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Newer Agents for Myasthenia Gravis

Systematic Review

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About This Research Product

A ***Systematic Review*** is the most comprehensive evidence synthesis research product Drug Effectiveness Review Project (DERP) participants can request. The scope of the topic is generally larger (e.g., drug class review) and uses gold-standard evidence synthesis methods. Because of the scope and approach, budget and timeline are generally larger for this research product, relative to others. This product is usually the result of a topic nomination or for a research need identified through surveillance.

Overview of All Research Products Available to DERP

Research Product Type	Scoping	Budget	Synthesis of Findings	RoB and GRADE	About the Product Goal of Product
PICOS and Key Questions	Yes	No	No	No	• Outlines the scope of DERP's research interests • DERP uses this product to determine if they want a topic brief
Topic Brief	Yes	Yes	No	No	• Developed from PICOS and Key Questions and identifies eligible studies or policy sources for the topic and proposes a budget • DERP uses this product to determine if they want to move the topic into the research work plan (e.g., systematic review)
Surveillance Report	No	No	No	No	• Identifies studies and FDA actions on existing topics (i.e., those completed in the last 3 years) since the previous research product was completed • DERP uses this product to determine if they want to commission an update or derivate of an existing research product
Surveillance Brief	No	No	Yes	Yes	• Summarizes and contextualizes the results of newly identified studies identified during surveillance • DERP uses this product to better understand newly published evidence, without commissioning a full update of another research product
Individual Topic Request (ITR)	No	No	Yes	Yes	• A brief and succinct research product synthesizing evidence on a narrow, requested topic (e.g., a new, high-cost drug) • DERP uses this product to better understand the evidence for a narrow topic, typically on a quick timeline
Policy Brief	No	No	Yes	No	• A synthesis of management strategies, on things such therapies or payment models, for DERP participants to consider • DERP uses this product to evaluate what is or might be occurring in Medicaid at a programmatic and clinical level
Systematic Review	**No**	**No**	**Yes**	**Yes**	• **The most comprehensive evidence synthesis product that uses gold-standard methods of evidence synthesis** • **DERP uses this product to understand the body of evidence for a larger topic, such as a drug class review**

Abbreviations. DERP: Drug Effectiveness Review Project; FDA: US Food and Drug Administration; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; ITR: individual topic request; PICOS: populations, interventions, comparators, outcomes, study designs; RoB: risk of bias.

Executive Summary

Background

Medicaid administrators are interested in the emerging agents for generalized myasthenia gravis (gMG), a chronic autoimmune disease characterized by muscle weakness, including body movement, facial expressions, speaking, swallowing, and breathing. Conventional treatments focus on increasing muscle strength and include acetylcholinesterase inhibition, thymectomy, immunosuppression, plasmapheresis, intravenous immunoglobulin, and light exercise. A rarer, closely related condition, Lambert-Eaton myasthenic syndrome (LEMS), is a chronic autoimmune disease that causes progressive muscle weakness starting with the limbs. Both gMG and LEMS are caused by miscommunications at the neuromuscular junction.

The new biologic drugs for gMG include complement inhibitors and neonatal Fc receptor blockers. The complement inhibitors currently approved by the FDA are eculizumab (Soliris), ravulizumab-cwvz (Ultomiris), and zilucoplan (Zilbrysq). The FDA-approved neonatal Fc receptor blockers are efgartigimod alfa-fcab (Vyvgart), efgartigimod alfa in combination with hyaluronidase-qvfc (Vyvgart Hytrulo), nipocalimab (Imaavy), and rozanolixizumab-noli (Rystiggo). Amifampridine phosphate, a sodium channel blocker, has been FDA-approved for LEMS and is under study for gMG.

PICOS and Key Questions

This review evaluates eligible randomized controlled trials (RCTs) investigating the use of new biologic agents to treat patients with gMG and LEMS. Comparators include placebo, standard of care, or another listed intervention. Outcomes include symptom control, function (e.g., activities of daily living), and quality of life, all using validated tools, along with safety outcomes such as adverse events (AEs) and serious adverse events (SAEs; e.g., hospitalization, exacerbations, disability or incapacity, mortality). Key questions include the effectiveness and harms of these agents and their place in therapy.

Methods

Researchers from the Center for Evidence-based Policy (Center) conducted a literature search of on December 12, 2024, without date limits to capture all relevant studies published. We also searched for ongoing studies of listed interventions, including both FDA-approved agents and pipeline agents. We conducted title-abstract and full-text level screening of search results, along with risk-of-bias assessments. We performed the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach on our selected outcomes, and assigned certainty-of-evidence (CoE) ratings from *very low* to *high*. Only RCTs published in English and conducted in countries categorized as very high on the United Nations Human Development Index were included. We also conducted a search for relevant clinical guidelines to determine place-in-therapy for these therapeutic agents.

Key Findings

In summary, we identified:

- 13 eligible placebo-controlled RCTs (11 in gMG and 2 in LEMS) evaluating 7 of the biologic drugs of interest; no head-to-head studies were identified
- 11 eligible ongoing studies of both the FDA-approved and pipeline agents
- Based on the included 11 placebo-controlled RCTs in gMG, we found:
    - For amifampridine phosphate, statistically significant and clinically meaningful improvements in symptoms, function, and quality of life, with very few AEs; however, the included study was very small, with only 7 participants. Overall, the certainty of evidence CoE was *very low*, based on 1 RCT
    - For eculizumab, statistically significant and generally clinically meaningful improvements in symptoms, function, and quality of life. Participants in both groups (treatment or placebo) experienced AEs, with no significant differences between groups. Overall, the CoE was *low to very low*, based on 2 RCTs
    - For efgartigimod, statistically significant and clinically meaningful improvements in symptoms, function, and quality of life after treatment; however, over time the effect waned and tended to return to the same or similar levels as at baseline. Participants in both groups (treatment or placebo) experienced AEs, with no significant differences between groups. The CoE, based on 2 RCTs, was *low*; however, for total AEs the CoE was assessed as being *moderate*
    - For nipocalimab, no significant differences between groups except for a significant increase in quality of life with the 30 mg/kg dosage compared with placebo. Participants in both groups (treatment or placebo) experienced AEs, with no significant differences between groups. The CoE, based on 1 RCT, was *low*; however, for total AEs the CoE was assessed as being *moderate*
    - For ravulizumab, significant but not clinically meaningful improvements in symptoms and function, and no significant difference in quality of life. Participants in both groups (treatment or placebo) experienced AEs, with no significant differences between groups. The CoE, based on 1 RCT, was *low*; however, for AEs the CoE was assessed as being *moderate*
    - For rozanolixizumab, findings were mixed with some statistically significant and clinically meaningful improvements in symptoms and function for the drug compared with placebo. Participants in both groups (treatment or placebo) experienced AEs, with no significant differences between groups. The CoE, based on 2 RCTs, was *very low*; however, for AEs the CoE was assessed as being *moderate*
    - For zilucoplan there were mixed results overall, mostly based on dosage, with the higher dosage having significant and clinically meaning improvements in symptoms and function, and significantly improved quality of life, compared with placebo. The lower dose had mixed results, either significant improvement or no difference in symptoms and function and significant improvement in quality of life, compared with placebo. Both dosages had no significant increases in AEs compared with placebo. The CoE, based on 2 RCTs, was *low*; however, for AEs the CoE was assessed as being *moderate*

- Based on the included 2 placebo-controlled RCTs in LEMS, we found:
    - For amifampridine phosphate, findings related to symptoms, function, and quality of life were mixed. Participants in both groups (treatment or placebo) experienced AEs, with no significant differences between groups. The CoE, based on 2 RCTs, was *very low*

State Considerations Overview

- Because of lack of head-to-head studies, it may be difficult to select drugs from those covered here, as these agents have similar effectiveness and safety profiles versus placebo.
- The treatment landscape for gMG is changing rapidly.
- High drug costs and varying routes of administration may be important factors to consider; intravenously administered therapies may require utilization of specific settings (e.g., clinic, infusion center, home health service), creating access barriers that subcutaneous or oral therapies may not have.
- These newer drugs may provide additional options for patients who are refractory to, or have had adverse reactions to, conventional therapy for gMG.

Conclusions

Myasthenia gravis is a rare disease with high morbidity that does not currently have any curative treatment. The current primary treatments are designed to reduce symptoms of the disease but are not always effective and have a notable AE burden. Overall, the new drugs for treatment of gMG and the closely-related LEMS show some statistically significant and clinically meaningful efficacy improvements over placebo; however, the CoE remains *low to very low*. In general, most study participants experienced an AE, regardless of group, with similar rates of AEs between groups. Head-to-head studies are not yet available and are needed. Also, there are notable risk of bias levels in the placebo-controlled trials. Nonetheless, these emerging therapies may provide a valuable option, particularly for patients nonresponsive to or unable to tolerate conventional treatments.

Background

Myasthenia gravis is a chronic autoimmune disease characterized by weakness in the voluntary muscles, including those for body movement, facial expression, speaking, swallowing, and breathing.[1-3] This weakness is caused by nerve signals failing to communicate to muscles at the neuromuscular junction.[1-3] Common symptoms include eyelid drooping, blurred or double vision, altered facial expressions, shortness of breath, difficulty swallowing, impaired speech, and extremity weakness (arms and legs, hands and feet).[1-3] Characteristically, the muscle weakness increases with activity and reduces with rest.[1-3] A myasthenic crisis happens when the breathing muscles weaken enough to require ventilatory support, a medical emergency that occurs in about 20% of myasthenia gravis patients.[1-3] When myasthenia gravis progresses to widely affect multiple muscle groups, it is referred to as generalized myasthenia gravis (gMG).[1] For people with myasthenia gravis, the immune system makes certain abnormal antibodies thought to trigger the disease symptoms.[1-3] The most common types of autoantibodies present in gMG are anti-acetylcholinesterase receptor antibodies (AChR-ab), anti-muscle-specific kinase antibodies (MuSK-ab), and anti-low-density lipoprotein–related protein 4 antibodies (LPR4-ab).[1,4] These proteins are essential to the function of the neuromuscular junction.[4,5]

As of 2021, it is estimated that 37 of every 100,000 people in the US have myasthenia gravis.[5] It has a lower age of onset in women (more likely to be before age 40) than men (more likely to be after age 50).[5] Overall, myasthenia gravis is more common over age 50, but it can occur at any age.[5] Myasthenia gravis affects all races and ethnicities, though it is slightly more common in people of African descent.[5] African Americans tend to develop myasthenia gravis at a younger age and are more likely to have gMG positive for MuSK-ab (MuSK-ab+).[5]

The initial diagnosis of myasthenia gravis can be challenging. The distinguishing clinical symptom is fluctuating muscle weakness that gets worse with physical activity and decreases with rest.[5] The presence of ocular symptoms, such as double vision and eye drooping, are also common.[5] A variety of factors can precipitate the disease, including infections, surgery, immunizations, pregnancy, some drugs, and other chronic medical illnesses.[4,5] The signs can often be subtle, such as coughing after swallowing and slower eating, vocal hoarseness, difficulty climbing stairs, and frequent errors in and slowness of writing and typing, most commonly late in the day.[4,5] As these symptoms may have multiple causes, identifying the disease clinically can be difficult, especially in primary care.[4,5] The occurrence of an acute myasthenic crisis may assist diagnosis.[4,5] Additionally, approximately 10% of patients have a thymoma (thymus gland tumor), which may be involved in the production of the autoantibodies.[4]

Once suspected, myasthenia gravis can be confirmed by a blood test for the presence of AChR-ab, as it is by far the most common antibody type for this disease (about 85% of patients have AChR-ab).[6,7] The test of the presence of the MuSK-ab is usually done in individuals with symptoms that are not positive for AChR-ab, or in individuals who are positive for AChR-ab (AChR-ab+) but are refractory to initial treatment.[8] Testing for LPR4-ab is less common, though the type of autoantibodies present or absent can be used to characterize the disease.[4] Most clinical studies include the AChR-ab+ type as the main population or as a subpopulation.

The Myasthenia Gravis Foundation of America (MGFA) provides a clinical categorization of myasthenia gravis into 5 main classes, with subcategories for classes II, III, and IV.[9] The

classification can affect the individual's response to treatment and prognosis.[9] Most clinical trials in this report focus on classes II through IV, as Class I is limited to ocular myasthenia gravis only and Class V is defined as requiring intubation with or without ventilation.[9] Classes II to IV, which each include subclasses a and b, denote gMG specifically, and range from mild to severe weakness.[9]

A rarer condition closely related to myasthenia gravis is Lambert-Eaton myasthenic syndrome (LEMS)[10] Like gMG, LEMS is caused by a miscommunication between the nerve and muscle cells at the neuromuscular junction, which results in progressive muscle weakness, starting from the limbs.[10] As well as a primary autoimmune version, it can also occur secondary to cancer, specifically small-cell lung cancer.[10] LEMS has a much lower prevalence and incidence than gMG, although the gender and age distribution of the primary autoimmune form are similar to gMG.[4] While we focus on gMG and LEMS in this report, there are ocular, congenital, and transient neonatal types of myasthenia gravis that fall outside the scope of the current report.[3]

There is no known cure for myasthenia gravis.[11] Treatments focus on improving muscle strength.[2,3,11] Standard approaches include pyridostigmine (an acetylcholinesterase inhibitor), immunosuppression agents (corticosteroids, azathioprine, mycophenolate mofetil, cyclosporin), B-cell directed therapy (rituximab), plasmapheresis (therapeutic plasma exchange), intravenous and subcutaneous immunoglobulin, and regular light exercise.[2,3,5,11] Thymectomy is also an available option, particularly in cases with thymus abnormalities such as hyperplasia or tumor.[11]

New biologic drugs for gMG include complement inhibitors and neonatal Fc receptor blockers.[12,13] The FDA-approved complement inhibitors are eculizumab (Soliris), ravulizumab-cwvz (Ultomiris), and zilucoplan (Zilbrysq).[13,14] The FDA-approved neonatal Fc receptor blockers are efgartigimod alfa-fcab (Vyvgart), efgartigimod alfa in combination with hyaluronidase-qvfc (Vyvgart Hytrulo), nipocalimab (Imaavy), and rozanolixizumab-noli (Rystiggo).[13,15] These agents increase the degradation of immunoglobulin G, including pathological autoantibodies.[13,15] Amifampridine phosphate, a potassium channel blocker, has been FDA-approved for LEMS and is under study for gMG.[16,17]

Pipeline agents in phase 3 testing include 3 additional complement inhibitors (pozelimab, gefurulimab, and iptacopan); 1 additional neonatal Fc receptor blocker (batoclimab); a small interfering RNA (siRNA) product that targets the complement system (cemdisiran); a B-cell–depleting anti-CD19 antibody (inebilizumab); an antimetabolite (cladribine); and a coinhibitor of B-lymphocyte stimulator and proliferation-inducing ligand (telitacicept). For descriptions of the FDA-approved and pipeline agents covered in this report, see the Interventions section below.

Outcomes and Minimal Clinically Important Differences

Clinical trials of drugs for treatment of gMG and LEMS rely on a variety of score measurements, either clinician-implemented or patient reported, as well as safety outcomes like adverse events (AEs) and laboratory values. While the serum immunoglobulin level was initially an outcome for this report, it was not provided in most of the studies. We examined the studies for their primary and secondary outcomes and selected the 4 most reported myasthenia gravis scores: Myasthenia Gravis Activities of Daily Living (MG-ADL), Myasthenia Gravis Composite (MGC) score, Myasthenia Gravis Quality of Life-15 revised (MG-QoL 15r), and Quantitative Myasthenia Gravis

(QMG). These are the same 4 scores described on the MGFA website's medical professional section.[18] However in a few cases, the longer original MG-QoL scale is used, rather than the revised form. Table 1 gives more details on the selected scores, along with the minimal clinically important difference (MCID), where known.

Table 1. Primary Efficacy Outcome Measures for Myasthenia Gravis

Score	Assessment	Interpretation	MCID
MG-ADL	Patient-reported functional activities of daily living including disability-related to ocular, bulbar, respiratory, and gross motor or limb impairment[19]	• 8 items (3 points per item) • 0 to 24 total points possible • Higher score means greater severity; a lower score is better	2 points[20] • Studies in this review use 2 points
MGC	Clinician examination and recorded patient medical history data assessing the function of ocular (ptosis, double vision), facial (talking, chewing), respiratory (breathing), neck, shoulder and hip muscles[21]	• 10 items (5 points per item) • 0 to 50 total points possible • Higher score means greater severity; a lower score is better	3 points[21] Studies in this review use 3 points
MG-QoL 15 (original)	Patient reported quality of life measures including MG-relevant physical, social, and psychological items[22]	• 15 items (4 points per item) • 0 to 60 total points possible • Higher score means greater severity; a lower score is better	Not determined
MG-QoL 15r	Patient reported quality of life measures including MG-relevant physical, social and psychological items[23]	• 15 items (2 points per item) • 0 to 30 total points possible • Higher score means greater severity; a lower score is better	Not determined
QMG	Clinician assessment of impairments of body functions and structures, including ocular, facial, bulbar, gross motor, axial and respiratory function[19]	• 13 items (3 points per item) • 0 to 39 total points possible • Higher score means greater severity; a lower score is better	2.6 to 3.5 points, depending on baseline severity of disease[24] Studies in this review use 3 points

Abbreviations. MCID: minimal clinically important difference; MG: myasthenia gravis; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGC: Myasthenia Gravis Composite; MG-QoL 15(r): 15-item Myasthenia Gravis Quality of Life scale (revised); QMG: Quantitative Myasthenia Gravis.

PICOS

Populations

- Adults with gMG or LEMS

Interventions

Table 2. FDA-Approved and Pipeline Agents for gMG or LEMS

Generic Name	Brand Name	Type	Route Dosage(s)	Indications	FDA Approval Date or Status
FDA-approved drugs					
Amifampridine phosphate	Firdapse	Potassium channel blocker	Oral 15 mg/kg to 30 mg/kg daily	LEMS for ages ≥ 6 years	November 28, 2018
Eculizumab	Soliris	Complement inhibitor	IV 900 mg weekly for 4 weeks, then 1,200 mg for 1 week, then 1,200 mg every 2 weeks	gMG in AChR-ab+ adults (≥ 18 years)	October 23, 2017
Efgartigimod alfa-fcab	Vyvgart	Neonatal Fc receptor blocker	IV 10 mg/kg weekly for 4 weeks, then further cycles as needed	gMG in AChR-ab+ adults (≥ 18 years)	December 17, 2021
Efgartigimod alfa with hyaluronidase-qvfc	Vyvgart Hytrulo	Neonatal Fc receptor blocker with hyaluronidase	IV 10 mg/kg weekly for 4 weeks, then further cycles as needed	gMG in AChR-ab+ adults (≥ 18 years)	June 20, 2023
Nipocalimab	Imaavy	Neonatal Fc receptor blocker	IV 30-mg/kg loading dose, then 15 mg/kg every 2 weeks	gMG in AChR-ab+ or MuSK-ab+ or LRP4-ab+ adults (≥ 18 years)	April 30, 2025
Ravulizumab-cwvz	Ultomiris	Complement inhibitor	IV 2,400-mg to 3,000-mg loading dose, then 3,000-mg to 3,600-mg maintenance doses every 8 weeks	gMG in AChR-ab+ adults (≥ 18 years)	April 28, 2022
Rozanolixizumab	Rystiggo	Neonatal Fc receptor blocker	SC 420 mg to 840 mg weekly for 6 weeks, then further cycles as needed	gMG in AChR-ab+ or MuSK-ab+ adults (≥ 18 years)	June 27, 2023
Zilucoplan	Zilbrysq	Complement inhibitor	SC 16.6 mg to 32.4 mg daily, based on body weight	gMG in AChR-ab+ adults (≥ 18 years)	October 17, 2023

Generic Name	Brand Name	Type	Route Dosage(s)	Indications	FDA Approval Date or Status
Pipeline agents[a]					
Batoclimab	IMVT-1401	Neonatal Fc receptor blocker	SC 340 mg to 680 mg weekly	gMG	Phase III
Cemdisiran	ALN-CC5	siRNA targeting complement	SC 200-mg to 400-mg doses weekly	gMG	Phase III
Cladribine	Mavenclad	Antimetabolite targeting autoantibody producing cells	Oral 3.5 mg/kg divided into 2 yearly (once per year) treatment courses	gMG in AChR-ab+ or MuSK-ab+ adults (≥ 18 years)	Phase III
Gefurulimab	ALXN1720	Complement inhibitor	SC Various dosages under testing	gMG	Phase III
Inebilizumab-cdon	Uplizna	Anti-CD19 antibody	IV 300-mg initial dose, 300 mg after 2 weeks, then 300 mg every 6 months	gMG	BLA under priority review January 9, 2025
Iptacopan	Fabhalta	Complement inhibitor	Oral 200 mg twice daily	gMG	Phase III
Pozelimab	Veopoz	Complement inhibitor	SC 30-mg/kg loading dose, then 10 mg/kg weekly	gMG in AChR-ab+ or LRP4-ab+ adults (≥ 18 years)	Phase III
Telitacicept	RC18	Anti-B-cell activating factor antibody and anti-A proliferation-inducing ligand antibody	SC 80 mg, 160 mg, or 240 mg weekly	gMG	Phase III

Note. [a] *Pipeline agents were included only for ongoing studies and not published studies.*
Abbreviations. AChR-ab+: positive for anti-acetylcholine receptor antibodies; FDA: US Food and Drug Administration; gMG: generalized myasthenia gravis; IV: intravenous; LEMS: Lambert-Eaton myasthenic syndrome; LRP4-ab+: positive for anti-low-density lipoprotein receptor–related protein 4 antibodies; MuSK-ab+: positive for anti–muscle-specific kinase antibodies; SC: subcutaneous; siRNA: small interfering RNA.

Comparators

- Another listed intervention
- Standard of care, including pyridostigmine bromide
- Placebo

Outcomes

- Levels of blood immunoglobulin
- Symptom control
- Function (e.g., activities of daily living), using a validated tool
- Quality of life, using a validated tool
- Time to first exacerbation
- Adverse events (AEs)
- Serious adverse events (SAEs; e.g., hospitalization, disability or incapacity, mortality)

Study Designs

- Randomized controlled trials (RCTs)
- Studies from countries that are *very high* on the United Nations Human Development Index

Key Questions

KQ1. What is the effectiveness of the listed interventions for adults with gMG or LEMS?

a. Does effectiveness vary by patient characteristics (e.g., age, disease severity)?

KQ2. What are the harms of the listed interventions for adults with gMG or LEMS?

a. Do harms vary by patient characteristics (e.g., age, disease severity)?

KQ3. What is the place in therapy for newer agents compared with standard of care?

KQ4. What are the characteristics of ongoing studies of the listed interventions for people with gMG or LEMS?

KQ5. What are the characteristics of pipeline therapies with a Prescription Drug User Fee Act (PDUFA) date within the next 12 months?

Methods

Researchers from the Center for Evidence-based Policy (Center) ran a literature search using Ovid MEDLINE ALL, the Cochrane Central Register of Controlled Trials (CENTRAL) via OVID, and Embase for any RCTs analyzing a listed intervention; specifically, the FDA-approved agents in Table 2. We conducted the searches on December 12, 2024, without date limits to capture all relevant studies. We also searched ClinicalTrials.gov and ScanMedicine to identify ongoing studies of listed interventions for gMG, including both FDA-approved agents and pipeline agents (see Table 2).

Two independent researchers conducted title-abstract and full-text level screening of literature search results and risk-of-bias (RoB) assessments; conflicts were handled through discussion, and any disagreements were resolved by a third independent senior researcher. We performed the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach[25] on select outcomes: MG-ADL, MGC, MG-QoL 15r, QMG, total AEs, and SAEs. Two independent researchers assigned certainty-of-evidence (CoE) ratings from *very low* to *high*; conflicts were handled through discussion, and any disagreements were resolved by a third independent senior researcher.

Only RCTs evaluating a listed intervention were included. Additional eligibility criteria were studies on human participants, studies conducted in countries categorized as *very high* on the United Nations Human Development Index, and publication in English. A full description of our methods can be found in Appendix A.

