Long-term Safety, Tolerability, and Efficacy of Efgartigimod in Patients With Generalized Myasthenia Gravis: Concluding Analyses From the ADAPT+ Study

Andreas Meisel,[1] Jan L. De Bleecker,[2] Jan Verschuuren,[3] Vera Bril,[4,5] Tuan Vu,[6] Chafic Karam,[7] Stojan Peric,[8] Hiroyuki Murai,[9] Said Beydoun,[10] Mamatha Pasnoor,[11] Sophie Steeland,[12] Benjamin Van Hoorick,[12] Caroline T'joen,[12] Kimiaki Utsugisawa,[13] Renato Mantegazza,[14] James F. Howard, Jr,[15] and the ADAPT Study Group

[1]Department of Neurology and NeuroCure Clinical Research Center, Charité – Universitätsmedizin Berlin, Germany; [2]Department of Neurology, Ghent University Hospital, Ghent, Belgium; [3]Department of Neurology, Leiden University Medical Center, Leiden, the Netherlands; [4]Ellen & Martin Prosserman Centre for Neuromuscular Diseases, University Health Network, Toronto, Ontario, Canada; [5]University of Toronto, Toronto, Ontario, Canada; [6]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, Florida, USA; [7]Penn Neuroscience Center - Neurology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania, USA; [8]Neurology Clinic, Clinical Center of Serbia, Faculty of Medicine, University of Belgrade, Belgrade, Serbia; [9]Department of Neurology, School of Medicine, International University of Health and Welfare, Tokyo, Japan; [10]Keck School of Medicine, University of Southern California, Los Angeles, California, USA; [11]Department of Neurology, The University of Kansas Medical Center, Kansas City, Kansas, USA; [12]argenx, Ghent, Belgium; [13]Department of Neurology, Hanamaki General Hospital, Hanamaki, Japan; [14]Department of Neuroimmunology and Neuromuscular Diseases, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; [15]Department of Neurology, The University of North Carolina, Chapel Hill, North Carolina, USA

