Long-Term Safety and Efficacy of Efgartigimod in Patients With gMG: Interim Results From ADAPT-SC+

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Encore presentation; presentation previously disclosed at the American Academy of Neurology Annual Meeting; April 22-27, 2023; Boston, MA, USA

The Japanese Society of Neurology (JSN)
COI Disclosure

Name of Lead Presenter: Akiyuki Uzawa

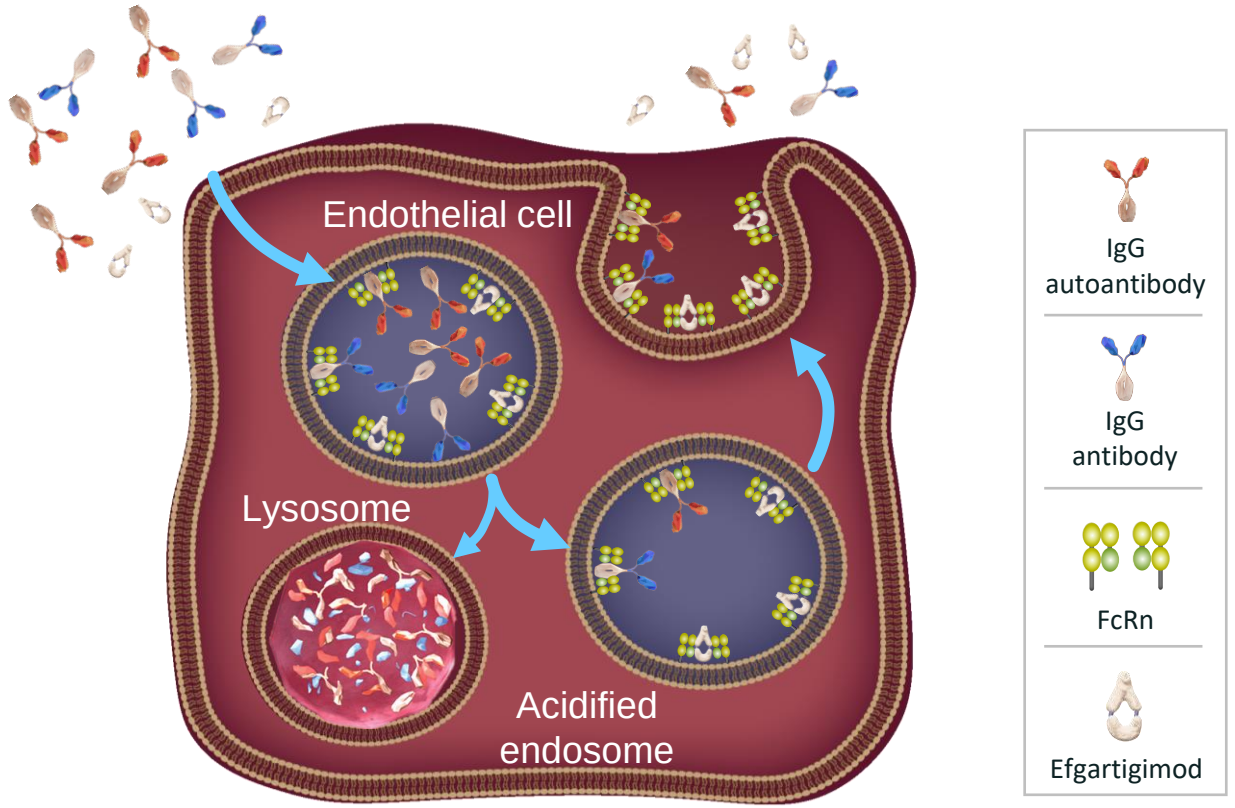
Companies, etc. in a relation of conflict of interest requiring disclosure in relation to the presentation:
(*Indicate "None" if not applicable.)

1) Advisor:	**None**
2) Stock ownership/capital gain:	**None**
3) Patent royalties:	**None**
4) Honoraria:	**None**
5) Writing fees:	**None**
6) Grants for commissioned/joint research:	**argenx, Alexion Pharmaceuticals, Inc.**
7) Scholarship grants:	**None**
8) Endowed chair:	**None**
9) Gifts or other forms of compensation:	**None**

Introduction

Efgartigimod Mechanism of Action: Blocking FcRn

- Efgartigimod is a human IgG1 Fc fragment engineered for increased affinity to FcRn, which prevents recycling of IgG without impacting its production[1-5]
  - Targeted reduction of all IgG subclasses
  - No impact on IgM, IgA, IgE, and IgD
  - No reduction in albumin levels
  - No increase in cholesterol
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[6]
- 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



Fc, crystallizable fragment; FcRn, neonatal Fc receptor; Ig, immunoglobulin; IV, intravenous; PD, pharmacodynamic; PH20, recombinant human hyaluronidase; PK, pharmacokinetic; SC, subcutaneous.

