Ocular symptoms in patients with generalised myasthenia gravis receiving rozanolixizumab: *Post hoc* analysis of MycarinG

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ICNMD 2024 | 25–29 October 2024

OS.07.04

Conflicts of interest

Ali A. Habib has received research support from Alexion Pharmaceuticals, argenx, Cabaletta Bio, Genentech/Roche, Immunovant, Regeneron Pharmaceuticals, UCB and Viela Bio (now Amgen). He has received honoraria from Alexion Pharmaceuticals, Alpine Immune Sciences, argenx, Genentech/Roche, Immunovant, Inhibrx, Regeneron Pharmaceuticals, NMD Pharma and UCB.

Robert M. Pascuzzi is Professor Emeritus of Neurology at Indiana University and receives compensation for his professional work from Indiana University Health. He has no financial relationship with any pharmaceutical company and receives no compensation from any pharmaceutical company (present or past). Robert M. Pascuzzi speaks at educational seminars on a broad variety of general neurology topics for primary care physicians through the organisation Medical Education Resources (an educational organisation with no links or ties to any pharmaceutical or healthcare business company). Therefore, Robert M. Pascuzzi has no conflicts of interest related to this research, manuscript, presentation, or publication.

John Vissing has been a Consultant on advisory boards for Amicus Therapeutics, Arvinas, Biogen, Fulcrum Therapeutics, Genethon, Horizon Therapeutics (now Amgen), Lupin, ML Biopharma, Novartis, Regeneron Pharmaceuticals, Roche, Sanofi Genzyme (now Sanofi), Sarepta Therapeutics and UCB. He has received research, travel support and/or speaker honoraria from Alexion Pharmaceuticals, argenx, Biogen, Edgewise Therapeutics, Fulcrum Therapeutics, Lupin, Sanofi Genzyme (now Sanofi) and UCB. He is a Principal Investigator in clinical trials for Alexion Pharmaceuticals, argenx, Genethon, Horizon Therapeutics (now Amgen), Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), ML Biopharma, Novartis, Regeneron Pharmaceuticals, Roche, Sanofi Genzyme (now Sanofi) and UCB.

Tuan Vu is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion/AstraZeneca Rare Disease, Amgen, argenx, Cartesian Therapeutics, COUR Pharmaceuticals, Dianthus Therapeutics, Immunovant, Johnson & Johnson, NMD Pharmaceuticals, Regeneron Pharmaceuticals and UCB, and has served as a speaker for Alexion/AstraZeneca Rare Disease, argenx, and CSL Behring. He performed consulting work for Alexion/AstraZeneca Rare Disease, argenx, Dianthus Therapeutics, ImmunAbs and UCB.

Thaïs Tarancón is an employee and shareholder of UCB.

Francesca Pannullo is a former contractor for UCB.

Asha Hareendran is an employee and shareholder of UCB.

Vera Bril is a Consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Momenta (now Johnson & Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Roche, Sanofi, Takeda Pharmaceuticals and UCB. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson & Johnson), Octapharma, Takeda Pharmaceuticals, UCB and Viela Bio (now Amgen).

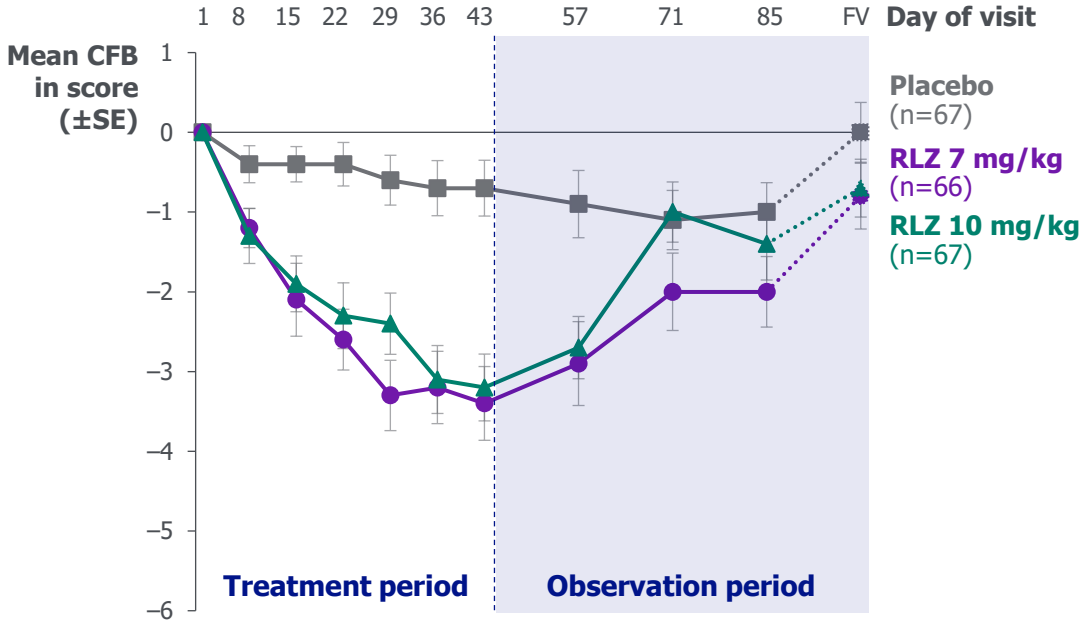
Statistical analyses were run by UCB.

