Achievement of Minimal Symptom Expression in Acetylcholine Receptor Antibody-Positive Participants Treated With Efgartigimod in ADAPT/ADAPT+

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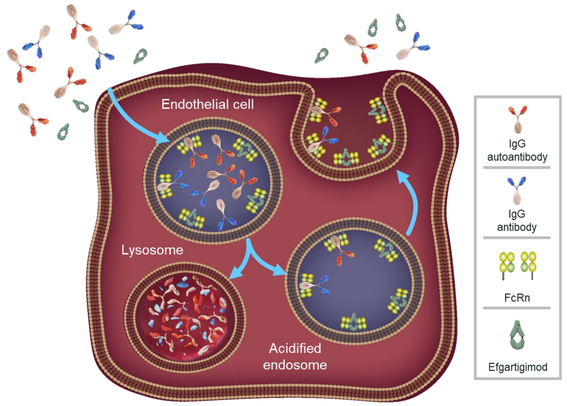
BACKGROUND

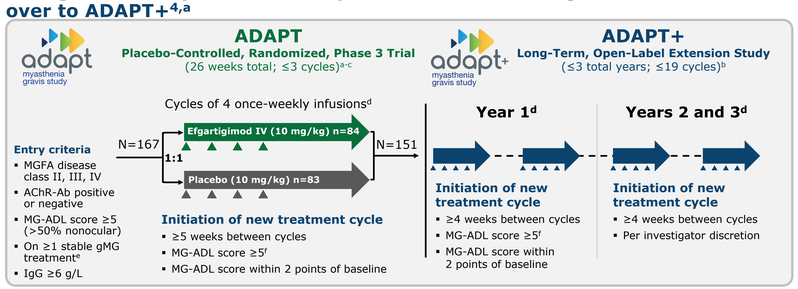
Efgartigimod Mechanism of Action: Blocking FcRn

- 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[5-8]



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 requiring rescue therapy 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.

RESULTS

Baseline Characteristics
(AChR-Ab+ Participants)

	Placebo		Efgartigimod	
Characteristics	**MSE[a] (n=7)**	**Non-MSE (n=57)**	**MSE[a] (n=29)**	**Non-MSE (n=36)**
Age, y, 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/m² (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)

- 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)

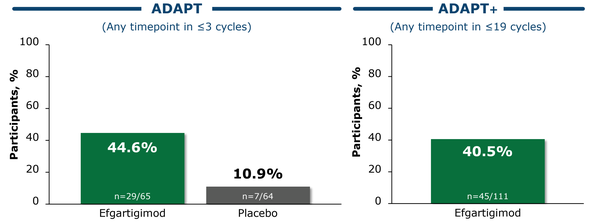
[a]MSE is defined as MG-ADL score of 0 or 1.

Summary of TEAEs
(Overall Participants)

	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.

Proportion of Participants With MSE in ADAPT/ADAPT+
(AChR-Ab+ Participants)



- 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+

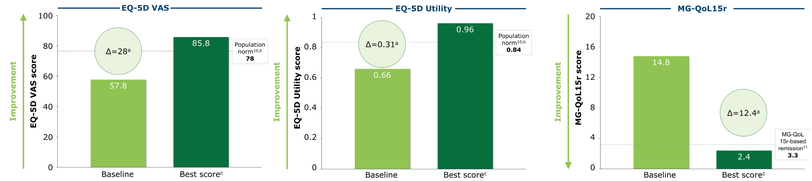
[a]61 of the 65 AChR-Ab+ participants treated with efgartigimod in ADAPT rolled over into ADAPT+.

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

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%

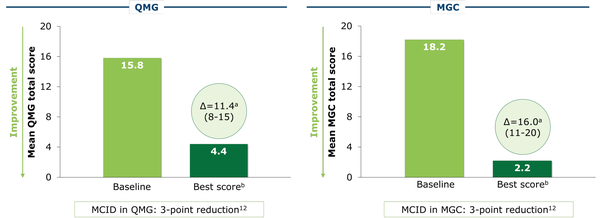
RESULTS (cont'd)

Change in HRQoL Outcomes Among Participants Who Achieved MSE in ADAPT (n=29)
(AChR-Ab+ Participants)



[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.