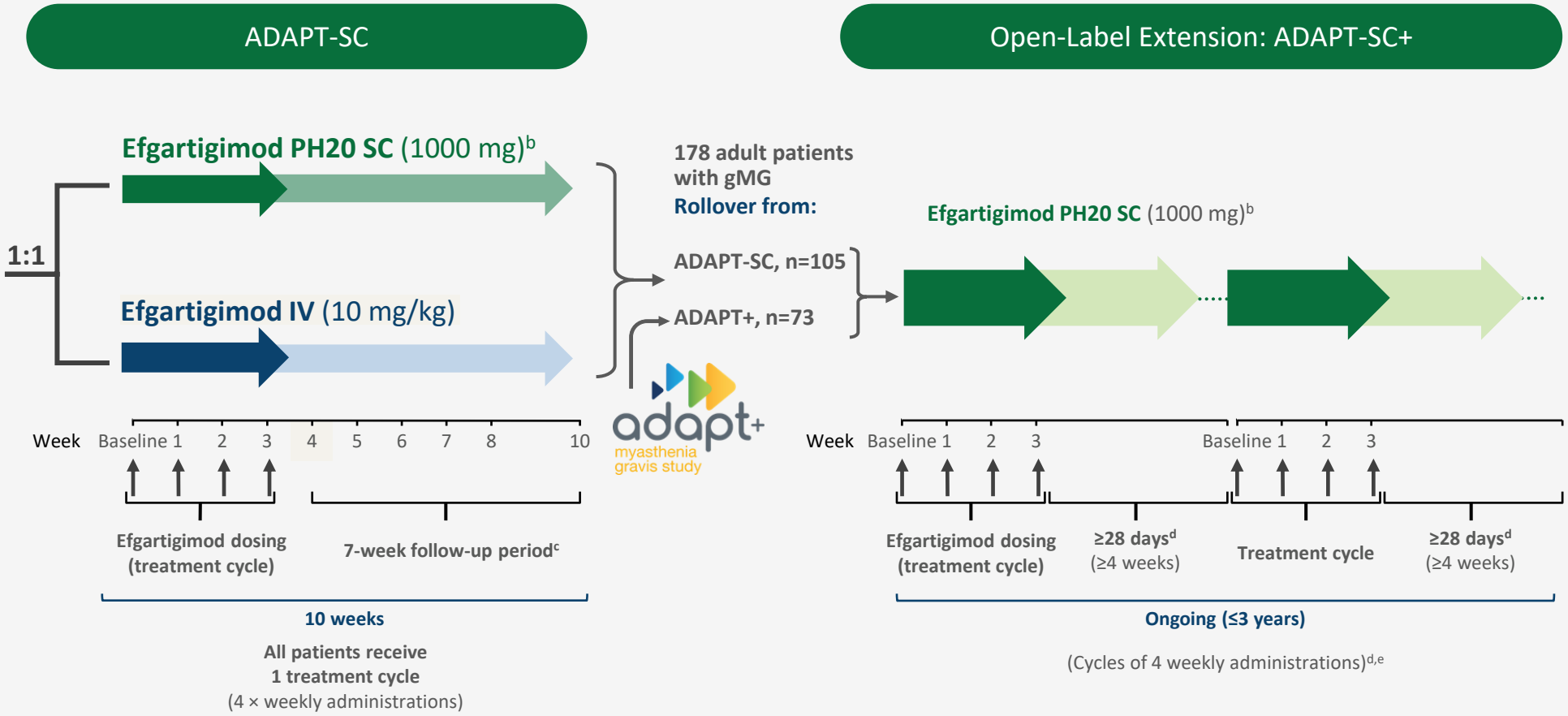
1. Ulrichts P, et al. *J Clin Invest.* 2018;128(10):4372-4386. **2.** Vaccaro C, et al. *Nat Biotech.* 2005;23(10):1283-1288. **3.** Howard JF, Jr, et al. *Lancet Neurol*. 2021;20(7):526-536. **4.** Nixon AE, et al. *Front Immunol.* 2015;6:176. **5.** Ward ES, et al. *Front Immunol.* 2022;13:892534. **6.** Locke KW, et al. *Drug Deliv.* 2019;26(1):98-106.

