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Reimagining Management of Generalized Myasthenia Gravis: A Focus on FcRn Inhibitors

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Learning Objective 1

Evaluate the mechanism of action, safety, and efficacy of FcRn antagonists for the treatment of gMG.

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Learning Objective 2

Identify patients with gMG who may be appropriate candidates for treatment with FcRn antagonists.

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Learning Objective 3

Develop optimized and individualized treatment plans for patients with gMG receiving FcRn antagonists.

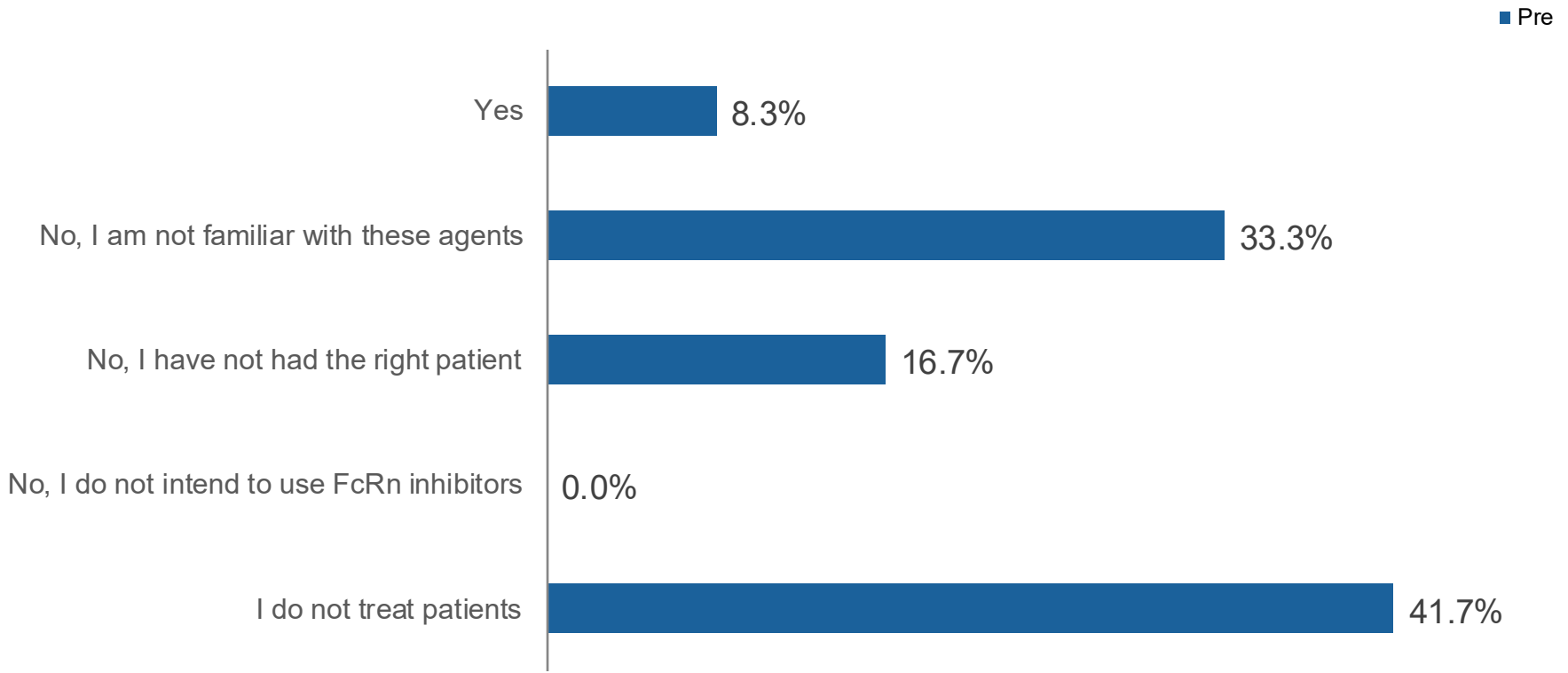
FcRn Antagonists in gMG: What Are They and How Do They Work?

Audience Response

Have you used an FcRn antagonist to treat myasthenia gravis in your clinical practice?

A. Yes
B. No, I am not familiar with these agents
C. No, I have not had the right patient
D. No, I do not intend to use FcRn inhibitors
E. I do not treat patients

Have you used an FcRn antagonist to treat myasthenia gravis in your clinical practice?



Results recorded on July 16, 2025.

Neonatal Fc Receptor Antagonists

- The neonatal **Fc receptor (FcRn)** rescues IgG from cellular degradation
- FcRn antagonists block this action, resulting in degradation of IgG
- In **generalized myasthenia gravis (gMG),** this reduces the amount of circulating pathogenic antibody

FDA-Approved:
Efgartigimod
Rozanolixizumab
Nipocalimab

In Development:
Batoclimab*

*This agent is not FDA-approved for the treatment of gMG.

Sanchez-Tejerina D, et al. *J Clin Med.* 2022;11(21):6394.

Mechanism of Action Animation

Measuring Outcomes: MG-ADL

	0 = Normal	1	2	3 = Most Severe
Talking	Normal	Intermittent slurring or nasal speech	Constant slurring or nasal speech, but can be understood	Difficult-to-understand speech
Chewing	Normal	Fatigue with solid food	Fatigue with soft food	Gastric tube
Swallowing	Normal	Rare episode of choking	Frequent choking necessitating changes in diet	Gastric tube
Breathing	Normal	Shortness of breath with exertion	Shortness of breath at rest	Ventilator dependence
Impairment of ability to brush teeth or comb hair	None	Extra effort, but no rest periods needed	Rest periods needed	Cannot do one of these functions
Impairment of ability to arise from a chair	None	Mild, sometimes uses arms	Moderate, always uses arms	Severe, requires assistance
Double vision	None	Occurs, but not daily	Daily, but not constant	Constant
Eyelid droop	None	Occurs but not daily	Daily, but not constant	Constant

- Maximum score is 24
- Minimal Symptomatic Expression (MSE) is 0 or 1
- Decrease of 2 points is considered clinically significant

MG-ADL = Myasthenia Gravis Activities of Daily Living.

Conquer Myasthenia Gravis [CMG]. 2022. https://myastheniagravis.org/mg-activities-of-daily-living-mg-adl-scale/.

Measuring Outcomes: QMG

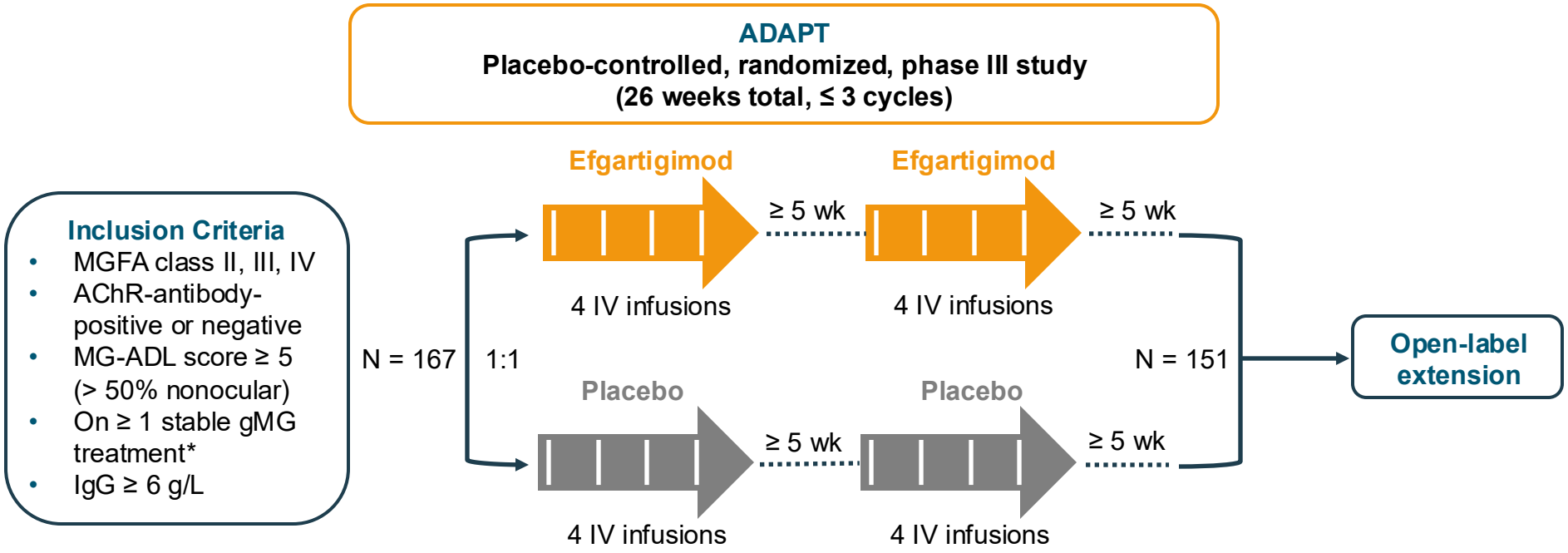
Test Item (Grade)	None (0)	Mild (1)	Moderate (2)	Severe (3)
Double vision on lateral gaze right or left (circle one), seconds	61	11-60	1-10	Spontaneous
Ptosis (upward gaze)	61	11-60	1-10	Spontaneous
Facial muscles	Normal lid closure	Complete, weak, some resistance	Complete, without resistance	Incomplete
Swallowing 4 oz water (1/2 cup)	Normal	Minimal coughing or throat clearing	Severe coughing/choking or nasal regurgitation	Cannot swallow (test not attempted)
Speech after counting aloud from 1 to 50 (onset of dysarthria)	None at 50	Dysarthria at 30-49	Dysarthria at 10-29	Dysarthria at 9
Right arm outstretched (90° sitting), seconds	240	90-239	10-89	0-9
Left arm outstretched (90° sitting), seconds	240	90-239	10-89	0-9
Forced vital capacity	≥ 80	65-79	50-64	≤ 50
Right-hand grip (kg) - Men	≥ 45	15-44	5-14	0-4
Right-hand grip (kg) - Women	≥ 30	10-29	5-9	0-4
Left-hand grip (kg) - Men	≥ 35	15-34	5-14	0-4
Left-hand grip (kg) - Women	≥ 25	10-24	5-9	0-4
Head lifted (45° supine), seconds	120	30-119	1-29	0
Right leg outstretched (45° supine), seconds	100	31-99	1-30	0
Left leg outstretched (45° supine), seconds	100	31-99	1-30	0

