MSE and Associated Outcomes in AChR-Ab+ Participants With gMG Receiving Efgartigimod in ADAPT/ADAPT+

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(Form 4-E)

If there is a state of conflict of interest requiring disclosure

The Japanese Society of Neurology (JSN)
COI Disclosure

Name of Lead Presenter: Hiroyuki Murai

Companies, etc. in a relation of conflict of interest requiring disclosure in relation to the presentation:
(*Indicate "None" if not applicable.)

1) Advisor:	**Alexion AstraZeneca Rare Disease, argenx, UCB Pharma, and Roche**
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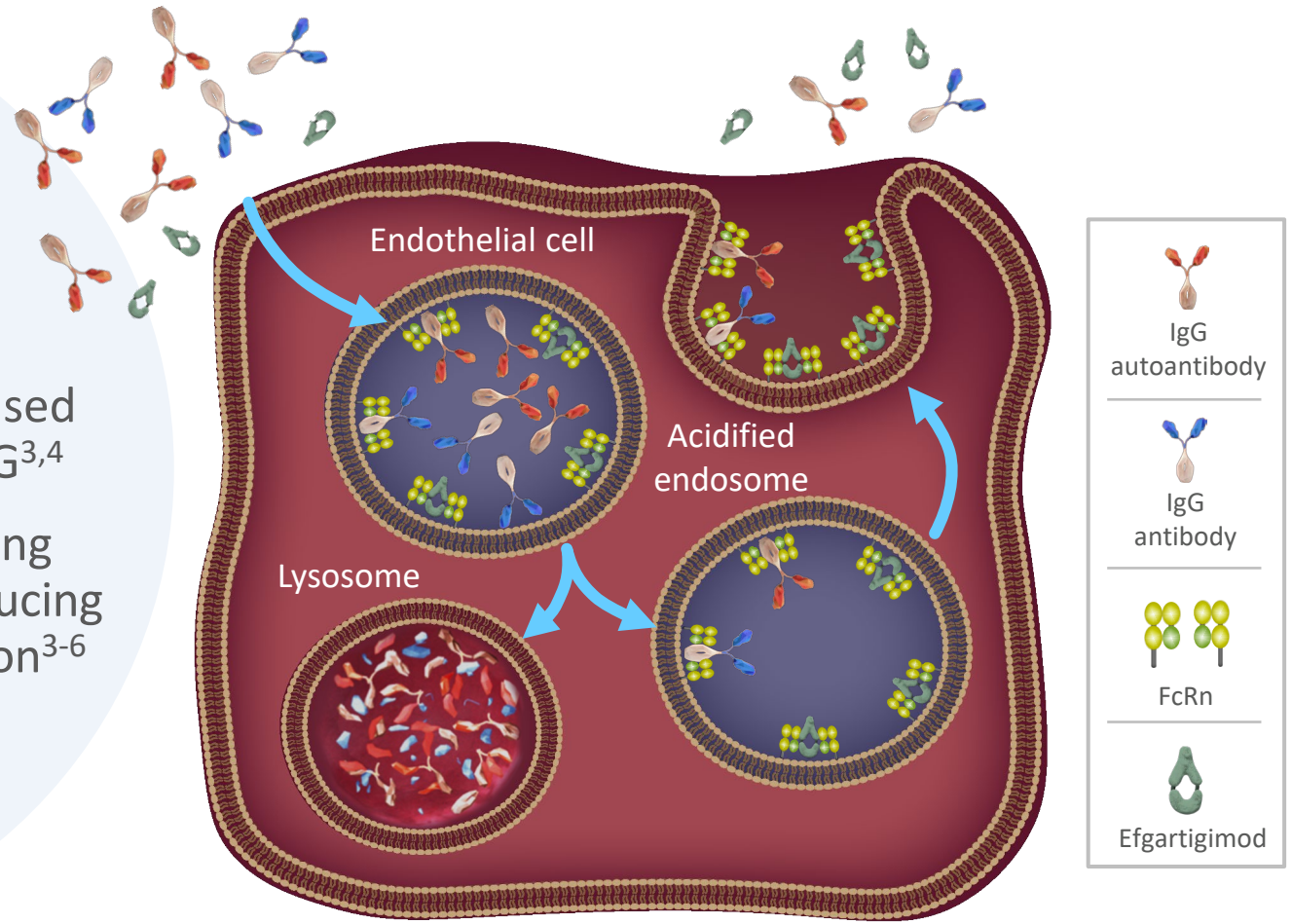
Efgartigimod Effectively Blocks FcRn and Reduces IgG Levels

- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
  - FcRn is additionally involved in other cellular processes such 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, thus reducing IgG levels without directly impacting IgG production[3-6]
  - Targeted reduction of all IgG subtypes[3,5]
  - No impact on IgM, IgA, IgE, or IgD[3,6]
  - No reduction in albumin or increase in cholesterol levels[5-8]



FC, crystallizable fragment; FcRn, neonatal Fc receptor; Ig, immunoglobulin.

