Subcutaneous Efgartigimod PH20 Demonstrates Improvements in gMG Patients Regardless of Prior Administration Route

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BACKGROUND

Efgartigimod Blocks FcRn and Reduces IgG Levels

- gMG is a rare, chronic, and potentially life-threatening neuromuscular autoimmune disease caused by pathogenic IgG autoantibodies binding to components of the neuromuscular junction and disrupting neuromuscular transmission[1,2]
- The neonatal Fc receptor, FcRn, recycles IgG, extending its half-life, and maintaining serum concentrations of both IgG and the pathogenic IgG autoantibodies in IgG-mediated diseases such as gMG[2,3]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity for FcRn[4]
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting lysosomal degradation of IgG, without impacting its production:[3–6]
  - Targeted reduction of all IgG subtypes
  - No impact on other immunoglobulins
  - No reduction in albumin or increase in cholesterol levels
- By reducing IgG levels, efgartigimod treatment results in clinical improvements in gMG symptoms[3]

Efgartigimod Mechanism of Action

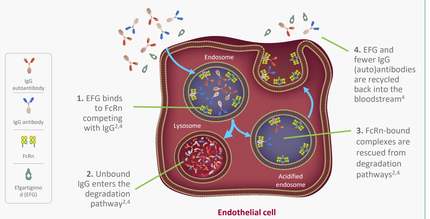


Image adapted from Kang TH, Jung ST. Boosting therapeutic potency of antibodies by taming Fc domain functions. *Exp Mol Med*. 2019;51:1–9 and distributed under the terms of the Creative Commons CC-BY license (https://creativecommons.org/licenses/by/4.0/).

- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20, which allows for rapid SC administration of larger volumes[7]
- Efgartigimod PH20 SC is approved for the treatment of gMG in patients positive for AChR antibodies in the US, as an add-on to standard therapy for the treatment of adult patients with gMG who are AChR-Ab+ in the EU, and in patients with or without AChR antibodies with insufficient response to steroids or NSISTs in Japan
- ADAPT-SC+ (NCT04818671) is an ongoing, open-label extension trial evaluating long-term safety and efficacy of efgartigimod PH20 SC in gMG

OBJECTIVE

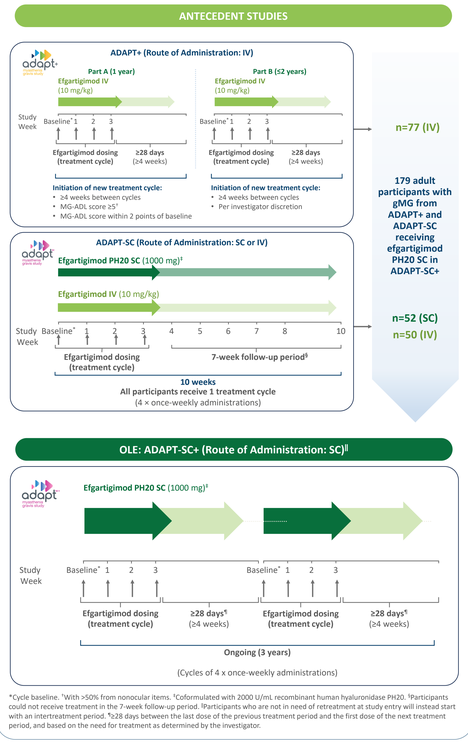
- To evaluate safety and efficacy of efgartigimod PH20 SC in the ADAPT-SC+ study in participants with gMG who previously received IV or SC formulations in antecedent studies (data cut-off: 01 December 2022)

METHODS

Study Design and Duration

- As of 01 December 2022, 184 participants rolled over to the ADAPT-SC+ study, and 179 received ≥1 dose of efgartigimod PH20 SC (**Figure 1**)
- Of these 179 participants, 127 received efgartigimod IV prior to receiving efgartigimod PH20 SC (denoted as 'IV-SC' herein) and 52 received only efgartigimod PH20 SC (denoted as 'SC-SC' herein) (**Table 1**)
- Median (min; max) duration in the ADAPT-SC+ study was 451.0 (67; 585) days (136.9 PYFU) and 444.5 (71; 515) days (56.5 PYFU) in the IV-SC and SC-SC subgroups, respectively

FIGURE 1 ADAPT-SC+ Study Design and Participant Origin



*Cycle baseline. †With >50% from nonocular items. ‡Coformulated with 2000 U/mL recombinant human hyaluronidase PH20. §Participants could not receive treatment in the 7-week follow-up period. ‖Participants who are not in need of retreatment at study entry will instead start with an intertreatment period. ¶≥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.

