Reducing burden of disease in gMG: Exploring the role of FcRn inhibitors

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Agenda

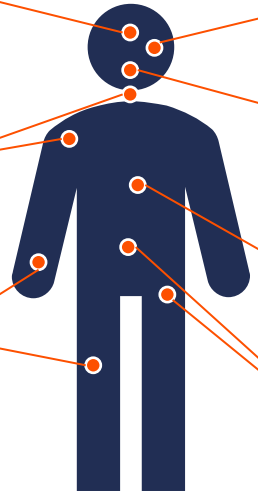
- Understanding disease and treatment burden in gMG
- Clinical evidence for the use of FcRn inhibitors in gMG
- Practical guidance for implementing FcRn inhibitors into clinical practice

Understanding disease and treatment burden in gMG

Clinical manifestations of generalized MG

MG is characterized by fatigable muscle weakness[1,2] which improves with rest[3]

Muscles typically affected in MG[1,2,4]



Ocular

- Blurry or double vision
- Ptosis

Neck and shoulders

- Pain holding head up
- Weakness

Limbs, hands and feet

- Difficulty lifting
- Weakness
- Pain
- Loss of dexterity and fine motor skills

Facial

- Difficulty making facial expressions

Bulbar

- Speech impairment
- Difficulty chewing
- Choking
- Aspiration

Breathing

- Shallow breathing
- Shortness of breath

Back, hips and core

- Weakness

gMG, generalized MG; MG, myasthenia gravis.

1. Kaminski HJ, et al. *J Clin Invest*. 2024;134:e179742; 2. DeHart-McCoyle M, et al. *BMJMED*. 2023;2:e000241; 3. Twork S, et al. *Health Qual Life Outcomes*. 2010;8:129; 4. Jackson K, et al. *Neurol Ther*. 2023;12:107–28.

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Various aspects of gMG that can affect QoL

- Fluctuating and unpredictable muscle weakness requiring constant adaptation of daily routines[1–3,5]
- Impairment of ability to perform daily tasks (e.g. driving, washing, or housework)[1–4]
- Speech and swallowing difficulties[5]
- Feelings of social isolation and loss of life control due to unresolved symptoms[3]
- Limitations to work-related capabilities[1–3,5]
- Generalized fatigue[2,3]

gMG, generalized myasthenia gravis; QoL, quality of life.

1. Schneider-Gold C, et al. *Ther Adv Neurol Discord*. 2019;12:1–16; 2. Lehnerer S, et al. *J Neurol*. 2022;269:3050–63; 3. Sacca F, et al. *Eur J Neurol*. 2024;31:e16180; 4. Berrih-Aknin S, et al. *BMJ Open*. 2021;11:e048198; 5. Twork S, et al. *Health Qual Life Outcomes*. 2010;8:129.

