Safety and efficacy of chronic weekly rozanolixizumab treatment in patients with generalised myasthenia gravis (MG0004)

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Conflicts of interest

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).

Julian Grosskreutz has served as a Consultant for Alexion Pharmaceuticals, Biogen and UCB, and his institution has received research support from the Boris Canessa Foundation.

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.

Renato Mantegazza has received funding for travel and meeting attendance or advisory board participation from Alexion Pharmaceuticals, argenx, BioMarin, Catalyst, Sanofi, Regeneron Pharmaceuticals and UCB.

Sabrina Sacconi has nothing to disclose.

Kimiaki Utsugisawa has served as a paid Consultant for argenx, Chugai Pharmaceutical, HanAll Biopharma, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Merck, Mitsubishi Tanabe Pharma, UCB and Viela Bio (now Amgen); and he has received speaker honoraria from Alexion Pharmaceuticals, argenx, the Japan Blood Products Organization 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 Pharma, 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.

Marion Boehnlein, **Franz Woltering** and **Bernhard Greve** are employees and shareholders of UCB.

Maryam Gayfieva is a former employee and shareholder of UCB.

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.

Statistical analyses were run by UCB.

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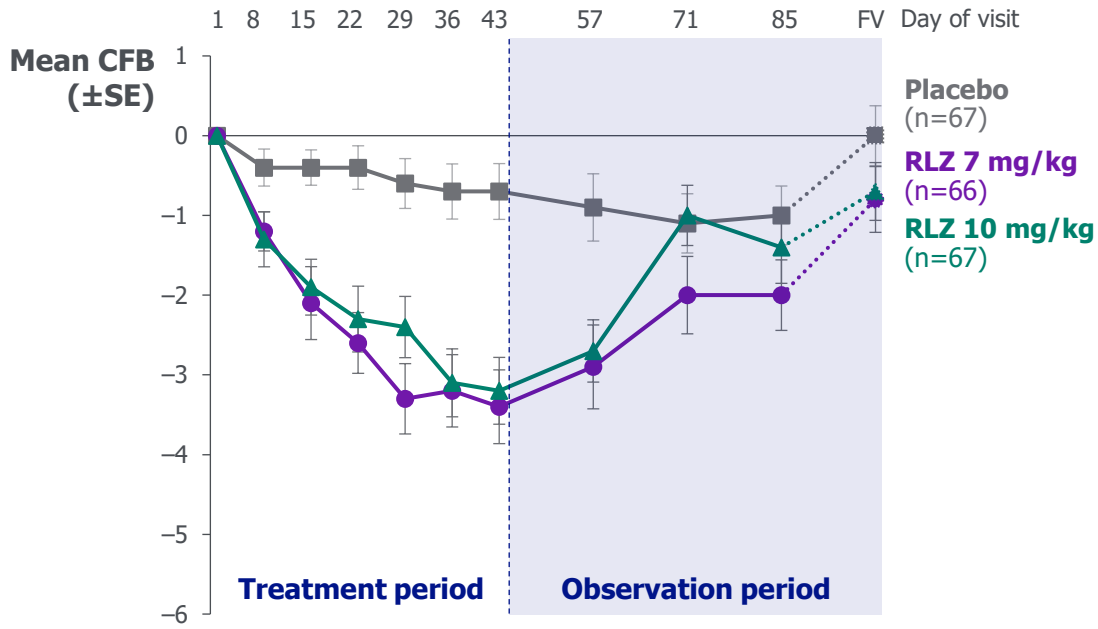
Rozanolixizumab: An FcRn inhibitor evaluated in the pivotal Phase 3 MycarinG study in patients with gMG

- **Six once-weekly infusions of rozanolixizumab significantly improved MG-specific outcomes** in patients with AChR Ab+ 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
- Patients from MycarinG could enrol in **MG0004** (NCT04124965), a Phase 3, multicentre, randomised, **OLE study of rozanolixizumab, for up to 52 weekly infusions**

MycarinG 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 **safety and efficacy of long-term treatment with rozanolixizumab** for up to 52 weekly infusions in patients with gMG

