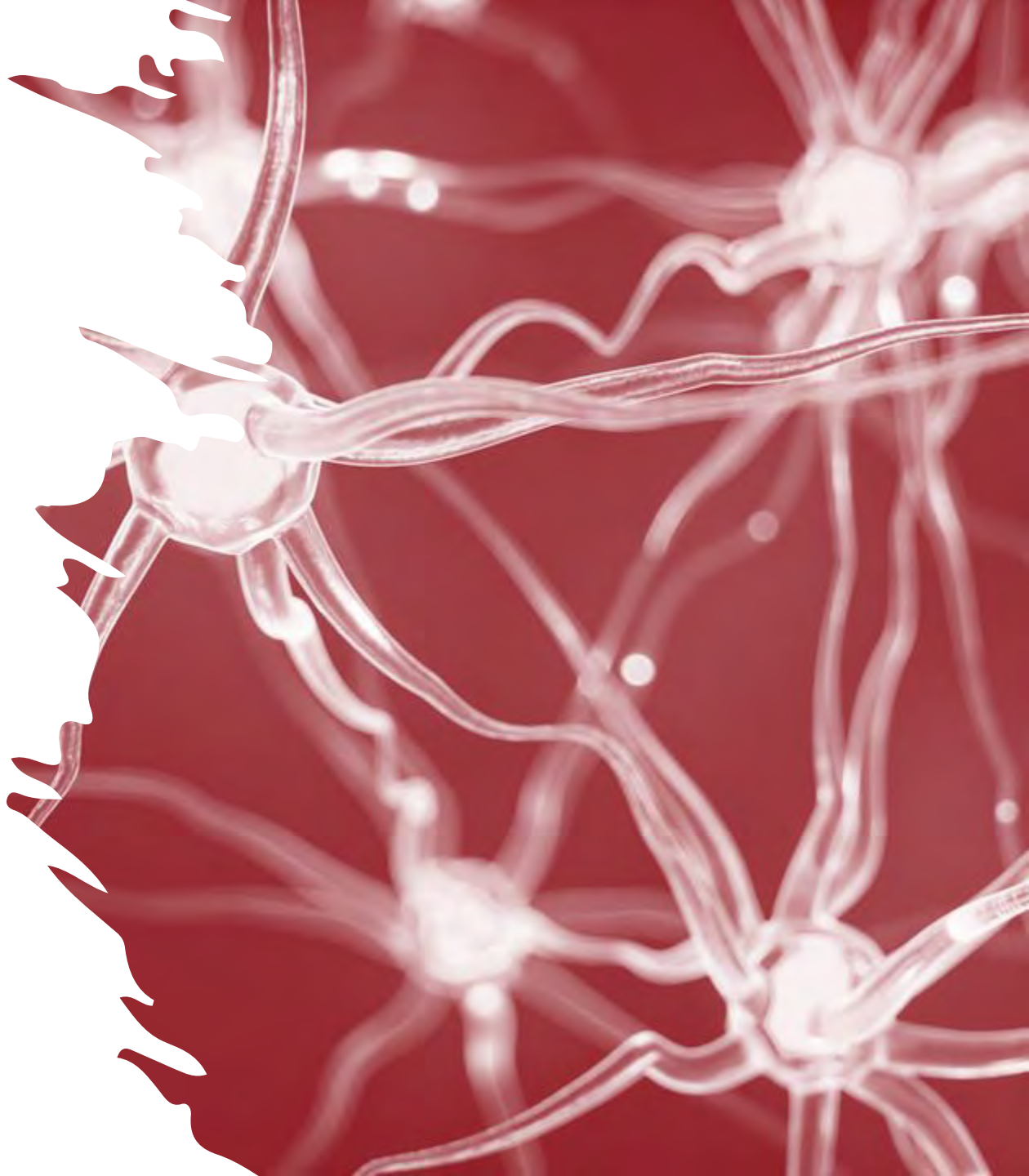
Myasthenia Gravis Clinical Research Highlights: AAN 2025

James Howard Jr, MD
Professor of Neurology
University of North Carolina



Continuing Education Information

In support of improving patient care, this activity has been planned and implemented by American Academy of CME, Inc. and CheckRare CE. American Academy of CME, Inc. is Jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

American Academy of CME, Inc., designates this enduring material for a maximum of 0.5 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Learning Objective: Describe the latest research about myasthenia gravis presented at AAN2025 and its clinical relevance.

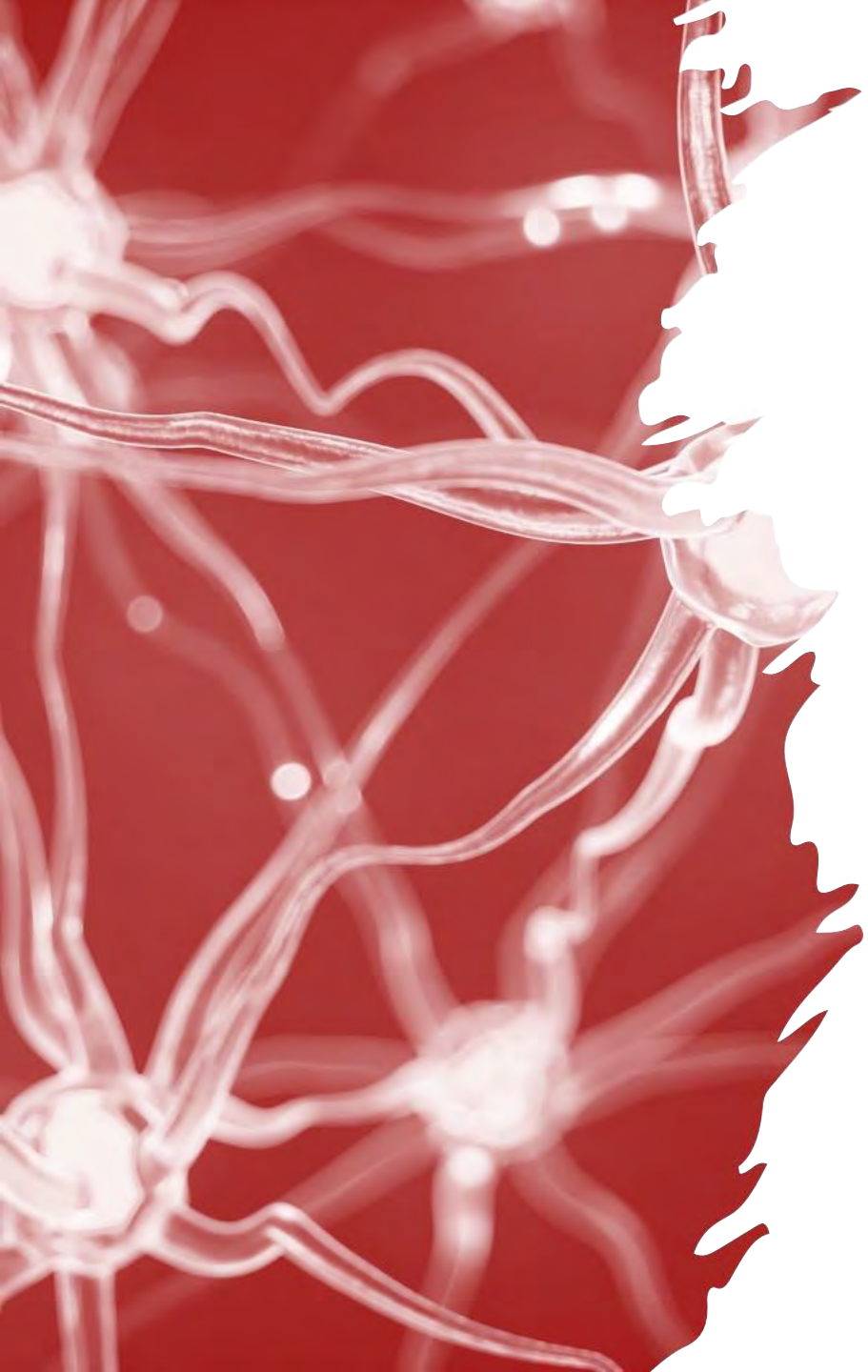
Planner/Faculty Educator Dr. Howard discloses the following relevant financial relationships with ineligible companies:

