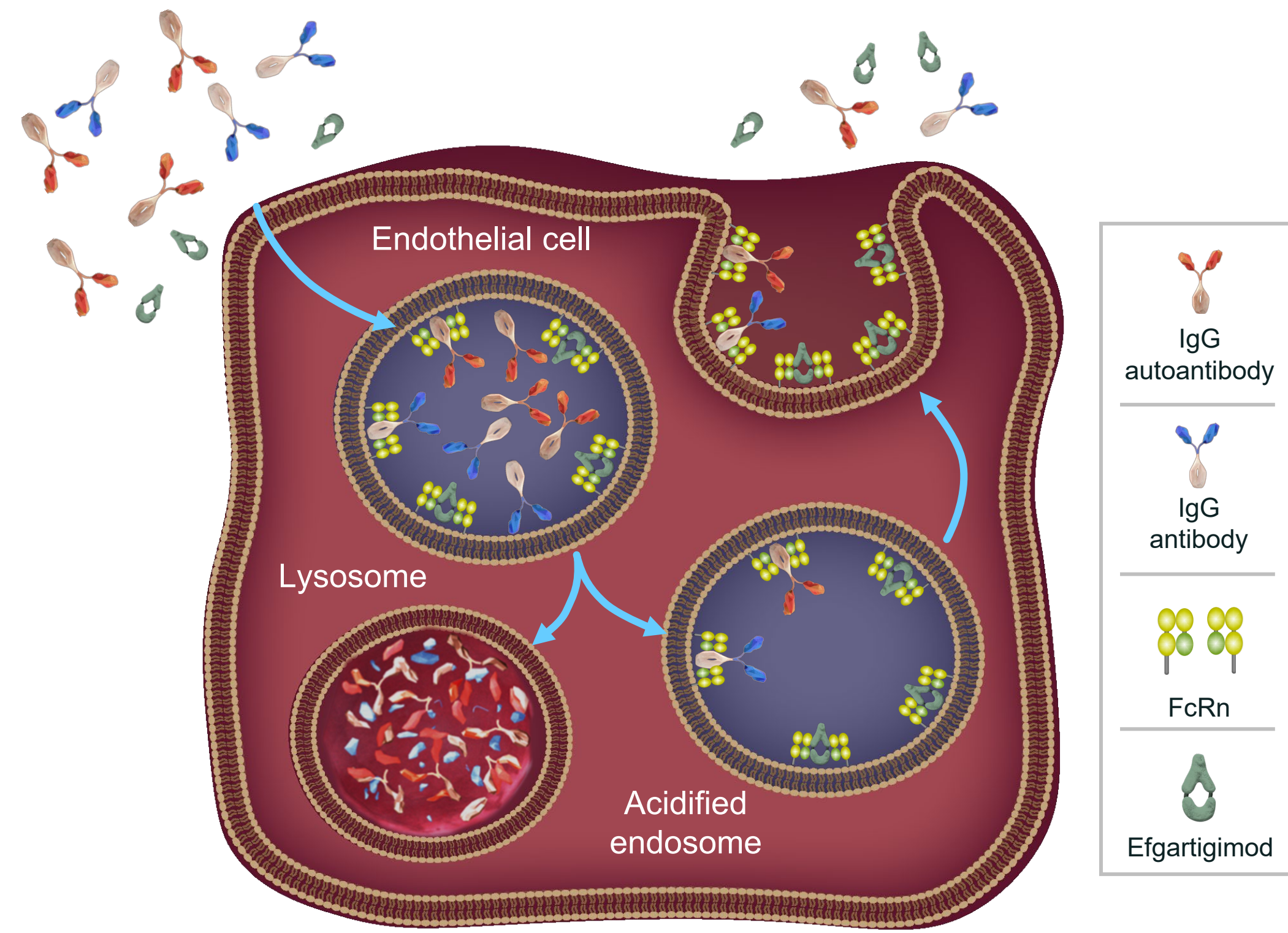




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INTRODUCTION

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 immunoglobulins¹⁻³
- Blocking FcRn to selectively reduce IgG levels is therefore a rational therapeutic approach in patients with IgG-mediated autoimmune diseases^{1,2}
- 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 FcRn¹
- 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 prevents IgG recycling by blocking IgG antibodies from binding to FcRn, with unbound IgG antibodies being degraded^{1,4}