Change in QMG and MGC Among Participants Who Achieved MSE in ADAPT (n=29)
(AChR-Ab+ Participants)



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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 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+**

DISCLOSURES AND ACKNOWLEDGEMENTS

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ABBREVIATIONS

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REFERENCES

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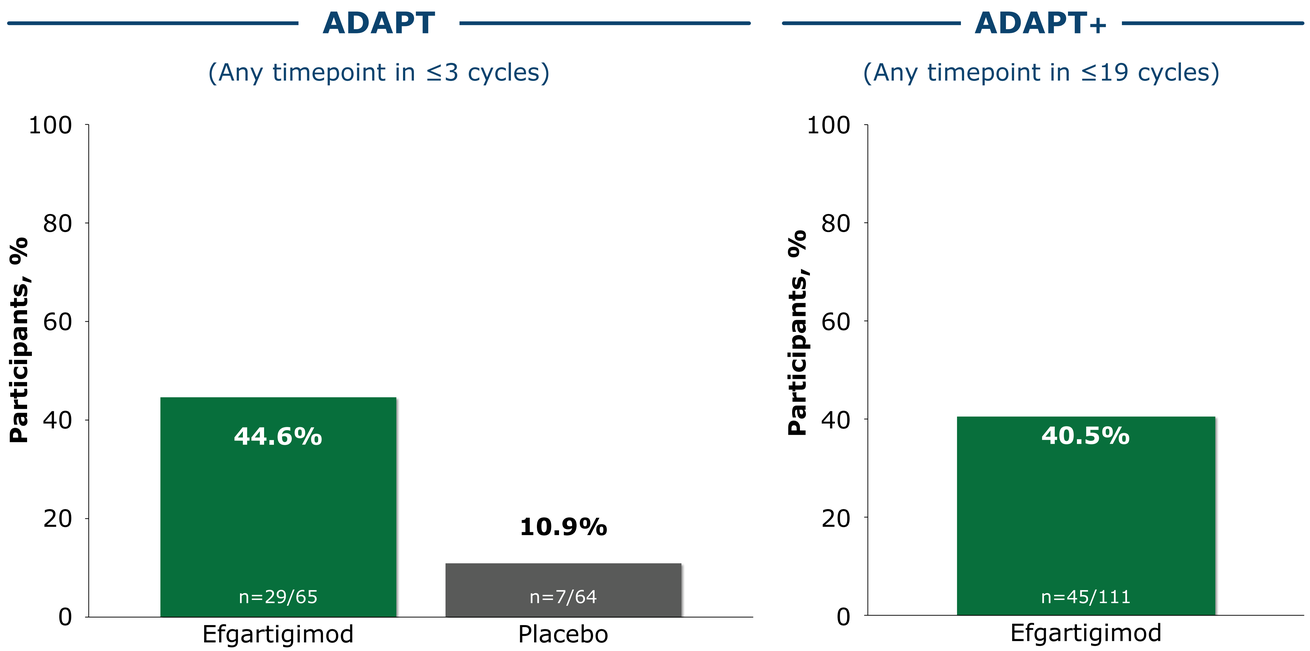
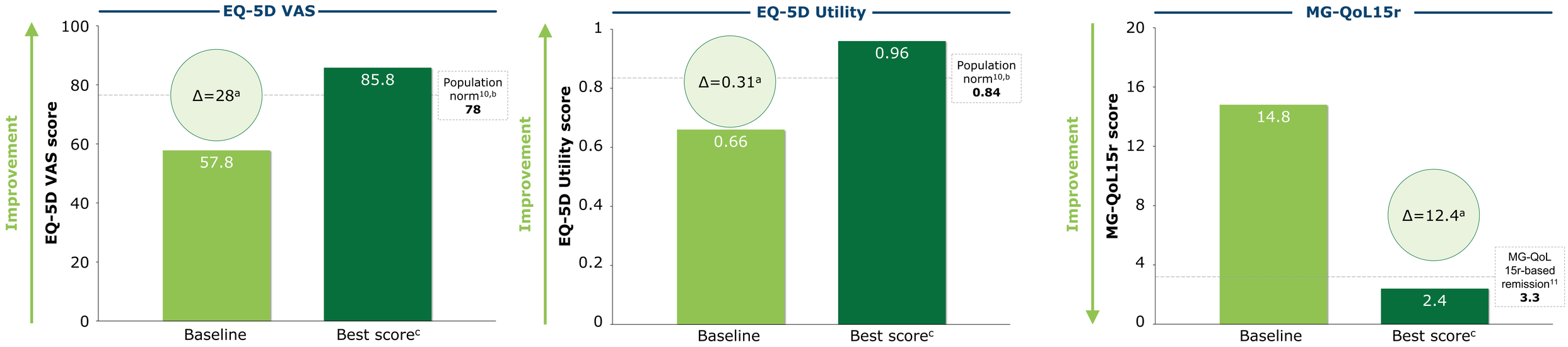
Proportion of Participants With MSE in ADAPT/ADAPT+