- Advisory Board/Consultant: Alexion AstraZeneca Rare Disease, Amgen, argenx, Biohaven Ltd, Cartesian Therapeutics, CoreEvitas, Curie.bio, Hansa Biopharma, H. Lundbeck A/S, Merck EMD Serono, NMD Pharma, Novartis Pharma, Regeneron Pharmaceuticals, Sanofi US, Seismic Therapeutics, TG Therapeutics, Toleranzia AB, and UCB Pharma.
- Grant/Research Support: Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, NMD Pharma, and UCB Pharma.
- Other Relationships: non-financial support (eg travel) Alexion AstraZeneca Rare Disease, argenx, Biohaven Ltd, Cartesian Therapeutics, Toleranzia AB, and UCB Pharma.

Planners and reviewers for this activity have no relevant financial relationships with any ineligible companies.

All relevant financial relationships listed have been mitigated. This activity will discuss off-label uses and investigational agents.

This accredited continuing education program is supported by an educational grant from UCB Inc.



What is Myasthenia Gravis?

- Group of rare autoimmune diseases **characterized by postsynaptic defect of neuromuscular transmission**, often due to the presence of antibodies against acetylcholine (AChR-Ab+).
  - **Trademark:** fluctuating but intense weakness in specific muscle groups – such as bulbar weakness, limb weakness, and ocular weakness
  - Ocular weakness - most common initial presentation of MG
  - **Six drugs approved** by the FDA:
    - Eculizumab
    - Efgartigimod
    - Ravulizumab
    - Rozanolixizumab
    - Zilucoplan
    - Nipocalimab

Global MG Management: Guidelines vs. Real-World Practice

- Intl survey assessed alignment with MG consensus guidelines and regional trends in care.
- N=210
- Providers in developed countries more frequently recommended guideline-based care, including thymectomy, IVIG, and cesarean delivery in MG pregnancies.

Outcome/Variable	Key Findings	Significance/Notes
Thymectomy for AChR-MG	Recommended by 53.3%	More common in experienced providers and developed countries
MuSK-MG 1st-line therapy	No clear consensus	Highlights therapeutic uncertainty
MMF in pregnancy	61.4% recommend discontinuation; 25.2% continue at lower dose	IVIG more recommended in developed countries (OR=2.97)
Cesarean delivery recommendation	More likely in developed countries (OR=4.86, p=.004)	Reflects differences in access and practice norms

Thawani S et al. Management of myasthenia gravis around the globe: Consensus guidelines versus realities of practice. *Neurology.* 2025; 104(7 Suppl. 1)

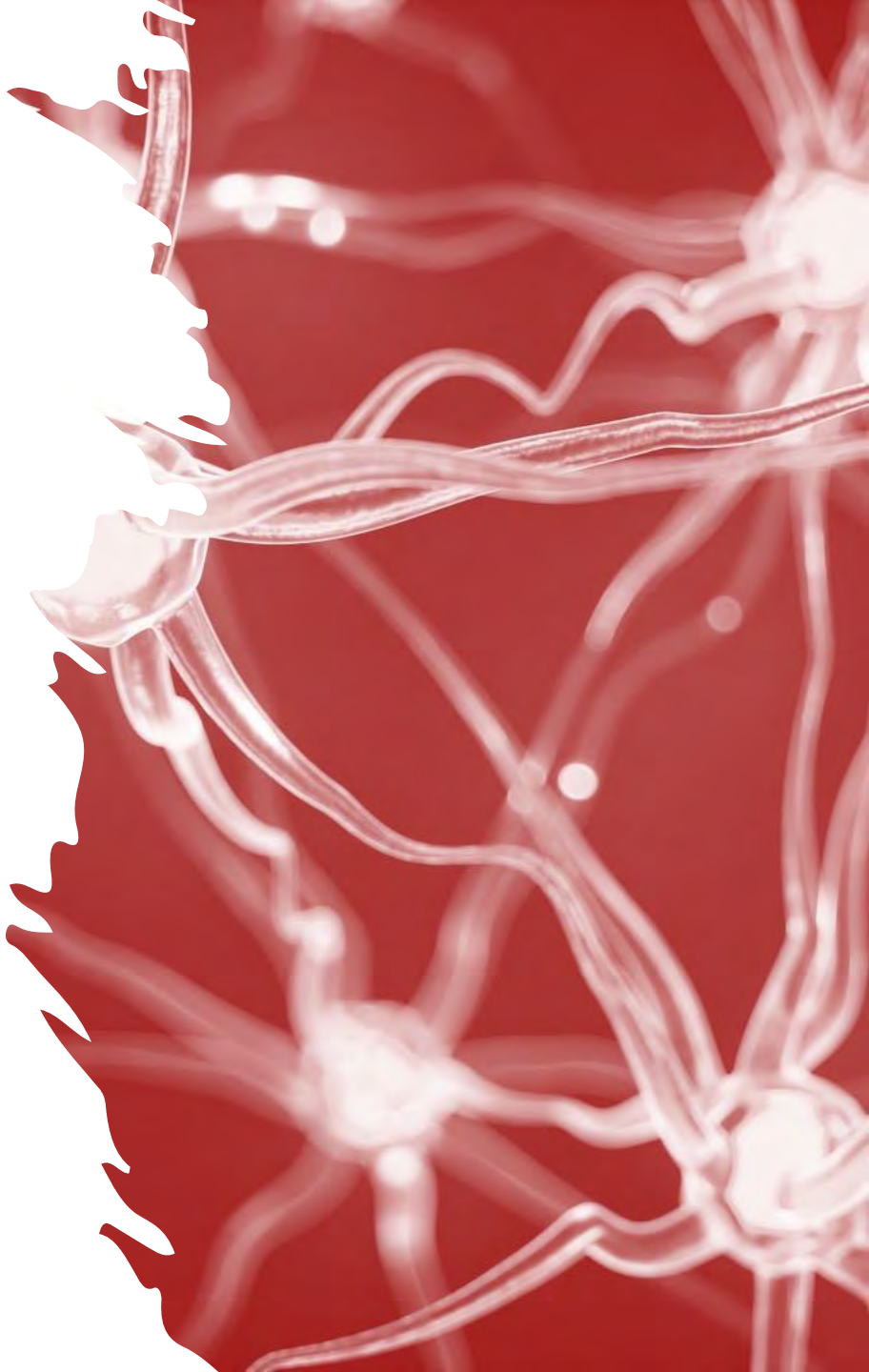
Real-World Treatment Patterns and Clinical Outcomes in gMG