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.** Howard JF Jr, et al. *Front Neurol*. 2024;14:1284444.

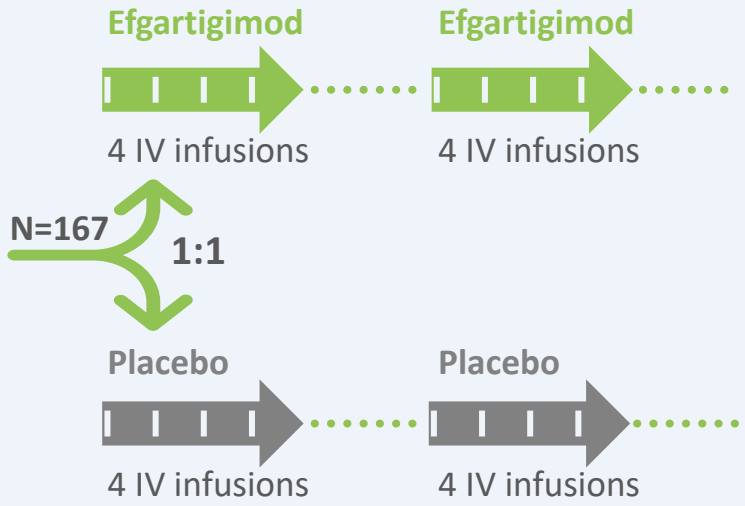
ADAPT Study Design

ADAPT

Placebo-controlled phase 3 study
(26 weeks total; ≤3 cycles)

Inclusion Criteria

- **MGFA Class II, III, IV**
- **AChR-Ab+ or –**
- **MG-ADL score ≥5 (>50% nonocular)**
- **On ≥1 stable gMG treatment**
- **IgG ≥6 g/L**



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

ADAPT+ OLE study
(≤3 total years; ≤19 cycles)

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 HRQoL measures among AChR-Ab+ participants who achieved MSE
- Characterize rate of MSE in ADAPT and ADAPT+ (OLE of ADAPT)

AChR-Ab, acetylcholine-receptor antibody; gMG, generalized myasthenia gravis; HRQoL, health-related quality of life; IgG, immunoglobulin G; IV, intravenous; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MSE, minimal symptom expression; OLE, open-label extension.

Baseline Demographics and Disease Characteristics for ADAPT and ADAPT+

	ADAPT		ADAPT+
Characteristics	**Placebo (n=83)**	**Efgartigimod (n=84)**	**Efgartigimod (n=145)**
Age, y, mean (SD)	48.2 (15.0)	45.9 (14.4)	47.0 (14.8)
Sex, n (%)			
Female	55 (66.3)	63 (75.0)	103 (71.0)
Male	28 (33.7)	21 (25.0)	42 (29.0)
Race, Japanese, n (%)	7 (8.4)	8 (9.5)	10 (6.9)
Time since gMG diagnosis, y, mean (SD)	8.8 (7.6)	10.1 (9.0)	9.7 (8.2)
MGFA class at screening, n (%)			
II	31 (37.3)	34 (40.5)	55 (37.9)
III	49 (59.0)	47 (56.0)	86 (59.3)
IV	3 (3.6)	3 (3.6)	4 (2.8)
AChR-Ab+, n (%)	64 (77.1)	65 (77.4)	111 (76.6)
Total MG-ADL score, mean (SD)	8.8 (2.3)	9.2 (2.6)	9.8 (3.2)
Total QMG score, mean (SD)	15.5 (4.6)	16.2 (5.0)	15.4 (5.7)
Commonly prescribed therapies, n (%)			
NSIST	51 (61.4)	51 (60.7)	89 (61.4)
Steroid	67 (80.7)	60 (71.4)	111 (76.6)

AChR-Ab, acetylcholine receptor antibody; gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; QMG, Quantitative Myasthenia Gravis.