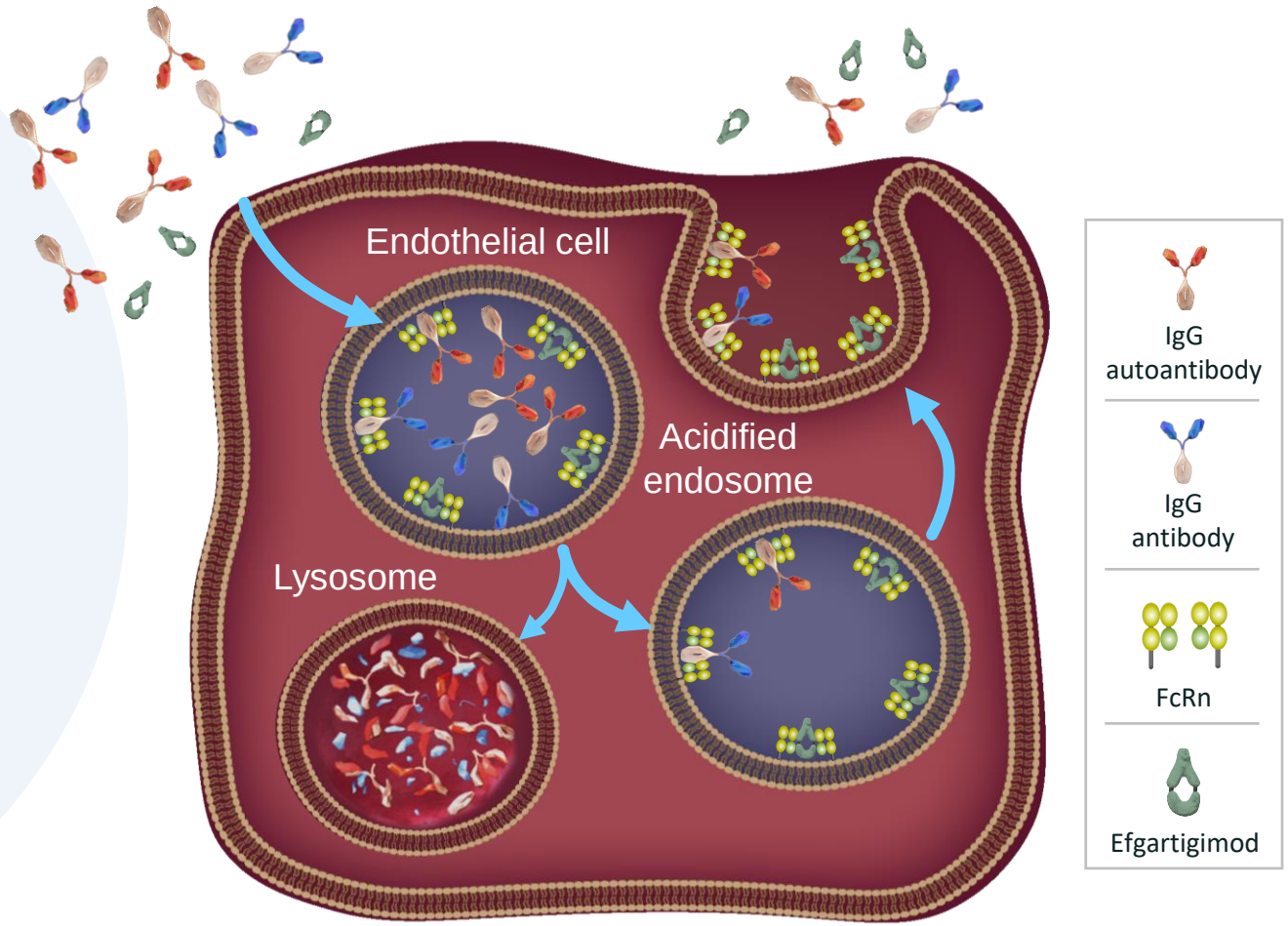
Disclosures

- The phase 3 ADAPT and ADAPT+ studies were funded by argenx
- Andreas Meisel has received speaker honoraria and financial research support from argenx BV

Andreas Meisel has also received speaker honoraria from Alexion Pharmaceuticals, Inc, Grifols, SA, and Hormosan Pharma GmbH; honoraria from Alexion Pharmaceuticals, Inc, UCB, Janssen, and Merck for consulting services; and financial research support (paid to his institution) from Octapharma and Alexion Pharmaceuticals, Inc. He is chairperson of the medical advisory board of the German Myasthenia Gravis Society.

Efgartigimod Blocks FcRn and Reduces IgG Levels

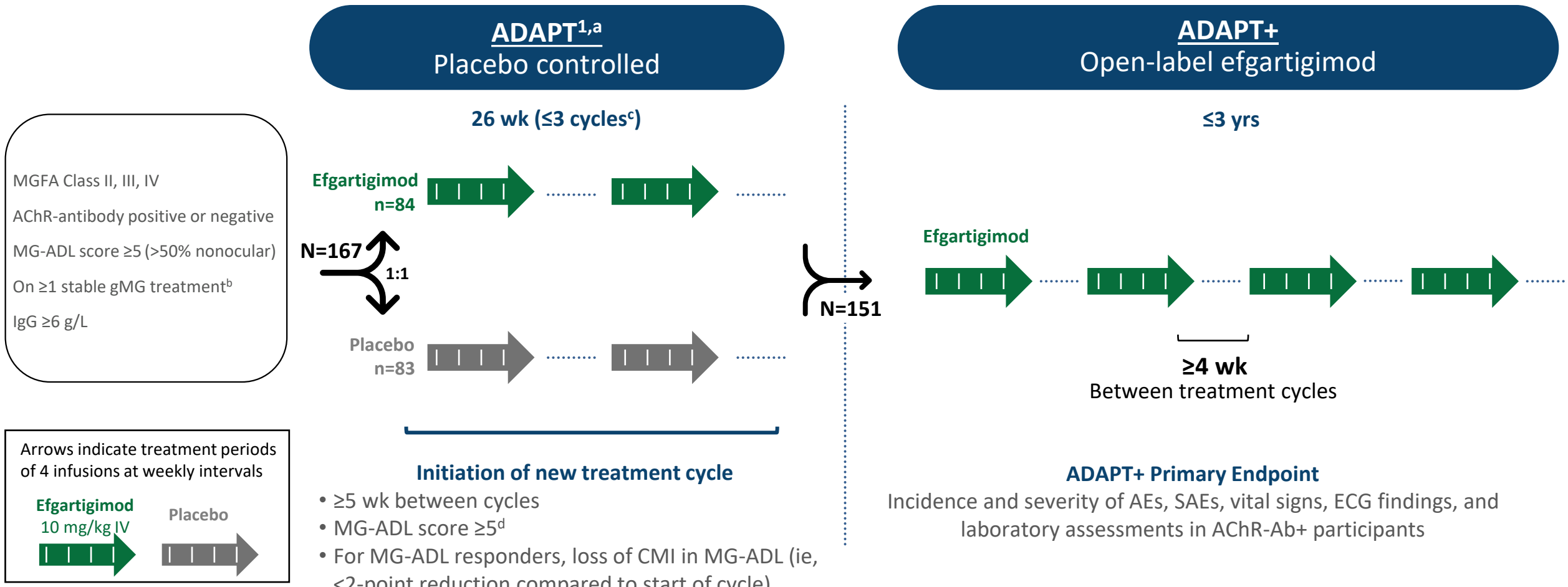
- FcRn recycles IgG, extending its half-life and maintaining serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn[2,3]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting IgG lysosomal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



