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

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Disclosures

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- MP has served as a medical advisor/consultant for argenx BV

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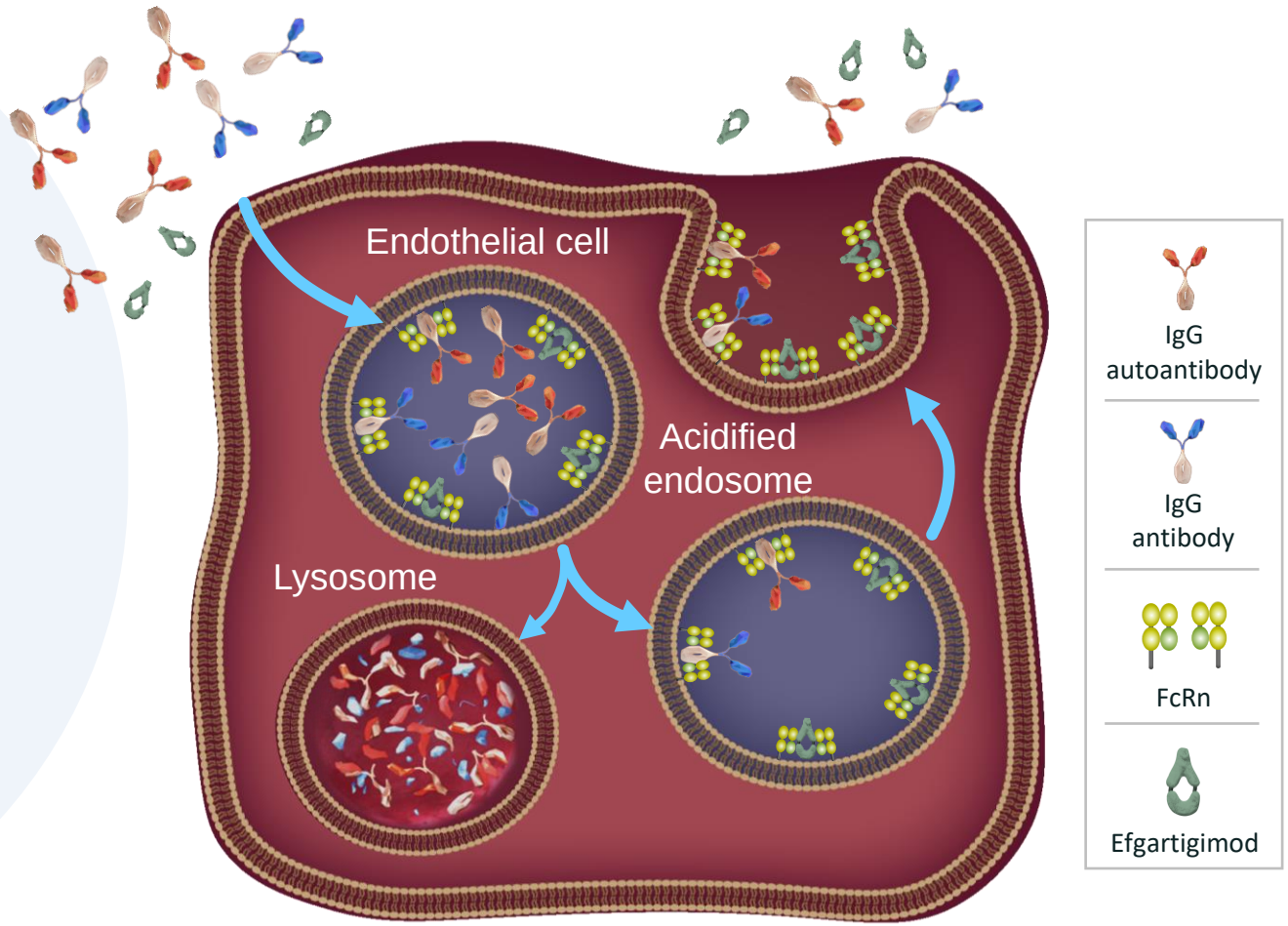
Efgartigimod Effectively Blocks FcRn and Reduces IgG Levels

