Poster #014

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

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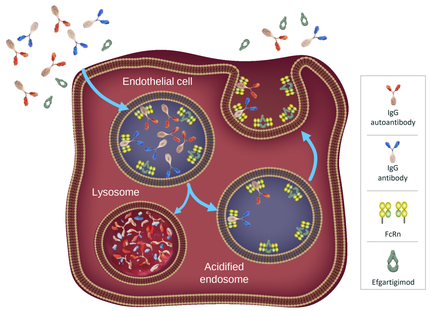
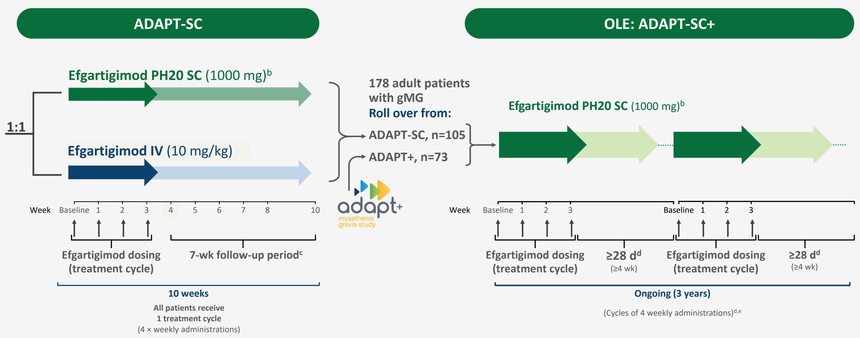
INTRODUCTION

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 subclasses
  - No impact on IgM, IgA, IgE, and IgD
  - No reduction in albumin levels
  - No increase in cholesterol
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[6]
- PK/PD modeling and phase 3 data (ADAPT-SC) suggest four weekly administrations of 1000 mg efgartigimod PH20 SC and 10 mg/kg efgartigimod IV result in comparable decreases in IgG levels

METHODS



[a]AChEIs, steroids, and/or NSISTs. [b]Coformulated with 2000 U/mL rHuPH20. [c]Patients could not receive treatment in the 7-week follow-up period. [d]≥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. [e]Patients 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 to 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 reductions in total IgG and anti-AChR-Ab levels. Improvements in MG-ADL and MG-QOL15r total scores occurred as early as the first administration and were achieved over multiple cycles in AChR-Ab+ and overall populations, including AChR-Ab- participants

The ADAPT-SC+ study is currently ongoing

RESULTS

Table 1. Patient Demographics and Baseline Characteristics
Safety Population

	Efgartigimod PH20 SC (n=164)
Age, mean y (SD)	50.7 (15.4)
Female, n (%)	106 (64.6)
Weight, kg, median (Q1 – Q3)	77 (63.5-90.0)
AChR-Ab positive, n (%)	134 (81.7)
Total MG-ADL score, mean (SD)	7.9 (3.5)
Total MG-QoL15r score, mean (SD)	13.7 (6.6)
MG therapy during the first year, n (%)	
Any steroid	112 (68.3)
Any NSIST	84 (51.2)
Any AChEI	140 (85.4)
Steroid + NSIST	62 (37.8)
AChEI only	30 (18.3)

- 178 participants rolled over from ADAPT-SC (n=105) and ADAPT+ (n=73)
- 134 AChR-Ab+ and 30 AChR-Ab- patients received ≥1 dose of efgartigimod PH20 SC in ADAPT-SC+ through March 2022, with a median (range) follow-up of 182 (24-311) days

Table 2. Summary of AEs
Safety Population

	Efgartigimod PH20 SC (N=164; PYFU=72.1)		
	IR[a]	Events	n (%)
Any AE, n (%)	11.0	790	125 (76.2)
Any AE grade ≥3, n (%)	0.6	41	19 (11.6)
Any SAE, n (%)	0.3	22	17 (10.4)
Any injection site reaction[b], n (%)	4.3	307	69 (42.1)
Any infection, n (%)	1.1	76	48 (29.3)
Fatal event[c]	<0.1	3	2 (1.2)
Discontinued study treatment owing to AEs[d], n (%)	0.1	4	3 (1.8)
Most commonly observed AEs[e], n (%)			
Injection site erythema	2.1	150	42 (25.6)
Headache	0.8	58	25 (15.2)
COVID-19	0.3	20	19 (11.6)
Injection site pain	0.4	28	15 (9.1)
Injection site pruritus	0.4	30	15 (9.1)
Injection site bruising	0.2	18	13 (7.9)
Diarrhea	0.3	20	12 (7.3)
Injection site rash	0.2	17	11 (6.7)
Nasopharyngitis	0.2	12	10 (6.1)
Injection site swelling	0.3	21	9 (5.5)

