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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

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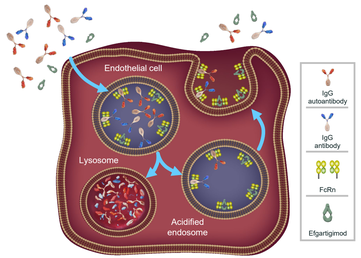
INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG antibodies and albumin. This recycling and salvage from lysosomal degradation results in IgG antibodies having the longest half-life and being the most abundant of all immunoglobulins[1-3]
- Efgartigimod is an IgG1 antibody Fc fragment that has been engineered for increased affinity to FcRn, and is uniquely composed of the only part of the IgG antibody that normally binds FcRn[1]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production, albumin levels, or other parts of the immune system[1,4,5]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[6,7]
- PK/PD modeling and phase 3 data (ADAPT-SC) have demonstrated that 4 once-weekly administrations of 1000 mg efgartigimod PH20 SC and 10 mg/kg efgartigimod IV result in comparable decreases in IgG levels[6,8]

RATIONALE

- 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[9,10]
- 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[11-13]
- Of patients with MG who initially presented with ocular symptoms (either ptosis or diplopia), up to 80% subsequently developed gMG[11]
- Anti-AChR antibodies are found in 40% to 77% of patients with oMG[14]
- Treatment 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[15,16]

OBJECTIVE To evaluate the efficacy and safety of subcutaneous (SC) efgartigimod coformulated with recombinant human hyaluronidase PH20 in participants with oMG

SUMMARY

ADAPT OCULUS is a randomized, double-blind, placebo-controlled study evaluating the efficacy and safety of subcutaneous (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**

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

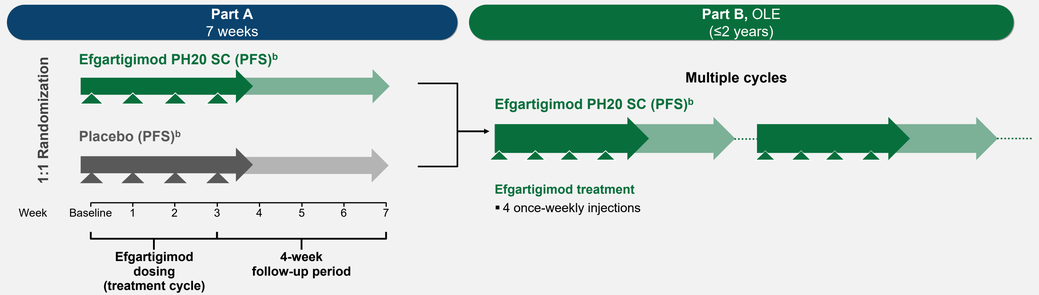
[a]Unless cancers were cured by adequate treatment with no evidence of recurrence for ≥3 years before the first dose of treatment. Adequately treated participants with basal cell or squamous cell skin cancer, carcinoma in situ of the cervix, carcinoma in situ of the breast, or incidental histological 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.

ENDPOINTS

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

ABBREVIATIONS
Ab, antibody; AChEI, acetylcholinesterase inhibitor; AChR, acetylcholine receptor; AE, adverse event; CS, corticosteroids; ECG, electrocardiogram; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; Ig, immunoglobulin; IVIg, intravenous immunoglobulin; 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; NAb, neutralizing antibodies; 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.

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