Interim Analyses of Efgartigimod PH20 SC in Participants With gMG in the ADAPT-SC+ Study

Masanori Takahashi,[1] James F. Howard Jr,[2] Yuebing Li,[3] Tuan Vu,[4] Denis Korobko,[5] Sophie Steeland,[6] Benjamin Van Hoorick,[6] Jana Podhorna,[6] Moana Hodari,[6] Kimiaki Utsugisawa,[7] Francesco Sacca,[8] Jan L. De Bleecker,[9] Renato Mantegazza,[10] and the ADAPT-SC+ Study Group

[1]Department of Neurology, Osaka University Graduate School of Medicine, Suita, Japan; [2]The University of North Carolina, Chapel Hill, North Carolina, USA; [3]Cleveland Clinic, Cleveland, Ohio, USA; [4]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, Florida, USA; [5]State Budgetary Healthcare Institution of Novosibirsk Region "State Novosibirsk Regional Clinical Hospital," Novosibirsk, Russia; [6]argenx, Ghent, Belgium; [7]Department of Neurology, Hanamaki General Hospital, Hanamaki, Japan; [8]NRSO Department, Federico II University of Naples, Naples, Italy; [9]Ghent University Hospital, Ghent, Belgium; [10]Department of Neuroimmunology and Neuromuscular Diseases, Fondazione Istituto Neurologico Carlo Besta, Milan, Italy

(Form 4-E)

If there is a state of conflict of interest requiring disclosure

The Japanese Society of Neurology (JSN)
COI Disclosure

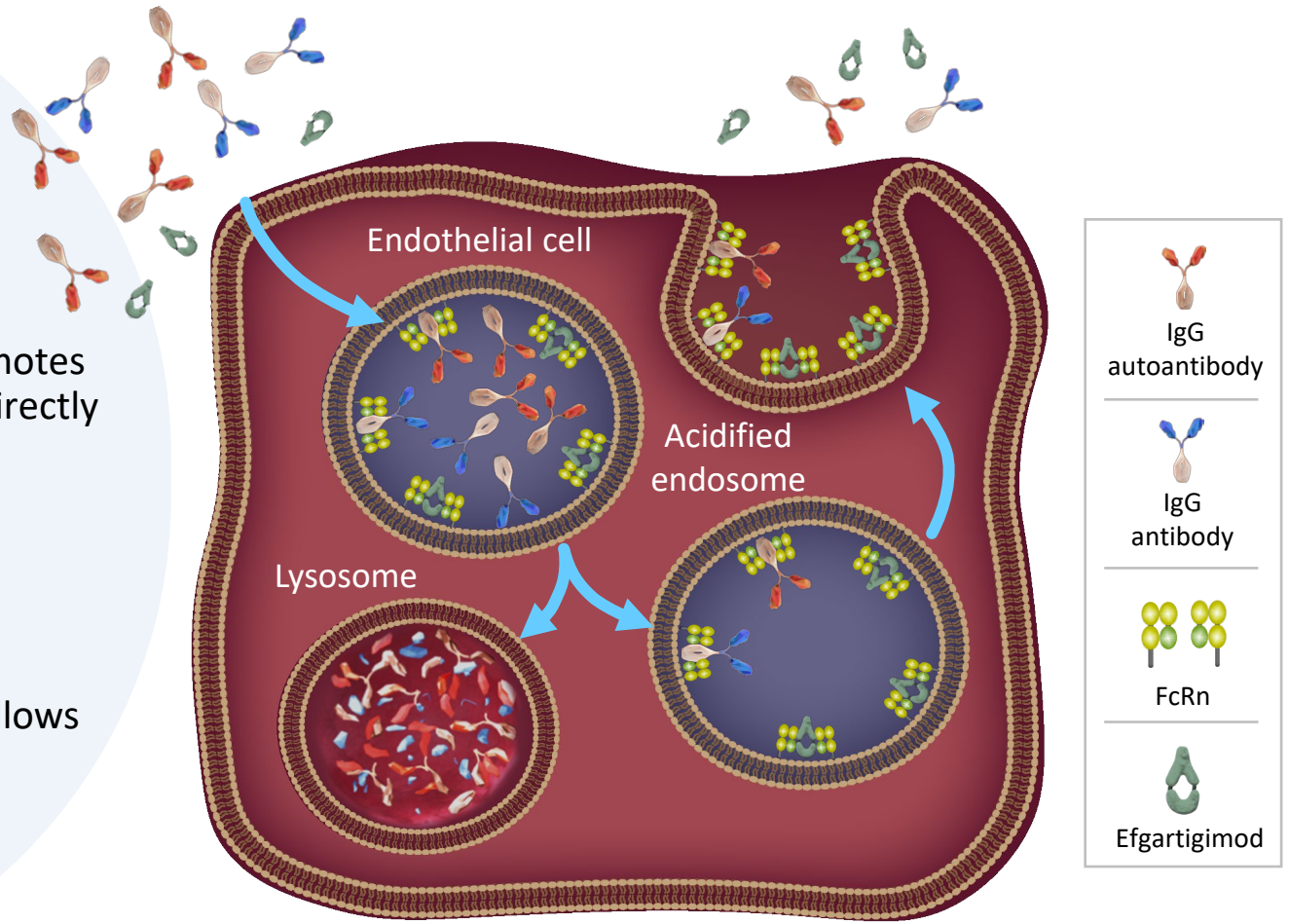
Name of Lead Presenter: Masanori Takahashi

