Myasthenia Gravis: The Evolving Therapeutic Landscape

Contemporary Neurology 2026
Clinical Neurology Society of America
January 17-20, 2026
Jupiter, FL

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Disclosure Information

Gil I. Wolfe MD

Disclosure of Relevant Financial Relationships

I have the following financial relationships to disclose:

Consultant for: Alexion, Argenx, BPL, Cartesian, Canopy, Dianthus Grifols, Johnson & Johnson, Takeda, UCB
Speaker's Bureau for: Grifols, Alexion, UCB
Grant/Research support from: ArgenX, Ra/UCB, Immunovant, Roche, Alexion, NINDS/NIH, MGFA
Stockholder in: N/A
Honoraria from: N/A
Employee of: N/A

Disclosure of Off-Label and/or investigative Uses

I will discuss the following off label use and/or investigational use in my presentation:

All agents except for pyridostigmine, eculizumab, efgartigimod, ravulizumab rozanolixizumab, zilucoplan, nipocalimab, and inebilizumab are either not approved or are investigational in the treatment of MG

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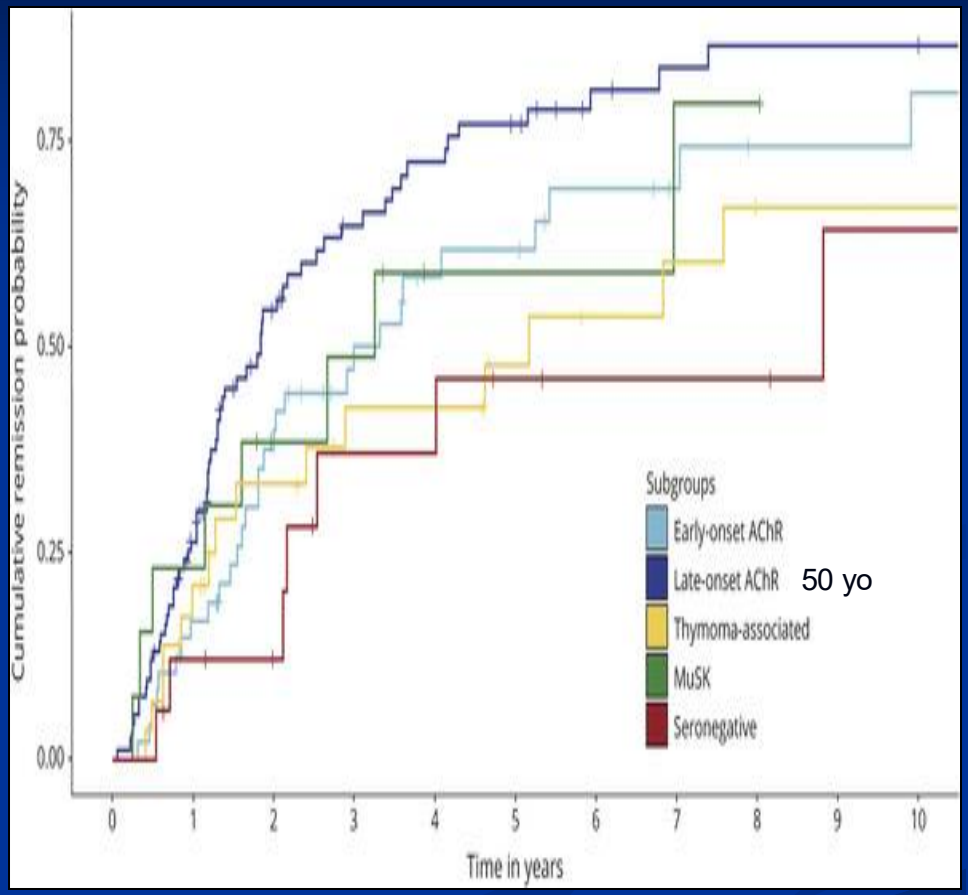
Educational objectives

1. To recognize the mechanisms of action being explored in new therapeutics for myasthenia gravis
2. To be informed about new agents available and those in late stages of investigation for myasthenia gravis and how they might be used
3. To be aware of updates to the International Consensus Guidance to manage myasthenia gravis

GMG Outcomes Since 2000

- n=199, onset after 2000
- Formalized evals up to 10 yrs
- Rx per Austrian guidelines
- Results
  - Only 5% experience nadir after yr 1
  - MMS or better at 1 yr in 51%
  - MMS or better >12 mos in 63%
  - Median time to MMS 30.9 mos
  - Pts asymptomatic for >12 mos by yr 2 do better
  - MuSK+ pts with better outcome than prior studies [rituximab]
  - 9 deaths, 7 in LOMG group
    - On par with Austrian mortality rates

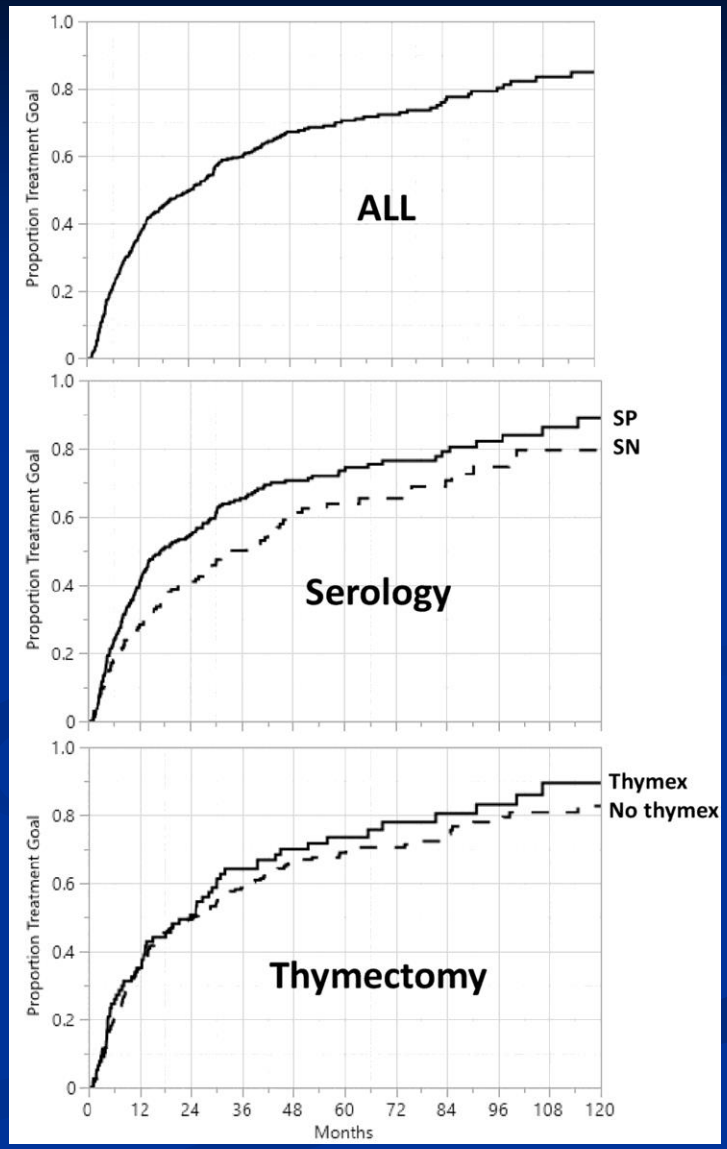


MMS or better >12 mos

Tomschik M et al. *Neurology* 2020;95:e1426-1436

MG Outcomes Since 2000

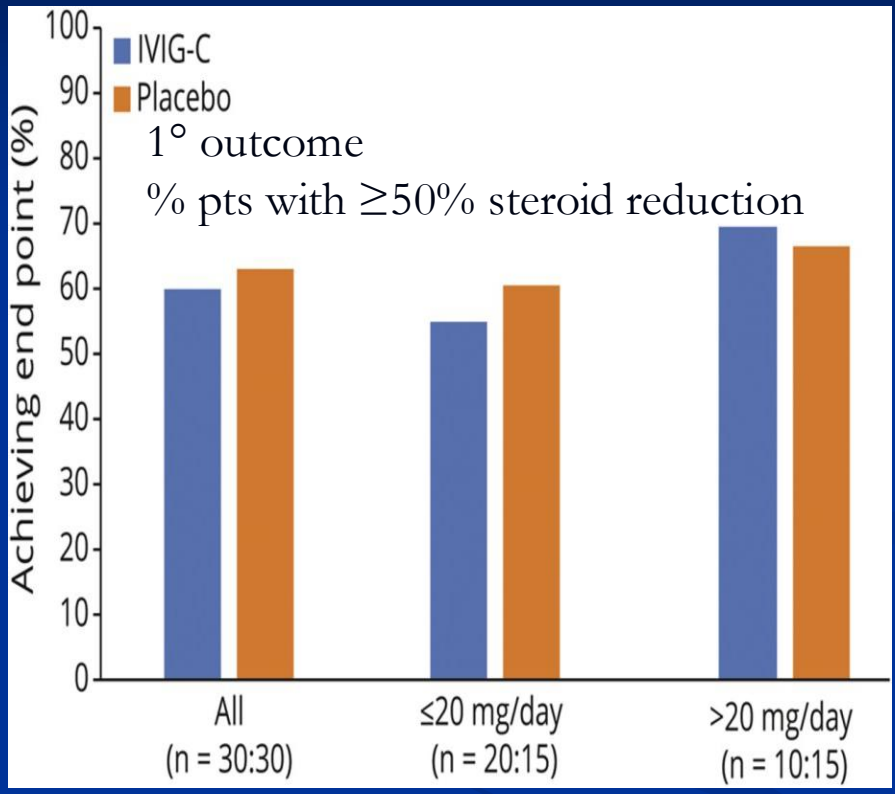
- n=367 followed ≥2 yrs
  - No C' inhibitors or FcRn antagonists used
- 72% achieved Tx goal within 2 yrs [MMS or better]
  - >80% within 10 yrs of first visit
- Variables predicting Tx goal
  - AChRAb+
  - Thymectomy (n=78)
    - Thymoma patients did just as well
  - Shorter disease duration (p=0.01)



Sanders DB et al. *Muscle Nerve* 2023;67:291-296

IVIg as steroid sparer

- DBPC trial, AChRAb+ on prednisone
  - ≥15 and ≤60 mg/d prednisone at least 3 mos
    - No Δ in IS agents x 6 mos
  - MGFA Class II-IVa (n=60)
  - IVIg 2 gm/kg followed by 1 gm/kg q3 wks to wk 36
  - Set taper schedule of 5-10 mg q3wks dependent on dosing and titration schedule [QMG dependent]
    - Tapering to 0 mg at physician discretion
    - Withdrawn if failed 2nd taper

