005

Long-Term Safety and Efficacy of Subcutaneous Efgartigimod PH20 in Adult Participants With Generalized Myasthenia Gravis: Interim Results of the ADAPT-SC+ Study

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

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

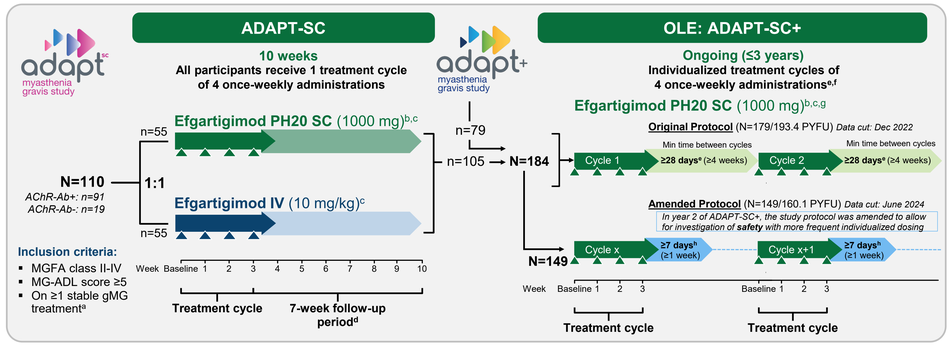
INTRODUCTION

- Efgartigimod is an IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn compared to endogenous IgG, and is uniquely composed of the only part of the IgG antibody that normally binds FcRn[1]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production or other parts of the immune system, and does not decrease albumin[1-3]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[4,5]

Efgartigimod Mechanism of Action: Blocking FcRn

1. Efgartigimod and IgG are internalized[1,6]
2. Efgartigimod competes with endogenous IgG for binding to FcRn[1]
3. Unbound IgG enters the lysosomal degradation pathway[1,6]
4. Efgartigimod and fewer IgGs are recycled back into the bloodstream[1]

METHODS



[a]AChEIs, steroids, and/or NSISTs. [b]Coformulated with 2000 U/mL rHuPH20. [c]Arrows indicate efgartigimod administration. [d]Participants did not receive efgartigimod 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]Participants were not required to have worsening of MG-ADL to be eligible for subsequent cycles. [h]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, with a minimum interval of 7 days after the last administration. Only safety data from Amended Protocol are included here; efficacy data will be presented in subsequent publications.

SUMMARY

- Efgartigimod PH20 SC was well tolerated, even after more frequent dosing (1-4 weeks between cycles) was allowed in ADAPT-SC+, with no new safety signals observed compared with previous efgartigimod studies
- No increase in injection site reactions or infections occurred after more frequent dosing (1-4 weeks between cycles) of efgartigimod PH20 SC was allowed
- Efgartigimod PH20 SC treatment resulted in consistent and repeatable improvements in MG-ADL and MG-QoL15r in AChR-Ab+ participants with gMG
- The majority of AChR-Ab+ participants experienced a CMI in MG-ADL, and a subset were able to achieve MSE; the proportions of AChR-Ab+ participants achieving CMI or MSE were consistent across multiple cycles
- The ADAPT-SC+ study is ongoing

RESULTS

Table 1. Participant Demographics and Baseline Characteristics
Overall and AChR-Ab+ Population

	Original Protocol ≥28 days between cycles		Amended Protocol ≥7 days allowed between cycles
	Efgartigimod PH20 SC *Overall (n=179)*	Efgartigimod PH20 SC *AChR-Ab+ (n=141)*	Efgartigimod PH20 SC *Overall (n=149)*
Age, years, mean (SD)	50.7 (15.5)	51.0 (15.9)	50.2 (15.4)
Sex, female, n (%)	119 (66.5)	90 (63.8)	102 (68.5)
Weight, kg, median (Q1-Q3)	76.9 (64.0-89.8)	77.0 (63.0-92.0)	76.6 (62.5; 89.8)
AChR-Ab+, n (%)	141 (78.8)	141 (100)	118 (79.2)
Total MG-ADL score, mean (SD)	7.9 (3.4)	7.6 (3.4)	7.7 (3.6)
Total MG-QoL15r score, mean (SD)	13.6 (6.9)	13.1 (6.8)	13.0 (6.9)
MG therapy during the first year, n (%)			
Any steroid	128 (71.5)	103 (73.0)	NR[a]
Any NSIST	89 (49.7)	67 (47.5)	NR[a]
Any AChEI	150 (83.8)	122 (86.5)	NR[a]
Steroid + NSIST	69 (38.5)	53 (37.6)	NR[a]
AChEI only	29 (16.2)	23 (16.3)	NR[a]

[a]The proportion of participants receiving concomitant MG therapies was consistent with the overall population at study initiation.

