144

Long-Term Safety and Efficacy of Efgartigimod PH20 SC in Generalized Myasthenia Gravis: Interim Analysis of Anti-Acetylcholine Receptor Antibody Seronegative Participants in ADAPT-SC+

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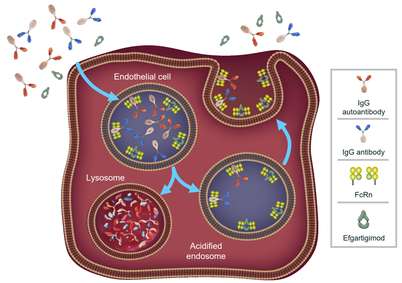
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn

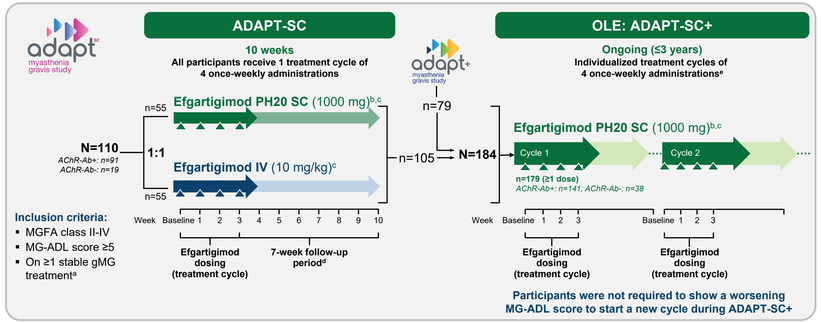


- Efgartigimod is an IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn, and is uniquely composed of the only part of the IgG antibody that normally binds FcRn[1]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production, albumin levels, or other parts of the immune system[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]
- PK/PD modeling and phase 3 data (ADAPT-SC) have demonstrated 4 once-weekly administrations of 1000 mg efgartigimod PH20 SC and 10 mg/kg efgartigimod IV result in comparable decreases in IgG levels[5]

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[2,6-8]
- The phase 3 ADAPT SERON clinical trial (NCT06298552) is currently ongoing to evaluate the safety and efficacy of efgartigimod IV in patients with AChR-Ab- gMG

METHODS



[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]Participants who are not in need of retreatment at study entry will instead start with an intertreatment period.

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
- The ADAPT SERON study is actively recruiting

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+, 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

ABBREVIATIONS
AChEI, acetylcholinesterase inhibitor; AChR-Ab-, acetylcholine receptor antibody seronegative; AChR-Ab+, acetylcholine receptor antibody seropositive; CMI, clinically meaningful improvement; EQ-5D-5L VAS, EuroQoL 5-Dimension, 5-Level Visual Analog Scale; ER, event rate per participant years of follow-up; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; 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; SC, subcutaneous; TEAE, treatment-emergent adverse event.

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RB-S: argenx. **Alexion, PTC. JFH:** Alexion AstraZeneca Rare Disease, argenx, Cartesian, US Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, US National Institutes of Health, Patient-Centered Outcomes Research Institute, 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, Altylam, 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, Avexxis, 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. **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 AQ and funded by argenx.

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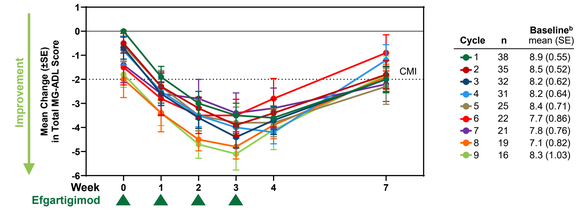
Table 2. Summary of TEAEs
Overall Population

	Efgartigimod PH20 SC (n=179; PYFU=193.4)	
	ER[a]	n (%)
Any TEAE, n (%)	9.0	152 (84.9)
Any TEAE grade ≥3, n (%)	0.4	36 (20.1)
Any serious TEAE, n (%)	0.3	33 (18.4)
Any ISR, n (%)	3.2	82 (45.8)
Fatal event[b]	<0.1	4 (2.2)
Discontinued study treatment owing to AEs,[c] 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]ER 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 10.3% (n=7/68) in Cycle 9
- 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



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

[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).

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

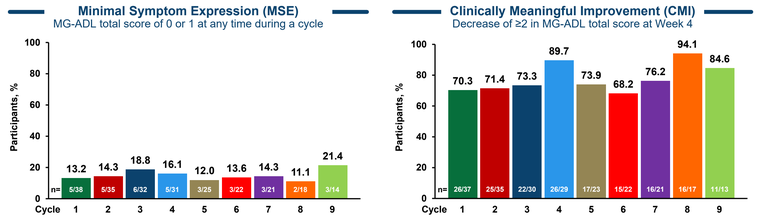
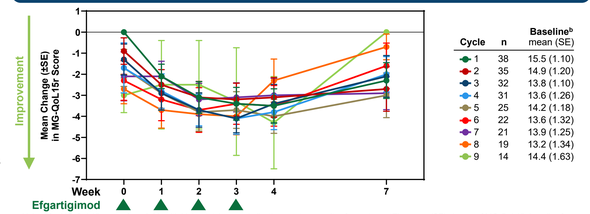


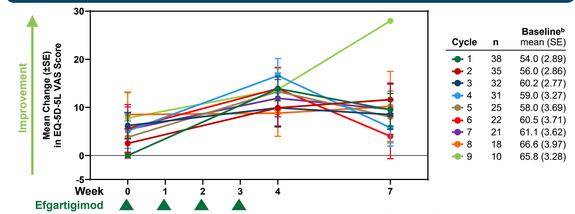
Figure 3. Mean Change in MG-QoL15r From Study Baseline[a]
AChR-Ab- Population



Cycle	n	Baseline[b] mean (SE)
1	38	15.5 (1.10)
2	35	14.9 (1.20)
3	32	13.8 (1.10)
4	31	13.6 (1.26)
5	25	14.2 (1.18)
6	22	13.6 (1.32)
7	21	13.9 (1.25)
8	19	13.2 (1.34)
9	14	14.4 (1.63)

[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 -3.0 (0.82).

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



Cycle	n	Baseline[b] mean (SE)
1	38	54.0 (2.89)
2	35	56.0 (2.86)
3	32	60.2 (2.77)
4	31	59.0 (3.27)
5	25	58.0 (3.69)
6	22	60.5 (3.71)
7	21	61.1 (3.62)
8	18	66.6 (3.97)
9	10	65.8 (3.28)

[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 9 was 7.8 (5.19).

Scan here to learn more about the ADAPT SERON study examining efgartigimod in participants with AChR-Ab- gMG

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