EPO-206

Efgartigimod Consistently Improved Health-Related Quality of Life in AChR-Ab+ Participants With gMG in IV and SC Trials

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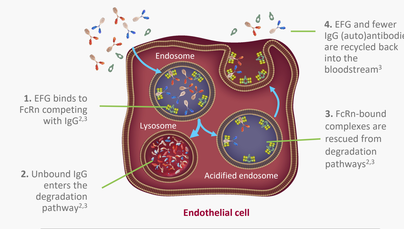
BACKGROUND

Efgartigimod Blocks FcRn and Reduces IgG Levels

- 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[1,2]
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity for FcRn[3]
- Efgartigimod outcompetes 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
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20, which allows for rapid SC administration of larger volumes[7]

Efgartigimod Mechanism of Action



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gMG and Burden on HRQoL

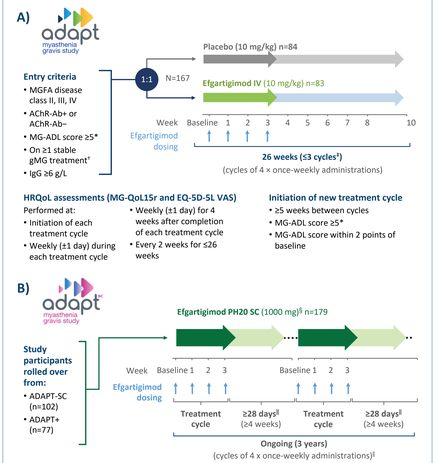
- gMG is a rare, chronic, and potentially life-threatening neuromuscular autoimmune disease caused by pathogenic IgG autoantibodies[4,8]
- Pathogenic IgG autoantibodies bind components of the neuromuscular junction, disrupting neuromuscular transmission and causing debilitating muscle weakness and fatigue[4,8]
- By reducing IgG levels, efgartigimod treatment results in clinical improvements in gMG symptoms[4]
- gMG causes substantial burdens on patient HRQoL, particularly for those whose symptoms are not well controlled or who experience a high level of treatment side effects[8,9]
- Recent guidelines indicate that the therapeutic goals for gMG should be the best possible disease control, with the best possible preservation or restoration of QoL[10]

OBJECTIVE

- To assess HRQoL outcomes following efgartigimod treatment of AChR-Ab+ gMG participants from trials with available HRQoL data:
  - The placebo-controlled, randomised, phase 3 ADAPT (IV) trial (NCT03669588; final data cut-off: 06 April 2020)(**Figure 1A**)
  - The ongoing open-label extension ADAPT-SC+ (SC) trial (NCT04818671; data cut-off: 01 December 2022)(**Figure 1B**)

METHODS

FIGURE 1 ADAPT and ADAPT-SC+ Trial Designs



*Within >50% from nonocular items. †AChEI, steroid +/or NSIST. Participants could not change concomitant therapies in ADAPT. ‡≤3 cycles dosed at ≥8 weeks after initial cycle. §Coformulated with 2000 U/mL recombinant human hyaluronidase PH20. ‖≥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. ¶Performed during the first year of study only.

HRQoL Assessments

MG-QoL15r[11]

- MG-QoL15r is a validated, commonly used, 15-item survey to assess patient perception of attributes associated with MG, including mobility (9 items), disease symptoms (3 items), general contentment (1 item) and emotional well-being (2 items); higher scores indicate worse QoL

EQ-5D-5L[12]

- EQ-5D-5L is a standardised, validated measure of health status
- It is widely used in clinical trials, population studies and real-world clinical settings, and is recommended as a key component of clinical/economic appraisals
- Patients report scores across 5 dimensions (mobility, self-care, usual activities, pain/discomfort, anxiety/depression) to generate a unique 5-digit code used to derive a utility and VAS score
- EQ-5D-5L VAS indicates an individual's daily perceived health status on a scale of 0 to 100 (higher score indicates better perceived overall health)

MG-QoL15r and EQ-5D-5L assessments are recommended in clinical practice, clinical trials, and telemedicine by a panel of European experts[13]