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:	**Alexion Pharma G.K., argenx Japan K.K., and UCB Japan**
5) Writing fees:	**None**
6) Grants for commissioned/joint research:	**None**
7) Scholarship grants:	**None**
8) Endowed chair:	**None**
9) Gifts or other forms of compensation:	**None**

Efgartigimod Effectively Blocks FcRn and Reduces IgG Levels

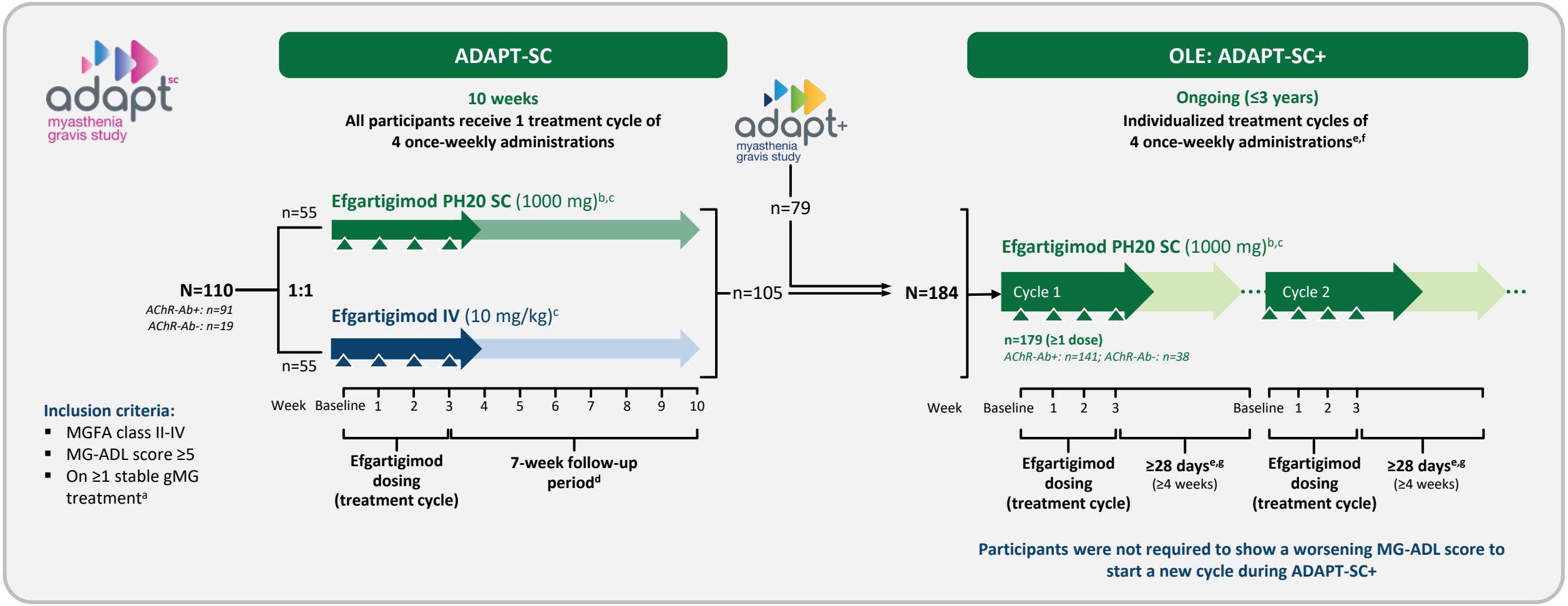
- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
  - FcRn is additionally involved in other cellular processes such as IgG-dependent phagocytosis and antigen presentation[2]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered to have 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



AChEI, acetylcholinesterase inhibitor; 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; NSIST, nonsteroidal immunosuppressive therapy; 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, y, mean (SD)	50.7 (15.5)	51.0 (15.9)	49.7 (14.2)
Sex, female, n (%)	119 (66.5)	90 (63.8)	29 (76.3)
Race, Japanese, n (%)	16 (8.9)	11 (7.8)	5 (13.2)
Weight, kg, median (Q1-Q3)	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)
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; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; NSIST, nonsteroidal immunosuppressive therapy; SC, subcutaneous.

