), Immunovant, Ionis, and Viela. **JV:** Roche, Sanofi Genzyme, Sarepta, Fulcrum, Biogen, Lupin, Amicus, Regeneron, argenx, UCB, Arvinas, ML Biopharma, Atamyo, Horizon, Dyne, Edgewise, and Alexion. The ADAPT trial was funded by argenx. Medical writing and editorial support for this presentation was provided by PRECISION Value & Health and funded by argenx.

Presented at American Academy of Neurology (AAN) 2024 Annual Meeting; April 13-18, 2024; Denver, Colorado