SUMMARY

- ✓ **ADAPT SERON is a randomized, double-blinded, placebo-controlled, phase 3, parallel-group trial evaluating efgartigimod IV in AChR-Ab- gMG**
- 👤 **Participants will all have confirmed acquired gMG based on review of an MG Diagnostic Adjudication Committee**
- 📋 **This phase 3 trial will provide important data on the efficacy and safety of efgartigimod IV in the treatment of AChR-Ab- gMG**
- 🔄 **Recruitment is ongoing**
- 📅 **Estimated primary completion date: Summer 2025**

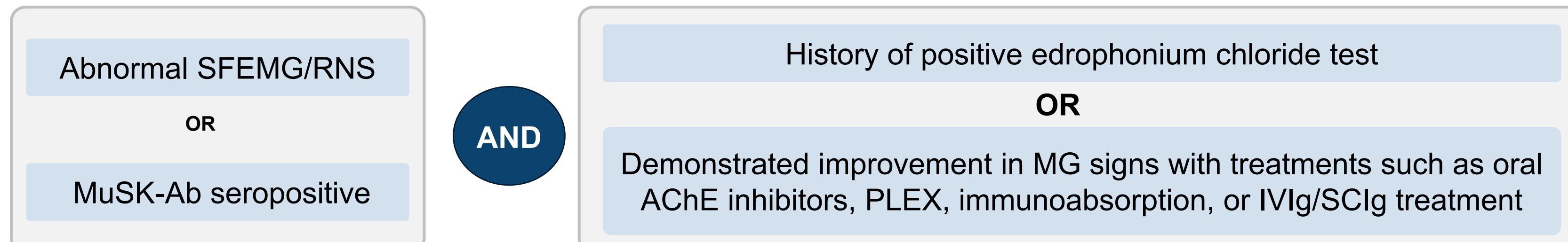
RATIONALE

- gMG is a rare, chronic, neuromuscular autoimmune disease caused by pathogenic IgGs targeting the neuromuscular junction, resulting in impaired neuromuscular transmission and debilitating and potentially life-threatening muscle weakness and chronic fatigue⁶
- Approximately 15% of patients with gMG do not have antibodies directed against AChR, which is referred to as AChR-Ab- gMG⁷
- The AChR-Ab- gMG population is heterogeneous and includes patients with autoantibodies targeting other components of the neuromuscular junction, including MuSK and LRP4⁸
 - MuSK and LRP4 autoantibodies have been detected in ≈5%, and ≈1%-5% of patients with gMG, respectively, while ≈10% of patients have no identifiable autoantibodies^{6,7,9,10}
 - In all known subgroups of acquired AChR-Ab- gMG, the disease is considered IgG mediated⁷
- Treatment for patients with AChR-Ab- gMG predominantly consists of off-label drug use and efficacy has not been proven for immunosuppressive treatments such as corticosteroids and NSiSTs^{11,12}
- Patients with AChR-Ab- gMG are often either excluded from clinical trials or represent a small subpopulation of the enrolled population, which limits the ability to draw conclusions¹³⁻¹⁷
- Recent evidence suggests clinical outcomes for patients with AChR-Ab- gMG treated with currently available treatments are worse than for patients with AChR-Ab+ gMG^{18,19}

DESIGN

INCLUSION CRITERIA

- Has no known weakness in infancy and develops fatigable weakness ≥ age 16
- Confirmed diagnosis of acquired gMG that meets one of the criteria in both of the following:



- AChR-Ab seronegative at screening (MuSK-Ab+/LRP4-Ab+ allowed)
- MGFA Class II, III, or IV
- MG-ADL total score ≥5 (>50% nonocular)
- Stable dose of gMG therapy prior to screening^{a-c}

^aNSiSTs initiated ≥6 months before screening with no change in dose during the 3 months before screening.
^bSteroids initiated ≥3 months before screening, with no change in dose during the month before screening.
^cAChEi with no change in dose during the 2 weeks before screening.