[a]Of the 184 participants enrolled, 179 received ≥1 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)

AE, adverse event; 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 10.3% (n=7/68) in Cycle 9.

[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.

Summary of AEs

Japanese Subpopulation

	Efgartigimod PH20 SC *(n=16; PYFU=18.2)*	
	Event Rate[a]	n (%)
Any AE	5.6	12 (75.0)
Any AE grade ≥3	0.2	3 (18.8)
Any SAE	0.2	3 (18.8)
Any ISR	1.2	8 (50.0)
Any infection	0.5	7 (43.8)
Fatal event	-	0 (0.0)
Discontinued study treatment owing to AEs	-	0 (0.0)
Most commonly observed AEs[b]		
Injection site pain	0.4	4 (25.0)
Anemia	0.2	3 (18.8)
Vertigo	0.2	3 (18.8)
Injection site erythema	0.3	3 (18.8)
Injection site rash	0.3	3 (18.8)
Headache	0.2	3 (18.8)
MG	0.2	3 (18.8)

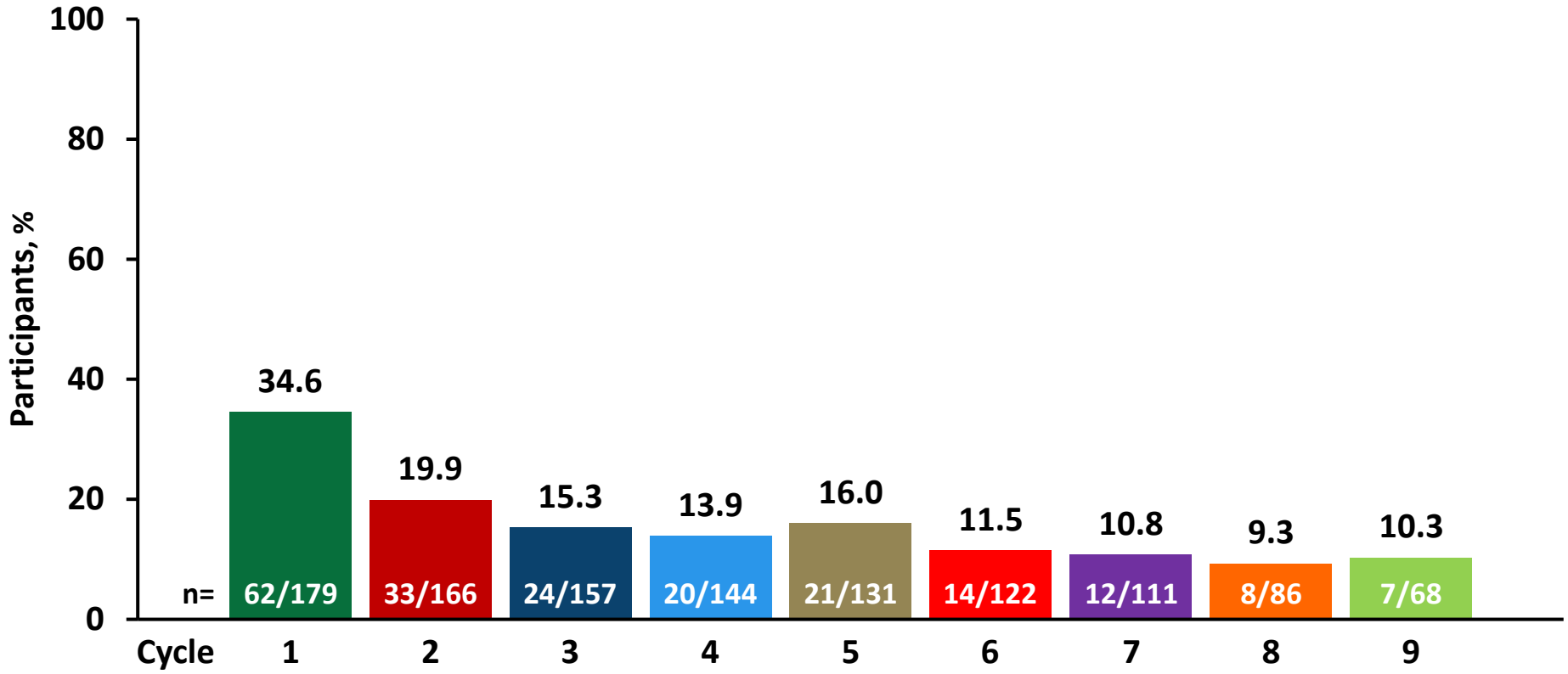
AE, adverse event; ISR, injection site reaction; MG, myasthenia gravis; PYFU, participant-years of follow-up; SAE, serious adverse event; SC, subcutaneous.