This study was funded by UCB.

Rozanolixizumab improved MG-specific outcomes in MycarinG[1]

- **Rozanolixizumab**, a humanised IgG4 mAb FcRn inhibitor, **significantly improved MG-specific outcomes** in patients with AChR or MuSK Ab+ gMG in the randomised, double-blind, placebo-controlled, Phase 3, MycarinG study (NCT03971422)[1]
  - Rozanolixizumab had an acceptable safety profile and was generally well tolerated
- Ocular symptoms in MG pose a substantial burden for patients, impacting their QoL and daily activities, including driving and working[2]
  - Ocular symptoms may respond differently to treatment than generalised symptoms[3,4]

Primary endpoint: CFB in MG-ADL score at Day 43[1]



Adapted from Bril V, et al. Lancet Neurol. 2023;22(5):383–394.

Objective: To assess the effect of rozanolixizumab treatment on the ocular subdomains of the MGSPRO, MGII, MG-ADL and QMG instruments in patients with gMG

Ab+, autoantibody positive; AChR, acetylcholine receptor; CFB, change from baseline; FcRn, neonatal Fc receptor; FV, final visit; (g)MG, (generalised) myasthenia gravis; IgG4, immunoglobulin G4; mAb, monoclonal antibody; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGII, Myasthenia Gravis Impairment Index; MGSPRO, Myasthenia Gravis Symptoms Patient-Reported Outcomes; MuSK, muscle-specific tyrosine kinase; QMG, Quantitative Myasthenia Gravis; QoL, quality of life; RLZ, rozanolixizumab; SE, standard error.

1. Bril V, et al. Lancet Neurol. 2023;22(5):383–394; 2. Meisel A, et al. Eur J Neurol. 2024;31(7):e16280; 3. Akaishi T, et al. BMC Neurol. 2016;16(1):225; 4. Barnett C, et al. Neurology. 2017;89(23):2357–2364.

The MGSPRO, MGII, MG-ADL and QMG instruments together cover all aspects of ocular MG symptoms

- Full evaluation of ocular symptoms can be time consuming and may not be feasible for every patient[1]
- We assessed ocular subscores from existing gMG instruments to evaluate specific ocular symptoms[1]

Instrument and subdomain	Underlying concepts	Recall period	Evaluated by	Scale structure
MGSPRO – Ocular Muscle Weakness scale	Severity of: • Diplopia • Ptosis • Blurry vision • Difficulty moving eyes side to side • Difficulty moving eyes up and down	7 days	Patient	4-point scale
MGII – ocular subdomain	Timing/duration, time to fatigability and severity of: • Diplopia • Ptosis Severity of: • Diplopia • Ptosis	14 days Current	Patient Clinician	
MG-ADL – ocular subdomain	Frequency of: • Diplopia • Ptosis	Current	Patient	
QMG[2] – ocular subdomain	Severity of: • Diplopia • Ptosis	Current	Clinician	

Higher score = more severe symptoms

*Range of response options for MGSPRO Ocular Muscle Weakness scale and QMG ocular subdomain scale: "none", "mild", "moderate" or "severe"; MGII ocular PRO scale: "none", "only evenings/after >1 hour/mild", "starting in the afternoon/after <1 hour/it affects my vision, but don't need to cover one eye, lift eyelid or tilt head" or "constant/starts immediately/I need to cover one eye/lift eyelid/tilt head to see"; MG-ADL ocular subdomain scale: "none", "occurs, but not daily", "daily, but not constant" and "constant".
(g)MG, (generalised) myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGII, Myasthenia Gravis Impairment Index; MGSPRO, Myasthenia Gravis Symptoms Patient-Reported Outcomes; PRO, patient-reported outcome; QMG, Quantitative Myasthenia Gravis.