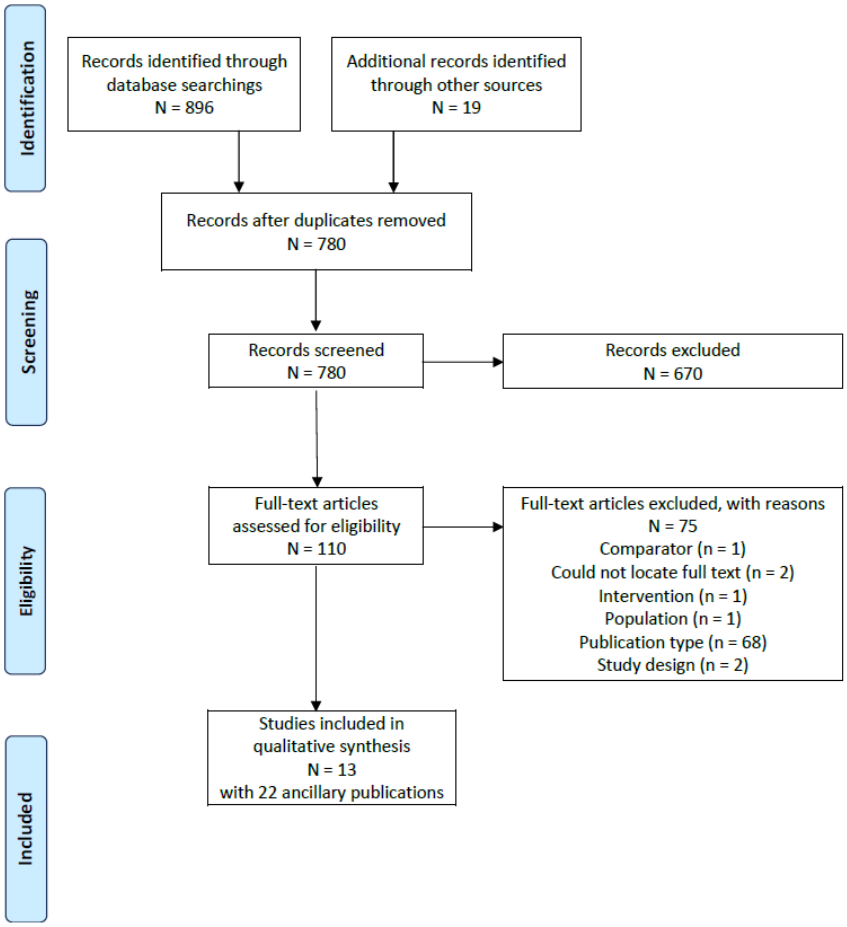
Statistics

We used the OpenEpi 2-by-2 table to calculate risk ratios and *P* values for AE outcomes.[26] We also use Pocock's 2006 method for calculating missing *P* values.[27] Finally, where needed we converted standard errors (SEs) to 95% confidence intervals (95% CIs) using the formula 95% CI = mean ± (1.96 x SE).

Findings

We found 896 records from database searches and 19 records from gray literature and guidelines searches. After deduplication, 780 citations were screened at the title and abstract level, with 110 selected for full text screening. Most exclusions at the full-text level were because of publication type, with guidelines, systematic reviews and meta-analyses labeled for citation tracking; we did not find anything new in the reference lists of those publications. In total, we identified 13 eligible RCTs with 22 ancillary publications for analysis in this report. See Figure 1 for the PRISMA flow diagram.

Figure 1. PRISMA Flow Diagram



Amifampridine Phosphate

We found 1 RCT reporting on amifampridine vs. placebo in people with gMG, specifically people with MuSK-ab+ myasthenia gravis (a rare subtype)[16]; and 2 RCTs in people with LEMS.[28,29] Amifampridine is FDA-approved for LEMS and is under investigation in gMG. All 3 studies had small sample sizes (N = 7, N = 26, and N = 38), short durations (4 days, or 2 to 3 weeks), and notable pharmaceutical company involvement, resulting in a *high* RoB assessment.[16,28,29] In the myasthenia gravis study, participants were in MGFA classes II, III, and IV, and were all MuSK-ab+; AChR-ab status was not specified.[16] Tables 3 and 4 report the GRADE findings for the key outcomes of interest for studies of amifampridine phosphate, separated by condition. Detailed study characteristics are in Appendix B, Table B1, and details about the outcome measures used can be found in Table 1.

Generalized Myasthenia Gravis

The MuSK-001 study by Bonanno and colleagues reported on amifampridine phosphate in gMG patients who all had the rare MuSK-ab+ subtype, using a crossover design with a very small number of participants (N = 7)[16]:

- 3 patients received 1 week each, in order, of amifampridine, placebo, and amifampridine (APA) for a total randomized period of 3 weeks.[16]
- 4 patients received 1 week each, in order, of placebo, amifampridine, placebo (PAP), for a total randomized period of 3 weeks.[16]

Table 3. Summary of Findings (GRADE) on Amifampridine Phosphate for gMG

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Symptom severity			
QMG 1 RCT[a16] N = 7	●○○○ Very low	Overall, QMG scores got worse (increased) for all participants. Amifampridine was associated with significantly smaller increase in QMG score (0.1 vs. 6.9; *P* < .001); difference was clinically meaningful (difference: 6.9) when compared with placebo	Downgraded 1 level each for RoB (funder COI) and indirectness (people with MuSK-ab+ gMG), and 2 levels for imprecision (very small sample size)
MGC 1 RCT[a16] N = 7	●○○○ Very low	Overall, MGC scores got worse (increased) for all participants. Amifampridine was associated with significantly smaller increase in MGC score (0.1 vs. 11.6; *P* < .001); difference was clinically meaningful (difference: 11.5) when compared with placebo	Downgraded 1 level each for RoB (funder COI) and indirectness (people with MuSK-ab+ gMG), and 2 levels for imprecision (very small sample size)

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Function			
MG-ADL 1 RCT[a16] N = 7	●○○○ Very low	Amifampridine was associated with significantly improved MG-ADL score (−0.1 vs. 5.6; *P* < .001); difference was clinically meaningful (difference: 5.7) when compared with placebo	Downgraded 1 level each for RoB (funder COI) and indirectness (people with MuSK-ab+ gMG), and 2 levels for imprecision (very small sample size)
Quality of life			
MG-QoL 15 1 RCT[a16] N = 7	●○○○ Very low	Amifampridine was associated with significantly improved MG-QoL 15 score (−2.1 vs. 16.4 *P* = .003)	Downgraded 1 level each for RoB (funder COI) and indirectness (people with MuSK-ab+ gMG), and 2 levels for imprecision (very small sample size)
Safety			
Total AEs 1 RCT[a16] N = 7	●○○○ Very low	Overall, 7 AEs were reported; the majority were paresthesias; however, these were not reported by treatment group	Downgraded 1 level each for RoB (funder COI) and indirectness (people with MuSK-ab+ gMG), and 2 levels for imprecision (very small sample size)
SAEs 1 RCT[a16] N = 7	●○○○ Very low	No difference between treatment groups, with no SAEs observed in either treatment group	Downgraded 1 level each for RoB (funder COI) and indirectness (people with MuSK-ab+ gMG), and 2 levels for imprecision (very small sample size)

Notes. [a] Where only 1 study is available, we were unable to assess inconsistency.
Abbreviations. AE: adverse event; CI: confidence interval; CoE: certainty of evidence; COI: conflict of interest; gMG: generalized myasthenia gravis; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGC: Myasthenia Gravis Composite; MG-QoL15: 15-item Myasthenia Gravis Quality of Life scale; MuSK-ab+: positive for anti-muscle-specific kinase antibodies; QMG: Quantitative Myasthenia Gravis; RCT: randomized controlled trial; RoB: risk of bias; SAE: serious adverse event.

There were no washout periods.[16] The study compared all patients receiving amifampridine with all patients receiving placebo across those 3 weeks, counting patients twice who received either amifampridine or placebo twice, resulting in a comparison of artificially larger groups of 10 patients on amifampridine and 11 patients on placebo.[16]

For patients in the combined amifampridine group, the MG-ADL, MGC, and QMG scores were significantly lower compared to patients in the placebo group (mean between-group differences: MG-ADL, −5.7; MGC least squares mean difference [LSMD], −11.5; QMG, −6.9; all *P* < .001).[16] The differences were also clinically meaningful for all 3 scores.[16] Additionally, the patients in the amifampridine group had significantly lower MG-QoL 15 scores than patients in the placebo

group (mean between-group difference, −18.5; *P* = .003).[16] For such a small study population, these are notably large effects. No other outcomes of interest were reported.[16]

Further, there were no significant differences in AEs between the 2 groups, with no serious AEs or discontinuations due to AEs reported in either patient group.[16] The most common AEs were oral and limb paresthesia (a "pins and needles" sensation).[16]

Lambert-Eaton Myasthenic Syndrome

Both studies in LEMS patients were "withdrawal" studies in which the patients started on amifampridine phosphate and then were randomized to either continue the drug or be changed to placebo.[28,29] The study by Oh and colleagues involved a 1-week taper of the drug followed by 1 week of placebo for those patients randomized to placebo, after which all patients received the drug for an extension period.[28] Thus, the RCT portion of this study was 2 weeks, although the slow dose taper meant that the true amifampridine vs. placebo part only occurred for 1 week.[28] Nonetheless, efficacy results were reported at the end of the 2-week period and AE outcomes were reported for at least 2 weeks.[28] The study by Shieh and colleagues randomized patients to a 4-day period of either amifampridine or placebo between 2 periods of all patients receiving the drug.[29] There was no dose-taper or washout period provided. Efficacy and safety outcomes were reported for the end of the 4-day RCT period.[29]

Table 4. Summary of Findings (GRADE) on Amifampridine Phosphate for LEMS

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Symptom severity			
QMG 2 RCTs[28,29] N = 64	●○○○ Very low	Overall, QMG scores got worse (increased) for all participants. Amifampridine was associated with significantly smaller increases in QMG score ($P < .05$) and were not always clinically meaningful	Downgraded 1 level each for RoB (funder COI), inconsistency (mixed findings), and imprecision (small sample sizes)
Function			
TFW25 and 3TUG[b] 2 RCTs[28,29] N = 64	●○○○ Very low	Measures of function (using the TFW25 and 3TUG) were mixed, with 1 study showing no difference and 1 study showing a significant improvement with amifampridine when compared with placebo	Downgraded 1 level each for RoB (funder COI), inconsistency (mixed findings), and imprecision (small sample sizes)
Quality of life			
No studies reported this outcome			

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Safety			
Total AEs 2 RCTs[28,29] N = 64	●○○○ Very low	Participants in both groups experienced AEs. One study reported no significant difference between groups (19% vs. 27%, *P* > .05); other study reported 3 events with amifampridine and 11 events with placebo in the 26 participants	Downgraded 1 level for RoB (funder COI) and 2 levels for imprecision (very wide CIs)
SAEs 2 RCTs[28,29] N = 64	●○○○ Very low	No difference between treatment groups; no SAEs observed in either treatment group	Downgraded 1 level for RoB (funder COI) and 2 levels for imprecision (very wide CIs)

Notes. [b] *TFW25 and 3TUG are clinical function scores used to assess muscle weakness and mobility in people with LEMS.*
Abbreviations. 3TUG: triple-timed up-and-go test; AE: adverse event; CI: confidence interval; CoE: certainty of evidence; COI: conflict of interest; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; QMG: Quantitative Myasthenia Gravis; RCT: randomized controlled trial; RoB: risk of bias; SAE: serious adverse event; TFW25: timed 25-foot walk test.

For both studies, the LEMS patients had significantly reduced QMG scores with amifampridine compared with placebo (mean difference [MD], −1.7; *P* = .045; and estimated LSMD, −2; given 95% CI, −0.78 to −3.29; *P* < .001).[28,29] Neither met the clinically meaningful difference of a reduction in mean difference of 3.[28,29]

In these studies the functional mobility in the LEMS participants was scored using timed walking scores, the triple-timed up-and-go test (3TUG) functional mobility task[30] and the timed 25-foot walk test (TFW25),[31] which are different measures than used in the gMG trial. The Oh and colleagues study reported that there was no significant difference in the TFW25 score for the amifampridine group compared with the placebo group at day 14.[28] For the Shieh and colleagues study, the proportion of patients with ≥ 20% increase in the time required to complete 3TUGtask was significantly higher in the placebo group compared with the amifampridine group, meaning that the patients on amifampridine had better mobility than the patients on placebo (*P* = .0112).[29]

Regarding total AEs, the Oh and colleagues study reported no significant differences between groups (18.8% vs 27.3%; *P* > .05), while the Shieh and colleagues study reported 3 AEs in 3 participants (24%) in the amifampridine group and 11 events (number of patients not reported) in the placebo group (significance not reported).[28,29] For serious AEs and discontinuations due to AEs, there were no significant differences between groups in either study.[28,29] The most common AEs included muscle weakness, fatigue, oral and digital paresthesia, headache, nausea, and diarrhea.[28,29]

Detailed outcomes for each of the 3 studies are shown in Appendix C, Table C1.

Eculizumab

Two RCTs described in 12 publications reported on eculizumab compared with placebo in adults with refractory gMG.[32-43]

- The 2013 study by Howard and colleagues had a very small sample size (N = 14), a crossover design, poor reporting of statistical measures, missing information on baseline characteristics, and pharmaceutical company involvement, resulting in a *high* RoB assessment.[32]
- The 2017 study by Howard and colleagues, called REGAIN, was reported in 11 publications (a primary publication and 10 ancillary publications), had a larger population (N = 126) with some minor methodological issues and pharmaceutical company involvement, resulting in a *moderate* RoB assessment.[33-43]

Participants enrolled in both studies were in MGFA classes II to IVb and were all AChR-ab+.[32,33] MuSK-ab status was not specified.[32,33] Patients demonstrated insufficient symptom control on standard immunotherapy.[32,33] Table 5 reports the GRADE findings for the key outcomes of interest. Detailed study characteristics are in Appendix B, Table B1, and details about the outcome measures used can be found in Table 1.

Table 5. Summary of Findings (GRADE) on Eculizumab for Myasthenia Gravis

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Symptom severity			
QMG 2 RCTs[32,33] N = 140	●○○○ Very low	Overall, QMG scores improved (decreased) for all participants. Eculizumab was associated with significantly greater decrease in QMG score in both studies (-4.6 vs. −1.6; −7.9 vs. −3.7; $P \leq .01$ for both); differences were likely clinically meaningful (difference: 3.0 to 4.0) when compared with placebo	Downgraded 1 level for RoB (funder COI) and 2 levels for imprecision (small sample size and incomplete washout).
MGC 1 RCT[a33] N = 126	●●○○ Low	Overall, MGC scores improved (decreased) for all participants. Eculizumab was associated with significantly greater decrease in MGC score (−8.1 vs. −4.8; $P = .01$); difference was clinically meaningful (difference: 3.3) when compared with placebo	Downgraded 1 level for RoB (funder COI) and 1 level for imprecision (not assessable)
Function			
MG-ADL 2 RCTs[32,33] N = 140	●○○○ Very low	Eculizumab was associated with a significantly improved MG-ADL score when compared with placebo (both $P < .05$); difference was clinically meaningful in 1 study (difference: 3.6 at end of period 1, but not overall) but not in the other (difference: 1.9)	Downgraded 1 level for RoB (funder COI), 1 level for imprecision (not assessable), and 1 level for inconsistency
Quality of life			
MG-QoL 15 1 RCT[a33] N = 126	●●○○ Low	Eculizumab was associated with significantly improved MG-QoL 15 score when compared with placebo (−12.6 vs. −5.4; $P = .001$)	Downgraded 1 level for RoB (funder COI) and 1 level for imprecision (not assessable)

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Safety			
Total AEs 1 RCT[a32] N = 14	●○○○ Very low	Participants in both groups experienced AEs; no significant difference between groups	Downgraded 1 level for RoB (funder COI) and 2 levels for imprecision (very small sample size)
SAEs 2 RCTs[32,33] N = 140	●●○○ Low	Participants in both groups experienced SAEs; however, no significant difference between groups (1% vs. 1% and 15% vs. 29%)	Downgraded 1 level each for RoB (funder COI) and imprecision (not assessable)

Note. [a] *Where only 1 study is available, we were unable to assess inconsistency.*

Abbreviations. AE: adverse event; CoE: certainty of evidence; COI: conflict of interest; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; MG-ADL: MG Activities of Daily Living; MGC: Myasthenia Gravis Composite; MG-QoL15: 15-item Myasthenia Gravis Quality of Life scale; QMG: Quantitative Myasthenia Gravis; RCT: randomized controlled trial; RoB: risk of bias; SAE: serious adverse event.

The 2013 crossover study by Howard and colleagues involved two 16-week eculizumab vs placebo periods with a 5-week washout period in between, and patients crossed from eculizumab to placebo or placebo to eculizumab, respectively.[32] The authors reported that the washout period was not fully effective for the QMG score, as it had not returned to baseline for the patients on eculizumab at the end of that period.[32] Thus, for QMG, the period 1 (16-week) data is preferred, although the full 37-week data is also reported.[32] Unfortunately, the loss of patients over the study duration was inconsistently reported, so the number of patients at the end of the 37 weeks varied for different outcomes.[32] Nonetheless, patients on eculizumab had a clinically meaningful decrease in QMG scores compared with patients on placebo at both the end of period 1 (MD, −4.7) and the full study (MD, −4.25).[32] The difference was significant for the full study (P = .01); statistical significance was not reported for period 1 alone.[32] The MG-ADL score showed a clinically meaningful and significant difference for patients on eculizumab compared with placebo for period 1 (MD, −3.57; P = .04), but no significant difference at the end of the full study.[32] MG-QoL 15r and MGC scores were not included outcomes.[32] There were no significant differences in any safety outcomes between groups in this study.[32] The most common AEs were nausea, back pain, nasopharyngitis, and headache.[32] No deaths were observed, and there was no difference between groups in the rate of exacerbations.[32] Discontinuations due to AEs and hospitalizations were not reported.

The larger 2017 Howard study compared the outcomes for 62 patients randomized to eculizumab and 63 patients randomized to placebo over a 26-week study duration.[33] Patients on eculizumab had significantly better QMG, MG-ADL MG-QoL 15, MGC, and neurological quality of life fatigue scores compared with patients on placebo (range of MDs, −1.9 to −7.1; P = .01 to P < .001).[33] The difference was clinically meaningful for QMG, MGC and fatigue.[33] For MG-ADL the difference was borderline clinically meaningful at −1.9, with a MCID of at least 2.[33] There were no significant differences between eculizumab and placebo groups for total AEs, SAEs, discontinuation due to AEs, hospitalizations, and deaths.[33] However, patients in the placebo group had significantly more disease exacerbations compared with patients on eculizumab (24%

vs 10%; *P* = .04).[33] The most common AEs were headache, upper respiratory infection, nasopharyngitis, nausea, and diarrhea.[33]

Details of outcomes for both studies are shown in Appendix C, Table C2.

Efgartigimod

We found 2 studies, presented in 6 publications, comparing efgartigimod with placebo in patients with gMG[44-49]:

- The 2019 study by Howard and colleagues had a small population size (N = 24) and was mostly exploratory for efficacy outcomes, with limited evidence, some concerns regarding baseline characteristics, a modified intention-to-treat population, and pharmaceutical company involvement. For these reasons, this study was assessed as being at *high* RoB.[44]
- The 2021 study by Howard and colleagues had 4 ancillary publications and a larger population (N = 167), but also had concerns with baseline characteristics, modified intention-to-treat, and pharmaceutical company involvement, as well as unbalanced attrition of patients.[45-49] Therefore, it was also assessed as being at as *high* RoB.

Both studies enrolled patients in MGFA Classes I, II and IV.[44,45] Participants in the 2019 Howard and colleagues study were all AChR-ab+, with MuSK-ab status not specified.[44] Patients in the 2021 Howard and colleagues study were 4% MuSK-ab+ in both placebo and drug groups, and 77% AChR-ab+ in both groups.[45]

Both studies investigated the use of efgartigimod without hyaluronidase.[44,45] No eligible studies were found for the combination drug, although the 2021 Howard and colleagues study was used in the FDA approval of the efgartigimod with hyaluronidase combination product, despite that product not being specifically tested in that study.[50] A second pharmacokinetic study was also used to support approval of the combination product, and was cited as demonstrating a comparable effect on antibody reduction to the efgartigimod-alone preparation.[50] Table 6 reports the GRADE findings for the key outcomes of interest. Detailed study characteristics are in Appendix B, Table B1, and details about the outcome measures used can be found in Table 1.

Table 6. Summary of Findings (GRADE) on Efgartigimod for Myasthenia Gravis

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Symptom severity			
QMG 2 RCTs[44,45] N = 191	●●○○ Low	Overall, QMG scores improved (decreased) for all participants. Efgartigimod was associated with a significantly greater decrease in QMG score; however, while the initial decreases were clinically meaningful, over time the differences between groups grew smaller, with QMG scores tending to rise after the active treatment phase (reported graphically)	Downgraded 1 level for RoB (funder COI, poorly reported data) and 1 level for imprecision (not assessable)

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
MGC 2 RCTs[44,45] N = 191	●●○○ Low	Overall, MGC scores improved (decreased) for all participants. Efgartigimod was associated with a significantly greater decrease in MGC score; while the initial decreases were clinically meaningful, over time the differences between groups grew smaller, with MGC scores tending to rise after the active treatment phase (reported graphically)	Downgraded 1 level for RoB (funder COI, poorly reported data) and 1 level for imprecision (not assessable)
Function			
MG-ADL 2 RCTs[44,45] N = 191	●●○○ Low	Overall, MG-ADL scores improved (decreased) for all participants. Efgartigimod was associated with a significantly greater decrease in MG-ADL score (*P* = .036); difference appears to be clinically meaningful for weeks 2 to 7. Over time the differences between groups grew smaller, with MG-ADL scores tending to rise after the active treatment phase (reported graphically)	Downgraded 1 level for RoB (funder COI, poorly reported data) and 1 level for imprecision (not assessable)
Quality of life			
MG-QoL 15r 2 RCTs[44,45] N = 191	●●○○ Low	Overall, MG-QoL 15r scores improved (decreased) for all participants. Efgartigimod was associated with a significantly greater decrease in MG-QoL 15r score (*P* = .049 to *P* = .01); the maximal difference was around week 4 and then over time the differences between groups grew smaller, with MG-QoL 15r scores tending to rise after the active treatment phase (reported graphically)	Downgraded 1 level for RoB (funder COI, poorly reported data) and 1 level for imprecision (not assessable)
Safety			
Total AEs 2 RCTs[44,45] N = 191	●●●○ Moderate	Most participants in each group experienced an AE. However, both studies report no difference between groups	Downgraded 1 level for RoB (funder COI, poorly reported data)
SAEs 2 RCTs[44,45] N = 191	●●○○ Low	Very few participants in either group experienced a SAE. Both studies reported no difference between groups	Downgraded 1 level for RoB (funder COI, poorly reported data) and 1 level for imprecision (few events)

Abbreviations. AE: adverse event; CoE: certainty of evidence; COI: conflict of interest; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGC: Myasthenia Gravis Composite; MG-QoL 15r: 15-item Myasthenia Gravis Quality of Life scale, revised; QMG: Quantitative Myasthenia Gravis; RCT: randomized controlled trial; RoB: risk of bias; SAE: serious adverse event.