Measure	Findings
Sample Size	6,195 pts (mean age: 61.1 yrs; 49.1% female)
Follow-up Duration	Mean 32.7 months
Treatment Trends (1st to 5th episode)	AChEI use ↓ from 81.1% to 58.5% Corticosteroids: 48.2–63.2%
	Non-steroidal IS use ↑ from 11.8% to 41.8%
	Immunoglobulin use ↑ from 6.3% to 15.6%
	FcRn inhibitor use ↑ from 0.1% to 2.7%
	C5 inhibitor use ↑ from 0.2% to 2.9%
Time to Initiation (Targeted Therapies)	FcRn: 20.7 months; C5 inhibitors: 15.8 months post-diagnosis
Exacerbations Post-Index	48.8% had exacerbations; highest in year 1 (41.5%), then declined yearly
Crises Post-Index	3.1% had MG crisis

- Assessed real-world treatment patterns and MG-related clinical events in U.S. pts with gMG.
- Retrospective observational study using Komodo Research Database (2017–2023); N=6,195
- Conventional therapies are often first-line; high early exacerbation rates suggest a need for earlier use of targeted treatments.

Grover K et al. Real-world treatment patterns among patients with generalized myasthenia gravis. *Neurology.* 2025; 104(7 Suppl. 1)

Clinical Trial Data



Efficacy of Nipocalimab in Generalized MG (Vivacity-MG3 Trial)

- Evaluated nipocalimab effect on QMG score in pts with gMG.
- N=153; QMG outcomes assessed over 24 weeks.
- Nipocalimab provided rapid, sustained improvement in disease severity, supporting its role as an effective FcRn-targeting therapy.

Measure	Nipocalimab	Placebo	Effect/p-value
LS Mean QMG Score Change (Week 22–24)	–4.9	–2.0	Δ = –2.81; p < .001
LS Mean QMG Change at Week 2	–3.6	–0.6	Δ = –3.1; p < .001
Mean Week to QMG-3 Improvement	3.8	7.5	—
QMG-3 Response within 8 Weeks	71.4% (55/77)	44.7% (34/76)	p < .001
Sustained QMG-3 ≥8 Weeks	55.8% (43/77)	26.3% (20/76)	p < .001
Odds of Sustaining QMG-3 ≥16 Weeks	OR: 4.31	—	—
Odds of Sustaining QMG-3 ≥20 Weeks	OR: 4.53	—	—
>75% Time with QMG-3 Response	36.4%	10.5%	p < .001

Ramchandren S et al. Efficacy of nipocalimab, a novel neonatal fragment crystallizable receptor blocker, as measured using quantitative myasthenia gravis assessment: Findings from the phase 3 placebo-controlled Vivacity-MG3 study. *Neurology.* 2025; 104(7 Suppl. 1)

Subgroup Analysis of Zilucoplan in gMG (RAISE Trial)

QMG Subdomain Scores (Mean CFB)

Subdomain	Zilucoplan	Placebo
Ocular	–2.0	–1.3
Bulbar	–1.6	–1.1
Respiratory	–0.6	–0.3
Limb/Axial	–2.9	–1.2

MG-ADL Subdomain Scores (Mean CFB)

Subdomain	Zilucoplan	Placebo
Ocular	–1.5	–0.8
Bulbar	–1.9	–1.1
Respiratory	–0.4	–0.3
Limb/Axial	–1.2	–0.8

Study Results

Outcome	Zilucoplan	Placebo	Difference/p-value
MG-ADL Total (LSM CFB)	–4.39	–2.30	Δ = –2.09; p = 0.0004
QMG Total (LSM CFB)	–6.19	–3.25	Δ = –2.94; p < 0.0001

- Assessed impact of zilucoplan on MG-ADL and QMG subdomains (ocular, bulbar, respiratory, limb/axial).
- N=174; daily SC injections over 12 weeks.
- Zilucoplan showed consistent benefit across all muscle groups, supporting its use for comprehensive symptom control in gMG.

Weiss MD et al. Effect of zilucoplan on myasthenia gravis–specific outcome subdomain scores in RAISE: A phase 3 study. *Neurology.* 2025; 104(7 Suppl. 1)

Efficacy and Safety of Inebilizumab in AChR+ and MuSK+ gMG

- Assessed efficacy and safety of inebilizumab in AChR+ or MuSK+ pts with gMG.
- N=238; (52-week RCP for AChR+; 26-week for MuSK+); primary endpoint at 26 weeks.
- Inebilizumab significantly improved MG-ADL and QMG scores across both antibody subtypes with favorable safety profile, supporting its potential as a B-cell–targeted therapy in gMG.

Measure	Inebilizumab	Placebo	Difference / p-value
Patients Randomized	119 (95 AChR+, 24 MuSK+)	119 (95 AChR+, 24 MuSK+)	—
MG-ADL Score (CFB at Week 26)	–4.2	–2.2	Δ = –1.9; p<0.001
QMG Score (CFB at Week 26)	–4.8	–2.3	Δ = –2.5; p<0.001
Any Adverse Events	80.7%	73.1%	—
Serious Adverse Events	8.4%	13.4%	—

Nowak RJ et al. Phase 3 myasthenia gravis inebilizumab trial (MINT): Efficacy and safety results in patients with generalized MG. *Neurology.* 2025; 104(7 Suppl. 1)

Dosing Flexibility of Efgartigimod in gMG (ADAPT NXT Trial)

Measure	Fixed-Cycle	Q2W Dosing
Participants Treated	17	52
MG-ADL Change from Baseline (Week 1–21)	–5.1	–4.6
Minimal Symptom Expression (MG-ADL 0–1)	47.1% (8/17)	44.2% (23/52)
Common Adverse Events	COVID-19, URTI, headache	COVID-19, URTI, headache
Safety/Tolerability	Well tolerated	Well tolerated

- Evaluated efficacy and tolerability of fixed-cycle vs biweekly efgartigimod dosing in AChR+ pts with gMG.
- N=69; 3:1 randomization to Q2W vs fixed-cycle dosing over 21 weeks; MG-ADL outcomes assessed.
- Both dosing regimens maintained efficacy, supporting flexible treatment schedules based on pt preference and clinical response.

Gwathmey K et al. Fixed cycle and every-other-week dosing of intravenous efgartigimod for generalized myasthenia gravis: Part B of ADAPT NXT. *Neurology.* 2025; 104(7 Suppl. 1)

Long-Term SC Efgartigimod in gMG (ADAPT-SC+ OLE)

- Assessed long-term safety and efficacy of subcutaneous efgartigimod PH20 in pts with gMG.
- OLE of ADAPT-SC/ADAPT+ (n=179); SC efgartigimod administered in cycles of 4 weekly doses based on clinical need.
- Long-term SC efgartigimod maintained symptom control with a favorable safety profile, offering a convenient and repeatable treatment option.