FC, crystallizable fragment; FcRn, neonatal Fc receptor; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M.

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.

ADAPT and ADAPT+ Study Design



AChEI, acetylcholinesterase inhibitor; AChR, acetylcholine receptor; AE, adverse evert; ECG, electrocardiograms; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; SAE, serious adverse events.. Note: Patients requiring rescue therapy in ADAPT and ADAPT+ Part A discontinued the study if they required rescue therapy; however, patients in ADAPT+ Part B did not. [a]Participants who required retreatment but were unable to complete a treatment cycle within the time frame of ADAPT were also eligible to be rolled over to ADAPT+. [b]AChEI, steroid, and/or NSIST; patients could not change concomitant therapies in ADAPT or during dosing in Part A of ADAPT+. Physicians could change concomitant therapies between doses in Part A and at any time in Part B of ADAPT+. [c]≤3 cycles dosed at ≥8 weeks after initial cycle. [d]With >50% from nonocular items.

Howard JF Jr, et al. *Lancet Neurol*. 2021;20(7):526-536.

ADAPT+ Baseline Characteristics and Treatment Exposure

Baseline Demographics and Disease Characteristics

Safety Population

Characteristics	Efgartigimod (N=145)
Age, y, mean (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, mean (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)

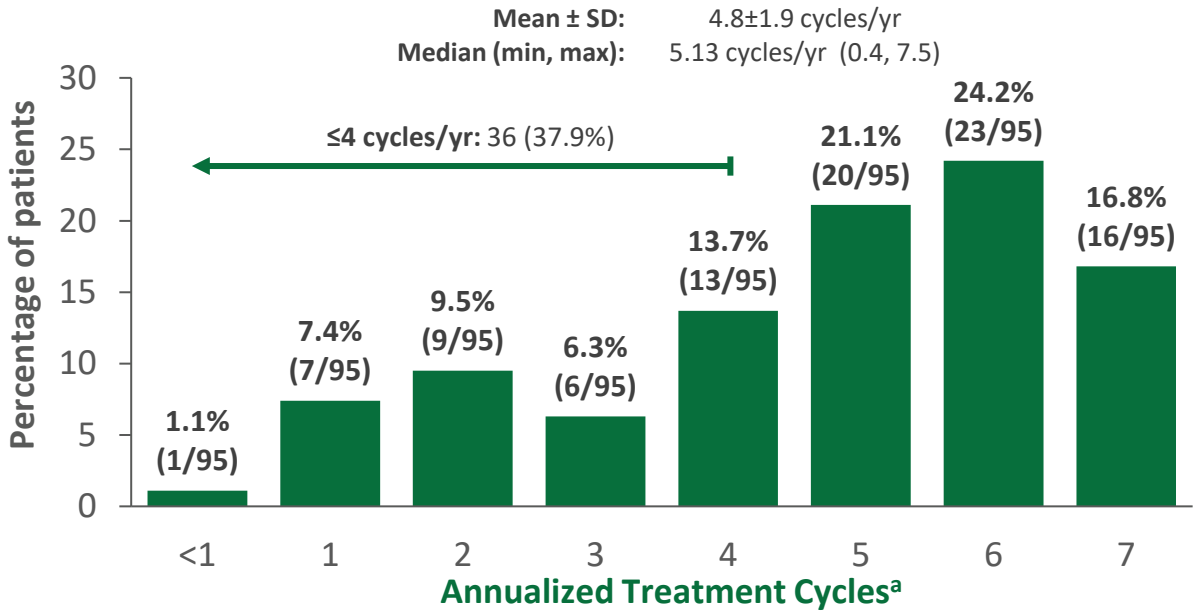
Treatment Exposure Through Conclusion of ADAPT+

