Achievement of Minimal Symptom Expression in Acetylcholine-Receptor Antibody-Positive Participants With Generalized Myasthenia Gravis in ADAPT/ADAPT+ Studies Resulted in Substantial Improvement in Disease-Specific Measures

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Disclosures

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- Srikanth Muppidi has participated in advisory board meetings for Alexion, argenx, UCB/Ra, and Horizon Pharma
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- Vera Bril has participated in scientific advisory boards for CSL Behring, Baxalta, Grifols, argenx, Octapharma, Alpha Technologies, Powell Mansfield Inc, Shire, Akcea, UCB, and Alnylam; she has received funding for travel or speaker honoraria from CSL Behring; and has consultancies with CSL Behring, Grifols, BioNevia, Octapharma, Powell Mansfield Inc, argenx, Alpha Technologies, Baxalta, Akcea, UCB, Alnylam, and Pfizer
- Glenn A. Phillips, Cynthia Z. Qi, Deborah Gelinas, Edward Brauer, and Sihui Zhao are employees of argenx
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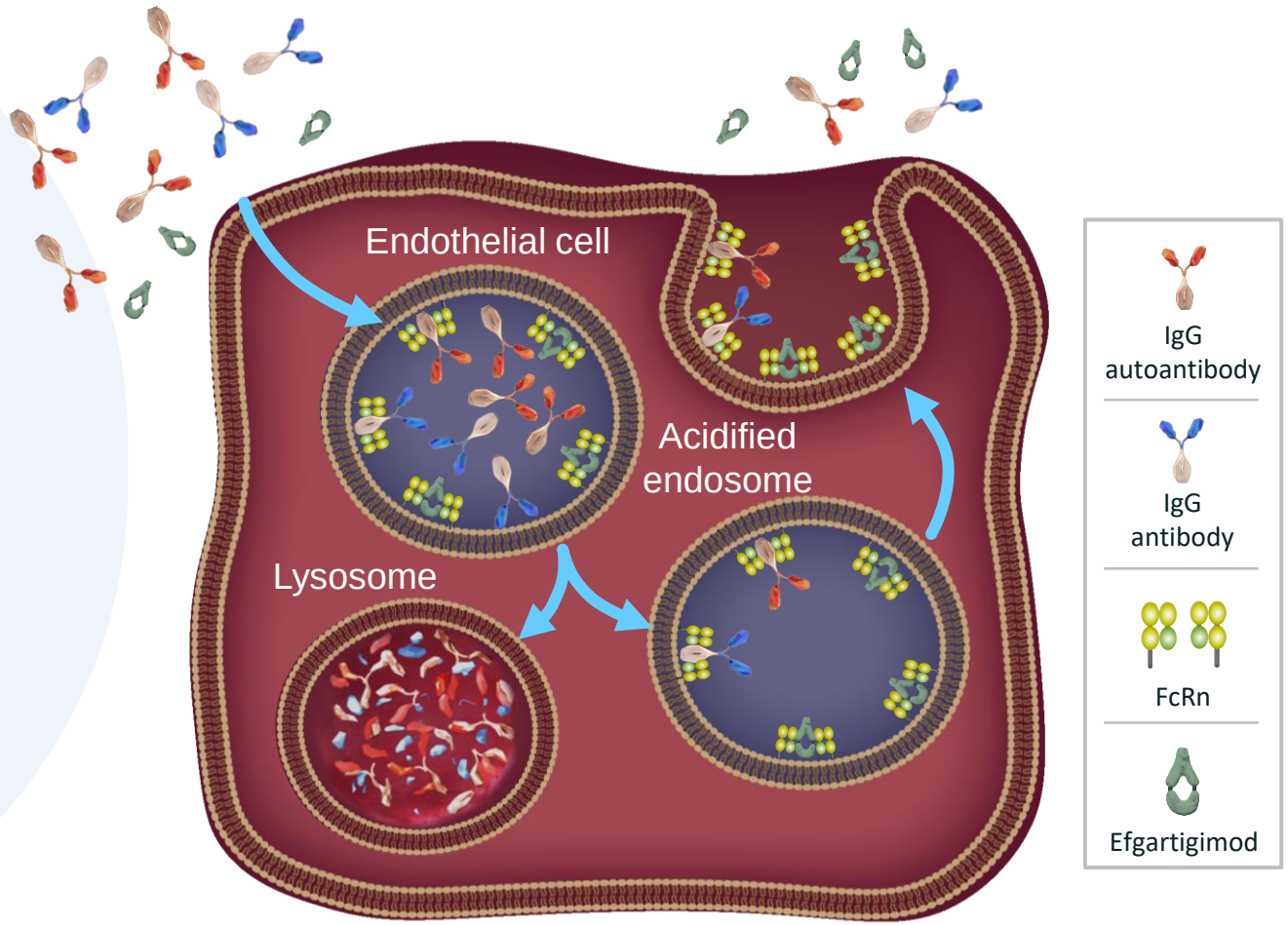
Efgartigimod Effectively Blocks FcRn and Reduces IgG Levels

