Subcutaneous Efgartigimod PH20 Treatment in Participants With Generalized Myasthenia Gravis in ADAPT-SC+: Interim Analyses on Quality of Life, Efficacy, Tolerability, and Long-Term Safety

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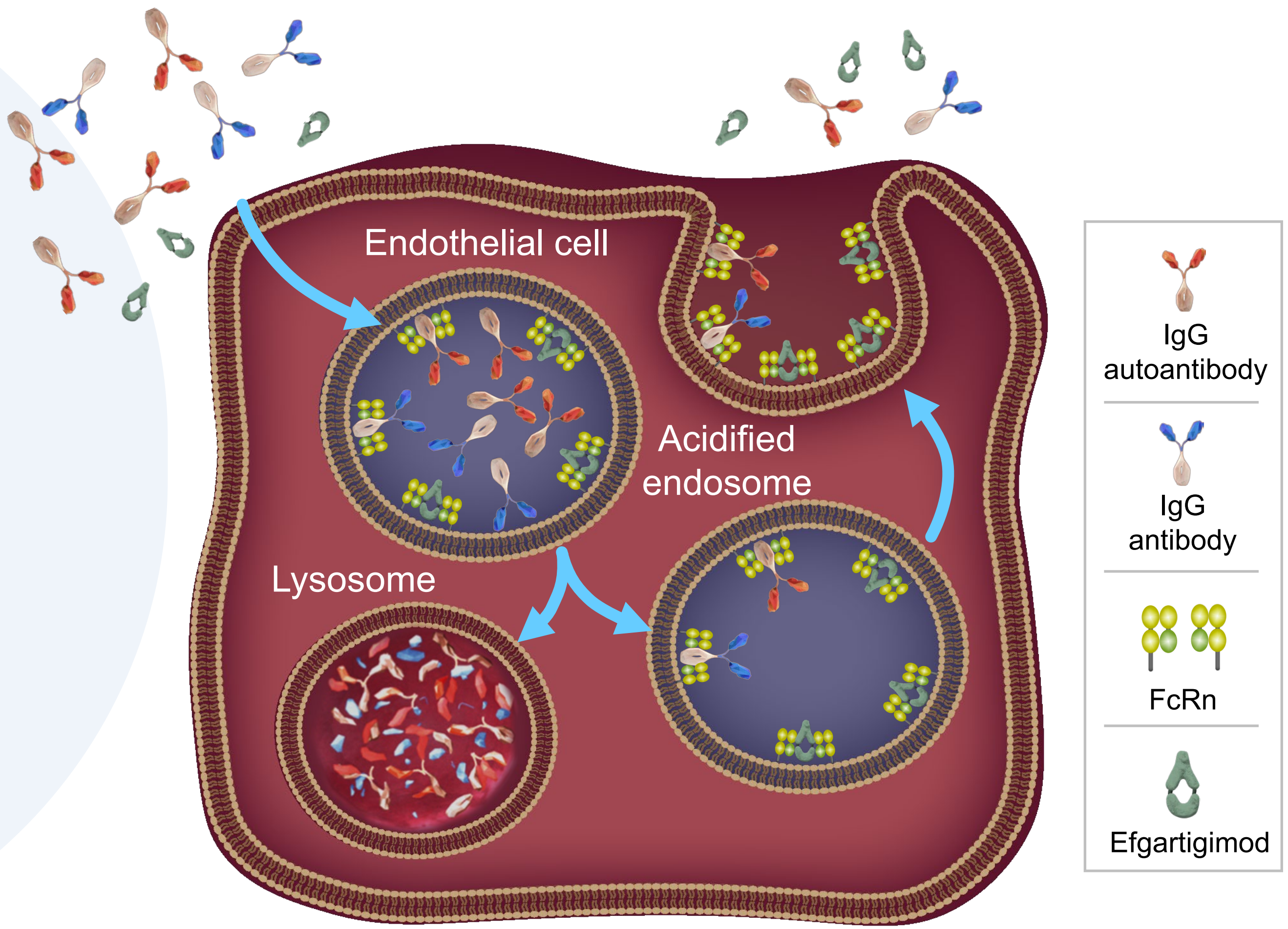
Disclosures

- The phase 3 ADAPT-SC and ADAPT-SC+ studies were funded by argenx
- TV has served as a speaker and consultant for argenx and participated in trials sponsored by argenx
- TV has also served as a speaker for Alexion, CSL Behring, and Allergan/AbbVie. He has performed consulting work related to MG for Alexion/AstraZeneca and UCB
- TV participated in MG trials sponsored by Alexion/AstraZeneca, argenx, UCB, Horizon, Johnson & Johnson, Dianthus, RemeGen, Regeneron, Immunovant, Cartesian, and Sanofi

MG, myasthenia gravis.