AChR-Ab+ Population



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

AChR-Ab+ Population



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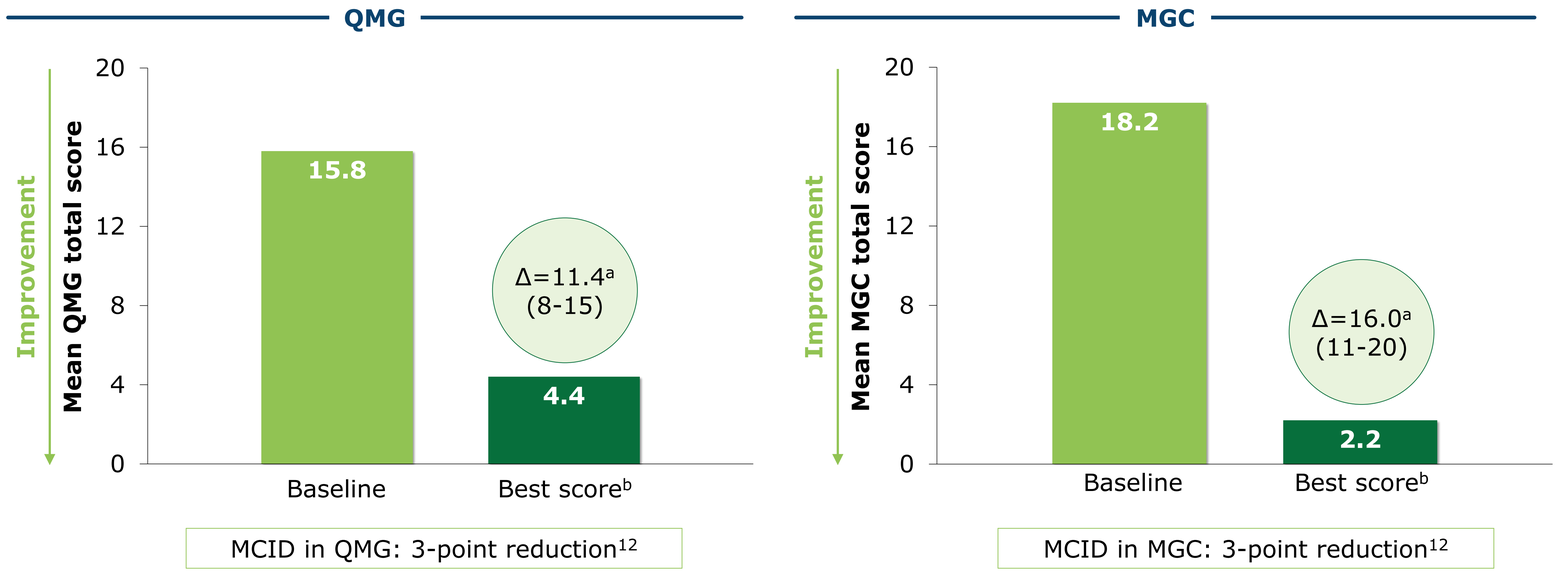
Change in QMG and MGC Among Participants Who Achieved MSE in ADAPT (n=29)

AChR-Ab+ Population



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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.

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