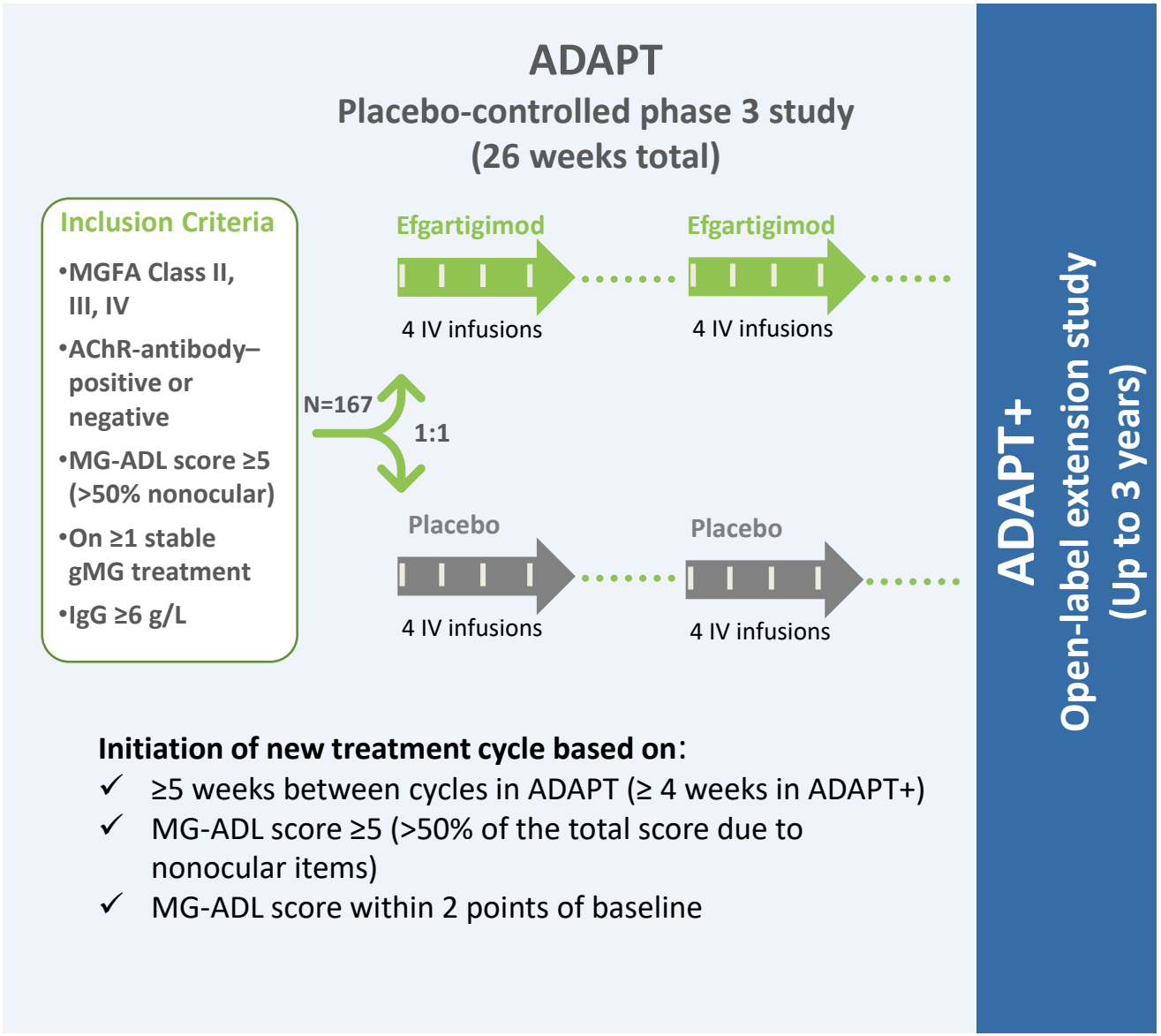
- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have increased affinity for FcRn and outcompete endogenous IgG[2,3]
- Efgartigimod binding to FcRn prevents IgG recycling and promotes its lysosomal degradation, reducing IgG levels without 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]