- A test of strength in 13 areas
- The higher the score, the more severe the disease
- 0 is normal; maximum score is 39
- A change of 3 or more points is considered clinically significant

QMG = Quantitative Myasthenia Gravis score.

Barohn RJ, et al. *Quantitative Myasthenia Gravis Score (QMG)*. 3rd ed. Myasthenia Gravis Foundation of America Website. 1997. https://myasthenia.org/wp-content/uploads/Portals/0/QMG.pdf.

Efgartigimod: Phase III ADAPT Trial Design



Primary endpoint (AChR+): % responders after first treatment cycle
Responder: ≥ 2 ADL point decline for at least 4 consecutive weeks any time within initial treatment cycle

*AChEI, corticosteroid, and/or non-steroidal immunosuppressive therapy (NSIST).
MGFA = Myasthenia Gravis Foundation of America; AChR = acetylcholine receptor; AChEI = acetylcholinesterase inhibitor; IV = intravenous.
Howard J, et al. *Lancet Neurol.* 2021;20:526-536.

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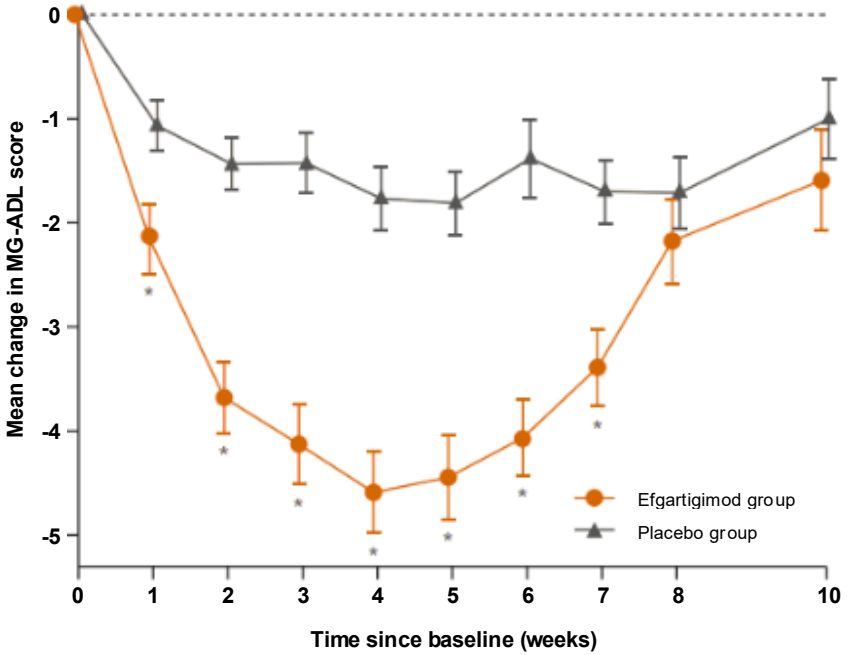
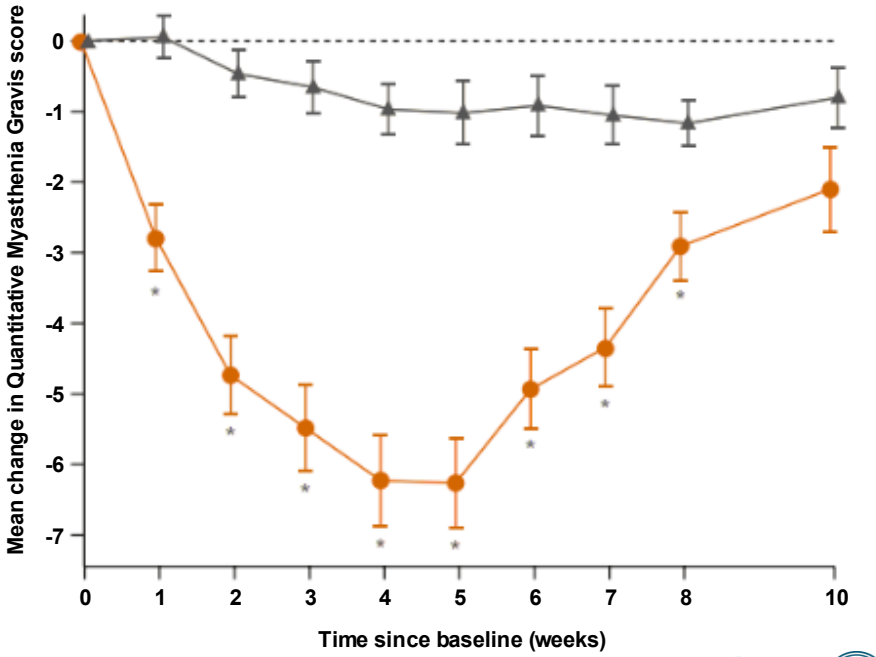
Efgartigimod: Phase III ADAPT Trial

MG-ADL



QMG



During cycle 1 in AChR-positive patients.

Howard J, et al. *Lancet Neurol*. 2021;20:526-536.

Rozanolixizumab: Phase III MycarinG Trial Design

Inclusion Criteria
- AChR or MuSK Ab+ gMG
- MGFA class II-IVa
- MG-ADL score ≥ 3
- QMG score of ≥ 11

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

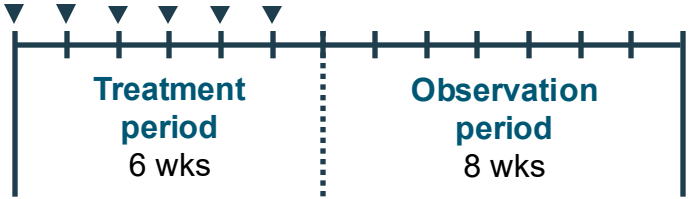
Randomization
N = 200
1:1:1

RLZ
10 mg/kg
n = 67

RLZ
7 mg/kg
n = 66

Placebo
n = 67

Open-label extension



MuSK = muscle-specific kinase.
Bril V, et al. *Lancet Neurol.* 2023;22(5):383-394.