Safety Population

	Efgartigimod (N=145)
Patients receiving ≥1 dose	145
Study duration, d	
Median (min, max)	651 (50, 1074)
Mean (SD)	610.2 (247.6)
Total follow-up, patient-years	229
Maximum number of cycles	≤19

Distribution of Annualized Treatment Cycles[a]

AChR-Ab+ Population With ≥350 Days of Follow-Up in ADAPT/ADAPT+ (N=95)



AChR-Ab+, acetylcholine receptor antibody seropositive; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; QMG, Quantitative Myasthenia Gravis. [a]Number of efgartigimod treatment cycles per year were captured in continuous intervals starting from 0.0 - < 0.5 cycles/year, and 1 cycle intervals thereafter. The x-axis represents the whole number rounding for each interval.

Rates of Adverse Events Were Similar Across ADAPT and ADAPT+

Safety Population

	ADAPT						ADAPT+ (Up to 3 yrs)		
	Placebo (n=83) [34.5 PY]			Efgartigimod (n=84) [34.9 PY]			Efgartigimod (n=145) [229.0 PY]		
	IR[a]	Events	n (%)	IR[a]	Events	n (%)	IR[a]	Events	n (%)
AEs[b]	**7.83**	270	70 (84)	**7.23**	252	65 (77)	**3.53**	809	124 (86)
SAEs	**0.29**	10	7 (8)	**0.11**	4	4 (5)[c]	**0.24**	56	36 (25)[c]
≥1 infusion-related reaction event	**0.26**	9	8 (10)	**0.09**	3	3 (4)	**0.09**	21	15 (10)
Infection AEs	**1.22**	42	31 (37)	**1.61**	56	39 (46)	**0.73**	168	80 (55)
Discontinued due to AEs	**0.09**	3	3 (4)	**0.20**	7	3 (4)	**0.06**	14	12 (8)
Severe AEs (grade ≥3)	**0.35**	12	8 (10)	**0.29**	10	9 (11)	**0.33**	76	40 (28)
Death[d]	-	0	0 (0)	-	0	0 (0)	**0.02**	5	5 (3)
Most frequent AEs									
Nasopharyngitis	**0.49**	17	15 (18)	**0.34**	12	10 (12)	**0.10**	24	20 (14)
Upper respiratory tract infection	**0.14**	5	4 (5)	**0.32**	11	9 (11)	**0.03**	7	6 (4)
Urinary tract infection	**0.12**	4	4 (5)	**0.26**	9	8 (10)	**0.08**	19	13 (9)
Headache	**1.13**	39	23 (28)	**1.15**	40	24 (29)	**0.45**	103	36 (25)
Nausea	**0.43**	15	9 (11)	**0.20**	7	7 (8)	**0.06**	13	9 (6)
Diarrhea	**0.41**	14	9 (11)	**0.17**	6	6 (7)	**0.08**	19	14 (10)
COVID-19[e]	-	0	0 (0)	-	0	0 (0)	**0.10**	24	23 (16)[f]

AE, adverse event; COVID-19, coronavirus disease 2019; IR, incidence rate; n, number of patients; PY, patient-year; SAE, serious adverse event; SARS-COV-2, severe acute respiratory syndrome coronavirus 2.

