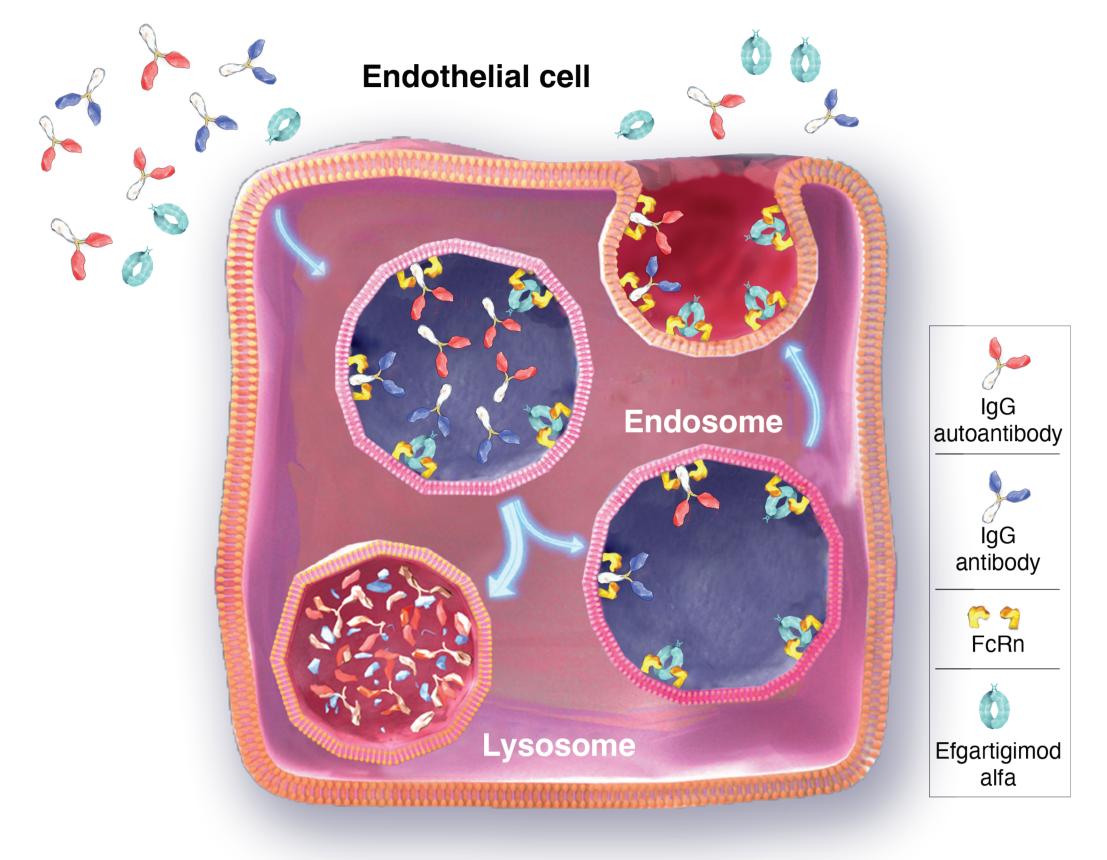


Study Design of Intravenous Efgartigimod in Children With Generalized Myasthenia Gravis

¹Division of Neurology, Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Illinois, USA; Peinberg School of Medicine, Chicago, Illinois, USA; Peinberg School o

INTRODUCTION

Efgartigimod Mechanism of Action: Blocking FcRn



- FcRn recycles IgG, extending its half-life and maintaining its serum
- Efgartigimod is a human IgG1 Fc fragment, a natural ligand of FcRn, engineered for increased affinity to FcRn²
- Efgartigimod was designed to outcompete endogenous IgG, preventing recycling and promoting lysosomal degradation of IgG²⁻⁵
- Targeted reduction of all IgG subclasses
- No impact on immunoglobulins M or A
- No reduction in albumin levels
- No increase in cholesterol
- No impact on IgG production or ability to mount an immune response

Nancy L. Kuntz,¹ Abigail Schwaede,¹ Anna Bogatyreva,² Jana Podhorna,² Sophie Steeland,² Tonke Van Bragt,² Benjamin Van Hoorick,² Antonio Guglietta,² James F. Howard Jr³

Generalized Myasthenia Gravis in Children: an IgG-Mediated Autoimmune Disease^{4,6}

- gMG is a rare, chronic, neuromuscular autoimmune disease mediated by pathogenic IgG autoantibodies that cause debilitating and potentially life-threatening muscle weakness⁴
- IgG autoantibodies against AChR have been identified in children with gMG (50%–71% in prepuberty, 68%–92% after puberty)⁶
- IgG autoantibodies are directly pathogenic in gMG, causing failure of neuromuscular transmission by targeting receptors and proteins of the neuromuscular junction⁴
- The medical need for effective and safe treatments for gMG in children remains high, owing to the limited options and lack of studies focusing on this age group⁶

Efgartigimod Has Been Shown to Effectively Reduce IgG Antibodies in Clinical Studies in Adults⁴

In the phase 3 trial (ADAPT Trial, NCT03669588, n=167) IV infusion of 10 mg/kg efgartigimod in a treatment cycle of 4 weekly infusions demonstrated clinical efficacy compared with placebo and was generally well tolerated in AChR-Ab+ patients⁴:

