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

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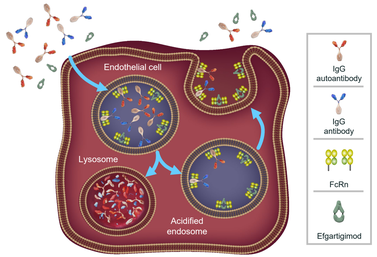
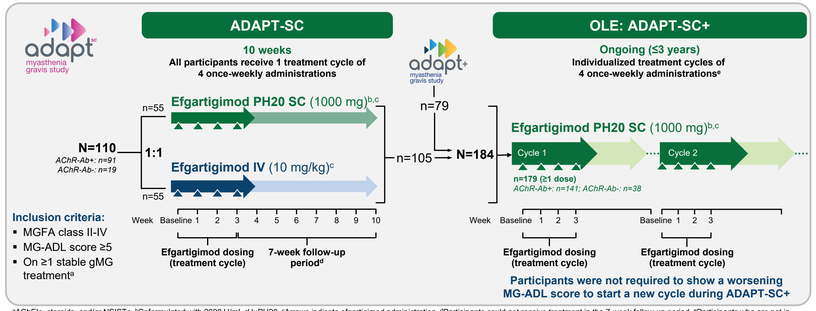
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG antibodies and albumin. This recycling and salvage from lysosomal degradation results in IgG antibodies having the longest half-life and being the most abundant of all immunoglobulins[1-3]
- Blocking FcRn to selectively reduce IgG levels is therefore a rational therapeutic approach in patients with IgG-mediated autoimmune diseases[1,2]
- 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[1,4,5]
- Efgartigimod prevents IgG recycling by blocking IgG antibodies from binding to FcRn, with unbound IgG antibodies being degraded[1,4]
- 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) 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[5,8]

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 over a total of 193.4 PYFU with no new safety signals observed compared with ADAPT-SC
- All injection site reactions were mild or moderate, decreased with subsequent cycles, and none led to treatment discontinuation
- Efgartigimod PH20 SC treatment resulted in consistent and repeatable improvements in MG-ADL, MG-QoL15r, and EQ-5D-5L VAS 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

	Efgartigimod PH20 SC *Overall* (n=179)	Efgartigimod PH20 SC *AChR-Ab+* (n=141)
Age, years, mean (SD)	50.7 (15.5)	51.0 (15.9)
Sex, female, n (%)	119 (66.5)	90 (63.8)
Weight, kg, median (Q1-Q3)	76.9 (64.0-89.8)	77.0 (63.0-92.0)
AChR-Ab+, n (%)	141 (78.8)	141 (100)
Total MG-ADL score, mean (SD)	7.9 (3.4)	7.6 (3.4)
Total MG-QoL15r score, mean (SD)	13.6 (6.9)	13.1 (6.8)
MG therapy during the first year, n (%)		
Any steroid	128 (71.5)	103 (73.0)
Any NSIST	89 (49.7)	67 (47.5)
Any AChEI	150 (83.8)	122 (86.5)
Steroid + NSIST	69 (38.5)	53 (37.6)
AChEI only	29 (16.2)	23 (16.3)

- 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 TEAEs

Overall Population

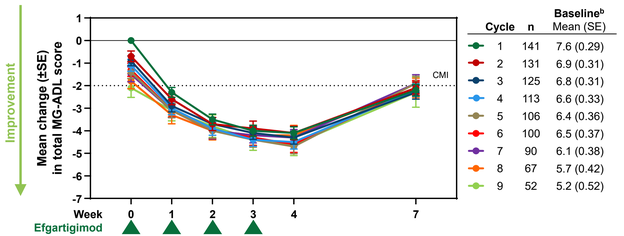
	Efgartigimod PH20 SC (n=179; PYFU=193.4)	
	ER[a]	n (%)
Any TEAE	9.0	152 (84.9)
Any TEAE grade ≥3	0.4	36 (20.1)
Any serious TEAE	0.3	33 (18.4)
Any injection site reaction	3.2	82 (45.8)
Fatal TEAE[b]	<0.1	4 (2.2)
Discontinued study treatment owing to TEAEs[c]	<0.1	4 (2.2)
Most commonly observed TEAEs[d]		
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]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]Most frequent AEs occurring in >10% of participants receiving efgartigimod PH20 SC.

- Participants experiencing injection site reaction events decreased over subsequent cycles; from 34.6% (n=62/179) in Cycle 1 to 10.3% (n=7/68) in Cycle 9
- No injection site reactions 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 9 was -2.1 (0.42).

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

AChR-Ab+ Population

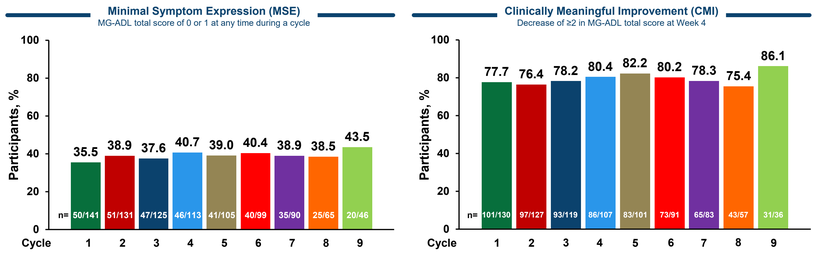
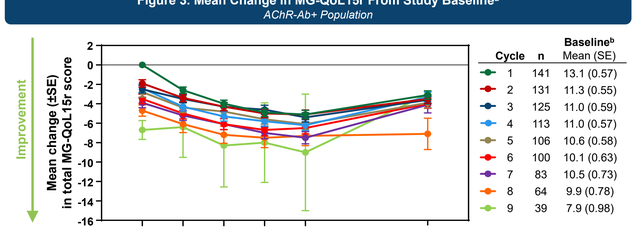


Figure 3. Mean Change in MG-QoL15r From Study Baseline[a]

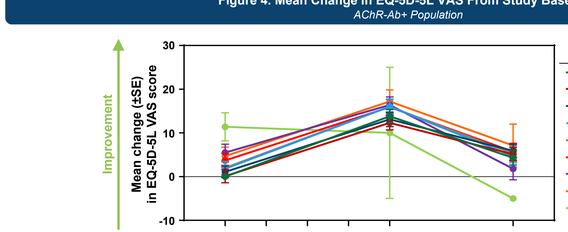
AChR-Ab+ Population



[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 9 was -6.7 (0.97).

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 9 was 11.4 (3.23).

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 crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IMP, investigational medicinal product; 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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