EPO-209

Efficacy and Safety of Efgartigimod IV and PH20 SC in gMG: Analysis of AChR-Ab– Participants in ADAPT+/ADAPT-SC+

Sarah Hoffmann,[1] James F. Howard Jr,[2] Tuan Vu,[3] Jan L. De Bleecker,[4] Kimiaki Utsugisawa,[5] Hiroyuki Murai,[6] Francesco Saccà,[7] Denis Korobko,[8] Caroline T'joen,[9] Sophie Steeland,[9] Benjamin Van Hoorick,[9] Jana Podhorna,[9] Andreas Meisel,[10] Renato Mantegazza,[11] and the ADAPT+/ADAPT-SC+ Study Groups

[1]Department of Neurology with Experimental Neurology, and the Neuroscience Clinical Research Center, Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität, Berlin, Germany; [2]Department of Neurology, The University of North Carolina, Chapel Hill, North Carolina, USA; [3]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, Florida, USA; [4]Department of Neurology, Ghent University Hospital, Ghent, Belgium; [5]Department of Neurology, Hanamaki General Hospital, Hanamaki, Japan; [6]Department of Neurology, School of Medicine, International University of Health and Welfare, Tokyo, Japan; [7]NRSO Department, Genesis Center, Federico II University of Naples, Naples, Italy; [8]State Budgetary Healthcare Institution of Novosibirsk Region "State Novosibirsk Regional Clinical Hospital", Novosibirsk, Russia; [9]argenx, Ghent, Belgium; [10]Department of Neurology with Experimental Neurology, Integrated Myasthenia Gravis Center, Neuroscience Clinical Research Center, Charité – Universitätsmedizin Berlin, Berlin, Germany; [11]Department of Neuroimmunology and Neuromuscular Diseases, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy

SCAN ME

argenx

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

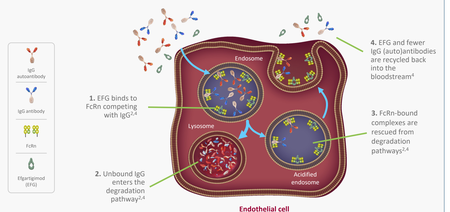


Image adapted from Kang TH, Jung ST. Boosting therapeutic potency of antibodies by taming Fc domain functions. *Exp Mol Med*. 2019;51:1–9 and distributed under the terms of the Creative Commons CC-BY license (https://creativecommons.org/licenses/by/4.0/).

Challenges in the Management of AChR-Ab– gMG

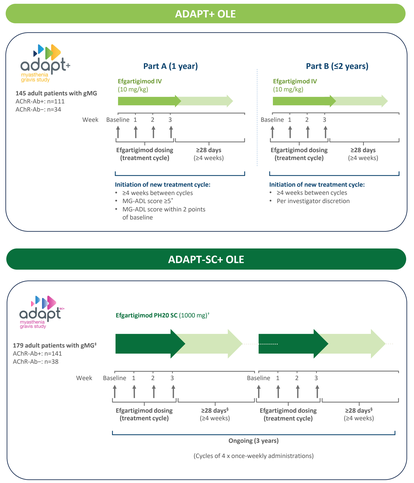
- ~15% of the gMG population are AChR-Ab– and this heterogeneous population have limited treatment options, are potentially difficult to diagnose and have a high unmet clinical need[3,7,8]
- ADAPT+ (NCT03770403) and ADAPT-SC+ (NCT04818671) evaluated the safety and efficacy of efgartigimod IV and efgartigimod PH20 SC (a coformulation of efgartigimod and PH20), respectively, in both AChR-Ab+ and AChR-Ab– individuals with gMG (**Figure 1**)

OBJECTIVE

- To analyse the efficacy of efgartigimod IV and efgartigimod PH20 SC in AChR-Ab– gMG participants in the completed ADAPT+ (final data cut-off: 20 September 2022) and ongoing ADAPT-SC+ trials (data cut-off: 01 December 2022)

METHODS

FIGURE 1 ADAPT+ and ADAPT-SC+ Trial Designs



*With >50% from nonocular items. †Coformulated with 2000 U/mL recombinant human hyaluronidase PH20. ‡Number of recruited participants who received ≥1 dose of efgartigimod PH20 SC. §≥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.