[a]Event rate was calculated as number of events per total PYFU. [b]Most frequent AEs occurring in >15% of patients receiving efgartigimod PH20 SC.

Incidence of ISRs Through Cycle 9

Overall Population

Percentage of Participants Experiencing ISRs by Cycle



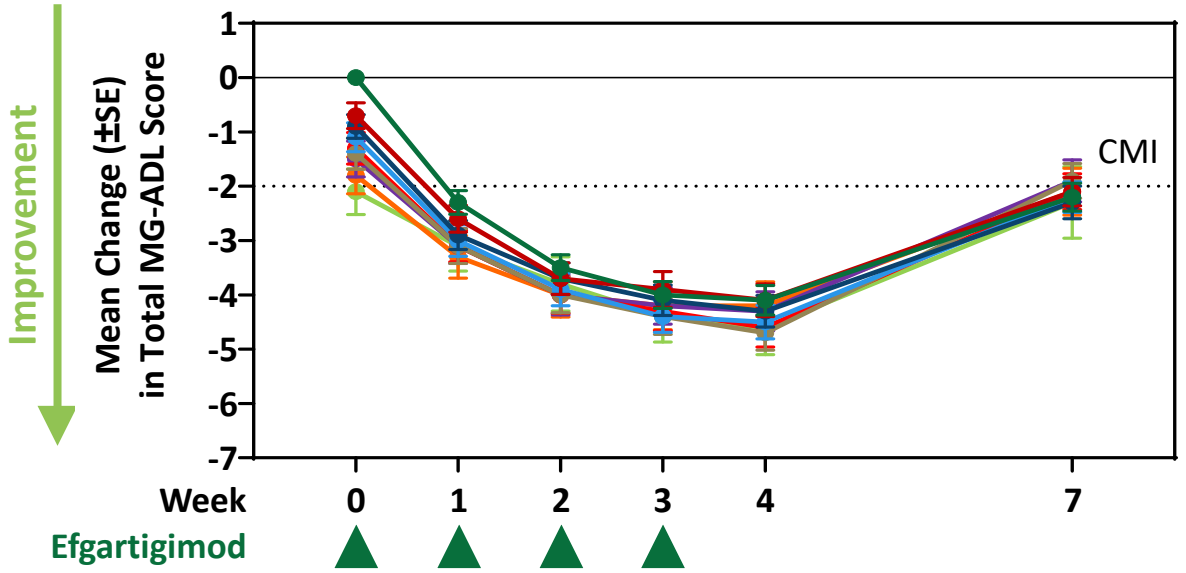
ISR, injection site reaction.