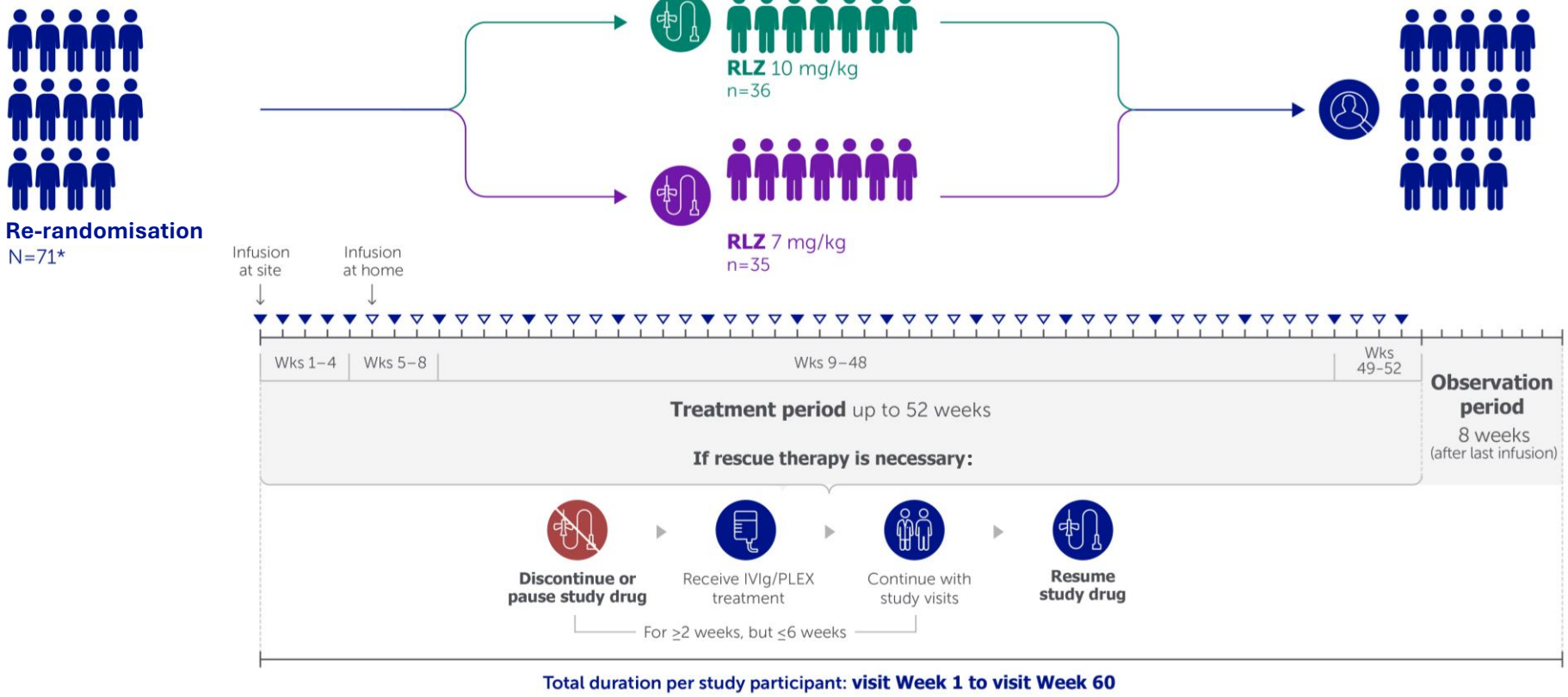
AChR Ab+, acetylcholine receptor autoantibody positive; CFB, change from baseline; FcRn, neonatal Fc receptor; FV, final visit; (g)MG, (generalised) myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK Ab+, muscle-specific tyrosine kinase autoantibody positive; OLE, open-label extension; RLZ, rozanolixizumab; SE, standard error.

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

MG0004: A Phase 3 OLE study of weekly rozanolixizumab in patients with gMG

Patients in MycarinG:
- ≥18 years of age
- AChR Ab+ or MuSK Ab+ gMG

Patients could enrol in MG0004 if they:
- Completed MycarinG, or
- Required rescue therapy during the observation period and opted to receive RLZ in MG0004 instead



Outcomes
- **Safety:** TEAEs by most recent dose
- **Efficacy:** CFB in MG-ADL, MGC and QMG scores up to Week 60

*Patients could switch dose from 10 mg/kg to 7 mg/kg and *vice versa* at the investigator's discretion.
AChR Ab+, acetylcholine receptor autoantibody positive; CFB, change from baseline; gMG, generalised myasthenia gravis; IVIg, intravenous immunoglobulin; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGC, Myasthenia Gravis Composite; MuSK Ab+, muscle-specific tyrosine kinase autoantibody positive; OLE, open-label extension; PLEX, plasma exchange; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event; Wks, weeks.