Measure	Result
Participants Treated	179
Mean Duration on Study	413 days
Safety	Mild/moderate AEs; injection-site reactions declined with time; no discontinuations due to ISR
MG-ADL Improvement (Cycle 1, Week 4)	–4.1
Sustained MG-ADL Response (Cycles 1–9)	Consistent, repeatable improvements
Minimal Symptom Expression (MG-ADL 0–1)	54.6% achieved at any point across 9 cycles
QoL Measures	Improvements mirrored MG-ADL pattern
Comparative Insight	Efficacy similar to IV efgartigimod

Vu T et al. Long-term safety and efficacy of subcutaneous efgartigimod PH20 in adult participants with generalized myasthenia gravis: Interim results of the ADAPT-SC+ study. *Neurology.* 2025; 104(7 Suppl. 1)

Rozanolixizumab and Ocular Symptom Control in gMG

Scale / Symptom	Rozano 7 mg/kg	Rozano 10 mg/kg	Placebo
MG-ADL: Double Vision	–0.6	–0.6	–0.2
MG-ADL: Ptosis	–0.5	–0.7	0.0
QMG: Double Vision	–0.6	–0.8	0.1
QMG: Ptosis	–0.5	–1.0	–0.5
PRO: Double Vision	–0.5	–0.6	–0.2
PRO: Eyelid Drooping	–0.5	–0.7	–0.1

- Evaluated effect of rozanolixizumab on ocular symptoms in pts with gMG.
- Post hoc analysis of Phase 3 RCT (N=200; 6-week SC dosing: 7 mg/kg, 10 mg/kg, or placebo); outcomes included MG-ADL, QMG, and MG Symptoms PRO ocular item scores.
- Rozanolixizumab improved ocular symptoms across patient- and clinician-reported outcomes, offering additional benefit for pts with gMG with ocular involvement.

Mahuwala ZK et al. Effect of rozanolixizumab on ocular symptoms in patients with generalized myasthenia gravis: A post hoc item-level analysis of myasthenia gravis-specific outcomes in MycarinG. *Neurology.* 2025; 104(7 Suppl. 1)

Switching from IV C5 Inhibitors to SC Zilucoplan

- Assessed safety, efficacy, and patient satisfaction when switching from IV eculizumab or ravulizumab to SC zilucoplan in AChR+ gMG.
- N=26; 12-week SC zilucoplan treatment.
- SC zilucoplan maintained symptom control, improved satisfaction, and was preferred by most pts over IV therapy.

Measure	Zilucoplan
Patients Enrolled / Completed	26 total / 23 completed
Previous Therapy	16 from eculizumab, 10 from ravulizumab
TEAEs	73.1% (mostly mild); 2 discontinuations due to TEAEs
MG Symptoms at Week 12	Improved or unchanged in ~75%
Patient Preference (SC vs IV)	76.9% preferred SC; 15.4% preferred IV
TSQM-9 Change from Baseline	**Global Satisfaction**: +19.4
	Effectiveness: +13.9
	Convenience: +21.7

Freimer M et al. Switching to subcutaneous zilucoplan from intravenous complement component 5 inhibitors in myasthenia gravis: Patient preference and satisfaction from a phase 3b study. *Neurology.* 2025; 104(7 Suppl. 1)

Real-World Effectiveness of Ravulizumab (MG SPOTLIGHT Registry)

Ravu-Only Subgroup

Measure	Pre-C5IT	Last Post-Ravu
MG-ADL (mean)	6.3	4.0
MGFA Class 0–II	64% (9/14)	86% (12/14)

Ecu-to-Ravu Subgroup

Measure	Pre-C5IT	Post-Eculizumab	Last Post-Ravu
MG-ADL (mean)	8.0	4.4	3.0
MSE (MG-ADL ≤1)	4% (1/24)	29% (7/24)	38% (9/24)
MGFA Class 0–II	24% (5/21)	90% (19/21)	95% (20/21)

Study Results

Measure	Pre-C5IT	First Post-Ravu	Last Post-Ravu
MG-ADL (mean)	7.6	3.9	3.4
Minimal Symptom Expression (≤1)	2% (1/52)	35% (18/52)	33% (17/52)
MGFA Class 0–II	40% (18/45)	91% (41/45)	89% (40/45)

- Evaluated updated safety and effectiveness data for ravulizumab in pts with gMG in clinical practice.
- Ongoing global registry analysis (N=114); includes pts newly treated with ravulizumab and those transitioned from eculizumab.
- Ravulizumab demonstrated sustained improvements in MG-ADL and MGFA classification across treatment groups, reinforcing its real-world efficacy and safety.

Narayanaswami P et al. Effectiveness and safety of ravulizumab in generalized myasthenia gravis (gMG): Updated analysis from a global registry. *Neurology.* 2025; 104(7 Suppl. 1)

Self-Administration of Rozanolixizumab (MG0020 Trial)

- Evaluated success, safety, and efficacy of self-administered rozanolixizumab via manual push (MP) and syringe driver (SD) in pts with gMG.
- Phase 3, open-label, randomized, crossover study (N=62)
  - Included training + two 6-week self-administration periods; success assessed by HCP.
- All pts successfully self-administered rozanolixizumab with either method, supporting home-based therapy for gMG.

Measure	Result
Patients Treated	62 total (55 randomized to SD→MP or MP→SD)
Self-Administration Success Rate	100%
IgG & MG-ADL Response	Improvements at Week 7 sustained through study
Any TEAE	75.8% (47/62 pts)
Most Common TEAE	Headache (21.0%; 13/62)
TEAEs by Method	SD: 31.5% (17 pts); MP: 34.0% (18 pts)
TEAE Severity	97.6% of events were mild/moderate

Bril V et al. Self-administration of rozanolixizumab in patients with generalized myasthenia gravis: The MG0020 study. *Neurology.* 2025; 104(7 Suppl. 1)

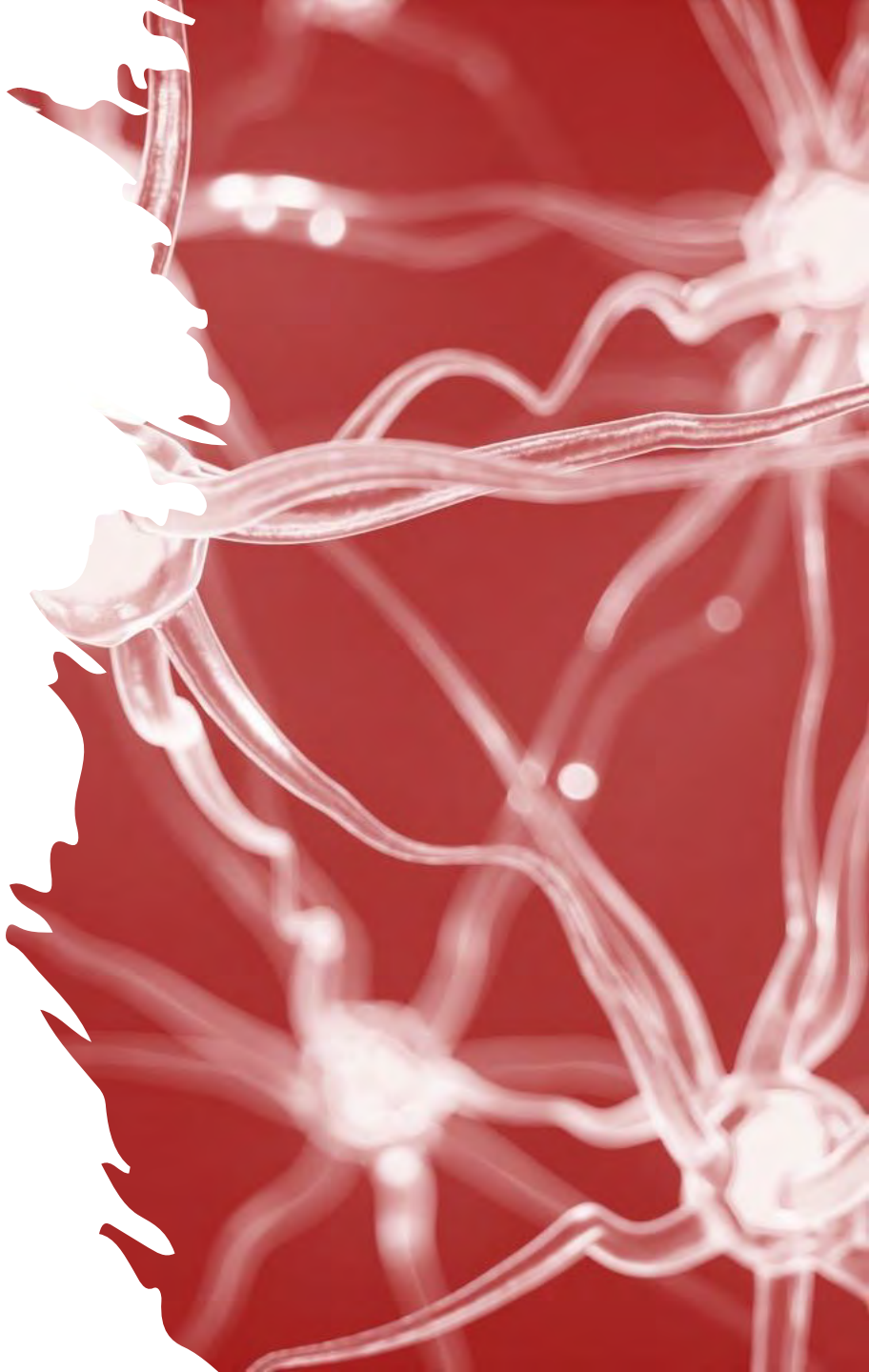
Long-Term Efficacy and Safety of Nipocalimab (Vivacity-MG3 OLE)