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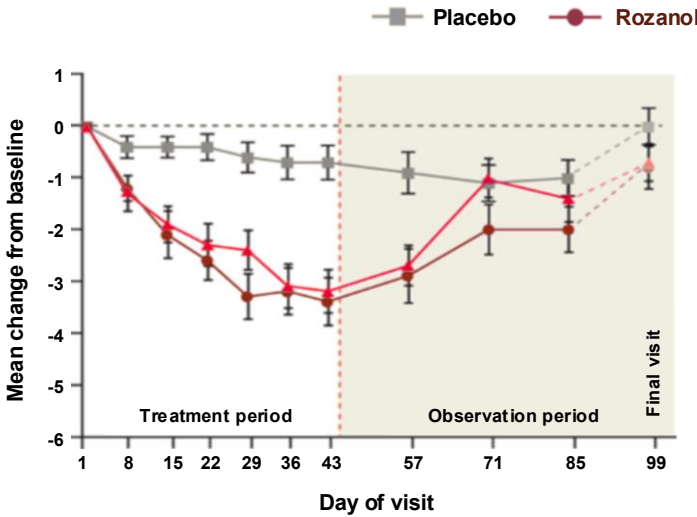
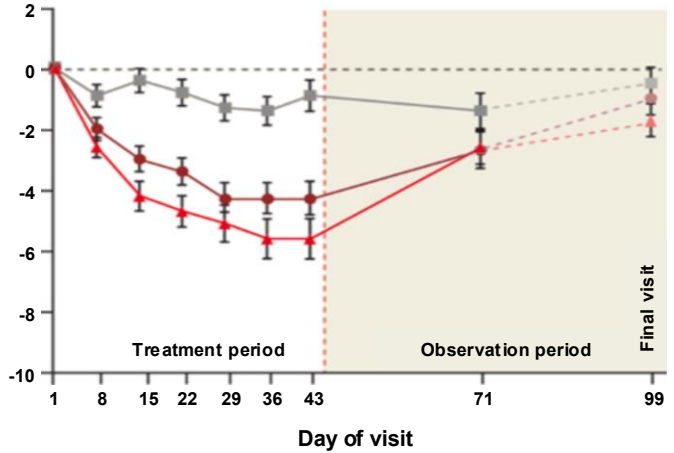
Rozanolixizumab: Phase III MycarinG Trial

MG-ADL



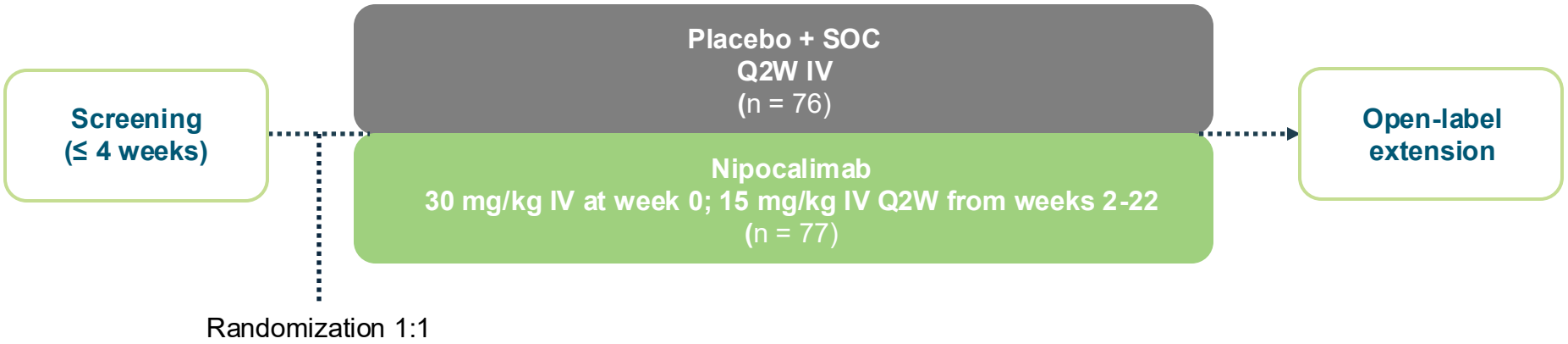
QMG



Bril V, et al. *Lancet Neurol.* 2023;22(5):383-394.

Nipocalimab: Phase III Vivacity MG3 Trial Design

n = 153 seropositive participants (including anti-AChR+ and/or anti-MuSK+ gMG)



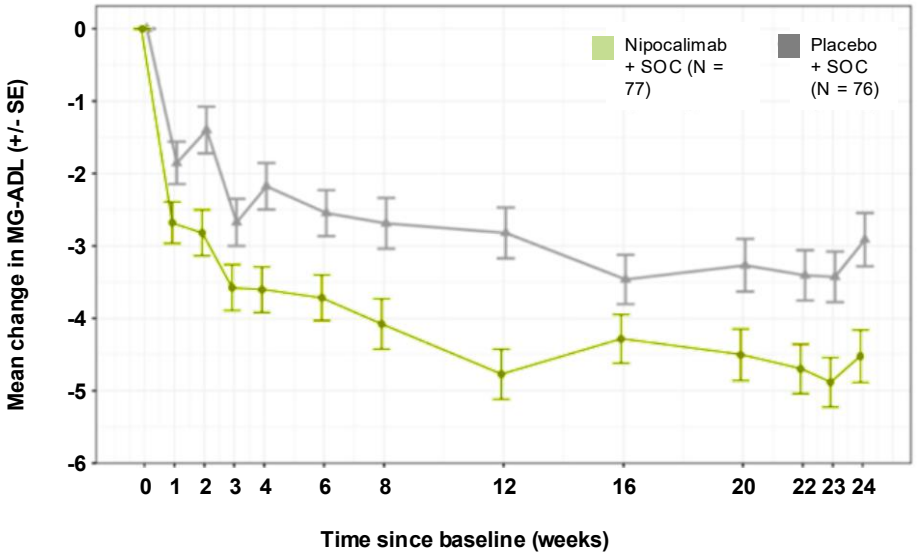
Primary endpoint: mean change in MG-ADL total score from baseline to weeks 22, 23, and 24

SOC = standard of care; Q2W = once every 2 weeks.

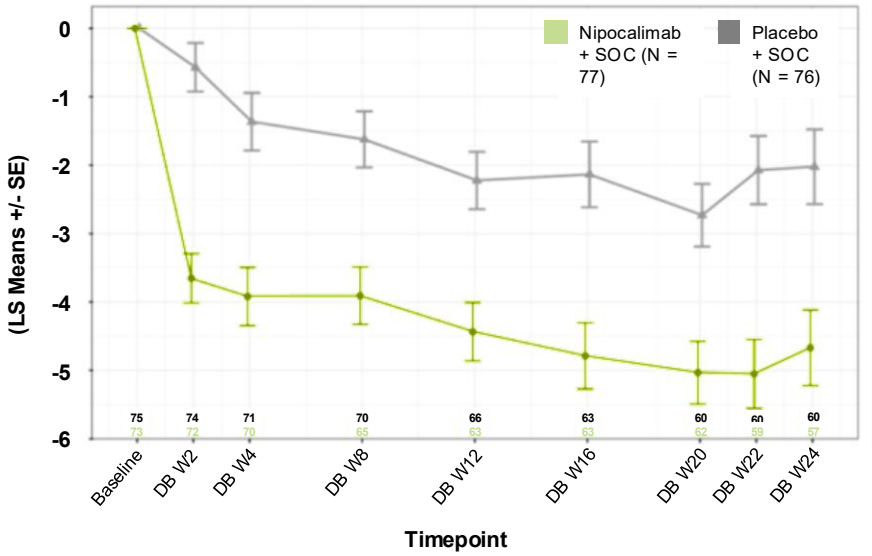
Antozzi C, et al. *Lancet Neurol.* 2025;24(2):105-116.

Nipocalimab: Phase III Vivacity MG3 Trial

MG-ADL



QMG



Antozzi C, et al. *Lancet Neurol.* 2025;24(2):105-116. Antozzi C, et al. *EMG Neurol.* 2024;12(1):51-55.

FcRn Antagonists: 5 Most Common Side Effects Occurring in > 5% of Patients

Efgartigimod (vs placebo)	Rozanolixizumab (7 mg or 10 mg vs placebo)	Nipocalimab (vs placebo)
Headache 29%, 28%	Headache 45.3%, 37.7%, 19.4%	Respiratory infection 18%, 13%
Nasopharyngitis 12%, 18%	Diarrhea 25.0%, 15.9%, 13.4%	Headache 14.3%, 17.0%
URI 11%, 5%	Pyrexia 12.5%, 20.3%, 1.5%	MG worsening 12.2%, 12.2%
UTI 10%, 5%	Nausea 7.8%, 11.6%, 7.5%	Muscle spasms 12.2%, 3.1%
Diarrhea 5%, 2%	Arthralgia 6.3%, 7.2%, 3.0%	Peripheral edema 11.2%, NS

Listed in order of decreasing frequency.
NS = not specified; URI = upper respiratory infection; UTI = urinary tract infection.
Howard J, et al. *Lancet Neurol*. 2021;20:526-536. Bril V, et al. *Lancet Neurol*. 2023;22:383-394. Antozzi C, et al. *Lancet Neurol*. 2025;24(2):105-116.

Which Patients Should Be Receiving FcRn Antagonists?

