467

Design of a Phase 3 Randomized, Double-Blinded, Placebo-Controlled Study Evaluating the Efficacy and Safety of Subcutaneous Efgartigimod PH20 Administered by Prefilled Syringe in Adults With Ocular Myasthenia Gravis

Carolina Barnett-Tapia,[1] Carlo Antozzi,[2] James F. Howard, Jr,[3] Jeff Guptill,[4,5] Rosa Jimenez,[4] Fien Gistelinck,[4] Sophie Steeland,[4] Fien Verhamme,[4] Sui H. Wong[6]

[1]Division of Neurology, University of Toronto, Toronto, Ontario, Canada; [2]Immunotherapy and Apheresis Unit, Fondazione IRCCS Istituto Neurologico C. Besta, Milan, Italy; [3]The University of North Carolina, Chapel Hill, NC, USA; [4]argenx, Ghent, Belgium; [5]School of Medicine, Duke University, Durham, NC, USA; [6]Moorfields Eye Hospital, London, UK

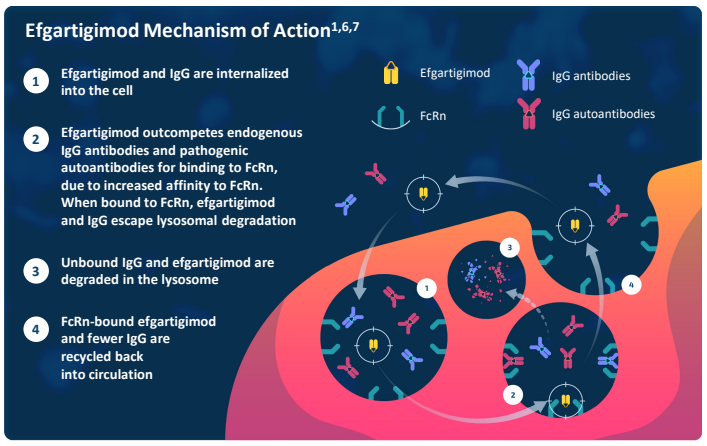
BACKGROUND | METHODS

- Efgartigimod is a human **IgG1 antibody Fc fragment** that has been engineered for **increased affinity to FcRn** compared to endogenous IgG and is **uniquely composed of the only part of the IgG antibody that normally binds FcRn**[1,2]
- By blocking FcRn, **efgartigimod selectively reduces IgG antibodies and pathogenic autoantibodies**, and does so **without**:[1,3–5]
  - Impacting antibody production (including other Ig antibodies) or other parts of the immune system
  - Decreasing albumin levels
  - Increasing LDL cholesterol levels

OBJECTIVE

To evaluate the efficacy and safety of SC efgartigimod coformulated with recombinant human hyaluronidase PH20 in participants with ocular myasthenia gravis

Efgartigimod Mechanism of Action[1,6,7]



- MG is a rare, chronic, neuromuscular autoimmune disease mediated by pathogenic IgGs that target components of the NMJ, resulting in reduced neuromuscular transmission and subsequent debilitating muscle weakness[8,9]
- MG can manifest as focal weakness, with ocular symptoms being the most common focal presentation, which can include fluctuating ptosis, diplopia, and eye closure weakness with intact pupillary reflexes[10-12]
- Of patients with MG who initially presented with ocular symptoms (either ptosis or diplopia), up to 80% subsequently developed gMG[10]
- Anti-AChR antibodies are found in 40% to 77% of patients with oMG[13]
- Treatments for patients with oMG predominantly consist of off-label drug use, and efficacy has not been proven for immunosuppressive treatments such as corticosteroids and NSISTs[14,15]

STUDY DESIGN

INCLUSION CRITERIA

- Adult participants diagnosed with MG with consistent clinical features and confirmed by documentation and supported by:

Seropositivity for AChR-Ab **OR** (Abnormal neuromuscular transmission (historical or during screening) **AND** History of positive edrophonium chloride test[a] or demonstrated improvement in MG signs[b])

- MGFA class I
- MGII (PRO) ocular score ≥6 with at least 2 ocular items with a score of ≥2 at screening and baseline
- On a stable dose of MG therapy prior to screening (AChEI, CS, NSISTs; alone or in combination)
- Symptom onset <3 years before screening[c]
- No pupillary abnormality other than that from previous local disease or surgery

[a]Evidenced by improvement in ptosis or diplopia. [b]Demonstrated improvement in MG signs with treatment such as oral AChEIs, PLEX, IVIg, or CS. [c]Unless evidence of MRI without fatty replacement in extraocular muscles or demonstrated response to treatment in the past year (ie, improvement in ≥1 oMG sign based on investigator judgment after treatment with IVIg, PLEX, pyridostigmine, and/or steroids).