1. Meisel A, et al. Eur J Neurol. 2024;31(7):e16280; 2. Barohn RJ, et al. Ann N Y Acad Sci. 1998;841(1):769–772.

MycarinG included a gMG population with broad-ranging MG severity

		Placebo (n=67)	RLZ 7 mg/kg (n=66)	RLZ 10 mg/kg (n=67)
Age, years, mean (SD)		50.4 (17.7)	53.2 (14.7)	51.9 (16.5)
Sex, female, n (%)		47 (70.1)	39 (59.1)	35 (52.2)
Duration of disease, years, mean (SD)		9.4 (9.3)	6.9 (6.8)	9.6 (9.9)
MG-ADL total score at baseline, mean (SD)		8.4 (3.4)	8.4 (3.8)	8.1 (2.9)
MG-ADL ocular score at baseline, mean (SD)		2.9 (1.6)	2.6 (1.8)	2.6 (1.7)
Patients with MG-ADL ocular subdomain score >0, n (%)		62 (92.5)	57 (86.4)	59 (88.1)
QMG total score at baseline, mean (SD)		15.8 (3.5)	15.4 (3.7)	15.6 (3.7)
MGFA Disease Class at baseline, n (%)	II	23 (34.3)	29 (43.9)	26 (38.8)
	III	41 (61.2)	34 (51.5)	39 (58.2)
	IVa/b*	3 (4.5)	3 (4.5)	2 (3.0)

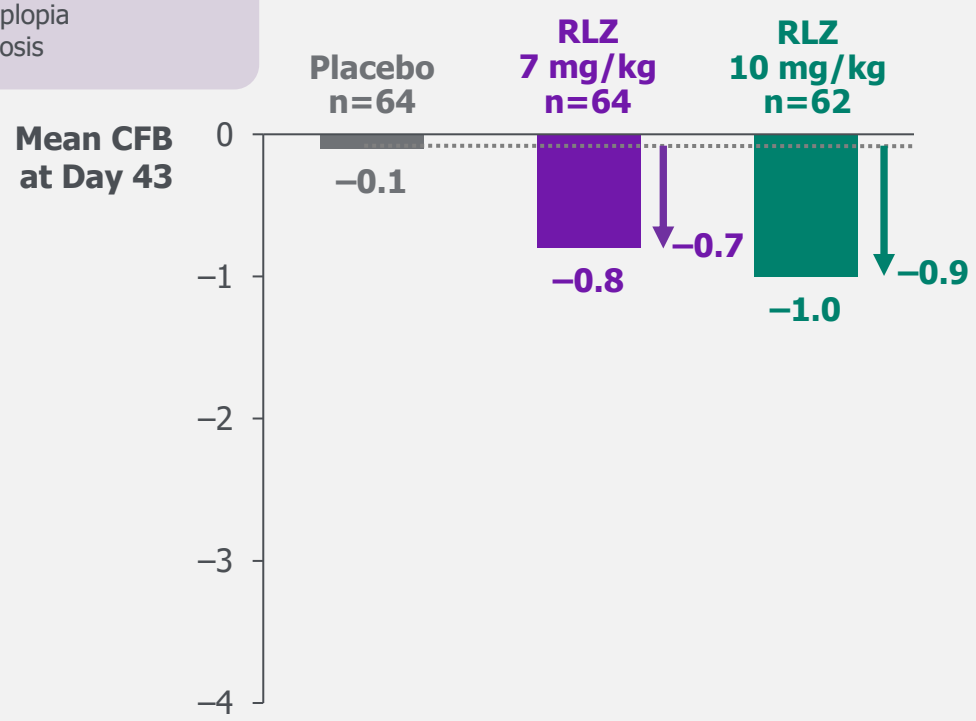
Randomised set.
*Only one patient, who was randomised to the placebo group, had Class IVb disease.
(g)MG, (generalised) myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation.

MG-ADL ocular subdomain score

Greater improvements with rozanolixizumab than placebo

Ocular subdomain

Frequency of:
- Diplopia
- Ptosis



	Placebo	RLZ 7 mg/kg	RLZ 10 mg/kg
Number of patients, n	67	66	67
Baseline MG-ADL ocular subdomain score, mean (SD)	2.9 (1.6)	2.6 (1.8)	2.6 (1.7)

Range of responses in MG-ADL (2 items):
- 0 = none
- 1 = occurs, but not daily
- 2 = daily, but not constant
- 3 = constant