RESULTS

TABLE 1 Patient Demographics and Baseline Disease Characteristics

AChR-Ab+ Participants

	ADAPT†		ADAPT-SC+†
	Efgartigimod IV (n=65)	Placebo (n=64)	Efgartigimod PH20 SC (n=141)
Age, mean (SD), years	44.7 (15.0)	49.2 (15.5)	51.0 (15.9)
Female, n (%)	46 (70.8)	40 (62.5)	90 (63.8)
MG-ADL total score, mean (SD)	9.0 (2.5)	8.6 (2.1)	7.6 (3.4)
MG-QoL15r total score, mean (SD)	15.7 (6.3)	16.6 (5.5)	13.1 (6.8)
Baseline EQ-5D-5L VAS score, mean (SE)	58.2 (17.4)	56.7 (17.1)	61.0 (18.6)
Concomitant MG therapy, n (%)			
Any steroid‡	46 (70.8)	51 (79.7)	103 (73.0)
Any NSIST§	40 (61.5)	37 (57.8)	67 (47.5)
Any AChEI‖	57 (87.7)	57 (89.1)	122 (86.5)
Steroid + NSIST¶	34 (52.3)	31 (48.4)	53 (37.6)
AChEI only	13 (20.0)	6 (9.4)	23 (16.3)

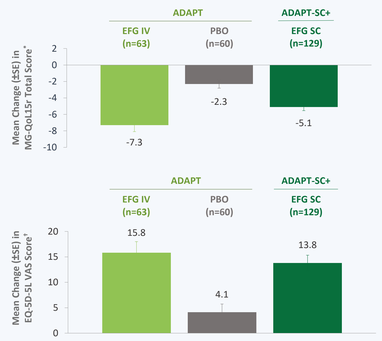
*Concomitant therapy received at a stable dosage during screening and throughout the study. †Concomitant therapy received during the first year of the study. ‡Deflazacort, hydrocortisone, methylprednisolone, methylprednisolone sodium succinate, prednisolone, prednisolone acetate and/or prednisone. §Azathioprine, ciclosporin, cyclophosphamide, methotrexate, mycophenolate and/or tacrolimus. ‖Ambenonium chloride, distigmine bromide, pyridostigmine and/or pyridostigmine bromide. ¶As dual or triple therapy, in combination with AChEI.

Efgartigimod Treatment Improved HRQoL During ADAPT and ADAPT-SC+

- In ADAPT, efgartigimod treatment led to improvements vs placebo in MG-QoL15r total score (**Figure 2A**) and EQ-5D-5L VAS score (**Figure 2B**) from baseline to Week 4 in cycle 1. Improvements in QoL were consistent in ADAPT-SC+

FIGURE 2 HRQoL Improvements at Week 4, Cycle 1

AChR-Ab+ Participants



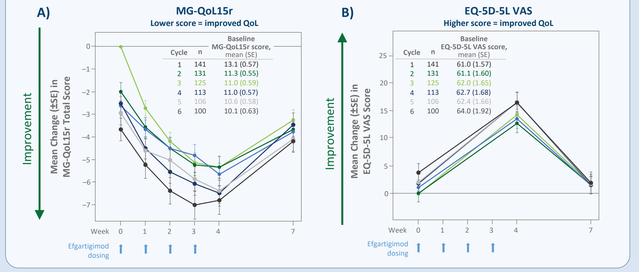
*Lower scores indicate better QoL. †Higher scores indicate better QoL.

Improvements in HRQoL Following Efgartigimod PH20 SC Treatment Were Consistent Across Multiple Cycles in ADAPT-SC+

- Efgartigimod PH20 SC treatment improved MG-QoL15r (**Figure 3A**) and EQ-5D-5L VAS scores (**Figure 3B**) from study baseline, with improvements in MG-QoL15r observed as early as one week after the first administration
- Baseline scores improved with subsequent cycles, indicating that participant HRQoL consistently improved as the duration of treatment increased
- In the efgartigimod arm, HRQoL measurements in ADAPT (measured only during cycles 1 and 2) demonstrated improvements consistent with those observed in ADAPT-SC+[8]

FIGURE 3 HRQoL Improvements Over Time in ADAPT-SC+

AChR-Ab+ Participants



- Efgartigimod was well tolerated across ADAPT and ADAPT-SC+, and most AEs were mild to moderate in severity (**Table 2**)