- 184 participants rolled over from ADAPT-SC (n=105) and ADAPT+ (n=79)
- 179 participants (141 AChR-Ab+ and 38 AChR-Ab-) received ≥1 dose of efgartigimod PH20 SC in ADAPT-SC+ through December 2022, with a mean (SD) study duration for all participants of 412.9 (104.5) days
- 180 participants (142 AChR-Ab+ and 38 AChR-Ab-; including both Original and Amended Protocol) received ≥1 dose of efgartigimod PH20 SC in ADAPT-SC+ through June 2024, with a mean (SD) duration for all participants of 849.3 (266.3) days

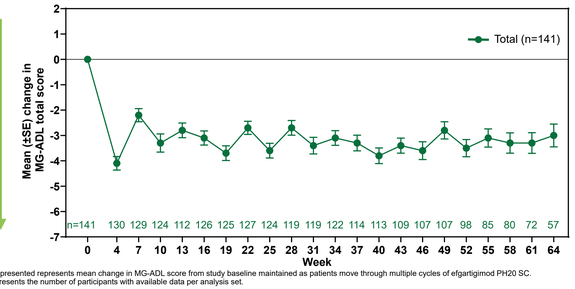
Table 2. Summary of AEs
Overall Population

	Original Protocol ≥28 days between cycles		Amended Protocol ≥7 days allowed between cycles	
	Efgartigimod PH20 SC *(n=179; PYFU=193.4)*		Efgartigimod PH20 SC *(n=149; PYFU=160.1)*	
	ER[a]	n (%)	ER[a]	n (%)
Any AE	9.0	152 (84.9)	5.4	112 (75.2)
Any AE grade ≥3	0.4	36 (20.1)	0.2	23 (15.4)
Any SAE	0.3	33 (18.4)	0.1	17 (11.4)
Any injection site reaction	3.2	82 (45.8)	2.3	23 (15.4)
Any infection	1.0	91 (50.8)	0.7	60 (40.3)
Fatal event[b]	<0.1	4 (2.2)	0	0
Discontinued study treatment owing to AEs	<0.1	4 (2.2)[c]	<0.1	2 (1.3)[d]
Most commonly observed AEs[e]				
Injection site erythema	1.7	52 (29.1)	1.3	19 (12.8)
COVID-19	0.2	40 (22.3)	<0.1	8 (5.4)
Upper respiratory tract infection	0.1	16 (8.9)	0.2	19 (12.8)
Headache	0.6	36 (20.1)	0.3	19 (12.8)
Nasopharyngitis	0.2	28 (15.6)	<0.1	11 (7.4)
Diarrhea	0.2	24 (13.4)	<0.1	9 (6.0)
Injection site pain	0.2	21 (11.7)	<0.1	3 (2.0)
Injection site pruritus	0.2	19 (10.6)	<0.1	5 (3.4)
Injection site bruising	0.2	18 (10.1)	0.2	8 (5.4)

[a]Event rate was calculated as number of events per total PYFU. [b]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. [c]Treatment discontinuations were 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). [d]Treatment discontinuations were due to Bowen's disease (Cycle 5), metastases to liver (Cycle 8), and rectal cancer stage IV (Cycle 8). [e]Most frequent AEs occurring in >10% of participants receiving efgartigimod PH20 SC in either data cut.

- Participants experiencing injection site reaction events decreased over subsequent cycles; from 34.6% (n=62/179) and 11.4% (n=17/149) in Cycle 1 to 10.3% (n=7/68) and 5.2% (n=3/58) in Cycle 9 for original and amended protocol data cuts, respectively
- In both the original and amended protocol data cuts, no injection site reactions were grade ≥3, serious, or resulted in treatment discontinuation

Figure 1. Mean Change From Baseline in Total MG-ADL Over Time[a,b]
Original Protocol AChR-Ab+ Population



[a]Data presented represents mean change in MG-ADL score from study baseline maintained as patients move through multiple cycles of efgartigimod PH20 SC. [b]n represents the number of participants with available data per analysis set.

Figure 2. Minimal Symptom Expression by Cycle
(MG-ADL total score of 0 or 1 at any time during a cycle)
Original Protocol AChR-Ab+ Population