Measure	Value
Patients in OLE (Autoantibody-Positive)	137
MG-ADL Change from DB Baseline	–5.73 at Week 24 (n=81)
	–5.97 at Week 48 (n=37)
Safety	Well tolerated; no new safety signals
Total Duration of Disease Control	Sustained improvement across 72 weeks

- Assessed long-term safety and efficacy of nipocalimab in pts with gMG during OLE of Phase 3 Vivacity-MG3 trial.
- Autoantibody-positive pts (N=137) entered ongoing OLE
- MG-ADL used for efficacy; safety assessed in all pts receiving ≥1 dose.
- Nipocalimab demonstrated sustained symptom improvement and consistent safety through 48 weeks of open-label treatment in pts with refractory, autoantibody-positive gMG.

Antozzi C et al. Long-term safety and efficacy of nipocalimab in generalized myasthenia gravis: Vivacity-MG3 open-label extension phase results. *Neurology.* 2025; 104(7 Suppl. 1)

Real World and Post–hoc studies



Efficacy of IV and SC Efgartigimod in AChR-Ab Negative gMG

Measure	Result
MG-ADL Change from Baseline (Week 3, Cycle 1)	–3.7 (n=55)
Clinically Meaningful Improvement (≥2-point MG-ADL)	76.4% (42/55)
Minimal Symptom Expression (MG-ADL 0–1)	23.2% (13/56) during Cycle 1
Durability	Similar results observed across all cycles
Safety	Comparable to AChR-Ab+ population

- Evaluated efficacy and safety of efgartigimod (IV and SC) in pts with AChR-Ab– gMG.
- Post hoc analysis from ADAPT/ADAPT+ and ADAPT-SC/ADAPT-SC+ trials; N=56
- Efgartigimod showed clinically meaningful benefit in AChR-Ab– population, addressing key unmet need in gMG.

Bril V et al. Combined analyses of participants with anti-acetylcholine receptor seronegative generalized myasthenia gravis treated with efgartigimod across clinical studies. *Neurology.* 2025; 104(7 Suppl. 1)

Impact of Ravulizumab on Hospitalization Rates in AChR-Ab+ gMG

- Compared hospitalization rates in AChR-Ab+ pts with gMG before and during ravulizumab treatment in real-world settings.
- Registry-based analysis (N=138).
- Subgroups:
  - ravulizumab-only vs. eculizumab-to-ravulizumab
  - pre- vs post-treatment comparisons
- Ravulizumab significantly reduced hospitalization rates and MG-related events, particularly in biologic-naïve pts.

Measure	Ravu-Only	Ecu-to-Ravu
Pts in Subgroup	61	77
≥1 Hospitalization (n)	25	42
Hospitalization Rate (Pre-Tx)	57.38 per 100 PY	27.86 per 100 PY (on eculizumab)
Hospitalization Rate (Post-Ravu)	15.44 per 100 PY	21.39 per 100 PY
MG Crisis/Exacerbation (Pre-Tx)	71.4% MG-related	51.8% MG-related
MG Crisis/Exacerbation (Post-Tx)	0%	0%

Tandan R et al. Assessment of hospitalizations in patients with generalized myasthenia gravis (gMG) before and during treatment with ravulizumab: Results from a global registry. *Neurology.* 2025; 104(7 Suppl. 1)

NSIST Dose Reduction After Efgartigimod Initiation

Cohort	Baseline ADD (mg/day)	12-Month ADD (mg/day)	p-value
Mycophenolate (n=103)	1629.4	1301.6	$p < 0.05$
Azathioprine (n=60)	131.1	92.4	$p < 0.05$

- Assessed changes in mycophenolate mofetil and azathioprine use after ≥1 year of efgartigimod treatment in pts with MG.
- Retrospective US claims database study.
- Pts with baseline mycophenolate mofetil or azathioprine use and continuous efgartigimod for 1 year.
- Efgartigimod use associated with significant reductions in mycophenolate mofetil and azathioprine dosing, suggesting potential steroid-sparing and immunosuppressant-sparing benefits.

Narayanaswami P et al. Changes in nonsteroidal immunosuppressive treatment usage before and after efgartigimod initiation in patients with myasthenia gravis. *Neurology.* 2025; 104(7 Suppl. 1)

Hospitalization and Exacerbation Outcomes After Efgartigimod Initiation

- Compared hospitalization, exacerbation, and crisis rates in the year before vs after efgartigimod initiation in pts with MG.
- Retrospective US claims and patient support program analysis (N=440); evaluated inpatient events and MG-ADL scores over a 1-year pre/post index period.
- Confirms significant reductions in MG-related hospitalizations and crises following sustained efgartigimod treatment.