Patient Case: Amber

- Amber is a 39-year-old woman who has been living with AChR-positive gMG for two years and is seeing you for a regularly scheduled visit

- Amber is currently receiving IVIG 2 g/kg every three weeks and mycophenolate mofetil 500 mg BID
- She previously received prednisone but discontinued due to intolerance
- While she has seen symptom improvement with IVIG, she suffers frequent migraines and meningeal symptoms
- Her MG-ADL score is 9

- Amber would like to discuss potentially changing her medication due to her continued symptoms, which are negatively impacting her QoL

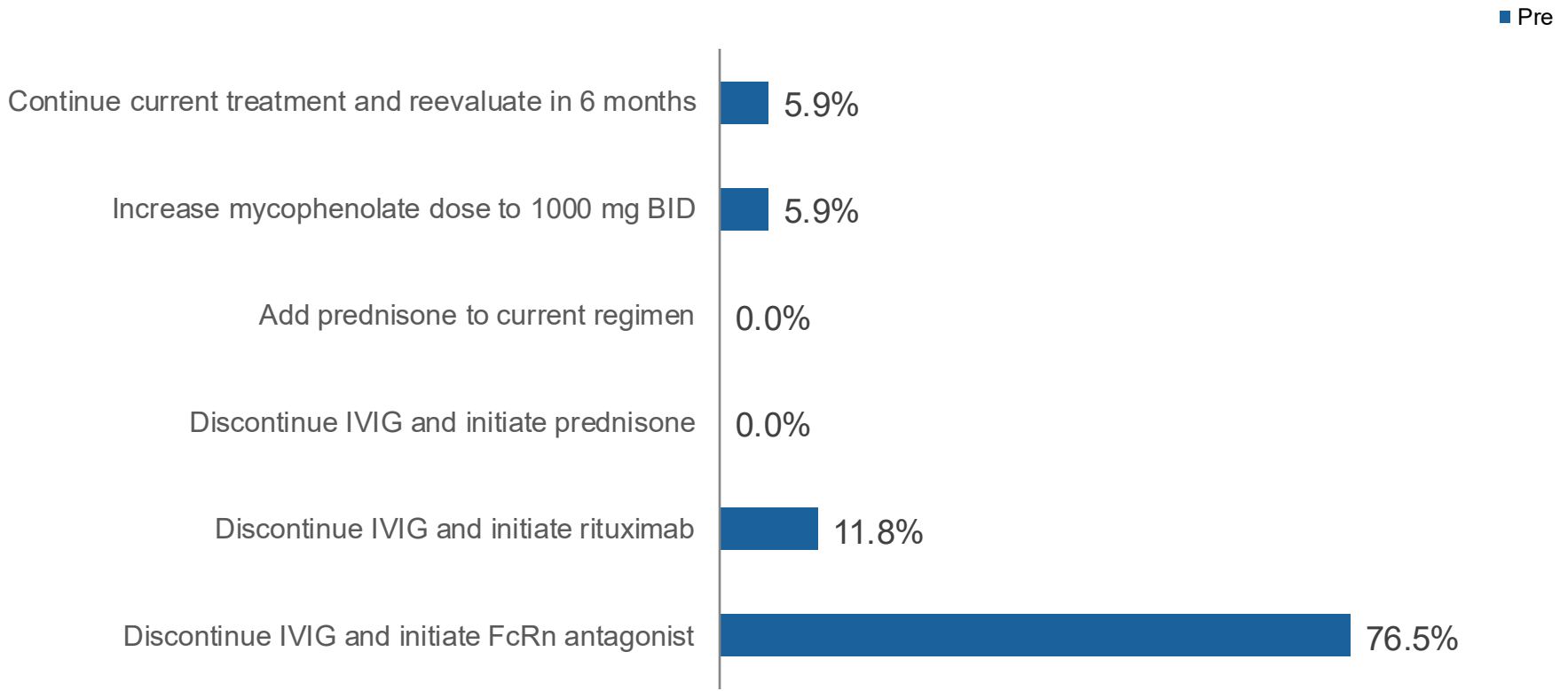
IVIG = intravenous immunoglobulin; BID = twice daily; QoL = quality of life.

Audience Response

Given this information, what would you recommend for Amber?

A. Continue current treatment and reevaluate in 6 months
B. Increase mycophenolate dose to 1000 mg BID
C. Add prednisone to current regimen
D. Discontinue IVIG and initiate prednisone
E. Discontinue IVIG and initiate rituximab
F. Discontinue IVIG and initiate FcRn antagonist

Given this information, what would you recommend for Amber?



Results recorded on July 16, 2025.

Conventional Therapy* for gMG

Treatments	Onset of Action	Maximum Efficacy
Tacrolimus	4-8 weeks	3 months
Cyclosporine	2-3 months	3-6 months
Cyclophosphamide	2-4 weeks	3-6 months
Methotrexate	1-3 months	3-6 months
Mycophenolate mofetil	4-12 months	6-18 months
Azathioprine	6-12 months	12-36 months
IVIG	1-2 weeks	
PLEX	1-2 exchanges	
Rituximab	1-3 months	

PLEX = plasma exchange.
*These agents are not FDA-approved for the treatment of gMG.
Farmakidis C, et al. *Neurol Clin*. 2018;36:311-337. Palace J, et al. *Neurol.* 1998;50:1778-1783.

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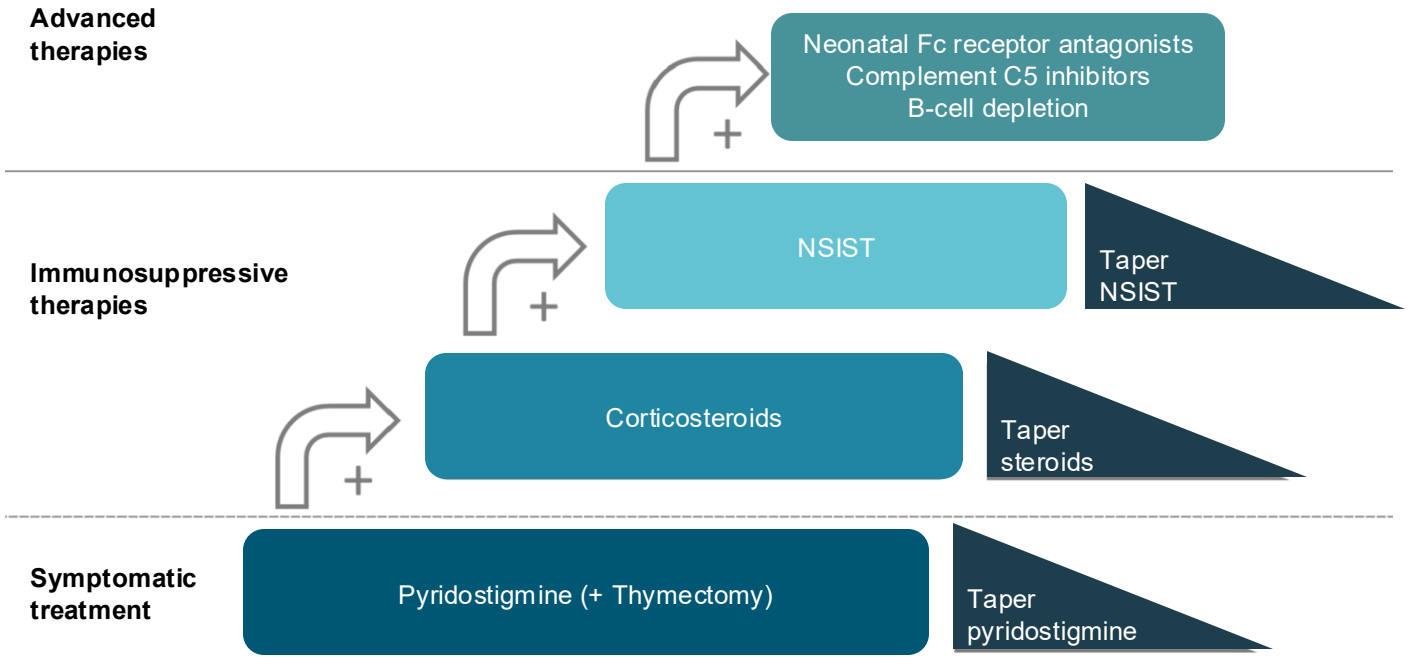
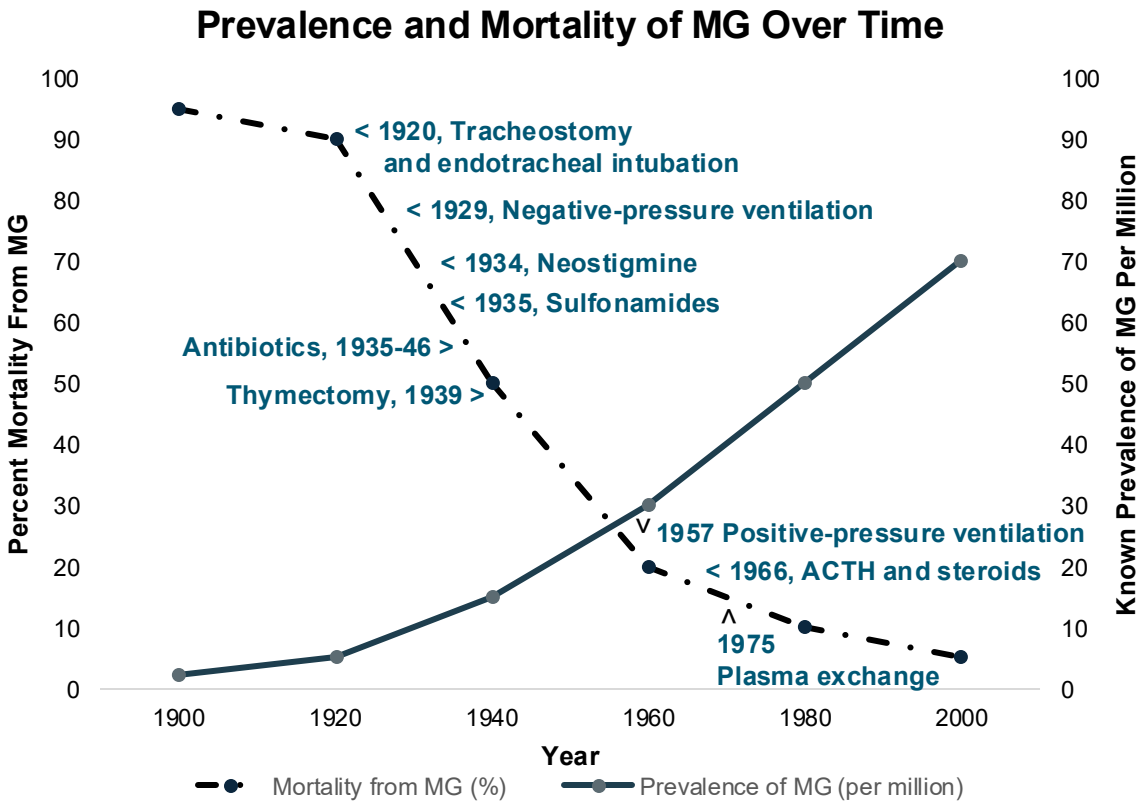
Current Recommendations By International Guidelines