Treatment burden in myasthenia gravis

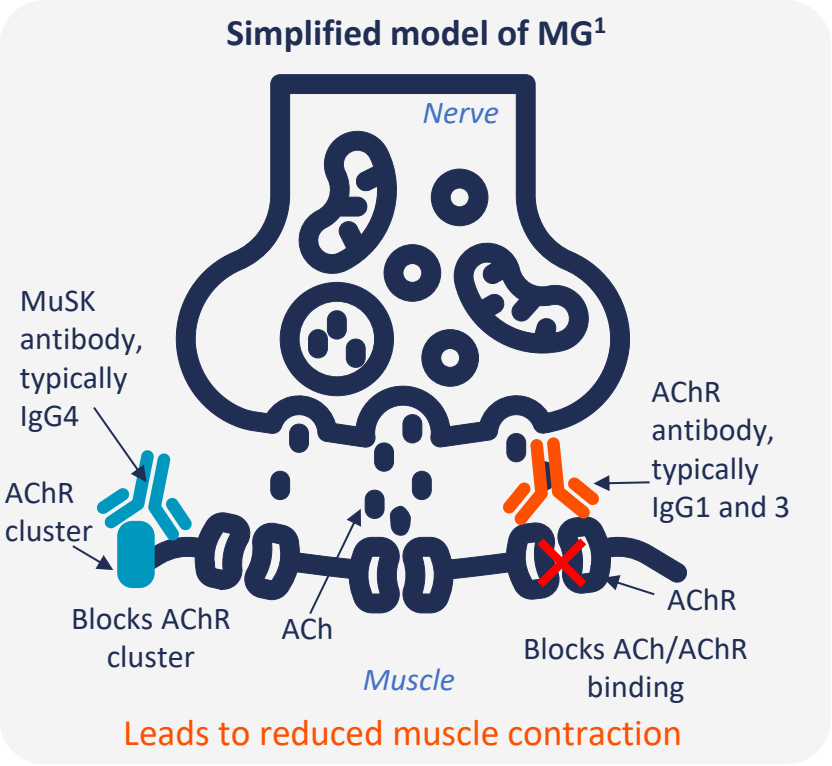
Treatment burden

- **Need for multiple treatments** to control disease*[1]
- It can take a **long time for the effect** of treatment to be seen[3]
- **Limited treatment options** in pregnancy or patients with comorbidities[3]
- Increased **hospital dependence** (for treatment administration or monitoring)[3]
- Treatment **side effects** (e.g. GI symptoms, weight gain, nausea and brain fog)[1]
- **Treatment-related complications** (e.g. osteoporosis with corticosteroids; infections of central catheters for plasma exchange; bacterial/viral infections with immunomodulatory therapies)[3]
- Long-term corticosteroid use can lead to **corticosteroid withdrawal** symptoms mimicking MG[3]

*Defined as being free of MG symptoms or having minimal symptom expression.
GI, gastrointestinal; gMG, generalized MG; MG, myasthenia gravis.
1. Ruzhansky K, et al. Presented at: 74th American Academy of Neurology Annual Meeting, Seattle, WA, USA, 2–7 April 2022. Abstr 3; 2. Schneider-Gold C, et al. *Ther Adv Neurol Discord*. 2019;12:1–16; 3. Sacca F, et al. *Eur J Neurol*. 2024;31:e16180.

Clinical evidence for the use of FcRn inhibitors in gMG

MoA of approved and emerging FcRn inhibitors



- FcRn antagonists prevent the binding of IgG to FcRn on the cell endothelium[2]
- This increases the breakdown of IgG, leading to the depletion of circulating IgG antibodies[2]

ACh, acetylcholine; AChR, ACh receptor; FcRn, neonatal FC receptor; gMG, generalized MG; IgG, immunoglobulin G; MG, myasthenia gravis; MoA, mechanism of action; MuSK, muscle specific kinase.

1. DeHart-McCoyle M, et al. *BMJMED*. 2023;2:e000241; 2. Burton LB, Guidon AC. *Practical Neurology*. 2020. Available at: https://practicalneurology.com/articles/2020-may/neuromuscular-notes-next-generation-treatments-for-myasthenia-gravis (accessed 19 February 2025).

FcRn inhibitors in gMG: Approved options

	Efgartigimod[1,2]	Rozanolixizumab[1,2]
Dose	10 mg/kg (IV) 1000 mg (SC)	7 mg/kg, 10 mg/kg, 15 mg/kg
Dosing regimen	Weekly IV for 4 weeks*† Weekly SC for 4 weeks*†	Weekly SC for 6 weeks*
Pharmacokinetic advantage	Rapid onset of action	SC administration convenient
US FDA and EMA approval status	Approved for use in AChR+ gMG	Approved in AChR+ and MuSK+ gMG

*Further continuation depending on treatment response; †Safety of starting subsequent cycles sooner than 50 days from the start of the previous cycle has not been established.[1,2]

AChR, acetylcholine receptor; EMA, European Medicines Agency; FcRn, neonatal Fc receptor; FDA, Food and drug administration; gMG, generalized myasthenia gravis; IV, intravenous; MuSK, muscle specific kinase; SC subcutaneous.

1. FDA. Prescribing information. Available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm (accessed 06 February 2025); 2. EMA. Summary of product characteristics. Available at: https://www.ema.europa.eu/en/medicines (accessed 26 March 2025).