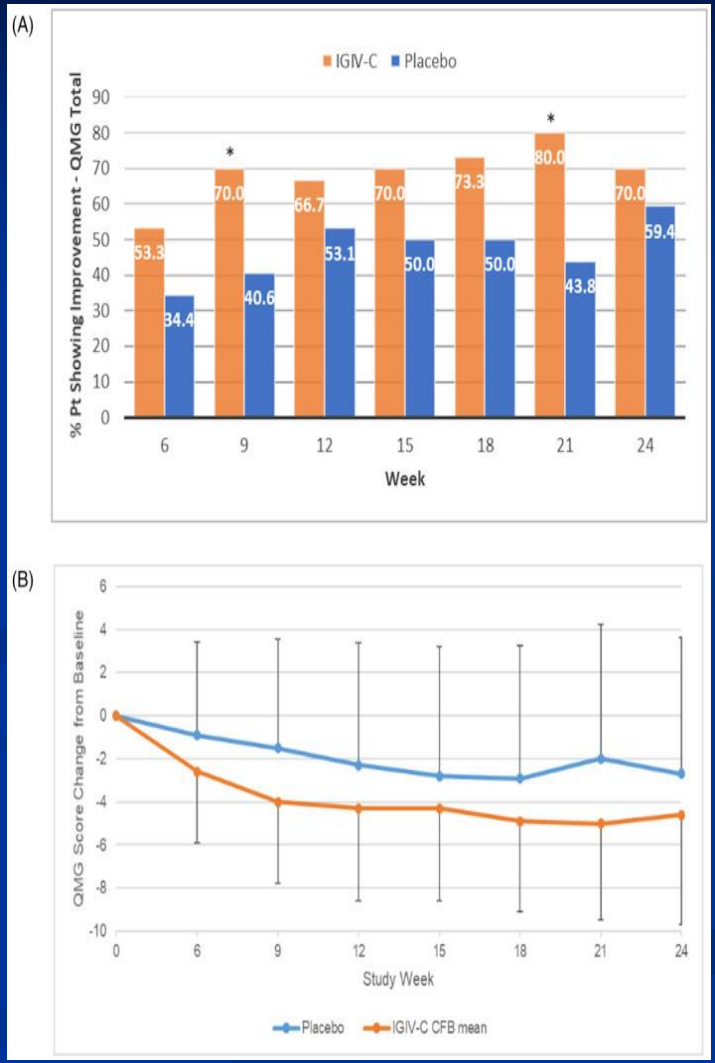


Bril V et al. *Neurology* 2023;100:e671-e682

IVIG as maintenance Rx

- n=62 AChRAb+; phase 2 multicenter study
- IVIG 2 gm/kg, then 1 gm/kg q3wks vs placebo (1:1)
- QMG ≥10
  - BL for IVIG group was 14.6
  - BL for placebo group was 16.2
- Results at wk 24
  - 1°: ΔQMG -5.1 vs. -3.1 (p=0.187)
  - 2°: ≥3 pt difference in QMG or MGC (p=0.442; 0.610)

    ≥2 pt difference in MG-ADL (p=0.025)
- Authors comment assumed impact of maintenance IVIG in MG likely overestimated historically
  - Bril V et al. *Muscle Nerve* 2025;71:43-54

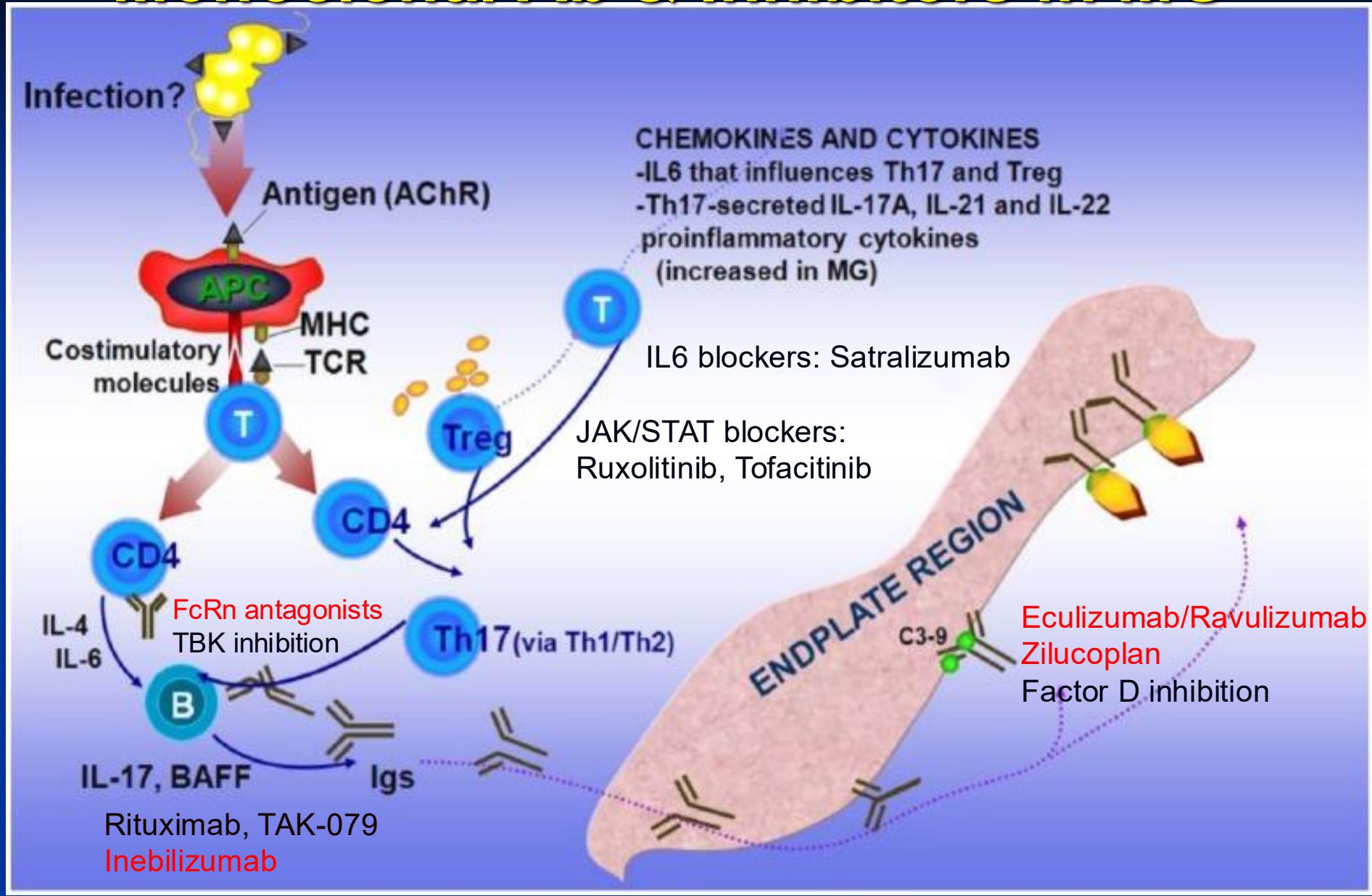


MG: Unmet treatment needs

- 10% of refractory patients
- 20% of patients with problematic AEs
- MuSK MG patients?
- MG during pregnancy/breast feeding
- MG crisis
  - When IVIg (or PE) ineffective
    - Many medical centers do not have access to PE
  - Something that has more “persistence”
- From International Treatment Guideline:

“The use of xxx as maintenance therapy should be considered for patients with refractory MG and in those in whom immunosuppressive medications are relatively contraindicated because of comorbidity or pregnancy.”