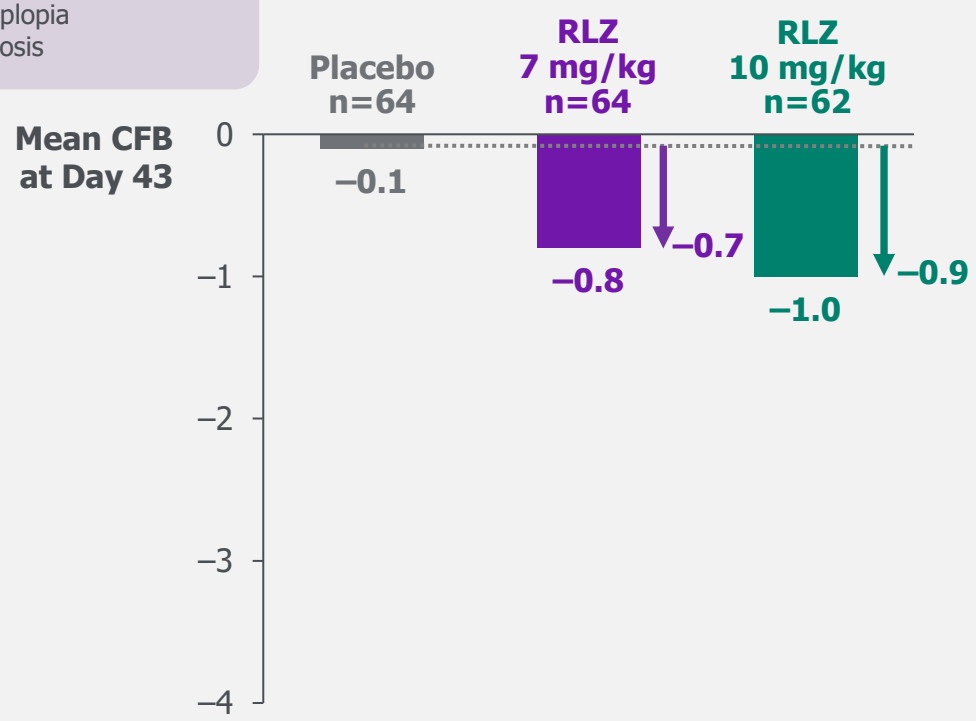
Randomised set. Higher score = more severe symptoms (0–6 for ocular subdomain, 0–24 for total scores). Ocular subdomain scores are *post hoc* change from baseline values whereas the total scores are primary and secondary analyses using the hypothetical and treatment policy strategy. Questionnaire completion rates at Day 43 were 92.5–97.0% for the MG-ADL ocular items. The proportion of patients with an MG-ADL ocular score >0 was 92.5% (placebo), 86.4% (RLZ 7 mg/kg) and 88.1% (RLZ 10 mg/kg).
CFB, change from baseline; MG-ADL, Myasthenia Gravis Activities of Daily Living; RLZ, rozanolixizumab; SD, standard deviation.

MG-ADL ocular subdomain score

Greater improvements with rozanolixizumab than placebo

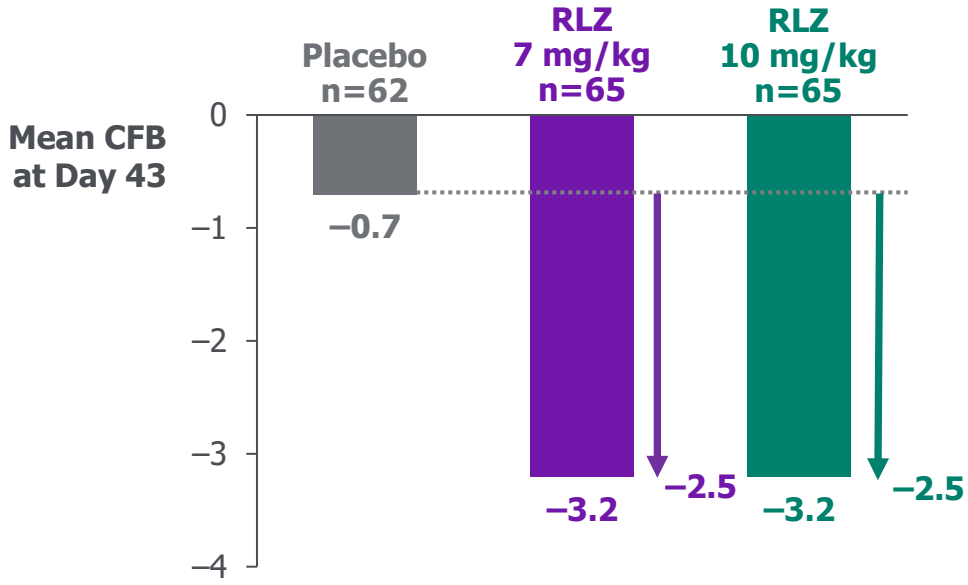
Ocular subdomain

Frequency of:
- Diplopia
- Ptosis



	Placebo	RLZ 7 mg/kg	RLZ 10 mg/kg
Number of patients, n	67	66	67
Baseline MG-ADL ocular subdomain score, mean (SD)	2.9 (1.6)	2.6 (1.8)	2.6 (1.7)