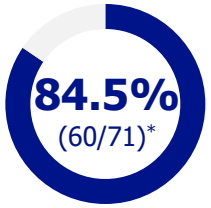
Baseline demographics and patient characteristics were generally balanced between rozanolixizumab dose groups

		RLZ 7 mg/kg n=35	RLZ 10 mg/kg n=36	RLZ total N=71
	Age, years, mean (SD)	50.6 (14.2)	53.7 (17.2)	52.2 (15.8)
	Sex, female, n (%)	19 (54.3)	19 (52.8)	38 (53.5)
	Prior thymectomy, n (%)	14 (40.0)	15 (41.7)	29 (40.8)
	AChR Ab+, n (%)	30 (85.7)	32 (88.9)	62 (87.3)
	MuSK Ab+, n (%)	5 (14.3)	4 (11.1)	9 (12.7)
	MG-ADL score, mean (SD)	8.4 (3.6)	8.4 (3.7)	8.4 (3.6)
	QMG score, mean (SD)	15.2 (5.1)	15.4 (5.5)	15.3 (5.3)
	Duration of disease, years, mean (SD)*	8.7 (9.7)	8.2 (8.4)	8.5 (9.0)
Prior gMG medication, n (%)	Corticosteroids (systemic)	24 (68.6)	20 (55.6)	44 (62.0)
	Immunosuppressants	19 (54.3)	18 (50.0)	37 (52.1)
	Parasympathomimetics	30 (85.7)	30 (83.3)	60 (84.5)

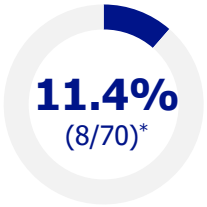
Randomised set.
*From diagnosis; data obtained at MycarinG baseline.
AChR Ab+, acetylcholine receptor autoantibody positive; gMG, generalised myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK Ab+, muscle-specific tyrosine kinase autoantibody positive; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation.

Mean treatment duration in the MG0004 study was 23 weeks

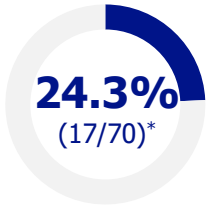
After ≥6 visits, patients could roll over into MG0007 (NCT04650854), an OLE study of cyclic rozanolixizumab[1–3]



enrolled in MG0007†



completed 52 doses of weekly treatment



remained in MG0004 at Week 33

In MG0004:

	RLZ 7 mg/kg n=35	RLZ 10 mg/kg n=35*
Treatment duration, weeks, mean (SD)	22.9 (14.6)	23.7 (14.6)
Number of infusions, mean (SD)	21.7 (13.0)	21.6 (12.3)

Patients could switch dose
at the investigator's discretion

5/35‡ switched from **7 mg/kg** to **10 mg/kg**
3 remained on the higher dose after switching

14/35‡ switched from **10 mg/kg** to **7 mg/kg**
12 remained on the lower dose after switching

*1 patient in the randomised set was not treated in MG0004 and was not included in the safety set; the patient who was not treated rolled over into MG0007. †52/70 (74.3%) patients who were treated in MG0004 discontinued early to enrol in MG0007. ‡Excluding patients who switched for a single week.
OLE, open-label extension; RLZ, rozanolixizumab; SD, standard deviation.

1. Bril V, et al. Long-term efficacy and safety of symptom-driven cyclical rozanolixizumab treatment in patients with generalized myasthenia gravis: a pooled analysis of a Phase 3 study and two open-label extension studies [poster]. AAN 2023. Poster P1-5-012; 2. Vissing J, et al. Rozanolixizumab responder and minimal symptom expression rates in generalized MG: pooled Phase 3 and extension studies [poster]. EAN 2023. Poster EPO-412;
3. Vu T, et al. Long-term safety of repeated cycles of rozanolixizumab treatment in patients with generalized myasthenia gravis [poster]. AANEM 2023. Poster 269.

Rozanolixizumab was generally well tolerated, and most TEAEs were mild or moderate

	Patients experiencing TEAEs, n (%)		
	RLZ 7 mg/kg n=50*	**RLZ 10 mg/kg** n=42*	**RLZ total** N=70
Any TEAEs	38 (76.0)	33 (78.6)	60 (85.7)
Serious TEAEs†	7 (14.0)	2 (4.8)	9 (12.9)
Permanent discontinuation from study due to TEAEs	4 (8.0)	0	4 (5.7)
Permanent discontinuation of study drug due to TEAEs	3 (6.0)‡	0	3 (4.3)‡
TEAEs requiring dose change	0	1 (2.4)	1 (1.4)
Treatment-related TEAEs	25 (50.0)	18 (42.9)	41 (58.6)
Severe TEAEs§	12 (24.0)	5 (11.9)	17 (24.3)
Headache	3 (6.0)	2 (4.8)	5 (7.1)
MG	2 (4.0)	1 (2.4)	3 (4.3)
All deaths (AEs leading to death)	0	0	0

Safety set by most recent dose; 1 patient was not treated and was not included in the safety set.
*Participants who switched doses may be counted in both RLZ treatment groups but only once in the RLZ total group. †Serious TEAEs were reported in no more than 1 patient each except for MG (3 cases in 7 mg/kg; 1 case in 10 mg/kg); no serious TEAEs were considered to be related to rozanolixizumab. ‡Myasthenia gravis (n=2) and congestive cardiac failure (n=1). §75.7% of TEAEs were mild or moderate; specific severe TEAEs listed are those occurring in >1 patient overall.
AE, adverse event; MG, myasthenia gravis; RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event.