RESULTS

TABLE 1 Demographics and Baseline Disease Characteristics
Safety Population

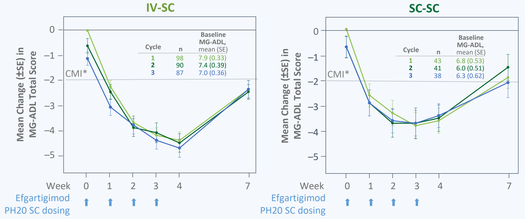
	IV-SC (n=127)	SC-SC (n=52)	Overall Population (N=179)
Age, mean (SD), years	50.4 (15.3)	51.4 (16.2)	50.7 (15.5)
Female, n (%)	90 (70.9)	29 (55.8)	119 (66.5)
Weight, mean (SD), kg	78.8 (19.8)	78.9 (21.4)	78.8 (20.3)
AChR-Ab+, n (%)	98 (77.2)	43 (82.7)	141 (78.8)
MG-ADL total score, mean (SD)	8.2 (3.4)	7.1 (3.4)	7.9 (3.4)
MG-QoL15r total score, mean (SD)	14.0 (6.8)	12.6 (7.0)	13.6 (6.9)
Baseline EQ-5D-5L VAS score, mean (SD)	58.7 (18.6)	61.3 (18.8)	59.5 (18.6)
MG therapy during the first year, n (%)			
Any steroid*	88 (69.3)	40 (76.9)	128 (71.5)
Any NSIST†	66 (52.0)	23 (44.2)	89 (49.7)
Any AChEI‡	105 (82.7)	45 (86.5)	150 (83.8)
Steroid* + NSIST†	50 (39.4)	19 (36.5)	69 (38.5)
AChEI only	21 (16.5)	8 (15.4)	29 (16.2)

*Deflazacort, hydrocortisone, methylprednisolone, methylprednisolone sodium succinate, prednisolone, prednisolone acetate, and/or prednisone. †Azathioprine, ciclosporin, cyclophosphamide, methotrexate, mycophenolate, and/or tacrolimus. ‡Ambenonium chloride, distigmine bromide, pyridostigmine, and/or pyridostigmine bromide.

Efficacy of efgartigimod PH20 SC was consistent between IV-SC and SC-SC subgroups

- In AChR-Ab+ participants (IV-SC: n=98; SC-SC: n=43; **Table 1**), mean [SE] MG-ADL total score improved from study baseline to Week 4, Cycle 1 (IV-SC: −4.3 [0.33]; SC-SC: −3.6 [0.49]) and was consistent over subsequent cycles in both subgroups (**Figure 2**)

FIGURE 2 Mean Change in MG-ADL Total Score From Baseline
AChR-Ab+ Participants

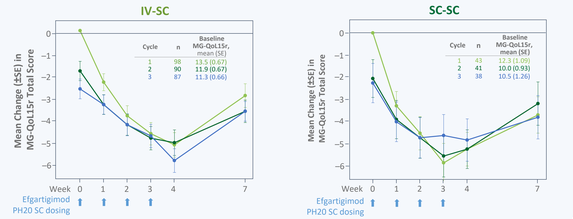


*≥2 point improvement in the total MG-ADL score from study baseline.

