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Study Design of Subcutaneous Efgartigimod PH20 in Juvenile Generalized Myasthenia Gravis

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INTRODUCTION

- Efgartigimod is an 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]
- Efgartigimod selectively reduces IgG by blocking FcRn-mediated IgG recycling without impacting antibody production or other parts of the immune system, and does not decrease albumin[1-3]
- Efgartigimod PH20 SC is a coformulation of efgartigimod and recombinant human hyaluronidase PH20 (rHuPH20), which allows for rapid SC administration of larger volumes[4,5]

Efgartigimod Mechanism of Action: Blocking FcRn

1. Efgartigimod and IgG are internalized[1,6]
2. Efgartigimod competes with endogenous IgG for binding to FcRn[1]
3. Unbound IgG enters the lysosomal degradation pathway[1,6]
4. Efgartigimod and fewer IgGs are recycled back into the bloodstream[1]

RATIONALE

- The incidence of juvenile gMG (1-5:1,000,000) is considerably lower than adult gMG[7]
- There remains an unmet need for effective and safe treatments in this population[8]
- A clinical trial assessing efgartigimod IV in juvenile gMG (NCT04833894) is currently underway[9]

OBJECTIVE

To confirm the age-appropriate dose of subcutaneous efgartigimod coformulated with recombinant hyaluronidase (efgartigimod PH20 SC)

SUMMARY

ADAPT JR SC is an open-label, single-arm, uncontrolled, multicenter study

This is the first trial evaluating efgartigimod PH20 SC in pediatric patients

This trial will provide important data on the dosing, efficacy, and safety of efgartigimod PH20 SC in pediatric patients with gMG

Recruitment is ongoing

Estimated primary completion date: Fall 2026

DESIGN

INCLUSION CRITERIA

- Aged 2 to <18 years at the time of informed consent/assent
- Diagnosed with gMG supported by physical examination and confirmed seropositivity for AChR-Ab
- Unsatisfactory response to immunosuppressants, corticosteroids, or AChEI
- On a stable concomitant MG therapy (must be on stable dose ≥1 month if on corticosteroids or immunosuppressants)

EXCLUSION CRITERIA

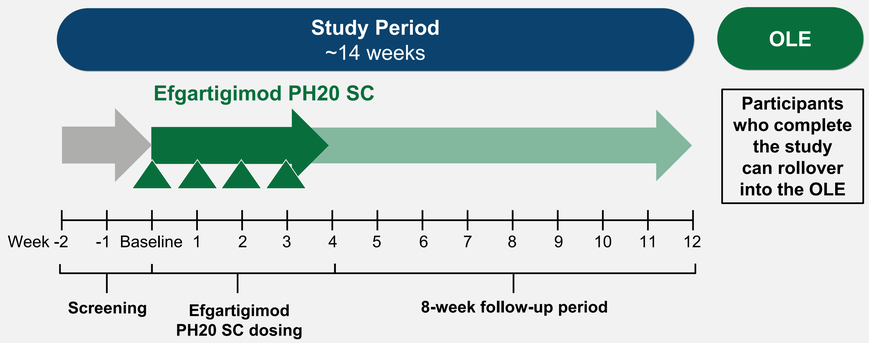
- MGFA class I, IVb, or V
- Worsening muscle weakness secondary to a concurrent infection or medication
- Documented lack of clinical response to PLEX
- Received a live or live-attenuated vaccine within <4 weeks before screening
- Thymectomy 3 months before screening or is planning to get a thymectomy during trial period
- Autoimmune disease or medical condition that would interfere with an accurate assessment of clinical symptoms or puts the participant at undue risk
- Clinically significant active infection or positive screening test for: HBV, HCV, HIV, or SARS-CoV-2
- Has laboratory abnormalities (eg LFTs, hemoglobin, eGFR)
- IgG below normal limit based on sex/age
- Has previously received efgartigimod while enrolled in a clinical study
- Has received IVIg, SCIg, or PLEX within <2 weeks, rituximab within 6 months, eculizumab within 1 month, or MAb within 5 half-lives before screening, or is participating in another study

ADAPT JR SC (ARGX-113-2207) TRIAL DESIGN

An Open-Label, Single-Arm, Uncontrolled, Multicenter Study

adapt JR.SC myasthenia gravis study

Total anticipated enrollment:
N≥12 total
n≈6 aged 12 to <18 years
n≈6 aged 2 to <12 years



ENDPOINTS

PRIMARY OUTCOME MEASURES

PK/PD parameters, including efgartigimod serum concentrations, total IgG levels, and AChR-Ab levels

SECONDARY OUTCOME MEASURES

Safety
- Incidence and severity of AEs, SAEs, injection site reactions
- Laboratory tests, vital signs, body weight, ECG parameters
- Prevalence of anti-drug antibodies against efgartigimod and rHuPH20

PK/PD
- Efgartigimod serum concentrations
- Serum AChR-Ab and total IgG

Antibody Response to Vaccinations
- Changes in protective antibody titers to vaccines

Age-Adjusted Efficacy Assessments
- MG-ADL[a] total score
- QMG[b] total score
- EQ-5D-Y[c] total score
- Neuro-QoL PF[c] score
- CGI-I change from baseline

[a]For participants <12 years of age, caregiver assistance can be provided during the MG-ADL assessment. The MG-ADL should not be performed for participants <6 years of age; instead, a dedicated neurological assessment should be performed; [b]Participants aged ≥12 at screening will be administered the traditional QMG version, while a modified version of the QMG will be administered for participants <12 years at screening. The modified version omits the grip strength assessment and modifies the swallowing assessment (slurp test) with total scores ranging from 0 to 21; the QMG assessment should not be performed on participants <6 years of age. [c]The assessment will be completed by the caregiver or with caregiver assistance for participants <12 years of age, and the proxy version will be used to evaluate participants <8 years of age.

ABBREVIATIONS

AChEI, AChEI, acetylcholinesterase inhibitor; AChR-Ab, acetylcholine receptor autoantibodies; AE, adverse event; CGI-I, Clinical Global Impression of Improvement; ECG, electrocardiogram; eFGR, estimated glomerular filtration rate; EQ-5D-Y, EuroQoL 5-Dimension Youth; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; Ig, immunoglobulin; IV, intravenous; IVIg, intravenous immunoglobulin; LFT, liver function test; MAb, monoclonal antibody; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; Neuro-QoL-PF, Quality of Life in Neurological Disorders Questionnaire – Pediatric Fatigue (score); OLE, open-label extension; PD, pharmacodynamics; PK, pharmacokinetics; PLEX, plasma exchange; QMG, Quantitative Myasthenia Gravis (scale); QW, once weekly; rHuPH20, recombinant human hyaluronidase PH20; SAE, serious adverse event; SARS-CoV-2; severe acute respiratory syndrome coronavirus 2; SC, subcutaneous; SCIg, subcutaneous immunoglobulin.

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