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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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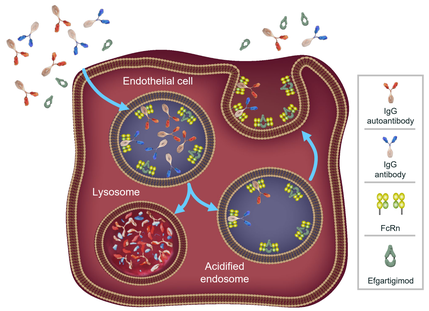
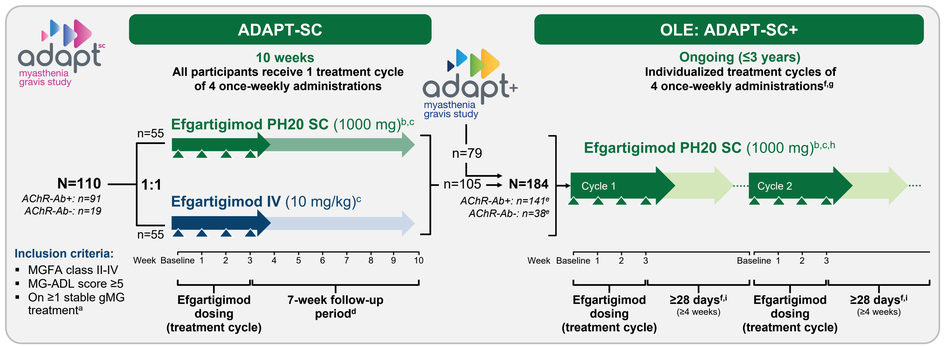
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG to extend its half-life and maintain its high serum concentration[1]
  - FcRn is additionally involved in other cellular processes such as albumin recycling, as well 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, reducing IgG levels without 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[5-7]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[8,9]
- 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[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]AChR-Ab status is reported only for the population who received ≥1 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, with a minimum interval of 7 days after the last administration.

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 ISRs were mild or moderate and decreased with subsequent cycles; no ISRs led to treatment discontinuation
- Efgartigimod PH20 SC treatment resulted in consistent and repeatable improvements in MG-ADL and MG-QoL15r total scores in AChR-Ab+ participants over multiple cycles, with improvements noted as early as the week after the first administration; similar improvements in MG-ADL were observed for AChR-Ab- participants
- 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 ongoing

RESULTS

Table 1. Participant Demographics and Baseline Characteristics

	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

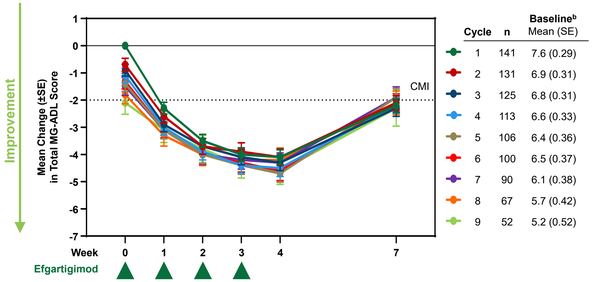
Table 2. Summary of AEs
Overall Population

	Efgartigimod PH20 SC (n=179; PYFU=193.4)	
	ER[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	3.2	82 (45.8)
Any infection	1.0	91 (50.8)
Fatal event[b]	<0.1	4 (2.2)
Discontinued study treatment owing to AEs[c]	<0.1	4 (2.2)
Most commonly observed AEs[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 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	141	7.6 (0.29)
2	131	6.9 (0.31)
3	125	6.8 (0.31)
4	113	6.6 (0.33)
5	106	6.4 (0.36)
6	100	6.5 (0.37)
7	90	6.1 (0.38)
8	67	5.7 (0.42)
9	52	5.2 (0.52)

[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

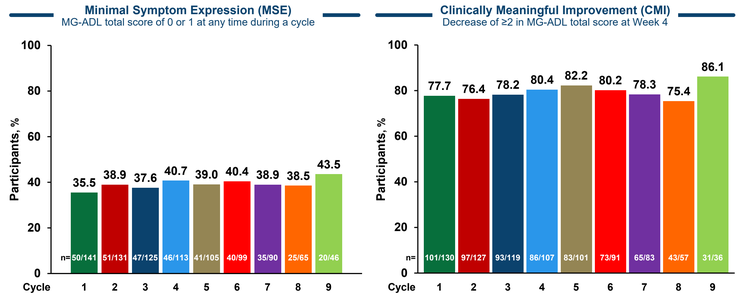
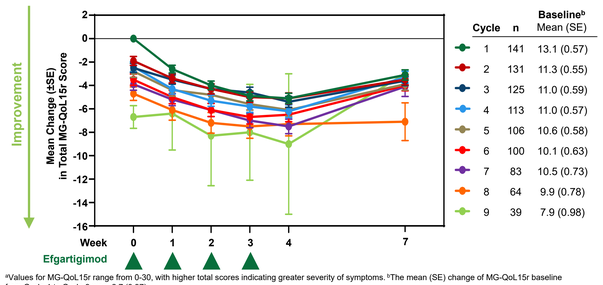


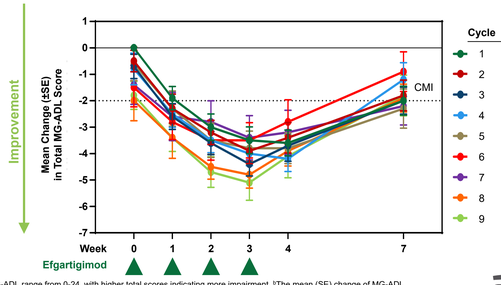
Figure 3. Mean Change in MG-QoL15r From Study Baseline[a]
AChR-Ab+ Population



Cycle	n	Baseline[b] Mean (SE)
1	141	13.1 (0.57)
2	131	11.3 (0.55)
3	125	11.0 (0.59)
4	113	11.0 (0.57)
5	106	10.6 (0.58)
6	100	10.1 (0.63)
7	83	10.5 (0.73)
8	64	9.9 (0.78)
9	39	7.9 (0.98)

[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 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).

ABBREVIATIONS
AChEI, acetylcholinesterase inhibitor; AChR-Ab-, acetylcholine receptor antibody seronegative; AChR-Ab+, acetylcholine receptor antibody seropositive; AE, adverse event; CMI, clinically meaningful improvement; ER, event rate; 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; SAE, serious adverse event; SC, subcutaneous; SE, standard error.

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