Long-Term Safety, Tolerability, and Efficacy of Subcutaneous Efgartigimod PH20 in Participants With Generalized Myasthenia Gravis: Interim Analysis of Anti-Acetylcholine Receptor Autoantibody Seronegative Participants in the ADAPT-SC+ Study

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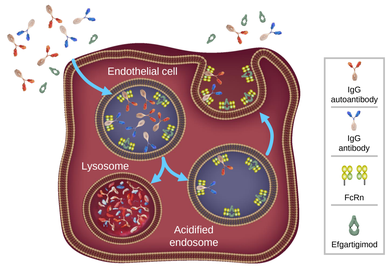
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn

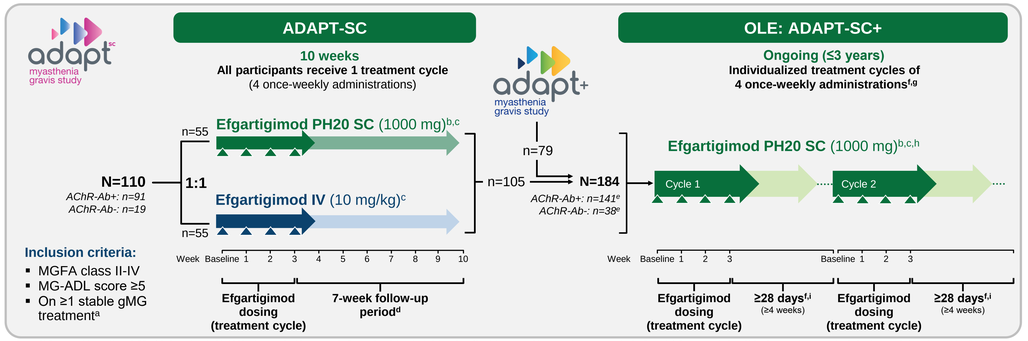


- Efgartigimod is a human IgG1 Fc fragment engineered for increased affinity to FcRn, which prevents recycling of IgG without impacting its production[1-5]
  - Targeted reduction of all IgG subtypes
  - No impact on IgM, IgA, IgE, or IgD
  - No reduction in albumin or increase in cholesterol levels
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[6,7]
- PK/PD modeling and phase 3 data (ADAPT-SC) suggest 4 once-weekly administrations of 1000 mg efgartigimod PH20 SC and 10 mg/kg efgartigimod IV result in comparable decreases in IgG levels[6]

Clinical Challenges in the Management of AChR-Ab- gMG

- AChR-Ab- gMG affects a heterogenous and potentially difficult-to-diagnose and treat patient population with high unmet clinical need who have historically been excluded from clinical trials[3,8-10]

METHODS



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

[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]AChR-Ab status is reported only for the population who received at least one dose of efgartigimod PH20 SC (n=179). [f]≥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. [g]Participants who are not in need of retreatment at study entry will instead start with an intertreatment period. [h]Participants were not required to have worsening of MG-ADL to be eligible for subsequent cycles. [i]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.

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, MG-QoL15r, and EQ-5D-5L VAS total scores over multiple cycles in AChR-Ab- participants, with improvements noted as early as the week after the first administration**
- **The majority of 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**

RESULTS

Table 1. Participant Demographics and Baseline Characteristics

	Efgartigimod PH20 SC *Overall (n=179)*	Efgartigimod PH20 SC *AChR-Ab- (n=38)*
Age, y, mean (SD)	50.7 (15.5)	49.7 (14.2)
Sex, female, n (%)	119 (66.5)	29 (76.3)
Weight, kg, median (Q1-Q3)	76.9 (64.0-89.8)	76.1 (67.7-85.6)
AChR-Ab positive, n (%)	141 (78.8)	-
Total MG-ADL score, mean (SD)	7.9 (3.4)	8.9 (3.4)
Total MG-QoL15r score, mean (SD)	13.6 (6.9)	15.5 (6.8)
EQ-5D-5L VAS, mean (SD)	59.5 (18.6)	54.0 (17.8)
MG therapy during the first year, n (%)		
Any steroid	128 (71.5)	25 (65.8)
Any NSIST	89 (49.7)	22 (57.9)
Any AChEI	150 (83.8)	28 (73.7)
Steroid + NSIST	69 (38.5)	16 (42.1)
AChEI only	29 (16.2)	6 (15.8)

- 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), median, and maximum study duration for all participants of 412.9 (104.52), 451, and 585 days, respectively

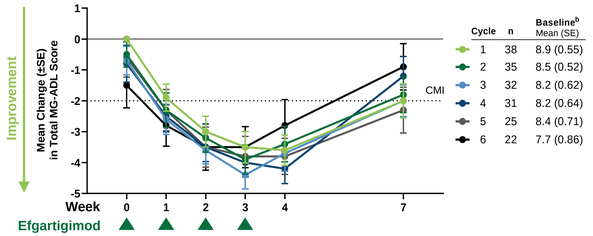
Table 2. Summary of AEs
Overall Population

	Efgartigimod PH20 SC (n=179; PYFU=193.4)	
	IR[a]	n (%)
Any AE, n (%)	9.0	152 (84.9)
Any AE grade ≥3, n (%)	0.4	36 (20.1)
Any SAE, n (%)	0.3	33 (18.4)
Any ISR, n (%)	3.2	82 (45.8)
Any infection, n (%)	1.0	91 (50.8)
Fatal event[b]	<0.1	4 (2.2)
Discontinued study treatment owing to AEs[d], n (%)	<0.1	4 (2.2)
Most commonly observed AEs[d], n (%)		
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)

[a]IR 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 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). [d]Most frequent AEs occurring in >10% of participants receiving efgartigimod PH20 SC.