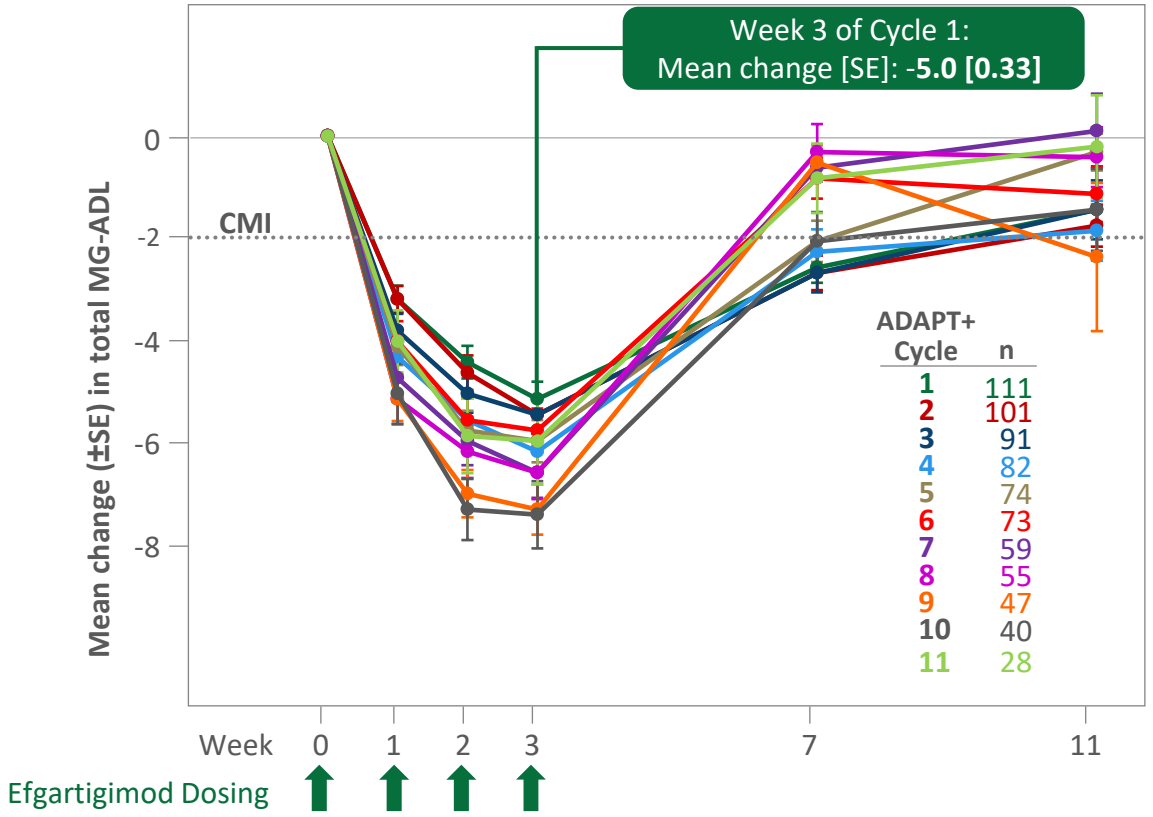
[a]IR was calculated as number of events per total PY of follow-up. [b]AEs were predominantly mild or moderate. [c]Only 1 SAE was considered treatment related per investigator. [d] Myocardial infarction, septic shock, MG crisis, lung neoplasm malignant, and unknown cause. None of the deaths in ADAPT+ 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 patients reporting COVID-19 during ADAPT+, 83% had not received prior COVID-19 vaccination.

Efgartigimod Demonstrated Consistent and Repeatable Improvement in Both MG-ADL and QMG Over Multiple Cycles in ADAPT+