EXCLUSION CRITERIA

- Total IgG <4 g/L at screening
- Use of IVIg, SCiG, or intramuscular Ig within 4 weeks, any other investigational product within 3 months or 5 half-lives, monoclonal antibody within 6 months (eculizumab within 3 months), PLEX within 4 weeks, anti-CD20 or anti-CD19 antibody within 6 months, prior treatment with any CAR T-cell therapy or IL-6(R) inhibitor, prior treatment with an FcRn inhibitor
- Received a live or live-attenuated vaccine <4 weeks before screening
- History of malignancy
 - Adequately treated basal cell or squamous cell skin cancer, carcinoma *in situ* of the cervix or breast, or incidental histological findings of stage T1a or T1b prostate cancer are allowed
- Received a thymectomy <3 months before screening or thymectomy planned during study
- Active infection
- Documented lack of clinical response to PLEX
- Severe renal impairment with eGFR <30 mL/min/1.73 m² at screening

ENDPOINTS

PRIMARY ENDPOINT

MG-ADL total score change from baseline to Day 29 (Week 4) in part A

SECONDARY ENDPOINTS

Key Secondary Endpoints

- QMG total score change from baseline to Day 29 (Week 4) in part A
- Proportion of participants who are both MG-ADL and QMG responders^{a,b} in part A

Other Secondary Endpoints

- Proportion of participants with MSE (defined as an MG-ADL total score of 0 or 1)
- Proportion of participants who are MG-ADL responders^a or QMG responders^b
- Proportion of participants who are early MG-ADL responders^c
- MG-ADL and QMG total score actual value and change from baseline over time
- MG-QoL15r score change from baseline to Day 29 (Week 4) in part A
- MG-QoL15r and EQ-5D-5L VAS actual values and change from baseline over time
- Incidence and severity of adverse events, serious adverse events, laboratory test results, vital signs, and electrocardiogram results
- Total IgG concentration actual values and percent changes from baseline over time