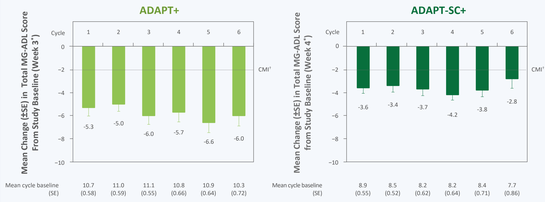
TABLE 1 Patient Demographics and Baseline Disease Characteristics

	ADAPT+		ADAPT-SC+	
	AChR-Ab– (n=34)	AChR-Ab+ (n=111)	AChR-Ab– (n=38)	AChR-Ab+ (n=141)
Age, mean (SD), years	46.7 (12.2)	47.1 (15.5)	49.7 (14.2)	51.0 (15.9)
Female, *n* (%)	28 (82.4)	75 (67.6)	29 (76.3)	90 (63.8)
Weight, median (Q1–Q3), kg	78.1 (65.2–93.9)	74.0 (62.8–94.0)	76.1 (67.7–85.6)	77.0 (63.0–92.0)
MG-ADL total score, mean (SD)	10.7 (3.4)	9.5 (3.1)	8.9 (3.4)	7.6 (3.4)
MG therapy during the first year, n (%)				
Any steroid	26 (76.5)	85 (76.6)	25 (65.8)	103 (73.0)
Any NSIST*	22 (64.7)	67 (60.4)	22 (57.9)	67 (47.5)
Any AChEI†	22 (64.7)	100 (90.1)	28 (73.7)	122 (86.5)
Steroid + NSIST*	19 (55.9)	57 (51.4)	16 (42.1)	53 (37.6)
AChEI only†	4 (11.8)	16 (14.4)	6 (15.8)	23 (16.3)

*Azathioprine, cyclosporine, cyclophosphamide, methotrexate, mycophenolate mofetil, and/or tacrolimus. †Ambenonium chloride, distigmine bromide, pyridostigmine, and/or pyridostigmine bromide.

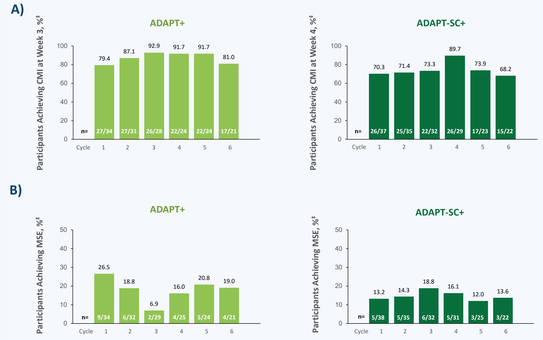
RESULTS

FIGURE 2 Improvement in Mean MG-ADL Score Across 6 Cycles
AChR-Ab– Participants



*MG-ADL was measured at Week 3 during ADAPT+ (no data captured at Week 4 when maximal IgG reduction and clinical improvement may have occurred) and Week 4 during ADAPT-SC+. †≥2-point improvement in the total MG-ADL score.

FIGURE 3 Clinically Meaningful Improvement* (A) and Minimal Symptom Expression† (B) Achieved, by Cycle, in ADAPT+ and ADAPT-SC+
AChR-Ab– Participants



*≥2-point improvement in the total MG-ADL score from study baseline. †Total MG-ADL score of 0 or 1 at any time during a cycle. ‡Percentage of participants achieving MSE is calculated based on the number of participants completing each cycle.