Methods

110 adult patients with gMG

Inclusion criteria:

- MGFA class II-IV
- MG-ADL score ≥5
- On ≥1 stable gMG treatment[a]



[a]AChE inhibitors, steroids, and/or NSIST. [b]Coformulated with 2000 U/mL rHuPH20. [c]Patients could not receive treatment in the 7-week follow-up period. [d]≥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. [e]Patients who are not in need of re-treatment at study entry will instead start with an intertreatment period.
AChE, acetylcholinesterase; gMG, generalized myasthenia gravis; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; PH20, recombinant human hyaluronidase; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

Patient Demographics and Baseline Characteristics (Safety Population)

- 178 participants rolled over from ADAPT-SC (n=105) and ADAPT+ (n=73)
- 134 AChR-Ab+ and 30 AChR-Ab- patients received ≥1 dose of efgartigimod PH20 SC in ADAPT-SC+ through March 2022, with a median (range) follow-up of 182 (24-311) days

	Efgartigimod PH20 SC (n=164)
Age, y, mean (SD)	50.7 (15.4)
Female, n (%)	106 (64.6)
Weight, kg, median (Q1-Q3)	77 (63.5-90.0)
AChR-Ab+, n (%)	134 (81.7)
Total MG-ADL score, mean (SD)	7.9 (3.5)
Total MG-QoL15r score, mean (SD)	13.7 (6.6)
MG therapy during the first year, n (%)	
Any steroid	112 (68.3)
Any NSIST	84 (51.2)
Any AChEI	140 (85.4)
Steroid + NSIST	62 (37.8)
AChEI only	30 (18.3)

AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor antibody; 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; PH20, recombinant human hyaluronidase; Q1/3; quartile 1/3; SC, subcutaneous; SD, standard deviation.

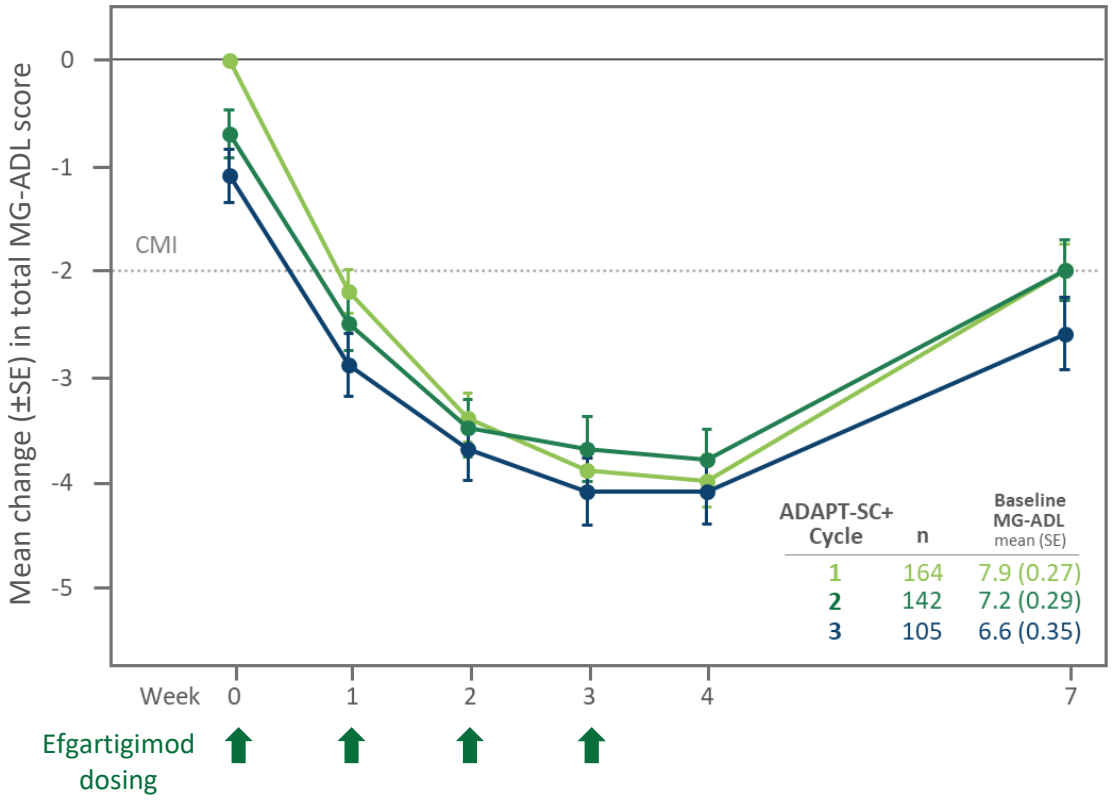
Summary of Adverse Events (Safety Population)