Efgartigimod Effectively Blocks FcRn and Reduces IgG Levels

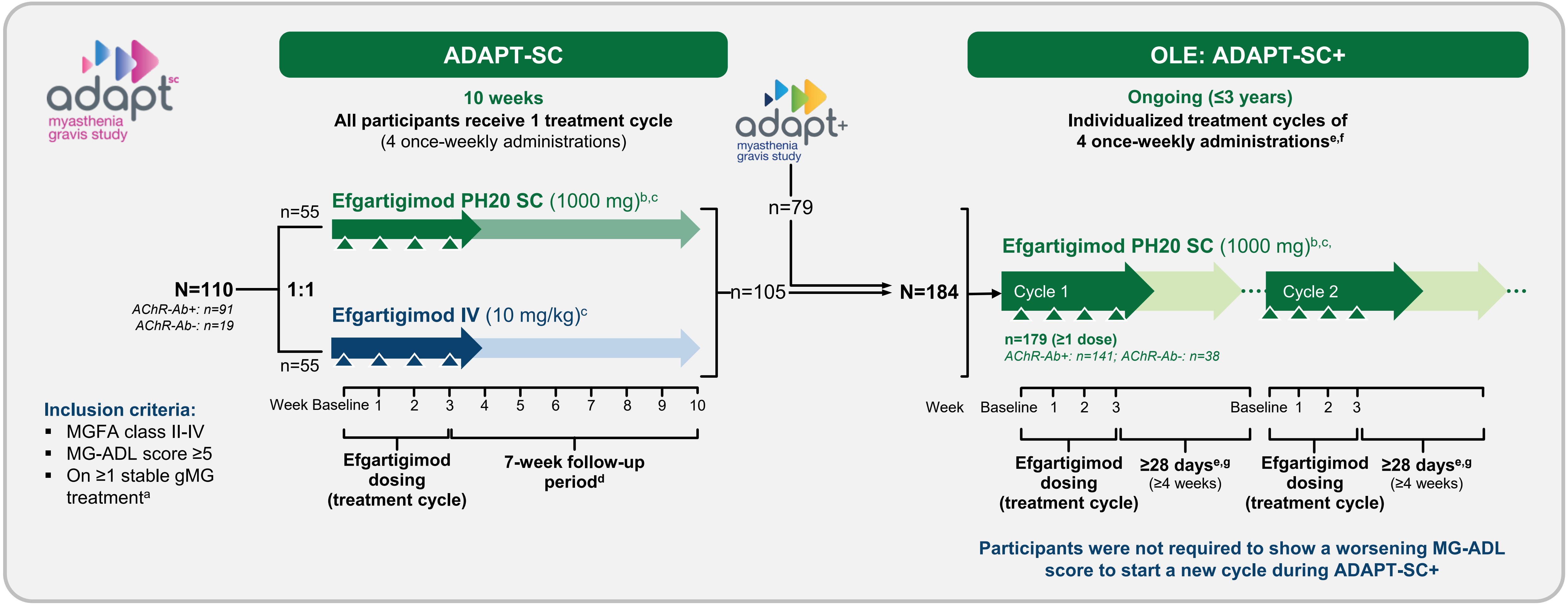
- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
  - FcRn is additionally involved in other cellular processes such as IgG-dependent phagocytosis and antigen presentation[2]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have 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]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[9,10]
- PK/PD modeling and phase 3 data (ADAPT-SC) suggest 4 weekly administrations of 1000 mg efgartigimod PH20 SC and 10 mg/kg efgartigimod IV result in comparable decreases in IgG levels[9]



FC, crystallizable fragment; FcRn, neonatal Fc receptor; Ig, immunoglobulin; IV, intravenous; PD, pharmacodynamic; PK, pharmacokinetic; SC, subcutaneous.

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. **9.** Study ARGX-113-2001 (ADAPT-SC) Clinical Trial Protocol v2.0, 02 Jul 2021. **10.** Locke KW, et al. *Drug Deliv.* 2019;26(1):98-106.

ADAPT-SC/ADAPT-SC+ Study Design



AChEIs, acetylcholinesterase inhibitors; AChR-Ab, acetylcholine receptor antibody; gMG, generalized myasthenia gravis; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSISTs, nonsteroidal immunosuppressive therapies; OLE, open-label extension; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

[a]AChEIs, steroids, and/or NSISTs. [b]Coformulated with 2000 U/mL rHuPH20. [c]Arrows indicate efgartigimod administration. [d]Participants could not receive treatment in the 7-week follow-up period. [e]≥28 days between the last dose of the previous treatment period and the first dose of the next treatment period and based on the need for treatment as determined by the investigator. [f]Participants who are not in need of retreatment at study entry will instead start with an intertreatment period. [g]During the second year onward, it is recommended to have ≥28 days between treatment cycles. However, a subsequent treatment period can be administered earlier based on clinical evaluation at the discretion of the investigator.

ADAPT-SC+ Participant Demographics and Baseline Characteristics

Overall, AChR-Ab+, and AChR-Ab- Populations

	Efgartigimod PH20 SC *Overall* *(n=179)*[a]	Efgartigimod PH20 SC *AChR-Ab+* *(n=141)*	Efgartigimod PH20 SC *AChR-Ab-* *(n=38)*
Age, mean (SD), y	50.7 (15.5)	51.0 (15.9)	49.7 (14.2)
Sex, female, n (%)	119 (66.5)	90 (63.8)	29 (76.3)
Weight, median (Q1-Q3), kg	76.9 (64.0-89.8)	77.0 (63.0-92.0)	76.1 (67.7-85.6)
AChR-Ab+, n (%)	141 (78.8)	141 (100)	-
Total MG-ADL score, mean (SD)	7.9 (3.4)	7.6 (3.4)	8.9 (3.4)
Total MG-QoL15r score, mean (SD)	13.6 (6.9)	13.1 (6.8)	15.5 (6.8)
MG therapy during the first year, n (%)			
Any steroid	128 (71.5)	103 (73.0)	25 (65.8)
Any NSIST	89 (49.7)	67 (47.5)	22 (57.9)
Any AChEI	150 (83.8)	122 (86.5)	28 (73.7)
Steroid + NSIST	69 (38.5)	53 (37.6)	16 (42.1)
AChEI only	29 (16.2)	23 (16.3)	6 (15.8)

AChEI, acetylcholinesterase inhibitor; AChR-Ab+, acetylcholine receptor antibody seropositive; AChR-Ab-, acetylcholine receptor antibody seronegative; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; NSIST, nonsteroidal immunosuppressive therapy; SC, subcutaneous.
[a]Of the 184 participants enrolled, 179 received at least one dose of efgartigimod PH20 SC.