EXCLUSION CRITERIA

- Presence of other autoimmune diseases that would interfere with an accurate assessment of clinical symptoms of oMG
- History of malignancy[a]
- Clinically significant active infection
- Total IgG levels <4 g/L at screening
- Clinically significant disease, recent major surgery (within 3 months of screening), or intention to have surgery during the study; or any other medical condition that would confound the results of the study or put the participant at undue risk in the investigator's opinion
- Other diseases that lead to eyelid drooping, peripheral muscle weakness, or diplopia
- Received a thymectomy <3 months before screening or thymectomy planned during study

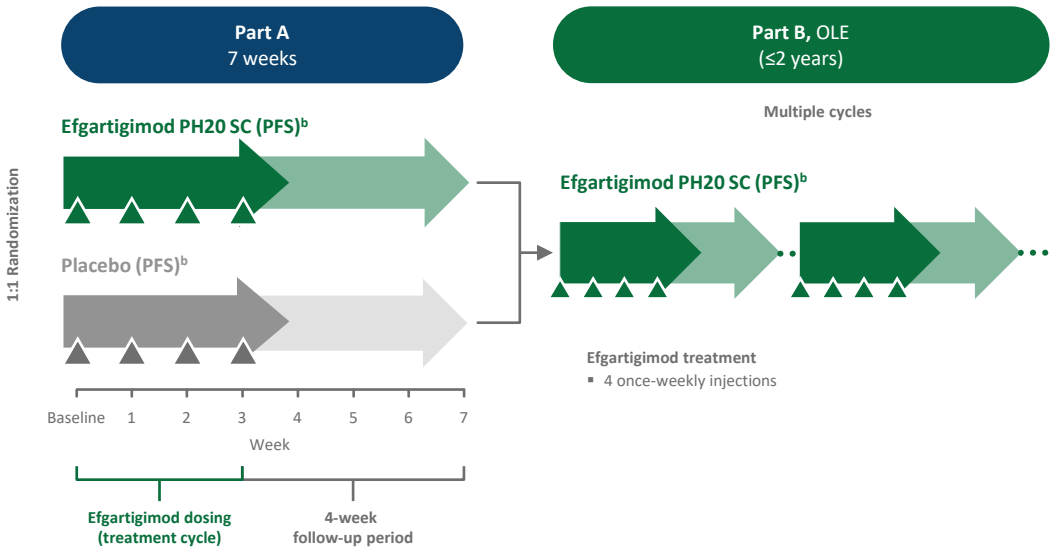
[a]Unless cancers were cured by adequate treatment with no evidence of recurrence for ≥3 years before the first dose of treatment. Adequately treated participants with basal cell or squamous cell skin cancer, carcinoma in situ of the cervix, carcinoma in situ of the breast, or incidental histological findings of prostate cancer (TNM stage T1a or T1b) can be included at any time.

ADAPT OCULUS (ARGX-113-2315) TRIAL DESIGN

Phase 3, Randomized, Double-Blinded, Placebo-Controlled, Parallel-Group Trial With Efgartigimod PH20 SC in oMG

adapt Oculus myasthenia gravis study

Total anticipated enrollment:
Approximately 124 oMG participants with confirmed diagnosis
Reviewed by MG Diagnostic Adjudication Committee[a]



[a]AChR-Ab seropositive participants do not have to be reviewed by the adjudication committee. [b]Triangles indicate efgartigimod or placebo administration.

PRIMARY ENDPOINT

MGII (PRO) ocular score change from baseline to Day 29 in part A

SECONDARY ENDPOINTS

Key Secondary Endpoints (Hierarchical Testing)

- MGII (PRO+PE) ocular score change from baseline to Day 29 in part A
- MG-ADL ocular domain score change from baseline to Day 29 in part A
- MGII total score change from baseline to Day 29 in part A

Other Secondary Endpoints

- MGII ocular scores (PRO, PRO+PE, and PE), generalized score, and total score; actual values and changes from baseline in part A and parts A+B
- MG-ADL total score, ocular domain score, and generalized domain score; actual values and changes from baseline in part A and parts A+B
- Incidence and severity of AEs and SAEs in part A and parts A+B
- Clinically relevant changes in laboratory parameters, vital signs, and ECGs in part A and parts A+B
- MG-QoL15r total score actual values and changes from baseline in part A and parts A+B
- NEI VFQ-25 total score actual values and changes from baseline in part A and parts A+B
- Actual values and percent changes from baseline in total IgG levels over time in part A and parts A+B
- Actual values and percent change from baseline in AChR-Ab levels in AChR-Ab seropositive participants over time in part A and parts A+B

