A Pharmacodynamic Noninferiority Study Comparing SC Efgartigimod PH20 With IV Efgartigimod: Results of ADAPT-SC

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- James F. Howard Jr has previously received speaker honoraria from argenx

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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[1-4]
  - Targeted reduction of all IgG subclasses
  - No impact on IgM or IgA
  - No reduction in albumin levels
  - No increase in cholesterol
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20)[5]
- PK/PD modeling predicts comparable decreases in IgG levels with 1000 mg efgartigimod PH20 SC injections and 10 mg/kg efgartigimod IV infusions[5]

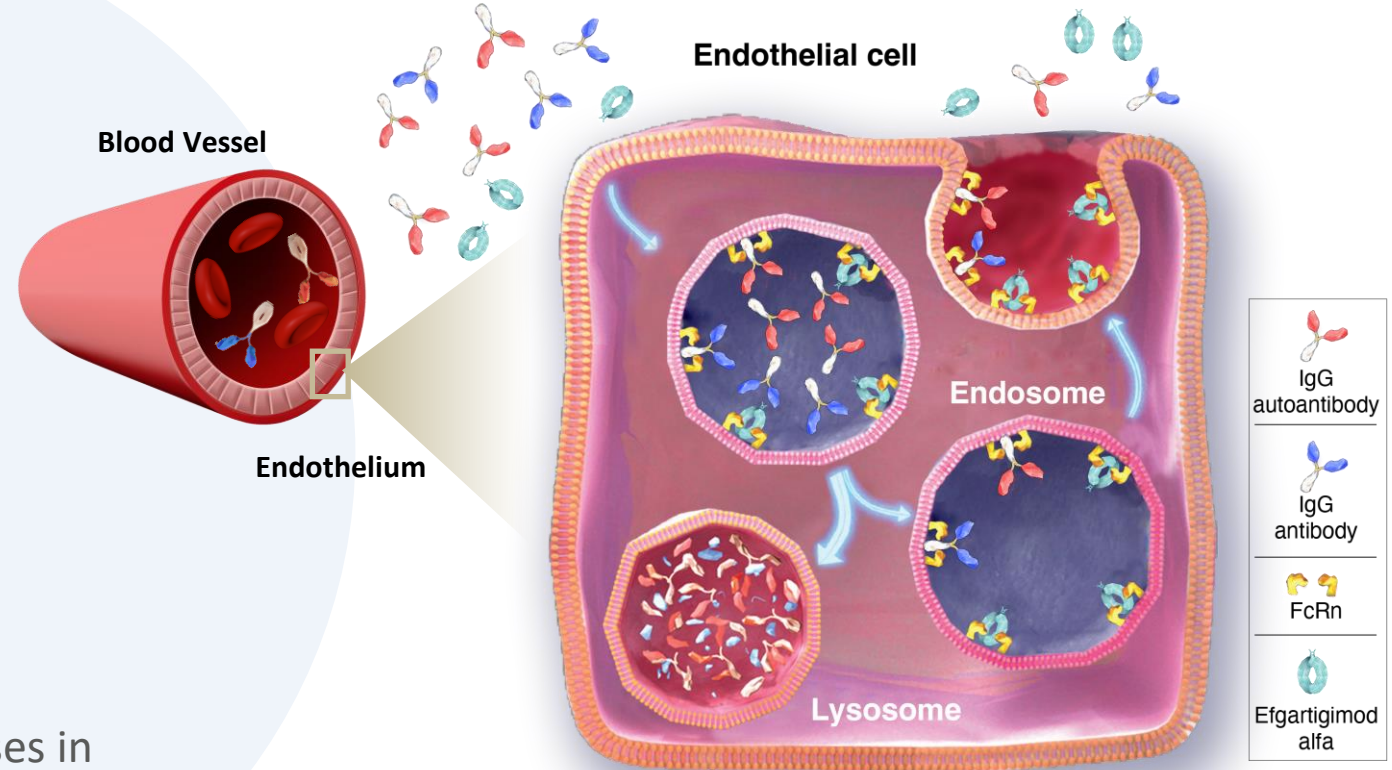


Image adapted from Kang TH, Jung ST. *Exp Mol Med*. 2019;51(11):1-9.

Fc, crystallizable fragment; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgA, immunoglobulin A; IgG, immunoglobulin G; IgM, immunoglobulin M; PD, pharmacodynamics; PK pharmacokinetics; SC, subcutaneous.