Monoclonal Ab & Inhibitors in MG



Modified from Dalakas MC. *Ther Adv Neurol Disord* 2015;8:316-327

Complement role in MG

Howard JF Jr. *Ann NY Acad Sci* 2018; 1412:113-128

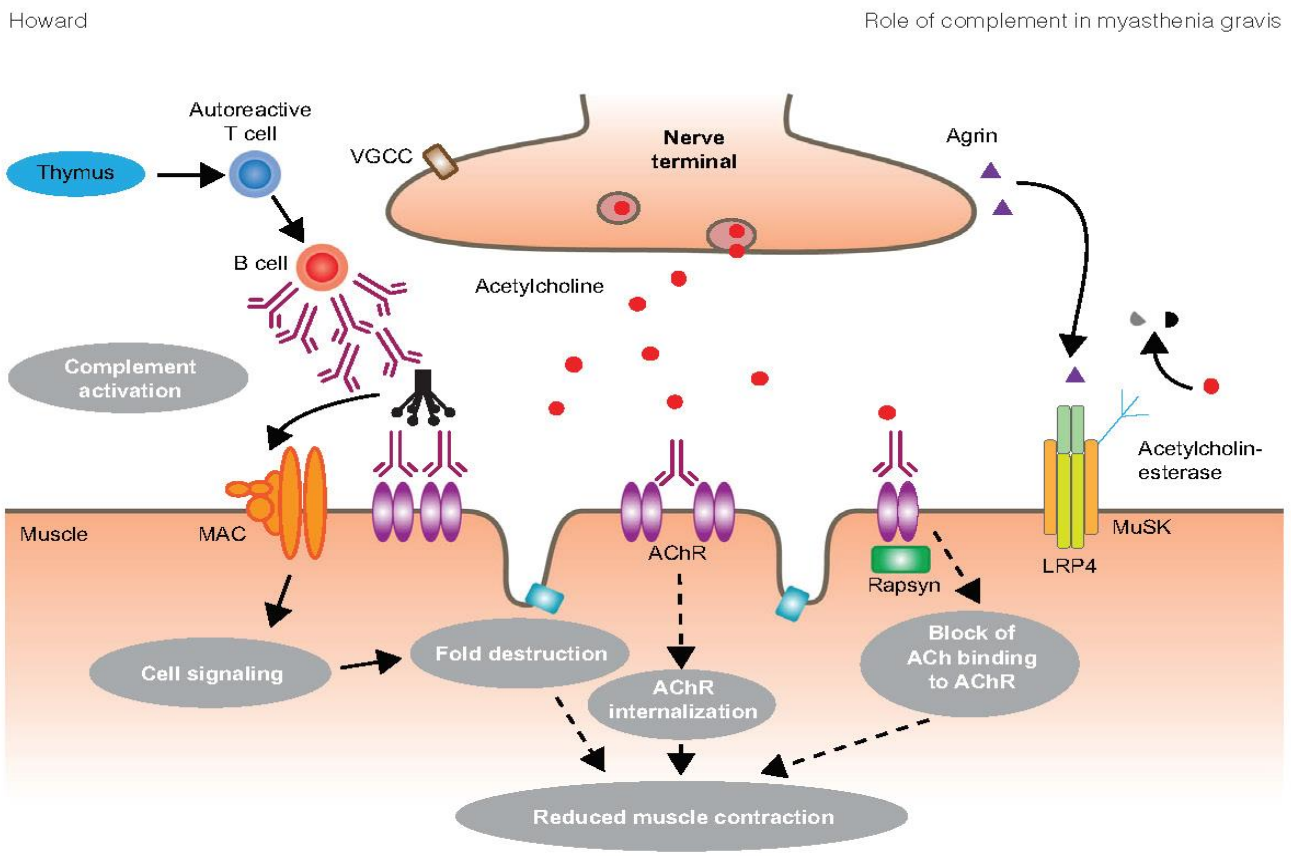


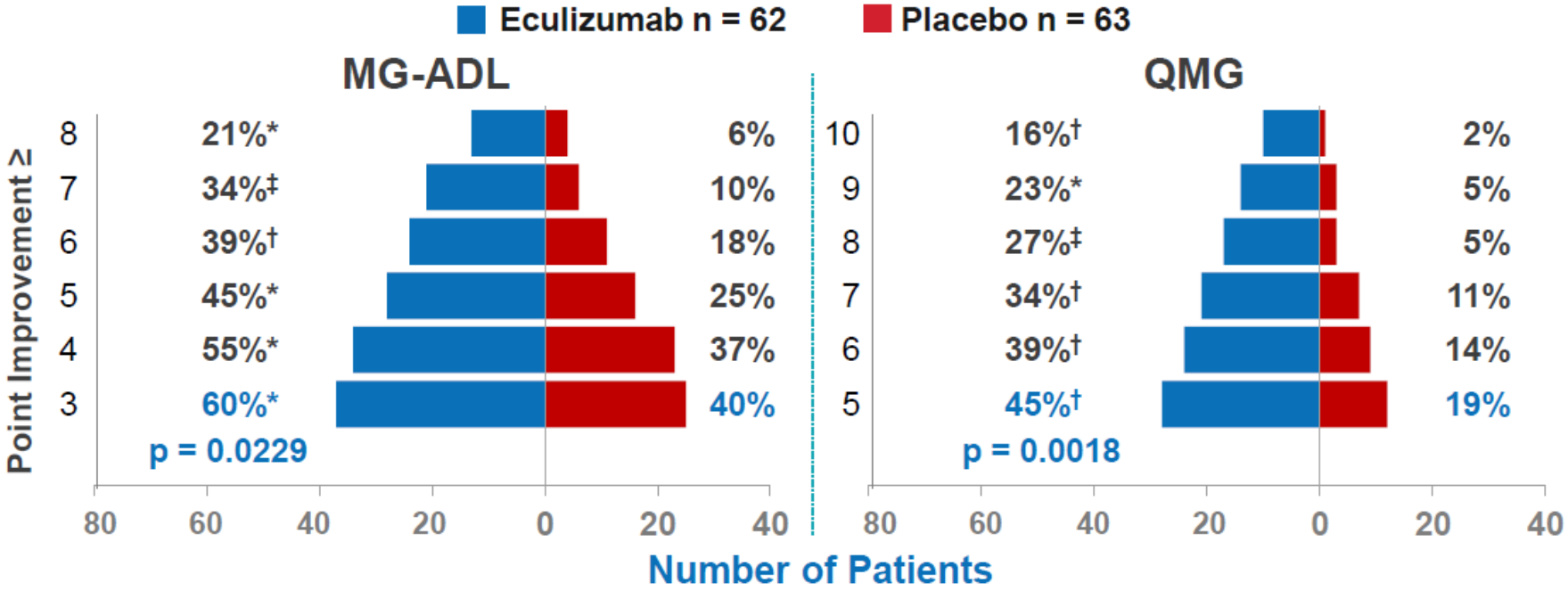
Figure 2. Pathophysiology of anti-AChR$^+$ MG. The three major pathogenic mechanisms of AChR autoantibodies in MG include complement activation at the neuromuscular junction, which causes the formation of MACs on the muscle membrane and destruction of the typical folds in the motor endplate; antigenic modulation that results in the internalization and degradation of surface AChRs; and binding of AChR antibodies at the AChR ligand binding site, which could directly block ACh binding and, consequently, channel opening. ACh, acetylcholine; AChR, acetylcholine receptor; LRP4, low-density lipoprotein receptor–related protein 4; MAC, membrane attack complex; MG, myasthenia gravis; MuSK, muscle-specific kinase; VGCC, voltage-gated Ca^{2+} channel; VGSC, voltage-gated Na^+ channel. Adapted by permission from Ref. 2.

REGAIN Eculizumab Study

- Parallel-group, multicenter Phase 3 study of 125 subjects completed
- 26 wk duration
- Looser entry criteria regarding PE/IGIV
- 900/1200 mg dosing was slightly higher than Phase 2
- Results
  - Δ MG-ADL was 1º outcome
    - p=0.0698 by worst rank analysis
  - 18/22 pre-specified endpoint analyses with p≤0.05 based on 1º and five 2º outcomes
    - Worst rank analysis for QMG ($p<0.05$)
    - Responder analyses for MG-ADL and QMG ($p<0.05$)
      - Howard JF et al. *Lancet Neurology* 2017;16:976-986

REGAIN Eculizumab Study

2nd and 3rd Secondary Endpoints: MG-ADL and QMG Responder Analyses[1]



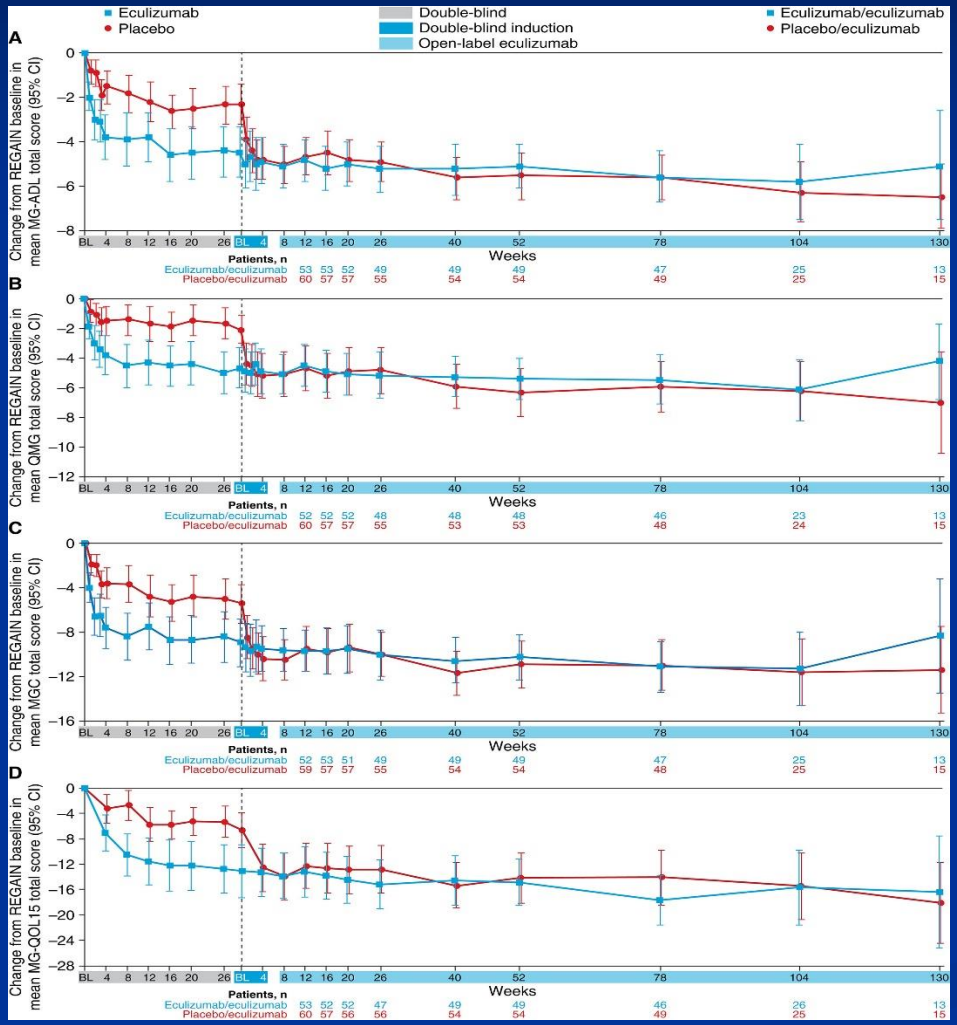
1. Proportion of patients with improvement in total score and **no rescue therapy** at week 26 from baseline
2. Secondary Endpoints: ≥ 3-point reduction in MG-ADL, ≥ 5-point reduction in QMG and **no rescue therapy**

*p ≤ 0.05; †p ≤ 0.01; ‡p ≤ 0.001

REGAIN Study

PL2.3: - REGAIN: A Randomized, Double-Blind, Placebo-Controlled Multi-Center Phase 3 Study Of The Safety And Efficacy Of Eculizumab In Subjects With Refractory Generalized Myasthenia Gravis - Dr. James F. Howard, Jr.

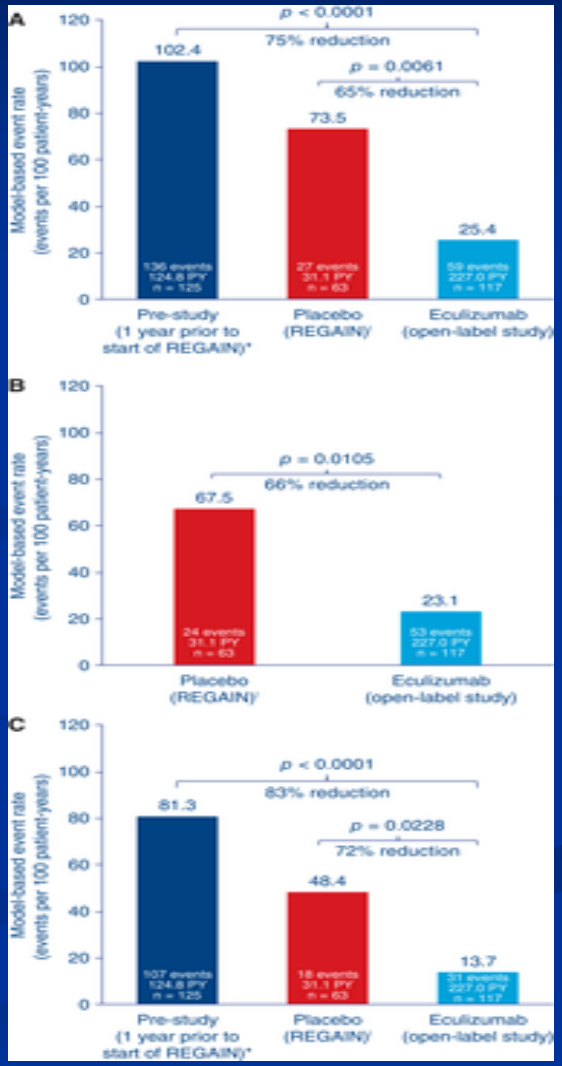
REGAIN Eculizumab Study
Long-term results



All exacerbations

Rescue Rx

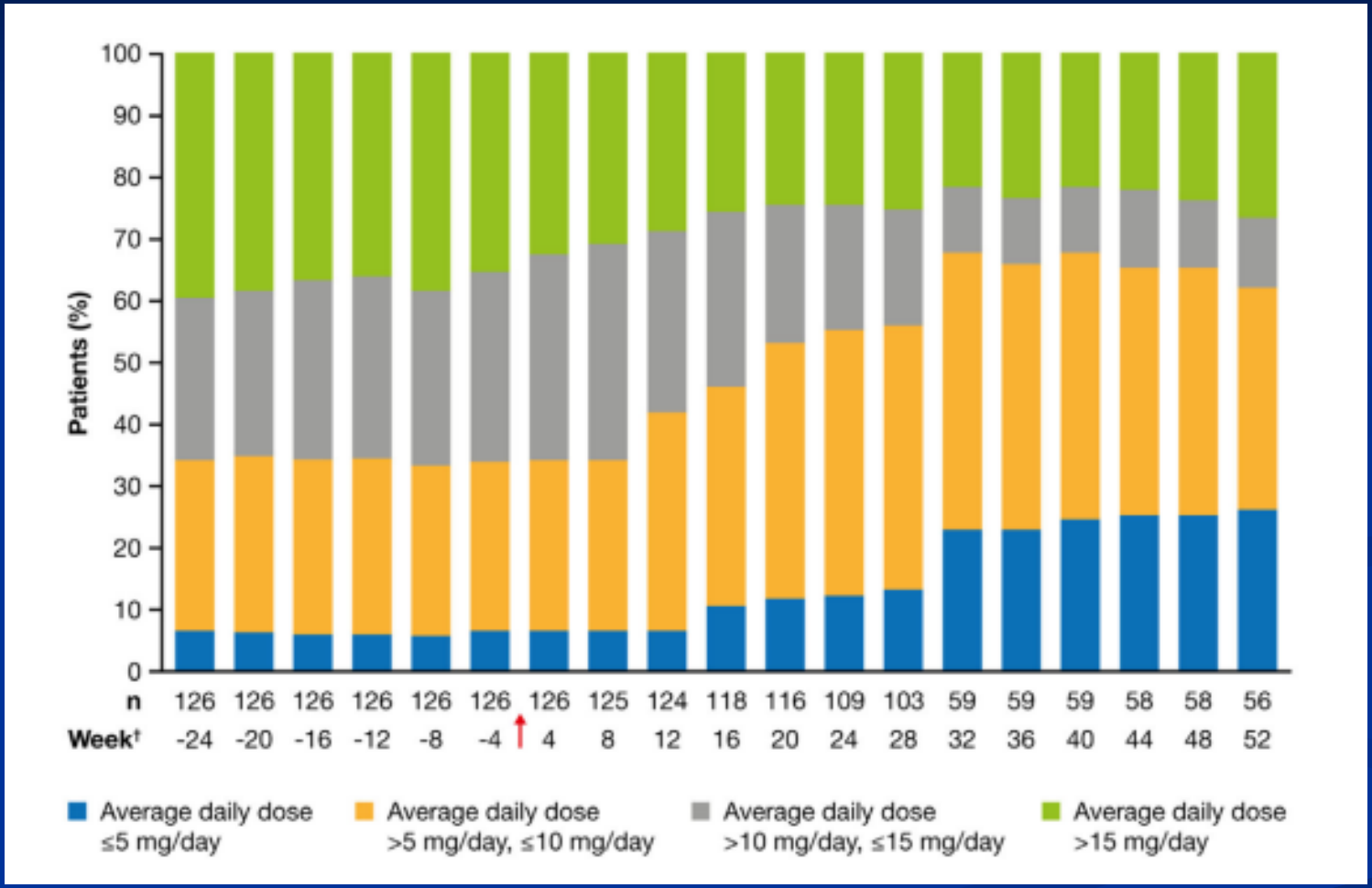
Hospitalization



Muppidi S et al. *Muscle Nerve* 2019;60:14-24

Japan: Eculizumab 1 year experience

Corticosteroid tapering (n=130)