	Efgartigimod PH20 SC (N=164; PYFU=72.1)		
	IR[a]	m	n (%)
Any AE, n (%)	11.0	790	125 (76.2)
Any AE grade ≥3, n (%)	0.6	41	19 (11.6)
Any SAE, n (%)	0.3	22	17 (10.4)
Any injection site reaction,[b] n (%)	4.3	307	69 (42.1)
Any infection, n (%)	1.1	76	48 (29.3)
Fatal event[c]	<0.1	3	2 (1.2)
Discontinued study treatment owing to AEs,[d] n (%)	0.1	4	3 (1.8)
Most commonly observed AEs,[e] n (%)			
Injection site erythema	2.1	150	42 (25.6)
Headache	0.8	58	25 (15.2)
COVID-19	0.3	20	19 (11.6)
Injection site pain	0.4	28	15 (9.1)
Injection site pruritus	0.4	30	15 (9.1)
Injection site bruising	0.2	18	13 (7.9)
Diarrhea	0.3	20	12 (7.3)
Injection site rash	0.2	17	11 (6.7)
Nasopharyngitis	0.2	12	10 (6.1)
Injection site swelling	0.3	21	9 (5.5)

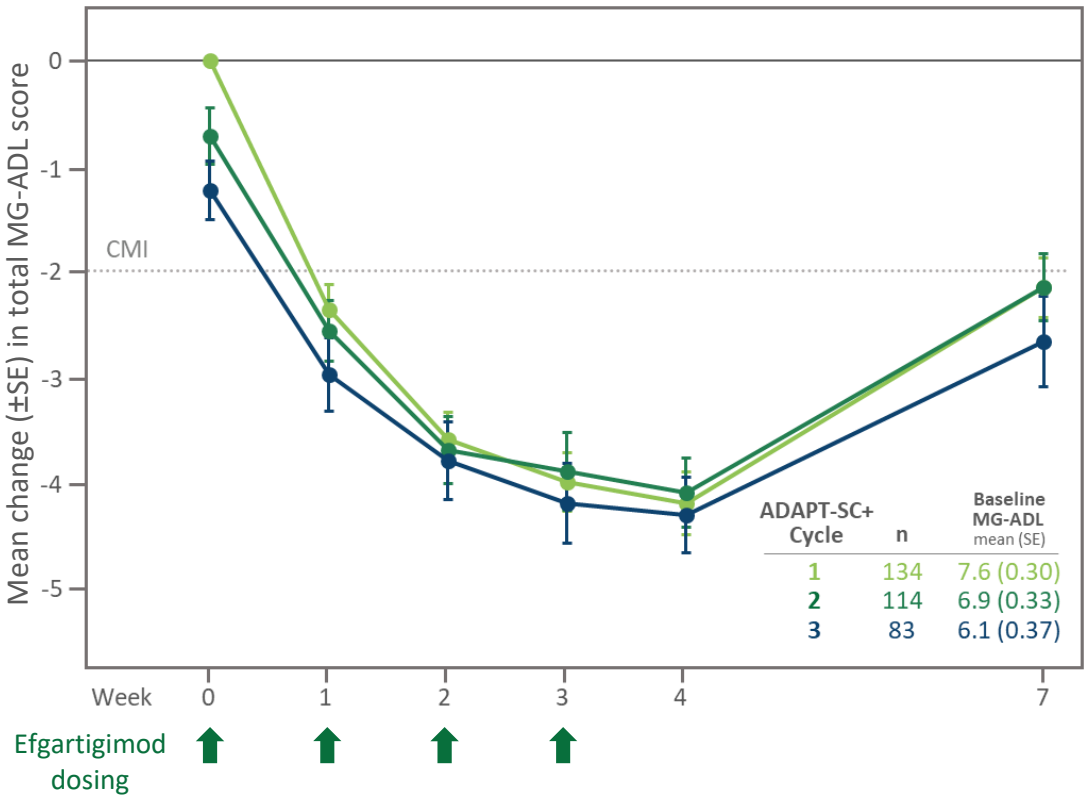
[a]IR was calculated as number of events per total PYFU. [b]ISR events decreased over subsequent cycles; cycle 1 (n=56, 34.1%), cycle 2 (n=24, 16.9%), cycle 3 (n=14, 13.3%), and cycle 4 (n=8, 11.8%). [c]Fatal events (metastatic renal cell cancer and COVID-19) were not related to efgartigimod PH20 SC treatment, as determined by investigators. [d]Treatment discontinuation due to metastatic renal cell cancer (cycle 1, death), COVID-19 (cycle 3, death), and MG crisis (cycle 1).
[e]Most frequent AEs occurring in >5% of patients receiving efgartigimod PH20 SC.
AE, adverse event; COVID-19, coronavirus disease 2019; IR, incidence rate (or event rate) per patient years of follow-up; ISR, injection site reaction; m, number of events; MG, myasthenia gravis; PH20, recombinant human hyaluronidase; PYFU, patient-year follow-up (sum of follow-up time of all participants expressed in years in the applicable period); SAE, serious adverse event; SC, subcutaneous.