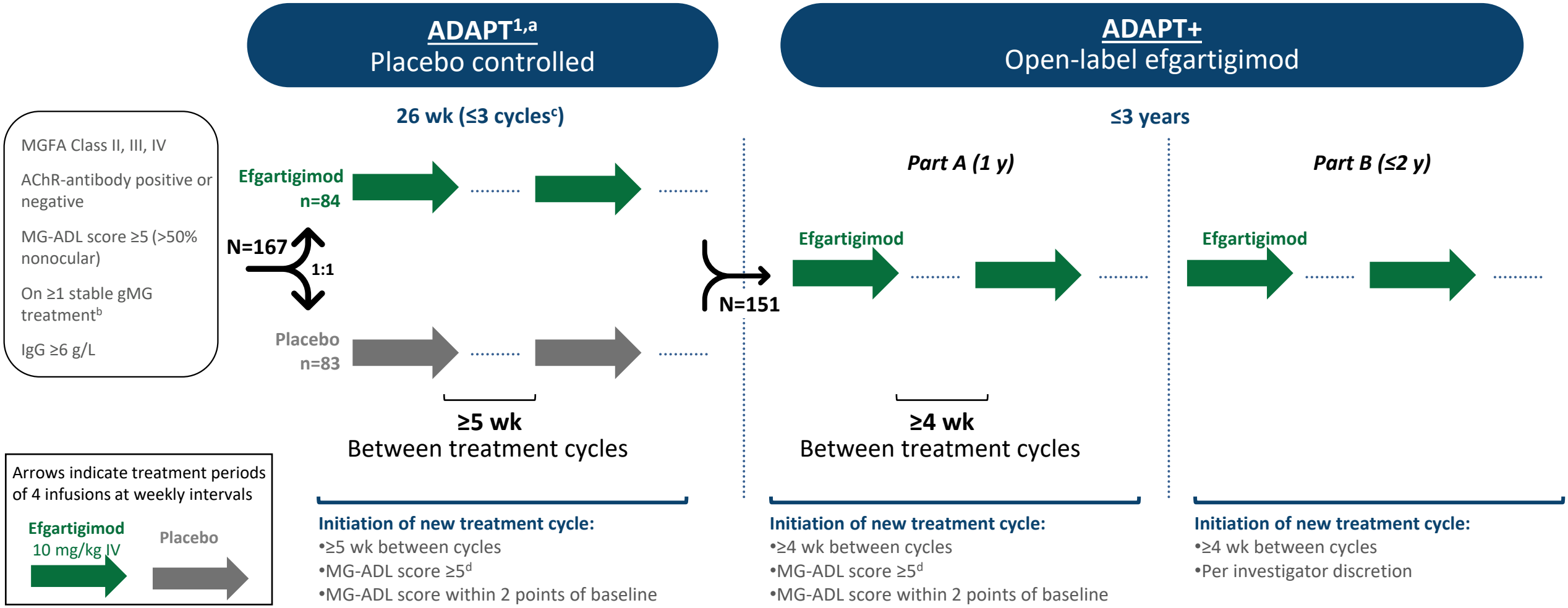
- FcRn recycles IgG, extending its half-life and maintaining serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn[2,3]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting IgG lysosomal 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 levels
  - No increase in cholesterol



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/ADAPT+ Study Design



AChEI, acetylcholinesterase inhibitor; AChR, acetylcholine receptor; 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. 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

Safety Population

Baseline Demographics and Disease Characteristics

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)

Treatment Exposure Through Conclusion of ADAPT+

	Efgartigimod (N=145)
Patients receiving ≥1 dose	145
Study duration, d	
Median (min, max)	651 (50, 1074)
Mean (SD)	610.2 (247.6)
Follow-up since first treatment in study, patient-years	229
Max number of cycles	Up to 19

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.

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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]	m	n (%)	IR[a]	m	n (%)	IR[a]	m	n (%)
AEs[b]	**7.8**	270	70 (84)	**7.2**	252	65 (77)	**3.5**	809	124 (86)
SAEs	**0.3**	10	7 (8)	**0.1**	4	4 (5)[c]	**0.2**	56	36 (25)[c]
≥1 infusion-related reaction event	**0.3**	9	8 (10)	**0.1**	3	3 (4)	**0.1**	21	15 (10)
Infection AEs	**1.2**	42	31 (37)	**1.6**	56	39 (46)	**0.7**	168	80 (55)
Discontinued due to AEs	**0.1**	3	3 (4)	**0.2**	7	3 (4)	**0.1**	14	12 (8)
Severe AEs (grade ≥3)	**0.4**	12	8 (10)	**0.3**	10	9 (11)	**0.3**	76	40 (28)
Death[d]	**-**	0	0 (0)	**-**	0	0 (0)	**<0.1**	5	5 (3)
Most frequent AEs									
Nasopharyngitis	**0.5**	17	15 (18)	**0.3**	12	10 (12)	**0.1**	24	20 (14)
Upper respiratory tract infection	**0.1**	5	4 (5)	**0.3**	11	9 (11)	**<0.1**	7	6 (4)
Urinary tract infection	**0.1**	4	4 (5)	**0.3**	9	8 (10)	**0.1**	19	13 (9)
Headache	**1.1**	39	23 (28)	**1.1**	40	24 (29)	**0.4**	103	36 (25)
Nausea	**0.4**	15	9 (11)	**0.2**	7	7 (8)	**0.1**	13	9 (6)
Diarrhea	**0.4**	14	9 (11)	**0.2**	6	6 (7)	**0.1**	19	14 (10)
COVID-19[e]	**-**	0	0 (0)	-	0	0 (0)	**0.1**	24	23 (16)[f]

AE, adverse event; COVID-19, coronavirus disease 2019; IR, incidence rate; m, number of events; 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]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.