De Bleecker JL, et al. *Acta Neurologica Belgica*. 2024;124:1371-1383.

Impact of Conventional Therapy on MG

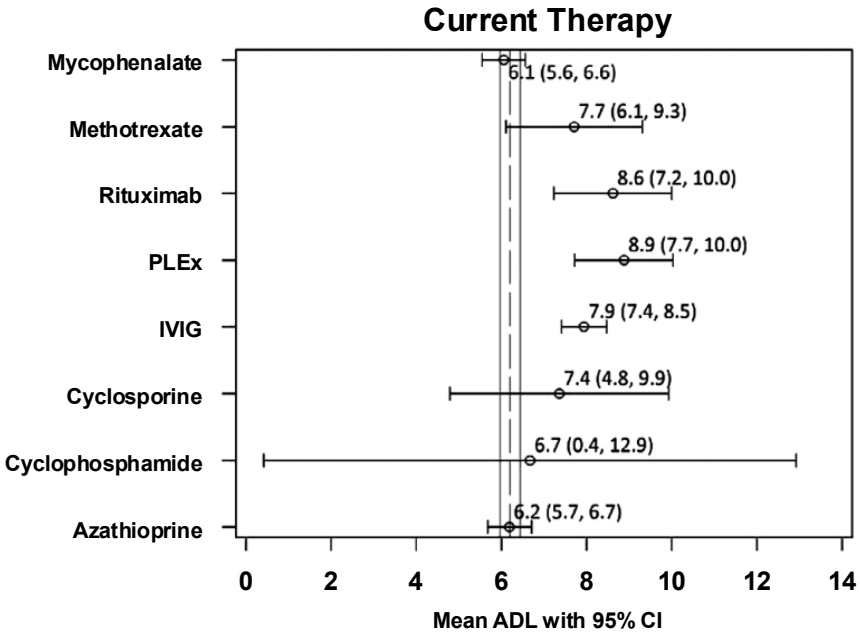


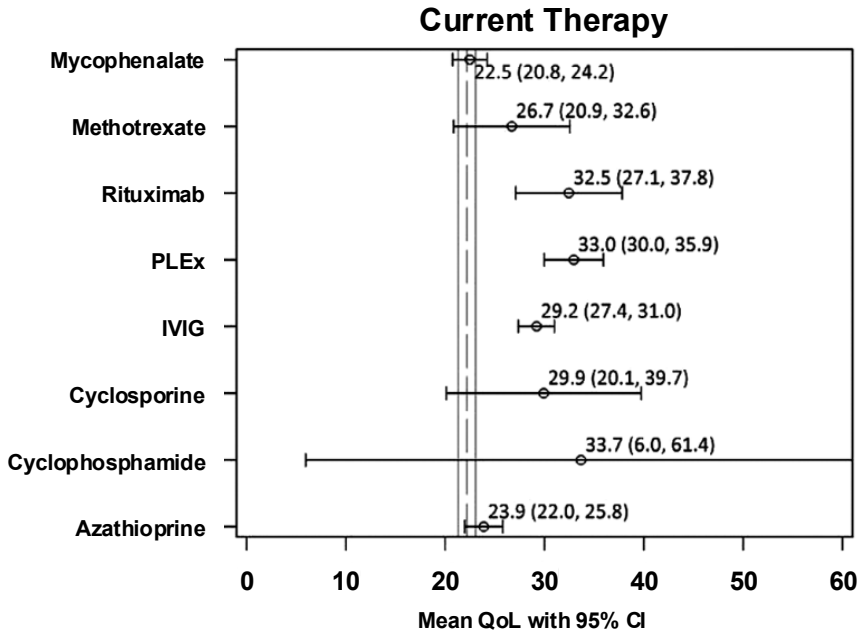
- Development of more effective treatments has **improved lifespan** for patients with MG, but 10% to 15% of cases are treatment refractory
- Half of patients are **dissatisfied** with disease control on current treatment
- Symptom suppression **insufficient**

ACTH = adrenocorticotropic hormone.

Grob D, et al. *Muscle Nerve.* 2008;37:141-149. Mantegazza R, et al. *Ther Adv Neurol Disord.* 2018;11:1756285617749134. Atkins C, et al. *Neurology.* 2021;97(14):663-664.

Does Conventional Therapy* Improve QoL?





*These agents are not FDA-approved for the treatment of gMG.

Cutter G, et al. *Muscle Nerve.* 2019;60(6):707-715.

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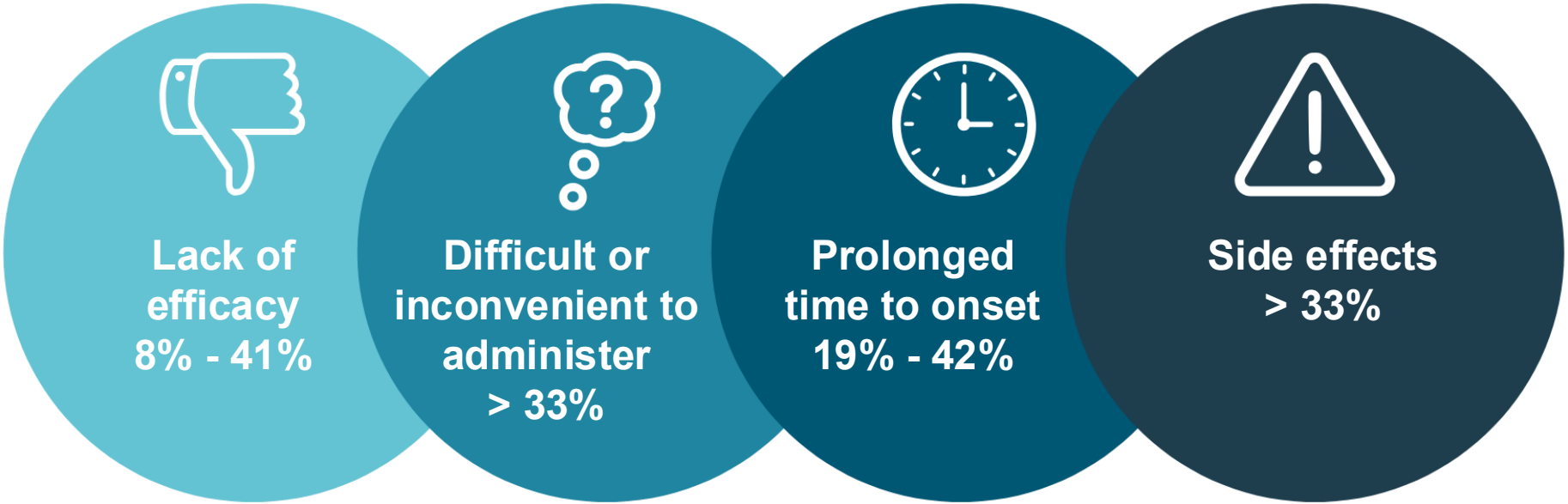
Treatment Dissatisfaction on Conventional Therapy



Lee I, et al. *Muscle Nerve.* 2018;58(1):90-98. Lee I, et al. *Neurol Neuroimmunol Neuroinflamm.* 2018;5(6):e507.