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.** argenx Data on File, 2022.

ADAPT-SC Study Design

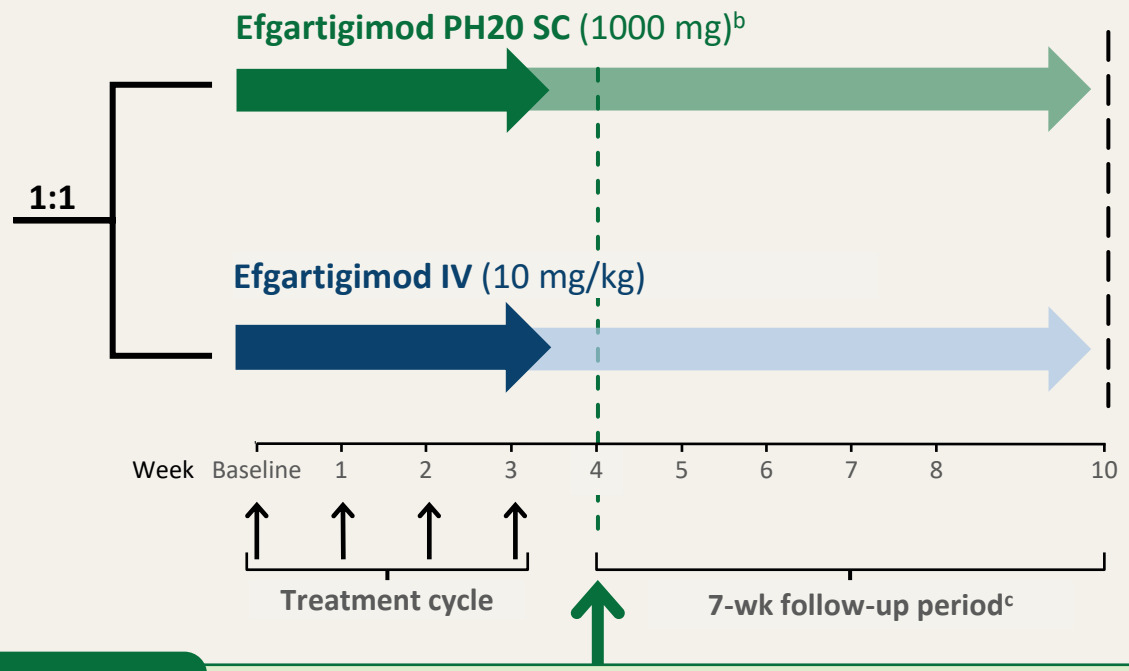
Objective: To demonstrate that the pharmacodynamic effect of efgartigimod PH20 SC is noninferior to that of efgartigimod IV

110 adult patients with gMG

Inclusion criteria:

- MGFA class II - IV
- MG-ADL score ≥5
- On ≥1 stable gMG treatment[a]

All patients receive 1 treatment cycle
(4 weekly single injections or 1-h infusions)



OLE: ADAPT-SC+

- 105 patients from ADAPT-SC & 73 patients from ADAPT+ rolled over to the OLE
- Time between treatment cycles was ≥28 d and based on the need for treatment as determined by the investigator
- Ongoing

Primary Endpoint

Percent reduction from baseline in total IgG levels at day 29

gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PLEX, plasma exchange; rHuPH20, recombinant human hyaluronidase PH20; SC, subcutaneous.
[a]Acetylcholinesterase inhibitors, steroids, and/or NSIST. [b]Coformulated with 2000 U/mL rHuPH20. [c]Patients could not receive treatment in the 7-week follow-up period, except rescue therapy (steroids, IVIg, and PLEX).

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Patient Demographics and Baseline Characteristics

	Efgartigimod PH20 SC (n=55)	Efgartigimod IV (n=55)
Age, y (SD)	50.9 (15.8)	55.8 (15.4)
Female, n (%)	31 (56.4)	34 (61.8)
Weight, kg, median (min–max)	78.30 (42.0–150.2)	78.00 (45.0–139.3)
Time since diagnosis, y (SD)	6.3 (6.4)	7.7 (8.5)
MGFA classification at screening, n (%)		
Class II	29 (52.7)	22 (40.0)
Class III	24 (43.7)	30 (54.5)
Class IV	2 (3.6)	3 (5.5)
Previous thymectomy, n (%)	16 (29.1)	13 (23.6)
AChR-Ab positive, n (%)	45 (81.8)	46 (83.6)
Total MG-ADL score, mean (SD)	8.8 (2.6)	8.5 (2.6)
Total QMG score, mean (SD)	14.9 (4.4)	15.5 (4.5)
Myasthenia gravis therapy at baseline, n (%)		
Any steroid	40 (72.7)	33 (60.0)
Any NSIST	23 (41.8)	25 (45.5)
Any AChE inhibitor	48 (87.3)	47 (85.5)
Steroid + NSIST	19 (34.5)	16 (29.1)
AChE inhibitor only	11 (20.0)	12 (21.8)