FC, crystallizable fragment; FcRn, neonatal Fc receptor; IgA, immunoglobulin A; IgD, immunoglobulin D; IgE, immunoglobulin E; 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.

Achieving MSE in ADAPT



Initiation of new treatment cycle based on:

- ✓ ≥5 weeks between cycles in ADAPT (≥ 4 weeks in ADAPT+)
- ✓ MG-ADL score ≥5 (>50% of the total score due to nonocular items)
- ✓ MG-ADL score within 2 points of baseline

Minimal Symptom Expression (MSE):
Total score of 0 or 1 on MG-ADL scale

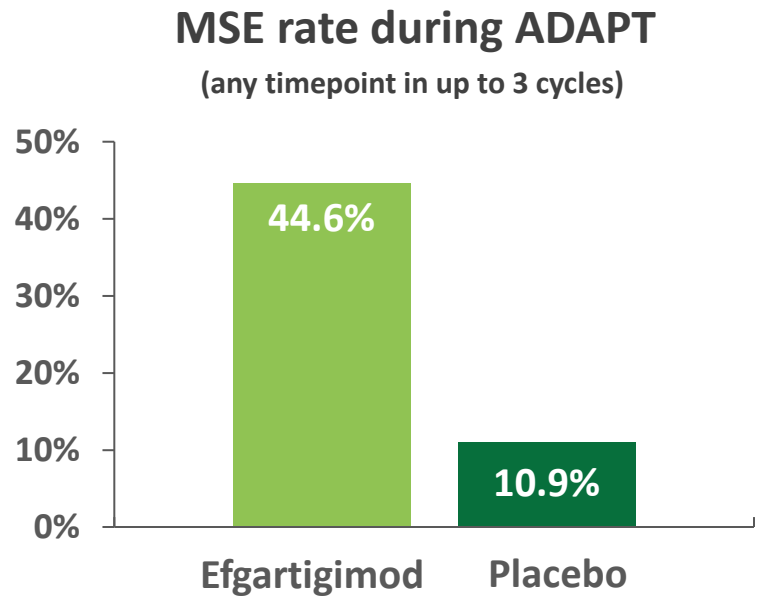
Objectives:

- Comparison of baseline demographics and characteristics of AChR-Ab+ participants who achieved MSE during ADAPT vs those who did not achieve MSE
- Assess changes in other disease-specific and health-related quality-of-life measures among AChR-Ab+ participants who achieved MSE
- Characterize rate of MSE in ADAPT and ADAPT+ (open-label extension of ADAPT)

AChR-Ab+=acetylcholine-receptor antibody–positive; IgG=immunoglobulin G; IV=intravenous; MG-ADL=Myasthenia Gravis-Activities of Daily Living; MGFA=Myasthenia Gravis Foundation of America.

Baseline Characteristics of AChR-Ab+ Participants in ADAPT Treated With Efgartigimod

	MSE (n=29)	Non-MSE (n=36)
Age, mean, y (SD)	42.4 (15.5)	46.5 (14.5)
Sex at birth, n (%)		
Female	21 (72.4)	25 (69.4)
Male	8 (27.6)	11 (30.6)
BMI, kg/m² (SD)	26.3 (5.0)	29.6 (9.7)
Time since gMG diagnosis, y (SD)	9.0 (6.8)	10.2 (9.3)
MGFA class at screening, n (%)		
II	11 (37.9)	17 (47.2)
III	18 (62.1)	17 (47.2)
IV	0	2 (5.6)
Previous thymectomy, n (%)	22 (75.9)	23 (63.9)
MG-ADL total score, mean (SD)	8.2 (1.8)	9.7 (2.7)*
QMG total score, mean (SD)	15.8 (4.9)	16.2 (5.4)
MG-QoL15r total score, mean (SD)	14.8 (5.8)	16.4 (6.6)
MGC total score, mean (SD)	18.2 (5.7)	18.9 (6.4)
Concomitant MG therapy, n (%)		
NSIST	18 (62.1)	20 (55.6%)
Steroid	21 (72.4)	25 (69.4%)