Mean Change in MG-ADL From Study Baseline

Overall Population

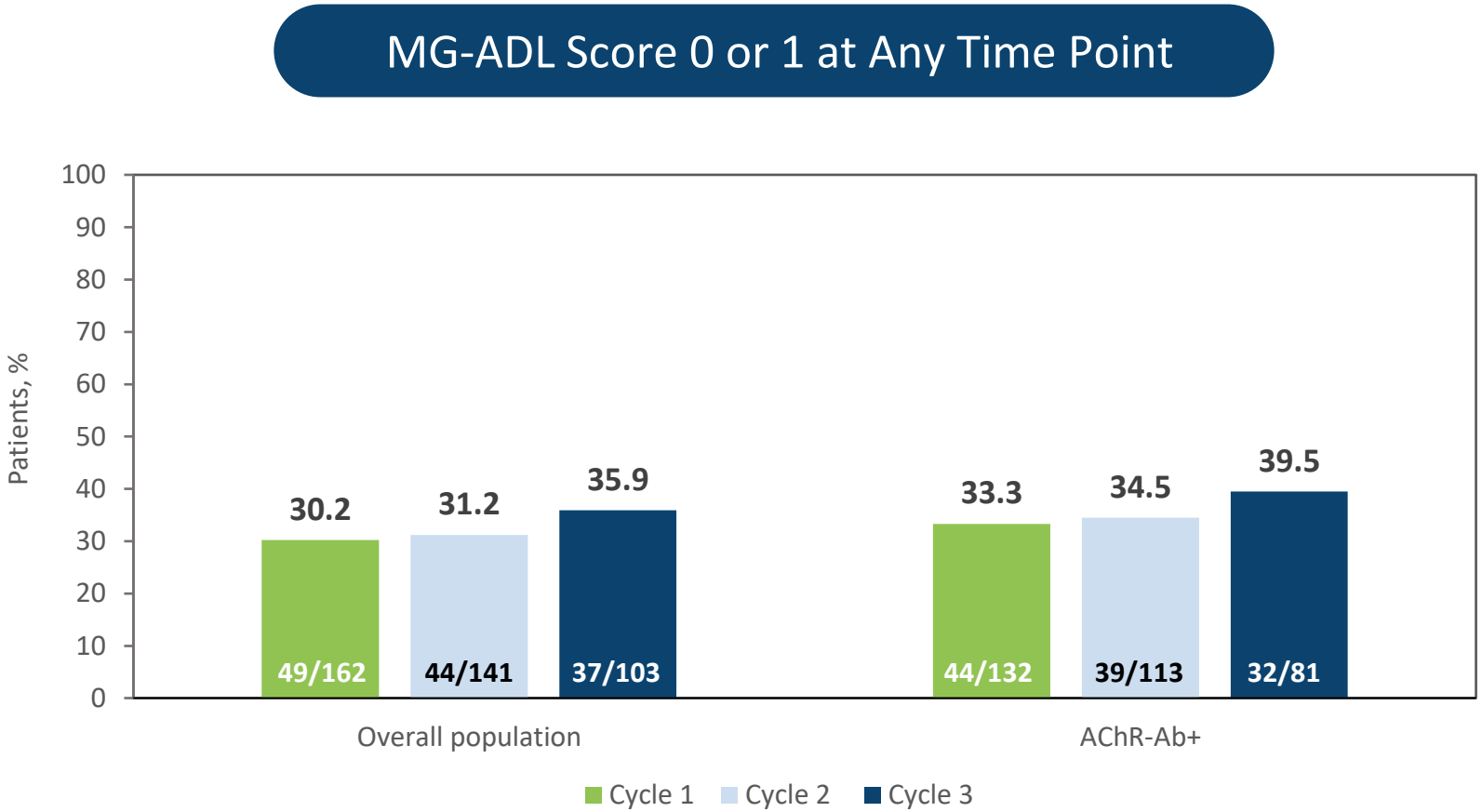


AChR-Ab+ Population



AChR-Ab, acetylcholine receptor antibody; CMI, clinically meaningful improvement; MG-ADL, Myasthenia Gravis Activities of Daily Living; SE, standard error.