Summary of AEs

Overall Population

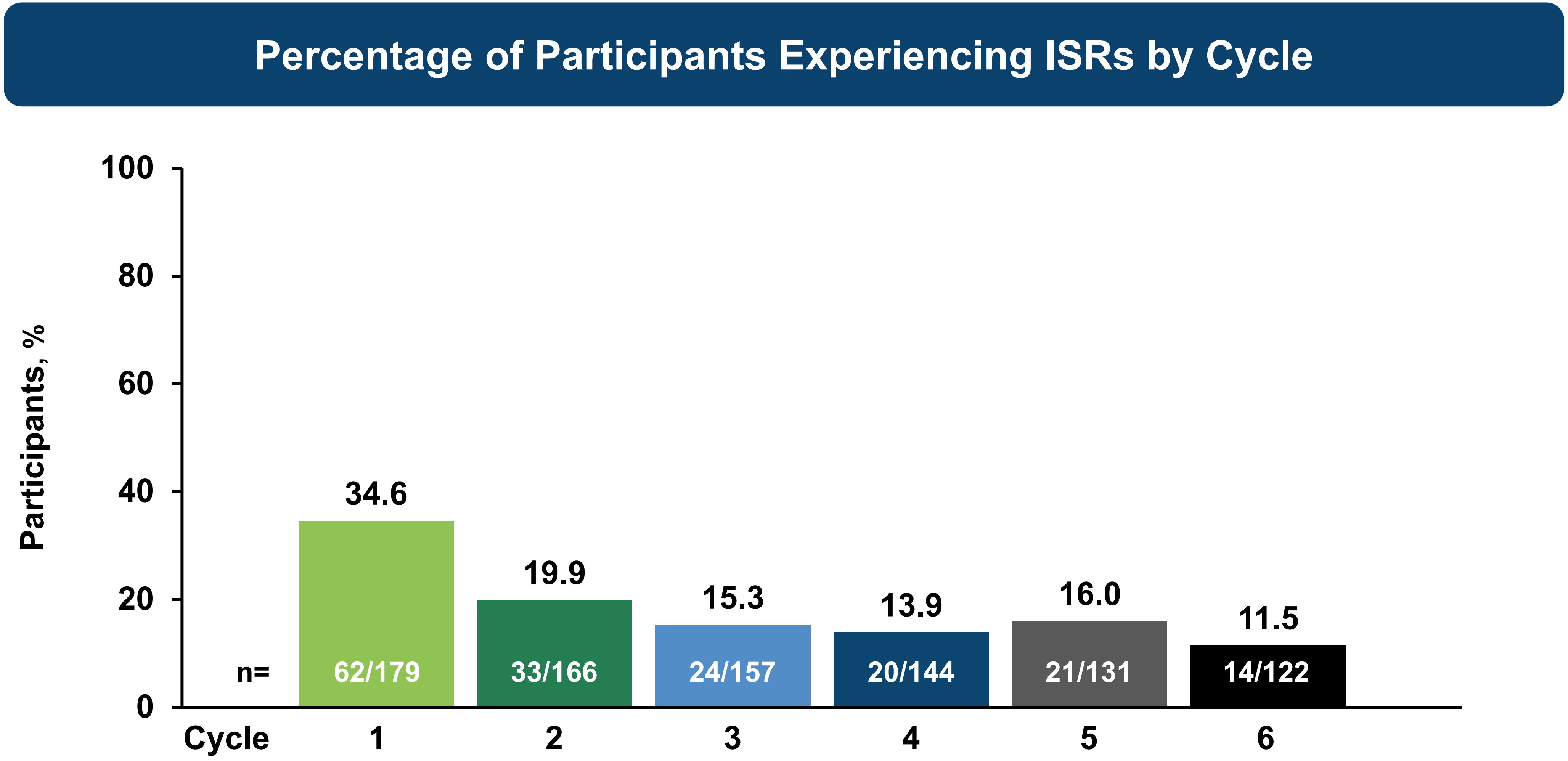
	Efgartigimod PH20 SC (n=179; PYFU=193.4)	
	Event Rate[a]	n (%)
Any AE	9.0	152 (84.9)
Any AE grade ≥3	0.4	36 (20.1)
Any SAE	0.3	33 (18.4)
Any ISR[b]	3.2	82 (45.8)
Any infection	1.0	91 (50.8)
Fatal event[c]	<0.1	4 (2.2)
Discontinued study treatment owing to AEs[d]	<0.1	4 (2.2)
Most commonly observed AEs[e]		
Injection site erythema	1.7	52 (29.1)
COVID-19	0.2	40 (22.3)
Headache	0.6	36 (20.1)
Nasopharyngitis	0.2	28 (15.6)
Diarrhea	0.2	24 (13.4)
Injection site pain	0.2	21 (11.7)
Injection site pruritus	0.2	19 (10.6)
Injection site bruising	0.2	18 (10.1)

AEs, adverse events; ISR, injection site reaction; MG, myasthenia gravis; PYFU, participant-years of follow-up; SAE, serious adverse event; SC, subcutaneous.

[a]Event rate was calculated as number of events per total PYFU. [b]Percentage of participants experiencing events decreased over subsequent cycles, from 34.6% (n=62/179) in Cycle 1 to 11.5% (n=14/122) in Cycle 6. [c]Fatal events (metastatic renal cell cancer, cardiac arrest, pulmonary mass, and COVID-19/respiratory failure) were not related to efgartigimod PH20 SC treatment, as determined by investigators. [d]Treatment discontinuation due to metastatic renal cell cancer (Cycle 1, death), cardiac arrest (Cycle 2, death), COVID-19/respiratory failure (Cycle 3, death), and MG crisis (Cycle 1). [e]Most frequent AEs occurring in >10% of patients receiving efgartigimod PH20 SC.

Incidence of ISRs Through Cycle 6

Overall Population



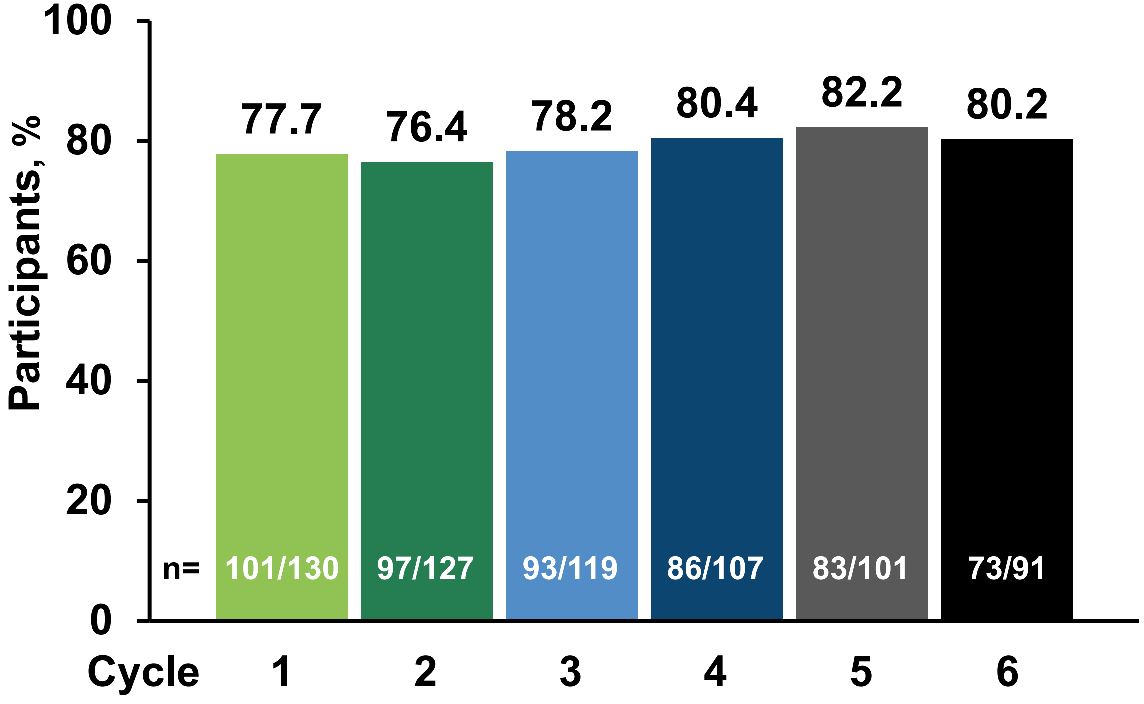
ISRs, injection site reactions.