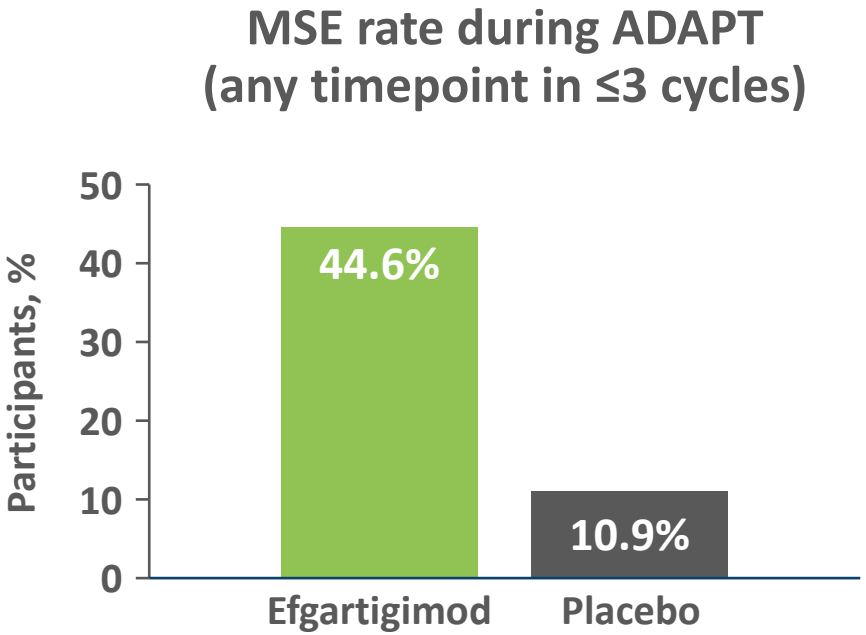
Summary of TEAEs

	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]
≥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]

ER, event rate; PY, participant-year; SAE, serious adverse event; TEAE, treatment-emergent adverse event.
[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. [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.

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

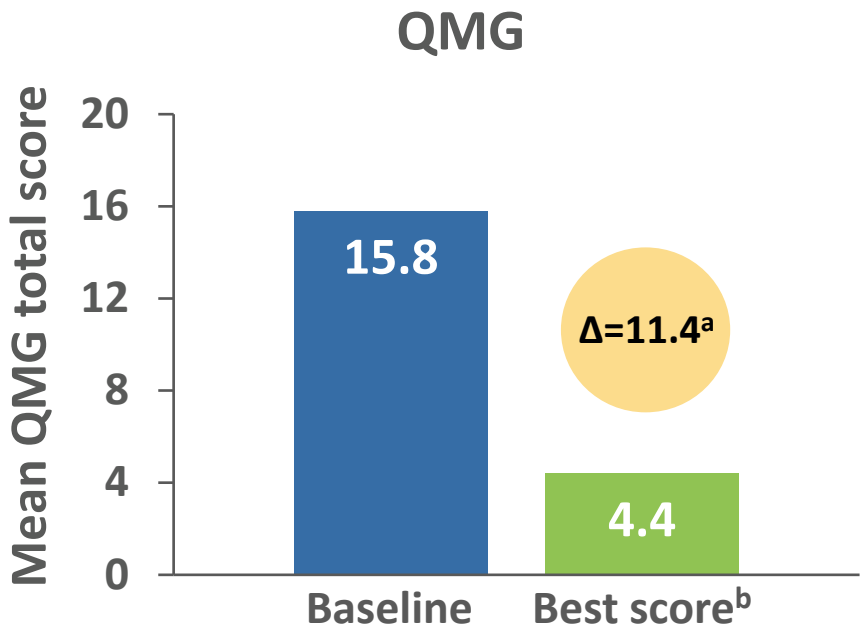
	MSE (n=29)	Non-MSE (n=36)
Age, y, mean (SD)	42.4 (15.5)	46.5 (14.5)
Sex, n (%)		
Female	21 (72.4)	25 (69.4)
Male	8 (27.6)	11 (30.6)
BMI, kg/m^2, mean (SD)	26.3 (5.0)	29.6 (9.7)
Time since gMG diagnosis, y, mean (SD)	9.0 (6.8)	10.2 (9.3)
MGFA class at screening, n (%)		
II	11 (37.9)	17 (47.2)
III	18 (62.1)	17 (47.2)
IV	0	2 (5.6)
Previous thymectomy, n (%)	22 (75.9)	23 (63.9)
Total MG-ADL score, mean (SD)	8.2 (1.8)	9.7 (2.7)*
Total QMG score, mean (SD)	15.8 (4.9)	16.2 (5.4)
Total MG-QoL15r score, mean (SD)	14.8 (5.8)	16.4 (6.6)
Total MGC score, mean (SD)	18.2 (5.7)	18.9 (6.4)
Commonly prescribed therapies, n (%)		
NSIST	19 (65.5)	21 (58.3)
Steroid	21 (72.4)	25 (69.4)