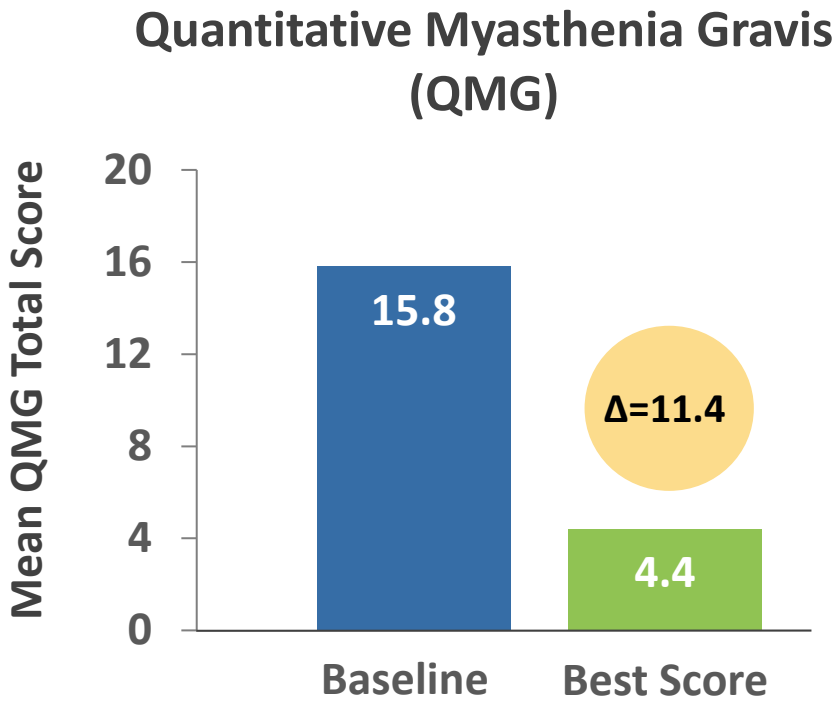


Baseline MG-ADL was the only characteristic with a significant between-group difference (*P*=0.0084), although the difference (1.5) was not clinically meaningful

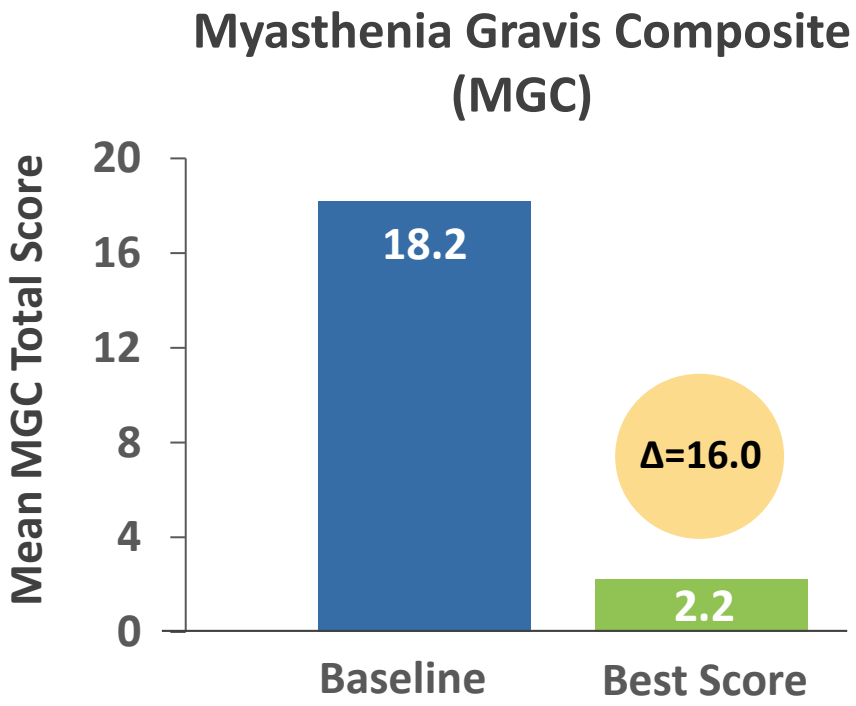
*Difference is statistically significant (*P*=0.0084).