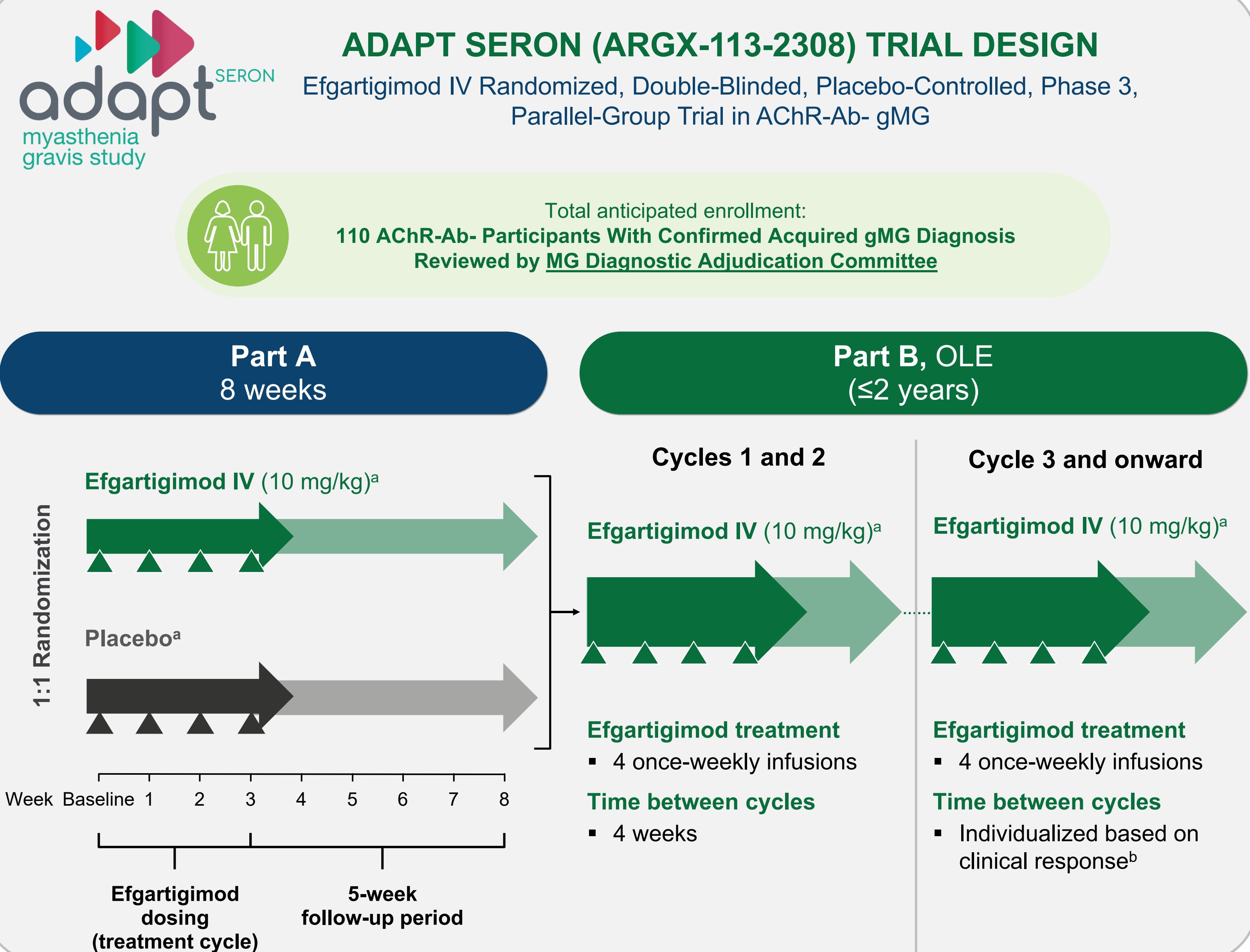
^aMG-ADL responder is defined as a participant achieving ≥2-point reduction in the MG-ADL total score compared to baseline that is maintained for the next 4 consecutive weeks, with the first reduction occurring no later than 1 week after the last administration of IMP in part A. ^bQMG responder is defined as a participant achieving ≥3-point reduction in the QMG score compared to baseline and maintained for the next 4 consecutive weeks, with the first reduction occurring no later than 1 week after the last administration of IMP in part A. ^cEarly MG-ADL responder is defined as a participant having onset of MG-ADL response no later than 2 weeks after the first administration of IMP in part A.

OBJECTIVE

To determine the efficacy and safety of 10 mg/kg IV efgartigimod compared with placebo in AChR-Ab- participants with gMG

ADAPT SERON (ARGX-113-2308) TRIAL DESIGN

Efgartigimod IV Randomized, Double-Blinded, Placebo-Controlled, Phase 3, Parallel-Group Trial in AChR-Ab- gMG



^aTriangles indicate efgartigimod or placebo administration. ^bTime between cycles will be no shorter than 7 days since previous efgartigimod IV infusion.

Scan here for more information on the ADAPT SERON website



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ABBREVIATIONS
 AChEi, acetylcholinesterase inhibitor; AChR, acetylcholine receptor; AChR-Ab, acetylcholine receptor antibody; CAR, chimeric antigen receptor; eGFR, estimated glomerular filtration rate; EQ-5D-5L VAS, EuroQol 5-Dimension 5-Level Visual Analog Scale; Fc, fragment crystallizable region; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; Ig, immunoglobulin; IL6(R), interleukin 6 receptor; IMP, investigational medicinal product; IV, intravenous; IVIg, intravenous Ig; LRP4, low-density lipoprotein receptor-related protein 4; LRP4-Ab+, low-density lipoprotein receptor-related protein 4 antibody positive; 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; MSE, minimal symptom expression; MuSK, muscle-specific tyrosine kinase; MuSK-Ab, muscle-specific tyrosine kinase antibody; NSiST, nonsteroidal immunosuppressive therapy; OLE, open-label extension; PLEX, plasma exchange; QMG, Quantitative Myasthenia Gravis; RNS, repetitive nerve stimulation; SCiG, subcutaneous Ig; SFEMG, single-fiber electromyography.

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