Efgartigimod was administered in 4 weekly infusions, and then participants were followed for about 8 to 10 weeks, after which another treatment cycle was conducted.[44,45] Both studies

represent the results in graphical form.[44,45] The 2019 Howard and colleagues study followed patients for 80 days, while the 2021 Howard and colleagues study reports results by treatment cycle, primarily the first treatment cycle (10 weeks).[44,45]

The 2019 Howard and colleagues study reported efficacy outcomes over 80 days, comparing 12 patients on efgartigimod with 12 patients on placebo.[44] For the QMG score, the patients receiving the drug had a significant and clinically meaningful decrease compared with patients receiving placebo by week 1 (mixed-model repeated measures, −2.38; 95% CI, −4.63 to −0.13; $P = .04$).[44] This remained significant through 80 days, with the maximal decrease at week 5 (a 5.7-point reduction from baseline).[44] The MG-ADL reached a clinically meaningful reduction by week 1 and statistically significant reduction for weeks 4 and 5, then increased but remained clinically meaningful through day 80.[44] The MG-QoL reached a significant decrease for patients receiving efgartigimod compared with patients receiving placebo at day 22 (MD, −3.72; 95% CI, −7.41 to −.02; $P = .049$), day 29 (MD, −3.87; 95% CI, −7.69 to −0.05; $P = .048$) and day 43 (MD, −4.38; 95% CI, −8.56 to −0.20; $P = .04$).[44] The score for the efgartigimod group falls at week 1, reaches a maximal reduction at 5 weeks, then rises to approach the level for the placebo group at 80 days.[44]

Results are similar for the efgartigimod group on the MG-ADL and MGC, with a significant decrease at week 1, maximal reduction around weeks 4 to 5, and then a slow rise to approach the level for the placebo group by day 80, while staying clinically meaningful from week 1 to 80 days.[44] The MGC shows a similar pattern, although the significant and relationship to the MCID are not shown.[44] There were no significant differences between efgartigimod and placebo groups for total AEs, SAEs, discontinuations to AEs, and deaths.[44] The most common AEs were headache and itching.[44]

The 2021 Howard and colleagues study reported efficacy outcome for the AChR-ab+ subgroups, comparing 63 patients on efgartigimod with 59 patients on placebo over 2 treatment cycles, each a maximum of 8 weeks in duration, with graphs representing the data for treatment cycle 1.[45] The results are similar to those for the 2019 study, with all 4 scores reaching a significant decrease for efgartigimod compared with placebo by week 1 ($P < .05$) and a maximal reduction around weeks 4 to 5.[45] The scores for the efgartigimod group then increase to approach the scores for the placebo group by the end of the 10-week treatment cycle.[45] The difference in scores between drug and placebo is clinically meaningful for the QMG, MG-ADL, and MGC approximately between weeks 1 to 2 and weeks 7 to 8.[45]

This study, however, reported safety outcomes in the total, mixed-AChR-ab-status population, comparing 84 patients on efgartigimod to 83 patients on placebo.[45] No significant differences between the groups were found.[45] The most common AEs were headache, nasopharyngitis, nausea, diarrhea, upper respiratory tract infection, and urinary tract infection.[45]

Details of outcomes for both studies are shown in Appendix C, Table C3.

Nipocalimab

We found 1 RCT called Vivacity-MG that compared nipocalimab with placebo in patients with refractory gMG.[51] This phase 2 study compared placebo patients with patients on 4 different nipocalimab dosage schedule regimens: 5 mg/kg every 2 weeks, 30 mg/kg every 4 weeks,

60 mg/kg single dose, and 60 mg/kg every 2 weeks; there were 13 or 14 patients per group, studied over a total of 8 weeks.[51] The primary issues with this study are concerns with pharmaceutical company involvement and missing patients and data due to COVID-19 interruptions, resulting in a *moderate* RoB assessment.[51] Enrolled patients were in MGFA Classes IIa to IVa, and were 7.1% MuSK-ab+ and around 92% to 93% AChR-ab+ in all groups.[51] The patients had all demonstrated insufficient symptom control on standard immunotherapy.[51] Table 7 reports the GRADE findings for the key outcomes of interest. Detailed study characteristics are in Appendix B, Table B1, and details about the outcome measures used can be found in Table 1.

Table 7. Summary of Findings (GRADE) on Nipocalimab for Myasthenia Gravis

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Symptom severity			
QMG 1 RCT[a51] N = 68	●●○○ Low	No difference among the 5 study groups (4 nipocalimab dosages and 1 placebo group)	Downgraded 1 level each for RoB (funder COI) and imprecision (wide confidence intervals)
MGC	*NA*	No included studies of nipocalimab used the MGC measure	*NA*
Function			
MG-ADL 1 RCT[a51] N = 68	●●○○ Low	No difference among the 5 study groups (4 nipocalimab dosages and 1 placebo group)	Downgraded 1 level each for RoB (funder COI) and imprecision (wide confidence intervals)
Quality of life			
MG-QoL 15r 1 RCT[a51] N = 68	●●○○ Low	Overall, there was no difference between nipocalimab and placebo. However, 1 of the 4 dosages (30 mg/kg every 4 weeks) did significantly improve QoL (P = .005).	Downgraded 1 level each for RoB (funder COI) and imprecision (wide confidence intervals)
Safety			
Total AEs 1 RCT[a51] N = 68	●●●○ Moderate	Most participants in all groups experienced an AE; however, there were no difference in AE incidence between nipocalimab dosages and placebo	Downgraded 1 level for RoB (funder COI)
SAEs 1 RCT[a51] N = 68	●●○○ Low	Very few participants in any group experienced a SAE; no differences between groups	Downgraded 1 level each for RoB (funder COI) and imprecision (very few events)

Note. [a] *Where only 1 study is available, we were unable to assess inconsistency.*
Abbreviations. AE: adverse event; CoE: certainty of evidence; COI: conflict of interest; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGC: Myasthenia Gravis Composite; MG-QoL 15r: 15-item Myasthenia Gravis Quality of Life scale (revised); NA: not applicable; QMG: Quantitative Myasthenia Gravis; QoL: quality of life; RCT: randomized controlled trial; RoB: risk of bias; SAE: serious adverse event.

There were no significant differences between placebo and any of the 3 nipocalimab dosages for QMG, MG-ADL and MG-QoL 15r score, with 1 exception.[51] Patients receiving the 30 mg/kg every 4 weeks dosage had significantly lower MG-QoL 15r compared with patients receiving placebo (LSMD, −5.1; *P* = .005).[51] As no other significant differences were found,[51] it is unclear how valid this single finding is, particularly given the lack of a defined MCID for the MG-QoL 15r score.[51] Additionally, there were no differences among patient groups for total AEs, SAEs, and discontinuations due to AEs.[51] The most common AEs were headache, diarrhea, nasopharyngitis, and rash.[51] Details of outcomes for this study are shown in Appendix C,Table C4.

A phase 3 trial of nipocalimab in gMG was published in January 2025, after our search date in December 2024, so it is not included here.[52] That study is still listed in the Ongoing Studies section below.

Ravulizumab

We found 1 RCT called CHAMPION MG, represented by 5 publications, which compared ravulizumab with placebo in patients with gMG.[53] This 26-week international trial included 175 patients and had a duration of 26 weeks.[53] We had some concern with baseline characteristic discrepancies as well as pharmaceutical company involvement, resulting in a *moderate* RoB assessment.[53] Enrolled patients were in MGFA Classes II to IVb and 100% were AChR-ab+.[53] MuSK-ab status was not specified.[53] Table 8 reports the GRADE findings for the key outcomes of interest. Detailed study characteristics are in Appendix B, Table B1, and details about the outcome measures used can be found in Table 1.

Table 8. Summary of Findings (GRADE) on Ravulizumab for Myasthenia Gravis

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Symptom severity			
QMG 1 RCT[a53] N = 175	●●○○ Low	Overall, QMG scores improved (decreased) for all participants. Ravulizumab was associated with a significantly greater decrease in QMG score (−2.8 vs. −0.8; *P* < .001); however, the difference was not clinically meaningful when compared with placebo (difference: 2.0)	Downgraded 1 level each for RoB (funder COI) and imprecision (wide confidence interval)
MGC	*NA*	No included studies of ravulizumab used the MGC measure	*NA*
Function			
MG-ADL 1 RCT[a53] N = 175	●●○○ Low	Overall, MG-ADL scores improved (decreased) for all participants. Ravulizumab was associated with a significantly greater decrease in MG-ADL score (−3.1 vs. −1.4; *P* < .001); however, the difference was not clinically meaningful when compared with placebo (difference: 1.6)	Downgraded 1 level each for RoB (funder COI) and imprecision (wide confidence interval)

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Quality of life			
MG-QoL 15r 1 RCT[a53] N = 175	●●○○ Low	Overall, MG-QoL 15r scores improved (decreased) for all participants. Ravulizumab was associated with a nonsignificant decrease in MG-QoL score (−3.3 vs. −1.6; *P* = .06)	Downgraded 1 level for RoB (funder COI) and imprecision (wide confidence interval)
Safety			
Total AEs 1 RCT[a53] N = 175	●●●○ Moderate	Most participants in both groups experienced an AE; however, only around 34% of participants in each group experienced an AE attributed to treatment. No significant difference between groups	Downgraded 1 level for RoB (funder COI).
SAEs 1 RCT[a53] N = 175	●●●○ Moderate	Participants in both groups experienced SAEs (23% vs. 16%). No significant difference between groups	Downgraded 1 level for RoB (funder COI)

Note. [a] *Where only 1 study is available, we were unable to assess inconsistency.*

Abbreviations. AE: adverse event; CoE: certainty of evidence; COI: conflict of interest; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGC: Myasthenia Gravis Composite; MG-QoL 15r: 15-item Myasthenia Gravis Quality of Life scale, revised; NA: not applicable; QMG: Quantitative Myasthenia Gravis; RCT: randomized controlled trial; RoB: risk of bias; SAE: serious adverse event.

Patients receiving ravulizumab had significantly reduced QMG and MG-ADL scores compared with patients receiving placebo (both *P* < .001), but neither difference was clinically meaningful.[53] However, the 95% CIs did cross the MCID for both scores (MD, −2.0; 95% CI, −3.2 to −0.8 for QMG; MD, −1.6; 95% CI, −2.6 to −0.7 for MG-ADL).[53] There were no significant differences between groups for the MG-QoL 15r score or any of the safety outcomes, including for total AEs, SAEs, discontinuations due to AEs, death and exacerbations.[53] The most common AEs were headache, diarrhea, and nausea.[53] Details of outcomes for this study are shown in Appendix C, Table C5.

Rozanolixizumab

We found 2 RCTs, represented by 3 publications, that compared rozanolixizumab with placebo in patients with gMG[54-56]:

- A 2021 phase 2a study by Bril and colleagues that had a small sample size (N = 43), concerns with baseline characteristics, and pharmaceutical company involvement resulting in a *high* RoB assessment.[54] Enrolled patients were in classes II, III, and IV.[54] The intervention group was 5% MuSK-ab+ and 90% AChR-ab+, while the placebo group was 0% MuSK-ab+ and 95% AChR-ab+.[54]
- A 2023 phase 3 study by Bril and colleagues, with 1 ancillary publication, that had pharmaceutical company involvement and poorly reported attrition, resulting in as assessment of *moderate* RoB.[55,56] Enrolled patients were in MGFA Classes IIa to IVb.[55] The placebo group was 12% MuSK-ab+ and 88% AChR-ab+, while the 7 mg/kg dosage group was

8% MuSK-ab+ and 91% AChR-ab+, and the 10 mg/kg dosage group was 12% MuSK-ab+ and 90% AChR-ab+.[55]

Table 9 reports the GRADE findings for 6 outcomes in these studies. Detailed study characteristics are in Appendix B, Table B1, and details about the outcome measures used can be found in Table 1.

Table 9. Summary of Findings (GRADE) on Rozanolixizumab for Myasthenia Gravis

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Symptom severity			
QMG 2 RCTs[54,55] N = 243	●○○○ Very low	In 1 study, 2 dosages of rozanolixizumab both significantly decreased QMG score compared with placebo (*P* < .001), and both met MCID (though 95% CIs cross MCID). The other study reports no difference between groups	Downgraded 1 level each for RoB (funder COI), inconsistency (mixed results), and imprecision (wide confidence intervals)
MGC 2 RCTs[54,55] N = 243	●○○○ Very low	In 1 study, 2 dosages of rozanolixizumab both significantly decreased MGC score compared with placebo (*P* < .001), and both met MCID. The other study does not report significance, with difference (LSMD, −1.8; upper CI, 0.4) not meeting MCID	Downgraded 1 level each for RoB (funder COI), inconsistency (mixed results), and imprecision (wide confidence intervals)
Function			
MG-ADL 2 RCTs[54,55] N = 243	●○○○ Very low	In 1 study, 2 dosages of rozanolixizumab both significantly decreased MG-ADL score compared with placebo (*P* < .001), both meeting MCID (though 95% CIs cross MCID). The other study does not report significance, with difference (LSMD, −1.4; upper CI, 0.4) not meeting MCID	Downgraded 1 level each for RoB (funder COI), inconsistency (mixed results), and imprecision (wide confidence intervals).
Quality of life			
MG-QoL 15r	*NA*	No included studies of rozanolixizumab used the MG-QoL 15r measure	*NA*
Safety			
Total AEs 2 RCTs[54,55] N = 243	●●●○ Moderate	No differences compared with placebo for the 7-mg/kg dosage group in either study. In 1 study, the 10-mg/kg dosage group had significantly more AEs compared with placebo (83% vs 67%, *P* = .04)	Downgraded 1 level for RoB (funder COI).
SAEs 2 RCTs[54,55] N = 243	●●●○ Moderate	No difference between study groups (0% vs 3% for both 7-mg/kg and 10-mg/kg dosages)	Downgraded 1 level for RoB (funder COI).

Abbreviations. AE: adverse event; CI: confidence interval; CoE: certainty of evidence; COI: conflict of interest; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; LSMD: least squares mean difference; MCID: minimal clinically important difference; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGC: Myasthenia Gravis Composite; MG-QoL 15r: 15-item Myasthenia Gravis Quality of Life scale, revised; NA: not applicable; QMG: Quantitative Myasthenia Gravis; RCT: randomized controlled trial; RoB: risk of bias; SAE: serious adverse event.

There was no significant difference in the QMG score among the rozanolixizumab and placebo groups in the phase 2 study.[54] The significance was not reported for the difference in MG-ADL and MGC scores among groups (LSMD, −1.4 and LSMD, −1.8, respectively) and those differences do not meet the respective MCIDs.[54] Additionally, there were no significant differences among groups for total AEs, SAEs, exacerbations, and discontinuations due to AEs.[54] The most common AEs were nausea, vomiting, diarrhea, headache, fatigue, dizziness, and nasopharyngitis.[54]

However, in the phase 3 study, there were significant and clinically meaningful differences between both rozanolixizumab groups (7 mg/kg and 10 mg/kg) and the placebo group for QMG (MD, −3.48 and MD, −4.76; both $P < .001$), MG-ADL (MD, −2.59 and MD, −2.62; both $P < .001$), and MGC (MD, −5.93 and MD, −5.53; both $P < .001$), although the 95% CIs of all these mean differences either hit or cross the MCID (see Table C6 in Appendix C).[55] There are no significant differences in total AEs, SAEs, exacerbations, or discontinuations due to AEs between rozanolixizumab and placebo groups, except for 1 result: patients receiving 10 mg/kg rozanolixizumab had significantly more total AEs than patients receiving placebo (83% vs 67%; $P = .04$).[55] The most common AEs were headache, diarrhea, fever, nausea, nasopharyngitis, muscle pain, and vomiting.[55]

Details of outcomes for these studies are shown in Appendix C, Table C6.

Zilucoplan

We found 2 RCTs, represented by 5 publications, that compared zilucoplan with placebo in patients with gMG, 1 phase 2 and 1 phase 3[57-61]:

- A 2020 phase 2 trial by Howard and colleagues had gender variation between groups, limited reporting of the randomization process, a small sample size (N = 45), and pharmaceutical company involvement, resulting in a *high* RoB assessment.[58] Enrolled patients were MGFA Classes II, III, and IV and 100% AChR-ab+.[58] MuSK-ab status was not specified.[58]
- A 2023 phase 3 trial by Howard and colleagues, called RAISE, had 3 ancillary publications and minimal methodological issues, but pharmaceutical company involvement resulted in a *moderate* RoB assessment.[57,59-61] Enrolled patients were MGFA Classes II, III, and IV, 100% AChR-ab+ and 0% MuSK-ab+.[57]

Table 10 reports the GRADE findings for 6 outcomes in these studies. Detailed study characteristics are in Appendix B, Table B1, and details about the outcome measures used can be found in Table 1.

Table 10. Summary of Findings (GRADE) on Zilucoplan for Myasthenia Gravis

Outcome Number of Studies Sample Size	CoE	Relationship	Rationale for CoE Rating
Symptom severity			
QMG 2 RCTs[57,58] N = 219	●●○○ Low	Both studies reported that zilucoplan significantly decreases QMG score compared with placebo ($P < .001$ to $P = .05$) for their 0.3-mg/kg dosage groups, and both groups were borderline clinically meaningful (−2.8 and −2.94). One study reported no difference for the 0.1-mg/kg dosage ($P = .09$)	Downgraded 1 level each for RoB (funder COI) and imprecision (wide confidence intervals)
MGC 2 RCTs[57,58] N = 219	●●○○ Low	Both studies report that zilucoplan significantly decreases MGC score compared with placebo ($P = .002$ to $P = .04$) for the 0.3-mg/kg dosage groups, and both were clinically meaningful. One study reports no difference for the 0.1-mg/kg dose ($P = .19$).	Downgraded 1 level each for RoB (funder COI) and imprecision (wide confidence intervals)
Function			
MG-ADL 2 RCTs[57,58] N = 219	●●○○ Low	Both studies report that zilucoplan significantly decreased MG-ADL score compared with placebo for all dosage groups ($P < .001$ to $P = .05$), and all were clinically meaningful	Downgraded 1 level each for RoB (funder COI) and imprecision (wide confidence intervals)
Quality of life			
MG-QoL 15r 2 RCTs[57,58] N = 219	●●○○ Low	In the 0.3-mg/kg dosage groups, zilucoplan significantly decreased MG-QoL 15r score compared with placebo ($P = .013$) in 1 study, while in the other study no difference was reported ($P = .06$). For the 0.1 mg/kg group, zilucoplan significantly decreased MG-QoL 15r score ($P = .02$) in 1 study	Downgraded 1 level each for RoB (funder COI) and Inconsistency (mixed results).
Safety			
Total AEs 2 RCTs[57,58] N = 219	●●●○ Moderate	Participants in all groups experienced AEs, and AEs were more common with the study drug for all doses and in both studies: 100% vs 80% for the 0.1 mg/kg dosage group; 77% to 86% vs 70% to 80% for 0.3 mg/kg dosage groups; none of these differences were significant	Downgraded 1 level for RoB (funder COI).
SAEs 2 RCTs[57,58] N = 219	●●●○ Moderate	Observed SAEs ranged from 0% to 20%, with no clear association to treatment group. For the 0.1-mg/kg dosage, there were fewer AEs in the zilucoplan group vs. placebo (0% vs 20%), but this was not significant. For the 0.3 mg/kg groups, the results were also not significant in both studies (36% drug vs 20% placebo and 13% drug vs 15% placebo, respectively)	Downgraded 1 level for RoB (funder COI).

Abbreviations. AE: adverse event; CoE: certainty of evidence; COI: conflict of interest; GRADE: Grading of Recommendations, Assessment, Development, and Evaluations approach; MG-ADL: Myasthenia Gravis Activities of Daily Living; MGC: Myasthenia Gravis Composite; MG-QoL 15r: 15-item Myasthenia Gravis Quality of Life scale, revised; QMG: Quantitative Myasthenia Gravis; RCT: randomized controlled trial; RoB: risk of bias; SAE: serious adverse event.

The 2020 phase 2 trial by Howard and colleagues investigated 2 zilucoplan dosages (0.1 mg/kg and 0.3 mg/kg) compared to placebo over 12 weeks.[58] The 2023 phase 3 trial by Howard and colleagues only compared the 0.3 mg/kg dosage with placebo.[57] For QMG, both trials found that patients receiving the 0.3 mg/kg zilucoplan dosage had significantly decreased scores compared with patients receiving placebo (MD, −2.9; 95% CI, −4.39 to −1.49; *P* < .001; and MD, −2.8; 95% CI, -6.1 to 0.5; *P* = .05).[57,58] This difference between groups was a borderline clinically meaningful difference, with 95% CIs that cross the MCID.[57,58] However, the patient group receiving 0.1 mg/kg zilucoplan had no significant difference in QMG score compared with the placebo group (MD, −2.3; 95% CI, −5.6 to 1.0; *P* = .09), although the 95% CI crossed the MCID.[58]

Similarly, the differences between groups for the MG-ADL score are significant and clinically meaningful, with patients receiving both dosages of zilucoplan in both studies having decreased scores compared with placebo (MD, −2.2; 95% CI, −4.75 to 0.35; *P* = .05 for 0.1 mg/kg; and MD, −2.3; 95% CI, −4.75 to 0.35; *P* = .04; and MD, −2.1; 95% CI, −3.24 to −0.95; *P* < .001 for 0.3 mg/kg).[57,58] For the MGC score, both studies report that patients on the 0.3 mg/kg dosage had significantly decreased scores compared with patients on placebo (MD, −4.1; *P* = .04; and MD, −3.2; *P* = .002); both differences are clinically meaningful.[57,58] However, the phase 2 study found that there was no significant difference between the 0.1 mg/kg group and the placebo group for MGC score.[58]

For quality of life, the 0.1 mg/kg group had a significantly decreased MG-QoL 15r score compared with placebo (MD, −5.3; 95% CI, −10.0 to −0.6; *P* = .02), while there were mixed results for the 0.3 mg/kg group.[57,58] For that group, 1 study reported no significant difference compared with placebo (MD, −3.7; 95% CI, −8.4 to 1.0; *P* = .06) and the other study reported a significantly improved score compared to the placebo group (MD, −3.2; 95% CI, −5.26 to −1.16; *P* = .013).[57,58]

Both studies reported no significant difference between groups for all safety outcomes including total AEs, SAEs, discontinuations due to AEs, and deaths.[57,58] The most common AEs were headache, injection-site reactions, nausea, vomiting, diarrhea, rash, and urinary tract infections.[57,58]

Details of outcomes for these studies are shown in Appendix C, Table C7.

Evidence Summary

Given that this report includes 7 drugs and 6 outcomes, Table 11 provides a summary of the findings by drug, along with their associated GRADE ratings.

Table 11. Overall Outcome Summary of Newer Drugs for Myasthenia Gravis and LEMS

Number of RCTs *Number of participants*
✓ *Significantly favors drug* ⊘ *No significant difference* ✗ *Significantly favors placebo*
* *Clinically meaningful* NR *Not reported*
●○○○ GRADE Very low ●●○○ GRADE Low ●●●○ GRADE Moderate

Drugs	Outcomes					
	QMG	MG-ADL	MG-QoL15r[a]	MGC	Total AEs	Serious AEs
Amifampridine phosphate *for generalized myasthenia gravis*	1 7 1 ✓* ●○○○	1 7 1 ✓* ●○○○	1[c] 7 1 ✓ ●○○○	1 7 1 ✓* ●○○○	NR[b]	1 7 1 ⊘ ●○○○
Amifampridine phosphate *for Lambert-Eaton myasthenic syndrome*	2 64 2 ✓ ●○○○	NR	NR	NR	2 64 2 ⊘ ●○○○	2 64 1 NR 1 ⊘ ●○○○
Eculizumab	2 140 2 ✓* ●○○○	2 140 1 ✓* 1 ⊘ ●○○○	1[c] 126 1 ✓ ●●○○	1 126 1 ✓* ●●○○	1 14 1 ⊘ ●○○○	2 140 2 ⊘ ●●○○
Efgartigimod	2 191 2 ✓* ●●○○	2 191 2 ✓* ●●○○	2 191 2 ✓ ●●○○	2 191 2 ✓* ●●○○	2 191 2 ⊘ ●●●○	2 191 2 ⊘ ●●○○
Nipocalimab	1 68 1 ⊘ ●●○○	1 68 1 ⊘ ●●○○	1 68 1 ⊘ (30 mg/kg dosage ✓) ●●○○	NR	1 68 1 ⊘ ●●●○	1 68 1 ⊘ ●●○○

Drugs	Outcomes					
	QMG	MG-ADL	MG-QoL15r[a]	MGC	Total AEs	Serious AEs
Ravulizumab	1 175 1 ✓ ●●○○	1 175 1 ✓ ●●○○	1 175 1 ⊘ ●●○○	NR	1 175 1 ⊘ ●●●○	1 175 1 ⊘ ●●●○
Rozanolixizumab *higher dose: 10 mg/kg*	2 243 1 ✓* 1 ⊘ ●○○○	2 243 1 ✓* 1 NR ●○○○	NR	2 243 1 ✓* 1 NR ●○○○	2 243 1 ⊘ 1 ✗ ●●●○	2 243 2 ⊘ ●●●○
Rozanolixizumab *lower dose: 7 mg/kg*	2 243 1 ✓* 1 ⊘ ●○○○	2 243 1 ✓* 1 NR ●○○○	NR	2 243 1 ✓* 1 NR ●○○○	2 243 2 ⊘ ●●●○	2 243 2 ⊘ ●●●○
Zilucoplan *higher dose: 0.3 mg/kg*	2 219 2 ✓* ●●○○	2 219 2 ✓* ●●○○	2 219 1 ✓ 1 ⊘ ●●○○	2 219 2 ✓* ●●○○	2 219 2 ⊘ ●●●○	2 219 2 ⊘ ●●●○
Zilucoplan *lower dose: 0.1 mg/kg*	1 45 1 ⊘ ●●○○	1 45 1 ✓* ●●○○	1 45 1 ✓ ●●○○	1 45 1 ⊘ ●●○○	2 219 2 ⊘ ●●●○	2 219 2 ⊘ ●●●○

Notes. [a] There is no reported MCID for the MG-QoL15r score. [b] 7 total AEs reported but no comparison reported between groups. [c] This study uses the non-revised MG-QoL 15.
Abbreviations. AE: adverse event; LEMS: Lambert-Eaton myasthenic syndrome; MGC: Myasthenia Gravis Composite; MG-ADL: Myasthenia Gravis Activities of Daily Living; MG-QoL15r: 15-item Myasthenia Gravis Quality of Life, revised; NR: not reported; NS: no significant difference; QMG: Quantitative Myasthenia Gravis.