Change in MG-ADL Through Cycle 9

AChR-Ab+ Population

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

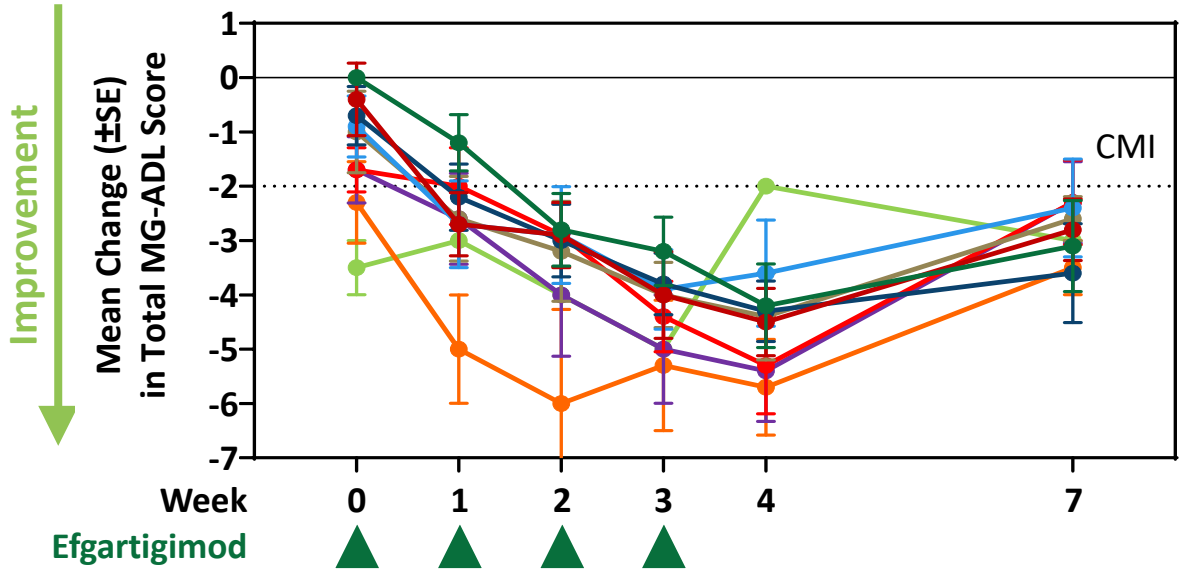
Overall AChR-Ab+ Population



Cycle	n	Baseline[b] mean (SE)	Cycle	n	Baseline[b] mean (SE)
1	141	7.6 (0.29)	6	100	6.5 (0.37)
2	131	6.9 (0.31)	7	90	6.1 (0.38)
3	125	6.8 (0.31)	8	67	5.7 (0.42)
4	113	6.6 (0.33)	9	52	5.2 (0.52)
5	106	6.4 (0.36)			

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

Japanese AChR-Ab+ Subpopulation



Cycle	n	Baseline mean (SE)	Cycle	n	Baseline mean (SE)
1	11	8.6 (0.93)	6	9	7.3 (1.15)
2	10	8.6 (1.11)	7	7	6.7 (1.30)
3	10	8.3 (1.01)	8	4	7.0 (1.08)
4	9	8.1 (1.14)	9	2	6.5 (1.50)
5	9	8.0 (1.33)			

AChR-Ab, acetycholine receptor antibody; 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 9 was -2.1 (0.42).

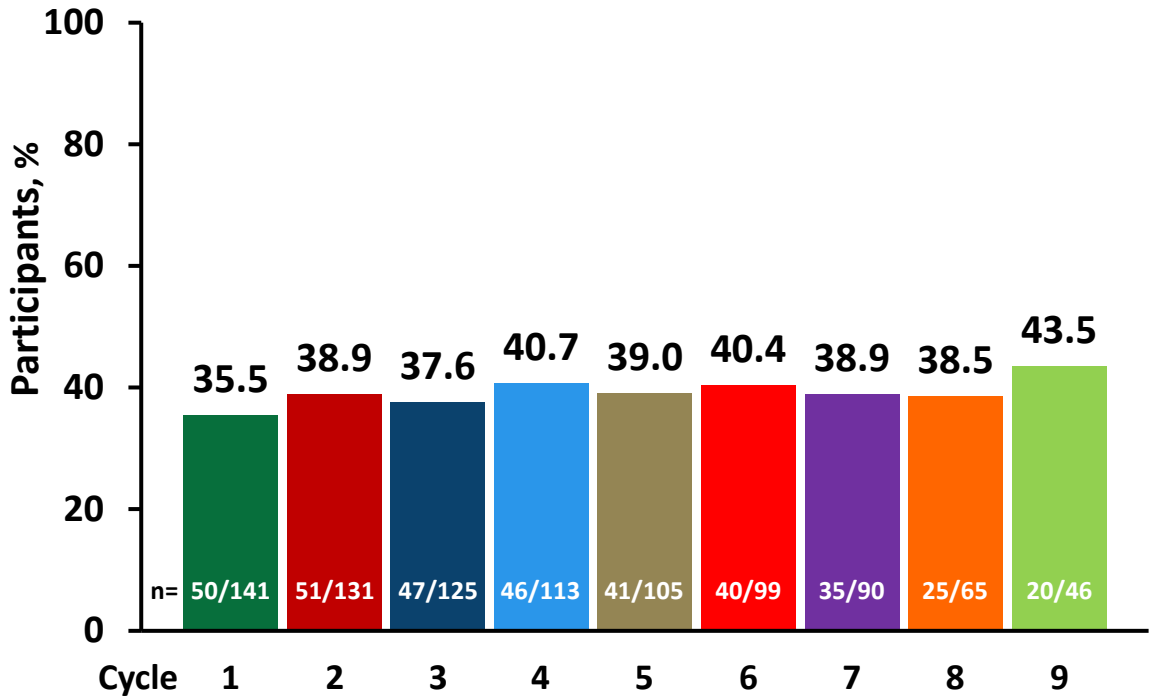
Minimal Symptom Expression and Clinically Meaningful Improvement Through Cycle 9