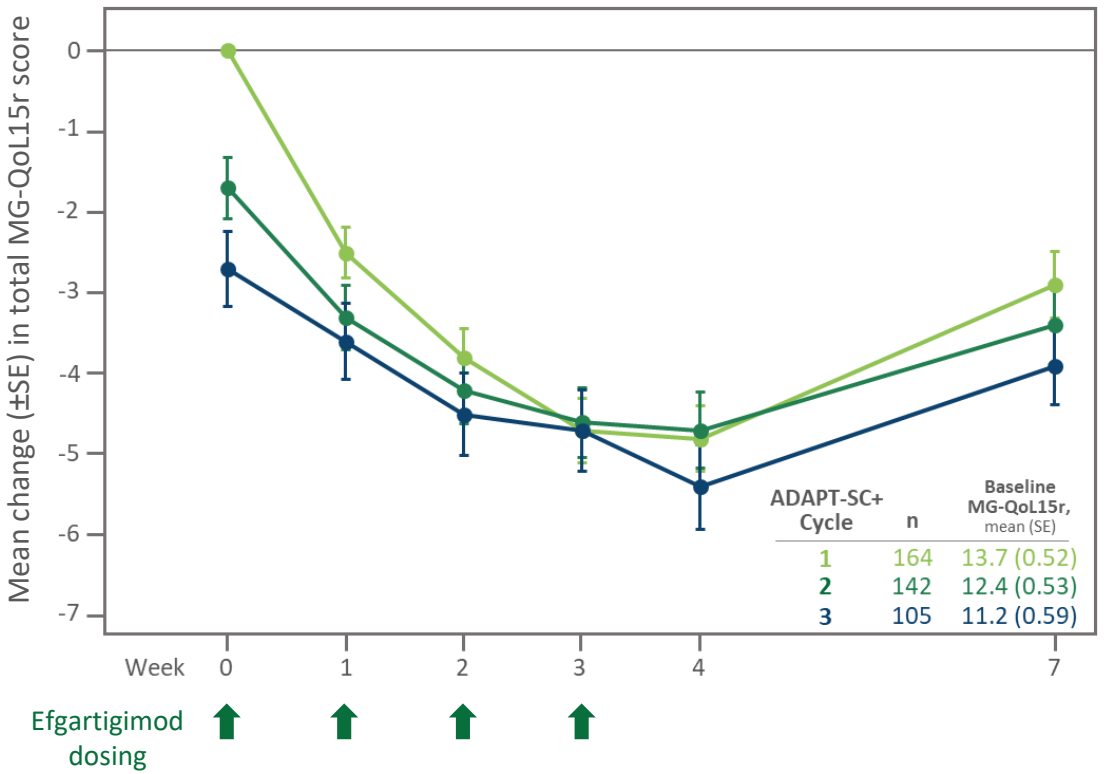
Minimal Symptom Expression by Cycle



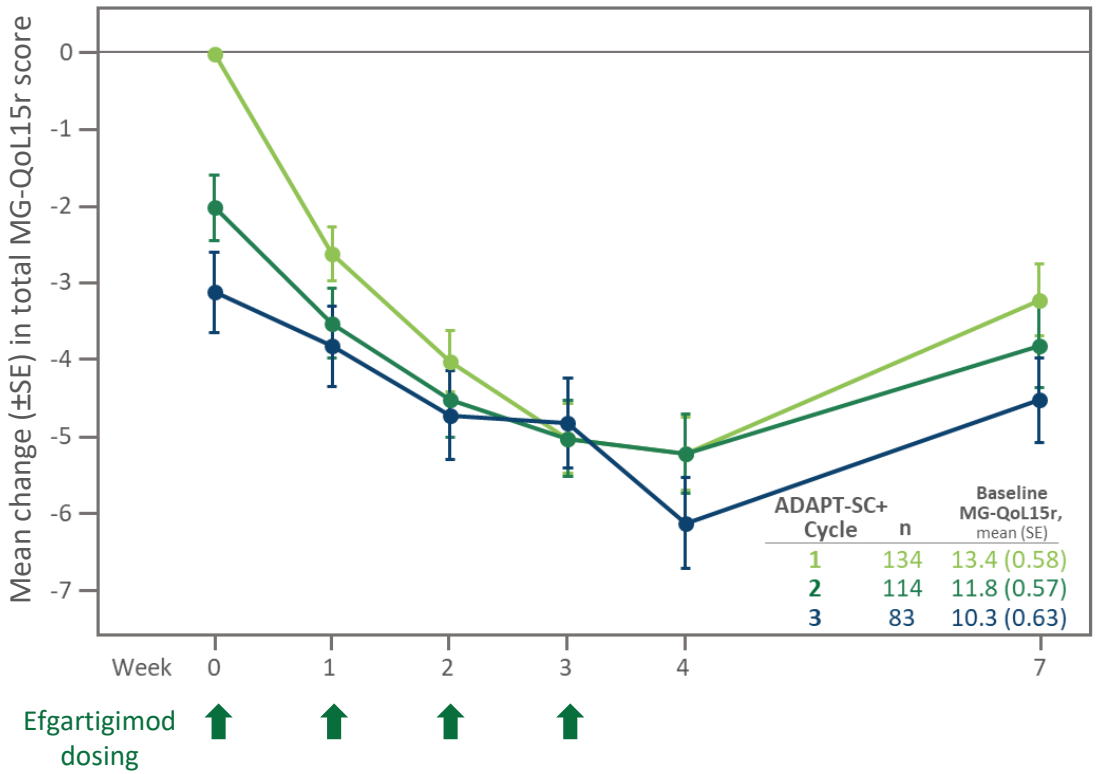
AChR-Ab, acetylcholine receptor antibody; MG-ADL, Myasthenia Gravis Activities of Daily Living.