Clinical Guidelines (Place in Therapy)

We did not identify any clinical practice guidelines meeting our inclusion criteria; however, we did identify 1 report published in the last 5 years that included more than 2 of these new drugs and had acceptable evidentiary methodology.[62] A 2022 Canadian Agency for Drugs and Technologies in Health (CADTH) *Horizon Scan on Emerging Drugs for Generalized Myasthenia Gravis* summarized the evidence for batoclimab, efgartigimod, nipocalimab, rozanolixizumab, and zilucoplan.[62] Although not a formal clinical practice guideline, it did provide brief summaries on what is known about new and emerging health technologies for gMG.[62]

Based on a systematic horizon scan, the authors concluded that primary treatment of gMG remains anticholinesterase inhibitors, corticosteroids, and nonsteroidal immunosuppressive agents.[62] Additionally, intravenous immunoglobulin and plasma exchange can be used for patients with severe or acutely decompensating gMG, but both have high cost, adverse effects, require intravenous treatment, and can be burdensome to use.[62] Thymectomy, a surgical intervention, may be an additional option for patients who fail to respond to immunotherapy or have serious AEs.[62] In summary, the CADTH report recommends that these emerging agents may provide a new option for patients with disease that is refractory to the primary treatment options or for patients with adverse reactions to those options.[62] However, the report also concluded that information for the emerging therapies was limited (most of the available evidence comes from a mix of phase 2 and 3 RCTs with small sample sizes, short trial duration, and narrow participant inclusion criteria) and may not reflect current standard of care for gMG.[62]

Ongoing Studies

We identified 11 eligible ongoing studies of both FDA-approved and pipeline agents in gMG patients,[63-73] including:

- Amifampridine: 2 studies (MSK-002 and IMPACT-MG)[63,64]
- Batoclimab: 1 study (NCT05403541)[65]
- Cladribine: 1 study (MyClad)[72]
- Efgartigimod: 1 study (ADAPT SERON)[68]
- Gefurulimab: 1 study (PREVAIL)[73]
- Inebilizumab: 1 study (MINT)[66]
- Iptacopan: 1 study (NCT06517758)[71]
- Nipocalimab: 1 study (Vivacity MG3)[67]
- Pozelimab and cemdisiran: 1 study (NIMBLE)[69]
- Telitacicept: 1 study (RemeMG)[70]

Please note that the Vivacity MG3 study has been published in January 2025, after the December 12, 2024 search date for this report.[52]

The actual or estimated completion dates for these trials range from 2020 to 2030.[63-73] NIMBLE is the only study that directly compares 2 drugs (pozelimab and cemdisiran), as well as comparing them both to placebo.[69] The rest of the trials compare the drug to placebo, and 1 study, (IMPACT-MG) also includes pyridostigmine, which is not an intervention relevant to this report.[63] The most widely-used primary outcome for these ongoing studies is MG-ADL score. The only other score, beyond the 4 described in this report, being used as a primary outcome in these ongoing studies is the Myasthenia Gravis Impairment Index.[63] All populations are adults with

gMG, though the MINT study also accepts adolescents (aged ≥ 12 years).[66] Many, but not all, of the studies distinguish their population by antibody status:

- No specification: 3 studies[65,67,73]
- AChR-ab+: 3 studies[63,68,71]
- AChR-ab+ or MuSK-ab+: 4 studies[64,66,70,72]
- AChR-ab+ or LRP4-ab+: 1 study[69]

Table 12. Ongoing RCTs of Pipeline Agents for Myasthenia Gravis

Trial Number Trial Name	Population	Intervention	Primary Outcome(s)	Completion Date
NCT03304054[64] MSK-002	Patients aged ≥ 18 years with gMG that is AChR-ab+ or MuSK-ab+ N = 93	• Amifampridine Phosphate • Placebo	• MG-ADL by time and gMG type	March 2020 (actual)
NCT04951622[67] Vivacity MG3	Patients aged ≥ 18 years with gMG N = 196	• Nipocalimab • Placebo	• Change in MG-ADL	November 2023 (actual) Publication January 2025[52]
NCT05919407[63] IMPACT-MG	Patients aged ≥ 18 years with gMG that is AChR-ab+ N = 24	• Amifampridine Phosphate • Placebo • Pyridostigmine	• Change in Myasthenia Gravis Impairment Index (MGII)	September 2024 (actual)
NCT05403541[65]	Patients aged ≥ 18 years with gMG N = 240	• Batoclimab (2 dosages and 2 dosage schedules) • Placebo	• Change in MG-ADL in AChR-ab+ participants	March 2025 (estimated)
NCT05070858[69] NIMBLE	Patients aged ≥ 18 years with gMG that is AChR-ab+ or LRP4-ab+ N = 235	• Pozelimab • Cemdisiran • Pozelimab + cemdisiran • Placebo	• Change in MG-ADL	May 2025 with extension to March 2028 (estimated)
NCT06456580[70] RemeMG	Patients aged ≥ 18 years with gMG that is AChR-ab+ or MuSK-ab+ N = 180	• Telitacicept • Placebo	• Change in MG-ADL	July 2026 (estimated)
NCT06517758[71]	Patients aged 18-75 years with gMG that is AChR-ab+ N = 146	• Iptacopan • Placebo	• Change in MG-ADL	December 2026 with extension to January 2029 (estimated)
NCT06298552[68] ADAPT SERON	Patients aged ≥ 18 years with gMG that is AChR-ab+ N = 110	• Efgartigimod • Placebo	• Change in MG-ADL	July 2027 (estimated)

Trial Number Trial Name	Population	Intervention	Primary Outcome(s)	Completion Date
NCT05556096[73] PREVAIL	Patients aged ≥ 18 years with gMG N = 260	• Gefurulimab (ALXN1720) • Placebo	• Change in MG-ADL	August 2027 (estimated)
NCT04524273[66] MINT	Patients aged ≥ 12 years with gMG that is AChR-ab+ or MuSK-ab+ N = 238	• Inebilizumab • Placebo	• Change in MG-ADL score	November 2027 (estimated)
NCT06463587[72] MyClad	Patients aged ≥ 18 years with gMG that is AChR-ab+ or MuSK-ab+ N = 240	• Cladribine low dosage • Cladribine high dosage • Placebo	• Change in MG-ADL	May 2028 with extension to July 2030 (estimated)

Abbreviations. AChR-ab+: positive for anti-acetylcholine receptor antibodies; gMG: generalized myasthenia gravis; MG-ADL: Myasthenia Gravis Activities of Daily Living; MuSK-ab+: positive for anti–muscle-specific kinase antibodies; RCT: randomized controlled trial.

State Considerations

- State administrators may find it difficult to select preferred agents from this list, as these therapies have similar effectiveness and safety profiles versus placebo; we also did not identify any head-to-head comparisons
- The treatment landscape for gMG is changing rapidly, with multiple drugs either recently approved or in the approval process
- Routes of administration for these agents may be a consideration, as several of these drugs are administered intravenously. The setting of intravenous drug administration, such as a clinic, infusion center, or home health service, may create barriers to access, compared with those therapies that are taken through subcutaneous or oral routes
- Newer drugs may provide additional options for patients who are refractory to or cannot tolerate the conventional therapy for gMG. The 2 eculizumab studies and 1 nipocalimab study in this report were conducted in patients with refractory gMG

Discussion

We investigated 7 new biological agents for the treatment of gMG and LEMS; each was compared to placebo in our included studies. While there was some variation between studies and mixed results within studies for individual drugs, overall, the data demonstrated these drugs may perform better than placebo for gMG; however, the CoE related to effectiveness is *low to very low*, highlighting some significant degree of uncertainty in how well these drugs perform. Similarly, there remains significant uncertainty in the effectiveness of amifampridine phosphate for LEMS.

The most-reported AEs across the newer drugs were headache, gastrointestinal symptoms (nausea, vomiting and diarrhea), and nasopharyngitis. The most reported serious AEs were worsening myasthenia gravis and myasthenic crisis. Overall, the data suggested these drugs do not cause more AEs than placebo; however, most study participants did experience at least 1 AE.

Generalized myasthenia gravis is a rare disease with limited population sizes. Additionally, given the large number of new drugs under investigation, several of the relevant trials are phase 2, crossover, and withdrawal studies, with short durations, methodological issues, and often a high RoB assessment. Therefore, we are limited in drawing conclusions. Nonetheless, the significant and clinically meaningful results in favor of the drugs, despite these concerns, indicate these drugs may be efficacious in improving gMG symptoms and quality of life, at least compared to placebo.

Although there is a lack of head-to-head drug comparison, we did identify a 2024 network meta-analysis with well-detailed procedures based on PRISMA and Cochrane methodology.[74] This analysis included 6 of the target drugs as well as additional pipeline agents and reviewed many of the same RCTs as this report.[74] This network meta-analysis reported that batoclimab, a pipeline agent, was the most effective in reducing QMG score when compared with placebo; however, none of the other agents (including eculizumab, efgartigimod, nipocalimab, ravulizumab, rozanolixizumab, and zilucoplan) were significantly better than placebo.[74] In terms of safety, batoclimab was, again, the top-ranked drug, and the only one with significantly fewer AEs relative to placebo, followed in the ranking by belimumab and efgartigimod, with zilucoplan ranking last in terms of safety.[74]

The safety results of this network meta-analysis are similar to our findings, in that there were only very few significant differences between these drugs and placebo.[74] Regarding efficacy, our results did not show much variation among the drugs for QMG score, with most of them demonstrating both statistically significant and clinically meaningful reductions relative to placebo. The absence of head-to-head studies does not allow us to make a comparison in our data, but it is interesting that the pipeline agent, batoclimab, performed best in the network meta-analysis rankings.[74] It is also interesting that nipocalimab, the only drug in our findings that was not better than placebo in reduction of QMG score, was also the lowest ranked among the drugs in the network meta-analysis.[74] This may change, however, based on the phase 3 Vivacity-MG3 trial of nipocalimab, which was published in January 2025, and outside of our date cutoff for analysis herein.

Limitations

There are several limitations of this review. No RCT phase or sample size limitations were applied, which resulted in the inclusion of some phase 2 studies with very small study populations. However, we made this decision to encompass all possible data, given the rarity of the disease. Additionally, the included studies all had significant pharmaceutical company involvement and funding, such as authors employed by those companies, which also contributed to concern about bias, leading to lower certainty of evidence. Finally, we found no head-to-head trials; instead, all drugs were compared to placebo. Given a rapidly changing landscape with multiple drugs in the approval process, such head-to-head clinical trials are needed. However, we did not identify any ongoing relevant head-to-head studies, other than 1 study of pipeline agents pozelimab and cemdisiran.

Conclusions

Myasthenia gravis is a rare disease with high morbidity that does not have any curative treatment to-date. The current primary treatments used to reduce disease symptoms are not

always effective and have a notable AE burden. Overall, the new drugs for treatment of gMG and related LEMS condition demonstrate a relative lack of AEs, as well as statistically significant and clinically meaningful efficacy improvements over placebo. Head-to-head studies are not yet available and are needed. Also, there are notable risk of bias levels in the placebo-controlled trials. Nonetheless, these emerging drugs may provide a valuable option, particularly for patients nonresponsive to or unable to tolerate conventional treatments.

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Appendix A. Methods

Clinical Evidence Methods

Search Strategy

We searched OVID MEDLINE All, Cochrane Central Register of Controlled Trials in OVID, and Embase, from database inception to December 12, 2024. Searches were limited to English language. We reviewed the references lists of systematic reviews identified in the searches rather than using them as evidence sources. We also identified relevant clinical guidelines. Our searches were conducted on December 12, 2024.

Bibliographic Databases

Table A1: Bibliographic Databases

Database	Platform	Dates	Total Number of Records Retrieved
CENTRAL	Ovid	1991 to December 12, 2024	4
MEDLINE ALL	Ovid	1946 to December 12, 2024	309
Embase	Elsevier	1947 to December 12, 2024	563

Abbreviations. CENTRAL: Cochrane Central Register of Controlled Trials.

Ovid MEDLINE ALL Search Strategy

1 Myasthenia Gravis/

2 'myasthenia gravis'.mp.

3 Lambert-Eaton Myasthenic Syndrome/

4 ('lambert-eaton* myasthenic syndrome' or LEMS).mp.

5 or/1-4

6 (Eculizumab* or soliris or Elizaria or Epysqli or Bekemv or H5-G1-1).mp.

7 (ravulizumab* or ultomiris or ALXN-1810 or ALXN-1210).mp.

8 (zilucoplan* or zilbrysq or RA101495).mp.

9 (Efgartigimod* or vyvgart or hytrulo or ARGX-113).mp.

10 (Rozanolixizumab* or rystiggo or UCB-7665).mp.

11 (Inebilizumab* or uplizna or MEDI-551).mp.

12 ('Amifampridine Phosphate*' or Firdapse).mp.

13 (Nipocalimab* or M281).mp.

14 or/6-13

15 5 and 14

16 limit 15 to english language

CENTRAL via OVID Search Strategy

1 Myasthenia Gravis/

2 'myasthenia gravis'.mp.

3 Lambert-Eaton Myasthenic Syndrome/

4 ('lambert-eaton* myasthenic syndrome' or LEMS).mp.

5 or/1-4

6 (Eculizumab* or soliris or Elizaria or Epysqli or Bekemv or H5-G1-1).mp.

7 (ravulizumab* or ultomiris or ALXN-1810 or ALXN-1210).mp.

8 (zilucoplan* or zilbrysq or RA101495).mp.

9 (Efgartigimod* or vyvgart or hytrulo or ARGX-113).mp.

10 (Rozanolixizumab* or rystiggo or UCB-7665).mp.

11 (Inebilizumab* or uplizna or MEDI-551).mp.

12 ('Amifampridine Phosphate*' or Firdapse).mp.

13 (Nipocalimab* or M281).mp.

14 or/6-13

15 5 and 14

16 limit 15 to english language

Embase Search Strategy

(('myasthenia gravis'/exp OR 'eaton lambert syndrome'/exp OR 'myasthenia gravis' OR 'eaton' NEAR/1 'lambert') AND ((eculizumab* OR soliris OR elizaria OR epysqli OR bekemv OR 'h5 g1 1') OR (ravulizumab* OR ultomiris OR 'alxn 1810' OR 'alxn 1210') OR (zilucoplan* OR zilbrysq OR ra101495) OR (efgartigimod* OR vyvgart OR hytrulo OR 'argx 113') OR (rozanolixizumab* OR rystiggo OR 'ucb 7665') OR (inebilizumab* OR uplizna OR 'medi 551') OR ('amifampridine phosphate*' OR firdapse) OR (nipocalimab* OR m281)) AND [english]/lim AND [embase]/lim) NOT (('myasthenia gravis'/exp OR 'eaton lambert syndrome'/exp OR 'myasthenia gravis' OR 'eaton' NEAR/1 'lambert') AND ((eculizumab* OR soliris OR elizaria OR epysqli OR bekemv OR 'h5 g1 1') OR (ravulizumab* OR ultomiris OR 'alxn 1810' OR 'alxn 1210') OR (zilucoplan* OR zilbrysq OR ra101495) OR (efgartigimod* OR vyvgart OR hytrulo OR 'argx 113') OR (rozanolixizumab* OR rystiggo OR 'ucb 7665') OR (inebilizumab* OR uplizna OR 'medi 551') OR ('amifampridine phosphate*' OR firdapse) OR (nipocalimab* OR m281)) AND [english]/lim AND [medline]/lim)

Gray Literature Searches

We searched for gray literature using Google and DuckDuckGo with the following search terms: *myasthenia gravis*, *amifampridine*, *eculizumab*, *efgartigimod*, *ravulizumab*, *nipocalimab*, *rozanolixizumab*, *zilucoplan*, *soliris*, *vyvgart*, *ultomiris*, *rystiggo*, *zilbrysq*, *rystiggo*, *zilbrysq*, *inebilizumab*,

cemdisiran, *pozelimab*, *batoclimab*, *gefurulimab*, *cladribine*, *telitacicept*, *iptacopan*, *uplizna*, *veopoz*, *mavenclad*, and *fabhalta*.

Ongoing Studies

We searched the following DERP sources for ongoing studies using the search terms: *myasthenia gravis*, *amifampridine*, *eculizumab*, *efgartigimod*, *ravulizumab*, *nipocalimab*, *rozanolixizumab*, *zilucoplan*, *soliris*, *vyvgart*, *ultomiris*, *rystiggo*, *zilbrysq*, *inebilizumab*, *cemdisiran*, *pozelimab*, *batoclimab*, *gefurulimab*, *cladribine*, *telitacicept*, *iptacopan*, *uplizna*, *veopoz*, *mavenclad*, and *fabhalta*

- ClinicalTrials.gov
- ScanMedicine

Clinical Practice Guidelines

We searched DERP clinical practice guideline sources to identify guidelines using the search term: *myasthenia gravis*. We searched the following sources for clinical practice guidelines published in the last 5 years:

- Agency for Healthcare Research and Quality (AHRQ)
- Canadian Agency for Drugs and Technologies in Health
- Epistemonikos
- Guidelines International Network (GIN)
- Institute for Clinical and Economic Review
- International HTA (Health Technology Assessment) Database
- National Institute for Health and Care Excellence (NICE)
- Oregon Health Evidence Review Commission
- Ovid MEDLINE ALL
- Scottish Intercollegiate Guidelines Network (SIGN)
- (Department of Veterans Affairs) VA/DoD (Department of Defense) Clinical Practice Guidelines
- Washington Health Technology Assessment

We used Google, Google Scholar, and DuckDuckGo for identifying additional relevant clinical practice guidelines using the following search terms: *myasthenia gravis*, and *guideline*.

Inclusion Criteria

Population

Adults with generalized myasthenia gravis (gMG) or Lambert-Eaton myasthenic syndrome (LEMS)

Interventions

Drugs specified in Table 2

Comparisons

- Head-to-head
- Placebo
- Standard care, usual care
- Attention control

Outcomes

- Levels of blood immunoglobulin
- Symptom control
- Function (e.g., activities of daily living), using a validated tool
- Quality of life, using a validated tool
- Time to first exacerbation
- Adverse events
- Serious adverse events (e.g., hospitalization, disability or incapacity, mortality)

Study Types

- Randomized controlled trials (RCTs)
- Studies from countries that are *very high* on the United Nations' Human Development Index

Exclusion Criteria

We excluded studies if they were not published in English.

Screening

Two experienced researchers independently screened all titles and abstracts of identified documents. In cases in which there was disagreement about eligibility, a third experienced researcher resolved the disagreement. This method was repeated for full-text review of documents that could not be excluded by title and abstract screening.

Data Abstraction

One experienced researcher abstracted and entered data from eligible studies in a standardized way using Distiller. A second experienced researcher reviewed all the data entered. We attempted to resolve discrepancies through discussion. When discussion did not resolve the issue, a third experienced researcher settled disagreements.

Participant Characteristics and Association with Outcomes

When discussing risk and protective factors or variables in statistical models in DERP research products, in almost all cases, we are referring to associations of participant characteristics with outcomes, and not causation of outcomes. This is important because participant characteristics, such as race and ethnicity, serve as proxy or surrogate measures for underlying etiological factors not measured or evaluated in analyses. Etiological factors that might cause differences in outcomes for subgroups of participants could include systemic racism or other forms of systemic discrimination, stress, poverty, housing instability, or epigenetics. For example, by describing any differences in outcomes by race and ethnic groups, we are noting observed associations; these associations are not caused by biological determinants of being Black, White, or Hispanic.

Risk of Bias Assessment

We assessed the risk of bias of the included RCTs using standard instruments developed and adapted by DERP that are modifications of instruments used by national and international standards for quality.[75-77] Two experienced researchers independently rated all included studies.

In cases in which there was disagreement about the risk of bias of a study, it was managed by discussion.

Systematic Reviews and Randomized Controlled Trials

If a meta-analysis or network meta-analysis was conducted, the risk of bias of the analyses was considered in the overall rating for the systematic review. In brief, low-risk-of-bias systematic reviews include a clearly focused question, a literature search sufficiently rigorous to identify all relevant studies, criteria used to assess study quality and select studies for inclusion (e.g., randomized controlled trials), and assessments of heterogeneity to determine whether a meta-analysis would be appropriate. Low-risk-of-bias randomized controlled trials include a clear description of the population, setting, intervention, and comparison groups; a random and concealed allocation of patients to study groups; low dropout rates; and intention-to-treat analyses. Low-risk-of-bias systematic reviews and randomized controlled trials also have low potential for bias from conflicts of interest and funding source(s). Moderate-risk-of-bias systematic reviews and randomized controlled trials have incomplete information about methods that might mask important limitations. High-risk-of-bias systematic reviews and randomized controlled trials have clear flaws that could introduce significant bias.

Systematic Reviews

If a meta-analysis or network meta-analysis was conducted, the risk of bias of the analyses was considered in the overall rating for the systematic review. In brief, low-risk-of-bias systematic reviews include a clearly focused question, a literature search sufficiently rigorous to identify all relevant studies, criteria used to assess study quality and select studies for inclusion (e.g., randomized controlled trials), and assessment of similarities between studies to determine whether combining them is appropriate for evidence synthesis. Moderate-risk-of-bias systematic reviews have incomplete information about methods that might mask important limitations or a meaningful conflict of interest. High-risk-of-bias systematic reviews have clear flaws that could introduce significant bias.

Randomized Controlled Trials

Low-risk-of-bias randomized controlled trials include a clear description of the population, setting, intervention, and comparison groups; a random and concealed allocation of patients to study groups; low dropout rates; and intention-to-treat analyses. Low-risk-of-bias randomized controlled trials also have low potential for bias from conflicts of interest and funding source(s). Moderate-risk-of-bias randomized controlled trials have incomplete information about methods that might mask important limitations or a meaningful conflict of interest. High-risk-of-bias randomized controlled trials have clear flaws that could introduce significant bias.

Clinical Practice Guidelines

We assessed the methodological quality of the guidelines using an instrument adapted from the Appraisal of Guidelines Research and Evaluation (AGREE) Collaboration.[78,79] Each rater assigned the study a rating of good, fair, or poor based on its adherence to recommended methods and potential for biases. A good-quality guideline fulfills all or most of the criteria outlined in the instrument. A fair-quality guideline fulfills some of the criteria, and its unfulfilled criteria are not likely to alter the recommendations. A poor-quality guideline met few or none of the criteria.