AChR-Ab+ Population

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

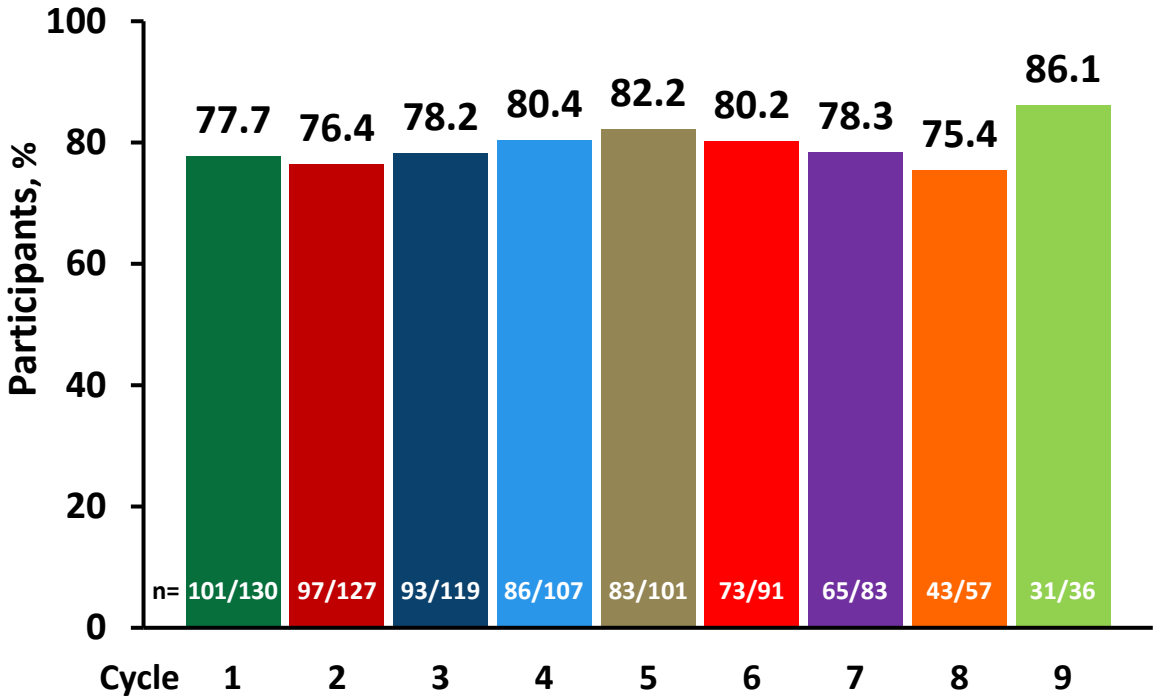
Minimal Symptom Expression (MSE)

MG-ADL total score of 0 or 1 at any time during a cycle



Clinically Meaningful Improvement (CMI)

Decrease of ≥2 in MG-ADL at Week 4



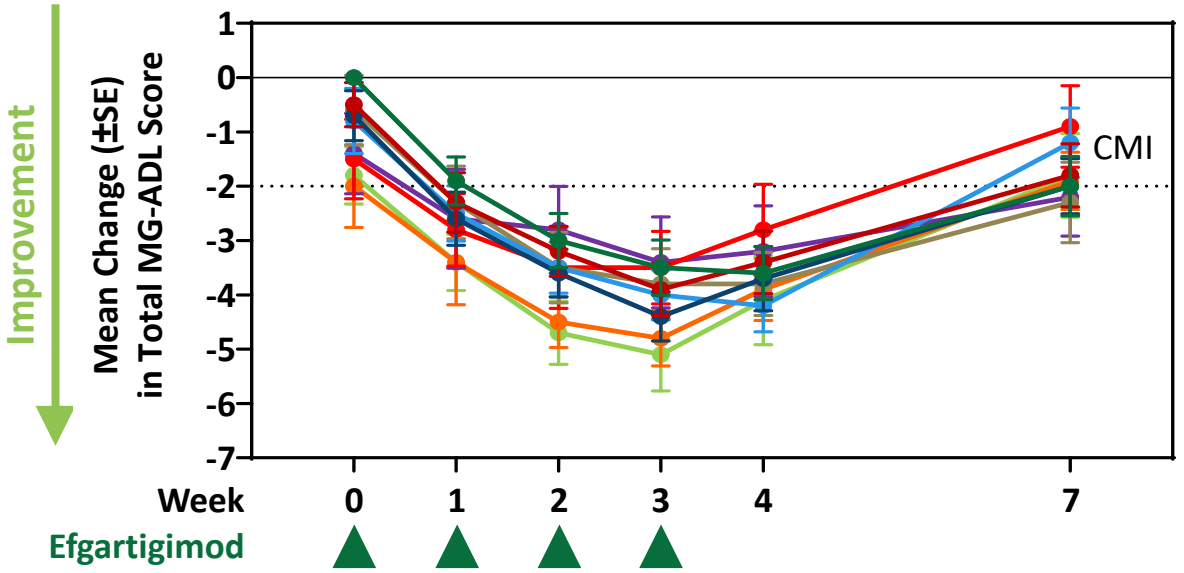
AChR-Ab, acetylcholine receptor antibody; MG-ADL, Myasthenia Gravis Activities of Daily Living.