Minimal Symptom Expression and Clinically Meaningful Improvement Through Cycle 6

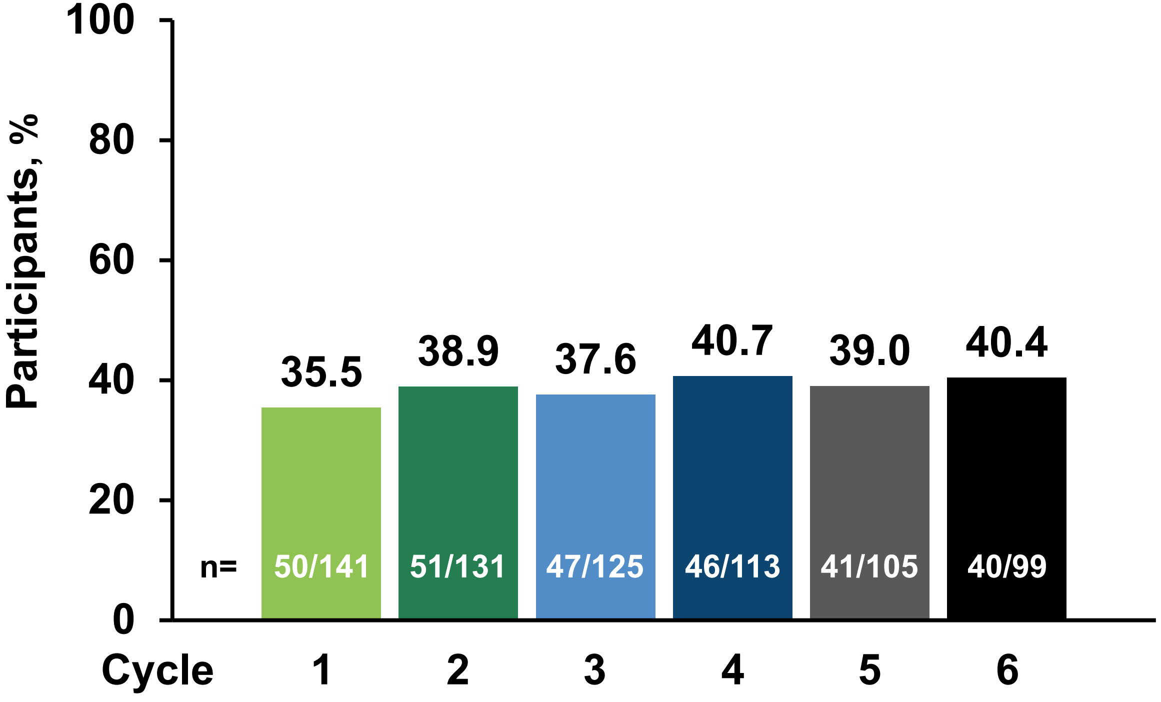
AChR-Ab+ Population

Minimal Symptom Expression and Clinically Meaningful Improvement in MG-ADL by Cycle

Clinically Meaningful Improvement (CMI)
Decrease of ≥2 in MG-ADL at Week 4



Minimal Symptom Expression (MSE)
MG-ADL total score of 0 or 1 at any time during a cycle