Certainty of Evidence Assessment

We assigned each outcome a summary judgment for the overall certainty of evidence based on the system developed by the Grading of Recommendations, Assessment, Development, and Evaluation Working Group (GRADE).[80,81] Two independent experienced researchers assigned ratings, with disagreements resolved by a third rater. The GRADE system defines the overall certainty of a body of evidence for an outcome in the following manner:

- **High:** Raters are very confident that the estimate of the effect of the intervention on the outcome lies close to the true effect. Typical sets of studies are randomized controlled trials with few or no limitations, and the estimate of effect is likely stable.
- **Moderate:** Raters are moderately confident in the estimate of the effect of the intervention on the outcome. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is different. Typical sets of studies are randomized controlled trials with some limitations or well-performed nonrandomized studies with additional strengths that guard against potential bias and have large estimates of effects.
- **Low:** Raters have little confidence in the estimate of the effect of the intervention on the outcome. The true effect may be substantially different from the estimate of the effect. Typical sets of studies are randomized controlled trials with serious limitations or nonrandomized studies without special strengths.
- **Very low:** Raters have no confidence in the estimate of the effect of the intervention on the outcome. The true effect is likely to be substantially different from the estimate of effect. Typical sets of studies are nonrandomized studies with serious limitations or inconsistent results across studies.
- **Not applicable:** Researchers did not identify any eligible articles.

Appendix B. Study Characteristics and Baseline Data

Table B1. Summary of Key Study and Participant Characteristics for Included RCTs of Newer Treatments for gMG and LEMS

Study Characteristics					Baseline Characteristics (Drug vs. Placebo)					Risk of Bias
Author, Year Number (NCT) Study Name	Location	N Randomized N vs N (Drug vs PBO)	Study Duration, weeks	Age Criteria, years	Mean Age, years	% Female	Mean Duration of disease, years	MGFA classes	Antibody Status (MuSK+, AChR+)	
Amifampridine phosphate										
Bonanno 2018[16] AIFA 46/2015 MuSK-001	Italy	N = 7 Placebo-amifampridine-placebo (PAP) group 4 vs amifampridine-placebo-amifampridine (APA) group 3	3	≥ 18	PAP group 46.3 vs APA group 39.7	PAP group 100 vs APA group 66.7	PAP group 7 vs APA group 7	II, III, IV	MuSK+ 100% AChR+ NR	High RoB
Oh, 2016[28] NCT01377922	International, including US	N = 38 16 vs 22	2	≥ 18	51.6 vs 51.5	9 vs 14	NR	NA (LEMS)	NA (LEMS)	High RoB
Shieh, 2019[29] NCT02970162	US	N = 26 13 vs 13	4 days	≥ 18	54.9 vs 53.4	54 vs 69	NR	NA (LEMS)	NA (LEMS)	High RoB
Eculizumab										
Howard 2013[32] NCT00727194	Canada, UK, US	N = 14 7 vs 7	16	19 to 80	48 (crossover)	57 (crossover)	7 (crossover)	II, IIa, IIb, III, IIIa, IIIb, IVa	MuSK+ NR AChR+ 100%	High RoB
Howard, 2017[33] NCT01997229 REGAIN	International, including US	N = 126 62 vs 63	26	≥ 18	47.5 vs 46.9	66 vs 65	9.9 vs 9.2	II, IIa, IIb, III, IIIa, IIIb, IV, IVa, IVb	MuSK+ NR AChR+ 100%	Moderate RoB

Study Characteristics					Baseline Characteristics (Drug vs. Placebo)					Risk of Bias
Author, Year Number (NCT) Study Name	Location	N Randomized N vs N (Drug vs PBO)	Study Duration, weeks	Age Criteria, years	Mean Age, years	% Female	Mean Duration of disease, years	MGFA classes	Antibody Status (MuSK+, AChR+)	
Efgartigimod										
Howard, 2019[44] NCT02965573	International, including US	N = 24 12 vs 12	11.4 weeks (80 days)	≥ 18	55.3 vs 43.5	58.3 vs 66.7	8.2 vs 13.3	II, III, IV	MuSK+ NR AChR+ 100%	High RoB
Howard, 2021[45] NCT03669588 ADAPT	International, including US	N = 167 All: 84 vs 83 AChR-ab+: 65 vs 64	26 (≤ 3 treatment cycles)	≥ 18	45.9 vs 48.2	75 vs 66	10.1 vs 8.8	II, III, IV	MuSK+ 4% vs 4% AChR+ 77% vs 77%	High RoB
Nipocalimab										
Antozzi, 2024[51] NCT03772587 Vivacity-MG	International, including US	N = 68 5 mg/kg: 14 vs 14 30 mg/kg: 13 vs 14 60 mg/kg single dose: 13 vs 14 60 mg/kg Q2W dose: 14 vs 14	8 (57 days)	≥ 18	5 mg/kg dose: 53 vs 60.5 30 mg/kg dose: 44 vs 60.5 60 mg/kg single dose: 47 vs 60.5 60 mg/kg Q2W dose: 63 vs 60.5	5 mg/kg dose: 43 vs 57 30 mg/kg dose: 69 vs 57 60 mg/kg single dose: 69 vs 57 60 mg/kg Q2W dose: 36 vs 57	5 mg/kg dose: 8 vs 13.2 30 mg/kg dose: 8.4 vs 13.2 60 mg/kg single dose: 7 vs 13.2 60 mg/kg Q2W dose: 6 vs 13.2	IIa, IIb, IIIa, IIIb, IVa	MuSK+ Placebo 7.1% 5 mg/kg dose: 7.1% 30 mg/kg dose: 7.1% 60 mg/kg single dose: 0% 60 mg/kg Q2W dose: 7.1% AChR+ Placebo: 92.9% 5 mg/kg dose: 92.9%: 30 mg/kg dose: 92.3%	Moderate RoB

Study Characteristics					Baseline Characteristics (Drug vs. Placebo)					Risk of Bias
Author, Year Number (NCT) Study Name	Location	N Randomized N vs N (Drug vs PBO)	Study Duration, weeks	Age Criteria, years	Mean Age, years	% Female	Mean Duration of disease, years	MGFA classes	Antibody Status (MuSK+, AChR+)	
									60 mg/kg single dose: 100% 60 mg/kg Q2W dose: 92.9%	
Ravulizumab										
Vu, 2022[53] NCT03920293 CHAMPION MG	International, including US	N = 175 86 vs 89	26	≥ 18	58 vs 53.3	51 vs 51	9.8 vs 10	II, IIa, IIb, III, IIIa, IIIb, IV, IVa, IVb	MuSK+ NR AChR+ 100%	Moderate RoB
Rozanolixizumab										
Bril, 2021[54] NCT03052751	International, including US	N = 43 21 vs 22	4 (29 days)	≥ 18	50.5 vs 53.3	62 vs 64	NR	II, III, IV	MuSK+: 5% vs 0% AChR+ 90% vs 95%	High RoB
Bril, 2023[55] NCT03971422 MycarinG	International, including US	N = 200 7 mg/kg dose: 66 vs 67 10 mg/kg dose: 67 vs 67	6	≥ 18	7 mg/kg dose: 53.2 vs 50.4 10 mg/kg dose: 51.9 vs 50.4	7 mg/kg dose: 59 vs 70 10 mg/kg dose: 52 vs 70	7 mg/kg dose: 5.3 vs 6.8 10 mg/kg dose: 5.7 vs 6.8	IIa, IIB, IIIa, IIIb, Iva, IVb	MuSK+ 7 mg/kg dose: 8% vs 12% 10 mg/kg dose: 12% vs 12% AChR+ 7 mg/kg dose: 91% vs 88% 10 mg/kg dose: 90% vs 88%	Moderate RoB

Study Characteristics					Baseline Characteristics (Drug vs. Placebo)					Risk of Bias
Author, Year Number (NCT) Study Name	Location	N Randomized N vs N (Drug vs PBO)	Study Duration, weeks	Age Criteria, years	Mean Age, years	% Female	Mean Duration of disease, years	MGFA classes	Antibody Status (MuSK+, AChR+)	
Zilucoplan										
Howard, 2020[58] NCT03315130	Canada and US	N = 45 0.1 mg/kg-dose: 15 vs 15 0.3 mg/kg dose: 14 vs 15	12	18 to 85	0.1 mg/kg dose: 45.5 vs. 48.4 0.3 mg/kg dose: 54.6 vs. 48.4	0.1 mg/kg dose: 53.3 vs. 73.3 0.3 mg/kg dose: 28.6 vs. 73.3	0.1 mg/kg dose: 6.5 vs. 6.3 0.3 mg/kg dose: 5.3 vs. 6.3	II, III, IV	0.1 mg/kg dose: 8 vs. 5 0.3 mg/kg dose: 7 vs. 5	High RoB
Howard, 2023[57] NCT04115293 RAISE	International, including US	N = 174 86 vs 84	12	18 to 74	52.6 vs 53.3		9.3 vs 9.0	II, III, IV	MuSK+ 0% AChR+ 100%	Moderate RoB

Abbreviations. AChR-ab+: positive for anti-acetylcholine receptor antibodies; gMG: generalized myasthenia gravis; LEMS: Lambert-Eaton myasthenic syndrome; MuSK+: positive for anti–muscle-specific kinase antibodies; NR: not reported; Q2W: every 2 weeks; RCT: randomized clinical trial; RoB: risk of bias

Appendix C. Data Outcomes by Drug

Table C1. Outcomes for Amifampridine Phosphate

Study	Condition	Comparison Groups (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Generalized myasthenia gravis					
Symptom severity					
Quantitative Myasthenia Gravis (QMG) score					
Bonanno 2018[16] AIFA 46/2015 MuSK-001	MuSK-MG	Amifampridine-30 to 100 mg (10) vs placebo (11)	7 days	0.1 vs. 6.9 CFB LSMD, −6.9 (95% CI, −9.75 to −3.98); *P* < .001	Clinically meaningful and significant favoring drug
MG Composite (MGC) score					
Bonanno 2018[16] AIFA 46/2015 MuSK-001	MuSK-MG	Amifampridine-30 to 100 mg (10) vs placebo (11)	7 days	0.1 vs 11.6 CFB LSMD, −11.5 (95% CI, −15.25 to −7.70); *P* < .001	Clinically meaningful and significant favoring drug
Function					
MG Activities of Daily Living (MG-ADL) score					
Bonanno 2018[16] AIFA 46/2015 MuSK-001	MuSK-MG	Amifampridine-30 to 100 mg (10) vs placebo (11)	7 days	-0.1 vs 5.6 CFB LSMD, −5.7 (95% CI, −8.33 to −3.12); *P* < .001	Clinically meaningful and significant favoring drug
Quality of life					
Myasthenia Gravis Quality of Life−15 (MG-QoL 15) score					
Bonanno 2018[16] AIFA 46/2015 MuSK-001	MuSK-MG	Amifampridine-30 to 100 mg (10) vs placebo (11)	7 days	-2.1 vs 16.4 CFB LSMD, −18.5 (95% CI, −28.79 to −8.21; *P* = .003	Significant favoring drug; MCID not known
Serum immunoglobulin levels					
NR					
Responder analyses					
NR					

Study	Condition	Comparison Groups (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Safety					
Total adverse events					
Bonanno 2018[16] AIFA 46/2015 MuSK-001	MuSK-MG	Amifampridine-30 to 100 mg (10) vs placebo (11)	7 days	A total of 7 patients reported AEs, no comparison between groups provided.	NR
Serious adverse events					
Bonanno 2018[16] AIFA 46/2015 MuSK-001	MuSK-MG	Placebo–amifampridine– placebo (4) vs amifampridine– placebo–amifampridine (3)	3 weeks	0% vs 0%	No significant difference.
Discontinuation due to adverse events					
Bonanno 2018[16] AIFA 46/2015 MuSK-001	MuSK-MG	Placebo–amifampridine– placebo (4) vs amifampridine– placebo–amifampridine (3)	3 weeks	0% vs 0%	No significant difference.
Deaths					
NR					
Exacerbations					
NR					
Hospitalizations					
NR					
Lambert-Eaton myasthenic syndrome					
Symptom severity					
Quantitative Myasthenia Gravis (QMG) score					
Oh, 2016[28] NCT01377922	LEMS	Amifampridine-30 to 80 mg (16) vs placebo- withdrawal of drug (22)	2 weeks	0.3 vs 2.2 CFB MD, -1.7 (95% CI, -3.4 to 0.0); *P* = .045	Marginally significant favoring drug; not clinically meaningful

Study	Condition	Comparison Groups (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Shieh, 2019[29] NCT02970162	LEMS	Amifampridine-30 to 80 mg (13) vs placebo - withdrawal of drug (13)	4 days	0.7 vs 7.1 CFB MD, estimated[a] as -2, (95% CI, -0.78 to -3.29); *P* < .001	Significant favoring drug; neither clinically meaningful
MG Composite (MGC) score					
NR					
Function					
MG Activities of Daily Living (MG-ADL) score					
NR					
Timed 25-foot walk test (TFW25)					
Oh, 2016[28] NCT01377922	LEMS	Amifampridine-30 to 80 mg (16) vs placebo- withdrawal of drug (22)	2 weeks	253 ± 126 vs 244 ± 116 feet/minute *P* > .05	No significant difference between groups
Triple-timed up-and-go test (3TUG)					
Shieh, 2019[29] NCT02970162	LEMS	Amifampridine-30 to 80 mg (13) vs placebo - withdrawal of drug (13)	4 days	1/13 (7.7%) vs 8/13 (61.5%) with increased time in test *P* = .01	Significant favoring drug
Quality of life					
Revised Myasthenia Gravis Quality of Life—15 (MG-QoL 15r) score					
NR					
Serum immunoglobulin levels					
NR					
Responder analyses					
NR					

Study	Condition	Comparison Groups (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Safety					
Total adverse events					
Oh, 2016[28] NCT01377922	LEMS	Amifampridine-30 to 80 mg (16) vs placebo - withdrawal of drug* (22)	2 weeks	18.8% vs 27.3% (part 3, treatment phase) RR = 0.69 (95% CI, 0.2 to 2.35); *P* = .60	No significant difference.
Shieh, 2019[29] NCT02970162	LEMS	Amifampridine-30 to 80 mg (13) vs placebo - withdrawal of drug (13)	4 days	3 AEs in 3 patients (24%) vs 11 AEs but number of patients not reported	More AEs with the placebo compared to the drug but significance NR
Serious adverse events					
Oh, 2016[28] NCT01377922	LEMS	Amifampridine-30 to 80 mg (16) vs placebo - withdrawal of drug (22)	≥ 2 weeks	0% vs 0%	No significant difference.
Shieh, 2019[29] NCT02970162	LEMS	Amifampridine-30 to 80 mg (13) vs placebo - withdrawal of drug (13)	4 days	0% vs 0%	No significant difference.
Discontinuation due to adverse events					
Shieh, 2019[29] NCT02970162	LEMS	Amifampridine-30 to 80 mg (13) vs placebo - withdrawal of drug (13)	4 days	0% vs 0%	No significant difference.
Oh, 2016[28] NCT01377922	LEMS	Amifampridine-30 to 80 mg (16) vs placebo - withdrawal of drug (22)	≥ 2 weeks	0% vs 0%	No significant difference.
Deaths					
NR					
Exacerbations					
NR					
Hospitalizations					
NR					

Notes. [a] *LSMD not reported in study; estimated as midpoint in reported 95% CI.*

Abbreviations. AE: adverse event; CFB: change from baseline; LSMD: least squares mean difference; MD: mean difference; NR: not reported; RR: risk ratio; SE: standard error.

Table C2. Outcomes for Eculizumab

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Quantitative Myasthenia Gravis (QMG) score				
Howard 2013[32] NCT00727194	Period 1: eculizumab-900 mg (7) vs placebo (7)	16 weeks	-7.4 vs -2.7 CFB MD, -4.7 (NR), NR	Clinically meaningful difference favoring drug; significance not provided but unlikely to be statistically significant as CIs overlap
	Over 2 periods and washout: eculizumab-900 mg (13) vs placebo (13)	37 weeks	-7.92 vs -3.67 CFB MD, -4.25 (NR), *P* = .014	Clinically meaningful and significant favoring drug; washout not fully effective
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	-4.6 vs -1.6 CFB MD, -3.0 (NR), *P* < .001	Clinically meaningful and significant favoring drug
MG Activities of Daily Living (MG-ADL) score				
Howard 2013[32] NCT00727194	Period 1: eculizumab-900 mg (7) vs placebo (7)	16 weeks	4.29 vs 7.86 score MD, -3.57 (95% CI, -6.97 to -0.17); *P* = .04	Clinically meaningful and significant favoring drug
	Overall: eculizumab-900 mg (12) vs placebo (12)*	37 weeks	5.42 vs 7.0 MD, -1.58 (95% CI, -4.08 to 0.91); *P* = .19	No significant difference
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	-4.2 vs -2.3 CFB MD, -1.9 (NR), *P* = .006	Significant favoring drug; borderline clinically meaningful (MCID ≥ 2)
Myasthenia Gravis Quality of Life—15 (MG-QoL 15) score				
Howard 2013[32] NCT00727194	NR			
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	-12.6 vs -5.4 CFB MD, -7.2 (NR), *P* = .001	Significant favoring drug; MCID not known
MG Composite (MGC) score				
Howard 2013[32] NCT00727194	NR			

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	-8.1 vs -4.8 CFB MD, -3.3 (NR), *P* = .01	Clinically meaningful and significant favoring drug
Neuro-QoL fatigue score				
Howard 2013[32] NCT00727194	NR			
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	-16.3 vs -7.7 CFB −8.6 (95% CI −14.8 to −2.3); *P* = .008	Clinically meaningful and significant favoring drug
Serum immunoglobulin levels				
Howard 2013[32] NCT00727194	NR			
Howard, 2017[33] NCT01997229 REGAIN	NR			
Responder analyses				
Howard 2013[32] NCT00727194	Period 1: eculizumab-900 mg (7) vs placebo (7)	26 weeks	≥3-point reduction QMG from baseline 86% vs. 57% ≥5-point reduction of QMG from baseline 57% vs. 29%	NR
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-900 mg (13) vs placebo (13)	37 weeks	≥5-point reduction of QMG from baseline 45% vs. 19%; *P* = .0018 ≥3-point reduction of MG-ADL from baseline 60% vs. 40%; *P* = .023	Clinically meaningful and significant favoring drug
Total adverse events				
Howard 2013[32] NCT00727194	Eculizumab-900 mg (13) vs placebo (13)	37 weeks	100% vs 84.6% RR, 1.18 (95% CI, 0.93 to 1.49); *P* = .26	No significant difference.
Howard, 2017[33] NCT01997229 REGAIN	NR			

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Serious adverse events				
Howard 2013[32] NCT00727194	Eculizumab-900 mg (13) vs placebo (13)	37 weeks	7.7% vs 7.7%	No significant difference.
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	15% vs 29% RR, 0.51 (95% CI, 0.25 to 1.04); *P* = .06	No significant difference.
Discontinuations due to adverse events				
Howard 2013[32] NCT00727194	Eculizumab-900 mg (13) vs placebo (13)	37 weeks	0% vs 0%	No significant difference.
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	5% vs 0% RR, 80 (95% CI, 0.01 to 537400); *P* = .06	No significant difference.
Deaths				
Howard 2013[32] NCT00727194	Eculizumab-900 mg (13) vs placebo (13)	37 weeks	0% vs 0%	No significant difference.
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	0% vs 0%	No significant difference.
Exacerbations				
Howard 2013[32] NCT00727194	Eculizumab-900 mg (13) vs placebo (13)	37 weeks	7.7% vs 7.7%	No significant difference.
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	10% vs 24% RR, 0.4 (95% CI, 0.17 to 0.96); *P* = .04	Significant favoring drug
Hospitalizations				
Howard 2013[32] NCT00727194	NR			
Howard, 2017[33] NCT01997229 REGAIN	Eculizumab-1,200 mg (62) vs placebo (63)	26 weeks	15% vs 29% RR, 0.5 (95% CI, 0.25 to 1.0); *P* = .06	No significant difference.

Abbreviations. AE: adverse event; CFB: change from baseline; LSMD: least squares mean difference; MD: mean difference; RR: risk ratio; SE: standard error.

Table C3. Outcomes for Efgartigimod

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Quantitative Myasthenia Gravis (QMG) score				
Howard, 2021[45] NCT03669588 ADAPT	AChR-ab+ subgroup: Efgartigimod-10 mg/kg (63) vs. placebo (59)	Treatment cycle 1 (≥ 8 weeks)	Significant decrease in QMG score by week 1 (after first infusion) and continuing through to remain significant ($P < .05$) for 8 weeks with maximum reduction at weeks 4-5, then increasing, but still significant through week 8. Become non-significant at week 10. Difference appears clinically meaningful weeks 1 to 7 (graphically represented).	Clinically meaningful and significant favoring drug
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	80 days	Significant decrease in QMG score by week 1 (after first infusion): 3-point reduction vs placebo with MMRM, -2.38 (95% CI, -4.63 to -0.13); $P = .04$ QMG reduction with efgartigimod vs. placebo remains clinically significant through 80 days with maximal decrease around week 5 (5.7-point reduction; graphically represented	Clinically meaningful and significant favoring drug
MG Activities of Daily Living (MG-ADL) score				
Howard, 2021[45] NCT03669588 ADAPT	AChR-ab+ subgroup: Efgartigimod-10 mg/kg (63) vs. placebo (59)	Treatment cycle 1 (≥ 8 weeks)	Significant decrease in MG-ADL score by week 1 (after first infusion) and continuing through to remain significant ($P < .05$) for 7 weeks with maximum reduction at week 4, then increasing, but still significant through week 7, become non-significant at week 8. Difference appears clinically meaningful weeks 2 to 7 (graphically represented).	Clinically meaningful and significant favoring drug
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg of body weight (12) vs placebo (12)	80 days	At 29 days: MD, −2.05 (95% CI, −3.95 to −0.15); $P = .04$ At 36 days: MD, −2.08 [95% CI, −4.12 to −0.04]; $P = .046$ MG-ADL reduction reaches clinically meaningful level at week 1 and reaches statistical significance for weeks 4 and 5, then increases but remains clinically meaningful through day 80 (graphically represented	Clinically meaningful and significant favoring drug

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15r) score				
Howard, 2021[45] NCT03669588 ADAPT	AChR-ab+ subgroup: Efgartigimod-10 mg/kg (63) vs. placebo (59)	Treatment cycle 1 (≥ 8 weeks)	Significant decrease in MG-QoL 15r score by week 1 (after first infusion) and continuing through to remain significant ($P < .05$) for 8 weeks with maximum reduction at week 5, then increasing, but still significant through week 8, become non-significant at week 10 (graphically represented).	Significant favoring drug; MCID not known
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	22 days (3 weeks)	Statistically significant differences between efgartigimod and placebo occur at: Day 22: MD, −3.72 (95% CI, −7.41 to −0.02); $P = .049$ Day 29: MD, −3.87 (95% CI, −7.69 to −0.05); $P = .048$ Day 43: MD, −4.38 (95% CI, −8.56 to −0.20); $P = .04$ Efgartigimod MGC score falls below placebo score at week 1, decreases to a maximal reduction in MGC score for efgartigimod (-6 points, 31% reduction) compared to placebo (-2.1 points, 14%) at 5 weeks, and rises to come close to (but still below) placebo at 80 days (graphically reported).	Significant favoring drug; MCID not known
MG Composite (MGC) score				
Howard, 2021[45] NCT03669588 ADAPT	AChR-ab+ subgroup: Efgartigimod-10 mg/kg (63) vs. placebo (59)	Treatment cycle 1 (≥ 8 weeks)	Significant decrease in MG-QoL 15r score by week 1 (after first infusion) and continuing through to remain significant ($P < .05$) for 7 weeks with maximum reduction at week 4, then increasing, but still significant through week 7, become non-significant at week 8. Difference appears clinically meaningful weeks 2 to 7 (graphically represented).	Significant and clinically meaningful favoring drug
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	80 days	Reported graphically: Maximal reduction of MGC score occurred at week 7: -9.4 points (56% reduction) vs. -4.4 points (30% reduction) MGC for efgartigimod falls below placebo level at week 1 and remains reduced compared to placebo for 80 days	NR

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Serum immunoglobulin levels				
Howard, 2021[45] NCT03669588 ADAPT	AChR-ab+ subgroup: Efgartigimod-10 mg/kg (63) vs. placebo (59)	Treatment cycle 1 (≥ 8 weeks)	Serum IgG was maximally reduced to 61.3 % (SD 0.9) at week 4 of treatment cycle 1. By week 10 it had increased back to about 10% below baseline.	NR
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	80 days	Serum IgG was reduced by 40% from baseline in week 1, to a maximum reduction of 70.7% just after 3 weeks. It increased slowly after that to reach about 20% below baseline at 80 days.	NR
Responder Analyses				
Howard, 2021[45] NCT03669588 ADAPT	Efgartigimod-10 mg/kg (84) vs. placebo (83)	26 weeks	≥2-point reduction of MG-ADL from baseline 77.8% vs. 48.3% ≥3-point reduction QMG from baseline 74.2% vs. 25.9%	NR
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	80 days	≥2-point reduction of MG-ADL from baseline 75% vs. 25% Difference 50.3% (95% CI, 15.9 to 84.7); *P* = .039	Significant and clinically meaningful favoring drug
Total adverse events				
Howard, 2021[45] NCT03669588 ADAPT	Efgartigimod-10 mg/kg (84) vs. placebo (83)	26 weeks	77% vs 84% RR, 0.92 (95% CI, 0.79 to 1.06); *P* = .26	No significant difference.
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	80 days	83% vs 83% (as reported in ≥ 2 patients) RR, 1 (95% CI, 0.7 to 1.43); *P* = 1	No significant difference.
Serious adverse events				
Howard, 2021[45] NCT03669588 ADAPT	Efgartigimod-10 mg/kg (84) vs. placebo (83)	26 weeks	5% vs 8% RR, 0.57 (95% CI, 0.17 to 1.86); *P* = .36	No significant difference.
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	80 days	0% vs 0%	No significant difference.