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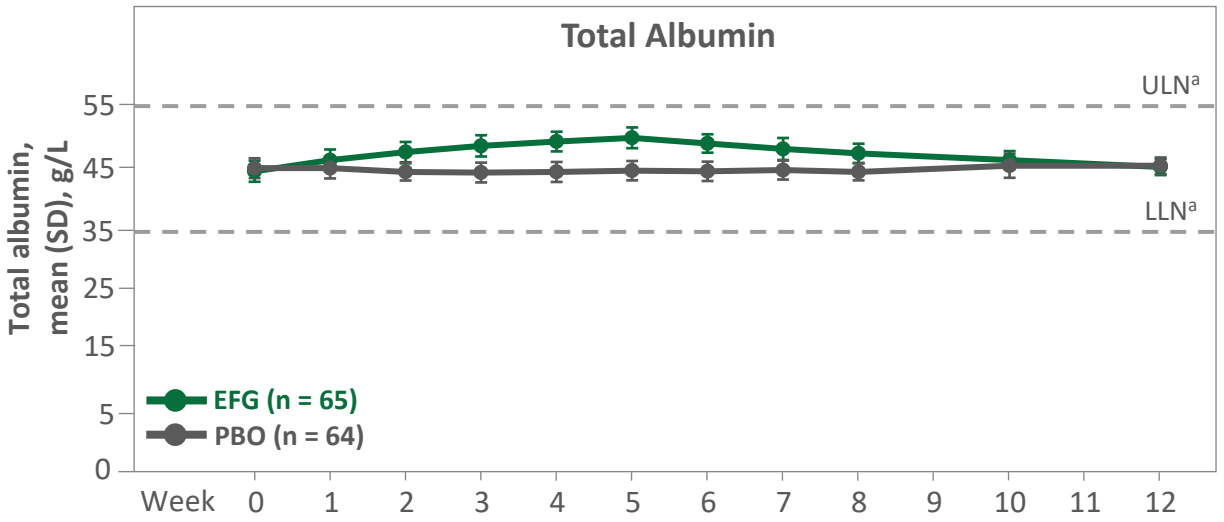
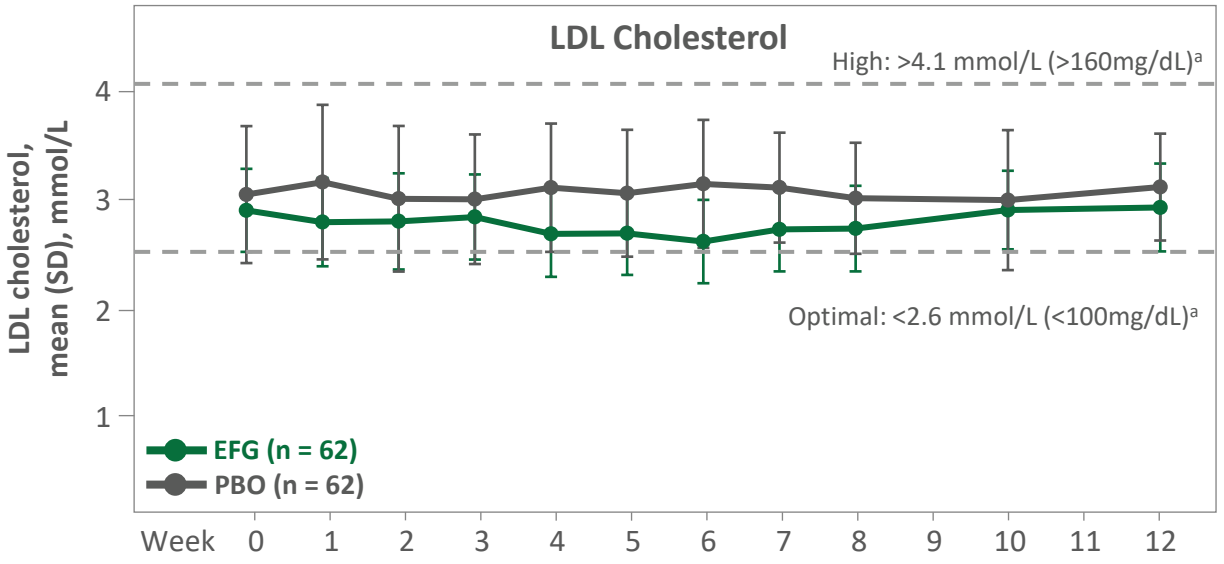
No Clinically Meaningful Reductions in Albumin and No Increases in LDL With Efgartigimod

