Efficacy and Safety of Nipocalimab vs Efgartigimod in a Randomized, Open-Label, Phase 3b, Interventional Trial Including Within Class Switching from Efgartigimod to Nipocalimab (EPIC): Study Design

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This plain language summary infographic was prepared from a poster presented at the 2025 American Association of Neuromuscular & Electrodiagnostic Medicine Annual Meeting

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For more information on this study, go to: https://clinicaltrials.gov/study/NCT07217587

EPIC
A Myasthenia Gravis study

WHAT IS MYASTHENIA GRAVIS (MG)?

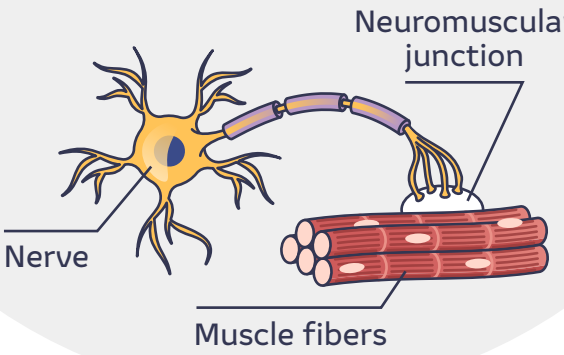
A rare, chronic autoimmune disease affecting **700,000** people worldwide[1]

Symptoms often start as **eye-related** (i.e., droopy eyelids, double vision)[1]

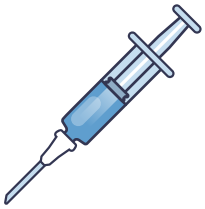
Often **progressing to other muscles** used for **talking**, **chewing**, and even **breathing**[1]

MG affecting **multiple muscle groups** across the body is referred to as **generalized MG (gMG)**[2]

In MG, the body's **immune system mistakenly attacks** its own **muscles at the neuromuscular junction**, leading to **muscle weakness** that worsens with activity and improves with rest[1,3]



Conventional therapies for gMG include **acetylcholinesterase inhibitors** to temporarily increase muscle strength and **immunosuppressants** to slow down the activity of the entire immune system



More advanced treatments include **therapeutic agents that target only specific parts of the immune system** directly related to gMG[4]

WHAT ARE NIPOCALIMAB AND EFGARTIGIMOD?

Nipocalimab **Efgartigimod** } **FDA-approved treatments** for gMG[5,6]

They work by targeting a specific part of the immune system called the **neonatal Fc receptor (FcRn)** to reduce the harmful **immunoglobulin G (IgG)** antibodies that impair the neuromuscular junction and lead to muscle weakness associated with gMG[7–9]

Although **nipocalimab** and **efgartigimod** are both **FcRn-targeting treatments**, they **differ in:**

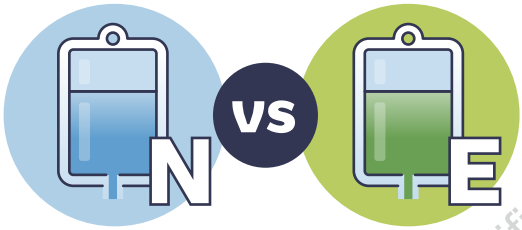
molecular structure

binding strength

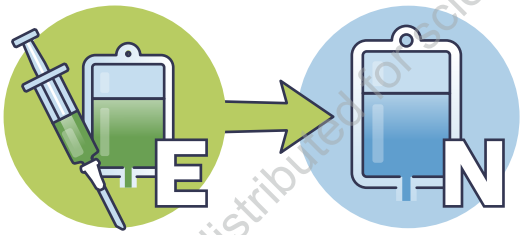
dosing schedule

which may lead to differences in patient outcomes[5,6,10,11]

WHY IS THE EPIC TRIAL BEING CONDUCTED?



EPIC is the **first randomized clinical trial** designed to directly **compare the efficacy** of **nipocalimab** **vs** **efgartigimod** for treatment of **gMG**



It also aims to understand the **efficacy** and **safety** of **switching** from **efgartigimod** to **nipocalimab**

FDA=US Food and Drug Administration, **gMG**=generalized myasthenia gravis.

HOW WILL THE STUDY BE PERFORMED?