Efgartigimod provides clinically meaningful improvement for AChR-Ab– participants

- Efgartigimod improved mean (SE) MG-ADL total scores consistently across multiple cycles (**Figure 2**)
- Most AChR-Ab– participants achieved CMI at Week 3 in Cycle 1 (**Figure 3A**), and a subset achieved MSE at some point during cycle 1 (**Figure 3B**); these observations were consistent across multiple cycles in both trials

TABLE 2 Summary of AEs (Overall Population)

	ADAPT+ (N=145; PYFU=228.9)		ADAPT-SC+ (N=179; PYFU=193.4)	
	ER*	Incidence, n (%)	ER*	Incidence, n (%)
Any AE	3.53	124 (85.5)	8.95	1.52 (84.9)
Any SAE	0.24	36 (24.8)	0.26	33 (18.4)
Any serious infection	0.05	9 (6.2)	0.02	4 (2.2)
Any grade ≥3 AE	0.33	40 (27.6)	0.39	36 (20.1)
Any infusion-related reaction	0.10	15 (10.3)	-	-
Any injection site reaction	-	-	3.25	82 (45.8)
Fatal event†	0.02	5 (3.4)	0.03	4 (2.2)
Discontinued study treatment due to AEs‡	0.06	12 (8.3)	0.03	4 (2.2)
Most commonly observed AEs,§				
Injection site erythema	-	-	1.73	52 (29.1)
Headache	0.45	36 (24.8)	0.63	36 (20.1)
COVID-19¶	0.10	23 (15.9)	0.24	40 (22.3)
Nasopharyngitis	0.10	20 (13.8)	0.19	28 (15.6)
Diarrhoea	0.08	14 (9.7)	0.18	24 (13.4)
Injection site pain	-	1 (0.7)	0.21	21 (11.7)
Injection site pruritus	-	-	0.24	19 (10.6)
Injection site bruising	-	1 (0.7)	0.24	18 (10.1)

*ER was calculated as number of events per total PYFU. †Fatal events in ADAPT+ (septic shock, MG crisis, acute myocardial infarction, lung cancer, and unknown cause of death) were not related to efgartigimod IV treatment, as determined by investigators. Fatal events in ADAPT-SC+ (metastatic renal cancer, cardiac arrest, pulmonary mass, and COVID-19/respiratory failure) were not related to efgartigimod PH20 SC treatment, as determined by investigators. ‡During ADAPT, treatment was discontinued due to myasthenia gravis (n=4), COVID-19 pneumonia (n=2), spinal compression fracture, cerebral venous sinus thrombosis, lung neoplasm malignant, acute myocardial infarction, adenocarcinoma of colon, and irritable bowel syndrome. A total of 2 TEAEs of myalgia and headache led to efgartigimod discontinuation in 1 participant. Treatment discontinuation during ADAPT-SC+ (n=4) were due to participant fatality. §Most frequent AEs occurring in >10% of the overall population receiving efgartigimod IV (ADAPT+) or efgartigimod PH20 SC (ADAPT-SC+). ¶Includes all preferred terms of COVID-19, COVID-19 pneumonia, coronavirus infection, exposure to SARS-CoV-2, and SARS-CoV-2 test-positive.

Efgartigimod was well tolerated in AChR-Ab– and AChR-Ab+ participants across trials

- Efgartigimod was well tolerated (**Table 2**); most AEs were mild to moderate in severity
- Safety observations from the overall population were consistent across AChR-Ab– and AChR-Ab+ populations

ADAPT^{seron}: A phase 3 trial of efgartigimod IV in AChR-Ab– gMG

- ADAPT^{seron} (NCT06298552) is a randomised, double-blinded, placebo-controlled, phase 3, parallel-group trial to evaluate the efficacy and safety of efgartigimod IV in adult participants with AChR-Ab– gMG
- **Study Part A:** Participants randomised to receive efgartigimod IV or placebo
- **Study Part B:** Open-label efgartigimod IV (participants completing Part A)
- **Primary outcome measure:** MG-ADL total score change from baseline at Week 4
- **Secondary outcomes:** QMG total score change from baseline at Week 4; proportion of participants who are both MG-ADL and QMG responders during Part A
- **Estimated enrolment:** 110
- **Primary completion estimate:** 25 July 2025

KEY TAKEAWAYS

- **Efgartigimod improved mean MG-ADL total scores in AChR-Ab– participants across multiple cycles in both IV and SC trials**
- **Most participants receiving efgartigimod demonstrated clinically meaningful improvements in MG-ADL total score during each cycle**
- **Proportions of AChR-Ab– participants achieving MSE were consistent across cycles in both IV and SC trials**
- **Efgartigimod was well-tolerated, with safety observations from the overall population consistent between trials**
- **The phase 3 ADAPT^{seron} trial will assess the safety and efficacy of efgartigimod IV in adult participants with AChR-Ab– gMG**