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Discontinuations due to adverse events				
Howard, 2021[45] NCT03669588 ADAPT	Efgartigimod-10 mg/kg (84) vs. placebo (83)	26 weeks	4% vs 4%	No significant difference.
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	80 days	1 (8%) vs 0%	No significant difference.
Deaths				
Howard, 2021[45] NCT03669588 ADAPT	Efgartigimod-10 mg/kg (84) vs. placebo (83)	26 weeks	0% vs 0%	No significant difference.
Howard, 2019[44] NCT02965573	Efgartigimod-10 mg/kg (12) vs. placebo (12)	80 days	0% vs 0%	No significant difference.
Exacerbations				
Howard, 2021[45] NCT03669588 ADAPT	Efgartigimod-10 mg/kg (84) vs. placebo (83)	26 weeks	1 occurred in the placebo group compared to 0 in the efgartigimod group.	NR
Howard, 2019[44] NCT02965573	NR			
Hospitalizations				
Howard, 2021[45] NCT03669588 ADAPT	NR			
Howard, 2019[44] NCT02965573	NR			

Abbreviations. AChR-ab+: positive for anti-acetylcholine receptor antibodies; AE: adverse event; CFB: change from baseline; LSMD: least squares mean difference; MD: mean difference; MMRM: mixed-model repeated measures; NR: not reported; RR: risk ratio; SE: standard error.

Table C4. Outcomes for Nipocalimab

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Quantitative Myasthenia Gravis (QMG) score				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	Nipocalimab-5 mg/kg (14) vs placebo (14)	57 days (8 weeks)	-3.5 vs -3.4 CFB LSMD, −0.1 (95% CI, −3.1 to 2.9); *P* = .93	No significant difference.
	Nipocalimab-30 mg/kg (13) vs placebo (14)	57 days (8 weeks)	-3.9 vs -3.4 CFB LSMD, −0.5 (95% CI, −3.6 to 2.6); *P* = .73	No significant difference.
	Nipocalimab-60 mg/kg single dose (13) vs placebo (14)	57 days (8 weeks)	-1.3 vs -3.4 CFB LSMD, -2.1 (95% CI, −1.0 to 5.2); *P* = .18	No significant difference.
	Nipocalimab-60 mg/kg Q2W (14) vs placebo (14)	57 days (8 weeks)	-5.2 vs -3.4 CFB LSMD, −1.8 (95% CI, −4.8 to 1.2); *P* = .23	No significant difference.
MG Activities of Daily Living (MG-ADL) score				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	Nipocalimab-5 mg/kg (14) vs placebo (14)	57 days (8 weeks)	-2.4 vs -2.4 CFB LSMD, −0.0 (95% CI, −2.1 to 2.1); *P* = .99	No significant difference.
	Nipocalimab-30 mg/kg (13) vs placebo (14)	57 days (8 weeks)	-3.7 vs -2.4 CFB LSMD, −1.3 (95% CI, −3.5 to 0.9); *P* = .24	No significant difference.
	Nipocalimab-60 mg/kg single dose (13) vs placebo (14)	57 days (8 weeks)	-1.4 vs -2.4 CFB LSMD, 1.0 (95% CI, −1.2 to 3.1); *P* = .36	No significant difference.
	Nipocalimab-60 mg/kg Q2W (14) vs placebo (14)	57 days (8 weeks)	-3.7 vs -2.4 CFB LSMD, −1.3 (95% CI, −3.4 to 0.8); *P* = .22	No significant difference.
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15) score				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	Nipocalimab-5 mg/kg (14) vs placebo (14)	57 days (8 weeks)	-2.1 vs -1.9 CFB LSMD, −0.2 (95% CI, −3.7 to 3.2); *P* = .90	No significant difference.
	Nipocalimab-30 mg/kg (13) vs placebo (14)	57 days (8 weeks)	-6.9 vs -1.9 CFB LSMD, −5.1 (95% CI, −8.6 to −1.5); *P* = .005	Significant favoring drug; MCID not known
	Nipocalimab-60 mg/kg single dose (13) vs placebo (14)	57 days (8 weeks)	-1.3 vs -1.9 CFB LSMD, 0.6 (95% CI, −3.0 to 4.1); *P* = .754	No significant difference.
	Nipocalimab-60 mg/kg Q2W (14) vs placebo (14)	57 days (8 weeks)	-4.0 vs -1.9 CFB LSMD, −2.2 (95% CI, −5.6 to 1.3); *P* = .21	No significant difference.

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Serum immunoglobulin levels				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	Nipocalimab-5 mg/kg (14) vs placebo (14)	57 days (8 weeks)	Peak reduction was seen at 1 week (42%) but returned to baseline (matching placebo) at 16 weeks (reported graphically)	NR
	Nipocalimab-30 mg/kg (13) vs placebo (14)	57 days (8 weeks)	Peak reduction was seen at 2 weeks (72%) but returned close to baseline (matching placebo) at 16 weeks (reported graphically)	NR
	Nipocalimab-60 mg/kg single dose (13) vs placebo (14)	57 days (8 weeks)	Peak reduction was seen at 2 weeks (80%) but returned close to baseline (matching placebo) at 16 weeks (reported graphically)	NR
	Nipocalimab-60 mg/kg Q2W (14) vs placebo (14)	57 days (8 weeks)	Peak reduction was seen at 6 weeks (83%) but returned close to baseline (matching placebo) at 16 weeks (reported graphically). This dose remained lowest compared to all others at 16 weeks.	NR
Responder analyses				
NR				
Total adverse events				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	Nipocalimab-5 mg/kg (14) vs placebo (14)	57 days (8 weeks)	85.7% vs 78.6% RR, 1.1 (95% CI, 0.77 to 1.54); *P* = .7	No significant difference.
	Nipocalimab-30 mg/kg (13) vs placebo (14)	57 days (8 weeks)	69.2% vs 78.6% RR, 0.88 (95% CI, 0.56 to 1.39); *P* = .6	No significant difference.
	Nipocalimab-60 mg/kg single dose (13) vs placebo (14)	57 days (8 weeks)	92.3% vs 78.6% RR, 1.18 (95% CI, 0.86 to 1.61); *P* = .4	No significant difference.
	Nipocalimab-60 mg/kg Q2W (14) vs placebo (14)	57 days (8 weeks)	85.7% vs 78.6% RR, 1.1 (95% CI, 0.77 to 1.54); *P* = .7	No significant difference.

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Serious adverse events				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	Nipocalimab-5 mg/kg (14) vs placebo (14)	57 days (8 weeks)	0% vs 14.3% RR, 0.025 (95% CI, 0 to 173.1); *P* = .23	No significant difference.
	Nipocalimab-30 mg/kg (13) vs placebo (14)	57 days (8 weeks)	7.7% vs 14.3% RR, 0.54 (95% CI, 0.055 to 5.26); *P* = .65	No significant difference.
	Nipocalimab-60 mg/kg single dose (13) vs placebo (14)	57 days (8 weeks)	0% vs 14.3% RR, 0.025 (95% CI, 0 to 173.1); *P* = .23	No significant difference.
	Nipocalimab-60 mg/kg Q2W (14) vs placebo (14)	57 days (8 weeks)	0% vs 14.3% RR, 0.025 (95% CI, 0 to 173.1); *P* = .23	No significant difference.
Discontinuations due to adverse events				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	Nipocalimab-5 mg/kg (14) vs placebo (14)	57 days (8 weeks)	0% vs 14.3% RR, 0.025 (95% CI, 0 to 173.1); *P* = .23	No significant difference.
	Nipocalimab-30 mg/kg (13) vs placebo (14)	57 days (8 weeks)	0% vs 14.3% RR, 0.025 (95% CI, 0 to 173.1); *P* = .23	No significant difference.
	Nipocalimab-60 mg/kg single dose (13) vs placebo (14)	57 days (8 weeks)	0% vs 14.3% RR, 0.025 (95% CI, 0 to 173.1); *P* = .23	No significant difference.
	Nipocalimab-60 mg/kg Q2W (14) vs placebo (14)	57 days (8 weeks)	0% vs 14.3% RR, 0.025 (95% CI, 0 to 173.1); *P* = .23	No significant difference.
Deaths				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	No deaths reported in study			
Exacerbations				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	NR			
Hospitalizations				
Antozzi, 2024[51] NCT03772587 Vivacity-MG	NR			

Abbreviations. AE: adverse event; CFB: change from baseline; LSMD: least squares mean difference; MD: mean difference; NR: not reported; RR: risk ratio; SE: standard error.

Table C5. Outcomes for Ravulizumab

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Quantitative Myasthenia Gravis (QMG) score				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	-2.8 vs -0.8 CFB MD, -2.0 (95% CI, -3.2 to -0.8); *P* < .001	Significant favoring drug; does not meet MCID
MG Activities of Daily Living (MG-ADL) score				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	-3.1 vs -1.4 CFB MD, -1.6 (95% CI, -2.6 to -0.7); *P* < .001	Significant favoring drug; does not meet MCID
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15r) score				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	-3.3 vs -1.6 CFB MD, -1.7 (95% CI, -3.4 to 0.1); *P* = .06	No significant difference.
Neuro-QoL fatigue score				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	-7.0 vs -4.8 CFB MD, -2.2 (95% CI, -6.9 to 2.6); NR	Study states no significant difference.; MCID not known
Serum immunoglobulin levels				
NR				
Responder Analyses				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	≥5-point reduction of QMG from baseline 30% vs. 11.3%, *P* = .005 ≥3-point reduction of MG-ADL from baseline 56.7% vs. 34.1% (significance NR)	Significant and clinically meaningful favoring drug for QMG score; clinically meaningful but significance NR for MG-ADL

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Total adverse events				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	91% vs 87% RR, 1.05 (95% CI, 0.94 to 1.17); *P* = .4	No significant difference.
Serious adverse events				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	23% vs 16% RR, 1.48 (95% CI, 0.8 to 2.74); *P* = .22	No significant difference.
Discontinuations due to adverse events				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	2% vs 3% RR, 0.69 (95% CI, 0.12 to 4.03); *P* = .7	No significant difference.
Deaths				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	2% vs 0% RR, 41.4 (95% CI, 0.0058 to 294100); *P* = .25	No significant difference.
Exacerbations				
Vu, 2022[53] NCT03920293 CHAMPION MG	Ravulizumab-3,000, 3,300, or 3,600 mg (86) vs placebo (89)	26 weeks	1% vs 3% RR, 0.35 (95% CI, 0.037 to 3.25); *P* = .4	No significant difference.
Hospitalizations				
Vu, 2022[53] NCT03920293 CHAMPION MG	NR			

Abbreviations. AE: adverse event; CFB: change from baseline; LSMD: least squares mean difference; MD: mean difference; NR: not reported; RR: risk ratio; SE: standard error.

Table C6. Outcomes for Rozanolixizumab

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Quantitative Myasthenia Gravis (QMG) score				
Bril, 2023[55] NCT03971422 MycarinG	Rozanolixizumab-7 mg/kg (66) vs placebo (67)	6 weeks	-5.4 vs -1.92 CFB MD, −3.48 (95% CI, −5.61 to −1.58); *P* < .001	Clinically meaningful and significant favoring drug
	Rozanolixizumab-10 mg/kg (66) vs placebo (67)	6 weeks	-6.67 vs -1.92 CFB MD, −4.76 (95% CI −6.82 to −2.86); *P* < .001	Clinically meaningful and significant favoring drug
Bril, 2021[54] NCT03052751	Rozanolixizumab-7 mg/kg (21) vs placebo (22)	29 days (4 weeks)	-1.8 vs -1.2 CFB LSMD, -0.7 (95% upper CI, 0.8); *P* = .22	No significant difference.
MG Activities of Daily Living (MG-ADL) score				
Bril, 2023[55] NCT03971422 MycarinG	Rozanolixizumab-7 mg/kg (66) vs placebo (67)	6 weeks	-3.7 vs -0.78 CFB MD, −2.59 (95% CI, −4.09 to −1.25); *P* < .001	Clinically meaningful and significant favoring drug
	Rozanolixizumab-10 mg/kg (66) vs placebo (67)	6 weeks	-3.4 vs -0.78 CFB MD, −2.62 (95% CI, −3.99 to −1.16); *P* < .001	Clinically meaningful and significant favoring drug
Bril, 2021[54] NCT03052751	Rozanolixizumab-7 mg/kg (21) vs placebo (22)	29 days (4 weeks)	-1.8 vs -0.4 CFB LSMD, -1.4 (95% upper CI, 0.4); NR	Significance not reported, does not meet MCID
MG Composite (MGC) score				
Bril, 2023[55] NCT03971422 MycarinG	Rozanolixizumab-7 mg/kg (66) vs placebo (67)	6 weeks	-5.93 vs -2.03 CFB MD, −3.90 (95% CI, −6.63 to −1.25); *P* < .001	Clinically meaningful and significant favoring drug
	Rozanolixizumab-10 mg/kg (66) vs placebo (67)	6 weeks	-7.55 vs -2.03 CFB MD, −5.53 (95% CI, −8.30 to −2.97); *P* < .001	Clinically meaningful and significant favoring drug
Bril, 2021[54] NCT03052751	Rozanolixizumab-7 mg/kg (21) vs placebo (22)	29 days (4 weeks)	-3.1 vs -1.2 LSMD, -1.8 (95% upper CI, 0.4); NR	Significance not reported, does not meet MCID
Serum immunoglobulin levels				
Bril, 2023[55] NCT03971422 MycarinG	Rozanolixizumab-7 mg/kg (66) vs placebo (67)	6 weeks	IgG mean reduction (change from baseline) was < 10% for placebo and close to 70% for rozanolixizumab, significance not reported (represented graphically)	NR
	Rozanolixizumab-10 mg/kg (66) vs placebo (67)	6 weeks	IgG mean reduction (change from baseline) was < 10% for placebo and close to 70% for rozanolixizumab, significance not reported (represented graphically)	NR

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Bril, 2021[54] NCT03052751	Rozanolixizumab-7 mg/kg (21) vs placebo (22)	29 days (4 weeks)	IgG mean reduction for rozanolixizumab was largest at day 22 (61%) and was 52% vs 4% for the placebo at day 29, significance not reported.	NR
Responder analyses				
Bril, 2023[55] NCT03971422 MycarinG	Rozanolixizumab-7 mg/kg (66) vs placebo (67)	6 weeks	≥ 2-point reduction of MG-ADL from baseline 71.9% vs. 31.3% ≥3-point reduction of QMG from baseline 54.7% vs. 39.1% ≥ 3-point reduction of MGC from baseline 60.9% vs. 40.6%	Clinically meaningful; significance NR
	Rozanolixizumab-10 mg/kg (66) vs placebo (67)	6 weeks	≥ 2-point reduction of MG-ADL from baseline 69.4% vs. 31.3% ≥ 3-point reduction of QMG from baseline 72.6% vs. 39.1% ≥ 3-point reduction of MGC from baseline 74.2% vs. 40.6%	Clinically meaningful; significance NR
Bril, 2021[54] NCT03052751	Rozanolixizumab-7 mg/kg (21) vs placebo (22)	29 days (4 weeks)	≥ 3-point reduction of QMG from baseline 38% vs 23% ≥ 3-point reduction of MG-ADL from baseline 48% vs 14% ≥ 3-point reduction of MGC from baseline 48% vs 27%	Clinically meaningful; significance NR
Total adverse events				
Bril, 2023[55] NCT03971422 MycarinG	Rozanolixizumab-7 mg/kg (64) vs placebo (67)	6 weeks	81% vs 67% RR, 1.21 (95% CI, 0.99 to 1.48); *P* = .07	No significant difference.
	Rozanolixizumab-10 mg/kg (69) vs placebo (67)	6 weeks	83% vs 67% RR, 1.23 (95% CI, 1.0 to 1.5); *P* = .04	Significant - more AEs with drug compared to placebo (favors placebo)
Bril, 2021[54] NCT03052751	Rozanolixizumab-7 mg/kg (21) vs placebo (22)	29 days (4 weeks)	76% vs 73% RR, 1.05 (95% CI, 0.74 to 1.49); *P* = .81	No significant difference.
Serious adverse events				
Bril, 2023[55] NCT03971422	Rozanolixizumab-7 mg/kg (64) vs placebo (67)	6 weeks	8% vs 9% RR, 0.87 (95% CI, 0.28 to 2.7); *P* = .82	No significant difference.

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
MycarinG	Rozanolixizumab-10 mg/kg (69) vs placebo (67)	6 weeks	10% vs 9% RR, 1.13 (95% CI, 0.40 to 3.2); *P* = .82	No significant difference.
Bril, 2021[54] NCT03052751	Rozanolixizumab-7 mg/kg (21) vs placebo (22)	29 days (4 weeks)	0% vs 9% RR, 0.026 (95% CI, 0 to 183.3); *P* = .25	No significant difference.
Discontinuations due to adverse events				
Bril, 2023[55] NCT03971422 MycarinG	Rozanolixizumab-7 mg/kg (64) vs placebo (67)	6 weeks	3% vs 3% RR, 1 (95% CI, 0.15 to 7.2); *P* = 1	No significant difference.
	Rozanolixizumab-10 mg/kg (69) vs placebo (67)	6 weeks	6% vs 3% RR, 1.94 (95% CI, 0.38 to 10.25); *P* = .47	No significant difference.
Bril, 2021[54] NCT03052751	Rozanolixizumab-7 mg/kg (21) vs placebo (22)	29 days (4 weeks)	5% vs 0% RR, 20.95 (95% CI, 0 to 163,300); *P* = .5	No significant difference.
Deaths				
Bril, 2023[55] NCT03971422 MycarinG	No deaths occurred in trial			
Bril, 2021[54] NCT03052751	No deaths occurred in trial			
Exacerbations				
Bril, 2023[55] NCT03971422 MycarinG	Rozanolixizumab-7 mg/kg (64) vs placebo (67)	6 weeks	0% vs 3% RR, 0.026 (95% CI, 0 to 185.7); *P* = .25	No significant difference.
	Rozanolixizumab-10 mg/kg (69) vs placebo (67)	6 weeks	0% vs 3% RR, 0.026 (95% CI, 0 to 185.7); *P* = .25	No significant difference.
Bril, 2021[54] NCT03052751	NR			
Hospitalizations				
Bril, 2023[55] NCT03971422 MycarinG	NR			
Bril, 2021[54] NCT03052751	NR			

Abbreviations. AE: adverse event; CFB: change from baseline; LSMD: least squares mean difference; MD: mean difference; NR: not reported; RR: risk ratio; SE: standard error.

Table C7. Outcomes for Zilucoplan

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Quantitative Myasthenia Gravis (QMG) score				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	-5.5 vs -3.2 CFB MD, −2.3 (95% CI, -5.6 to 1.0); *P* = .09	No significant difference
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	-6.0 vs -3.2 CFB MD. −2.8 (95% CI, -6.1 to 0.5); *P* = .05	Significant favoring drug; borderline clinically meaningful
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	-6.19 vs -3.25 CFB MD, −2.94 (95% CI, −4.39 to −1.49); *P* < .001	Significant favoring drug; borderline clinically meaningful
MG Activities of Daily Living (MG-ADL) score				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	-3.3 vs -1.1 CFB MD, −2.2 (95% CI, -4.75 to 0.35); *P* = .05	Clinically meaningful and significant favoring drug
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	-3.4 vs -1.1 CFB MD, −2.3 (95% CI, -4.75 to 0.35); *P* = .04	Clinically meaningful and significant favoring drug
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	-4.39 vs -2.3 CFB MD, −2.09 (95% CI, −3.24 to −0.95); *P* < .001	Clinically meaningful and significant favoring drug
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15) score				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	-7.4 vs -2.1 CFB MD, −5.3 (95% CI, -10.0 to -0.6); *P* = .02	Significant favors drug; MCID not known
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	-5.9 vs -2.1 CFB MD, −3.7 (95% CI, -8.4 to 1.0); *P* = .06	No significant difference.
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	-5.65 vs -3.16 CFB MD, -2.49 (95% CI, -4.45 to -0.54); *P* = .013	Significant favors drug; MCID not known

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
MG Composite (MGC) score				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	-5.3 vs -3.3 CFB MD, −2.0 (95% CI, 2.3 to -6.3); *P* = .19	No significant difference.
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	-7.4 vs -3.3 CFB MD, −4.1 (95% CI, 0.2 to -8.4); *P* = .04	Clinically meaningful and significant favoring drug
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	-8.62 vs -5.42 CFB MD, −3.20 (95% CI, −5.24 to −1.16); *P* = .002	Clinically meaningful and significant favoring drug
Neuro-QoL fatigue score				
Howard, 2020[58] NCT03315130	NR			
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	-6.26 vs -2.65 CFB MD, -3.61 (95% CI, -6.18 to -1.05); *P* = .006	Significant favors drug; MCID not known
Serum immunoglobulin levels				
Howard, 2020[58] NCT03315130	NR			
Howard, 2023[57] NCT04115293 RAISE	NR			
Responder analyses				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	NR	
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	≥3-point reduction of QMG from baseline Graphically represented Approximately 70% vs. 55%; *P* ≥ .05	No significant difference
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	≥5-point reduction of QMG from baseline 58% vs 33%; RR, 2.87 (95% CI, 1.52 to 5.40); *P* = .0012 ≥3-point reduction of MG-ADL from baseline 73% vs. 46%; RR, 3.18 (95% CI, 1.66 to 6.10); *P* < .001	Significant and clinically meaningful favoring drug

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Total adverse events				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	100% vs 80% RR, 1.25 (95% CI, 0.97 to 1.6); *P* = .12	No significant difference.
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	86% vs 80% RR, 1.1 (95% CI, 0.77 to 1.49); *P* = .72	No significant difference.
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	77% vs 70% RR, 1.09 (95% CI, 0.9 to 1.3); *P* = .35	No significant difference.
Serious adverse events				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	0% vs 20% RR, 0.017 (95% CI, 0 to 111.5); *P* = .11	No significant difference.
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	36% vs 20% RR, 1.79 (95% CI, 0.52 to 6.12); *P* = .38	No significant difference.
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	13% vs 15% RR, 0.87 (95% CI, 0.41 to 1.83); *P* = .71	No significant difference.
Discontinuations due to adverse events				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	0% vs 7% RR, 0.05 (95% CI, 0 to 386.4); *P* = .49	No significant difference.
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	7% vs 7% RR, 1 (95% CI, 0.074 to 15.5); *P* = 1	No significant difference.
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	5% vs 2% RR, 2.05 (95% CI, 0.385 to 10.88); *P* = .43	No significant difference.