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FcRn inhibitors in gMG: Emerging options

	Nipocalimab	Batoclimab
Dose	30 mg/kg initial dose followed by 15 mg/kg	680 mg
Dosing regimen	IV every 2 weeks*	Weekly SC for 6 weeks*
Pharmacokinetic advantage	Significant and sustained IgG reduction	SC administration convenient
US FDA and EMA approval status	Granted priority review by the FDA	N/A

*Further continuation depending on treatment response.

EMA, European Medicines Agency; FcRn, neonatal Fc receptor; FDA, Food and drug administration; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IV, intravenous; N/A, not applicable; SC subcutaneous.

Menon D, Bhandari V. *Expert Opin Emerg Drugs*. 2025; doi.org/10.1080/14728214.2025.2458061.

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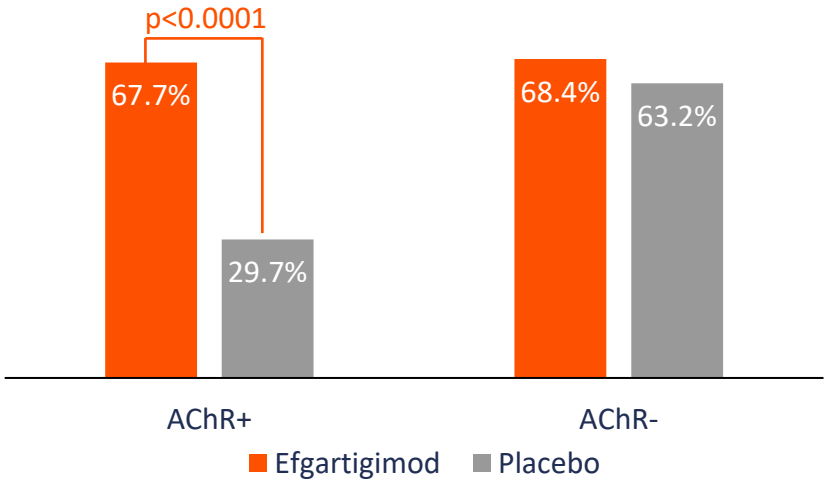
Efficacy and safety of approved FcRn inhibitors: Efgartigimod IV

ADAPT: Phase III trial of efgartigimod (10 mg/kg) vs placebo (N = 167; 77% were AChR+)

Primary endpoint: MG-ADL responder in cycle 1*



	Efgartigimod (n=84)	Placebo (n=83)
Any AE	77%	84%
Any SAE	5%	8%
Any AE leading to discontinuation	4%	4%

Most frequent AEs:

- Headache, GI symptoms, URTI, UTI
- All mild or moderate

*Defined as ≥2 point improvement (reduction) in MG-ADL score, sustained for ≥4 consecutive weeks with first improvement occurring by week 4 of the cycle (one week after 4th infusion). AE, adverse event; AChR, acetylcholine receptor; MG-ADL, myasthenia gravis activities of daily living; SAE, serious AE; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Howard JF, et al. *Lancet Neurol.* 2021;20:526–36.

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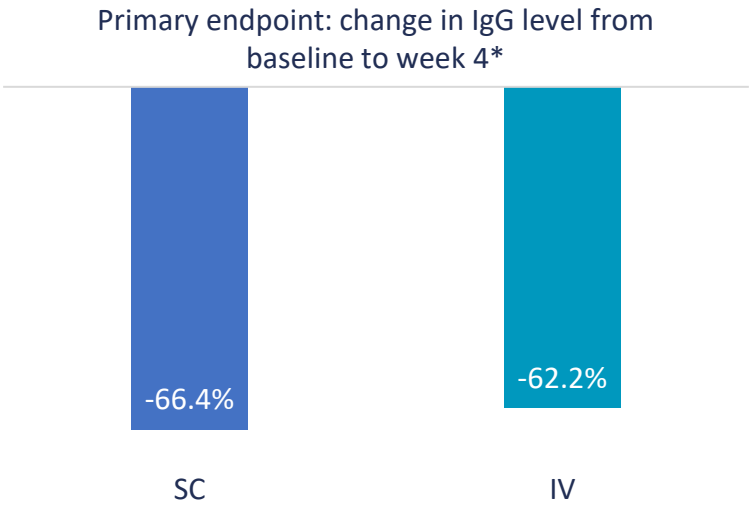
Efficacy and safety of approved FcRn inhibitors: Efgartigimod SC