AChR-Ab+ Population

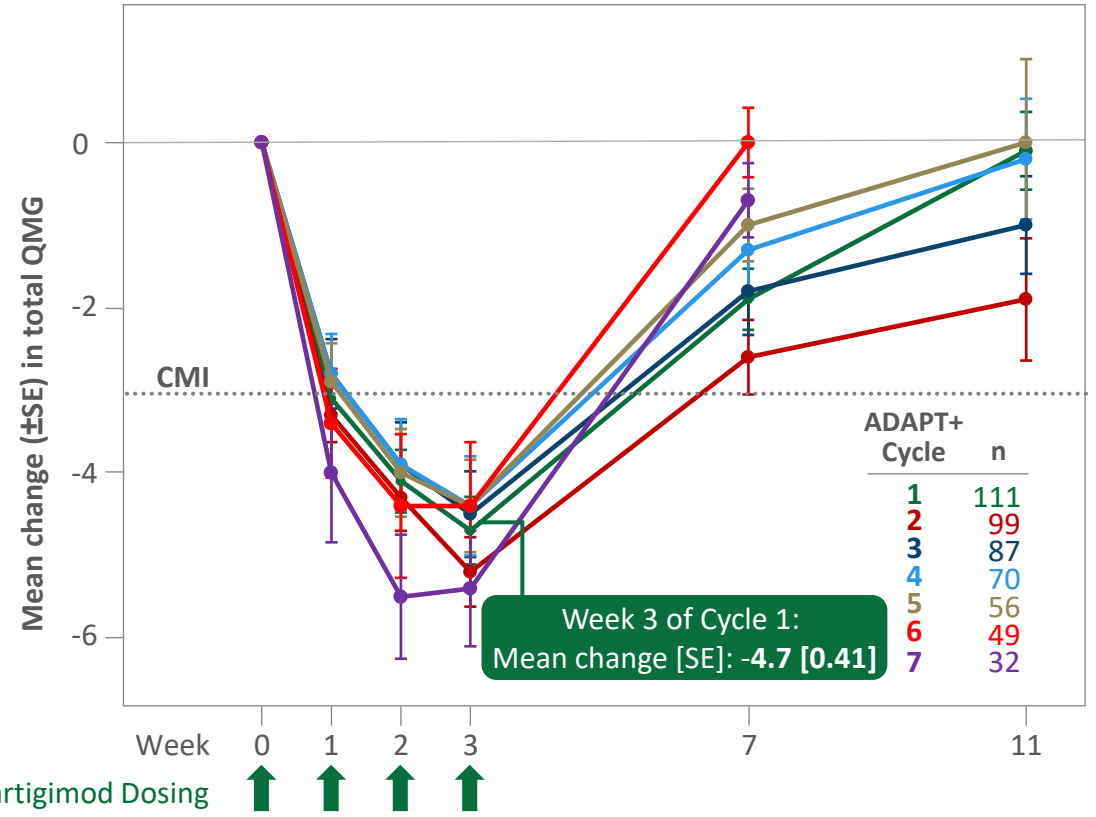
MG-ADL Total Score

Mean Change From Cycle Baseline by Cycle[a]