Head-to-head phase

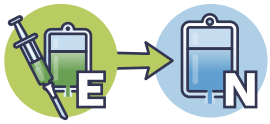
Patients with gMG who have never been treated with FcRn inhibitors are randomly assigned to receive either **nipocalimab** or **efgartigimod**

12-week, randomized, open-label treatment period

Nipocalimab is given every 2 weeks, while **efgartigimod** is administered weekly for 4 weeks

The study will compare how well these drugs treat gMG

Treatment switch phase

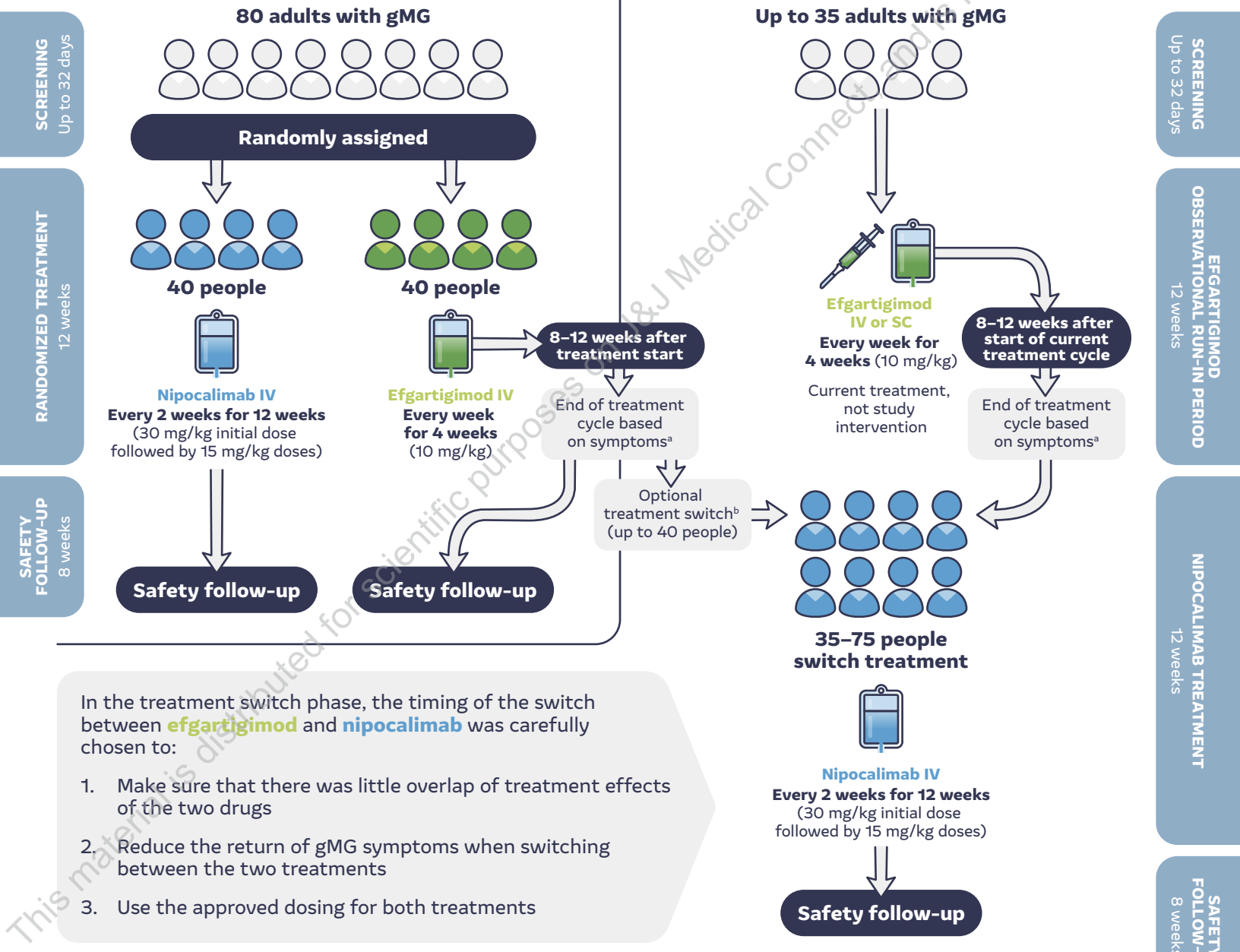


Patients with gMG taking **efgartigimod** in the head-to-head phase and additional eligible patients currently receiving **efgartigimod** switch to receiving **nipocalimab** treatment

12-week open-label **nipocalimab** treatment period

Nipocalimab is given every 2 weeks

The study will evaluate the effects of switching from **efgartigimod** to **nipocalimab**



In the treatment switch phase, the timing of the switch between **efgartigimod** and **nipocalimab** was carefully chosen to:

1. Make sure that there was little overlap of treatment effects of the two drugs
2. Reduce the return of gMG symptoms when switching between the two treatments
3. Use the approved dosing for both treatments

[a]Criteria for end of cycle/treatment switch 8 weeks after start of treatment are 1) current MG-ADL score shows less than a 2-point improvement from baseline, 2) current MG-ADL score shows at least a 2-point worsening vs peak MG-ADL improvement, or 3) any participant in the efgartigimod arm of the head-to head phase can switch and receive nipocalimab study intervention at 12 weeks after start of treatment.
[b]Researchers used computer modeling to find the best way to switch treatments.[12]
FcRn=neonatal FC receptor, **gMG**=generalized myasthenia gravis, **IV**=intravenous, **MG-ADL**=Myasthenia Gravis Activities of Daily Living, **SC**=subcutaneous.