Change in MG-ADL Through Cycle 9

AChR-Ab- Population

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

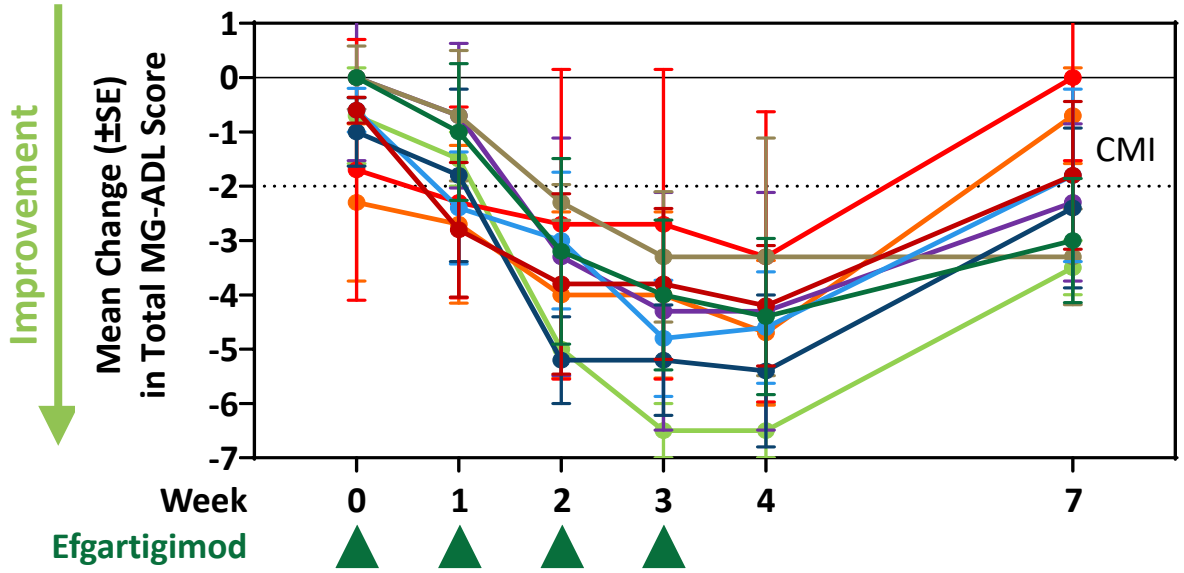
Overall AChR-Ab- Population



Cycle	n	Baseline[b] mean (SE)	Cycle	n	Baseline[b] mean (SE)
1	38	8.9 (0.55)	6	22	7.7 (0.86)
2	35	8.5 (0.52)	7	21	7.8 (0.76)
3	32	8.2 (0.62)	8	19	7.1 (0.82)
4	31	8.2 (0.64)	9	16	8.3 (1.03)
5	25	8.4 (0.71)			

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

Japanese AChR-Ab- Subpopulation



Cycle	n	Baseline mean (SE)	Cycle	n	Baseline mean (SE)
1	5	9.8 (0.66)	6	3	8.0 (2.08)
2	5	9.2 (0.49)	7	3	9.7 (1.20)
3	5	8.8 (0.37)	8	3	7.3 (1.20)
4	5	9.2 (0.58)	9	3	9.0 (0.58)
5	3	9.7 (0.67)			

AChR-Ab, acetylcholine receptor antibody; 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 9 was -1.8 (0.53).

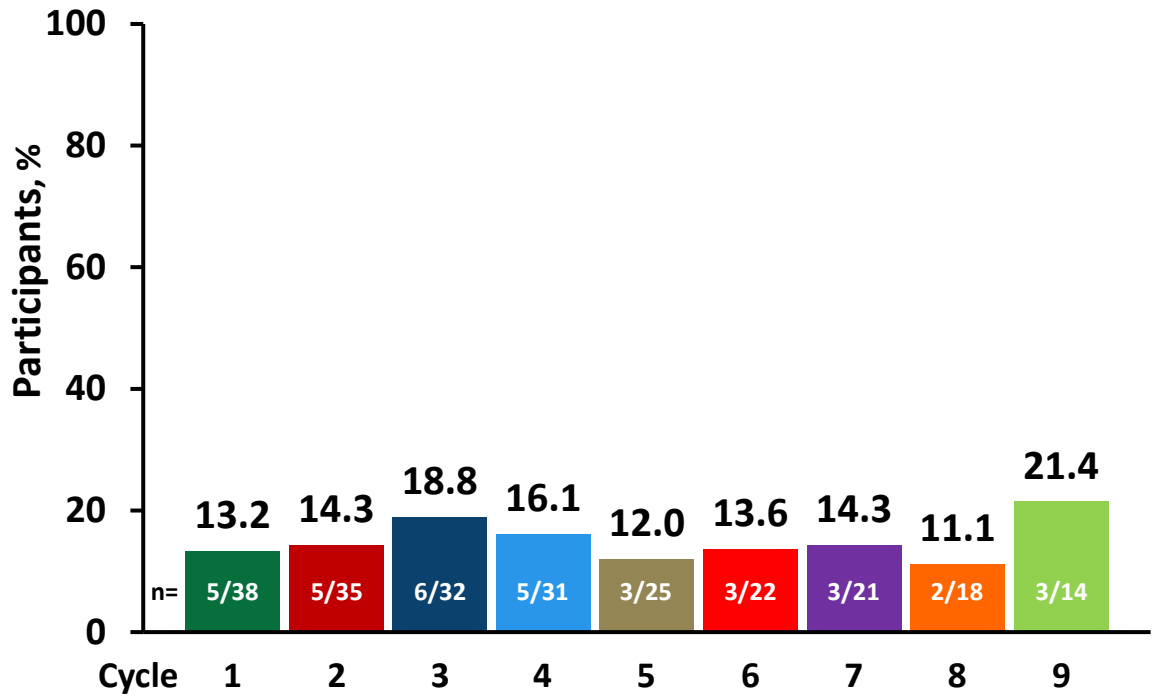
Minimal Symptom Expression and Clinically Meaningful Improvement Through Cycle 9