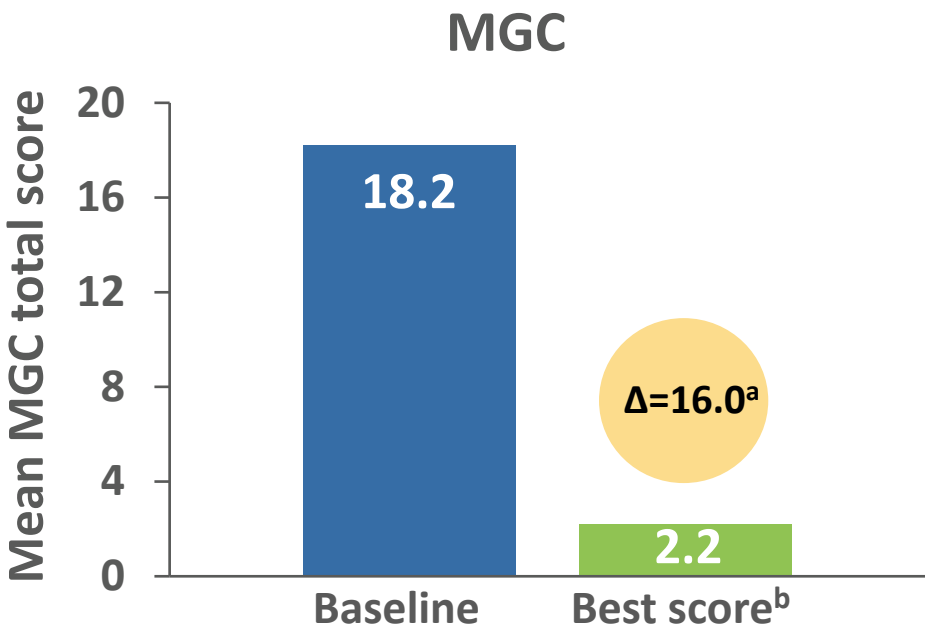


***Baseline MG-ADL was the only characteristic with a significant between-group difference (*P*=.0084), although the difference (1.5) was small**

AChR-Ab, acetylcholine receptor antibody; BMI, body mass index; gMG, generalized myasthenia gravis; MGC, Myasthenia Gravis Composite; MG-QoL15r, Myasthenia Gravis Quality of Life, 15-Item Questionnaire, 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**

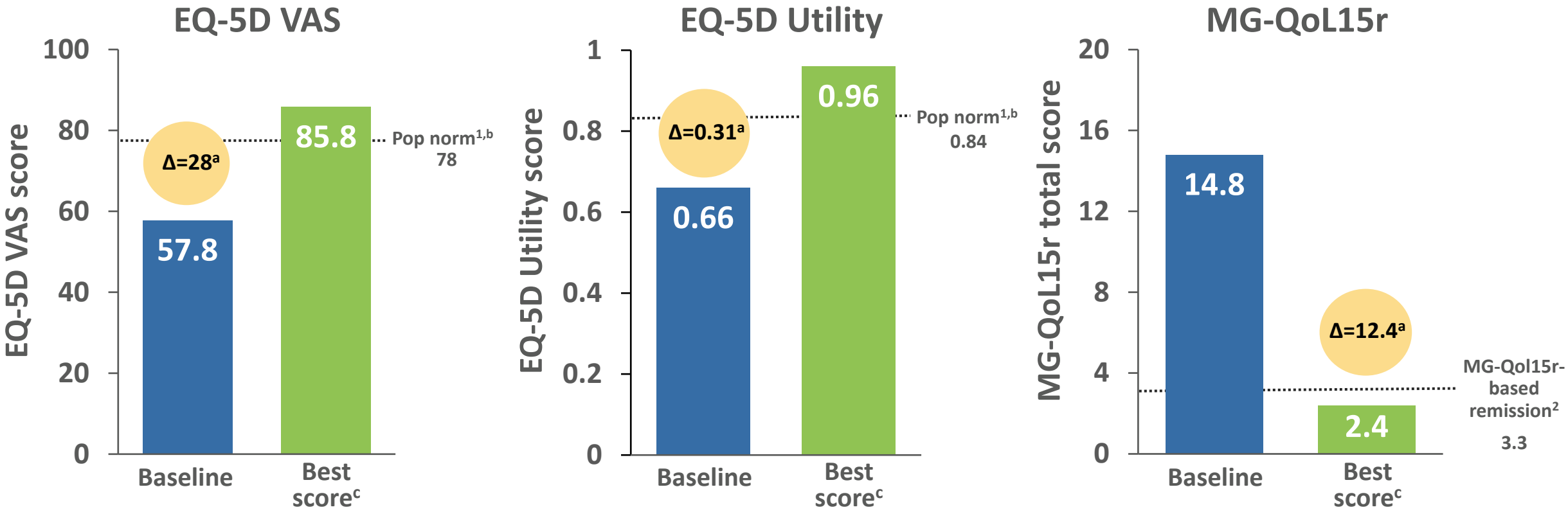
Achieving MSE resulted in substantial symptom improvements across multiple disease-specific measures