WHO WILL TAKE PART IN THE STUDY?

	Head-to-head phase	Treatment switch phase
Age	18–75 years old	
Health criteria	Diagnosed with gMG MG-ADL score of 5 or more with at least half of the symptoms being non-eye-related Seropositive for AChR antibodies	
Treatment history	No history of treatment with an FcRn-targeting therapy Did not respond well to current treatment	Completed at least one cycle of **efgartigimod** as per the approved schedule Participant and their doctor agree that switching to **nipocalimab** is appropriate
	Not currently using IgG monoclonal antibody treatments (except for **efgartigimod** in the switch phase) Has not received rituximab in the past 24 weeks or treatments like plasmapheresis or IVIg in the past 4 weeks	

HOW WILL RESEARCHERS EVALUATE THE EFFICACY AND SAFETY OF NIPOCALIMAB AND EFGARTIGIMOD?

Researchers will **compare how well nipocalimab and efgartigimod help treat gMG** and how safe each drug is by evaluating **predefined efficacy and safety endpoints**

The **efficacy endpoints** include changes in the **types of antibodies that cause gMG** (specifically IgG), patients' **self-reported symptom severity** as measured by the Myasthenia Gravis Activities of Daily Living (MG-ADL) score, and **physician-assessed symptom severity** as measured by the Quantitative Myasthenia Gravis (QMG) score[13,14]

For **safety**, participants will be monitored for any **adverse events** (AEs)

AChR=acetylcholine receptor, **FcRn**=neonatal Fc receptor, **gMG**=generalized myasthenia gravis, **IgG**=immunoglobulin G, **IVIg**=intravenous immunoglobulin.

EFFICACY AND SAFETY ENDPOINTS

Primary efficacy endpoint

Mean percent change from baseline in total IgG

Key secondary efficacy endpoints

Mean change from baseline in MG-ADL total score and QMG total score

Mean percent change in total IgG and MG-ADL total score after treatment switch

Key safety endpoints

Incidence of AEs, serious AEs, AEs of special interest[a]

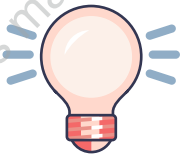
Efficacy endpoints will be analyzed:

1. Between weeks 8 and 12. This is the time when most decisions to proceed with a subsequent cycle of **efgartigimod** are made in clinical practice[15]
2. At week 8, when all participants have received the same number of treatment doses over the same time period (4 infusions in 8 weeks)

WHAT IMPACT WILL THE RESULTS OF THE EPIC TRIAL HAVE?

EPIC is the **first randomized trial comparing advanced treatments** for patients with **gMG**

The study addresses **whether nipocalimab works better than efgartigimod** in the latter part of **efgartigimod** cycles that cover most dosing patterns used by doctors in clinical practice



The results will provide **critical insights to help doctors make decisions** when **initiating** or **switching treatments** in the FcRn-targeting class

[a]AEs of special interest include infection, venous thromboembolism, and hypoalbuminemia of Grade 3 or higher.
AE=adverse event, **FcRn**=neonatal Fc receptor, **IgG**=immunoglobulin G, **MG-ADL**=Myasthenia Gravis Activities of Daily Living, **QMG**=Quantitative Myasthenia Gravis.

Glossary of technical terms

Acetylcholine receptor (AChR)
A receptor on muscle cells that receives signals from nerves, allowing muscles to move. AChR antibodies disrupt nerve-muscle communication and are often present in patients with generalized myasthenia gravis (gMG)

Acetylcholinesterase inhibitors
Blocks the enzyme that breaks down acetylcholine to increase acetylcholine at the neuromuscular junction and improve muscle strength in gMG

Immunoglobulin G (IgG) antibodies
A type of protein made by the immune system to fight infections. In gMG, these antibodies mistakenly attack the neuromuscular junction

Myasthenia Gravis Activities of Daily Living (MG-ADL) score
A scale used to measure how gMG symptoms affect daily activities like speaking, chewing, and walking

Neonatal Fc receptor (FcRn)
A protein in the immune system that helps control how long IgG antibodies stay in the bloodstream

Neuromuscular junction
The site where a nerve cell connects with a muscle cell and sends signals for the muscle to contract

Quantitative Myasthenia Gravis (QMG) score
A scoring system that evaluates muscle strength and function in individuals with gMG

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