Percent of patients on ≤5 mg/d increased from 7% to 26%

Murai H et al. *Neuroimmunol* 2022; DOI: 10.1111/cen3.12716

REGAIN Eculizumab Study: Long-term results

Event	Events, *n*	Patients experiencing an event, *n* (%)	Events per 100 PY
All adverse events	1,816	113 (96.6)	800.0
Most common adverse events >10% of all patients, *N* = 117			
Headache	71	44 (37.6)	31.3
Nasopharyngitis	76	37 (31.6)	33.5
Diarrhea	40	27 (23.1)	17.6
Upper respiratory tract infection	55	27 (23.1)	24.2
Myasthenia gravis exacerbations	40	23 (19.7)	17.6
Arthralgia	29	22 (18.8)	12.8
Nausea	26	21 (17.9)	11.5
Pain in extremity	21	18 (15.4)	9.3
Cough	21	17 (14.5)	9.3
Fatigue	21	17 (14.5)	9.3
Urinary tract infection	32	17 (14.5)	14.1
Influenza	24	16 (13.7)	10.6
Gastroenteritis	15	14 (12.0)	6.6
Bronchitis	22	13 (11.1)	9.7
Pyrexia	17	13 (11.1)	7.5
Fall	24	12 (10.3)	10.6
All serious adverse events	147	52 (44.4)	64.8

One case of meningococcal meningitis after data lock that resolved c Abx

Open-label study in 11 adolescents with refractory gMG with approval for ≥6 yo
600-900 mg induction; 300-1200 mg q2 wks
Brandsema JF et al. *Pediatr Neurol* 2024;156:198-207

Muppidi S et al. *Muscle Nerve* 2019; 60:14-24

Ravulizumab Phase 3 CHAMPION Trial

- Approved in 12/2018 for atypical HUS, then PNH
- Approved on 4/27/22 for AChRAb+ gMG
- Offers q8 wk IV administration
  - Dosing by weight: 2400-3600 mg
    - most adult pts will receive 2700 mg load followed 2 wks later by 3300 mg maintenance doses
  - n=175, MG-ADL ≥6, mean dz duration 10 yrs, mean baseline QMG 15
- Outcomes at 26 wks
  - 1°: MG-ADL -3.1 vs. -1.4 placebo ($p<0.001$)
  - QMG -2.8 vs. -0.8 placebo ($p<0.001$)
  - ≥5 pt QMG drop 3x as likely with active Rx (36% vs. 13%)
  - QOL-15r and fatigue measures did not reach significance
- AEs
  - HA actually lower on active Rx than placebo (19% vs. 26%)
  - 2 deaths on active Rx: COVID-19 and cerebral hemorrhage
  - No meningococcal infections
    - MGFA Scientific Session, 10/30/2021; AAN Meeting, 4/5/22
    - Vu T. et al. *NEJM Evid* 2022; 1(5) DOI 10.1056/EVIDoa2100066

Ravulizumab Phase 3 CHAMPION Trial

Vu T. et al. *NEJM Evid* 2022; 1(5) DOI 10.1056/EVIDoa2100066

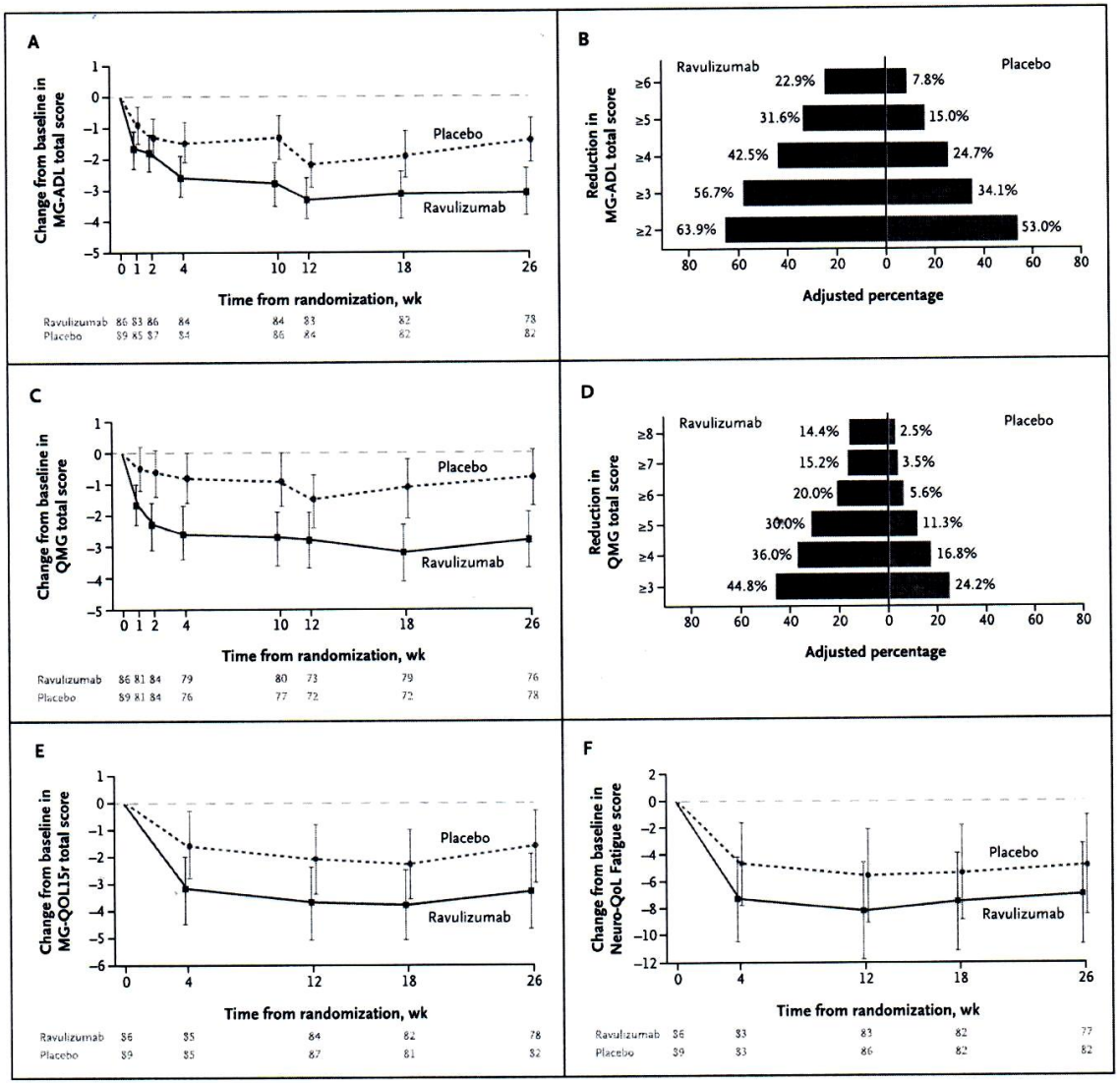
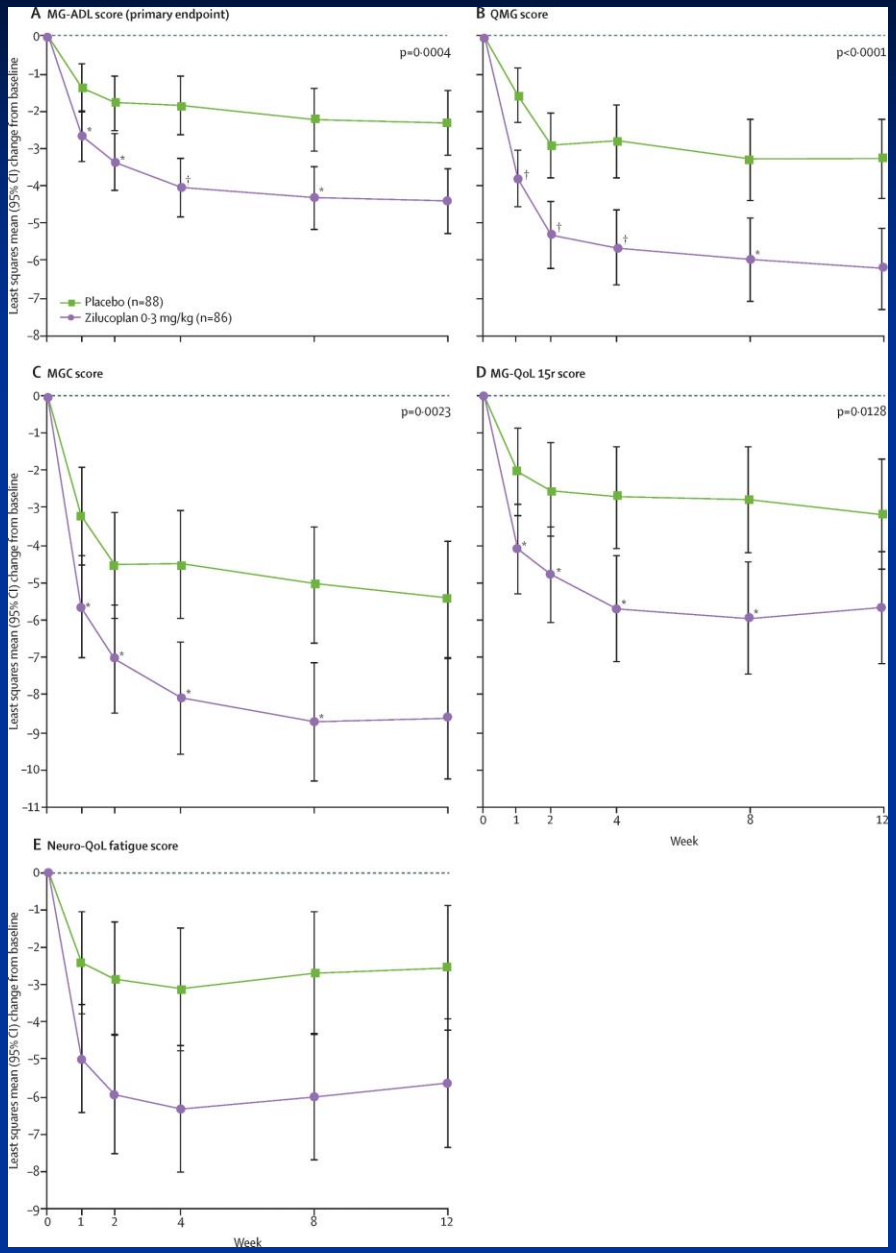