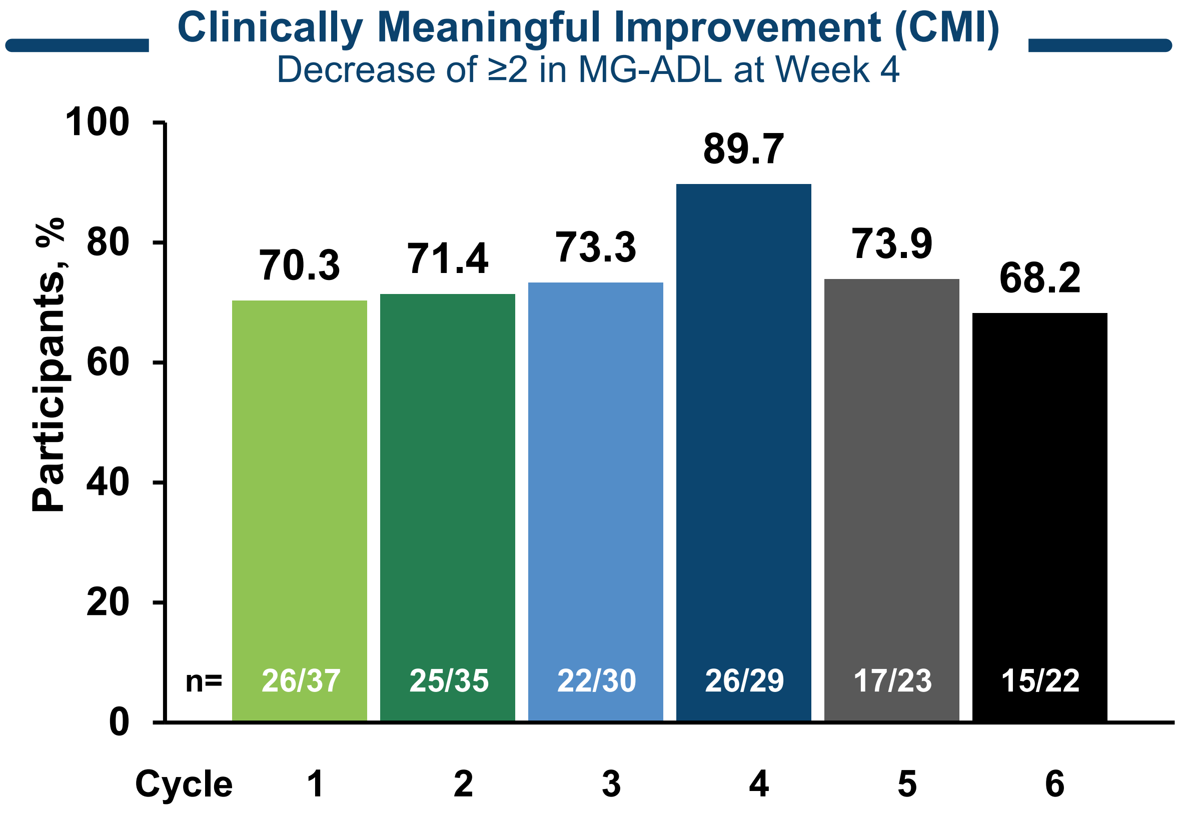


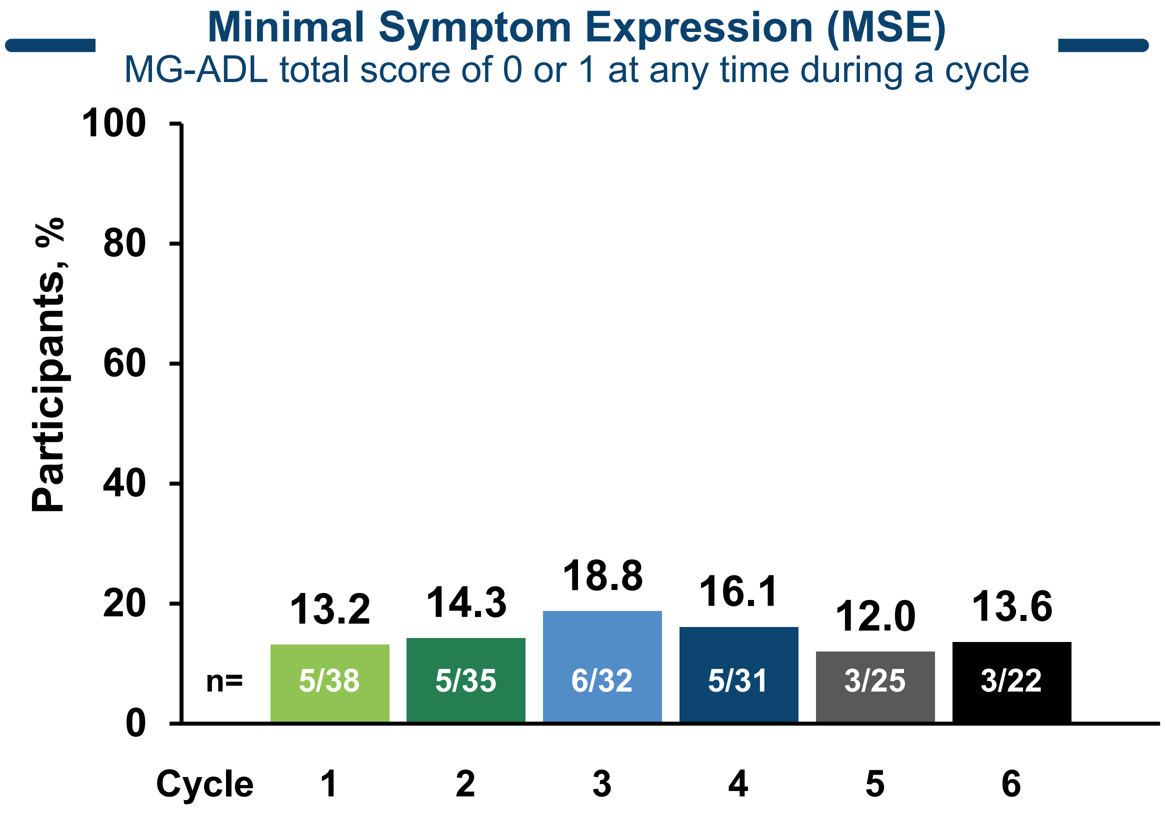
AChR-Ab+, acetylcholine receptor antibody seropositive; MG-ADL, Myasthenia Gravis Activities of Daily Living.

Minimal Symptom Expression and Clinically Meaningful Improvement Through Cycle 6

AChR-Ab- Population

Minimal Symptom Expression and Clinically Meaningful Improvement in MG-ADL by Cycle