BMI=body mass index; gMG=generalized myasthenia gravis; MGC=Myasthenia Gravis Composite; MG-QoL15r=Myasthenia Gravis Quality of Life, 15 item, revised; NSIST=nonsteroidal immunosuppressive therapy; QMG=Quantitative Myasthenia Gravis.

Change in QMG and MGC Among AChR-Ab+ Participants Who Were Treated With Efgartigimod and Achieved MSE (n=29)



MCID in QMG[1]: **3-point reduction**



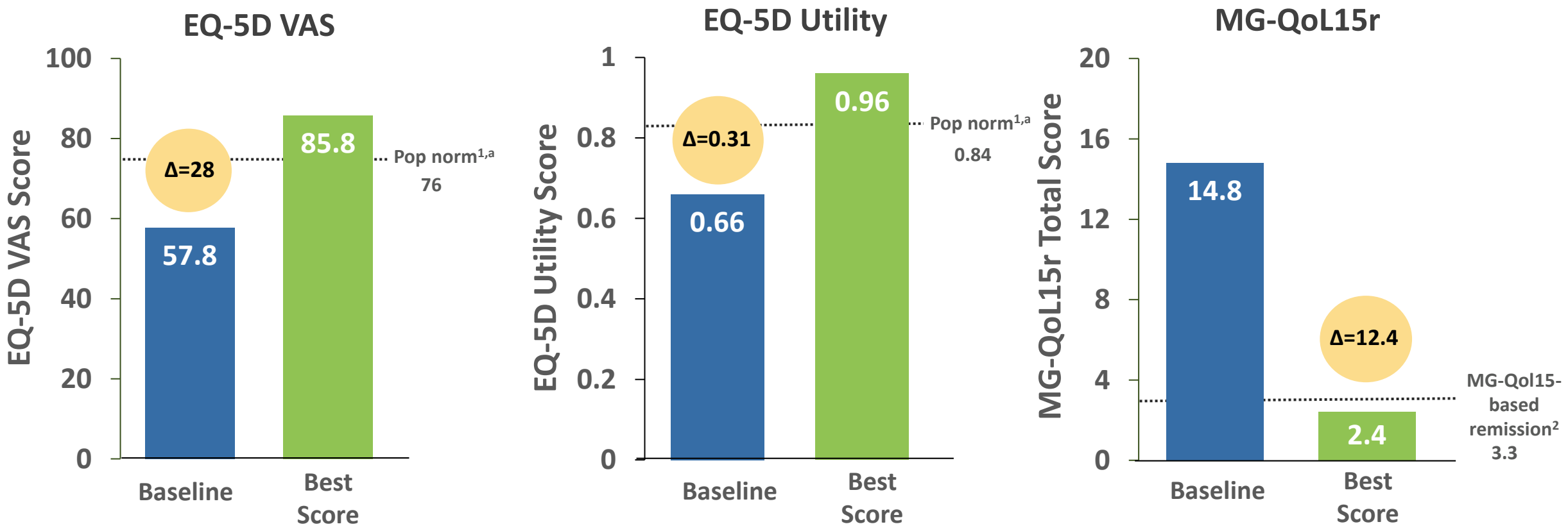
MCID in MGC[1]: **3-point reduction**

Achieving MSE resulted in substantial symptom improvements across multiple disease-specific measures

Best score=the minimal score/maximal reduction from study baseline across post-baseline visits at any cycle.
Δ=maximum change from study baseline across post-baseline visits of any treatment cycle of ADAPT.
MCID=minimal clinically important difference; MSE=minimum symptom expression; MGC=Myasthenia Gravis Composite; QMG=Quantitative Myasthenia Gravis.