MG-ADL total score



	Placebo	RLZ 7 mg/kg	RLZ 10 mg/kg
Number of patients, n	67	66	67
Baseline MG-ADL total score, mean (SD)	8.4 (3.4)	8.4 (3.8)	8.1 (2.9)

Range of responses in MG-ADL (2 items):
- 0 = none
- 1 = occurs, but not daily
- 2 = daily, but not constant
- 3 = constant

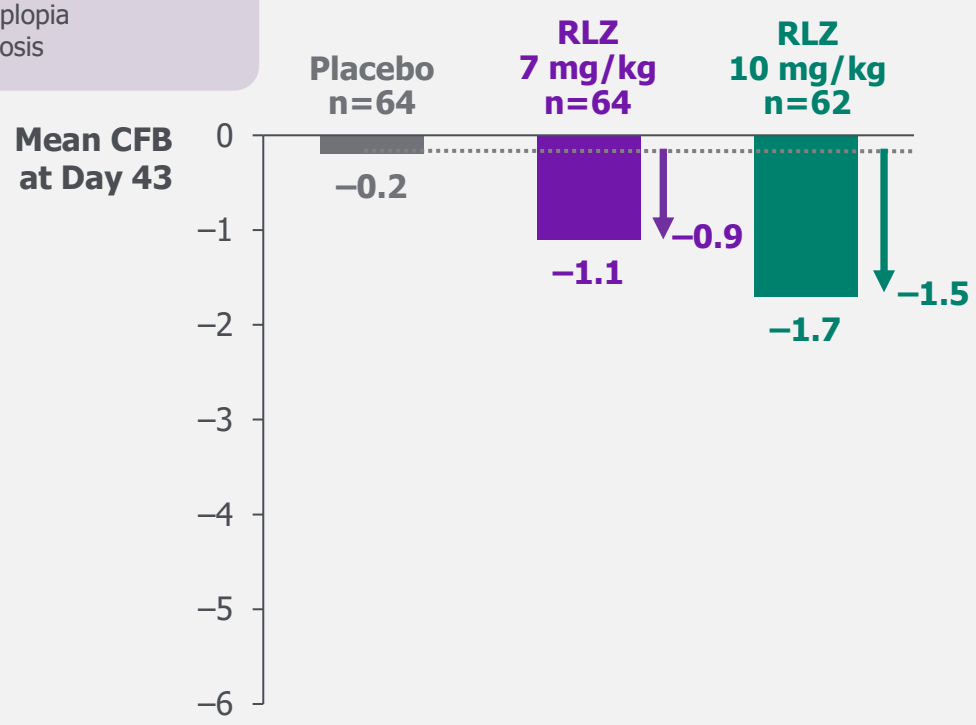
Randomised set. Higher score = more severe symptoms (0–6 for ocular subdomain, 0–24 for total scores). Ocular subdomain scores are *post hoc* change from baseline values whereas the total scores are primary and secondary analyses using the hypothetical and treatment policy strategy. Questionnaire completion rates at Day 43 were 92.5–97.0% for the MG-ADL ocular items. The proportion of patients with an MG-ADL ocular score >0 was 92.5% (placebo), 86.4% (RLZ 7 mg/kg) and 88.1% (RLZ 10 mg/kg).
CFB, change from baseline; MG-ADL, Myasthenia Gravis Activities of Daily Living; RLZ, rozanolixizumab; SD, standard deviation.