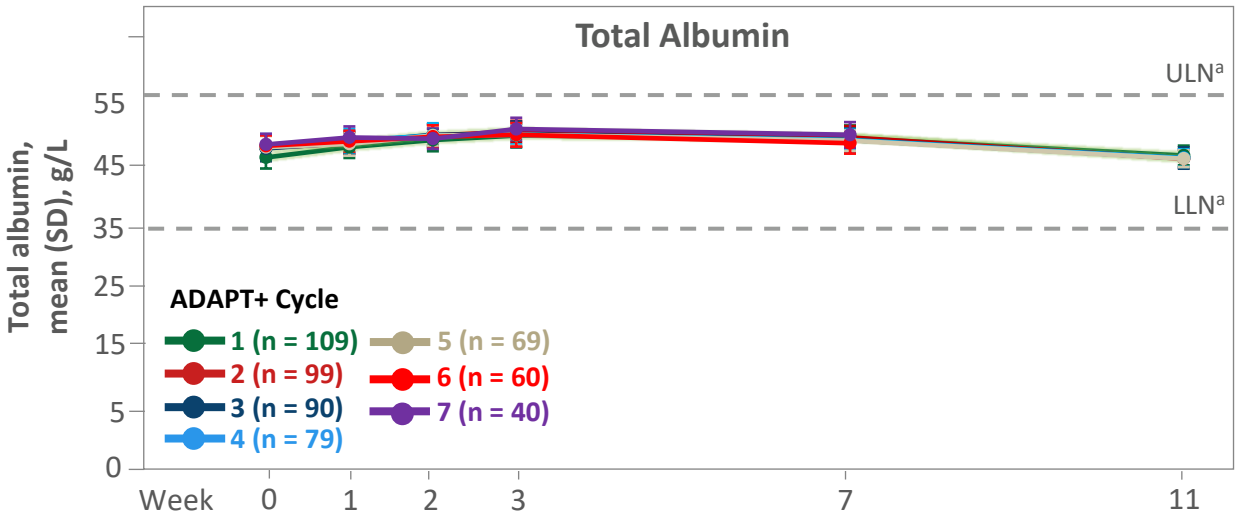
AChR-Ab+ Population

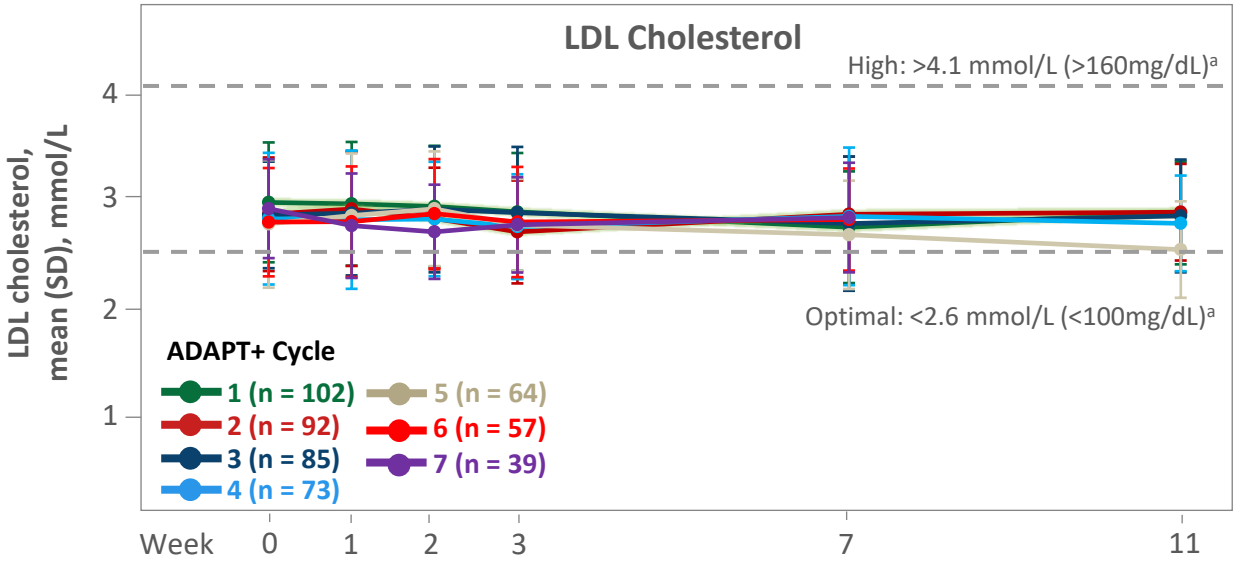
ADAPT





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.

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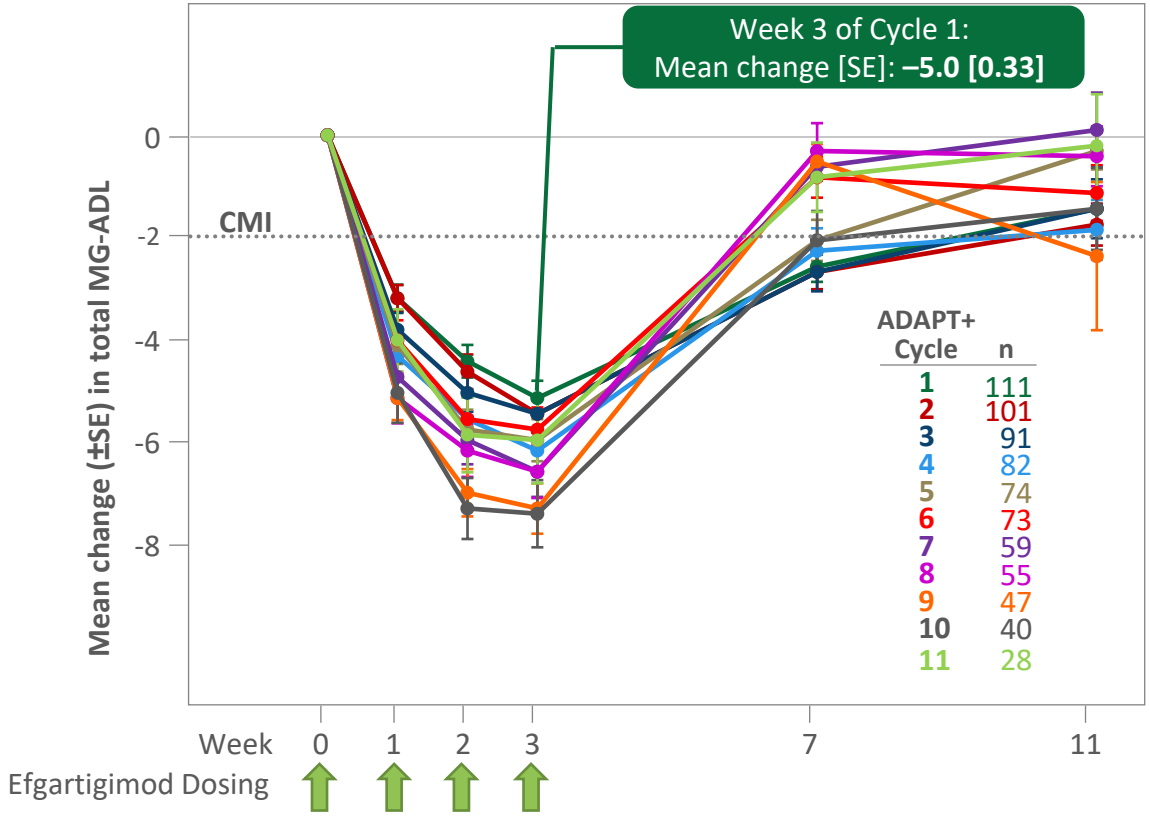
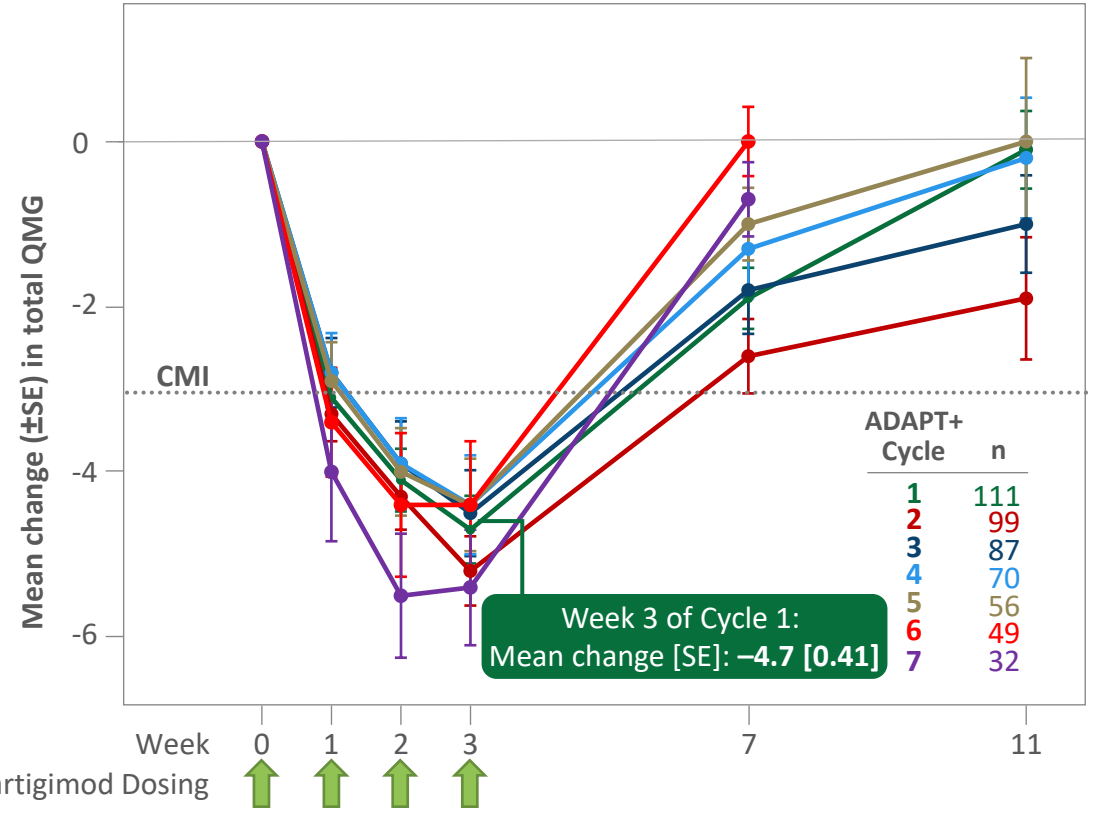
Efgartigimod Demonstrated Consistent and Repeatable Improvement in Both MG-ADL and QMG Over Multiple Cycles in ADAPT+