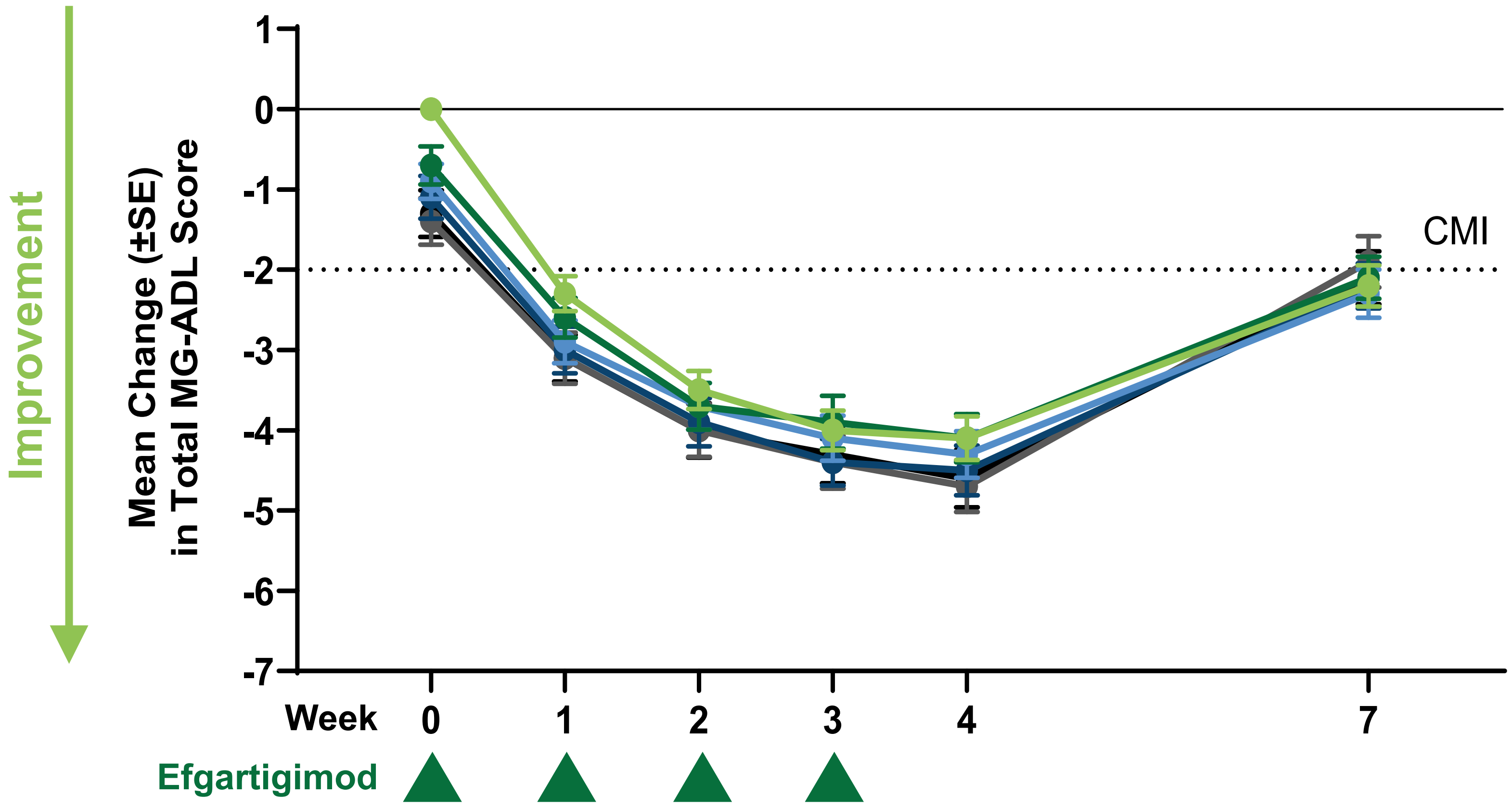


AChR-Ab-, acetylcholine receptor antibody seronegative; MG-ADL, Myasthenia Gravis Activities of Daily Living.

Change in MG-ADL Through Cycle 6

AChR-Ab+ Population

Mean Change in MG-ADL From Study Baseline[a]



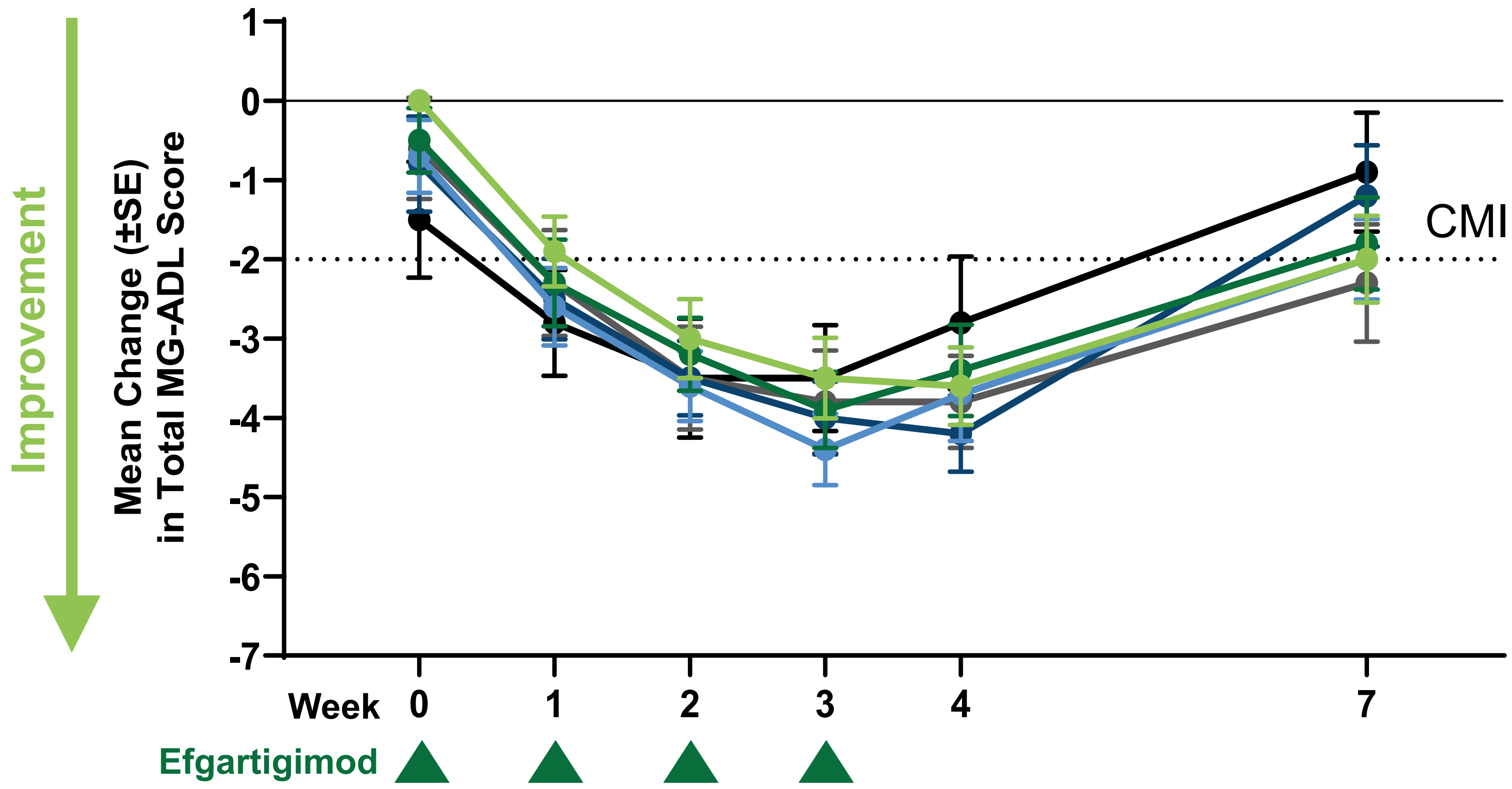
Cycle	n	Baseline[b] Mean (SE)	Week 4 Mean (SE)
1	141	7.6 (0.29)	-4.1 (0.27)
2	131	6.9 (0.31)	-4.1 (0.30)
3	125	6.8 (0.31)	-4.3 (0.29)
4	113	6.6 (0.33)	-4.5 (0.31)
5	106	6.4 (0.36)	-4.7 (0.32)
6	100	6.5 (0.37)	-4.6 (0.36)