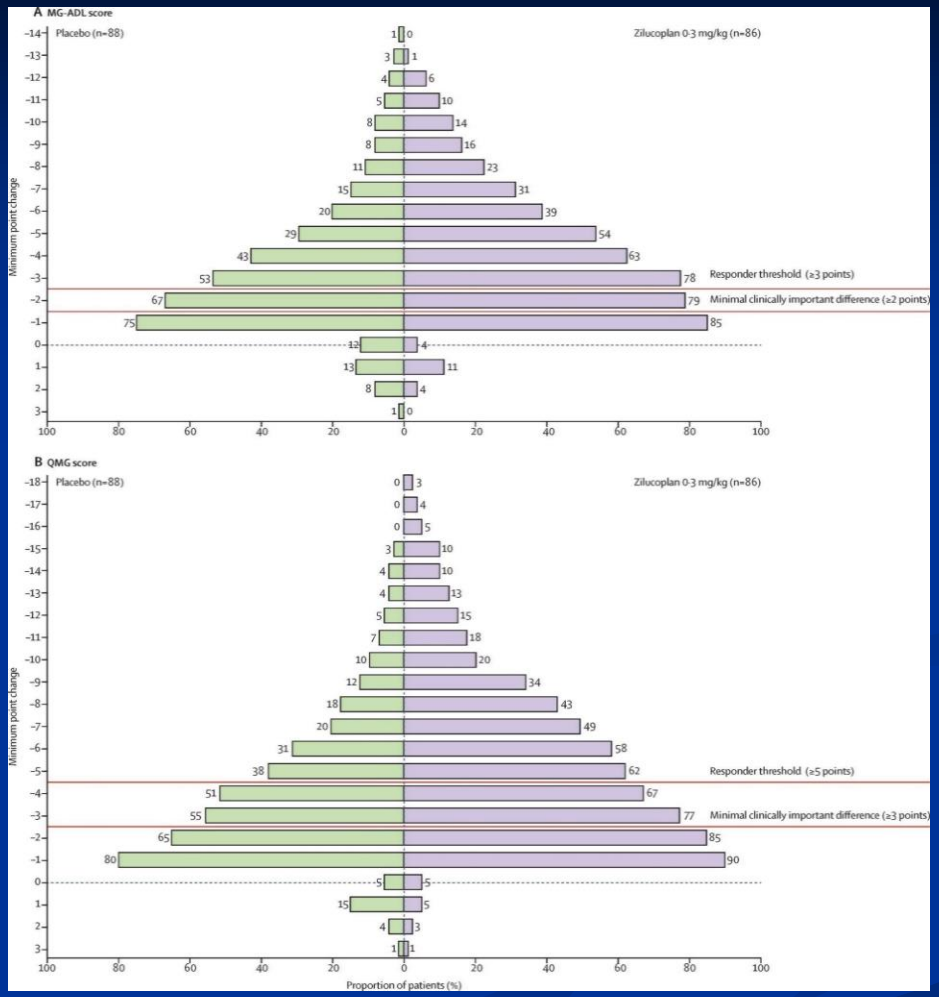
Figure 2. Trial Outcome Measures over Time, and Prespecified Responder Analyses at 26 Weeks.

Zilucoplan Phase 3 RAISE Trial

- n= 174 AChRAb+ gMG; MG-ADL≥6, QMG≥12
  - No thymectomy in prior 12 mos
  - 0.3 mg/kg sq qd vs placebo x 12 wks
  - Baseline QMG ~19 (sl worse than Phase 2 overall)
- Results
  - 1º Δ MG-ADL -4.39 vs -2.30 at wk 12 (p=0.0004)
    - 73% vs. 46% with MG-ADL decrease of ≥3 pts (p=0.0005)
    - 58% vs. 33% with QMG decrease of ≥5 pts (p=0.0012)
  - 2º: QMG, MGC, MG-QOL15r also hit statistical significance vs placebo
- AEs
  - HA ~15% in both arms; 23% in open label data
  - Injection site rxns 33% active vs. 15% placebo
  - <5% treatment-emergent AEs leading to withdrawal
  - Anti-drug Ab in 2 zilucoplan pts: no apparent impact
  - 1 death per arm: cerebral bleed on placebo; COVID-19 on active
    - Howard JF et al. *Lancet Neurology* 2023;23:395-406

Zilucoplan Phase 3 RAISE Trial





Howard JF et al. *Lancet Neurology* 2023;23:395-406

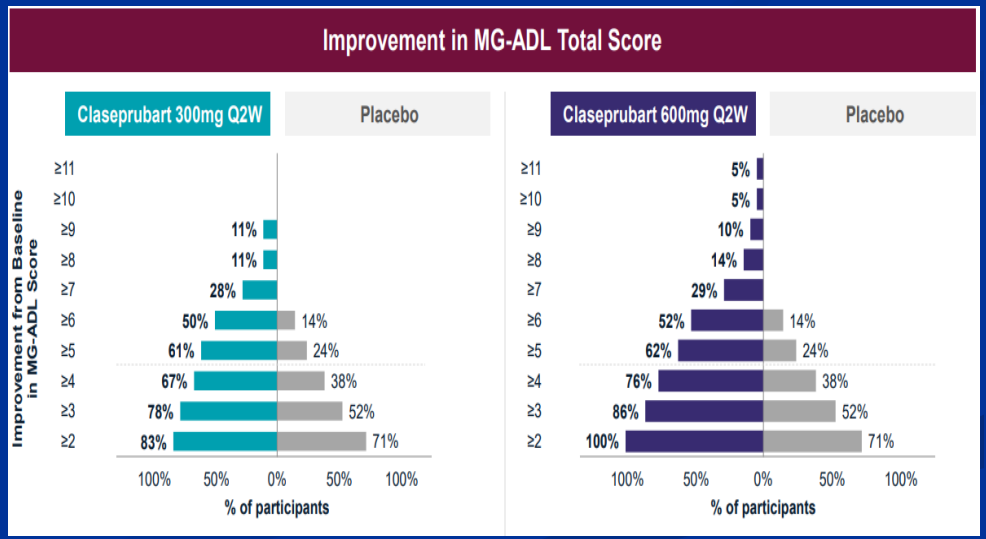
FDA approval for AChRAb+ gMG on 10/17/23
[5th distinct agent approved for gMG since 2017]

Claseprubart Phase 2 GMG Trial

- MAb that targets active form of C1s; selectively impacts classical pathway
- n=65 AChRAb+
- 300 or 600 mg sq q2wk to wk13
- Significant reductions in MG-ADL & QMG
  - MG-ADL improvement by wk 1
  - No significant difference between the two doses
- AEs
  - No infection signal
  - No SAEs
- Agent also in studies for CIDP (Phase 3) , MMN (Phase 2)

Efficacy Summary at Week 13

	Placebo N=22	Claseprubart 300mg Q2W N=21		Claseprubart 600mg Q2W N=22	
		Absolute	Placebo-Adjusted	Absolute	Placebo-Adjusted
MG-ADL mean change from baseline	-2.8	-4.6	-1.8 (P=0.0113)*	-5.4	-2.6 (P=0.0006)*
QMG mean change from baseline	-2.0	-4.4	-2.4 (P=0.0144)*	-4.5	-2.5 (P=0.0111)*
MSE	14%	37%	23% (P=0.0550)*	27%	13% (P=0.1031)
MGC mean change from baseline	-3.1	-8.7	-5.6 (P=0.0008)*	-8.6	-5.5 (P=0.0008)*
MG-QoL-15r mean change from baseline	-3.9	-6.1	-2.2 (P=0.0414)*	-5.4	-1.5 (P=0.1122)



Dianthus Therapeutics press release, 9/8/25

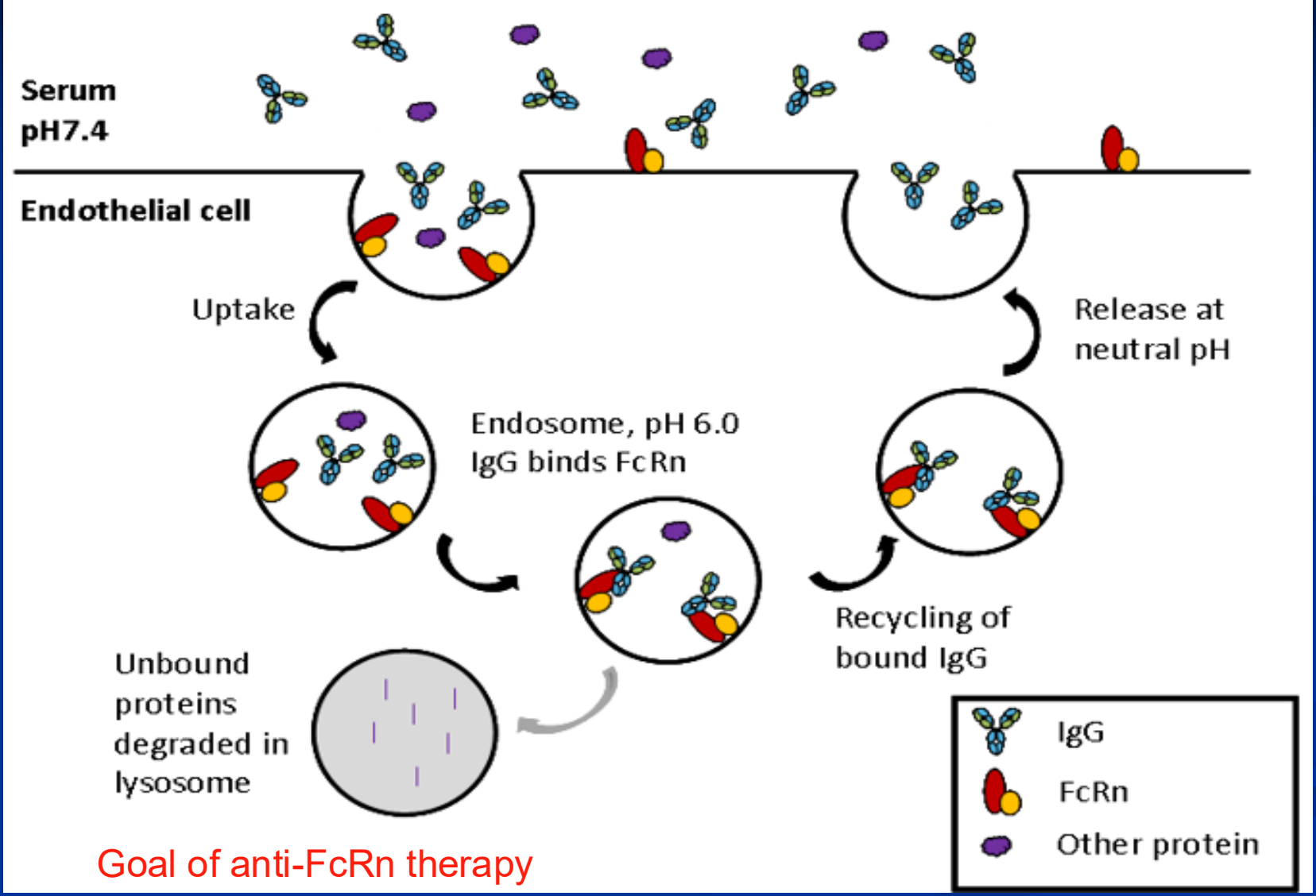
Advisory Cmte on Immunization Practices (ACIP)