AChR-Ab+ Population

MG-ADL Total Score
Mean Change From Cycle Baseline by Cycle[a]
(Efgartigimod + current TX)



QMG Total Score
Mean Change From Cycle Baseline by Cycle
(Efgartigimod + current TX)



AChR-Ab, acetylcholine receptor autoantibody; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis; TX, treatment.
[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.

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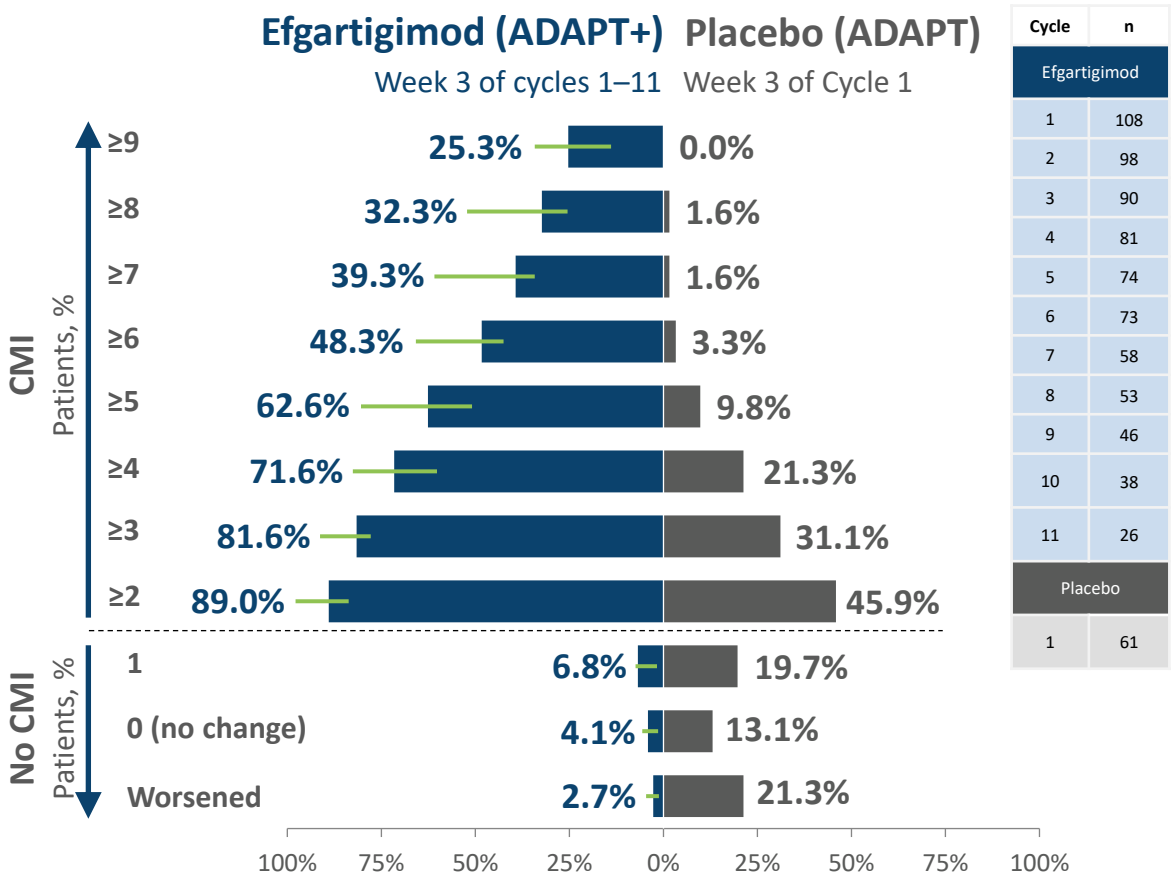
Efgartigimod Demonstrates Clinically Meaningful Improvements Across Increasing MG-ADL and QMG Thresholds Over Multiple Cycles in ADAPT+