AChR-Ab, acetylcholine receptor antibody; MCID, minimal clinically important difference; MGC, Myasthenia Gravis Composite; MSE, minimum symptom expression; QMG, Quantitative Myasthenia Gravis.

[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 minimal score/maximal reduction from study baseline across postbaseline visits at any cycle.

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

EQ-5D, EuroQoL 5-Dimension; HRQoL, health-related quality of life; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; MSE, minimum symptom expression; Pop norm, general population norm; VAS, visual analog scale.

[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.

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

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

	Participants Treated With Efgartigimod Who Achieved 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%

EQ-5D, EuroQoL 5-Dimension; MGC, Myasthenia Gravis Composite; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; MSE, minimal symptom expression; PASS, patient-acceptable symptom states; QoL, quality of life; QMG, Quantitative Myasthenia Gravis; VAS, visual analog scale.

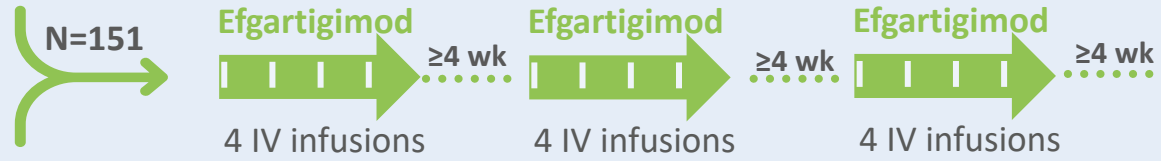
[a]MG-QoL15r threshold of ≤8 is based upon the PASS threshold for MG-QoL15 in Mendoza 2020.[1] EQ-5D Utility and EQ-5D VAS thresholds based on population normal values for individuals aged 35 to 44 years.[2]

1. Mendoza M, et al. *Neurology*. 2020;95(12):e1617-e1628. **2.** Jiang R, et al. *Qual Life Res*. 2021;30(3):803-816.

ADAPT+ Study Design

ADAPT
Placebo-controlled phase 3 study

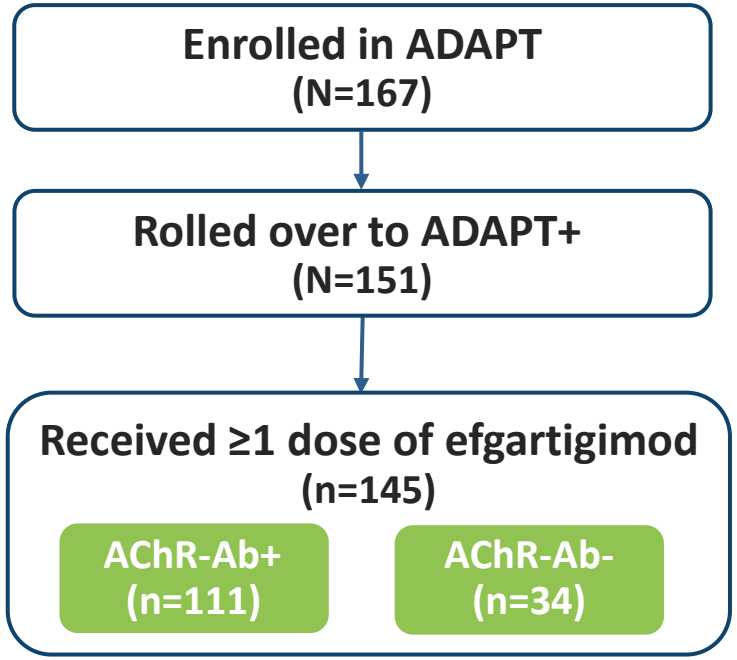
ADAPT+
Open-label extension (≤3 years)