Study	Comparison (N)	Study Duration	Drug vs. Placebo Between-group Comparison	MCID and Significance
Deaths				
Howard, 2020[58] NCT03315130	Zilucoplan-0.1 mg/kg (15) vs placebo (15)	12 weeks	0% vs 0%	No significant difference.
	Zilucoplan-0.3 mg/kg (14) vs placebo (15)	12 weeks	0% vs 0%	No significant difference.
Howard, 2023[57] NCT04115293 RAISE	Zilucoplan-0.3 mg/kg (86) vs placebo (88)	12 weeks	1% vs 1% RR, 1 (95% CI, 0.065 to 16.1); *P* = 1	No significant difference.
Exacerbations				
Howard, 2020[58] NCT03315130	NR			
Howard, 2023[57] NCT04115293 RAISE	NR			
Hospitalizations				
Howard, 2020[58] NCT03315130	NR			
Howard, 2023[57] NCT04115293 RAISE	NR			

Abbreviations. AE: adverse event; CFB: change from baseline; CI: confidence interval; LSMD: least squares mean difference; MD: mean difference; NR: not reported; RR: risk ratio; SE: standard error.

Appendix D. Complete GRADE Tables by Drug

Table D1. GRADE Profile for Amifampridine Phosphate

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Generalized myasthenia gravis							
Quantitative Myasthenia Gravis (QMG) score							
N = 7 1 RCT Bonanno, 2018[16]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not assessable (single study)	Serious (downgraded 1 level) for short study duration (7 days)	Serious (downgraded 1 level) for very small sample size (n = 7)	Not assessed	Study reports a significantly smaller increase in QMG score (0.1 vs. 6.9; *P* < .001). Meets MCID	●○○○ Very Low
MG Activities of Daily Living (MG-ADL) score							
N = 7 1 RCT Bonanno, 2018[16]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not assessable (single study)	Serious (downgraded 1 level) for short study duration (7 days)	Serious (downgraded 1 level) for very small sample size (n = 7)	Not assessed	Study reports a significantly smaller increase in MG-ADL score (-0.1 vs. 5.6; *P* < .001); Meets MCID	●○○○ Very Low
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15) score							
N = 7 1 RCT Bonanno, 2018[16]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not assessable (single study)	Serious (downgraded 1 level) for short study duration (7 days)	Serious (downgraded 1 level) for very small sample size (n = 7)	Not assessed	Study reports a significantly improved MG-QoL 15 score (-2.1 vs. 16.4; *P* = .003)	●○○○ Very Low
MG Composite (MGC) score							
N = 7 1 RCT Bonanno, 2018[16]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not assessable (single study)	Serious (downgraded 1 level) for short study duration (7 days)	Serious (downgraded 1 level) for very small sample size (n = 7)	Not assessed	Study reports a significantly smaller increase in QMG score (0.1 vs. 11.6; *P* < .001). Meets MCID	●○○○ Very Low

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Total adverse events							
N = 7 1 RCT Bonanno, 2018[16]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not assessable (single study)	Serious (downgraded 1 level) Only reported in patients with MuSK-MG	Serious (downgraded 1 level) Very small sample size (n = 7)	Not assessed	Study reports a total of 7 adverse events, but these were not reported by groups. Unable to make a comparison	●○○○ Very Low
Serious adverse events							
N = 7 1 RCT Bonanno, 2018[16]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not serious	Serious (downgraded 1 level)	Serious (downgraded 1 level) Very small sample size (n = 7)	Not assessed	No significant difference between groups - no events (0% vs 0%)	●○○○ Very Low
Lambert-Eaton myasthenic syndrome							
Quantitative Myasthenia Gravis (QMG) score							
N = 64 2 RCTs Oh, 2016[28] Shieh, 2019[29]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Serious (downgraded 1 level) Mixed results	Not serious	Serious (downgraded 1 levels) Small sample sizes	Not assessed	Amifampridine tended to be associated with significantly smaller increases in QMG score (differences -1.7 and estimated -2; *P* < .05). Neither meet MCID	●○○○ Very Low
MG Activities of Daily Living (MG-ADL) score							
NR							
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15) score							
NR							
MG Composite (MGC) score							
NR							

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Timed 25-foot walk test (TFW25) and triple-timed up-and-go test (3TUG)							
N = 64 2 RCTs Oh, 2016[28] Shieh, 2019[29]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Serious (downgraded 1 level) for mixed results. One study reports no difference while the other study reports a significant difference.	Not serious	Serious (downgraded 1 levels) Small sample sizes	Not assessed	One study reported no significant difference between groups ($P < .05$). The other study reported a significantly higher proportion of patients requiring more time to complete tasks compared with placebo ($P = .01$)	●○○○ Very Low
Total adverse events							
N = 64 2 RCTs Oh, 2016[28] Shieh, 2019[29]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not serious	Not serious	Serious (downgraded 2 levels) Small sample sizes and very wide CIs	Not assessed	One study reported no significant difference between groups (19% vs. 27%, $P > .05$). Other study reported 3 events with amifampridine and 11 events with placebo, but not number of patients, significance NR	●○○○ Very Low
Serious adverse events							
N = 64 2 RCTs Oh, 2016[28] Shieh, 2019[29]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not serious	Not serious	Serious (downgraded 2 levels) Small sample sizes and very wide CIs	Not assessed	No difference between treatment groups, with no SAEs in either treatment group	●○○○ Very Low

Abbreviations. AE: adverse event; CI: confidence interval; COI: conflict of interest; gMG: generalized myasthenia gravis; LEMS: Lambert-Eaton myasthenic syndrome; MCID: minimum clinically important difference; NR: not reported; RCT: randomized clinical trial.

Table D2. GRADE Profile for Eculizumab

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Quantitative Myasthenia Gravis (QMG) score							
N = 140 2 RCTs Howard, 2013[32] Howard, 2017[33]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not serious Note studies used different doses, 1 FDA-approved (1,200 mg) and 1 lower (900 mg). Doesn't affect results.	Not serious	Serious (downgraded 2 levels) 1 study has small sample size and washout period between crossover periods was not fully effective	Not assessed	Overall, QMG scores improved (i.e., decreased) for all participants Eculizumab was associated with a significantly greater decrease in QMG score in both studies (-4.6 vs. -1.6; -7.9 vs. -3.7; $P \leq .01$ for both); the differences were likely clinically meaningful (a difference of around 3.0 to 4.0) when compared with placebo	●○○○ Very Low
MG Activities of Daily Living (MG-ADL) score							
N = 140 2 RCTs Howard, 2013[32] Howard, 2017[33]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not serious *Some mixed results and different doses, but already very low.*	Not serious	Serious (downgrade 2 levels) Small sample size and number of patients completing study is variably reported.	Not assessed	Eculizumab was associated with a significantly improved MG-ADL score when compared with placebo (both $P < .05$); the difference was clinically meaningful in 1 study (a difference of 3.6 at the end of period 1 but not overall) but not in the other (a difference of 1.9)	●○○○ Very Low

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Myasthenia Gravis Quality of Life−15 (MG-QoL 15) score							
N = 126 1 RCT Howard, 2017[33]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not assessable (single study)	Not serious	Not serious	Not assessed	Eculizumab was associated with a significantly improved MG-QoL 15 score when compared with placebo (-12.6 vs. -5.4; *P* = .001).	●●○○ Low
MG Composite (MGC) score							
N = 126 1 RCT Howard, 2017[33]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not assessable (single study)	Not serious	Not serious	Not assessed	Overall, MGC scores improved (i.e., decreased) for all participants Eculizumab was associated with a significantly greater decrease in MGC score (-8.1 vs. -4.8; *P* = .01); the difference was clinically meaningful (a difference of 3.3) when compared with placebo.	●●○○ Low
Total adverse events							
N = 14 1 RCT Howard, 2013[32]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not serious	Not serious	Serious (downgraded 2 levels) Small sample size and number of patients completing study are variably reported.	Not assessed	Participants in both groups experienced AEs; however, there was no significant difference between groups.	●○○○ Very Low

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Serious adverse events							
N = 140 2 RCTs Howard, 2013[32] Howard, 2017[33]	Serious (downgraded 1 level) Funding related COI concerns; poorly reported methodology	Not serious	Not serious	Serious (downgraded 1 levels) Small sample size and number of patients completing study are variably reported.	Not assessed	Participants in both groups experienced SAEs; however, there was no significant difference between groups (1% vs. 1% and 15% vs. 29%) but no significant difference with *P* = .06.	●●○○ Low

Abbreviations. AE: adverse event; CI: confidence interval; COI: conflict of interest; gMG: generalized myasthenia gravis; LEMS: Lambert-Eaton myasthenic syndrome; MCID: minimum clinically important difference; NR: not reported; RCT: randomized clinical trial; SAE: serious adverse event.

Table D3. GRADE Profile for Efgartigimod

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Quantitative Myasthenia Gravis (QMG) score							
N = 191 2 RCTs Howard, 2019[44] Howard, 2021[45]	Serious (downgraded 1 level) High Funding related COI concerns and exploratory study with poorly reported data	Not serious	Not serious	Serious (downgraded 1 levels) Not assessable	Not assessed	Overall, QMG scores improved (i.e., decreased) for all participants. Efgartigimod was associated with a significantly greater decrease in QMG score; however, while the initial decreases were clinically meaningful, over time the differences between groups grew smaller, with QMG scores tending to rise over the period post active treatment (reported graphically)	●●○○ Low
MG Activities of Daily Living (MG-ADL) score							
N = 191 2 RCTs Howard, 2019[44] Howard, 2021[45]	Serious (downgraded 1 level) High Funding related COI concerns and exploratory study with poorly reported data	Not serious	Not serious	Serious (downgraded 1 level) Not assessable	Not assessed	Overall, MG-ADL scores improved (i.e., decreased) for all participants. Efgartigimod was associated with a significantly greater decrease in MG-ADL score (*P* = .036); difference appears to be clinically meaningful for weeks 2-7. Over time the differences between groups grew smaller, with MG-ADL scores tending to rise over the period post active treatment (reported graphically)	●●○○ Low

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15r) score							
N = 191 2 RCTs Howard, 2019[44] Howard, 2021[45]	Serious (downgraded 1 level) High Funding related COI concerns and 1 exploratory study with poorly reported data	Not serious	Not serious	Serious (downgraded 1 level) Not assessable	Not assessed	Overall, MG-QoL 15r scores improved (i.e., decreased) for all participants. Efgartigimod was associated with a significantly greater decrease in MG-QoL 15r score (*P* = .049 to *P* = .01); the maximal difference was around week 4 and then over time the differences between groups grew smaller, with MG-QoL 15r scores tending to rise over the period post active treatment (reported graphically)	●●○○ Low
MG Composite (MGC) score							
N = 191 2 RCTs Howard, 2019[44] Howard, 2021[45]	Serious (downgraded 1 level) High Funding related COI concerns and 1 exploratory study with poorly reported data	Not serious	Not serious	Serious (downgraded 1 level) Not assessable	Not assessed	Overall, MGC scores improved (i.e., decreased) for all participants. Efgartigimod was associated with a significantly greater decrease in MGC score; however, while the initial decreases were clinically meaningful, over time the differences between groups grew smaller, with MGC scores tending to rise over the period post active treatment (reported graphically)	●●○○ Low

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Total adverse events							
N = 191 2 RCTs Howard, 2019[44] Howard, 2021[45]	Serious (downgraded 1 level) High Funding related COI concerns and 1 exploratory study with poorly reported data	Not serious	Not serious	Not serious	Not assessed	The majority of participants in both groups experienced an AE. However, both studies report no difference between groups.	●●●○ Moderate
Serious adverse events							
N = 191 2 RCTs Howard, 2019[44] Howard, 2021[45]	Serious (downgraded 1 level) High Funding related COI concerns and 1 exploratory study with poorly reported data	Not serious	Not serious	Serious (downgraded 1 level) Few events	Not assessed	Very few participants in both groups experienced a SAE. Both studies report no difference between groups.	●●○○ Low

Abbreviations. AE: adverse event; CI: confidence interval; COI: conflict of interest; gMG: generalized myasthenia gravis; LEMS: Lambert-Eaton myasthenic syndrome; MCID: minimum clinically important difference; NR: not reported; RCT: randomized clinical trial.

Table D4. GRADE Profile for Nipocalimab

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Quantitative Myasthenia Gravis (QMG) score							
N = 68 1 RCT Antozzi, 2024[51]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Serious (downgraded 1 level due to loss of data and participants due to COVID-19 with unclear reporting)	Not assessed	No difference between study groups.	●●○○ Low
MG Activities of Daily Living (MG-ADL) score							
N = 68 1 RCT Antozzi, 2024[51]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Serious (downgraded 1 level due to loss of data and participants due to COVID-19 with unclear reporting)	Not assessed	No difference between study groups.	●●○○ Low
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15) score							
N = 68 1 RCT Antozzi, 2024[51]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Serious (downgraded 1 level due to loss of data and participants due to COVID-19 with unclear reporting)	Not assessed	Overall, there is no difference; however, 1 out of 4 doses (30 mg/kg) did significantly improve QoL (*P* = .005).	●●○○ Low
Myasthenia Gravis Composite (MGC) score							
Not reported							

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Total adverse events							
N = 68 1 RCT Antozzi, 2024[51]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Serious (downgraded 1 level due to loss of data and participants due to COVID-19 with unclear reporting)	Not assessed	Most participants in all groups experienced an AE; however, there were no difference in AE incidence between nipocalimab dosages and placebo	●●●○ Moderate
Serious adverse events							
N = 68 1 RCT Antozzi, 2024[51]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Serious (downgraded 1 level due to loss of data and participants due to COVID-19 with unclear reporting)	Not assessed	Very few participants in any group experienced a SAE; no differences between groups	●●○○ Low

Abbreviations. AE: adverse event; CI: confidence interval; COI: conflict of interest; gMG: generalized myasthenia gravis; MCID: minimum clinically important difference; NR: not reported; RCT: randomized clinical trial.

Table D5. GRADE Profile for Ravulizumab

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Quantitative Myasthenia Gravis (QMG) score							
N = 175 1 RCT Vu, 2022[53]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Serious (downgraded 1level) While MD (-2.0) does not meet MCID, the 95% CI crosses it (-3.2 to -0.8)	Not assessed	Overall, QMG scores improved (i.e., decreased) for all participants; ravulizumab was associated with a significantly greater decrease in QMG score (-2.8 vs. -0.8; *P* < .001); however, the difference was not clinically meaningful when compared with placebo (a difference of 2.0).	●●○○ Low
MG Activities of Daily Living (MG-ADL) score							
N = 175 1 RCT Vu, 2022[53]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Serious (downgraded 1level) While MD (-1.6) does not meet MCID, the 95% CI crosses it (-2.6 to -0.7)	Not assessed	Overall, MG-ADL scores improved (i.e., decreased) for all participants; ravulizumab was associated with a significantly greater decrease in MG-ADL score (-3.1 vs. -1.4; *P* < .001); however, the difference was not clinically meaningful when compared with placebo (a difference of 1.6).	●●○○ Low
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15) score							
N = 175 1 RCT Vu, 2022[53]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Not serious	Not assessed	Overall, MG-QoL 15 scores improved (i.e., decreased) for all participants; ravulizumab was associated with a nonsignificant decrease in MG-QoL score (-3.3 vs. -1.6; *P* = .06).	●●○○ Low

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Myasthenia Gravis Composite (MGC) score							
Not reported							
Total adverse events							
N = 175 1 RCT Vu, 2022[53]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Not serious	Not assessed	The majority of participants in both groups experienced an AE; however, only around 34% of participants in each group experienced an AE attributed to treatment. No significant difference between groups.	●●●○ Moderate
Serious adverse events							
N = 175 1 RCT Vu, 2022[53]	Serious (downgraded 1 level) High Funding related COI concerns	Not assessable (single study)	Not serious	Not serious	Not assessed	Participants in both groups experienced SAEs (23% vs. 16%). No significant difference between groups.	●●●○ Moderate

Abbreviations. AE: adverse event; CI: confidence interval; COI: conflict of interest; gMG: generalized myasthenia gravis; MCID: minimum clinically important difference; NR: not reported; RCT: randomized clinical trial.

Table D6. GRADE Profile for Rozanolixizumab

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Quantitative Myasthenia Gravis (QMG) score							
N = 243 2 RCTs Bril, 2021[54] Bril, 2023[55]	Serious (downgraded 1 level) High Funding related COI concerns	Serious (downgraded 1 level) One study reports a significant difference but the other shows no difference	Not serious	Serious (downgraded 1 level) For 1 study, 95% CIs cross MCID for both drug doses.	Not assessed	One study reports that Rozanolixizumab significantly decreases QMG score compared to placebo ($P < .001$) for two drug doses, both meeting MCID (though 95% CIs cross MCID). The other study reports no difference between groups.	●○○○ Very Low
MG Activities of Daily Living (MG-ADL) score							
N = 243 2 RCTs Bril, 2021[54] Bril, 2023[55]	Serious (downgraded 1 level) High Funding related COI concerns	Serious (downgraded 1 level) One study reports a significant difference while the other doesn't report significance of a not clinically meaningful difference.	Not serious	Serious (downgraded 1 level) For 1 study, 95% CIs cross MCID for both drug doses.	Not assessed	One study reports that Rozanolixizumab significantly decreases QMG score compared to placebo ($P < .001$) for two drug doses, both meeting MCID (though 95% CIs cross MCID). The other study does not report significance, with difference (LSMD = -1.8, upper CI 0.4). not meeting MCID.	●○○○ Very Low
Revised Myasthenia Gravis Quality of Life−15 (MG-QoL 15) score							
Not reported							

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
MG Composite (MGC) score							
N = 243 2 RCTs Bril, 2021[54] Bril, 2023[55]	Serious (downgraded 1 level) High Funding related COI concerns	Serious (downgraded 1 level) One study reports a significant difference while other doesn't report significance of a not clinically meaningful difference.	Not serious	Serious (downgraded 1 level) For 1 study, 95% CIs cross MCID for both drug doses.	Not assessed	One study reports that Rozanolixizumab significantly decreases QMG score compared to placebo ($P < .001$), meeting MCID, for 2 doses, while other study does not report significance, with difference (LSMD = -1.8, upper CI 0.4). not meeting MCID	●○○○ Very Low
Total adverse events							
N = 243 2 RCTs Bril, 2021[54] Bril, 2023[55]	Serious (downgraded 1 level) High Funding related COI concerns	Not serious	Not serious	Not serious	Not assessed	No difference between groups for 7 mg/kg dose groups in both studies. For 10 mg/kg dose in 1 study, there were significantly more AEs in Rozanolixizumab group compared to placebo (83% vs 67%, $P = .04$)	●●●○ Moderate
Serious adverse events							
N = 243 2 RCTs Bril, 2021[54] Bril, 2023[55]	Serious (downgraded 1 level) High Funding related COI concerns	Not serious	Not serious	Not serious	Not assessed	No difference between study groups (0% vs 3% for both 7mg/kg and 10 mg/kg doses).	●●●○ Moderate

Abbreviations. AE: adverse event; CI: confidence interval; COI: conflict of interest; gMG: generalized myasthenia gravis; LEMS: Lambert-Eaton myasthenic syndrome; MCID: minimum clinically important difference; NR: not reported; RCT: randomized clinical trial.

Table D7. GRADE Profile for Zilucoplan

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
Quantitative Myasthenia Gravis (QMG) score							
N = 219 2 RCTs Howard, 2020[58] Howard, 2023[57]	Serious (downgraded 1 level) High Funding related COI concerns	Not serious	Not serious	Serious (downgraded 1 level) All 95% CIs cross MCID	Not assessed	Both studies report that zilucoplan significantly decreases QMG score compared to placebo ($P < .001$ to $P = .05$) for 0.3 mg/kg dose, both borderline clinically meaningful (-2.8 and -2.94). One study reports no difference for 0.1 mg/kg dose ($P = .09$).	●●○○ Low
MG Activities of Daily Living (MG-ADL) score							
N = 219 2 RCTs Howard, 2020[58] Howard, 2023[57]	Serious (downgraded 1 level) High Funding related COI concerns	Not serious	Not serious	Serious (downgraded 1 level) All 95% CIs cross MCID	Not assessed	Both studies report that Zilucoplan significantly decreases MG-ADL score compared to placebo for all dose groups ($P < .001$ to $P = .05$), all clinically meaningful.	●●○○ Low
Revised Myasthenia Gravis Quality of Life −15 (MG-QoL 15) score							
N = 219 2 RCTs Howard, 2020[58] Howard, 2023[57]	Serious (downgraded 1 level) High Funding related COI concerns	Serious (downgraded 1 level) One study reports significant difference for 0.3 mg/kg group while other study reports no difference.	Not serious	Not serious	Not assessed	For 3 mg/kg group, 1 study reports that Zilucoplan significantly decreases MG-QoL 15 score ($P = .013$) while the other study reports no difference ($P = .06$). For the 0.1 mg/kg group, 1 study reports that Zilucoplan significantly decreases MG-QoL 15r score ($P = .02$).	●●○○ Low

Number of Participants (N) and Number of RCTs	Risk of Bias	Inconsistency	Indirectness	Imprecision	Publication Bias/Other	Effect	Overall Certainty of Evidence Rating
MG Composite (MGC) score							
N = 219 2 RCTs Howard, 2020[58] Howard, 2023[57]	Serious (downgraded 1 level) High Funding related COI concerns	Not serious	Not serious	Serious (downgraded 1 level) All 95% CIs cross MCID	Not assessed	Both studies report that zilucoplan significantly decreases MGC score compared to placebo (*P* = .002 to *P* = .04) for 0.3 mg/kg dose, both clinically meaningful. One study reports no difference for 0.1 mg/kg dose (*P* = .19).	●●○○ Low
Total adverse events							
N = 219 2 RCTs Howard, 2020[58] Howard, 2023[57]	Serious (downgraded 1 level) High Funding related COI concerns	Not serious	Not serious	Not serious	Not assessed	Participants in each group experienced AEs. While AEs were more numerous with the drug for all doses in both studies (100% vs 80% 0.1 mg/kg dose; 86% vs 80% 0.3 mg/kg dose; 77% vs 70% 0.3 mg/kg dose), none of these were significant differences.	●●●○ Moderate
Serious adverse events							
N = 219 2 RCTs Howard, 2020[58] Howard, 2023[57]	Serious (downgraded 1 level) High Funding related COI concerns	Not serious	Not serious	Not serious	Not assessed	Observed SAEs ranged from 0% to 20%, with no clear association to treatment group. For the 0.1 mg/kg dose, there were more AEs in the placebo vs drug group (0% drug vs 20% placebo), but this was not significant. For the 0.3 mg/kg groups, the results were also not significant in both studies (36% drug vs 20% placebo and 13% drug vs 15% placebo, respectively).	●●●○ Moderate

Abbreviations. AE: adverse event; CI: confidence interval; COI: conflict of interest; gMG: generalized myasthenia gravis; LEMS: Lambert-Eaton myasthenic syndrome; MCID: minimum clinically important difference; NR: not reported; RCT: randomized clinical trial.

Appendix E. Bibliography of Included Studies

Antozzi C, Guptill J, Bril V, et al. Safety and efficacy of nipocalimab in patients with generalized myasthenia gravis: results from the randomized phase 2 Vivacity-MG study. *Neurology*. 2024;102(2):e207937. doi: 10.1212/WNL.0000000000207937.