QMG Total Score

Mean Change From Cycle Baseline by Cycle

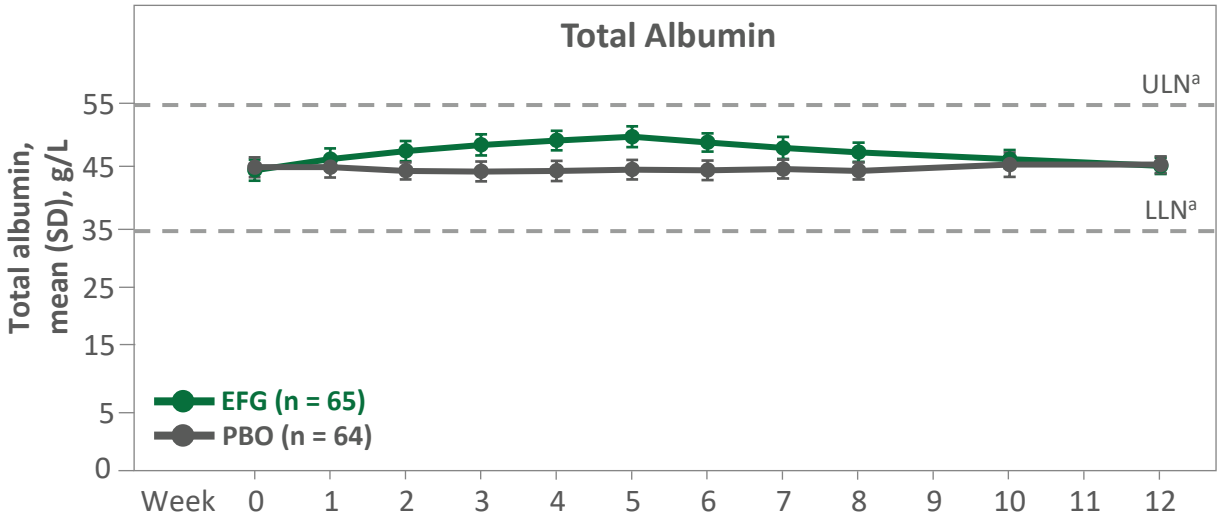


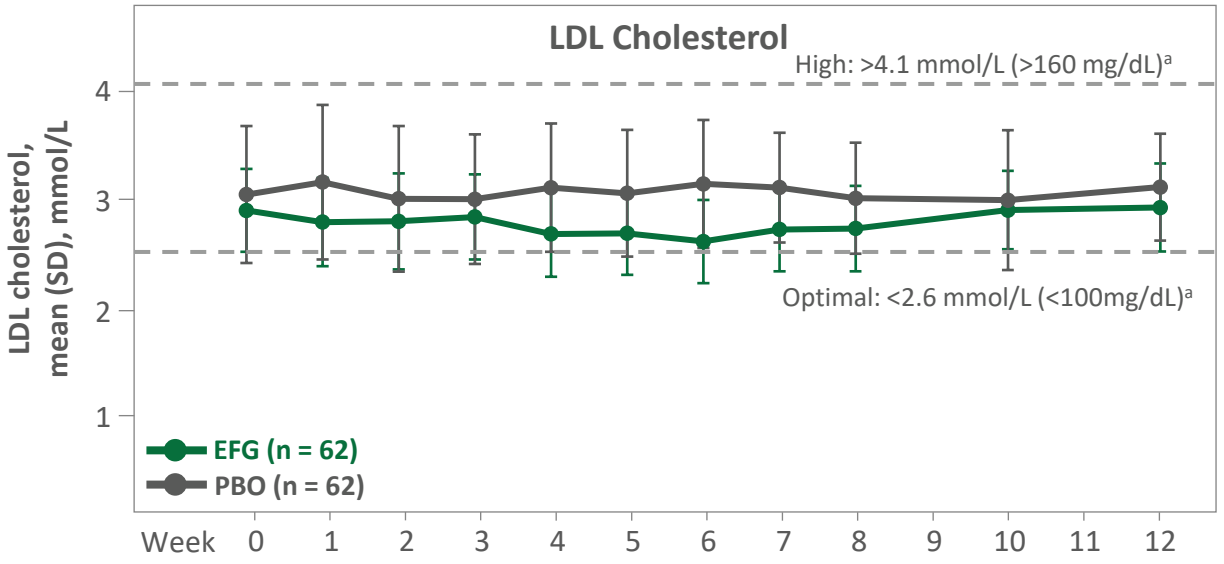
AChR-Ab, acetylcholine receptor autoantibody; CMI, clinically meaningful improvement; CT, current treatment; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis.
[a]Only cycles with data out to Week 11 are depicted. [b]QMG was not a required assessment in part B of ADAPT+; therefore, there are fewer data for cycles compared to MG-ADL.