Comparing Conventional Therapy and FcRn Antagonists

- Advantages of FcRn antagonists:
  - Quick onset of effect
  - More **tolerable** long-term side effects than steroids
  - Improved **QoL** scores
  - Choices = customization
  - Convenience
- Disadvantages:
  - **Cost**
  - "Step through" requirements
  - Employment-based health insurance coverage, but many patients with gMG are **unemployed or underemployed**
  - Poor/no coverage by health insurers for seronegative patients

Treatments	Onset of Action	Maximum Efficacy
Tacrolimus*	4-8 weeks	3 months
Cyclosporine*	2-3 months	3-6 months
Cyclophosphamide*	2-4 weeks	3-6 months
Methotrexate*	1-3 months	3-6 months
Mycophenolate mofetil*	4-12 months	6-18 months
Azathioprine*	6-12 months	12-36 months
FcRn Antagonists	< 1-2 weeks	4-5 weeks

*These agents are not FDA-approved for the treatment of gMG.

Farmakidis C, et al. *Neurol Clin*. 2018;36(2):311-337. Palace J, et al. *Neurol*. 1998;50(6):1778-1783.

FcRn Antagonists: Considerations

Patient selection

- **Efgartigimod** approved only for AChR-positive patients
- **Rozanolixizumab** and **nipocalimab** approved only for patients who are either AChR-positive **or** MuSK-positive
- **Nipocalimab** is approved for adolescents aged 12 to 17 in addition to adults

Administration

- Both **efgartigimod** and **rozanolixizumab** can be given as SC injections
- **Nipocalimab** is given by IV administration only

Infection

- Increased risk of infection − monitor IgG levels regularly during treatment to assess the risk of infection
- Immunization with live or live-attenuated vaccines not recommended

SC = subcutaneous.

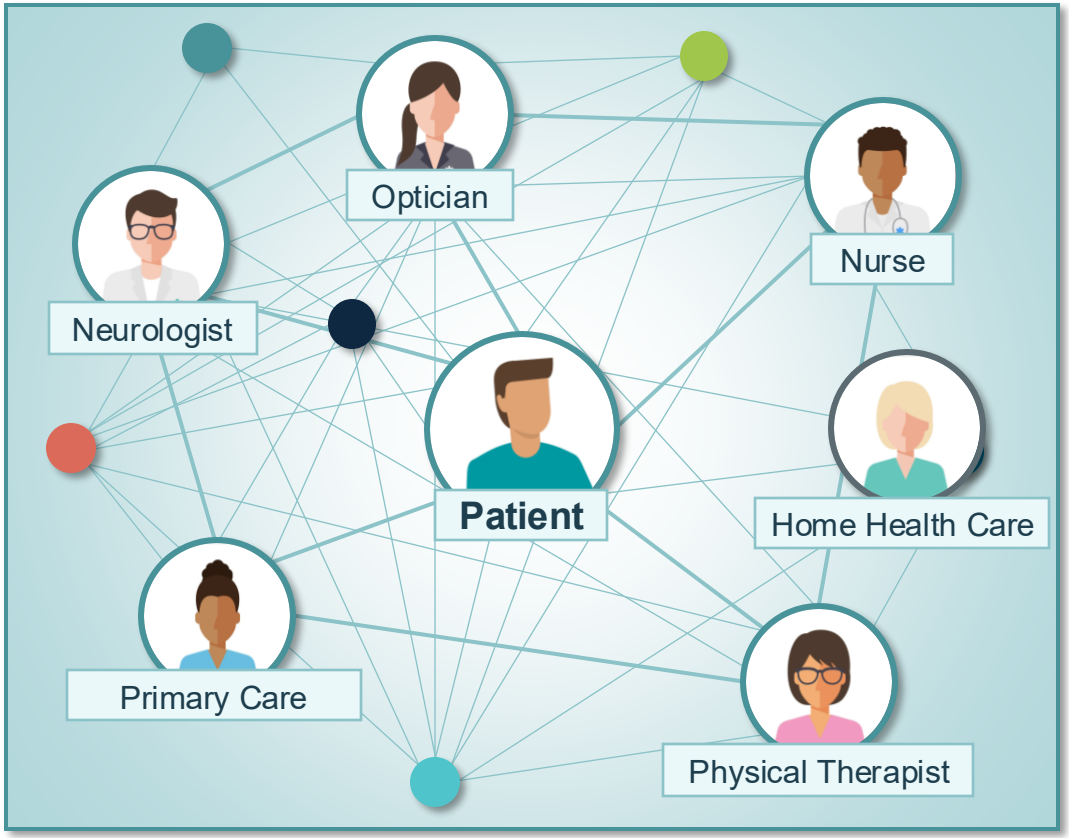
Efgartigimod [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2021/761195s000lbl.pdf.
Rozanolixizumab [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761286s000lbl.pdf.
Nipocalimab [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761430s000lbl.pdf.

Selecting Between Treatment Options

- Efficacy
  - All FcRn antagonists have phase III data showing efficacy, but no head-to-head comparisons:
    - Different definitions of treatment response for each trial
    - Different trial designs
    - Drug to drug comparison without head-to-head trial cannot be supported
- Response to treatment
  - How long should a drug be tried before changing to another?
  - Worth trying another agent within the same class if it is a different type of compound?
    - SC vs IV
    - Fc fragment (efgartigimod) vs monoclonal IgG (rozanolixizumab/nipocalimab)

Haminski HJ, et al. *J Clin Invest.* 2024;134(12):e179742.

Importance of a Team-Based Approach for the Management of gMG

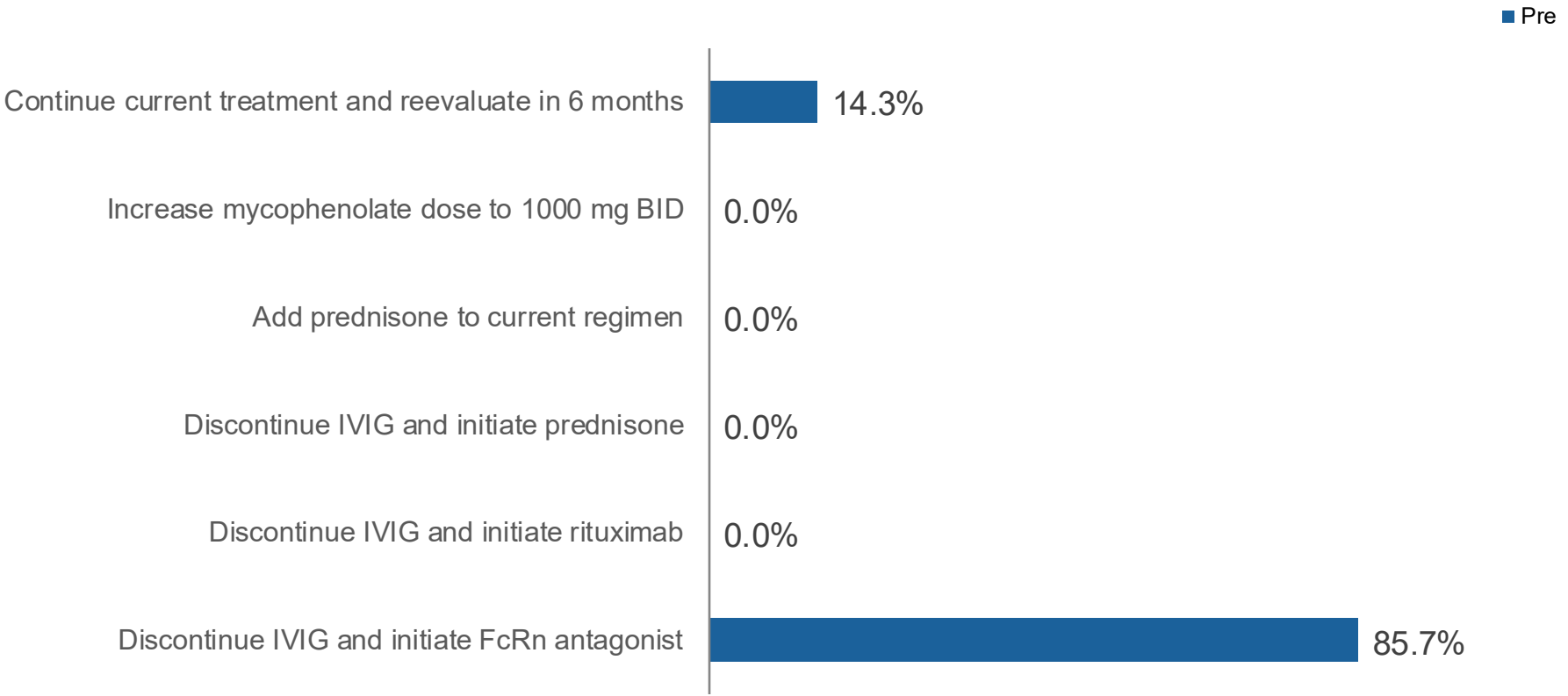


Audience Response

Now, what would you recommend for Amber?