Neisseria meningitides

Serogroup	Vaccine brand	Schedule (given IM)
ACWY (MenACWY) "Conjugate/Quadrivalent"	Menquadfi (replaced Menactra)	Initial: 2 doses separated by 2 mos Booster: q5 yrs
	Menveo	Same as above
B (MenB)	Bexsero	Initial: 2-3 doses with last at 6 mos Booster: 1 yr; then q2-3 yrs
Don't switch between MenB vaccines	Trumenba	Initial: 3 doses @ 0, 1-2, 6 mos Booster: 1 yr; then q2-3 yrs

Pentavalant Penbraya vaccine now FDA approved

Background: Anti-FcRn Strategy



Goal of anti-FcRn therapy

Reviewed in Wolfe GI et al. *J Neurol Sci* 2021;430:118074

Efgartigimod in MG

- Phase 3 ADAPT trial
- n=167 (77% AChRAb+)
  - Efgartigimod 10 mg/kg IV qwk x4 wks vs. placebo
    - Re-treat per clinical response (MG-ADL ≥5; lost response) no sooner than 8 wks
- Results [*4 consecutive wks]

Outcome at 26 wks	Efgartigimod	Placebo
MG-ADL ≥2 pt drop in AChRAb+ (1°)*	68%	30% (p<0.0001)
QMG ≥3 pt drop*	63%	14% (p<0.0001)
MSE (MG-ADL 0 or 1)	40%	11% (p<0.0001)

  - All MG Ab subgroups responded
  - Onset in first 2 wks in 57% vs. 25% on placebo
    - 23% with 8-11 wk durable response measured by MG-ADL
    - 34% with ≥12 wk durable response
  - Well tolerated (28% with HA in both groups; fewer SAEs on active Rx, 5% vs. 8%)
    - Howard JF et al. *Lancet Neurol* 2021;20:526-536

Efgartigimod in MG

- First in class FDA approval 12/17/21
- Adult AChRAb+ gMG patients
  - 1/26 update: SNMG approval based on further studies
- 10mg/kg IV qwk x 4wk cycles
  - Safety of repeat cycle within 50d of start of prior cycle unknown
- Warnings/AEs
  - Delay if active infection
  - ≥10%: RTI, UTI, headache

Efgartigimod IV q2 wks vs fixed cycles q8 wks

- n=69, ≥18 yo, AChRAb+, MG-ADL ≥5
  - n=52 on q2 wk schedule
- 1° ΔMG-ADL at wk 21
- Results

Outcome	q2 wks	Fixed cycles
ΔMG-ADL	-4.6	-5.1
MG-ADL decrease of ≥5 pts during study	73.1%	88.2%
MSE @ any time	44.2%	47.1%

- Study D/Cs
  - 2 in each arm

- Habib AA et al. *Ann Clin Transl Neurol* 2025; doi:10.1002/acn3.70051

Rozanolixizumab in MG

- Phase 3 MycarinG study (n=200); humanized IgG4
  - 7 mg/kg vs. 10 mg/kg vs placebo sq infusion qwk x6 wks
    - Included AChR and MuSK-Ab+ subjects
    - MG-ADL≥3 non ocular; QMG≥11
  - Results
    - 1° MG-ADL ~ -3.4 pt for both active arms vs. -0.8 ($p<0.001$) at day 43
      - All 12 MuSK pts on active Rx were MG-ADL responders
      - Improvements by day 8
    - QMG, MGC, MG Symptoms PRO significantly improved ($p\leq0.0002$)
    - HA 45% vs. 38% vs. 19% (placebo)
      - Mostly after 1st dose
    - Diarrhea, pyrexia, nausea other common AEs
    - SAEs 5% vs. 19% vs. 5% (placebo)
    - No serious infections in active arms
    - No deaths
    - FDA approval in June 2023 for AChR and MuSK Ab+ pts
      - Bril V et al. *Lancet Neurology* 2023;22:383-394

Rozanolixizumab in MG

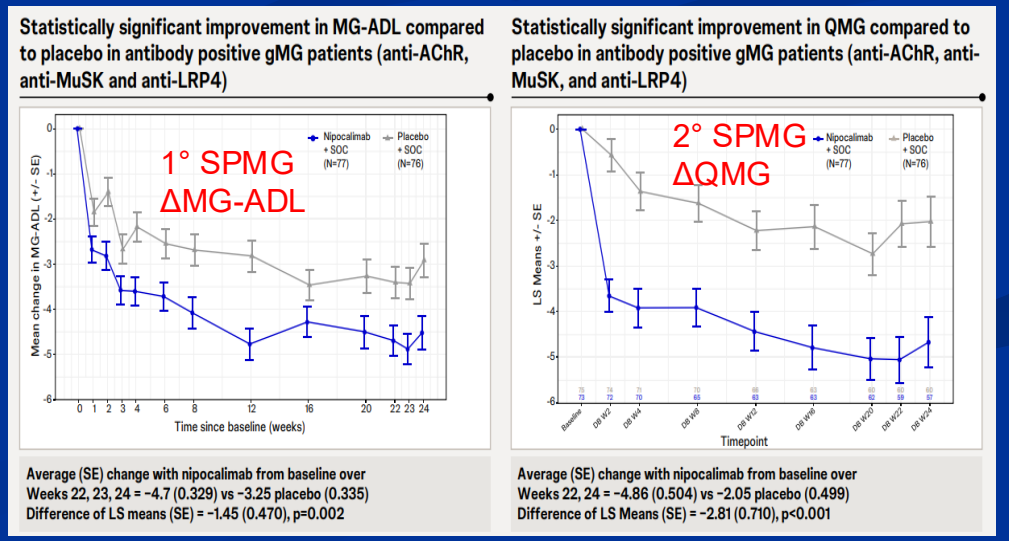
- FDA approved label
  - Adult AChRAb+ & MuSKAb+ GMG

Pt wt (kg)	Dose	Volume (sq)
<50	420 mg	3 mL
50 to <100	560 mg	4 mL
≥100	840 mg	6 mL

- Cycles
  - 6 weekly sq infusions (<15 min)
  - ≥63 days from start of prior cycle
  - 90% of pts had longer intervals

Anti-FcRn: Nipocalimab (IgG1)

- Phase III Vivacity trial, n=153 seropositive
- AChR, MuSK, LRP4 Abs; separate SNMG analysis
  - 88% AChRAb+ and 11% MuSKAb+
- MG-ADL ≥6
- IV q2wks to wk 24 (30 mg/kg load; then 15 mg/kg)
- 2º outcome: sustained response of ≥2 pt MG-ADL drop from wk 4 to 24 (2 excursions allowed)
  - 56% vs. 26% placebo
- AEs
  - HA 14% vs. 17% placebo
  - Severe infection 3-4%
  - No hypoalbuminemia
  - Edema 11% vs. 2% placebo
  - Agent does not cross placenta



Antozzi C et al. *Lancet Neurol* 2025;24:105-116

Anti-FcRn: Nipocalimab (IgG1)

- Open label Phase 2/3 in pediatric gMG
- n=7, mean MG-ADL ~4
- MG-ADL improved by >2 pts by wk 4-24
- Well tolerated
  - No SAEs thru wk 24

    - Strober J. MGFA Scientific Session, 10/15/24

Anti-FcRn: Nipocalimab (IgG1)

- FDA approval on April 29, 2025
- GMG ≥12 yo with AChRAb or MuSKAb
- Dosing
  - 30 mg/kg IV loading dose (30 min)
  - 15 mg/kg IV q2 wks thereafter

Anti-FcRn: Batoclimab (IMVT-1401)

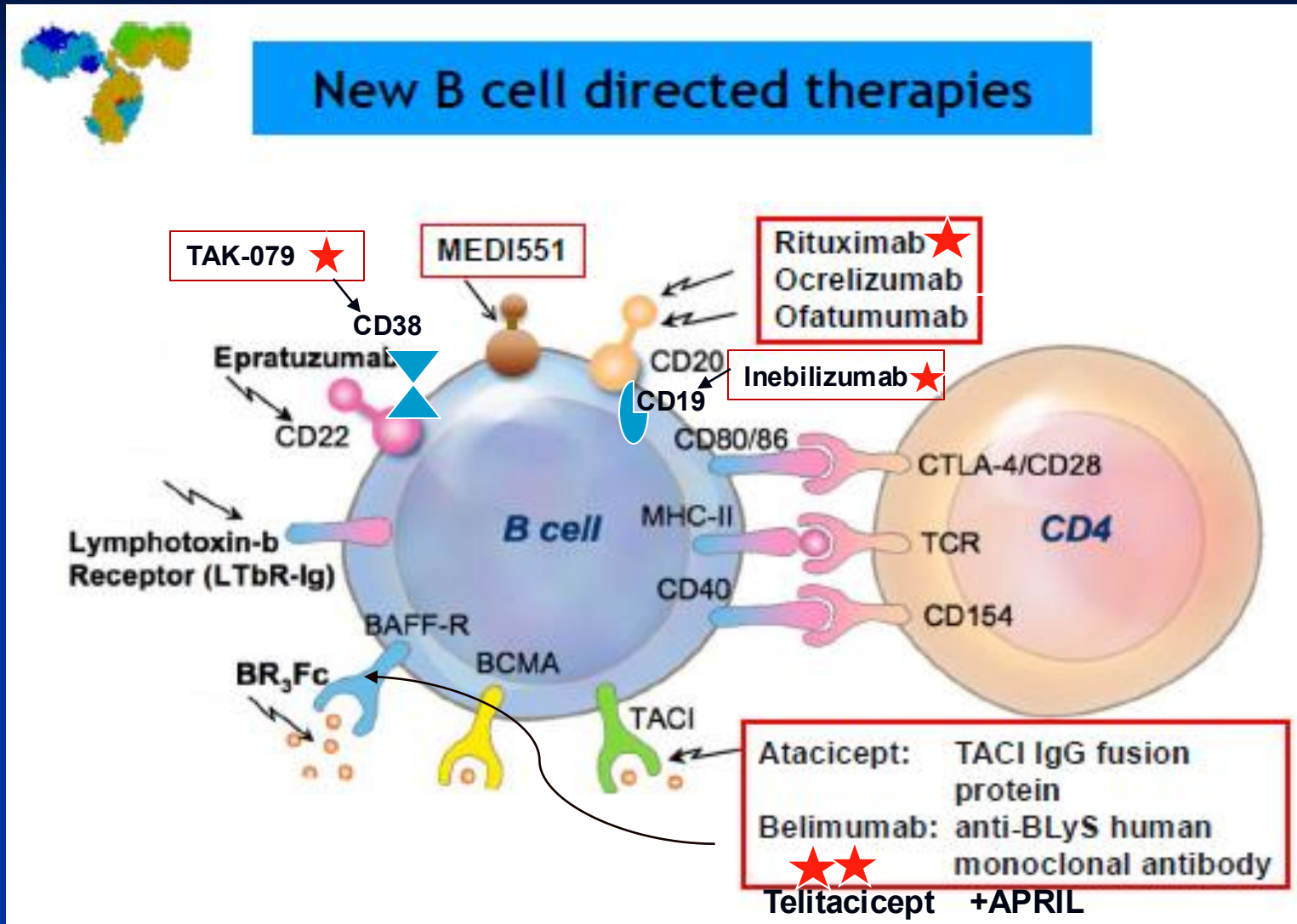
- Phase 3 1:1:1 study of 680 mg:340mg:placebo sq injection qwk x 12 wks followed by 340 mg wk:340 mg qowk: placebo in initial responders x 12 wks (MG-ADL ≥2 pt reduction)
- 1º ΔMG-ADL from baseline at wk 12
- Results
  - 5.6 point improvement on higher dose (74% mean IgG reduction)*
  - 4.7 point improvement on lower dose (64% mean IgG reduction)*
  - 3.6 point improvement on placebo