MG-ADL responders in cycle 1: 68% vs 30% placebo (P<.0001)



Efgartigimod (68%) Placebo Efgartigimod (63%)



KEY ELIGIBILITY CRITERIA

Inclusion criteria

- Patients aged 2 to <18 years (12 to <18 years in the US)
- Confirmed diagnosis of gMG, MGFA disease class II, III, IVa with the presence of AChR-Ab
- On stable concomitant gMG therapy of adequate duration before screening and documented unsatisfactory response (efficacy and/or safety) to immunosuppressants, steroids, or acetylcholinesterase

Exclusion criteria

- Confirmed diagnosis of MGFA disease class I, IVb, and V
- Active or chronic infection at screening
- History of malignancy^a
- Received a live or live-attenuated vaccine <28 days before screening
- Received a thymectomy <3 months before screening or performed during the trial period • Use of an investigational product within 3 months or 5 half-lives, monoclonal antibody within
- 6 months of first efgartigimod dose, or IVIg or plasma exchange within 4 weeks before
- Total IgG levels below the lower limit of normal for age and sex

^aParticipants may be included if they have adequately treated basal cell or squamous cell cancer, carcinoma in situ of the cervix or breast, or incidental histological findings of prostate cancer.

ABBREVIATIONS

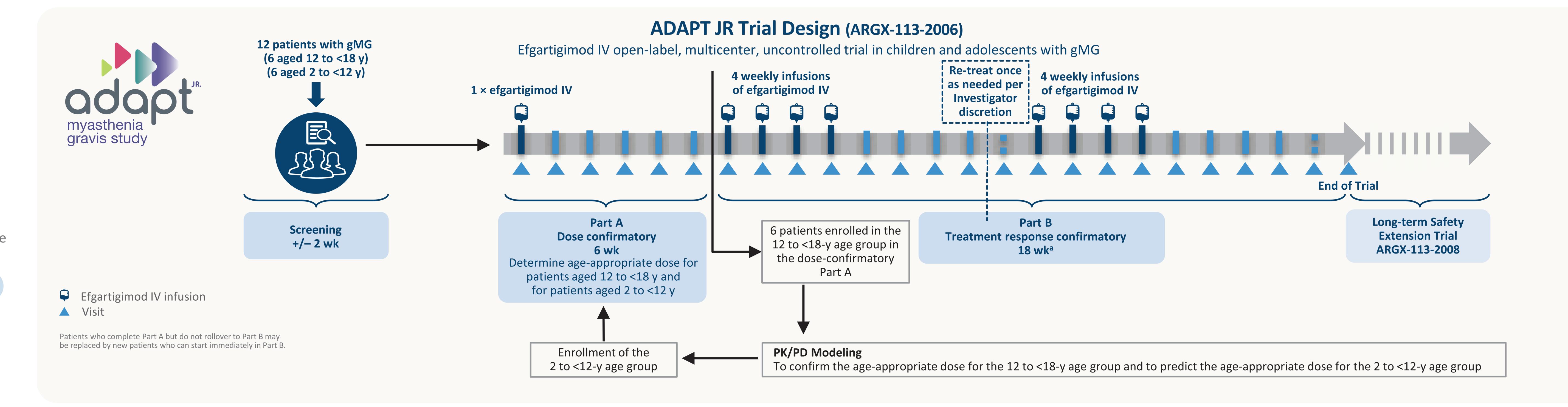
Ab, antibody; AChR, acetylcholine receptor; AChR antibody; AE, adverse event; EQ-5D-Y, EuroQoL 5-dimension QoL instrument for youth; FcRn, neonatal Fc receptor; gMG, generalized myasthenia Gravis; QMG, Quantitative Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; gMG, generalized myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, neonatal Fc receptor; activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; FcRn, activities of Daily Living; MGFA, Myasthenia Gravis; QoL, quality of life. Instrument for youth; PcRn, activities of Daily Living; MGFA, acti **REFERENCES**

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DESIGN

• The primary aim of this study is to confirm the age-appropriate dose of intravenous efgartigimod and provide (model-predicted) evidence for the treatment response



Primary Endpoints

Safety, tolerability, and

antidrug antibodies

during the study

immunogenicity based on:

Incidence and severity of AEs

Incidence and prevalence of

Change in protective Ab titers to

vaccines received prior to or

Pharmacokinetics

- Efgartigimod concentrations as input for PK/PD modeling analysis including:
- Clearance

Secondary and Additional Endpoints

Volume of distribution

Pharmacodynamics

- PD parameters as input for PK/PD modeling analysis:
- Total IgG levels
- Anti-AChR-Ab levels

Additional PK and PD

Serum levels of efgartigimod

Change from baseline in IgG

and anti-AChR-Ab levels

SUMMARY

Open-label, uncontrolled trial to evaluate PK, PD, safety, and clinical response of efgartigimod in children aged 2 to <18 years with gMG

ADAPT JR will determine age-appropriate dosing and safety of efgartigimod and provide evidence for the treatment response in children and adolescents aged 2 to <18 years with gMG



Recruitment is ongoing for 2- to <12-year age group

6 patients aged 12 to <18 years are already participating in the study



Efficacy (age-dependent) based on:

QoL and fatigue: EQ-5D-Y and

NeuroQoL Pediatric Fatigue Score

Detailed neurological assessment:

Daily function: MG-ADL

Strength: QMG

in children <6 y