ADAPT: Phase III trial of efgartigimod SC (1,000 mg) vs efgartigimod IV (10 mg/kg) (N = 111)



	SC (n=55)	IV (n=55)
Any AE	67.3%	50.9%
Any SAE	14.5%	7.3%
Any AE leading to discontinuation	3.6%	n=0

Most frequent AEs (occurring in >10%):

- Injection site reactions (localized), headache, COVID-19, MG
- Most mild or moderate

*Least-squares mean estimate one week after 4th infusion.
AE, adverse event; IV, intravenous; MG, myasthenia gravis; SAE, serious AE; SC, subcutaneous.
Howard JF, et al. *Neurotherapeutics*. 2024;21:e00378.

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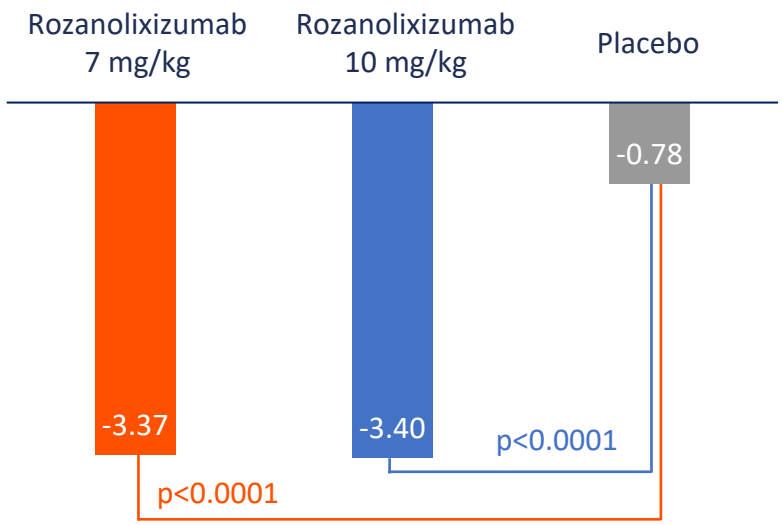
Efficacy and safety of approved FcRn inhibitors: Rozanolixizumab

MycarinG: Phase III trial of rozanolixizumab (7mg/kg or 10 mg/kg) vs placebo (N=200)

Primary endpoint: Change in MG-ADL from baseline to day 43



	Rozanolixizumab 7 mg/kg (n=64)	Rozanolixizumab 10 mg/kg (n=69)	Placebo (n=67)
Any TEAE	81%	83%	67%
Any STEAE	5%	19%	4%
Any TEAE leading to discontinuation	3%	6%	3%

Most frequent AEs:

- Headache, diarrhoea, pyrexia, nausea
- Most mild or moderate

AE, adverse event; MG-ADL, myasthenia gravis activities of daily living; STEAE, severe TEAE; TEAE, treatment emergent AE.

Bril V, et al. *Lancet Neurol*. 2023;22:383–94.

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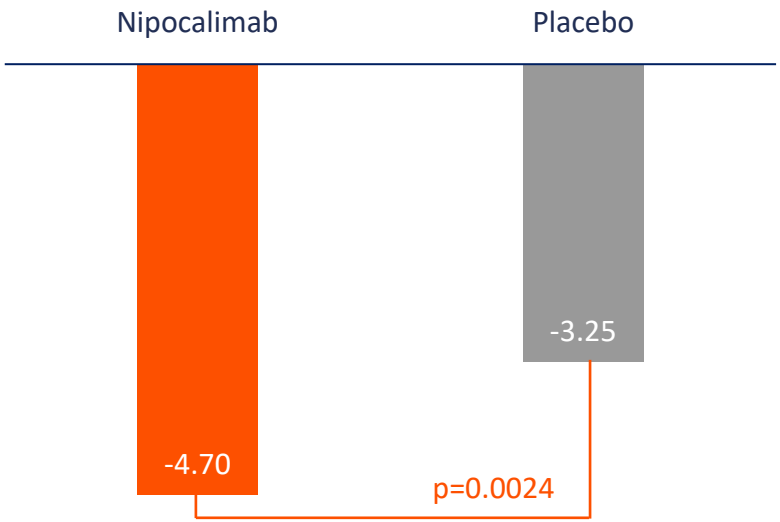
Efficacy and safety of investigational FcRn inhibitors: Nipocalimab