AChR-Ab+, acetycholine receptor antibody seropositive; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living.
[a]Values for MG-ADL range from 0-24, with higher total scores indicating more impairment. [b]The mean (SE) change of MG-ADL baseline from Cycle 1 to Cycle 6 was -1.3 (0.29).

Change in MG-ADL Through Cycle 6

AChR-Ab- Population

Mean Change in MG-ADL From Study Baseline[a]



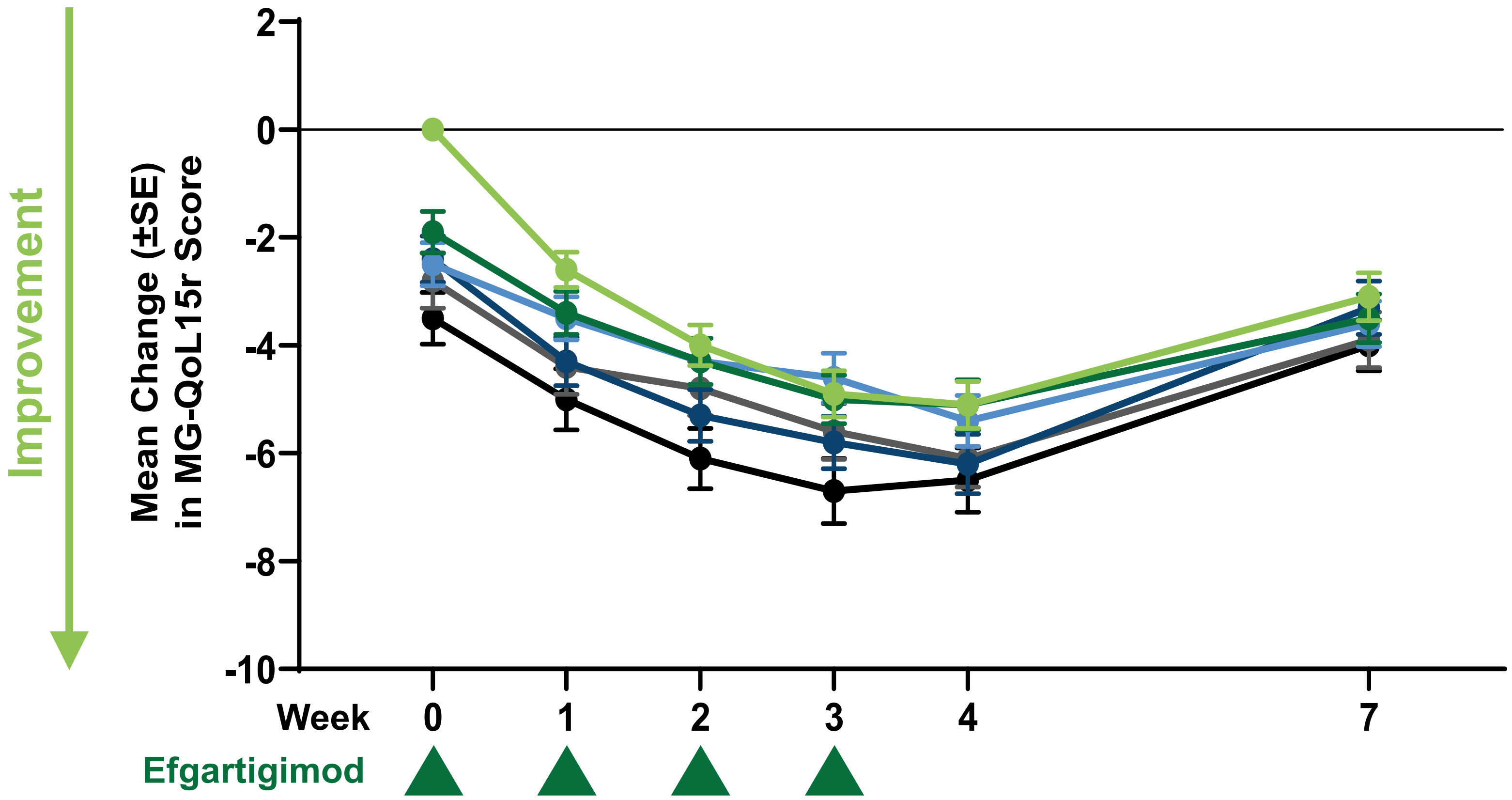
Cycle	n	Baseline[b] Mean (SE)	Week 4 Mean (SE)
1	38	8.9 (0.55)	-3.6 (0.49)
2	35	8.5 (0.52)	-3.4 (0.58)
3	32	8.2 (0.62)	-3.7 (0.59)
4	31	8.2 (0.64)	-4.2 (0.48)
5	25	8.4 (0.71)	-3.8 (0.58)
6	22	7.7 (0.86)	-2.8 (0.84)

AChR-Ab-, acetylcholine receptor antibody seronegative; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living; SE, standard error.
[a]Values for MG-ADL range from 0-24, with higher total scores indicating more impairment. [b]The mean (SE) change of MG-ADL baseline from Cycle 1 to Cycle 6 was -1.5 (0.73).