No Reductions in Albumin and No Increases in LDL With Efgartigimod

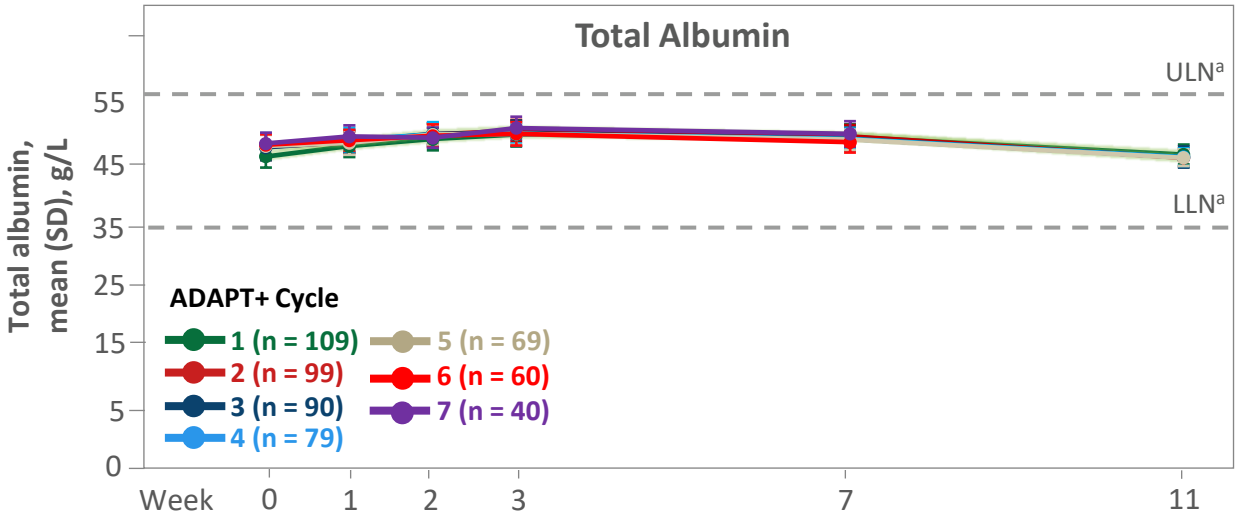
AChR-Ab+ Population

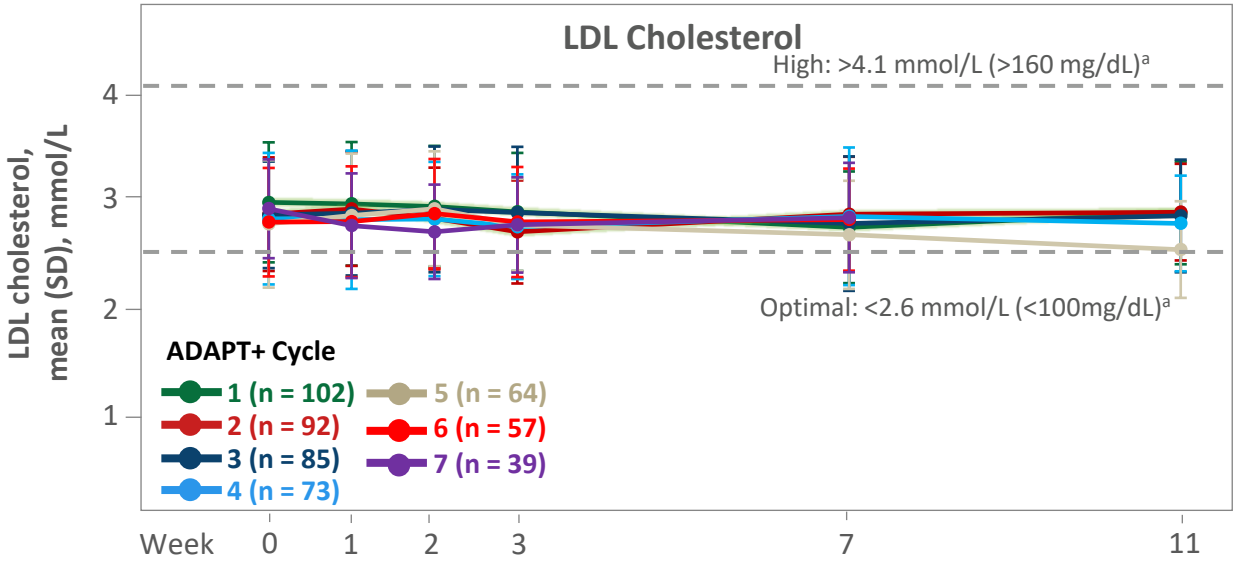
ADAPT





ADAPT+





AChR-Ab, acetylcholine receptor autoantibody; LDL, low-density lipoprotein; LLN, lower limit of normal; ULN, upper limit of normal. [a]Reference values are based on Kratz A, et al. *N Engl J Med*. 2004;351(15):1548-1563.

Summary

In AChR-Ab+ patients, efgartigimod treatment resulted in consistent and repeatable improvements in MG-ADL and QMG scores across multiple treatment cycles

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

No reductions in albumin or increases in LDL were observed with efgartigimod

AChR-Ab+ patients with ≥350 days of follow-up across ADAPT/ADAPT+ showed varying time between cycles, supporting an individualized treatment approach

This analysis suggests that long-term efgartigimod treatment is well tolerated and efficacious in patients with gMG

AChR-Ab, acetylcholine receptor autoantibody; AE, adverse event; gMG, generalized myasthenia gravis; LDL, low-density lipoprotein; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis.