SUPPLEMENTARY MATERIALS

Risk-Benefit Analysis of Novel Treatments for Patients with Generalized Myasthenia Gravis

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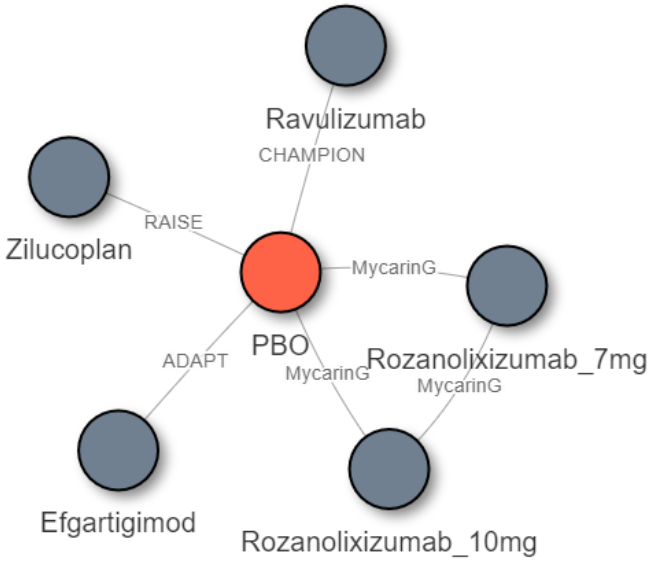
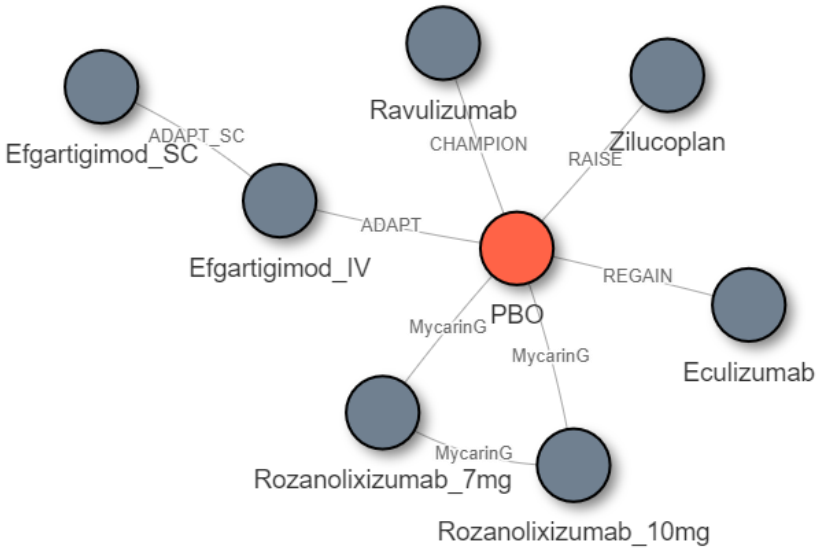
Supplementary Figure 1. NMA networks for the primary (a) and sensitivity (b) analyses.

a. NMA network of the primary analysis



b. NMA network of the sensitivity analysis



Abbreviations: IV, intravenous; NMA, network meta-analysis; PBO, placebo; SC, subcutaneous.

Supplementary Table 1. Summary of included trials

	ADAPT (NCT03669588)	CHAMPION-MG (NCT03920293)	MycarinG (NCT03971422)	RAISE (NCT04115293)	ADAPT-SC (NCT04735432)	REGAIN (NCT01997229)
Treatment[a]	-EFG IV -PBO	-RAV -PBO	-ROZ 10 mg/kg -ROZ 7 mg/kg -PBO	-ZIL -PBO	-EFG SC -EFG IV	-ECU -PBO
Study design	Phase III randomized double-blind trial	Phase III randomized double-blind trial	Phase III randomized double-blind trial	Phase III randomized double-blind trial	Phase III randomized open-label trial	Phase III randomized double-blind trial
Study population for the trial	Adults with gMG - MG-ADL score ≥5 - MGFA class II–IV	Adults with AChR Ab+ gMG - MG-ADL score ≥6 - MGFA class II–IV	Adults with AChR Ab+ or MuSK Ab+ gMG - MG-ADL score ≥3 - QMG score ≥11 - MGFA class II–IVa	Adults with AChR Ab+ gMG - MG-ADL score ≥6 - QMG score ≥12 - MGFA class II– IV	Adults with gMG - MG-ADL score ≥5 - MGFA class II–IV	Adults with AChR Ab+ gMG - MG- ADL score ≥6 - MGFA class II–IV - Refractory patients[b]
Sample size of the trial	N=167 - EFG IV: 84 - PBO: 83	N=175 - RAV: 86 - PBO: 89	N=200 (21 anti-MuSK Ab+) - ROZ 10 mg/kg: 67 - ROZ 7 mg/kg: 66 - PBO: 67	N=174 - Zilucoplan: 86 - PBO: 88	N=110 - EFG SC: 55 - EFG IV: 55	N=125 - ECU: 62 - PBO: 63
Key baseline characteristics for all patients	- Time since gMG diagnosis (years): 10.1 - MG-ADL: 9.0 - QMG: 15.9 - MGFA II: 40% - MGFA III: 56% - MGFA IV: 4%	- Time since gMG diagnosis (years): 9.9 - MG-ADL: 9.0 - QMG: 14.7 - MGFA II: 45% - MGFA III: 49% - MGFA IV: 6%	- Time since gMG diagnosis (years): 5.8 - MG-ADL: 8.3 - QMG: 15.6 - MGFA II: 39% - MGFA III: 57% - MGFA IV: 4%	- Time since gMG diagnosis (years): 9.1 - MG-ADL: 10.6 - QMG: 19.1 - MGFA II: 28% - MGFA III: 67% - MGFA IV: 5%	- Time since gMG diagnosis (years): 7.0 - MG-ADL: 8.7 - QMG: 15.2 - MGFA II: 46% - MGFA III: 49% - MGFA IV: 5%	- Time since gMG diagnosis (years): 9.6 - MG-ADL: 10.2 - QMG: 17.1 - MGFA II[c]: 38% - MGFA III: 53% - MGFA IV: 10%
Population used for the NMA	- AChR Ab+ gMG for efficacy - Overall trial population for safety	Overall trial population	- AchR Ab+ gMG for ≥3 points reduction in QMG and ≥2 points reduction in MG-ADL - Overall trial population for other outcomes	Overall trial population	- AChR Ab+ gMG for efficacy - Overall trial population for safety	Overall trial population
Sample size of population used for the NMA	N=129 for efficacy - EFG IV: 65 - PBO: 64 Overall trial population for safety	Overall trial population	N = 171 in AChR Ab+ subgroup: - ROZ 10 mg/kg: 55 - ROZ 7 mg/kg: 59 - PBO: 57 Overall trial population	Overall trial population	N=91 for efficacy - EFG SC: 45 - EFG IV: 46 Overall trial population for safety	Overall trial population

	ADAPT (NCT03669588)	CHAMPION-MG (NCT03920293)	MycarinG (NCT03971422)	RAISE (NCT04115293)	ADAPT-SC (NCT04735432)	REGAIN (NCT01997229)
Efficacy timepoint; safety timepoint	Week 4; Week 26	Week 26; Week 26	Week 6; Week 14	Week 12; Week 12	Week 4; Week 10	Week 26; Week 26

Abbreviations: Ab, antibody; AChR, acetylcholine receptor; ECU, eculizumab; EFG IV, efgartigimod intravenous; EFG SC, efgartigimod PH20 subcutaneous; gMG, generalized myasthenia gravis; IV, intravenous; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK, muscle-specific tyrosine kinase; NMA, network meta-analysis; PBO, placebo; QMG, Quantitative Myasthenia Gravis; RAV, ravulizumab; ROZ, rozanolixizumab; ZIL, zilucoplan.

Notes: [a] In all placebo-controlled trials, conventional therapy was used as background treatment(s) in both the active treatment and placebo arms.
[b] Refractory patients were defined by having received ≥2 immunosuppressive therapies, or ≥1 immunosuppressive therapy with IV immunoglobulin or plasma exchange given at least 4 times per year, for 12 months without symptom control.
[C] The percentages add up to more than 100% due to rounding issues.

Supplementary Table 2. Dosing schedules and cost inputs

Therapy	Dosing Schedule and Courses[a]	Annual Drug Costs[b,c]	Annual Admin Costs[b]	Annual Total Costs[d]
CT[e]	-	$1,843	$0	$1,843
Efgartigimod IV[f]	2.6 vials per infusion, 4 weekly infusions within a cycle; average of 4.6 cycles per year	$292,184	$1,452	$293,637
Ravulizumab	One loading dose of 2,786 mg (2.5 vials) at treatment start, followed by a maintenance dose of 3,387 mg (3 vials) every 8 weeks beginning 2 weeks after the loading dose for 50 weeks	$585,425	$862	$586,287
Rozanolixizumab	2.35 injection per infusion; 6 weekly infusions within a cycle; average of 4 cycles per year	$342,800	$433	$343,233
Zilucoplan	1 injection daily for 365 days	$482,166	$0	$482,166
Eculizumab	Weekly loading dose of 900 mg for 4 weeks, followed by a maintenance dose of 1,200 mg at week 5, and then every 2 weeks thereafter	$719,373	$2,249	$721,623
Efgartigimod PH20 SC[g]	4 weekly injections within a cycle; average of 4.6 cycles per year	$292,067	$332	$292,399

Abbreviations: admin, administration; AE, adverse event; CT, conventional therapy; IV, intravenous; SC, subcutaneous.

Notes: [a] For each treatment option, dosing schedule and treatment duration were based on evidence from their respective clinical trials and supplemented by real-world data as needed. Patients were assumed to be fully adherent to the prescribed regimen. [b] Drug and administration costs for all treatments were calculated based on the Wholesale Acquisition Cost from RED BOOK (IBM Watson Health. MicroMedex RED BOOK 2024. Available from: https://www.ibm.com/products/micromedex-red-book) and the 2024 Centers for Medicare & Medicaid Services Physician Fee Schedule (Centers for Medicare & Medicaid Services (CMS). 2024 Physician Fee Schedule. Available from: https://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/PhysicianFeeSched). [c] The weights distribution used for the drug cost calculation was informed by data on file from an Argenx ongoing study. [e] CT was comprised of monotreatment or combination treatments of acetylcholinesterase inhibitors and steroid and non-steroidal immunosuppressive drugs. The drug distributions were based on Argenx data on file from Symphony Integrated Dataverse (January 2014–December 2019) and Howard et al. (Howard JF, Jr., Utsugisawa K, Benatar M, Murai H, Barohn RJ, Illa I, 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):976-86). [f] Patients receiving efgartigimod IV treatment were assumed to follow an individualized dosing schedule based on clinical evaluation, as aligned with the intended clinical use of efgartigimod and the ADAPT trial design. Average number of treatment cycles, calculated based on a study of the real-world treatment patterns of efgartigimod IV, was considered in the model base-case (Qi C, Brauer E, Gelinas D, Goyal A, Bergin C, editors. Real-world usage patterns of Vyvgart in adults with generalized myasthenia gravis in the United States. 45th Annual Carrell-Krusen Neuromuscular Symposium; 2023 February 23–24, 2023; Dallas, TX, USA). [g] The total number of doses per year for efgartigimod PH20 SC was assumed to be the same as efgartigimod IV.

Supplementary Table 3. NMA results of efficacy outcomes for the primary and sensitivity analyses[a]

	Primary analysis	Sensitivity analysis
Effect on the proportion of patients with ≥3-point improvement in QMG, mean (95% CrI)		
Efgartigimod IV	0.45 (0.32, 0.55)	0.45 (0.32, 0.55)
Ravulizumab	0.23 (0.06, 0.38)	0.23 (0.06, 0.38)
Rozanolixizumab 7 mg/kg	0.11 (-0.07, 0.29)	0.11 (-0.07, 0.29)
Rozanolixizumab 10 mg/kg	0.31 (0.13, 0.46)	0.31 (0.13, 0.46)
Zilucoplan	0.25 (0.09, 0.39)	0.25 (0.09, 0.39)
Efgartigimod PH20 SC	-	0.47 (0.25, 0.60)
Effect on the proportion of patients with ≥5-point improvement in QMG, mean (95% CrI)		
Efgartigimod IV	0.52 (0.33, 0.67)	0.53 (0.33, 0.68)
Ravulizumab	0.27 (0.07, 0.48)	0.26 (0.07, 0.48)
Rozanolixizumab 7 mg/kg	0.35 (0.15, 0.55)	0.35 (0.15, 0.55)
Rozanolixizumab 10 mg/kg	0.37 (0.17, 0.57)	0.37 (0.17, 0.56)
Zilucoplan	0.21 (0.07, 0.36)	0.21 (0.07, 0.36)
Eculizumab	-	0.28 (0.09, 0.48)
Efgartigimod PH20 SC	-	0.46 (0.17, 0.68)
Effect on the proportion of patients with ≥2-point improvement in MG-ADL, mean (95% CrI)		
Efgartigimod IV	0.28 (0.14, 0.39)	0.28 (0.14, 0.39)
Ravulizumab	0.11 (-0.04, 0.25)	0.11 (-0.04, 0.25)
Rozanolixizumab 7 mg/kg	0.31 (0.18, 0.41)	0.31 (0.18, 0.40)
Rozanolixizumab 10 mg/kg	0.28 (0.14, 0.39)	0.28 (0.14, 0.39)
Zilucoplan	0.15 (-0.01, 0.28)	0.14 (-0.01, 0.28)
Efgartigimod PH20 SC	-	0.30 (-0.03, 0.46)
Effect on the proportion of patients with ≥3-point improvement in MG-ADL, mean (95% CrI)		
Efgartigimod IV	0.36 (0.20, 0.49)	0.36 (0.19, 0.49)
Ravulizumab	0.23 (0.07, 0.37)	0.22 (0.07, 0.37)
Rozanolixizumab 7 mg/kg	0.37 (0.21, 0.50)	0.37 (0.21, 0.50)
Rozanolixizumab 10 mg/kg	0.39 (0.23, 0.51)	0.39 (0.23, 0.51)
Zilucoplan	0.27 (0.12, 0.41)	0.27 (0.12, 0.41)
Eculizumab	-	0.20 (0.03, 0.36)
Efgartigimod PH20 SC	-	0.34 (0.02, 0.55)
Effect on the proportion of patients with ≥5-point improvement in MG-ADL, mean (95% CrI)		
Efgartigimod IV	0.50 (0.29, 0.68)	0.50 (0.30, 0.68)
Ravulizumab	0.20 (0.04, 0.40)	0.21 (0.04, 0.40)
Rozanolixizumab 7 mg/kg	0.28 (0.07, 0.52)	0.29 (0.07, 0.52)
Rozanolixizumab 10 mg/kg	0.31 (0.10, 0.54)	0.31 (0.10, 0.54)
Zilucoplan	0.20 (0.07, 0.35)	0.21 (0.07, 0.36)

	Primary analysis	Sensitivity analysis
Eculizumab	-	0.18 (0.02, 0.37)
Efgartigimod PH20 SC	-	0.59 (0.34, 0.75)
Effect on change in QMG from baseline, mean (95% CrI)		
Efgartigimod IV	-5.20 (-6.77, -3.62)	-5.21 (-6.77, -3.62)
Ravulizumab	-2.00 (-3.27, -0.73)	-2.00 (-3.26, -0.72)
Rozanolixizumab 7 mg/kg	-3.47 (-5.36, -1.57)	-3.45 (-5.37, -1.58)
Rozanolixizumab 10 mg/kg	-4.74 (-6.64, -2.84)	-4.73 (-6.63, -2.81)
Zilucoplan	-2.93 (-4.47, -1.38)	-2.94 (-4.47, -1.41)
Eculizumab	-	-3.01 (-4.67, -1.33)
Efgartigimod PH20 SC	-	-6.35 (-8.67, -4.01)
Effect on change in MG-ADL score from baseline, mean (95% CrI)		
Efgartigimod IV	-2.85 (-3.82, -1.88)	-2.86 (-3.83, -1.87)
Ravulizumab	-1.70 (-2.75, -0.65)	-1.70 (-2.74, -0.64)
Rozanolixizumab 7 mg/kg	-2.58 (-3.94, -1.22)	-2.57 (-3.95, -1.22)
Rozanolixizumab 10 mg/kg	-2.61 (-3.97, -1.26)	-2.60 (-3.97, -1.24)
Zilucoplan	-2.08 (-3.32, -0.84)	-2.09 (-3.32, -0.86)
Eculizumab	-	-1.91 (-3.29, -0.51)
Efgartigimod PH20 SC	-	-3.57 (-5.06, -2.08)
Effect on change in MGC score from baseline, mean (95% CrI)		
Efgartigimod IV	-6.04 (-8.76, -3.31)	-6.04 (-8.75, -3.33)
Rozanolixizumab 7 mg/kg	-3.91 (-6.42, -1.37)	-3.88 (-6.44, -1.32)
Rozanolixizumab 10 mg/kg	-5.54 (-8.09, -3.00)	-5.51 (-8.07, -2.94)
Zilucoplan	-3.19 (-5.44, -0.90)	3.19 (-5.44, -0.93)
Eculizumab	-	-3.30 (-5.97, -0.63)

Abbreviations: Ab, antibody; AChR, acetylcholine receptor; CrI, credible interval; gMG, generalized myasthenia gravis; IV, intravenous; MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGC, Myasthenia Gravis Composite; MuSK, muscle-specific tyrosine kinase; NNT, number needed to treat; QMG, Quantitative Myasthenia Gravis; SC, subcutaneous.

Note: [a] For rozanolixizumab, the effect on the proportions of patients with ≥3-point improvement in QMG and ≥2-point improvement in MG-ADL were estimated based on patients with AChR Ab+ gMG, and other outcomes were estimated based on patients with AChR Ab+ or MuSK Ab+ gMG due to lack of data. For eculizumab, all outcomes were estimated based on patients with anti-AChR Ab+ refractory gMG due to lack of data. For all other drugs, all outcomes were estimated based on patients with anti-AChR Ab+ gMG.

Supplementary Table 4. NMA results of safety outcomes for the primary and sensitivity analyses

	Primary analysis	Sensitivity analysis
Effect on the proportion of patients with SAE, mean (95% CrI)		
Efgartigimod IV	-0.04 (-0.11, 0.08)	-0.05 (-0.14, 0.10)
Ravulizumab	0.07 (-0.03, 0.21)	0.08 (-0.03, 0.24)
Rozanolixizumab 7 mg/kg	0.00 (-0.10, 0.17)	0.00 (-0.11, 0.20)
Rozanolixizumab 10 mg/kg	0.03 (-0.08, 0.22)	0.04 (-0.09, 0.25)
Zilucoplan	-0.01 (-0.08, 0.10)	-0.01 (-0.10, 0.11)
Eculizumab	-	-0.07 (-0.13, 0.00)
Efgartigimod PH20 SC	-	0.06 (-0.12, 0.43)
Effect on the proportion of patients with TEAE, mean (95% CrI)*		
Efgartigimod IV	-0.10 (-0.28, 0.05)	-0.09 (-0.28, 0.05)
Ravulizumab	0.06 (-0.10, 0.16)	0.06 (-0.10, 0.16)
Rozanolixizumab 7 mg/kg	0.10 (-0.01, 0.18)	0.10 (-0.01, 0.18)
Rozanolixizumab 10 mg/kg	0.11 (0.01, 0.18)	0.11 (0.01, 0.18)
Zilucoplan	0.05 (-0.07, 0.13)	0.05 (-0.07, 0.13)
Eculizumab	-	-
Efgartigimod PH20 SC	-	0.03 (-0.18, 0.16)
Effect on the proportion of patients with headache, mean (95% CrI)		
Efgartigimod IV	0.02 (-0.09, 0.15)	0.01 (-0.09, 0.15)
Ravulizumab	-0.06 (-0.15, 0.05)	-0.06 (-0.14, 0.05)
Rozanolixizumab 7 mg/kg	0.28 (0.10, 0.48)	0.28 (0.10, 0.47)
Rozanolixizumab 10 mg/kg	0.21 (0.03, 0.40)	0.20 (0.03, 0.40)
Zilucoplan	0.00 (-0.12, 0.16)	0.00 (-0.12, 0.15)
Eculizumab	-	-0.02 (-0.14, 0.15)
Efgartigimod PH20 SC	-	0.03 (-0.15, 0.30)
Effect on the proportion of patients with nasopharyngitis, mean (95% CrI)*		
Efgartigimod IV	-0.03 (-0.07, 0.03)	-0.03 (-0.08, 0.04)
Rozanolixizumab 7 mg/kg	-0.05 (-0.11, 0.10)	-0.05 (-0.12, 0.12)
Rozanolixizumab 10 mg/kg	0.08 (-0.05, 0.39)	0.09 (-0.06, 0.42)
Zilucoplan	0.09 (-0.05, 0.41)	0.10 (-0.06, 0.42)
Eculizumab	-	0.00 (-0.07, 0.11)
Effect on the proportion of patients with nausea, mean (95% CrI)		
Efgartigimod IV	-0.01 (-0.07, 0.08)	-0.02 (-0.08, 0.09)
Ravulizumab	0.01 (-0.05, 0.13)	0.01 (-0.06, 0.14)
Rozanolixizumab 7 mg/kg	0.02 (-0.07, 0.20)	0.02 (-0.07, 0.21)
Rozanolixizumab 10 mg/kg	0.07 (-0.04, 0.28)	0.07 (-0.05, 0.30)
Zilucoplan	0.03 (-0.05, 0.19)	0.03 (-0.06, 0.20)

	Primary analysis	Sensitivity analysis
Eculizumab	-	0.00 (-0.07, 0.12)
Efgartigimod PH20 SC	-	-0.10 (-0.13, -0.07)
Effect on the proportion of patients with diarrhea, mean (95% CrI)		
Efgartigimod IV	-0.03 (-0.08, 0.07)	-0.03 (-0.09, 0.07)
Ravulizumab	0.03 (-0.04, 0.15)	0.03 (-0.05, 0.16)
Rozanolixizumab 7 mg/kg	0.10 (-0.01, 0.28)	0.11 (-0.01, 0.29)
Rozanolixizumab 10 mg/kg	0.03 (-0.05, 0.16)	0.03 (-0.05, 0.17)
Zilucoplan	0.31 (0.03, 0.72)	0.33 (0.03, 0.75)
Eculizumab	-	0.01 (-0.07, 0.15)
Efgartigimod PH20 SC	-	-0.07 (-0.12, 0.09)
Effect on the proportion of patients with URTI, mean (95% CrI)*		
Efgartigimod IV	0.11 (-0.02, 0.35)	0.12 (-0.02, 0.40)
Ravulizumab	0.07 (-0.02, 0.22)	0.08 (-0.02, 0.26)
Rozanolixizumab 7 mg/kg	0.04 (-0.04, 0.23)	0.05 (-0.06, 0.29)
Rozanolixizumab 10 mg/kg	0.05 (-0.04, 0.24)	0.06 (-0.05, 0.31)
Zilucoplan	0.09 (-0.01, 0.26)	0.10 (-0.01, 0.31)
Eculizumab	-	-0.01 (-0.06, 0.07)
Effect on the proportion of patients with UTI, mean (95% CrI)		
Efgartigimod IV	0.07 (-0.02, 0.28)	0.07 (-0.02, 0.28)
Ravulizumab	0.03 (-0.03, 0.18)	0.03 (-0.04, 0.20)
Rozanolixizumab 7 mg/kg	-0.02 (-0.06, 0.07)	-0.02 (-0.06, 0.08)
Rozanolixizumab 10 mg/kg	-0.02 (-0.06, 0.07)	-0.02 (-0.06, 0.07)
Zilucoplan	0.06 (-0.02, 0.25)	0.06 (-0.02, 0.26)
Eculizumab	-	0.00 (-0.05, 0.11)
Efgartigimod PH20 SC	-	0.00 (-0.07, 0.25)

Abbreviations: Ab, antibody; AChR, acetylcholine receptor; CrI, credible interval; gMG, generalized myasthenia gravis; IV, intravenous; MuSK, muscle-specific tyrosine kinase; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Note: * Nasopharyngitis was not observed/reported for RAV and EFG SC; upper respiratory tract infection was not observed/reported for EFG SC; Treatment-emergent adverse events was not reported for ECU. [a] For rozanolixizumab, safety outcomes were estimated based on patients with AChR Ab+ or MuSK Ab+ gMG due to lack of data. For eculizumab, safety outcomes were estimated based on patients with anti-AChR Ab+ refractory gMG due to lack of data. For all other drugs, all outcomes were estimated based on patients with anti-AChR Ab+ gMG.

Supplementary Table 5. Comparison of baseline characteristics across the included trials

	ADAPT	CHAMPION	MycarinG	RAISE	ADAPT-SC	REGAIN
Sample size	129	175	200	174	110	125
Age, mean (SD)	46.9 (15.3)	55.6 (15.1)	51.8 (16.3)	53.0 (15.2)	53.4 (15.6)	38.1 (18.6)
Sex, female	67%	51%	61%	57%	59%	66%
Time since diagnosis, years, mean (SD)	9.3 (8.3)	9.9 (9.3)	5.8 (6.0)	9.1 (10.0)	7.0 (7.5)	9.6 (8.2)
MGFA class II	41%	45%	39%	28%	46%	38%
MGFA class III	55%	49%	57%	67%	49%	53%
MGFA class IV	4%	6%	4%	5%	5%	10%
Baseline MG-ADL score, mean (SD)	8.8 (2.3)	9.0 (2.5)	8.3 (3.4)	10.6 (3.0)	8.7 (2.6)	10.2 (2.8)
Baseline QMG score, mean (SD)	15.6 (4.8)	14.7 (5.2)	15.6 (3.6)	19.1 (4.1)	15.2 (4.5)	17.1 (5.3)

Abbreviations: MG-ADL, Myasthenia Gravis-Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; QMG, Quantitative Myasthenia Gravis; SD, standard deviation.

Note: ANOVA (for continuous variables) and multinomial logistic regression (for categorical variables) analysis indicated that there are significant differences in the reported baseline characteristics across these trials. These differences do not preclude the validity of a network meta-analysis as these factors are not necessarily effect modifiers.