QMG ocular subdomain score

Greater improvements with rozanolixizumab than placebo

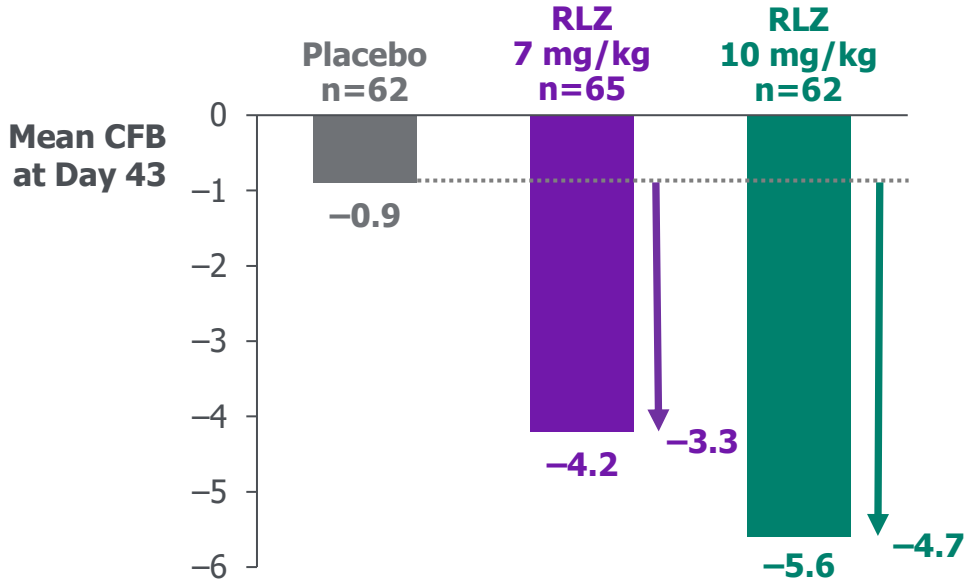
Ocular subdomain

Severity of:
- Diplopia
- Ptosis



	Placebo	RLZ 7 mg/kg	RLZ 10 mg/kg
Number of patients, n	67	66	67
Baseline QMG ocular subdomain score, mean (SD)	3.7 (2.1)	3.7 (2.0)	3.9 (1.9)

QMG total score



	Placebo	RLZ 7 mg/kg	RLZ 10 mg/kg
Number of patients, n	67	66	67
Baseline QMG total score, mean (SD)	15.8 (3.5)	15.4 (3.7)	15.6 (3.7)

Range of responses in QMG (2 items):
- 0 = none
- 1 = mild
- 2 = moderate
- 3 = severe

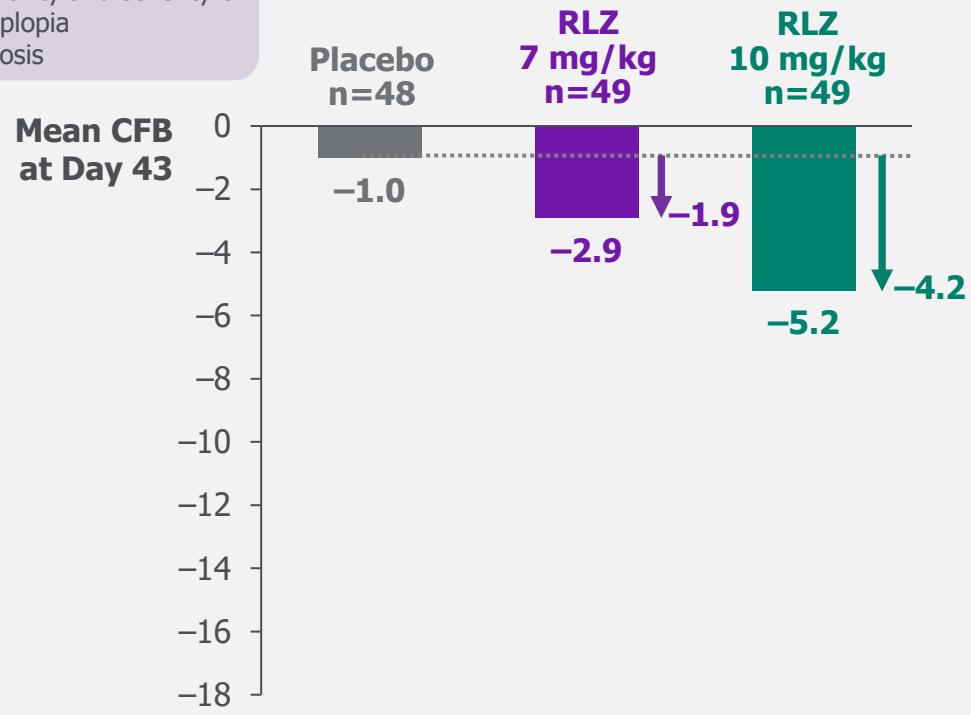
Randomised set. Higher score = more severe symptoms (0–6 for ocular subdomain, 0–39 for total score). Ocular subdomain scores are *post hoc* change from baseline values whereas the total scores are primary and secondary analyses using the hypothetical and treatment policy strategy. Questionnaire completion rates at Day 43 were 92.5–97.0% for the QMG ocular scale.
CFB, change from baseline; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation.