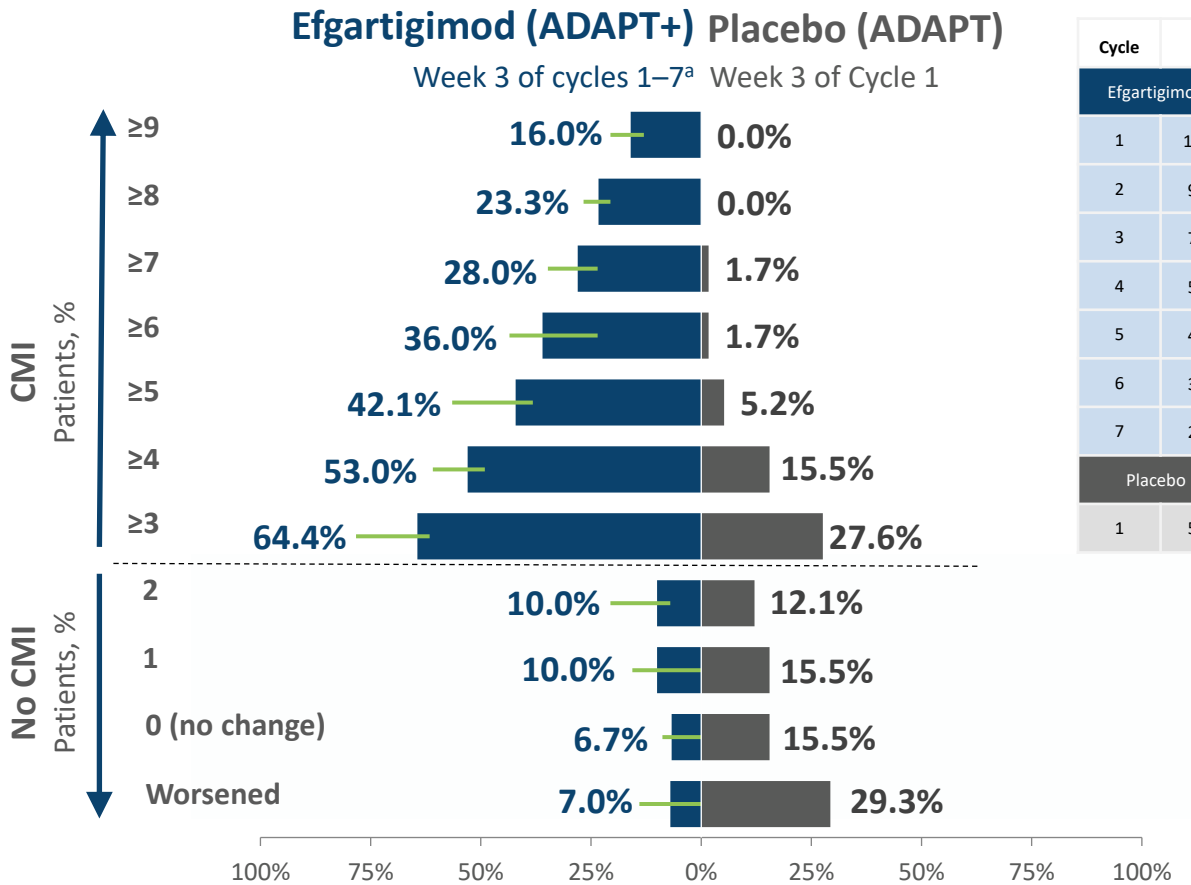
AChR-Ab+ Population

Change in MG-ADL Score[a]



Cycle	n
Efgartigimod	
1	108
2	98
3	90
4	81
5	74
6	73
7	58
8	53
9	46
10	38
11	26
Placebo	
1	61

Change in QMG Score[b]



Cycle	n
Efgartigimod	
1	100
2	90
3	73
4	57
5	45
6	34
7	23
Placebo	
1	58

Efgartigimod Median % (ADAPT+) — Range (ADAPT+) **Placebo** % (ADAPT cycle 1)

AChR-Ab, acetylcholine receptor autoantibody; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis. .

[a]Only cycles with data out to week 11 are included. [b]QMG was not a required assessment in part B of ADAPT+; therefore, there are fewer data for cycles compared to MG-ADL.