Mean Change in MG-QoL15r From Study Baseline

Overall Population



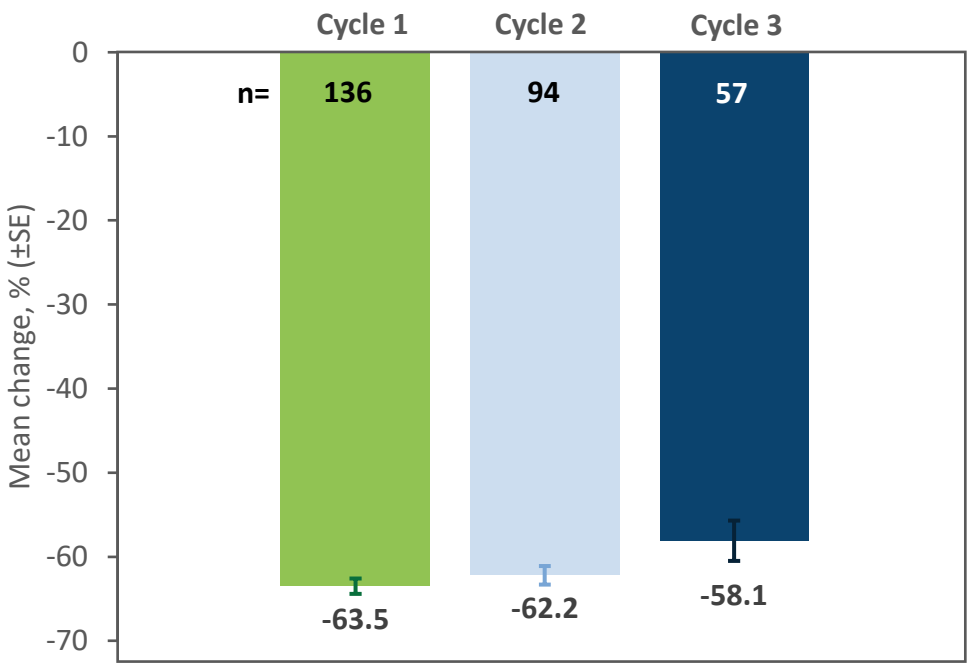
AChR-Ab+ Population



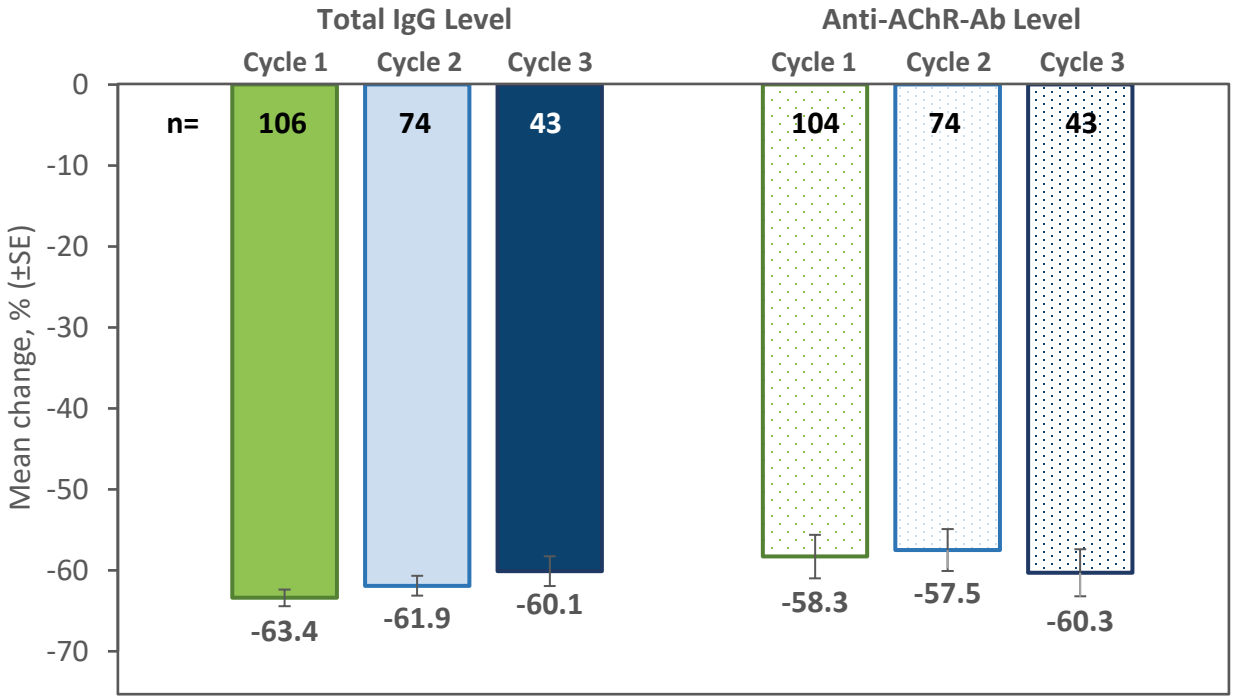
AChR-Ab, acetylcholine receptor antibody; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; SE, standard error.

Mean Percent Change in Total IgG and Anti–AChR-Ab Levels at Week 4 From Study Baseline

Mean Percent Change in Total IgG (Overall Population)



Mean Percent Change in Total IgG and Anti-AChR-Ab Levels (AChR-Ab+ Population)



AChR-Ab, acetylcholine receptor antibody; Ig, immunoglobulin; SE, standard error.

Summary

Efgartigimod PH20 SC was well tolerated, with no new safety signals observed compared to 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 reductions in total IgG and anti–AChR-Ab levels. Improvements in MG-ADL and MG-QoL15r total scores occurred as early as the first administration and were achieved over multiple cycles in AChR-Ab+ and overall populations, including AChR-Ab- participants

The ADAPT-SC+ study is currently ongoing

AChR-Ab, acetylcholine receptor antibody; Ig, immunoglobulin; ISR, injection site reaction; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QoL15r, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; PH20, recombinant human hyaluronidase; SC, subcutaneous.

Acknowledgments

The authors gratefully acknowledge the ADAPT SC and ADAPT SC+ trial participants and investigators.

The ADAPT-SC and ADAPT-SC+ trials were funded by argenx.

Medical writing and editorial support were funded by argenx and were provided by PRECISION Value & Health for the original presentation and by ProScribe – Envision Pharma Group for this encore presentation.