1. Thomsen JLS, Andersen H. *Front Neurol*. 2020;11:596382.

Change in HRQoL Outcomes Among AChR-Ab+ Participants Who Were Treated With Efgartigimod and Achieved MSE (n=29)



Achieving MSE resulted in substantial HRQoL benefits, with scores that were comparable to healthy populations

Best score=maximal score/change from study baseline across post-baseline visits at any cycle.

[a] population normal values were derived from an aged-matched cohort with individuals ranging from 35-44 years old

Δ=maximum change from study baseline across post-baseline visits of any treatment cycle of ADAPT.

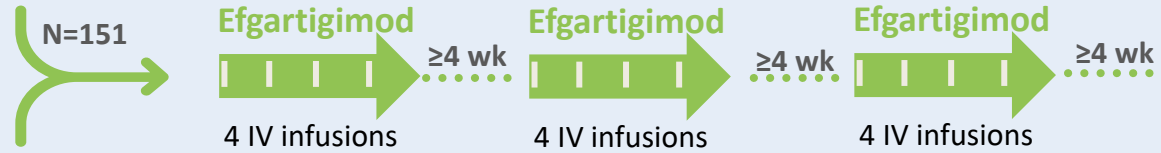
EQ-5D=EuroQoL 5 Dimensions; HRQoL=health-related quality of life; MSE=minimum symptom expression; Pop norm, general population norm; VAS=visual analog scale.

1. Jiang R, et al. Qual Life Res. 2021;30(3):803-816; **2**. Burns TM, et al; MG Composite and MG-QoL15 Study Group. *Muscle Nerve*. 2010;41(2):219-226.

Achieving MSE in ADAPT+

ADAPT
Placebo-controlled
phase 3 study

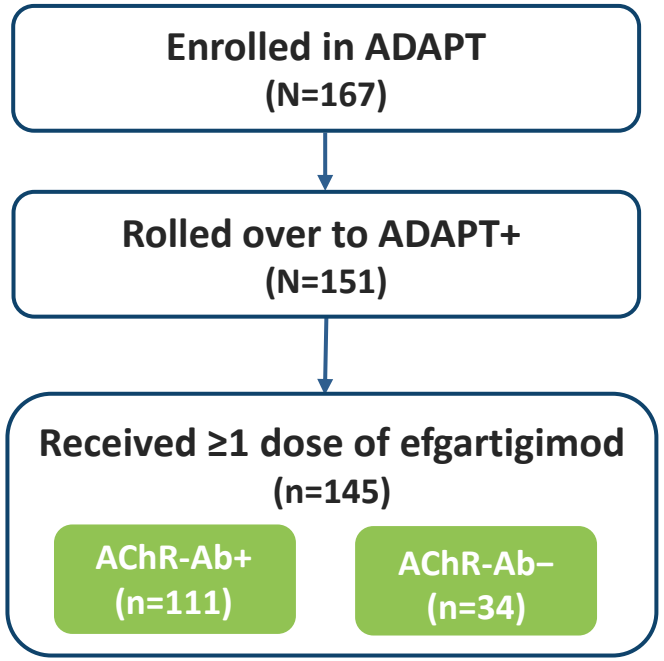
ADAPT+
Open-label extension
(Up to 3 years)



Subsequent treatment cycle initiated based on:

- ≥4 weeks since last treatment cycle
- MG-ADL total score ≥5 (>50% of the total score due to nonocular items)
- MG-ADL score within 2 points of baseline (not required after year 1)