Bonanno S, Pasanisi MB, Frangiamore R, et al. Amifampridine phosphate in the treatment of muscle-specific kinase myasthenia gravis: a phase IIb, randomized, double-blind, placebo-controlled, double crossover study. *SAGE Open Med*. 2018;6:2050312118819013. doi: 10.1177/2050312118819013

Bril V, Benatar M, Andersen H, et al. Efficacy and safety of rozanolixizumab in moderate to severe generalized myasthenia gravis: a phase 2 randomized control trial. *Neurology*. 2021;96(6):e853-e865. doi: 10.1212/WNL.0000000000011108

Bril V, Druzdz A, Grosskreutz J, et al. Safety and efficacy of rozanolixizumab in patients with generalised myasthenia gravis (MycarinG): a randomised, double-blind, placebo-controlled, adaptive phase 3 study. *Lancet Neurol*. 2023;22(5):383-394. doi: 10.1016/S1474-4422(23)00077-7

Habib AA, Sacconi S, Antonini G, et al. Efficacy and safety of rozanolixizumab in patients with muscle-specific tyrosine kinase autoantibody-positive generalised myasthenia gravis: a subgroup analysis of the randomised, double-blind, placebo-controlled, adaptive phase III MycarinG study. *Ther Adv Neurol Disord*. 2024;17:17562864241273036. doi: 10.1177/17562864241273036

Howard JF, Jr., Barohn RJ, Cutter GR, et al. A randomized, double-blind, placebo-controlled phase II study of eculizumab in patients with refractory generalized myasthenia gravis. *Muscle Nerve*. 2013;48(1):76-84. doi: 10.1002/mus.23839

Howard JF, Jr., Bresch S, Genge A, et al. Safety and efficacy of zilucoplan in patients with generalised myasthenia gravis (RAISE): a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet Neurol*. 2023;22(5):395-406. doi: 10.1016/S1474-4422(23)00080-7

Howard JF, Jr., Bresch S, Farmakidis C, et al. Long-term safety and efficacy of zilucoplan in patients with generalized myasthenia gravis: interim analysis of the RAISE-XT open-label extension study. *Ther Adv Neurol Disord*. 2024;17:17562864241243186. doi: 10.1177/17562864241243186

Utsugisawa K, Deguchi K, Konno S, et al. Efficacy and safety of zilucoplan in Japanese patients with generalized myasthenia gravis: A subgroup analysis of the phase III randomized RAISE study. *Clin Exp Neuroimmunol*. 2023;15(1):45-54. doi: 10.1111/cen3.12766

Weiss MD, Freimer M, Leite MI, et al. Improvement of fatigue in generalised myasthenia gravis with zilucoplan. *J Neurol*. 2024;271(5):2758-2767. doi: 10.1007/s00415-024-12209-3

Howard JF, Jr., Bril V, Burns TM, et al. Randomized phase 2 study of FcRn antagonist efgartigimod in generalized myasthenia gravis. *Neurology*. 2019;92(23):e2661-e2673. doi: 10.1212/WNL.0000000000007600

Howard JF, Jr., Bril V, Vu T, et al. Safety, efficacy, and tolerability of efgartigimod in patients with generalised myasthenia gravis (ADAPT): a multicentre, randomised, placebo-controlled, phase 3 trial. *Lancet Neurol*. 2021;20(7):526-536. doi: 10.1016/S1474-4422(21)00159-9

Bril V, Howard JF, Jr., Karam C, et al. Effect of efgartigimod on muscle group subdomains in participants with generalized myasthenia gravis: post hoc analyses of the phase 3 pivotal ADAPT study. *Eur J Neurol*. 2024;31(1):e16098. doi: 10.1111/ene.16098

Dewilde S, Griffiths A, Qi CZ, et al. Post-hoc analyses from the ADAPT clinical study demonstrate aggregate sustained benefit of Efgartigimod in generalized myasthenia gravis. *J Neurol Sci*. 2024;466:123264. doi: 10.1016/j.jns.2024.123264

Howard JF, Jr., Bril V, Vu T, et al. Long-term safety, tolerability, and efficacy of efgartigimod (ADAPT+): interim results from a phase 3 open-label extension study in participants with generalized myasthenia gravis. *Front Neurol*. 2023;14:1284444. doi: 10.3389/fneur.2023.1284444

Sacca F, Barnett C, Vu T, et al. Efgartigimod improved health-related quality of life in generalized myasthenia gravis: results from a randomized, double-blind, placebo-controlled, phase 3 study (ADAPT). *J Neurol*. 2023;270(4):2096-2105. doi: 10.1007/s00415-022-11517-w

Howard JF, Jr., Nowak RJ, Wolfe GI, et al. Clinical Effects of the self-administered subcutaneous complement inhibitor zilucoplan in patients with moderate to severe generalized myasthenia gravis: results of a phase 2 randomized, double-blind, placebo-controlled, multicenter clinical trial. *JAMA Neurol*. 2020;77(5):582-592. doi: 10.1001/jamaneurol.2019.5125

Howard JF, Jr., Utsugisawa K, Benatar M, et al. Safety and efficacy of eculizumab in anti-acetylcholine receptor antibody-positive refractory generalised myasthenia gravis (REGAIN): a phase 3, randomised, double-blind, placebo-controlled, multicentre study. *Lancet Neurol*. 2017;16(12):976-986. doi: 10.1016/S1474-4422(17)30369-1

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Howard JF, Jr., Karam C, Yountz M, O'Brien FL, Mozaffar T, Group RS. Long-term efficacy of eculizumab in refractory generalized myasthenia gravis: responder analyses. *Ann Clin Transl Neurol*. 2021;8(7):1398-1407. doi: 10.1002/acn3.51376

Jacob S, Murai H, Utsugisawa K, et al. Response to eculizumab in patients with myasthenia gravis recently treated with chronic IVIg: a subgroup analysis of REGAIN and its open-label extension study. *Ther Adv Neurol Disord*. 2020;13:1756286420911784. doi: 10.1177/1756286420911784

Mantegazza R, O'Brien FL, Yountz M, Howard JF, Jr., group Rs. Consistent improvement with eculizumab across muscle groups in myasthenia gravis. *Ann Clin Transl Neurol*. 2020;7(8):1327-1339. doi: 10.1002/acn3.51121

Mantegazza R, Wolfe GI, Muppidi S, et al. Post-intervention Status in patients with refractory myasthenia gravis treated with eculizumab during REGAIN and its open-label extension. *Neurology*. 2021;96(4):e610-e618. doi: 10.1212/WNL.0000000000011207

Muppidi S, Utsugisawa K, Benatar M, et al. Long-term safety and efficacy of eculizumab in generalized myasthenia gravis. *Muscle Nerve*. 2019;60(1):14-24. doi: 10.1002/mus.26447

Murai H, Uzawa A, Suzuki Y, et al. Long-term efficacy and safety of eculizumab in Japanese patients with generalized myasthenia gravis: A subgroup analysis of the REGAIN open-label extension study. *J Neurol Sci*. 2019;407:116419. doi: 10.1016/j.jns.2019.08.004

Nowak RJ, Muppidi S, Beydoun SR, O'Brien FL, Yountz M, Howard JF, Jr. Concomitant immunosuppressive therapy use in eculizumab-treated adults with generalized myasthenia gravis during the REGAIN open-label extension study. *Front Neurol*. 2020;11:556104. doi: 10.3389/fneur.2020.556104

Siddiqi ZA, Nowak RJ, Mozaffar T, et al. Eculizumab in refractory generalized myasthenia gravis previously treated with rituximab: subgroup analysis of REGAIN and its extension study. *Muscle Nerve*. 2021;64(6):662-669. doi: 10.1002/mus.27422

Vissing J, Jacob S, Fujita KP, O'Brien F, Howard JF, REGAIN Study Group. 'Minimal symptom expression' in patients with acetylcholine receptor antibody-positive refractory generalized myasthenia gravis treated with eculizumab. *J Neurol.* 2020;267(7):1991-2001. doi: 10.1007/s00415-020-09770-y

Oh SJ, Shcherbakova N, Kostera-Pruszczyk A, et al. Amifampridine phosphate (Firdapse) is effective and safe in a phase 3 clinical trial in LEMS. *Muscle Nerve*. 2016;53(5):717-725. doi: 10.1002/mus.25070

Shieh P, Sharma K, Kohrman B, Oh SJ. Amifampridine phosphate (Firdapse) is effective in a confirmatory phase 3 clinical trial in LEMS. *J Clin Neuromuscul Dis*. 2019;20(3):111-119. doi: 10.1097/CND.0000000000000239

Vu T, Meisel A, Mantegazza R, et al. Terminal complement inhibitor ravulizumab in generalized myasthenia gravis. *NEJM Evidence*. 2022;1(5):EVIDoa2100066. doi: 10.1056/EVIDoa2100066

Habib AA, Benatar M, Vu T, et al. Time to response with ravulizumab, a long-acting terminal complement inhibitor, in adults with anti-acetylcholine receptor antibody-positive generalized myasthenia gravis. *Eur J Neurol*. 2024;31(12):e16490. doi: 10.1111/ene.16490

Howard JF, Jr., Vu T, Mantegazza R, et al. Efficacy of ravulizumab in patients with generalized myasthenia gravis by time from diagnosis: a post hoc subgroup analysis of the CHAMPION MG study. *Muscle Nerve*. 2024;69(5):556-565. doi: 10.1002/mus.28044

Meisel A, Annane D, Vu T, et al. Long-term efficacy and safety of ravulizumab in adults with anti-acetylcholine receptor antibody-positive generalized myasthenia gravis: results from the phase 3 CHAMPION MG open-label extension. *J Neurol*. 2023;270(8):3862-3875. doi: 10.1007/s00415-023-11699-x

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Appendix F. Bibliography of Excluded Studies With Reasons

Table F1. Studies Excluded From This Systematic Review With Reasons

Excluded Studies	Exclusion Reason
CADTH Common Drug Reviews 2020. *Canadian Agency for Drugs and Technologies in Health*. 2020. 12:12	Publication Type
Efgartigimod alfa (VYVGART°) in generalised myasthenia gravis. *Prescrire Int*. 2024. 33:121-123	Unable to obtain full text
Ravulizumab (ULTOMIRIS°) in generalised myasthenia gravis. *Prescrire Int*. 2024. 33:126	Unable to obtain full text
Alderson D, Homer N, Dierick K. Pnd5 - a Literature Review Reporting the Side Effects and Any Related Consequences Caused by Current Chronic Myasthenia Gravis Treatments. *Value Health*. 2018. 21:S329. doi: 10.1016/j.jval.2018.09.1972	Publication Type
Antonini A, Vu, T, Druzdz A, Grosskreutz J, et al. Efficacy of rozanolixizumab in generalised Myasthenia Gravis: subgroup analyses from the randomised Phase 3 MycarinG study. *Acta Myol*. 2023. 42:58	Publication Type
Antozzi C, Freimer M, Leite MI, et al. RAISE-XT: An interim analysis of safety and efficacy in an open-label extension study of zilucoplan in patients with Myasthenia Gravis. *Acta Myol*. 2023. 42:58	Publication Type
Antozzi, C, Guptill J, Bril V, et al. Vivacity-MG: a phase 2, multicenter, randomized, double-blind, placebo-controlled study to evaluate the safety, tolerability, efficacy, pharmacokinetics, pharmacodynamics, and immunogenicity of nipocalimab administered to adults with generalized myasthenia gravis. *Clin Exp Rheumatol*. 2023. 41:498	Publication Type
Bril V, Benatar M, Brock M, et al. Proof-of-concept and safety of the anti-FcRn antibody rozanolixizumab in patients with moderate-to-severe generalized myasthenia gravis (GMG): a phase 2a study. *Neurology*. 2019. 92 (15_supplement): S43.001	Publication Type
Bril V, Gwathmey K, Goebeler M, et al. Overview of the safety profile of efgartigimod from clinical trials in participants with diverse immunoglobulin G–mediated autoimmune diseases. *J Neurol Sci*. 2023. 455. doi: 10.1016/j.jns.2023.121195	Publication Type
Bril V, Pasnoor M, Karam C, et al. Long-term safety, tolerability, and efficacy of efgartigimod in patients with generalized myasthenia gravis: Concluding analyses from the ADAPT+ study. *J Neurol Sci*. 2023. 455. doi: 10.1016/j.jns.2023.121089	Publication Type
Bril V, Vissing J, Drużdż A, et al. Rozanolixizumab responder and minimal symptom expression rates in generalized myasthenia gravis: Pooled phase 3 and extension studies. *J Neurol Sci*. 2023. 455. doi: 10.1016/j.jns.2023.122016	Publication Type
Channa H, Angela G, Miriam F, et al. H. Corticosteroid dose tapering in patients with generalised myasthenia gravis on zilucoplan: interim analysis of RAISE-XT. *J Neurol Neurosurg Psychiatry*. 2024. 95:A45-A46. doi: 10.1136/jnnp-2024-ABN.148	Publication Type
Chen H, Qiu Y, Yin Z, et al. Efficacy and safety of the innovative monoclonal antibodies in adults with generalized myasthenia gravis: a Bayesian network analysis. *Front Immunol*. 2023. 14:1280226. doi: 10.3389/fimmu.2023.1280226	Publication Type

Excluded Studies	Exclusion Reason
Feng X, Song Z, Wu M, et al. Efficacy and safety of immunotherapies in refractory myasthenia gravis: a systematic review and meta-analysis. *Front Neurol.* 2021. 12:725700. doi: 10.3389/fneur.2021.725700	Publication Type
Frangiamore R, Rinaldi E, Vanoli F, Andreetta F, Mantegazza R, Antozzi C. Efgartigimod improves triple-negative myasthenia gravis. *Neurol Sci.* 2024. 45:1307-1309. doi: 10.1007/s10072-023-07122-y	Publication Type
Garzon-Orjuela N, van der Werf L, Prieto-Pinto LC, Lasalvia P, Castaneda-Cardona C, Rosselli D. Quality of life in refractory generalized myasthenia gravis: a rapid review of the literature. *Intractable Rare Dis Res.* 2019. 8:231-238. doi: 10.5582/irdr.2019.01121	Publication Type
Gelinas D, Rahman O, Lambert E, Van Hoorick B. Baseline characteristics and demographics of patients enrolled in an expanded access program for efgartigimod in adult patients with generalized myasthenia gravis. *Neurology.* 2022. 98 (18_supplement): P3-1.001	Publication Type
Genge A, Bril V, Vu T, Brauer E, Kerstens R, Howard JF. Efgartigimod demonstrates consistent improvements in patients with generalized myasthenia gravis of shorter disease duration. *J Neurol Sci.* 2023. 455. doi: 10.1016/j.jns.2023.121088	Publication Type
Genge A, Leite MI, Bresch S, et al. Long-term safety, efficacy & self-injection satisfaction with zilucoplan in myasthenia gravis: RAISE-XT interim analysis. *J Neurol Sci.* 2023. 455. doi: 10.1016/j.jns.2023.122025	Publication Type
Gu J, Qiao Y, Huang R, Cong S. Efficacy and safety of immunosuppressants and monoclonal antibodies in adults with myasthenia gravis: a systematic review and network meta-analysis. *J Transl Med.* 2024. 22:955. doi: 10.1186/s12967-024-05751-1	Publication Type
Guptill J, Antozzi C, Bril V. Serum IgG and autoantibody lowering by the anti-FcRn monoclonal antibody, nipocalimab, correlates with improvement in MG-ADL in generalized myasthenia patients. *Neurology.* 2022. 98(18_supplement): S25.007	Publication Type
Howard JF, Bril V, Mantegazza R, et al. A double-blind placebo-controlled study to evaluate the safety and efficacy of FcRn antagonist ARGX-113 (efgartigimod) in generalized myasthenia gravis. *Neurology.* 2018. 90:e2193	Publication Type
Howard JF, Vu T, Li G, et al. Adapt-Sc Study. Subcutaneous efgartigimod PH20 in generalized myasthenia gravis: a phase 3 randomized noninferiority study (ADAPT-SC) and interim analyses of a long-term open-label extension study (ADAPT-SC+). *Neurotherapeutics.* 2024. 21:e00378. doi: 10.1016/j.neurot.2024.e00378	Publication Type
Howard JF, Li G, Vu T, et al. Long-term safety, tolerability, and efficacy of subcutaneous efgartigimod PH20 in patients with generalized Myasthenia Gravis: Interim results of the ADAPT-SC+ Study. *Acta Myol.* 2023. 42:58-59	Publication Type
Howard JF, Vu T, Mantegazza R, et al. Long-term efficacy and safety of ravulizumab, a long-acting terminal complement inhibitor, in adults with anti-acetylcholine receptor antibody-positive generalized myasthenia gravis: results from the phase 3 CHAMPION MG open-label extension. *Neurology.* 2022. 98(18_supplement): S25.005	Publication Type
Howard J, Barohn R, Freimer M, et al. Randomized, double-blind, placebo-controlled, crossover, multicenter, phase II study of eculizumab in patients with refractory generalized myasthenia gravis (GMG). *Neurology.* 2012. 78(1_supplement): S35.004. doi: 10.1212/WNL.78.1	Publication Type

Excluded Studies	Exclusion Reason
Howard J, Bril V, Mantegazza R, et al. Additional analyses of the phase 2 efgartigimod study in myasthenia gravis. *Neurology*. 2020. 94 (15_supplement): 4484.	Publication Type
Howard J, Bril V, Vu T, et al. Long-term safety, tolerability, and efficacy of efgartigimod in patients with generalized myasthenia gravis: interim results of the ADAPT+ study. *Neurology*. 2022. 98(18_supplement): S25.004.	Publication Type
Howard J, Bril V, Vu T, et al. Efficacy, safety, and tolerability of efgartigimod in patients with generalized myasthenia gravis: analysis of the phase 3 ADAPT study. *Neurology*. 2021. 96 (15_supplement): 4520.	Publication Type
Howard J, Jacob S, Guptill J, et al. Relieving the burden of myasthenia gravis: Eculizumab reduces exacerbation, hospitalization and rescue therapy rates. *Muscle Nerve*. 2018. 58:S115.	Publication Type
Howard J, Karam C, Yountz M, O'Brien F, Mozaffar T. Long-term efficacy of eculizumab in refractory generalized myasthenia gravis: Responder analyses. *Muscle Nerve*. 2019. 60:S133.	Publication Type
Howard J, Nowak R, Wolfe G, et al. Zilucoplan, a self-administered subcutaneous peptide inhibitor of complement component 5 (C5) for the treatment of generalized myasthenia gravis: phase 2 results. *Muscle Nerve*. 2019. 60:S129.	Publication Type
Howard J, Wang JJ, O'Brien F, Mantegazza R. Efficacy of eculizumab on myasthenia gravis-activities of daily living and its respiratory, bulbar, limb and ocular domains in patients with ACHR+ refractory generalized myasthenia gravis. *Muscle Nerve*. 2017. 56:649.	Publication Type
Howard J, Wang JJ, O'Brien F, Mantegazza R. Efficacy of eculizumab is maintained beyond 26 weeks in patients with ACHR+ refractory generalized myasthenia gravis. *Muscle Nerve*. 2017. 56:649.	Publication Type
Howard J, Wang J, O'Brien F, Mantegazza R. Efficacy of eculizumab is sustained over 52 weeks in patients with ACHR+ refractory generalized myasthenia gravis: interim results from the open-label extension of REGAIN. *Muscle Nerve*. 2017. 56:657.	Publication Type
Jacob S, Howard J, Bril V, et al. Long-term assessment of efgartigimod in patients with generalised myasthenia gravis: ADAPT+ study interim results. *J Neurol Neurosurg Psychiatry*. 2022. 93:1. doi: 10.1136/jnnp-2022-abn2.2	Publication Type
Landfeldt E, Pogoryelova O, Sejersen T, Zethraeus N, Breiner A, Lochmuller H. Economic costs of myasthenia gravis: a systematic review. *Pharmacoeconomics*. 2020. 38:715-728. doi: 10.1007/s40273-020-00912-8	Publication Type
Leu JH, Vermeulen A, Abbes C, Arroyo S, Denney WS, Ling LE. Pharmacokinetics and pharmacodynamics across infusion rates of intravenously administered nipocalimab: results of a phase 1, placebo-controlled study. *Front Neurosci*. 2024. 18:1302714. doi: 10.3389/fnins.2024.1302714	Population
Levine T, Mantegazza R, Oreja-Guevara C, et al. Infection risk in patients with complement-mediated neurological disorders receiving eculizumab: findings from two phase 3 studies and their extensions in aquaporin-4 antibody-positive neuromyelitis optica spectrum disorder (AQP4+ NMOSD) and acetylcholine-receptor antibody-positive refractory generalized myasthenia gravis (ACHR+ GMG). *Neurology*. 2020. 94(15_supplement): 1829.	Study Design

Excluded Studies	Exclusion Reason
Li J, Wu X, Chu T, et al. The efficacy and safety of FcRn inhibitors in patients with myasthenia gravis: a systematic review and meta-analysis. *J Neurol.* 2024. 271:2298-2308. doi: 10.1007/s00415-024-12247-x	Publication Type
Ma Y, Nie X, Zhu G, Qi W, Hao L, Guo X. The efficacy and safety of different targeted drugs for the treatment of generalized myasthenia gravis: a systematic review and bayesian network meta-analysis. *CNS Drugs.* 2024. 38:93-104. doi: 10.1007/s40263-024-01062-7	Publication Type
Mantegazza RE, Habib AA, Benata M, et al. Ravulizumab for the treatment of generalized myasthenia gravis: timing of response. *Acta Myol.* 2023. 42:110-111	Publication Type
Mantegazza RE, Levine TD, Oreja-Guevara C, et al. No change in risk of infection among NMOSD and refractory gMG patients treated with eculizumab: findings from two phase 3 studies and their extensions. *Eur J Neurol.* 2020. 27:381-382.	Study Design
Mantegazza R, Fujita K, O'Brien F, Howard J. Eculizumab shows consistent improvement across quantitative myasthenia gravis test muscle groups. *Muscle Nerve.* 2018. 58:S97.	Publication Type
Mantegazza R, Pasanisi B, Antozzi C, et al. MuSK MG patients showed a positive response to amifampridine phosphate in a randomized, placebo-controlled, crossover study. *Neuromuscul Disord.* 2017. 27:S249. doi: 10.1016/j.nmd.2017.06.553	Publication Type
Mantegazza R, Wolfe G, Muppidi S, et al. Minimal manifestations with eculizumab in myasthenia gravis. *Muscle Nerve.* 2018. 58:S98.	Publication Type
Mantegazza R, Bril V, Vu T, et al. Safety and tolerability of efgartigimod in patients with generalized myasthenia gravis: phase 3 adapt study results. *J Neurol Sci.* 2021. 429. doi: 10.1016/j.jns.2021.117764	Publication Type
Mantegazza R, Levine T, Oeja-Guevara C, et al. Safety of eculizumab in NMOSD and MG: analysis of the phase 3 studies PREVENT and REGAIN, and their extensions. *J Neurol Sci.* 2021. 429. doi: 10.1016/j.jns.2021.118787	Publication Type
Mishra AK, Varma A. Myasthenia gravis: a systematic review. *Cureus.* 2023. 15:e50017. doi: 10.7759/cureus.50017	Publication Type
Muppidi S, O'Brien F, Wang J, Fujita K, Howard J. Long-term effectiveness and safety of eculizumab in generalized myasthenia gravis: Beyond mg-adl and qmg. *Muscle Nerve.* 2018. 58:S115	Publication Type
Murai H, Howard JF, Wang JJ, O'Brien F, Utsugisawa K. Efficacy of eculizumab is maintained beyond 26 weeks in patients with acetylcholine receptor-positive refractory generalized myasthenia gravis. *Clin Exp Neuroimmunol.* 2017. 8:365	Publication Type
Murai H, Uzawa A, Suzuki Y, et al. Open label extension trial of REGAIN to evaluate the safety and efficacy of eculizumab in patients from Japan with refractory generalized myasthenia gravis. *J Neurol Sci.* 2017. 381:132-133. doi: 10.1016/j.jns.2017.08.397	Publication Type
Murai H, Utsugisawa K, Motomura M, Imai T, Uzawa A, Suzuki S. The Japanese clinical guidelines 2022 for myasthenia gravis and Lambert–Eaton myasthenic syndrome. *Clin Exp Neuroimmunol.* 2023. 14:19-27. doi: 10.1111/cen3.12739	Publication Type
Narayanaswami P, Sanders DB, Wolfe G, et al. International consensus guidance for management of myasthenia gravis: 2020 Update. *Neurology.* 2021. 96:114-122. doi: 10.1212/WNL.0000000000011124	Publication Type

Excluded Studies	Exclusion Reason
Ndegwa S, Mierzwinski-Urban M. CADTH Horizon Scan: emerging drugs for generalized myasthenia gravis. *Can J Health Technol.* 2022. 2(2):n.r. doi: 10.51731/cjht.2022.270	Publication Type
Oh S, Gorodetzky C, Winship D. Amifampridine phosphate (Firdapse™) is safe and effective in a pivotal phase 3 trial in LEMS patients. *Neurology.* 2015. 84(14_supplement): PL2.001.	Publication Type
Pasnoor M, Bril V, Karam C, et al. Long-term safety, tolerability, and efficacy of efgartigimod in patients with generalized myasthenia gravis: concluding analyses from the ADAPT+ study. *Acta Myol.* 2023. 42:108	Publication Type
Pastor S, García M, Sastre M, et al. Efficacy and safety of non-steroidal immunosuppressive treatments in generalized myasthenia gravis patients. a systematic review and meta-analysis. *Eur J Neurol.* 2020. 27:356-357	Publication Type
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