A. Continue current treatment and reevaluate in 6 months
B. Increase mycophenolate dose to 1000 mg BID
C. Add prednisone to current regimen
D. Discontinue IVIG and initiate prednisone
E. Discontinue IVIG and initiate rituximab
F. Discontinue IVIG and initiate FcRn antagonist

Now, what would you recommend for Amber?



Results recorded on July 16, 2025.

Faculty Q&A and Discussion

Recorded during live program on July 16, 2025.

Optimizing Dose, Schedule, and Route of Administration for Best Outcomes with FcRn Antagonists

Patient Case: Amber

- Amber begins treatment with the FcRn antagonist efgartigimod SC once weekly on a schedule of 4 weeks on, 4 weeks off

- She responds well to treatment and sees an improvement in symptoms within one cycle
- She continues to experience benefits with each subsequent cycle of efgartigimod

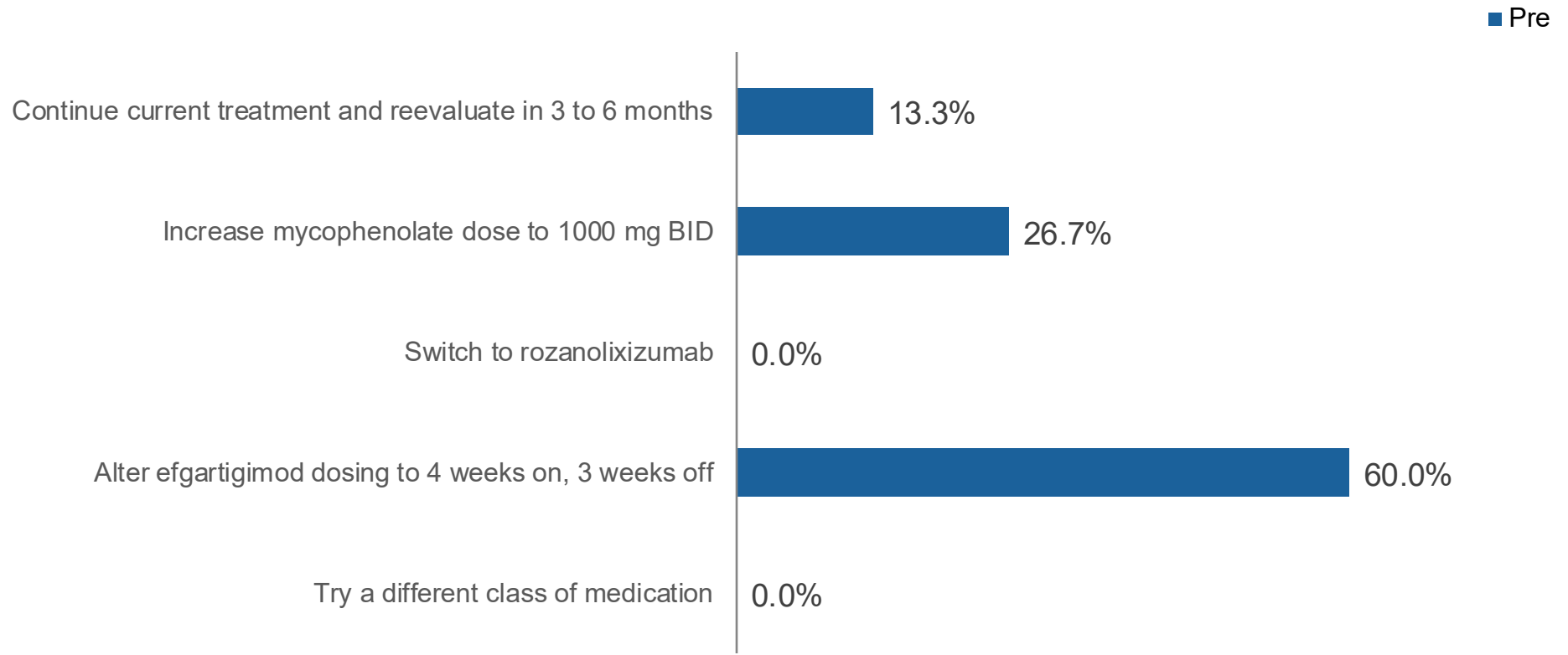
- While Amber's symptoms are improving during her treatment cycles, she reports an early return of symptoms, usually about 1 week before the beginning of each treatment cycle

Audience Response

What would you recommend for Amber?

A. Continue current treatment and reevaluate in 3 to 6 months
B. Increase mycophenolate dose to 1000 mg BID
C. Switch to rozanolixizumab
D. Alter efgartigimod dosing to 4 weeks on, 3 weeks off
E. Try a different class of medication

What would you recommend for Amber?



Results recorded on July 16, 2025.

Dosing of Approved FcRn Antagonists

Agent	Delivery	Infusion Duration	Dose	Schedule
Efgartigimod	IV	1 hour	10 mg/kg	Cycles of 4 weeks on, 4 weeks off
	SC	20 to 30 seconds	1,008 mg efgartigimod alfa + 11,200 units hyaluronidase	Cycles of 4 weeks on, 4 weeks off
	Prefilled syringe	20 to 30 seconds	1,000 mg efgartigimod alfa + 10,000 units of hyaluronidase per 5 mL syringe	Cycles of 4 weeks on, 4 weeks off
Rozanolixizumab	SC	15 minutes	420 mg (pt < 50 kg) 560 mg (50 kg to < 100 kg) 840 mg (≥ 100 kg)	Cycles of 6 weeks on, 4 weeks off
Nipocalimab	IV	30 minutes	Initial dose 30 mg/kg, 15 mg/kg for subsequent doses	Continuous therapy every 2 weeks

Efgartigimod alfa and hyaluronidase-qvfc [package insert]. https://www.accessdata.fda.gov/drugsatfda_docs/label/2024/761304s005,s006lbl.pdf.

Individualized Dosing of FcRn Antagonists

Cyclical dosing offers the option of personalization

- During treatment breaks between cycles, some patients experience an early return of symptoms
- Cycles can be shortened or lengthened to address continued symptoms or emergent adverse events

Efgartigimod

- During the ADAPT trial, each cycle of **efgartigimod** could be initiated based on patient response as measured by MG-ADL
- The ADAPT NXT trial evaluated two alternative dosing schedules for **efgartigimod**

Rozanolixizumab

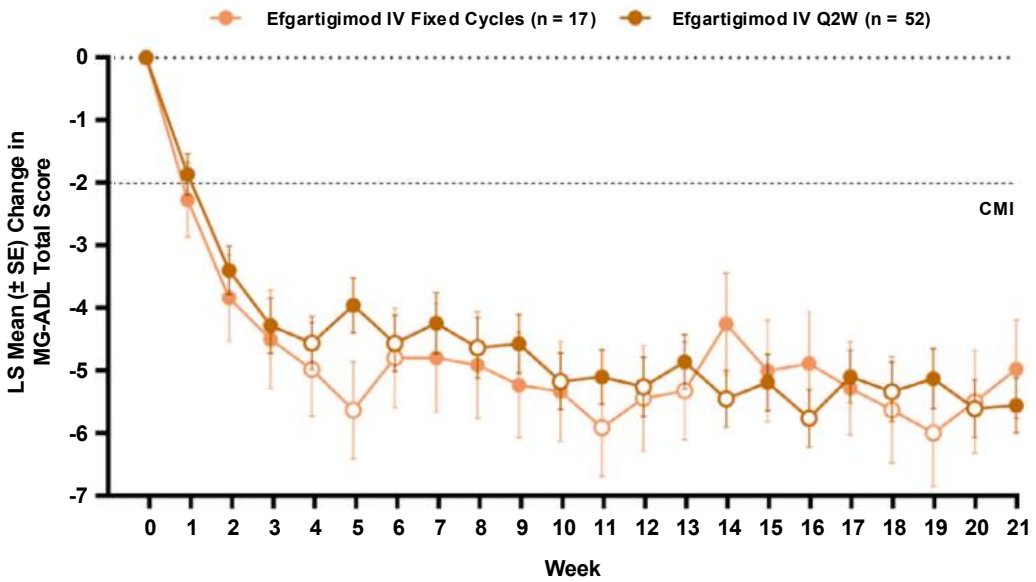
- In MycarinG, patients received 6 cycles of treatment followed by an 8-week observation period
- The open-label extension study MG0007 evaluated individualized dosing of **rozanolixizumab** based on symptom worsening (symptom-driven cycles)
- The open-label extension MG0004 evaluated continuous dosing of **rozanolixizumab**

Individualized dosing is not part of the FDA label for these agents.