Outcome	Pre-Efgartigimod	Post-Efgartigimod	% Reduction	p-value
All-Cause Hospitalizations (per pt)	0.65	0.31	52%	<0.05
MG-Specific Hospitalizations	0.41	0.15	63%	<0.05
MG Exacerbations	0.28	0.09	68%	<0.05
MG Crises	0.07	0.02	71%	<0.05
MG-ADL Score (n=190)	8.0	3.1	—	<0.05

Smith AG et al. Hospitalization outcomes after efgartigimod initiation in patients with myasthenia gravis. *Neurology.* 2025; 104(7 Suppl. 1)

MGFA Global Registry Analysis

Outcome	Associated Factors (↑ risk)	Associated Factors (↓ risk)	Outcome
≥1 Exacerbation in Prior 6 Months	• Comorbid anxiety/depression (2×) • Living alone (74%) • Corticosteroid use (36%) • Higher baseline MG-ADL (19% per point)	• Ocular onset symptoms (–51%) • NSIST use (–25%) • Time since diagnosis (–2%/year)	≥1 Exacerbation in Prior 6 Months
MG-ADL Score ↑ ≥2 Points	• Generalized vs ocular onset (138%) • Anxiety/depression (73%)	• Plasma exchange (–83%) • Physical activity (–37%) • Older age (–2%/year)	MG-ADL Score ↑ ≥2 Points

- Identified baseline factors associated with self-reported exacerbations and ≥2-point MG-ADL score increases at first follow-up.
- 1,319 U.S.-based adults from the MGFA Global Patient Registry (2013–2023).
- Analyzed self-reported data at enrollment and first follow-up (within 12 months).
- Psychosocial and clinical baseline factors, including anxiety/depression, generalized symptoms, and living alone, may help identify pts at higher risk of symptom worsening or exacerbation.

Choudhry Z et al. Identifying risk factors for exacerbation and symptom worsening—A retrospective cohort study of patients with myasthenia gravis in the United States. *Neurology.* 2025; 104(7 Suppl. 1)

Autologous HSCT in Refractory MG – Long-Term Retrospective Analysis

- Evaluated efficacy and safety of autologous HSCT in pts with severe, treatment-refractory MG.
- Retrospective review of 21 pts undergoing HSCT.
- HSCT may provide durable remission in refractory MG but carries substantial procedural risk, particularly in medically complex pts.

Measure	Result
Patients Included	21 total
Median Time from MG Diagnosis to HSCT	4.0 years
Primary Efficacy Outcome (PIS: remission without Rx)	16/18 evaluable (88.9%) at median 1.7 years
Durability of Remission	Median follow-up 6.7 years
Minimal Manifestations With Treatment	2/18 evaluable pts
Non-Evaluable Patients	3 (1 comorbid illness; 2 early deaths post-HSCT)
Deaths (unrelated to active MG)	4 total (2 early post-HSCT; 2 at 8.6 and 9.4 years)
HSCT-Related Mortality Rate	19%

Beland B et al. Refractory myasthenia gravis treated with autologous hematopoietic stem cell transplantation. *Neurology.* 2025; 104(7 Suppl. 1)

Phase 2b Trial of Descartes-08 CAR-T Therapy in gMG

Measure	Descartes-08	Placebo
Patients (Per Protocol)	18	13
≥5-Point MGC Response (Overall)	67%	31%
≥5-Point MGC Response (AChR+)	64%	20%
Mean MGC Change (AChR+)	–5.6	–0.5
Mean MGC Change (Overall)	–5.4	–2.7
Mean MG-ADL Change (AChR+)	–3.4	–0.9
Mean MG-ADL Change (Overall)	–3.8	–1.7
Safety	No cytokine release syndrome; infusion reactions resolved within 48 hrs	–

- Compared Descartes-08 vs placebo on MG Composite (MGC) score at Month 3.
- N=31 (18 Descartes-08, 13 placebo); 6 weekly outpatient infusions; non-MuSK+ gMG.
- Descartes-08 showed significant symptom improvement with no cytokine release syndrome, supporting its potential as a non-chemo CAR-T option in gMG.

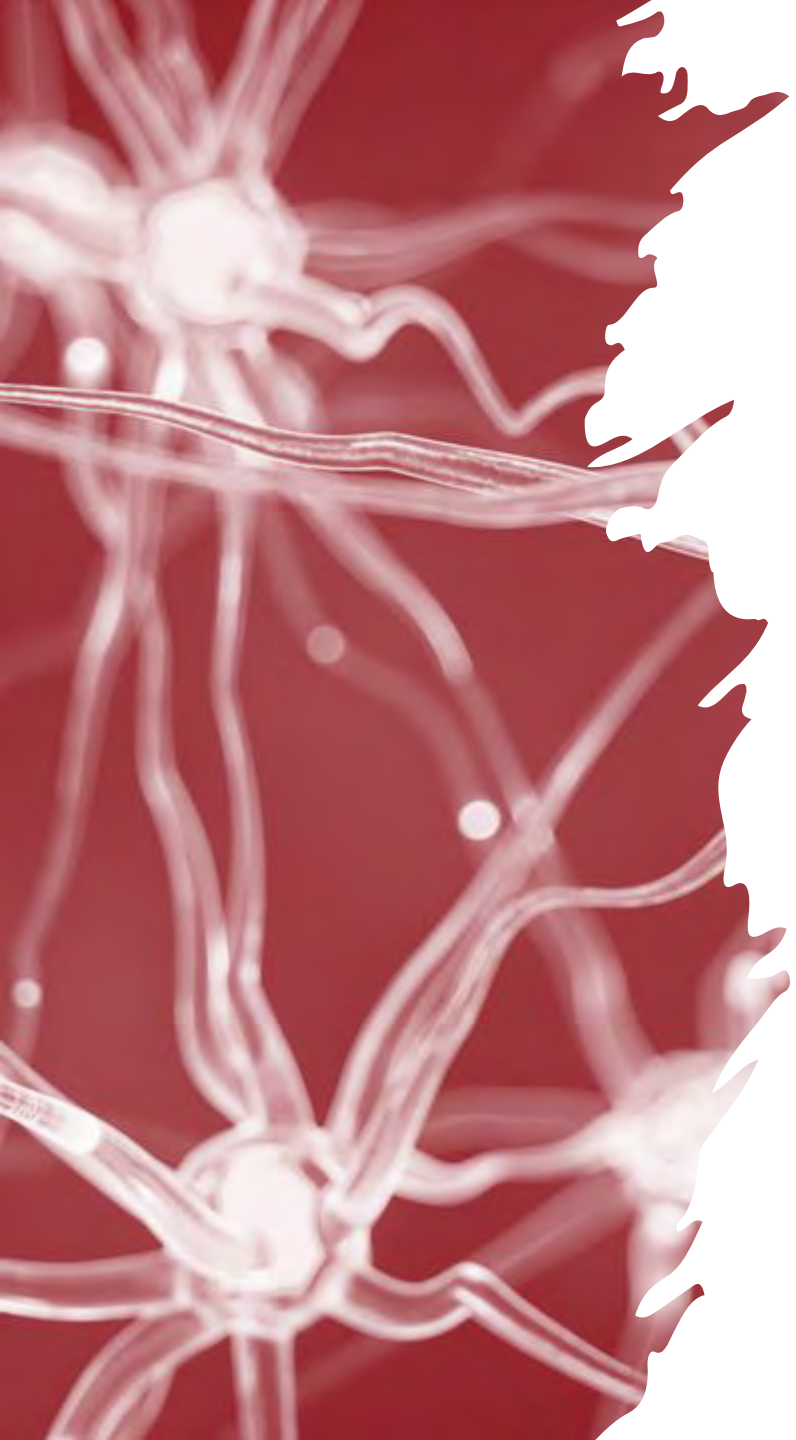
Vu T et al. Efficacy and safety of autologous BCMA-directed mRNA CAR T-cell therapy in generalized myasthenia gravis: Results from a phase 2b randomized placebo-controlled trial. *Neurology.* 2025; 104(7 Suppl. 1)
Chanin N et al. Durability of response to B-cell maturation antigen-directed mRNA cell therapy in myasthenia gravis. *Ann Clin Trans Neurol.* 2025 Aug 26. [online ahead of print]

Systematic Review of Long-Term Eculizumab in Refractory MG

- Evaluated long-term efficacy and safety of eculizumab in pts with refractory gMG.
- Meta-analysis of 4 RCTs (N=161); included AChR+ pts with MG-ADL ≥6 and prior IST.
- Eculizumab consistently improved functional and QoL outcomes in refractory MG, with stronger consistency seen in MGC and MGQOL15 scores.