[a]IR was calculated as number of events per total PYFU. [b]ISR events decreased over subsequent cycles; cycle 1 (n=56, 34.1%), cycle 2 (n=24, 16.9%), cycle 3 (n=14, 13.3%), and cycle 4 (n=8, 11.8%). [c]Fatal events (metastatic renal cell cancer and COVID-19) were not related to efgartigimod PH20 SC treatment, as determined by investigators. [d]Treatment discontinuation due to metastatic renal cell cancer (cycle 1, death), COVID-19 (cycle 3, death), and MG crisis (cycle 1). [e]Most frequent AEs occurring in >5% of patients receiving efgartigimod PH20 SC.

Figure 1. Mean Change in MG-ADL From Study Baseline
Overall Population

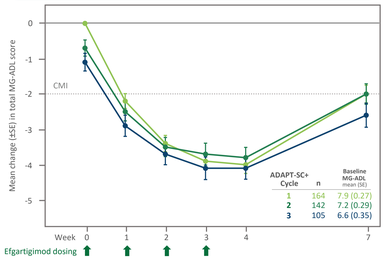


Figure 2. Mean Change in MG-ADL From Study Baseline
AChR-Ab+ Population

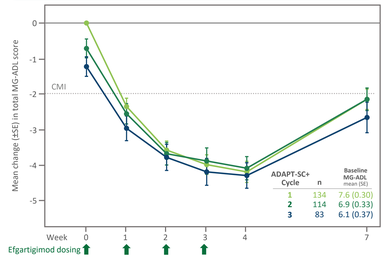


Figure 3. Minimal Symptom Expression by Cycle
(MG-ADL score 0 or 1 at any time point)

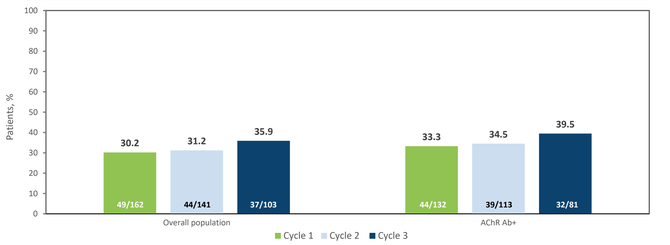


Figure 4. Mean Change in MG-QoL15r From Study Baseline; *Overall Population*

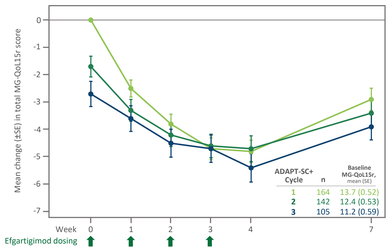


Figure 5. Mean Change in MG-QoL15r From Study Baseline; *AChR-Ab+ Population*

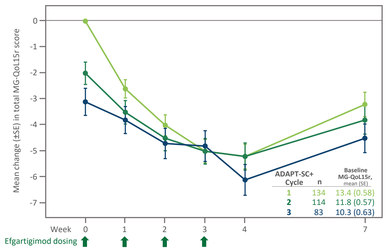


Figure 6. Mean Percent Change in Total IgG at Week 4 From Study Baseline
Overall Population

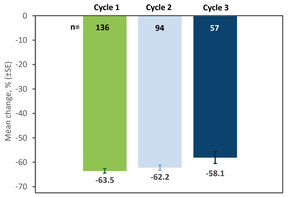
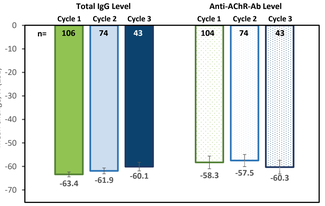


Figure 7. Mean Percent Change in Total IgG and Anti-AChR-Ab Levels at Week 4 From Study Baseline; *AChR-Ab+ Population*



ABBREVIATIONS
AChEI, acetylcholinesterase inhibitor; AChR-Ab+, acetylcholine receptor antibody seropositive; AE, adverse event; CMI, clinically meaningful improvement; COVID-19, coronavirus disease 2019; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IR, incidence rate (or event rate) per patient years of follow-up; ISR, injection site reaction; 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; NSIST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PD, pharmacodynamic; PH20, recombinant human hyaluronidase PH20; PK, pharmacokinetic; PYFU, patient year follow-up (sum of follow-up time of all participants expressed in years in the applicable period); SAE, serious adverse event; SC, subcutaneous; SE, standard error.

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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**. Locke KW, et al. *Drug Deliv*. 2019;26(1):98-106.

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