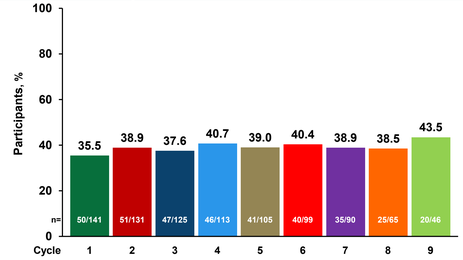
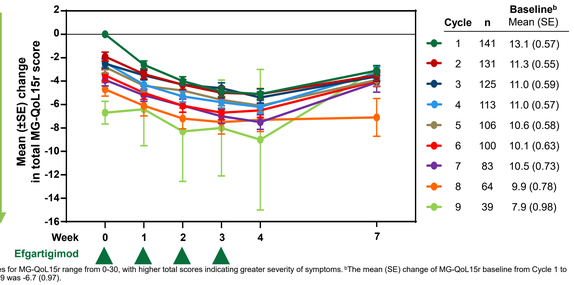
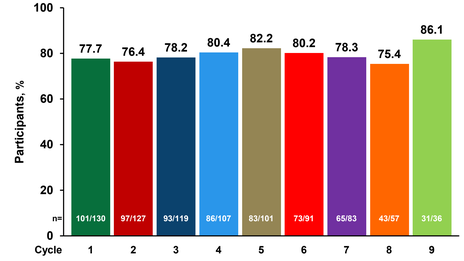


Figure 3. Mean Change From Study Baseline in MG-QoL15r Across Cycles[a]
Original Protocol AChR-Ab+ Population



[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 9 was -6.7 (0.97).

Figure 4. Clinically Meaningful Improvement by Cycle
(Decrease of ≥2 in MG-ADL total score at Week 4)
Original Protocol AChR-Ab+ Population



ABBREVIATIONS:
AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor antibody; AE, adverse event; CMI, clinically meaningful improvement; EQ-5D-5L VAS, EuroQol 5-Dimension, 5-Level Visual Analog Scale; ER, event rate; Fc, fragment crystallisable region; FcRn, neonatal Fc receptor; gMG, generalised myasthenia gravis; Ig, immunoglobulin; IV, intravenous; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MG-QoL15r, Myasthenia Gravis Quality of Life 15-item Questionnaire, Revised; MSE, minimal symptom expression; NR, not reported; NSIST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PD, pharmacodynamic; PK, pharmacokinetic; PYFU, participant years of follow-up (sum of follow-up time of all participants expressed in years in the applicable period); rHuPH20, recombinant human hyaluronidase PH20; SAE, serious adverse event; SC, subcutaneous; SE, standard error.

ACKNOWLEDGMENTS AND DISCLOSURES: **The authors gratefully acknowledge the ADAPT+, ADAPT-SC, and ADAPT-SC+ trial participants and investigators.**
TV: Alexion, argenx, CSL Behring, AllerganAbbVie, Alexion AstraZeneca, Dianthus, Remegen, ImmunoAbs, UCB, Amgen, Immunovant, Regeneron, Johnson & Johnson, and Cartesian. **YL:** argenx, UCB, Alexion, Catalyst, and Immunovant. **JFH:** Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, UCB, AcademicCME, Biologix, CheckRare CME, CoreEvitas, Curie.bio, Hansa Biopharma, Amgen, Biohaven, Medscape CME, Merck EMB Serono, NMD, Novartis, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron, Sanofi, TG Therapeutics, and Tolerancia AB. **DK:** AstraZeneca, Roche, Novartis Russia, Sanofi, Merck, Johnson & Johnson, UCB, argenx, Viela Bio (Amgen), TG Therapeutics, ValentaPharm, Generium, BIOCAD. **SS, BVH, JP,** and **MH** are employees of argenx. **KU**: UCB, Janssen, Horizon, Chugai, Hanall, Merck, Mitsubishi Tanabe, argenx, Alexion, and the Japan Blood Products Organization. **FS:** Alexion, Biogen, Mylan, Novartis, Roche, Sanofi, Teva, Almirall, argenx, Avexis, Forward, Lexeo, Merk, Pomona, Takeda, and Prilenia. **JLDB:** argenx, Alexion, CSL, UCB, Alnylam, Janssen, and Sanofi Genzyme. **RM:** Alexion, argenx, Ra, BioMarin, Catalyst, UCB, Teva, Merck, Roche, and Biogen. The ADAPT+, ADAPT-SC, and ADAPT-SC+ trials were funded by argenx. Medical writing and editorial support for this presentation was provided by Precision AQ and funded by argenx.

REFERENCES:
1. Ulrichts P, et al. *J Clin Invest.* 2018;10(10):128:4372-4386. **2.** Howard JF Jr, et al. [published correction appears in *Lancet Neurol.* 2021;20(8):e5.] *Lancet Neurol.* 2021;20(7):526-536. **3.** Guptill JT, et al. *Autoimmunity.* 2022;55(8):620-631. **4.** Study ARGX-113-2001 (ADAPT-SC) Clinical Trial Protocol v2.0, 02 Jul 2021. **5.** Locke KW, et al. *Drug Deliv.* 2019;26(1):98-106. **6.** Sesarman A, et al. *Cell Mol Life Sci.* 2010;67:2533–50.

Presented at the American Academy of Neurology (AAN) Annual Meeting; April 5-9, 2025; San Diego, California