ADAPT to ADAPT+ Rollover Disposition

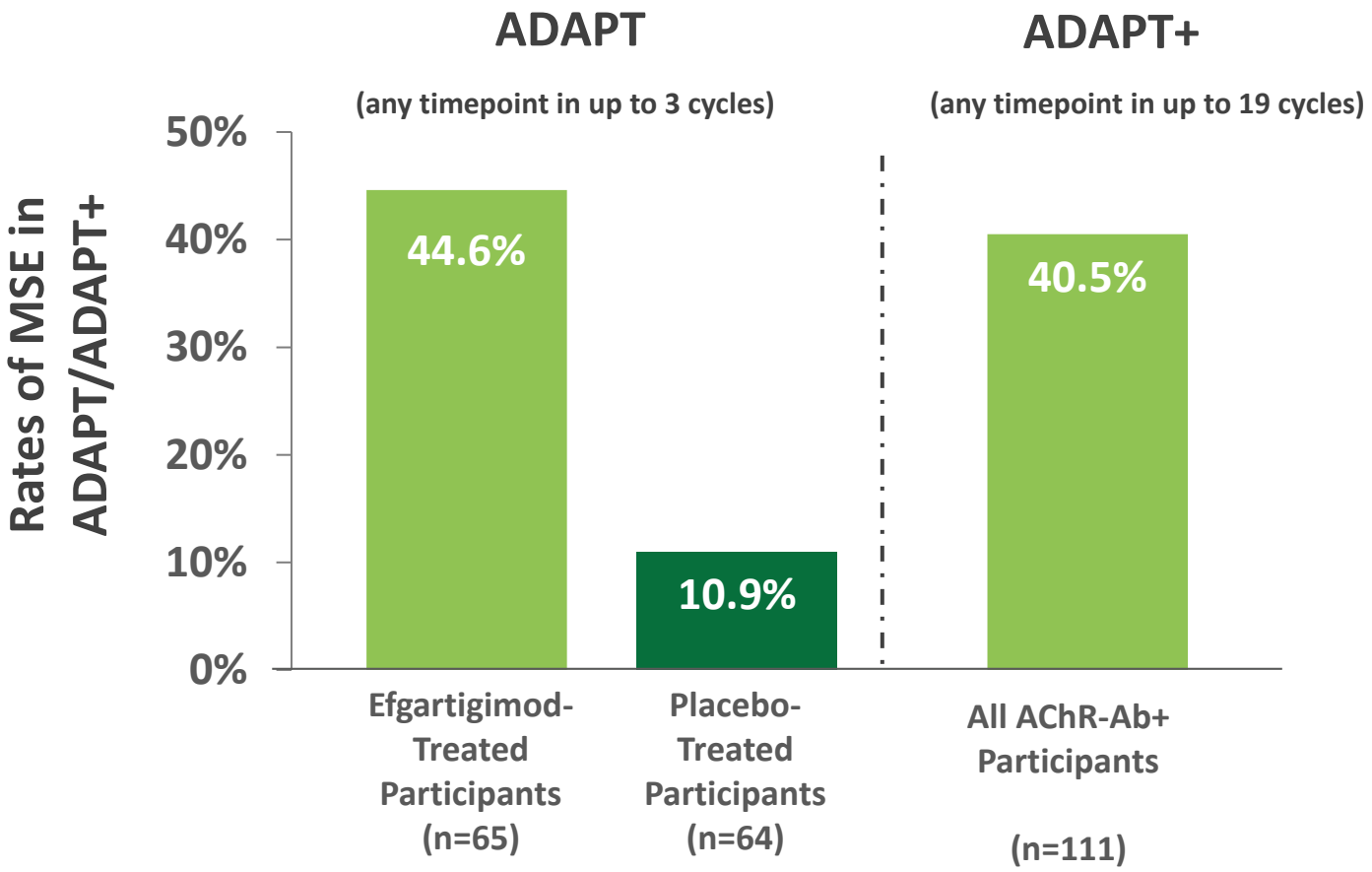


Key differences between ADAPT and ADAPT+:

- MG-ADL administered in ADAPT at baseline (week 0) and weeks 1, 2, 3, 4, 5, 6, 7, 8, and 10
- MG-ADL administered in ADAPT+ at baseline (week 0) and weeks 1, 2, 3, 7, and 11
- Time between initiating subsequent treatment cycles was ≥5 weeks in ADAPT and ≥4 weeks in ADAPT+

AChR-Ab–=acetylcholine-receptor antibody–negative; CMI=clinically meaningful difference.

Rates of MSE in AChR-Ab+ Participants in ADAPT and ADAPT+



Rates of MSE were consistent across both studies

- 40.5% of participants enrolled in ADAPT+ achieved MSE, which is comparable to the MSE rate observed in ADAPT (44.6%)
- 81% of participants from efgartigimod arm who achieved MSE during ADAPT regained MSE during ADAPT+
- 8 participants (23%) who did not achieve MSE in ADAPT did achieve MSE during ADAPT+

Summary

Minimal symptom expression (MSE) is an important treatment goal in gMG

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

Participants who achieved MSE during ADAPT had minimal disease symptoms across multiple disease measures and substantial improvements in health-related quality of life

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

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