MGII* ocular subdomain score

Greater improvements with rozanolixizumab than placebo

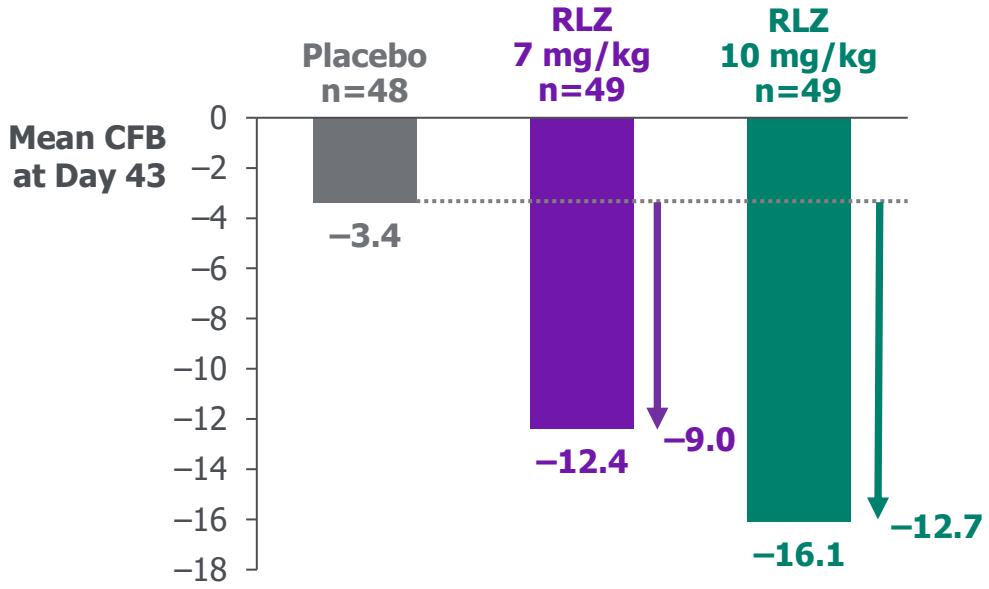
Ocular subdomain

Timing/duration, time to fatigability and severity of:
- Diplopia
- Ptosis



	Placebo	RLZ 7 mg/kg	RLZ 10 mg/kg
Number of patients, n	67	66	67
Baseline MGII ocular subdomain score, mean (SD)	11.0 (6.0)	10.7 (6.8)	11.5 (5.7)

MGII total score



	Placebo	RLZ 7 mg/kg	RLZ 10 mg/kg
Number of patients, n	53	55	54
Baseline MGII total score, mean (SD)	35.6 (12.4)	36.3 (15.2)	38.3 (12.1)

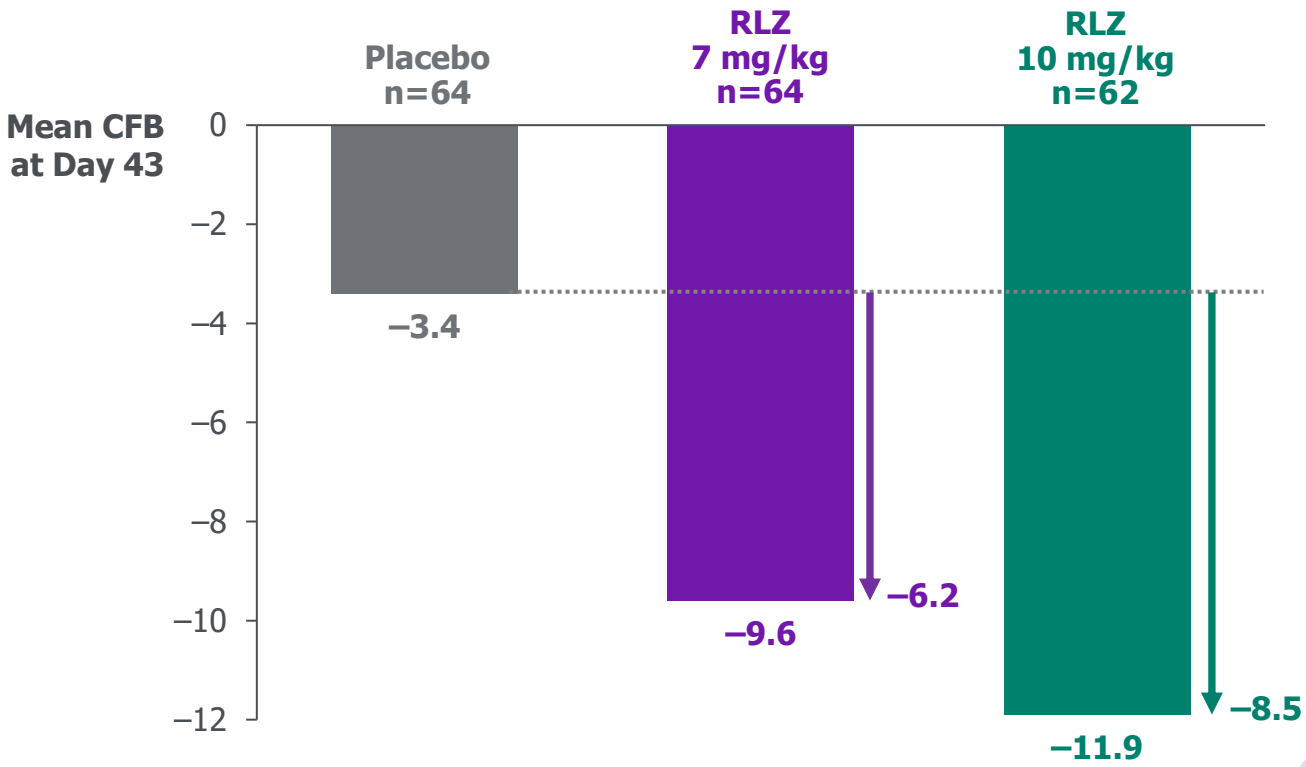
Range of responses in MGII (6 items):
- 0 = no double vision/eyelid drooping
- 1 = only in evenings/after >1 hour/mild
- 2 = in afternoon/after <1 hour/affects vision or activities
- 3 = constant/starts immediately/need to cover eye, lift eyelid or tilt head