Outcome Measure	Mean Difference	p-value	Heterogeneity (I^2)
MG-ADL	18.117	<0.001	100%
QMG	13.89	<0.001	100%
MGC	56.950	0.386	0%
MGQOL15	55.091	0.328	0%

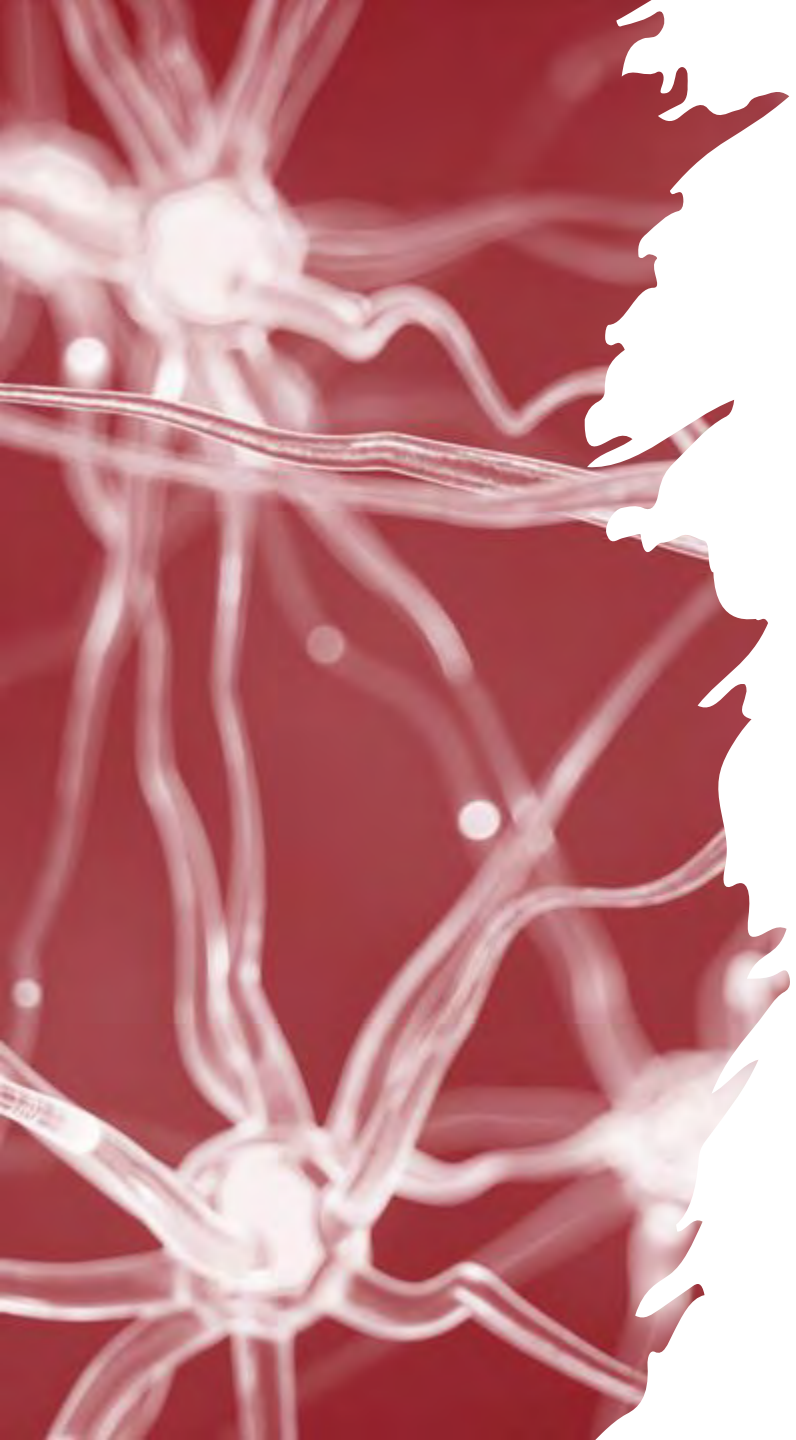
Bin Najeeb H et al. Efficacy and safety of eculizumab in refractory myasthenia gravis: A meta-analysis and systematic review. *Neurology.* 2025; 104(7 Suppl. 1)



Clinical Pearls

FcRn Inhibitors

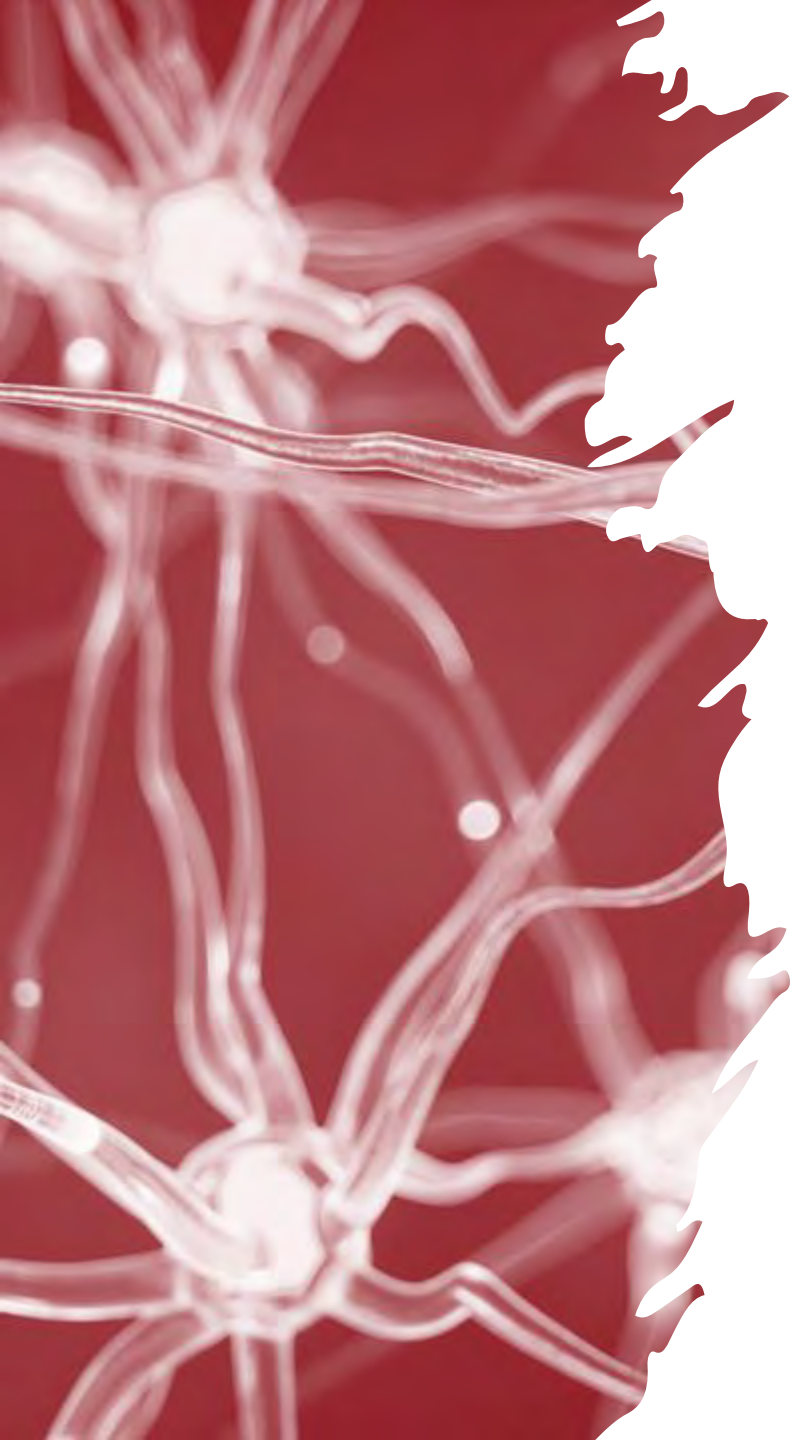
- **Nipocalimab**
  - Rapid, sustained improvement in MG symptoms (MG-ADL and QMG) with favorable safety.
  - Long-term disease control maintained over 48 weeks in open-label extension.
- **Efgartigimod (IV and SC)**
  - Maintains efficacy across both fixed-cycle and biweekly (Q2W) dosing.
  - SC formulation offers durable symptom improvement and good tolerability over repeated cycles.
  - Real-world use linked to reduced hospitalizations, exacerbations, and immunosuppressant use (MMF, AZA).
  - Provides clinically meaningful benefit even in AChR– pts.
- **Rozanolixizumab**
  - Improves ocular symptoms (ptosis, diplopia), supporting its role in ocular-dominant gMG.
  - Self-administration (manual push or syringe driver) is feasible, well tolerated, and maintains efficacy.