Vivacity-MG3: Phase III trial of nipocalimab (30 mg/kg loading dose then 15 mg/kg) vs placebo (N=196)

Primary endpoint: MG-ADL change from baseline*



	Nipocalimab (n=98)	Placebo (n=98)
Any AE	84%	84%
Any SAE	9%	14%
Any AE leading to discontinuation	5%	7%

Most frequent AEs for nipocalimab:

- COVID-19 associated AEs, headache, muscle spasms, MG, peripheral oedema
- Most mild or moderate

*Least-squares mean change from baseline averaged total score across weeks 22, 23 and 24.
AE, adverse event; MG, myasthenia gravis; MG-ADL, MG activities of daily living; SAE, serious AE.
Antozzi C, et al. *Lancet Neurol*. 2025;24:105–16.

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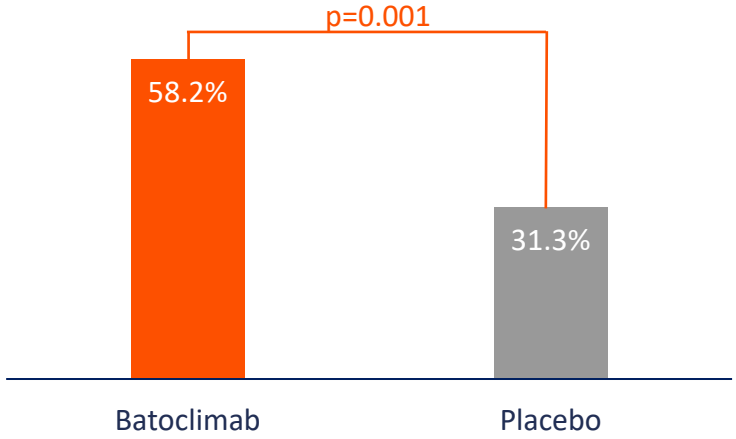
Efficacy and safety of investigational FcRn inhibitors: Batoclimab

Phase III trial in China of batoclimab (680 mg) vs placebo (N=132)

Primary endpoint: Rate of sustained MG-ADL improvement in the first cycle in antibody-positive patients (n=131)*



	Batoclimab (n=67)	Placebo (n=65)
Any TEAE	95.5%	92.3%
Any STEAE	3.0%	7.7%
Any TEAE leading to discontinuation	1.5%	3.1%

Most frequent TEAEs for batoclimab:

- Peripheral oedema, URTI, UTI
- Most mild or moderate

* ≥3-point reduction.

MG, myasthenia gravis; MG-ADL, MG activities of daily living; STEAE, severe TEAE; TEAE, treatment emergent adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Yan C, et al. *JAMA Neurol*. 2024;81:336–45.

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Practical guidance for implementing FcRn inhibitors into clinical practice

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Factors to consider when managing gMG with FcRn

- Method of administration[1,2]
- Type of gMG (AChR+ or MuSK+)[1,2]
- Frequency of administration[1,2]
- Concomitant use with other medications that also bind to FcRn[1,2,4]
- Dosing schedule: cyclic vs predictable dosing[3]
- Timing of vaccinations, particularly live or live-attenuated[1,2]
- Time taken to administer dose[1,2]
- Presence of active infections prior to treatment initiation[1,2]

AChR, acetylcholine receptor; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; MuSK, muscle specific kinase.

1. FDA. Prescribing information. Available at: www.accessdata.fda.gov/scripts/cder/daf/index.cfm (accessed 06 February 2025); 2. EMA. Summary of product characteristics. Available at: https://www.ema.europa.eu/en/medicines (accessed 26 March 2025); 3. Vissing J, et al. *EMJ Neurol*. 2024;12:33–41; 4. Mina-Osorio P, et al. *Transfus Med Rev*. 2024;38:150767.