Outcome	Placebo	340 mg qwk*	680 mg qwk*
MSE at wk 12	7%	31%	42%
ΔMG-ADL ≥5 drop at wk 12	11%	25%	40%

  - Higher dose superior on second randomization
  - AE/safety data consistent with prior experience

    - Topline results press release 3/19/25

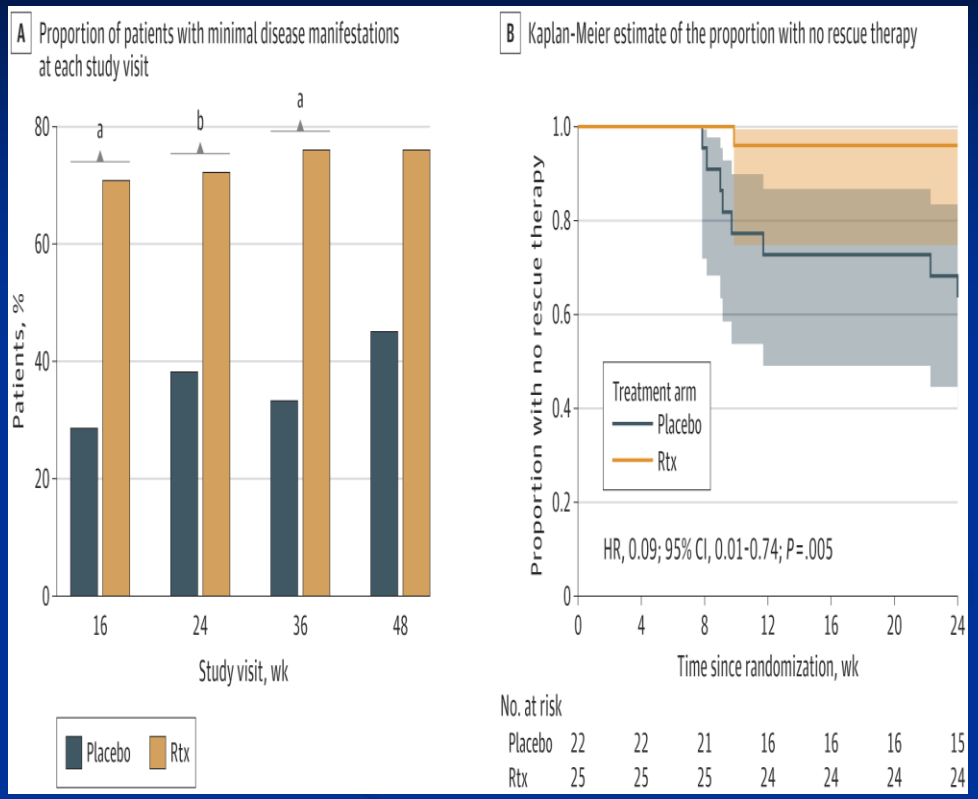
Monoclonal Ab approaches in MG



Courtesy of Hans-Peter Hartung, MD, FRCP

Rituximab in new-onset gMG (RINOMAX)

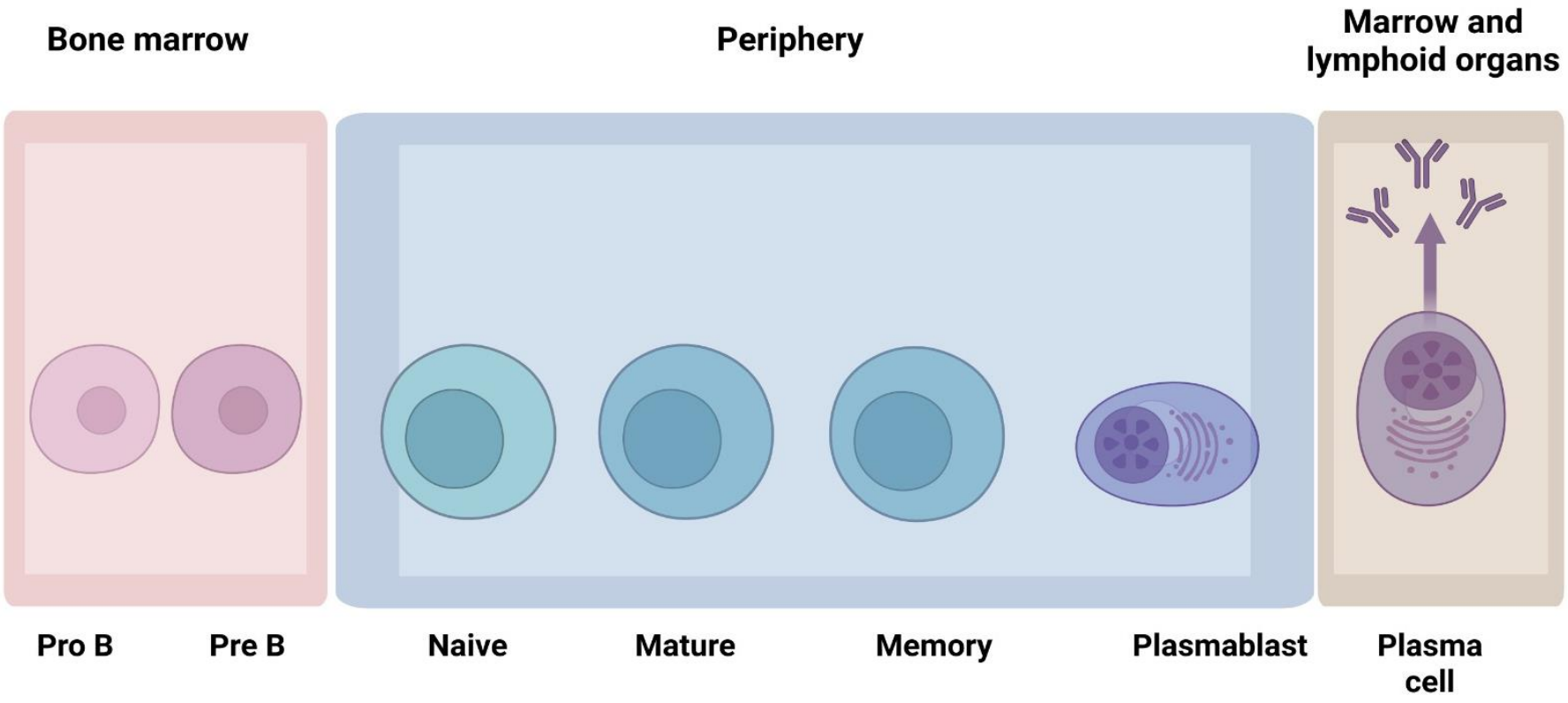
- n=47 (only 2 not AChRAb+); ≤12 mos sx, MGFA 2-4
- QMG ≥6 (9.4 at BL)
- RTX 500 mg x1
- 1° minimal dz manifestations at wk 16
  - Prednisolone tapered to ≤10 mg/d (max at entry 40 mg/d)
  - No rescue Rx wks 9-16 including prednisolone bump
  - QMG ≤4
- Results
  - 1°: 17/24 (71%) RTX vs. 6/21(29%) placebo (p=0.007)
  - 2°: QMG, MG-ADL, MG-QOL did not reach significance
  - Rescues/hospitalization only with placebo: 3x as many placebo pts with censored data for rescue



6 SAEs on RTX vs. 4 on placebo
1 fatality on RTX (cardiac event in pt with known heart dz)

Piehl F et al. *JAMA Neurology* 2022.2887

B-cell Lineage Comparison

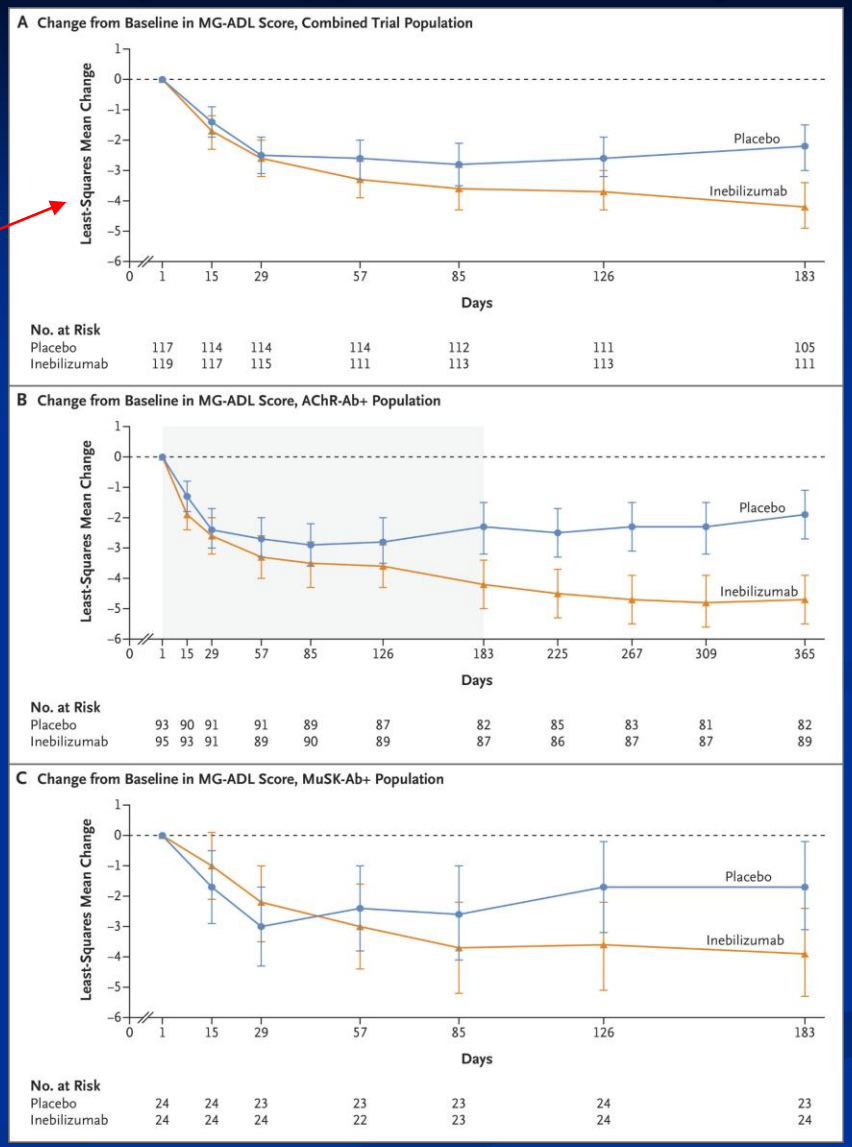


Inebilizumab in MG

- Monoclonal Ab to CD19
  - FDA approval for adult AChR and MuSK Ab+ GMG in December 2025
    - Prescreen for Hep B, TB, quantitative Ig
  - Phase 3 MINT study of AChR (n=172) and MuSK Ab+ MG (n=80); largest MG trial to date
    - MG-ADL≥6; QMG ≥11
    - AChRAb+: 300 mg IV on Days 1, 15, & 183 with q6 mos in OLE
    - MuSKAb+: 300 mg IV on Days 1 & 15 with q6 mos in OLE
    - 1°: ΔMG-ADL @ 26 wks for combined AChRAb+ & MuSKAb+ populations
    - Specified steroid taper to 5 mg qd from wk 4 to 24; 40 mg qd max dose at entry