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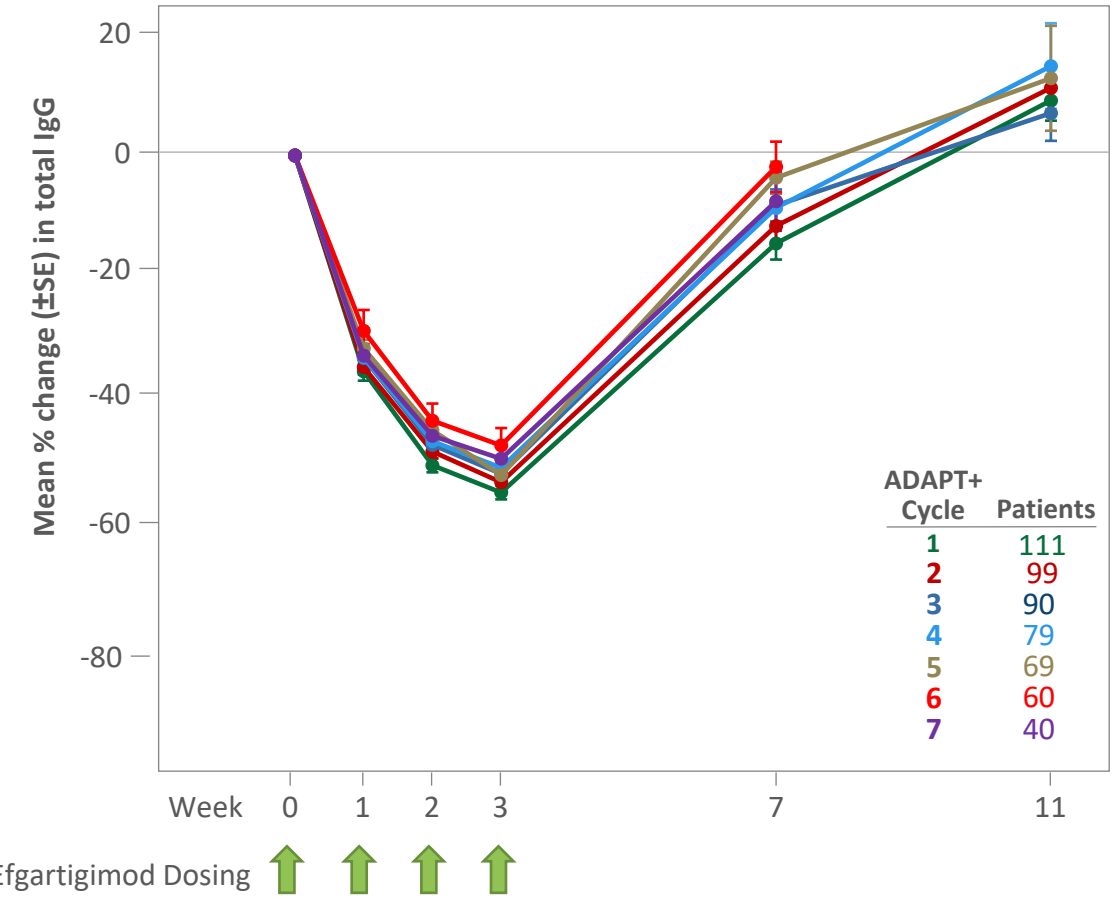
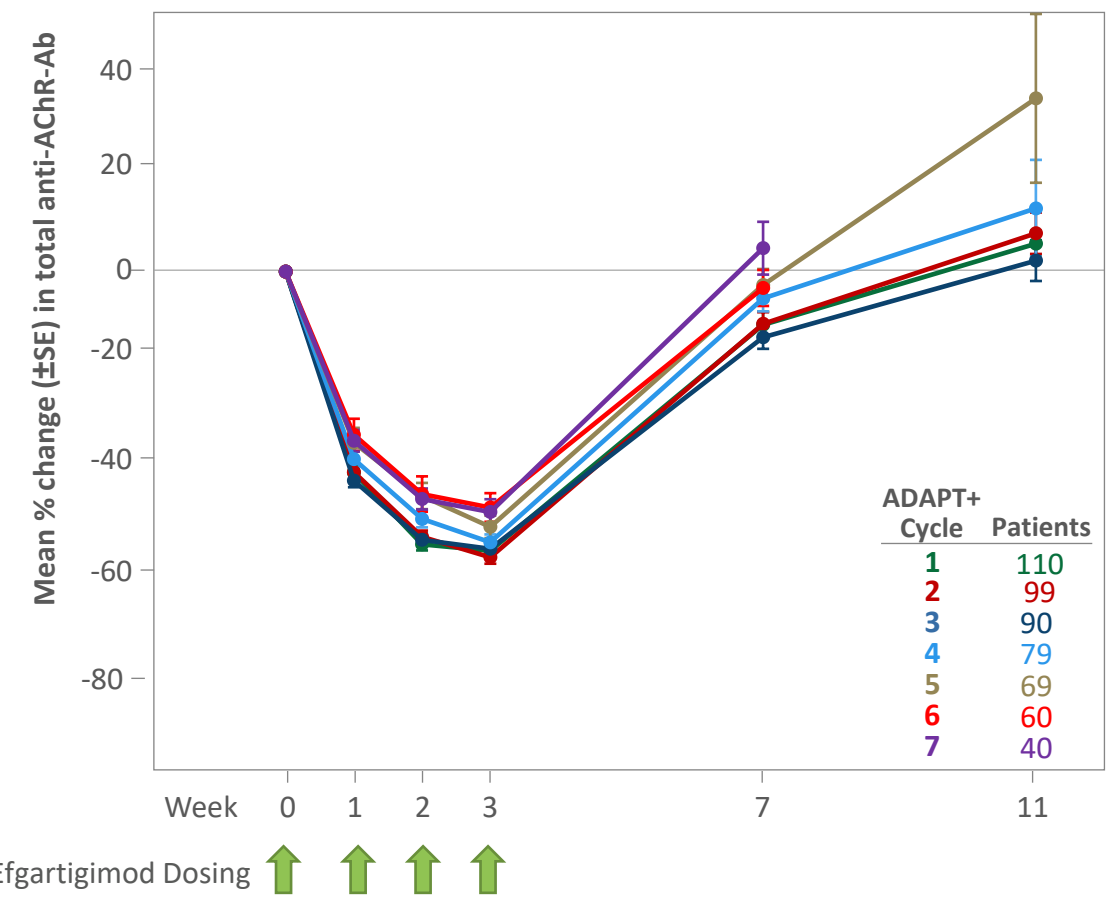
Efgartigimod Demonstrated Consistent Transient Reduction in IgG Levels Over Multiple Cycles in ADAPT+