TABLE 2 Summary of AEs

Overall Population

	ADAPT				ADAPT-SC+	
	Efgartigimod IV (n=84; PYFU=34.9)		Placebo (n=83; PYFU=34.5)		Efgartigimod PH20 SC (N=179; PYFU=193.4)	
	ER*	Incidence, n (%)	ER*	Incidence, n (%)	ER*	Incidence, n (%)
Any AE	7.23	65 (77.4)	7.83	70 (84.3)	8.95	152 (84.9)
Any SAE	0.11	4 (4.8)	0.29	7 (8.4)	0.26	33 (18.4)
Any grade ≥3 AE	0.29	9 (10.7)	0.35	8 (9.6)	0.39	36 (20.1)
Any serious infection	-	0 (0)	0.03	1 (1.2)	0.02	4 (2.2)
Any infusion-related reaction event†	0.09	3 (3.6)	0.26	8 (9.6)	3.25	82 (45.8)
Fatal event‡	-	0 (0)	-	0 (0)	0.03	4 (2.2)
Discontinued study treatment due to AEs	0.20	3 (3.6)	0.09	3 (3.6)	0.03	4 (2.2)§
Most commonly observed AEs,‖						
Injection site erythema	-	-	-	-	1.73	52 (29.1)
COVID-19¶	-	-	-	-	0.24	40 (22.3)
Headache	1.15	24 (28.6)	1.13	23 (27.7)	0.63	36 (20.1)
Nasopharyngitis	0.34	10 (11.9)	0.49	15 (18.1)	0.19	28 (15.6)
Nausea	0.20	7 (8.3)	0.43	9 (10.8)	-	-
Diarrhea	0.17	6 (7.1)	0.41	9 (10.8)	0.18	24 (13.4)
Upper respiratory tract infection	0.32	9 (10.7)	0.14	4. (4.8)	-	-
Injection site pain	-	-	-	-	0.21	21 (11.7)
Injection site pruritus	-	-	-	-	0.24	19 (10.6)
Injection site bruising	-	-	-	-	0.24	18 (10.1)

*ER was calculated as number of events per total PYFU. †Injection site reaction in ADAPT-SC+ study. ‡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 discontinuation during ADAPT-SC+ (n=4) were due to participant fatality. ‖Most commonly observed AEs occurring in >10% of participants receiving efgartigimod IV or 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

Recent guidelines highlight preservation and restoration of QoL as an important treatment goal in gMG[10]

Efgartigimod treatment resulted in consistent and repeatable improvements in MG-QoL15r and EQ-5D-5L VAS total scores over multiple cycles in AChR-Ab+ participants, with improvements noted as early as the week after the first administration

Both IV (ADAPT) and SC (ADAPT-SC+) formulations of efgartigimod were well tolerated

Efgartigimod meets the HRQoL-related treatment goal set by recent gMG treatment guidelines by rapidly and consistently improving HRQoL, as quantified using validated, commonly used and recommended scales[10–13]

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; AChR-Ab+, acetylcholine receptor antibody-positive; AE, adverse event; EFG, efgartigimod; ER, event rate; EQ-5D-5L, EuroQol 5-Dimension, 5-Level; Fc, fragment crystallisable; FcRn, neonatal Fc receptor; gMG, generalised myasthenia gravis; HRQoL, health-related quality of life; Ig, immunoglobulin; 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; NSIST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PBO, placebo; PH20, recombinant human hyaluronidase PH20; PYFU, participant-year(s) of follow-up; QoL, quality of life; SAE, serious adverse event; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SC, subcutaneous; SD, standard deviation; SE, standard error; VAS, visual analogue scale.

DISCLOSURES AND ACKNOWLEDGEMENTS

FS: Agenzia Italiana del Farmaco, Alexion, Almirall, argenx, Dianthus, Friedrich's Ataxia Research Alliance, Genpharm, Immunovant, Leadiant Biosciences, Lexeo Therapeutics, Madison Pharma, Medpharma, Novartis, Prilenia, Reata, Sandoz, Sanofi, Zai Lab; **JLDB:** Alexion, Alnylam, argenx, CSL Behring, Janssen, Sanofi Genzyme, UCB; **KU:** Alexion, Amgen, argenx, Chugai, Janssen, Japan Blood Products Organisation, Mitsubishi Tanabe, UCB; **DK:** argenx, Amgen, BIOCAD, Bristol Myers Squibb, Janssen, Merck, Novartis Russia, Roche, Sanofi, UCB; **SS, BVH, RK and 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.

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