Inebilizumab in MG (FDA approval 12/11/25)

- n=238 (190 AChRAb+; 48 MuSKAb+)
- Results
  - Baseline MG-ADL ~9
  - 1º: ΔMG-ADL -4.2 vs. -2.2 placebo ($p < 0.001$) for AChRAb+ & MuSKAb+ cohorts at wk 26
  - ΔQMG score -4.8 vs. -2.3 placebo ($p = 0.001$)
  - Prednisone: 87.4% vs. 84.6% on placebo hit 5 mg target
- AEs
  - No new safety signals
  - Similar safety events vs. placebo
    - HA, cough, nasopharyngitis, infusion-related rxns, UTIs
    - Fewer SAEs on inebilizumab (8.4 vs. 13.4%)



Nowak RJ et al. *NEJM* 2025;392:2309-2320
Editorial: Wolfe GI & Shelly S. *NEJM* 2025;392:2382-2384

Role of Newer Agents

- Refractory patients
  - Eculizumab trial program; refractory pts did as well or better as non-refractory in zilucoplan trial
- Exacerbations/impending & manifest crisis
  - Rapid onset
    - Caveat of *N. meningitides* vaccination for C' inhibitors; could cover x2 wks with penicillin/3rd generation cephalosporin
    - Avoid ciprofloxacin
- Steroid-sparing
  - Bridge therapy akin to IVIg
  - Longer term maintenance
  - Some agents easier to use with PE/IVIg
- Pregnancy (Nipocalimab)

Apples vs. Oranges vs. Strawberries

Outcome (time pt)	Eculizumab (26 wk)*	Ravulizumab (26 wk)	Efgartigimod IV (4 wk)	Rozanolixizumab (6 wk)	Zilucoplan (12 wk)	Nipocalimab (22-24 wks)
QMG ≥5 pt drop	45% (1.67x placebo)	30% (2.65x placebo)	60% (5.0x placebo)	47% (avg of 2 doses; 3.1x placebo)	62% (1.63x placebo)	42-46% (12-15% placebo)
MG-ADL ≥5 pt drop	45% (1.66x placebo)	31% (2.1x placebo)	55% (4.58x placebo)	31% (avg of 2 doses; 3.1x placebo)	54% (1.86x placebo)	44-48% (20-25% placebo)
MG-ADL ≥3 pt drop	60% (1.5x placebo)	57% (1.66x placebo)	73% (1.97x placebo)	57% (avg of 2 doses; 3.0x placebo)	78% (1.47x placebo)	60-69% (36-48% placebo)
NNT QMG ≥3 pt drop	6.3*	4.37	2.21 (p<0.05 vs. others)	5.39	4.03	N/A
NNT MG-ADL ≥3 pt drop	5.0*	4.39	2.73	2.59	3.61	N/A
MG-QOL15r	N/A	-3.30 vs. -1.60	-7.30 vs. -2.30 (p<0.0001)	-4.0/-5.3 vs. -1.3 (p significant)	-5.65 vs. -3.16 (p=0.013)	N/A
EQ-5D VAS	N/A	4.0 vs. 2.7	15.8 vs. 4.1 (p<0.0001)	12.2/11.4 vs. 6.1 (p significant)	N/A	N/A

NNH similar across treatments; some with lower AE risk than placebo (efgartigimod/zilucoplan)

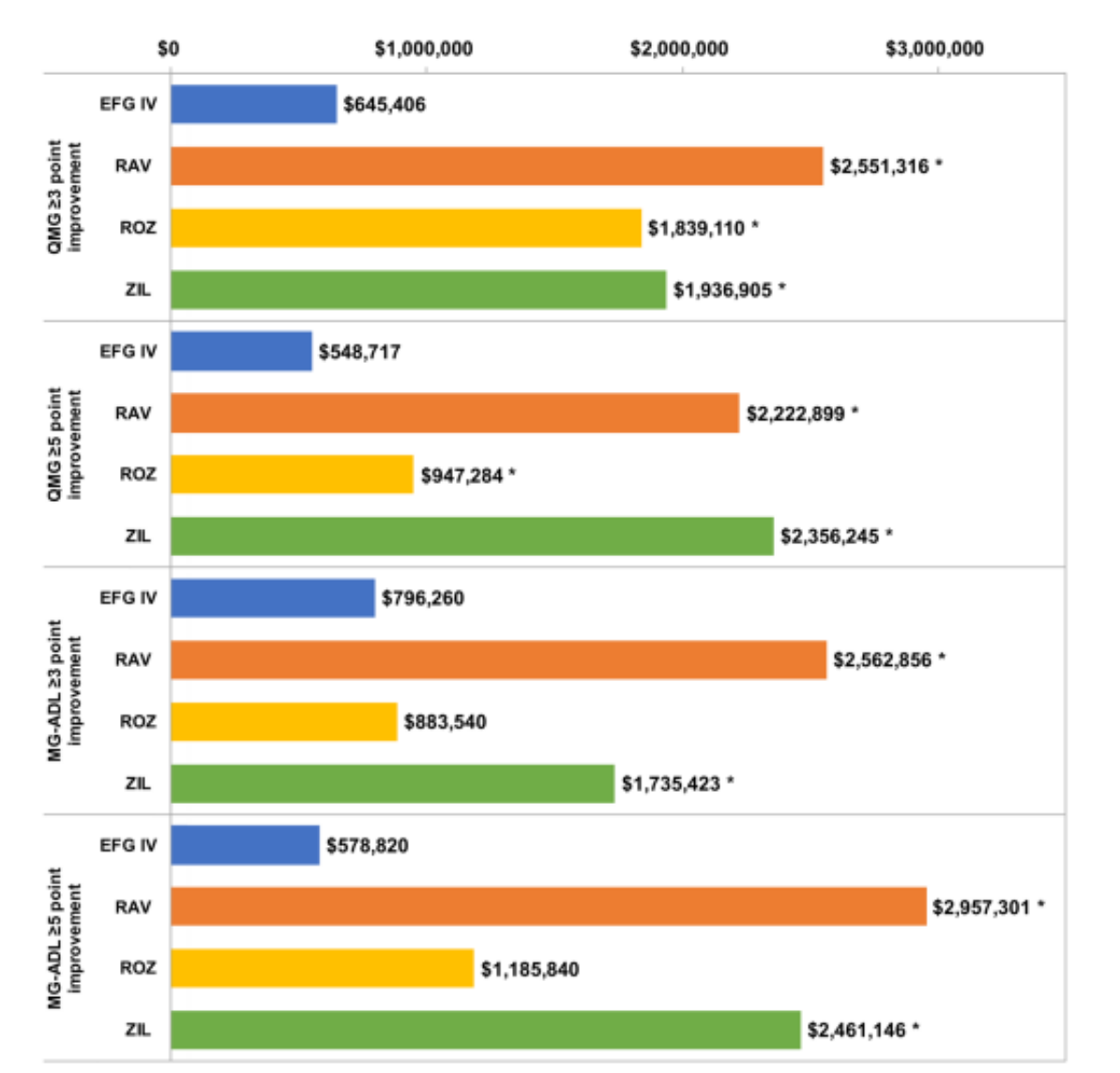
*Only refractory subjects enrolled

Smith AG, Wolfe GI, Habib AA et al. *Adv Ther* 2024;10.1007 [PMID:39470879] for NNT/NNH

Approximate Yearly Costs

Medication	Cost per unit	Yearly estimated cost
Rituximab (biosimilar, non-FDA approved)	$764 per 100 mg	1000mg twice then once in six months, total cost = $23,000
Eculizumab	$6820 per 300 mg	900mg loading then 1200mg Q2wks, total cost = $737,000
Ravulizumab	$6695 per 100 mg	For 80 kg pt, loading dose plus 6 treatment, total cost = $502,000
Efgartigimod	$5950 per 400 mg	For 80 kg pt, 7 cycles, total cost = $333,000
Efgartigimod Hyaluronidase	$ 15773 per 1008 mg	7 cycles, total cost = $442,000
Rozanolixizumab	$6050 per 280 mg	For 80 kg pt, 5.7 cycles, total cost = $414,000
Zilucoplan	$1047 per 23 mg	For 70 kg pt, total cost = $366,645
Intravenous immunoglobulins (non-FDA approved)	$200 per gram	For 80 kg pt, loading dose plus monthly treatment, total cost = $208,000

Cost Per Improved Outcome (CPIO)



Smith AG, Wolfe GI, Habib AA et al. *Adv Ther* 2024;10.1007 [PMID:39470879]

Traditional Vs. New Targeted MG Treatments
AChRAb+ GMG Achieving MMS/MSE

Traditional Medications			
	MM or Better	**Time**	**Study Type**
Prednisone	Combo with below		
Mycophenolate[1]	60% 80%	7-12 mo. 19-24 mo.	Retrospective
Azathioprine[2]	60-90%	6 – 24 mo.	RCT
Rituximab[3-5]	60-75% (AChR) 67% (MuSK)	4-6 mo.	RCT/Retro Retrospective

Next Gen Treatments			
	MM or MSE	**Time**	**Study Type**
Eculizumab[6, 7]	21%- 57%	6-24 mo.	RCT/OLE
Ravulizumab[8]	? Not reported		RCT/OLE
Zilucoplan[9]	19-39%	3-13 mo.	RCT/OLE
Efgartigimod[10]	40-45%	4-10 weeks	RCT/OLE
Rozanolixuzimab[11]	27-40%	6 weeks	Abstract only RCT/OLE

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Courtesy of M. Herir, Univ of Vermont

Intl Treatment Guidance in MG

Categories for 2021 update

- Thymectomy
- Ocular MG
- Rituximab
- Methotrexate
- Eculizumab
- Immune checkpoint inhibitors (AEs)

2026 update underway

- Voting commenced 2/25

VIEWS & REVIEWS | OPEN ACCESS | LEVEL OF RECOMMENDATION

International Consensus Guidance for Management of Myasthenia Gravis

2020 Update

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Neurology® 2021;96:114-122. doi:10.1212/WNL.0000000000011124

Abstract

Objective
To update the 2016 formal consensus-based guidance for the management of myasthenia gravis (MG) based on the latest evidence in the literature.

Methods
In October 2013, the Myasthenia Gravis Foundation of America appointed a Task Force to develop treatment guidance for MG, and a panel of 15 international experts was convened. The RAND/UCLA appropriateness method was used to develop consensus recommendations pertaining to 7 treatment topics. In February 2019, the international panel was reconvened with the addition of one member to represent South America. All previous recommendations were reviewed for currency, and new consensus recommendations were developed on topics that required inclusion or updates based on the recent literature. Up to 3 rounds of anonymous e-mail votes were used to reach consensus, with modifications to recommendations between rounds based on the panel input. A simple majority vote (80% of panel members voting "yes") was used to approve minor changes in grammar and syntax to improve clarity.

Results
The previous recommendations for thymectomy were updated. New recommendations were developed for the use of rituximab, eculizumab, and methotrexate as well as for the following topics: early immunosuppression in ocular MG and MG associated with immune checkpoint inhibitor treatment.

Conclusion
This updated formal consensus guidance of international MG experts, based on new evidence, provides recommendations to clinicians caring for patients with MG worldwide.

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Go to Neurology.org/N for full disclosures. Funding information and disclosures deemed relevant by the authors, if any, are provided at the end of the article.

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The Article Processing Charge was funded by the Myasthenia Gravis Foundation of America.

Narayanaswami P, Sanders DB, Wolfe G et al. *Neurology* 2021; 96:114-122 [PMID:33144515