- Participants experiencing ISR events decreased over subsequent cycles; from 34.6% (n=62/179) in Cycle 1 to 11.5% (n=14/122) in Cycle 6
- No ISRs were grade ≥3, serious, or resulted in treatment discontinuation

Figure 1. Mean Change in MG-ADL From Study Baseline[a]
AChR-Ab- Population



[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).

Figure 2. Minimal Symptom Expression and Clinically Meaningful Improvement in MG-ADL by Cycle
AChR-Ab- Population

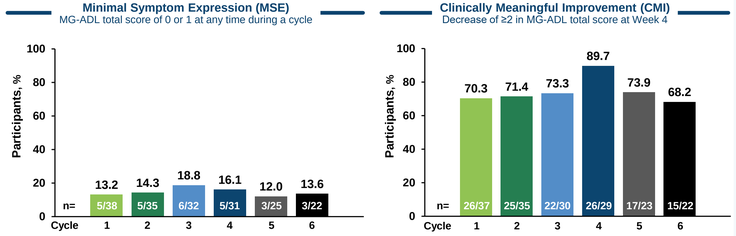
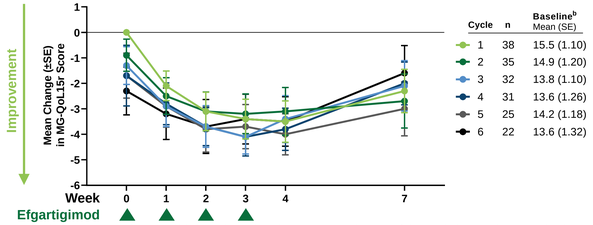
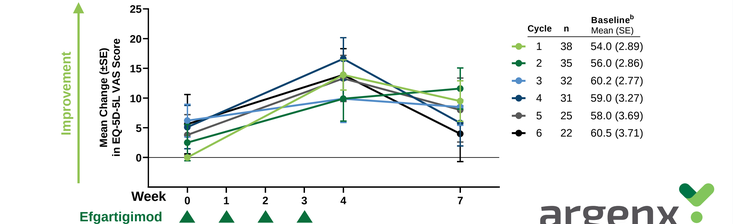


Figure 3. Mean Change in MG-QoL15r From Study Baseline[a]
AChR-Ab- Population



[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 6 was -2.3 (0.94).

Figure 4. Mean Change in EQ-5D-5L VAS From Study Baseline[a]
AChR-Ab- Population



[a]Values for EQ-5D-5L VAS range from 0-100, with higher total scores indicating greater overall health. [b]The mean (SE) change of EQ-5D-5L VAS baseline from Cycle 1 to Cycle 6 was 5.6 (4.99).

ABBREVIATIONS
AChEI, acetylcholinesterase inhibitor; AChR-Ab-, acetylcholine receptor antibody seronegative; AE, adverse event; CMI, clinically meaningful improvement; EQ-5D-5L VAS, EuroQol 5-Dimension, 5-Level Visual Analog Scale; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IR, incidence rate (or event rate) per participant years of follow-up; ISR, injection site reaction; 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; 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.
JFH: Alexion AstraZeneca Rare Disease, argenx, Cartesian, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, PCORI, Ra Pharmaceuticals/UCB Bioscience, Takeda, AcademicCME, Biologix, F. Hoffmann-LaRoche, Horizon, Medscape, Merck EMB Serono, NMD Pharma, Novartis, PeerView, PlatformQ, Regeneron, Sanofi, Zai Labs, and Tolerantia AB. **TV:** Alexion, argenx, CSL Behring, Allergan/AbbVie, AstraZeneca, UCB, Horizon/Viela Bio, Regeneron, Janssen/Momenta, Immunovant, Cartesian, and Sanofi. **JLDB:** argenx, Alexion, CSL, UCB, Almylam, and Sanofi Genzyme. **KU:** argenx, UCB, Janssen, Viela Bio, Chugai Pharma, Merck, Mitsubishi Tanabe, Alexion, and the Japan Blood Products Organization. **MP:** Terumo BCT, Alexion, CSL Behring, argenx, Momenta, Catalyst, UCB, Immunovant, and Janssen. **FS:** Alexion, Biogen, Mylan, Novartis, Roche, Sanofi, Teva, Almirall, argenx, Avexis, Forward, Lexeo, Merck, Pomona, Takeda, and Prilenia. **DK:** Roche, Novartis, Sanofi, Merck, Janssen, UCB, argenx, Horizon, Bristol Myers Squibb, and BIOCAD. **SS, BVH, LL, and JP**: argenx. **JN:** Curare Consulting and argenx. **RB-S:** argenx , Alexion, PTC. **AM:** Alexion, argenx, Grifols, Hormosan, UCB, Janssen, Merck, Octapharma, and German Myasthenia Gravis Society. **RM:** Alexion, argenx, UCB, 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 Value & Health and funded by argenx.

REFERENCES
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.** Study ARGX-113-2001 (ADAPT-SC) Clinical Trial Protocol v2.0, 02 Jul 2021. **7.** Locke KW, et al. *Drug Deliv.* 2019;26(1):98-106. **8.** Gilhus NE, Verschuuren JJ. *Lancet Neurology.* 2015;14(10):1023-1036. **9.** Vu T, et al. *NEJM Evid.* 2022;1(5):1-12. **10.** Howard JF Jr, et al. *Lancet Neurol.* 2017;16(12):976-986.

Presented at the American Association of Neuromuscular and Electrodiagnostic Medicine (AANEM) Annual Meeting; November 1-4, 2023; Phoenix, Arizona