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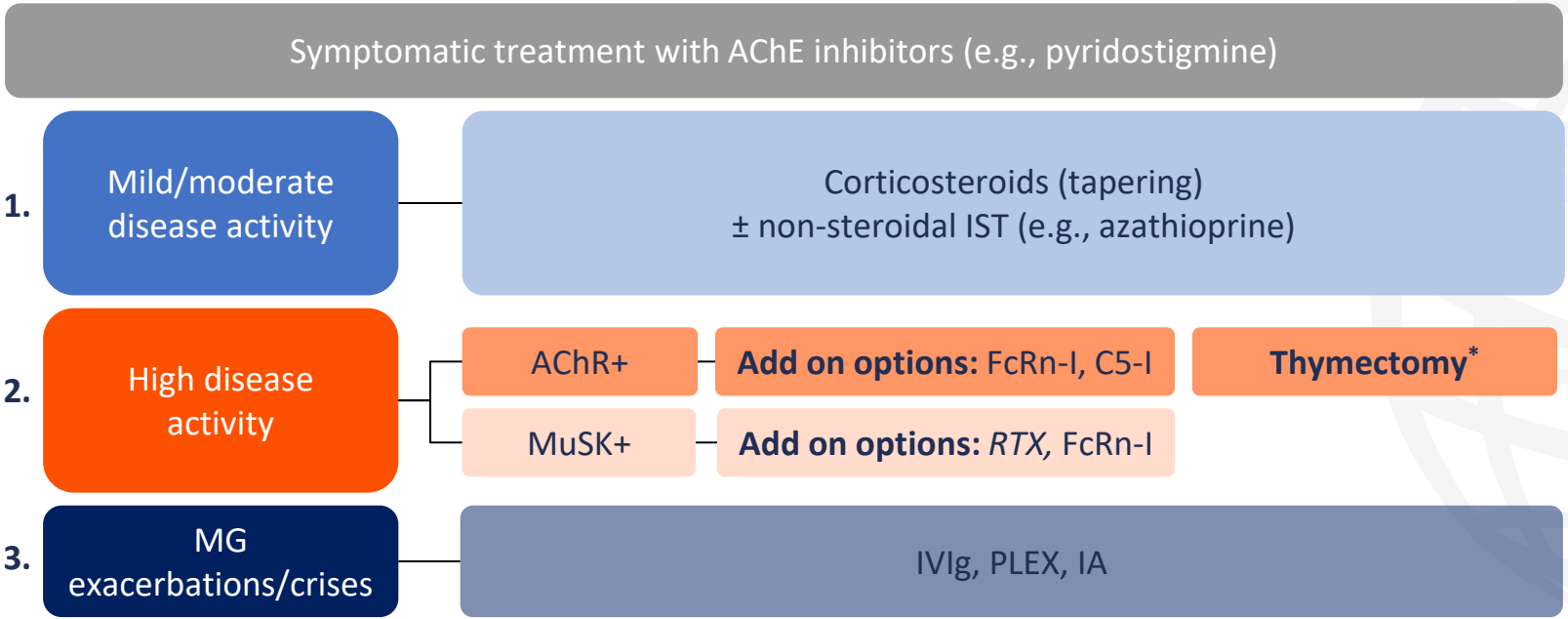
Treatment algorithm for gMG[1,2]



Treatments listed in italics are used off-label. *Thymectomy is recommended in AChR+ patients who are eligible and should be performed within 2 years after diagnosis.
AChE, acetylcholine esterase; AChR, acetylcholine receptor; C5, C5 component of complement; FcRn, neonatal Fc receptor; I, inhibitor; IA, immunoadsorption; IST, immunosuppressive therapy; IVIg, intravenous immunoglobulin; MG, myasthenia gravis; MuSK, muscle-specific tyrosine kinase; PLX, plasma exchange; RTX, rituximab.

1. Wiendl H, et al. *Ther Adv Neurol Disord*. 2023;16:1–31; 2. Gerischer L, et al. *BioDrugs*. 2025;39:185–213.