AChE, acetylcholinesterase; AChR-Ab, acetylcholine receptor antibody; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; NSIST, nonsteroidal immunosuppressive therapy; QMG, Quantitative Myasthenia Gravis; SC, subcutaneous.

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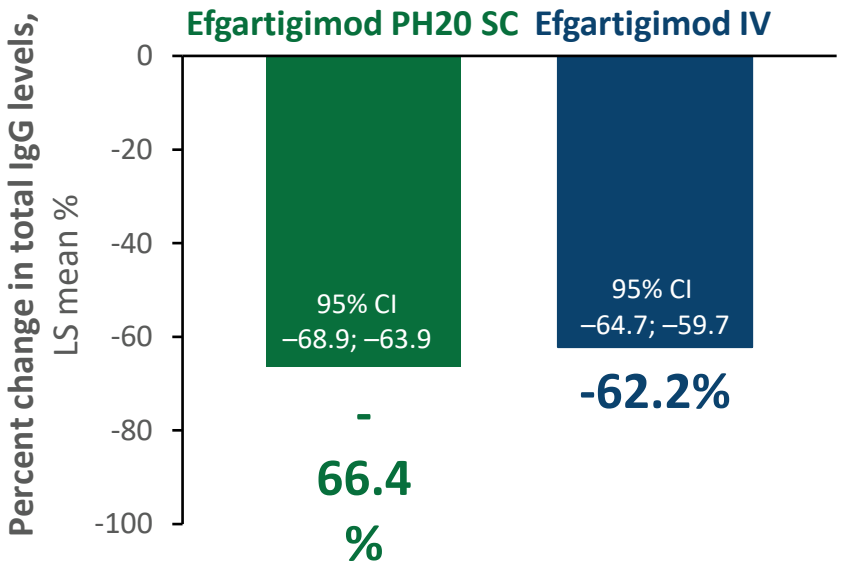
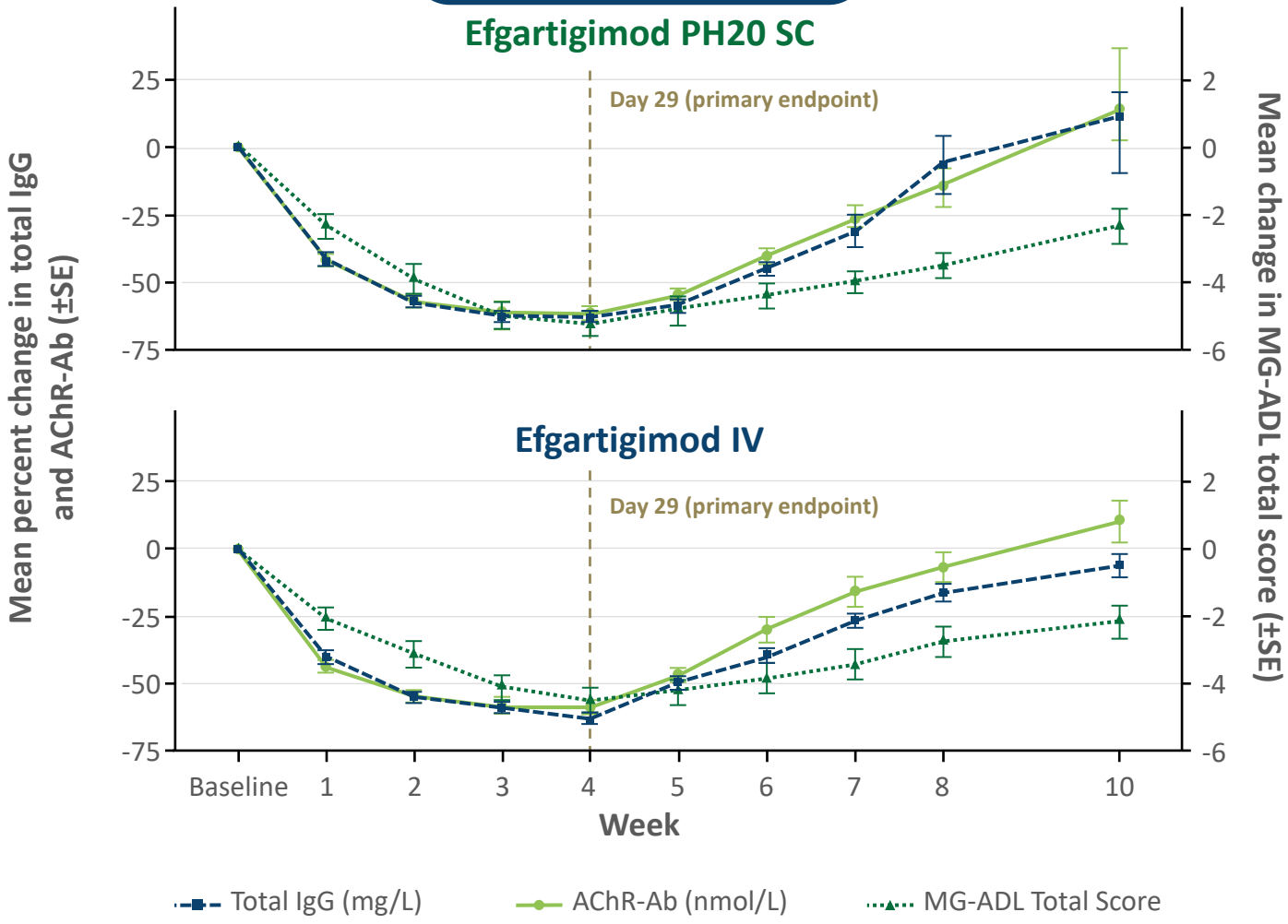
Primary and Secondary Efficacy Endpoints