AChR-Ab+ Population

Total IgG
Mean % Change From Cycle Baseline



Anti-AChR-Abs
Mean % Change From Cycle Baseline



AChR-Ab, acetylcholine receptor autoantibody; IgG, immunoglobulin G.
[a]Samples for pharmacodynamic biomarkers, including total IgG levels, were collected only during part A (year 1) of ADAPT+.

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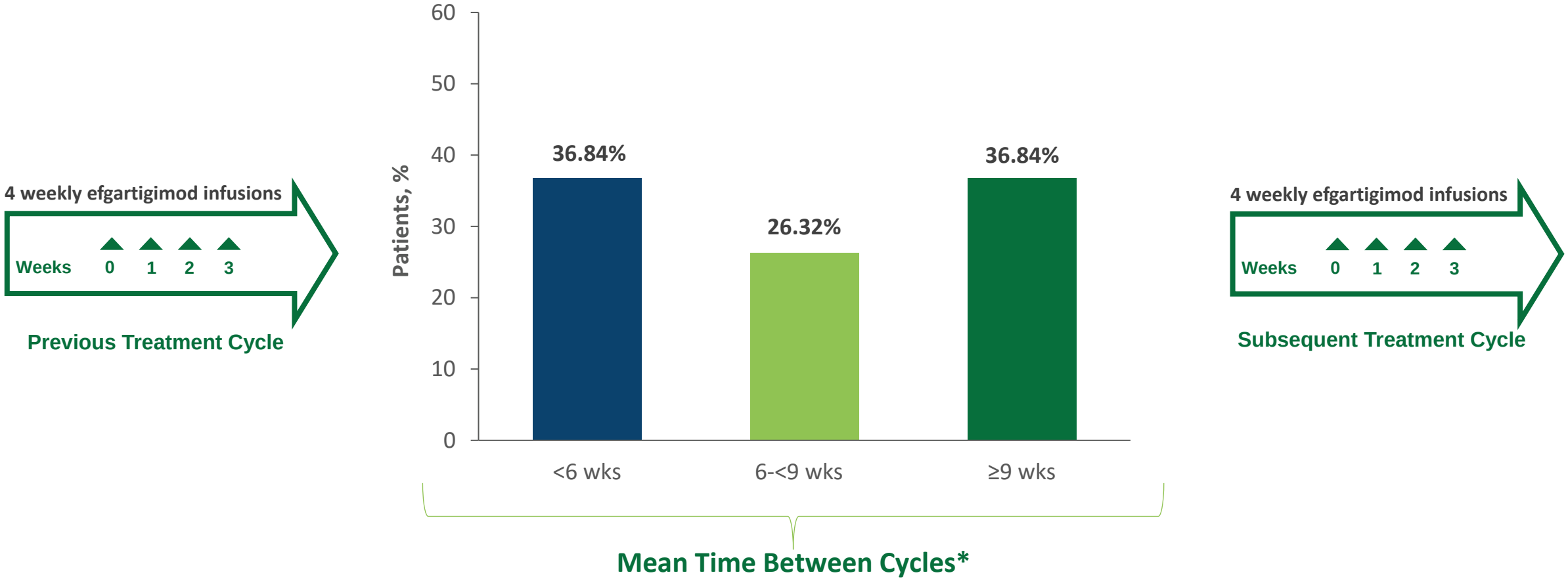
Distribution of Time Between Cycles Supports an Individualized Treatment Approach

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



ADAPT+ demonstrates that individualization of cycle dosing allows for flexible or fixed time between cycles[a]; and initiation of subsequent cycles is based on clinical evaluation and patient/HCP goals

AChR-Ab, acetylcholine receptor autoantibody.

*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.

[a]Median number of cycles per year was 5.1 (min-max, 0.5-7.5; mean ± SD, 4.8 ± 1.9 cycles).

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Summary

In AChR-Ab+ patients, efgartigimod treatment resulted in consistent and repeatable improvements in MG-ADL and QMG scores, and similar results were seen in the overall population

Incidence of AEs were similar across ADAPT and ADAPT+ (84% [placebo arm] and 77% [efgartigimod arm] of patients in ADAPT vs 86% of patients in ADAPT+)

Efgartigimod treatment led to no reductions in albumin and no increases in LDL cholesterol

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; gMG, generalized myasthenia gravis; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis.

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