Change in MG-QoL15r Through Cycle 6

AChR-Ab+ Population

Mean Change in MG-QoL15r From Study Baseline[a]



Cycle	n	Baseline[b] Mean (SE)	Week 4 Mean (SE)
1	141	13.1 (0.57)	-5.1 (0.44)
2	131	11.3 (0.55)	-5.1 (0.47)
3	125	11.0 (0.59)	-5.4 (0.47)
4	113	11.0 (0.57)	-6.2 (0.55)
5	106	10.6 (0.58)	-6.1 (0.53)
6	100	10.1 (0.63)	-6.5 (0.60)

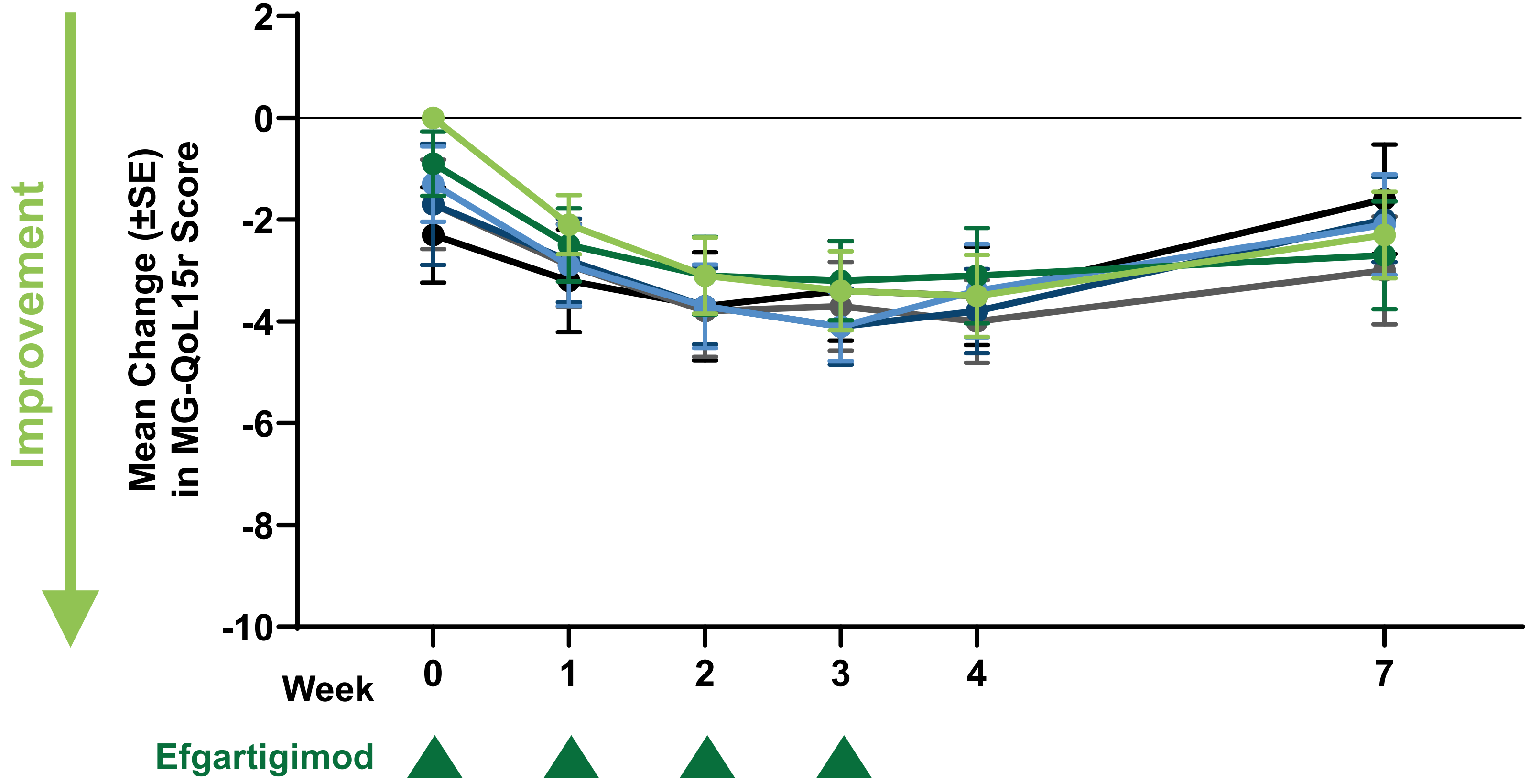
AChR-Ab+, acetycholine receptor antibody seropositive; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised.

[a]Values for MG-QoL15r range from 0-30, with higher total scores indicating greater severity of symptoms. [b]The mean (SE) change of MG-QoL15r baseline from Cycle 1 to Cycle 6 was -3.5 (0.48).

Change in MG-QoL15r Through Cycle 6

AChR-Ab- Population

Mean Change in MG-QoL15r From Study Baseline[a]



Cycle	n	Baseline[b] Mean (SE)	Week 4 Mean (SE)
1	38	15.5 (1.10)	-3.5 (0.81)
2	35	14.9 (1.20)	-3.1 (0.94)
3	32	13.8 (1.10)	-3.4 (0.92)
4	31	13.6 (1.26)	-3.8 (0.83)
5	25	14.2 (1.18)	-4.0 (0.81)
6	22	13.6 (1.32)	-3.5 (0.97)

AChR-Ab-, acetylcholine receptor antibody seronegative; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; SE, standard error.
[a]Values for MG-QoL15r range from 0-30, with higher total scores indicating greater severity of symptoms. [b]The mean (SE) change of MG-QoL15r baseline from Cycle 1 to Cycle 6 was -2.3 (0.94).

Summary

Efgartigimod PH20 SC was well tolerated, with no new safety signals observed compared with ADAPT-SC

All ISRs were mild or moderate and decreased with subsequent cycles, and no ISRs led to treatment discontinuation

Efgartigimod PH20 SC treatment resulted in consistent and repeatable improvements in MG-ADL and MG-QoL15r total scores over multiple cycles in AChR-Ab+ and AChR-Ab- participants, with improvements noted as early as the week after the first administration

The majority of AChR-Ab+ and AChR-Ab- participants experienced a CMI in MG-ADL, and a subset were able to achieve MSE; the proportions of participants achieving CMI or MSE were consistent across multiple cycles

The ADAPT-SC+ study is currently ongoing

AChR-Ab+, acetycholine receptor antibody seropositive; AChR-Ab-, acetycholine receptor antibody seronegative; CMI, clinically meaningful improvement; ISRs, injection site reactions; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; MSE, minimal symptom expression; SC, subcutaneous.