Randomised set. Higher score = more severe symptoms (0–24 for ocular subdomain, 0–84 for total scores). Questionnaire completion rates at Day 43 were 71.6–74.2% for the optional MGII ocular scale.
*Completion of MGII was optional.
CFB, change from baseline; MGII, Myasthenia Gravis Impairment Index; RLZ, rozanolixizumab; SD, standard deviation.

MGSPRO Ocular Muscle Weakness scale score

Greater improvements with rozanolixizumab than placebo

Severity of:
- Diplopia/ptosis/blurry vision
- Difficulty moving eyes side to side
- Difficulty moving eyes up and down



	Placebo	RLZ 7 mg/kg	RLZ 10 mg/kg
Number of patients, n	67	66	67
Baseline MGSPRO Ocular Muscle Weakness score, mean (SD)	37.4 (25.8)	30.1 (21.8)	30.8 (21.7)

Range of responses in MG Symptoms PRO (5 items):
- 1 = none
- 2 = mild
- 3 = moderate
- 4 = severe

Randomised set. Higher score = more severe symptoms (0–100 for each scale). No total score is available for MGSPRO. Questionnaire completion rates at Day 43 were 92.5–97.0% for the MGSPRO Ocular Muscle Weakness scale.
The sum of responses to the items composing each scale undergoes linear transformation to generate a score of 0–100.[1]
CFB, change from baseline; MGSPRO, Myasthenia Gravis Symptoms Patient-Reported Outcomes; RLZ, rozanolixizumab; SD, standard deviation.

1. Regnault A, et al. Front Neurol. 2024; doi: 10.3389/fneur.2024.1368525. [Epub ahead of print].

Rozanolixizumab was generally well tolerated at both doses and most TEAEs were mild or moderate

	Placebo n=67	RLZ 7 mg/kg n=64*	RLZ 10 mg/kg n=69*
Any TEAE, n (%)†	45 (67.2)	52 (81.3)	57 (82.6)
Headache	13 (19.4)	29 (45.3)	26 (37.7)
Diarrhoea	9 (13.4)	16 (25.0)	11 (15.9)
Pyrexia	1 (1.5)	8 (12.5)	14 (20.3)
Serious TEAE, n (%)	6 (9.0)	5 (7.8)	7 (10.1)
TEAE resulting in withdrawal from study, n (%)	2 (3.0)	2 (3.1)	5 (7.2)
Treatment-related TEAE, n (%)	22 (32.8)	32 (50.0)	39 (56.5)
Severe TEAE, n (%)	3 (4.5)	3 (4.7)	13 (18.8)
TEAEs leading to death, n (%)	0	0	0

Safety set.
*Two patients in the 7 mg/kg group who incorrectly received 10 mg/kg were analysed in the 10 mg/kg group for safety analyses.
†Specific TEAEs listed are the three most commonly occurring overall.
RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event.

Conclusions

- Ocular symptoms in MG pose a substantial burden for patients, impacting QoL and daily activities including driving and working,[1] and may respond differently to treatment than generalised symptoms[2,3]
- In the Phase 3, randomised, placebo-controlled, double-blind, MycarinG study, patients with gMG received one 6-week cycle of rozanolixizumab 7 mg/kg or 10 mg/kg
- Greater improvements in the ocular scale scores for MG-ADL, QMG, MGII and MGSPRO were observed with rozanolixizumab than with placebo
- Rozanolixizumab was generally well tolerated and most TEAEs were mild or moderate
- These data further support rozanolixizumab as a treatment option for patients with gMG, including those with ocular signs and symptoms

(g)MG, (generalised) myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGII, Myasthenia Gravis Impairment Index; MGSPRO, Myasthenia Gravis Symptoms Patient-Reported Outcomes; QMG, Quantitative Myasthenia Gravis; QoL, quality of life; TEAE, treatment-emergent adverse event.

1. Meisel A, et al. Eur J Neurol. 2024;31(7):e16280; 2. Akaishi T, et al. BMC Neurol. 2016;16(1):225; 3. Barnett C, et al. Neurology. 2017;89(23):2357–2364.