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

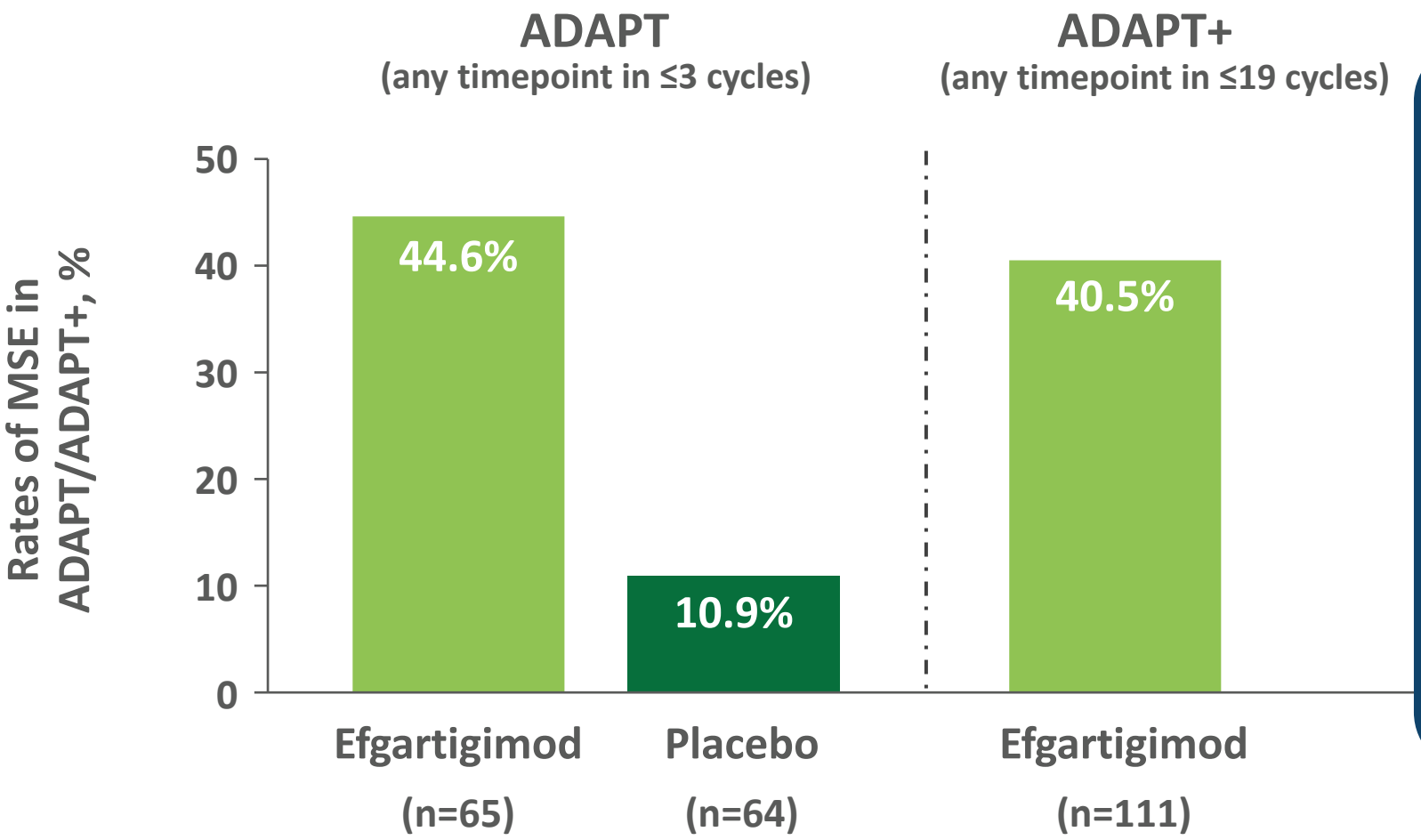


Key differences between ADAPT and ADAPT+:

- 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; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension.

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%)**
- **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+**

AChR-Ab, acetylcholine receptor antibody; MSE, minimal symptom expression.
[a]61 of the 65 AChR-Ab+ participants treated with efgartigimod in ADAPT rolled over into ADAPT+.

Summary

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 HRQoL

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

gMG, generalized myasthenia gravis; HRQoL, health-related quality of life; MSE, minimal symptom expression.