Clinical Pearls

Complement C5 Inhibitors

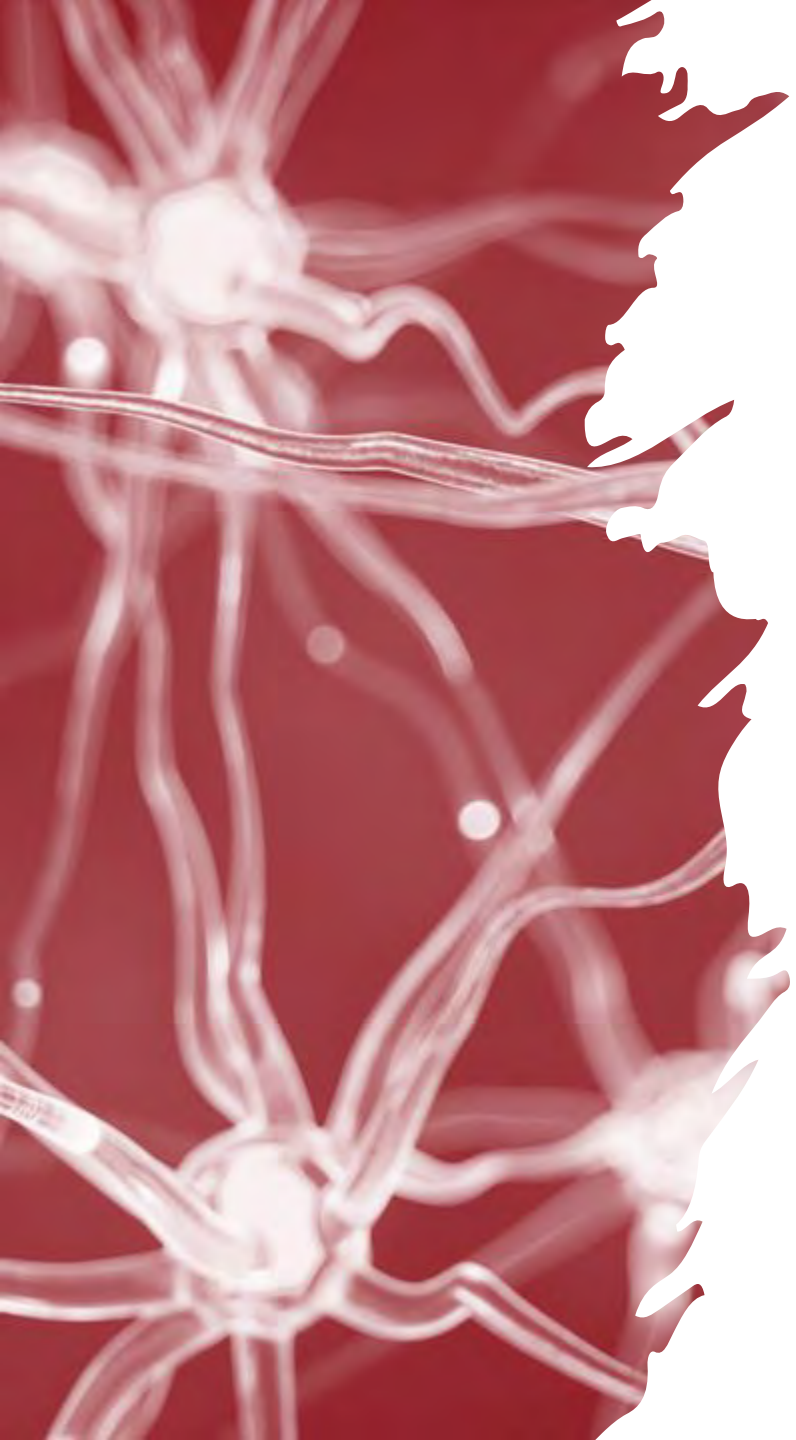
- **Ravulizumab**
  - Long-term real-world data show durable improvements in MG-ADL and MGFA status.
  - Significantly reduces hospitalization rates, especially in biologic-naïve pts.
  - Post-treatment admissions are mostly unrelated to MG, with no reported MG crises/exacerbations.
- **Eculizumab**
  - Meta-analysis confirms its efficacy in refractory MG, with consistent improvement in MGC and quality of life.
- **Zilucoplan**
  - Offers rapid, comprehensive improvement across all MG subdomains (ocular, bulbar, respiratory, limb/axial).
  - High patient satisfaction and preference when switching from IV C5 inhibitors to SC zilucoplan.



Clinical Pearls

Cell-Based & Immunomodulatory Therapies

- **Descartes-08 (BCMA-directed CAR-T)**
  - Outpatient CAR-T therapy showed significant disease activity reduction vs placebo without cytokine release syndrome.
  - Encouraging efficacy signals ahead of planned Phase 3 evaluation.
- **Autologous HSCT**
  - Induced durable remission in most pts with refractory MG.
  - Carries high treatment-related mortality in medically complex populations, highlighting need for prospective trials.



Clinical Pearls

Other / Observational Insights

- **Real-world Treatment Patterns**
  - Targeted therapies are typically used later in the treatment course; early exacerbations suggest the need for earlier intervention.
- **MGFA Registry Analysis**
  - Risk factors for exacerbation and symptom worsening include generalized onset, comorbid anxiety/depression, corticosteroid use, and living alone.
  - Protective factors: physical activity, NSIST use, plasma exchange, and older age.