Efgartigimod PH20 SC improved QoL in both IV-SC and SC-SC subgroups

- Mean MG-QoL15r total scores improved from study baseline in both subgroups, with mean (SE) change of −5.1 (0.55) and −5.1 (0.74) in the AChR-Ab+ IV-SC and SC-SC populations, respectively, at Week 4 in Cycle 1 (**Figure 3**). EQ-5D-5L VAS showed comparable improvements (data not shown)
- MG-QoL15r cycle baseline scores improved with subsequent treatment cycles in both subgroups, indicating improved QoL over time

FIGURE 3 Mean Change in MG-QoL15r Total Score From Study Baseline
AChR-Ab+ Participants



Efgartigimod was well tolerated with a favourable safety profile

- AEs were mild to moderate in severity, and consistent between subgroups (**Table 2**)

TABLE 2 Overview of AEs
Safety Population

	IV-SC (n=127; PYFU=136.9)		SC-SC (n=52; PYFU=56.5)		Overall Population (N=179; PYFU=193.4)	
	ER*	Incidence, n (%)	ER*	Incidence, n (%)	ER*	Incidence, n (%)
Any AE	7.82	105 (82.7)	11.69	47 (90.4)	8.95	152 (84.9)
Any SAE	0.20	18 (14.2)	0.39	15 (28.8)	0.26	33 (18.4)
Any serious infection	0.03	4 (3.1)	-	0	0.02	4 (2.2)
Any grade ≥3 AE	0.32	22 (17.3)	0.55	14 (26.9)	0.39	36 (20.1)
Any injection site reaction	3.28	57 (44.9)	3.17	25 (48.1)	3.25	82 (45.8)
Fatal event†	0.04	4 (3.1)	-	0	0.03	4 (2.2)
Discontinued study treatment due to AEs	0.04	4 (3.1)	-	0	0.03	4 (2.2)‡
Most commonly observed AEs,§						
Injection site erythema	1.80	39 (30.7)	1.54	13 (25.0)	1.73	52 (29.1)
Headache	0.36	22 (17.3)	1.29	14 (26.9)	0.63	36 (20.1)
COVID-19‖	0.26	30 (23.6)	0.19	10 (19.2)	0.24	40 (22.3)
Diarrhoea	0.15	15 (11.8)	0.25	9 (17.3)	0.18	24 (13.4)
Nasopharyngitis	0.19	20 (15.7)	0.19	8 (15.4)	0.19	28 (15.6)
Injection site pain	0.21	15 (11.8)	0.21	6 (11.5)	0.21	21 (11.7)
Injection site pruritis	0.24	13 (10.2)	0.23	6 (11.5)	0.24	19 (10.6)
Injection site bruising	0.23	13 (10.2)	0.28	5 (9.6)	0.24	18 (10.1)

*ER was calculated as number of events per total PYFU. †Fatal events (metastatic renal cancer, cardiac arrest, pulmonary mass, and COVID-19/respiratory failure) were not related to efgartigimod PH20 SC treatment, as determined by investigators. ‡Treatment discontinuations during ADAPT-SC+ (n=4) were due to participant fatality. §Most commonly observed AEs occurring in >10% of the overall population of participants receiving efgartigimod PH20 SC. ‖Includes all preferred terms of COVID-19. COVID-19 pneumonia, coronavirus infection, exposure to SARS-CoV-2, and SARS-CoV-2 test positive.

KEY TAKEAWAYS

- **Efgartigimod PH20 SC improved MG-ADL total scores, demonstrating consistent and robust efficacy in participants with gMG independent of prior route of efgartigimod administration in antecedent studies**
- **Participant QoL improved with subsequent treatment cycles with efgartigimod PH20 SC**
- **AEs were mild to moderate in severity and consistent between subgroups**
- **Efgartigimod PH20 SC demonstrated comparable efficacy and safety in gMG participants, regardless of prior administration route**

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ABBREVIATIONS

AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor antibody; AChR-Ab+, acetylcholine receptor antibody-positive; AE, adverse event; CMI, clinically meaningful improvement; ER, event rate; EQ-5D-5L VAS, EuroQol 5-Dimension 5-Level visual analogue scale; GI, gastrointestinal; gMG, generalised myasthenia gravis, Ig, immunoglobulin; IV, intravenous; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MG-QoL15r, Myasthenia Gravis Quality of Life 15-item, revised; NSIST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PH20, recombinant human hyaluronidase PH20; PYFU, participant-year(s) of follow-up; SAE, serious adverse event; SC, subcutaneous; QoL, quality of life; SD, standard deviation; SE, standard error.

DISCLOSURES AND ACKNOWLEDGEMENTS

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