KEY TAKEAWAYS

ADAPT OCULUS is a randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of SC efgartigimod coformulated with recombinant human hyaluronidase PH20 in oMG

This phase 3 trial will provide important data on the efficacy and safety of efgartigimod PH20 SC prefilled syringe in the treatment of oMG, including patients early in their disease course

Recruitment is ongoing

Estimated primary completion date: Q4 2025

PRESENTED AT THE 55TH CONGRESS OF THE ITALIAN SOCIETY OF NEUROLOGY (SIN); OCTOBER 24–28, 2025; PADUA, ITALY

ABBREVIATIONS

Ab, antibody; **AChEI**, acetylcholinesterase inhibitor; **AChR**, acetylcholine receptor; **AE**, adverse event; **CS**, corticosteroids; **ECG**, electrocardiogram; **Fc**, fragment crystallizable region; **FcRn**, neonatal Fc receptor; **gMG**, generalized myasthenia gravis; **Ig**, immunoglobulin; **IgG**, immunoglobulin G; **IV**, intravenous; **IVIg**, intravenous immunoglobulin; **LDL**, low-density lipoprotein; **MG**, myasthenia gravis; **MG-ADL**, Myasthenia Gravis Activities of Daily Living; **MGFA**, Myasthenia Gravis Foundation of America; **MGII**, myasthenia gravis impairment index; **MG-QoL15r**, Myasthenia Gravis Quality of Life 15-Item Questionnaire, Revised; **MRI**, magnetic resonance imaging; **NEI VFQ-25**, 25-item National Eye Institute Visual Function Questionnaire; **NMJ**, neuromuscular junction; **NSIST**, nonsteroidal immunosuppressive therapy; **OLE**, open-label extension; **oMG**, ocular myasthenia gravis; **PD**, pharmacodynamics; **PE**, physical examination; **PFS**, prefilled syringe; **PK**, pharmacokinetics; **PLEX**, plasma exchange; **PRO**, patient-reported outcome; **SAE**, serious adverse event; **SC**, subcutaneous; **TNM**, tumor, necrosis, metastasis.

DISCLOSURES AND ACKNOWLEDGMENTS

The authors gratefully acknowledge the clinicians, patient organizations, and scientists who have collaborated on the design of this trial.

CB-T: Consultant and advisory board participation from Argenx, Alexion, Janssen, and UCB; **CA:** Funding for travel, meeting attendance, and advisory board participation from Alexion, Amgen, argenx, Janssen, Johnson & Johnson, Momenta, UCB; **JFH:** Academic CME, Ad Scientiam, Alexion AstraZeneca Rare Disease, Amgen, argenx, Biohaven Ltd, Biologix, Cartesian Therapeutics, Centers for Disease Control and Prevention, CheckRare CME, CoreEvitas, Curie.bio, Hansa Biopharma, Medscape CME, Merck EMB Serono, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, Novartis, PCORI, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, Teleranzia AB, UCB; **JG:** argenx; **RJ, FG, SS, and FV:** Employees of argenx; **SHW:** Visual Snow Initiative, myaware, MGFA, argenx, and Immunovant. Formatting and editing assistance was provided by Envision Ignite, an Envision Medical Communications Agency, part of Envision Pharma Group, funded by argenx. Previously presented at the American Academy of Neurology (AAN) Annual Meeting 2025; San Diego, CA, USA.

REFERENCES

1. Ulrichts P, et al. *J Clin Invest*. 2018;128:4372–86. **2.** Vaccaro C, et al. *Nat Biotechnol*. 2005;23:1283–8. **3.** Howard JF, Jr., et al. *Lancet Neurol*. 2021;20:526–36 **4.** Guptill JT, et al. *Autoimmunity*. 2022;55:620–31. **5.** argenx, data on file. **6.** Roopenian DC, Akilesh S. *Nat Rev Immunol*. 2007;7:715–25. **7.** Ward ES, Ober RJ. *Trends Pharmacol Sci*. 2018;39:892–904. **8.** Behin A, Le Panse R. *J Neuromuscul Dis*. 2018;5:265–77. **9.** Lazaridis K, Tzartos SJ. *Front Immunol*. 2020;11:1–13. **10.** Grob D, et al. *Muscle Nerve*. 2008;37:141–9. **11.** Jayam TA, et al. *Autoimmune Dis*. 2012;2012:874680. **12.** Evoli A, Iorio R. *Front Neurol*. 2020;11:605902. **13.** Nair AG, et al. *Indian J Ophthalmol*. 2014;62:985–91. **14.** Behbehani R. *Eye Brain*. 2023;15:1–13. **15.** Benatar M, et al. *Muscle Nerve*. 2012;45:909–17.