Presented at the 10th Congress of the European Academy of Neurology (EAN): June 29–July 2, 2024, Helsinki, Finland

ABBREVIATIONS

AChEI, acetylcholinesterase inhibitor; AChR-Ab–, acetylcholine receptor antibody-negative; AChR-Ab+, acetylcholine receptor antibody-positive; AE, adverse event; CMI, clinically meaningful improvement; ER, event rate; Fc, fragment crystallizable; FcRn, neonatal Fc receptor; gMG, generalised myasthenia gravis; Ig, immunoglobulin; IV, intravenous; MG-ADL, Myasthenia Gravis Activities of Daily Living; MSE, minimal symptom expression; NSIST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PYFU, patient-year(s) of follow-up; Q, quartile; QMG, quantitative myasthenia gravis; PH20, recombinant human hyaluronidase PH20; SAE, serious adverse event; SC, subcutaneous; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event.

DISCLOSURES AND ACKNOWLEDGEMENTS

SH: Alexion, argenx, UCB; **JFH:** Academic CME, Ad Scientiam, Alexion, Amgen, AstraZeneca Rare Disease, argenx, Biologix, Cartesian Therapeutics, Centers for Disease Control and Prevention, CheckRare CME, F. Hoffmann-LaRoche Ltd, Medscape CME, Merck EMB Serono, MGFA, Muscular Dystrophy Association, National Institutes of Health (NIH), NMD Pharma, Novartis, PCORI, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, Tolerancia AB, UCB, Zai Lab; **TV:** Alexion, Amgen, argenx, Cartesian Therapeutics, Dianthus, ImmunAbs, Immunovant, Johnson and Johnson, Regeneron, Sanofi Genzyme, UCB; **JLDB:** Alexion, Alnylam, argenx, CSL Behring, Janssen, Sanofi Genzyme, UCB; **KU:** Alexion, Amgen, argenx, Chugai, Janssen, Japan Blood Products Organisation, Mitsubishi Tanabe, UCB; **HM:** Alexion, argenx, AstraZeneca, Chugai, Japan Blood Products Organisation, Ministry of Health, Labour and Welfare of Japan, Roche, UCB; **FS:** Agenzia Italiana del Farmaco, Alexion, Almirall, argenx, Dianthus, Friedrich Ataxia Research Alliance, Genpharm, Immunovant, Lediant, Lexeo Therapeutics, Madison Pharma, Medpharma, Novartis, Prilenia, Reata, Sandoz, Sanofi, Zai Lab; **DK:** argenx, BIOCAD, Bristol Myers Squibb, Horizon, Janssen, Merck, Novartis Russia, Roche, Sanofi, UCB; **CT'J, SS, BVH, JP:** Employees of argenx; **AM:** Alexion, argenx, Axunio, Grifols, Hormosan, Janssen, Merck, Novartis, Octapharma, UCB; **RM:** Alexion, argenx, Biogen, BioMarin, Catalyst, Merck, Roche, Teva, UCB.

This study was sponsored by argenx. Medical writing support was provided by Envision Pharma Group, funded by argenx.

The authors gratefully acknowledge the trial participants and investigators involved in these studies.

REFERENCES

1. Howard JF Jr, et al. *Front Neurol.* 2024;14:1284444. **2.** Sesarman A, et al. *Cell Mol Life Sci.* 2010;67:2533–50. **3.** Howard JF Jr, et al. *Lancet Neurol.* 2021;20:526–36. **4.** Ulrichts P, et al. *J Clin Invest.* 2018;128:4372–86. **5.** Vaccaro C, et al. *Nat Biotech.* 2005;23:1283–8. **6.** Nixon AE, et al. *Front Immunol.* 2015;6:176. **7.** Gilhus NE, Verschuuren JJ. *Lancet Neurology*. 2015;14:1023–36. **8.** Vu T, et al. *NEJM Evid*. 2022;1:1–12.