AChR-Ab- Population

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

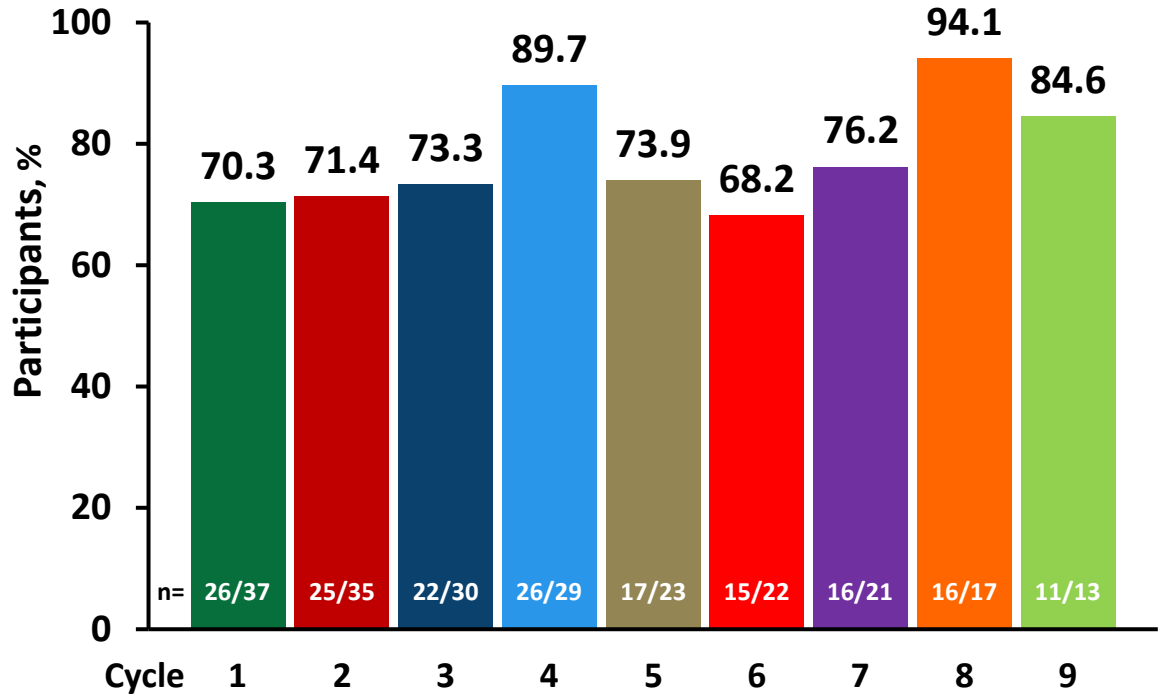
Minimal Symptom Expression (MSE)

MG-ADL total score of 0 or 1 at any time during a cycle



Clinically Meaningful Improvement (CMI)

Decrease of ≥2 in MG-ADL at Week 4



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

Summary

Efgartigimod PH20 SC was well tolerated in the overall and Japanese populations, 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

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

Efgartigimod PH20 SC treatment resulted in consistent and repeatable improvements in MG-ADL total score over multiple cycles in the Japanese subpopulation in AChR-Ab+ and AChR-Ab-participants, mirroring trends observed in the overall population

The ADAPT-SC+ study is currently ongoing

AChR-Ab, acetycholine receptor antibody; CMI, clinically meaningful improvement; ISR, injection site reaction; MG-ADL, Myasthenia Gravis Activities of Daily Living; MSE, minimal symptom expression; SC, subcutaneous.