Primary Endpoint

Percent total IgG reduction from baseline at day 29



Secondary Endpoints



AChR-Ab, acetylcholine receptor antibody; IgG, immunoglobulin G; IV, intravenous; LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; SC, subcutaneous; SE, standard error.

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ADAPT-SC Safety: Summary of AEs

	Efgartigimod PH20 SC (n=55)	Efgartigimod IV (n=55)
Any AE, n (%)	37 (67.3)	28 (50.9)
Any AE Grade ≥3[a], n (%)	9 (16.4)	4 (7.3)
Any SAE, n (%)	8 (14.5)	4 (7.3)
≥1 injection-site reaction (localized), n (%)	21 (38.2)[b]	1 (1.8)[c]
Any infection, n (%)	10 (18.2)	9 (16.4)
Discontinued study treatment owing to AEs, n (%)	2 (3.6)[d]	0 (0.0)
Most commonly observed AEs occurring in ≥5 participants, n (%)		
Injection site rash	8 (14.5)[e]	0 (0)
Headache	7 (12.7)	7 (12.7)
Injection site erythema	7 (12.7)	0 (0)
Myasthenia gravis	6 (10.9)[f]	1 (1.8)
Injection site pruritus	5 (9.1)	0 (0)

AEs were predominantly mild or moderate in severity. No deaths were reported

AE, adverse event; COVID-19, coronavirus 2019; IV, intravenous; OLE, open-label extension; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.
[a]No Grade 4 or 5 AEs reported. [b]Injection site reactions were mild (18/21 patients) or moderate (3/21 patients) and most (19/21 patients) were transient and resolved without treatment. [c]No preferred term AEs of injection-site reaction recorded. This AE was incorrectly coded (should have been catheter site reaction). [d]1 treatment discontinuation due to COVID-19 infection and the other to MG worsening on Day 1. [e]Incidence of injection site reactions did not increase with subsequent injections. [f]Re-emergence of symptoms typically happened at the end of the follow-up period, and all of the patients who rolled over to the OLE were responders when treated again with efgartigimod.

Summary

The primary endpoint of ADAPT-SC was met as efgartigimod PH20 SC was noninferior to efgartigimod IV in reducing total IgG levels

Safety and tolerability of efgartigimod PH20 SC was similar to efgartigimod IV, except for mild to moderate, transient injection site reactions

The availability of both SC and IV formulations of efgartigimod could provide the best route of administration for each patient

IgG, immunoglobulin G; IV, intravenous; gMG, generalized myasthenia gravis; SC, subcutaneous.

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