Habib AA, et al. *Ann Clin Transl Neurol.* 2025;12(6):1162-1170. Bril V, et al. *J Neuromuscular Dis.* 2025;12(2):218-230.

Efgartigimod Individualized Dosing: ADAPT NXT

- ADAPT NXT evaluated alternative dosing of efgartigimod
- All patients received 4 weekly cycles as a lead-in before randomization to:
  - Fixed cycles of 4 weeks on and 4 weeks off
  - Q2W administration
- Both dosing schemas were well-tolerated with similar rates of AEs
  - COVID-19, headache, and URI were the most common treatment emergent AEs

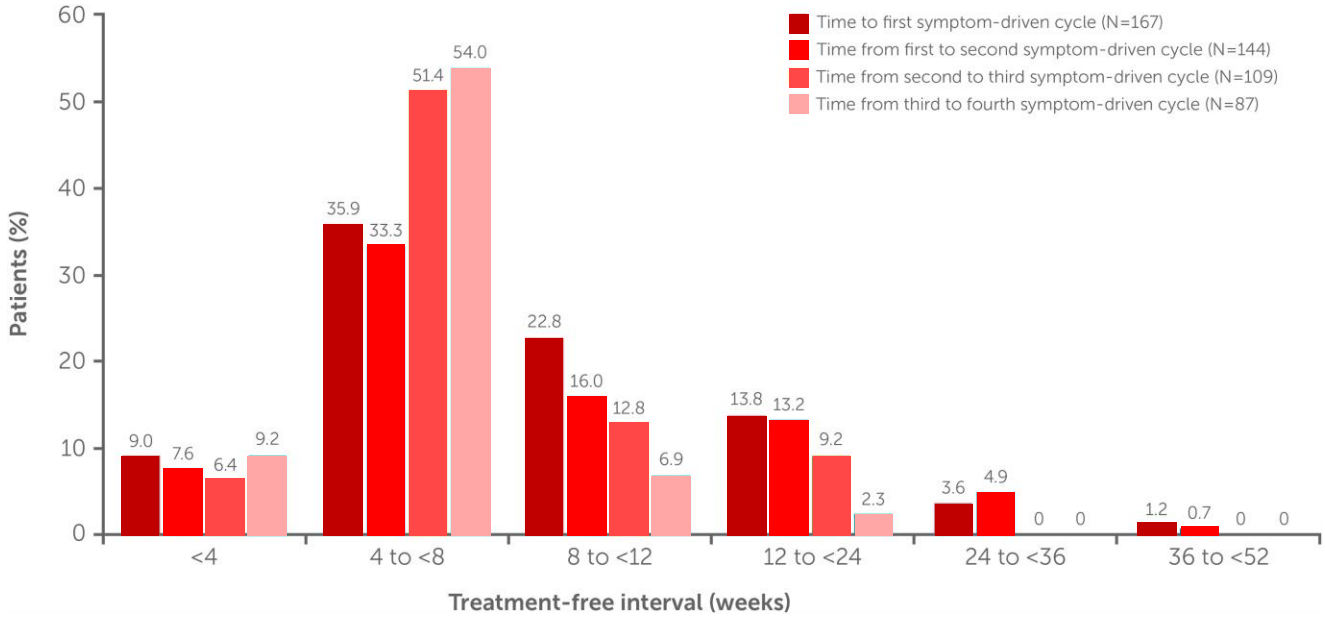


AEs = adverse events.

Habib AA, et al. *Ann Clin Transl Neurol.* 2025;12(6):1162-1170.

Rozanolixizumab Individualized Dosing: MG0007

MG0007 evaluated “symptom-driven cycles” of **rozanolixizumab** in patients completing 52 weeks of treatment on MycarinG, with patients receiving new cycles after worsening of MG-ADL or QMG scores



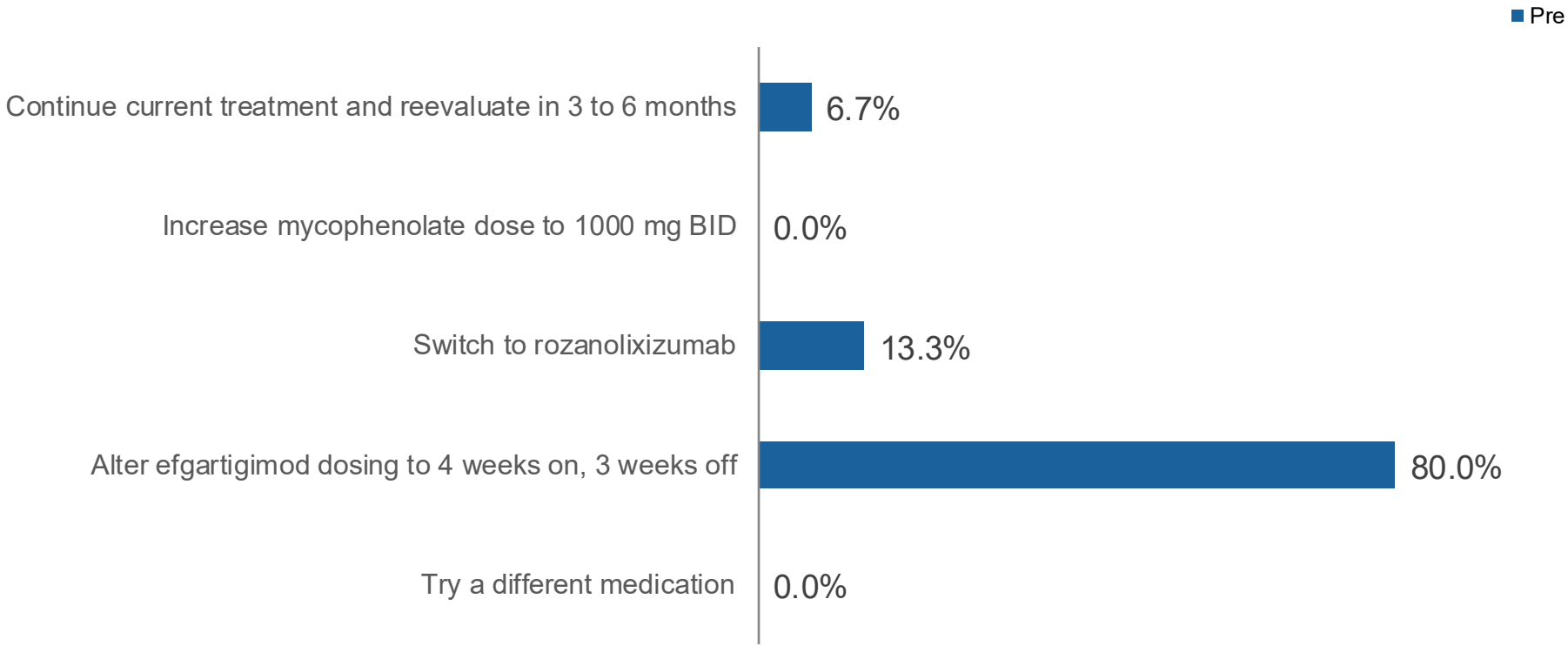
Bril V, et al. *J Neuromuscular Dis.* 2025;12(2):218-230.

Audience Response

Now, what would you recommend for Amber?

A. Continue current treatment and reevaluate in 3 to 6 months
B. Increase mycophenolate dose to 1000 mg BID
C. Switch to rozanolixizumab
D. Alter efgartigimod dosing to 4 weeks on, 3 weeks off
E. Try a different medication

Now, what would you recommend for Amber?



Results recorded on July 16, 2025.

Faculty Q&A and Discussion

Recorded during live program on July 16, 2025.

SMART Goals

Specific, Measurable, Attainable, Relevant, Timely

- Consider FcRn antagonists for appropriate patients with gMG who have suboptimal responses to standard therapy
- Routinely evaluate quality of life when assessing treatment responses
- Discuss treatment options and set realistic treatment goals with your patient
- Monitor response to FcRn antagonists and consider symptom-adapted treatment dosing when appropriate

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