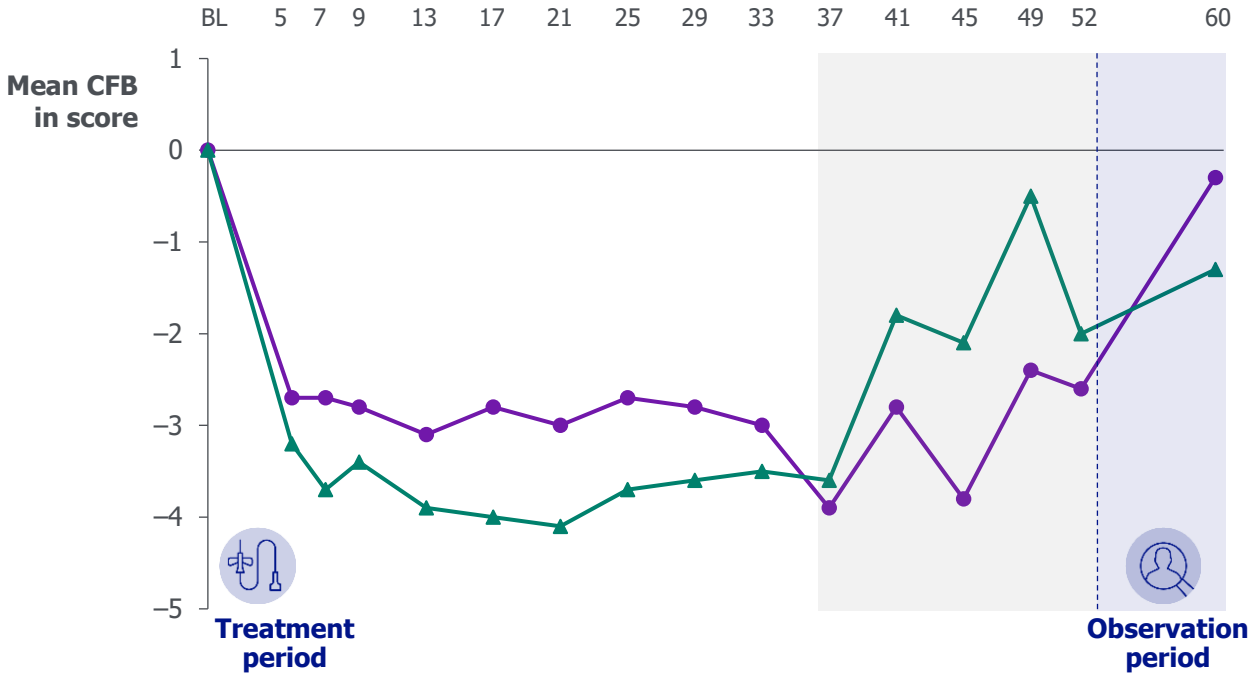
Rozanolixizumab was generally well tolerated with a safety profile similar to repeated cycles of treatment

	Patients experiencing TEAEs, n (%)		
	RLZ 7 mg/kg n=50*	**RLZ 10 mg/kg** n=42*	**RLZ total** N=70
Any TEAEs†	38 (76.0)	33 (78.6)	60 (85.7)
Headache	15 (30.0)	12 (28.6)	25 (35.7)
Diarrhoea	6 (12.0)	7 (16.7)	13 (18.6)
Decreased blood IgG	6 (12.0)	5 (11.9)	11 (15.7)
Nausea	4 (8.0)	5 (11.9)	9 (12.9)
Pyrexia	4 (8.0)	3 (7.1)	7 (10.0)
UTI	5 (10.0)	2 (4.8)	7 (10.0)

- **Infections** were reported in 26.0% (n=13) of the 7 mg/kg group and 21.4% (n=9) of the 10 mg/kg group
  - There were no serious, severe or opportunistic infections
  - No infections led to study discontinuation
- There were no clinically relevant reductions in **albumin** or TEAEs related to albumin reductions
- The safety profile was similar to that with repeated cycles of treatment in the MG0007 study[1]

Safety set by most recent dose; 1 patient was not treated and was not included in the safety set.
*Participants who switched doses may be counted in both RLZ treatment groups but only once in the RLZ total group. †Specific TEAEs listed are those occurring in ≥10% of patients overall.
IgG, immunoglobulin G; RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event; UTI, urinary tract infection.
1. Vu T, et al. Long-term safety of repeated cycles of rozanolixizumab treatment in patients with generalized myasthenia gravis [poster]. AANEM 2023. Poster 269.

Clinically relevant improvements in MG-ADL score were observed with rozanolixizumab treatment



Visit (Week)	BL	5	7	9	13	17	21	25	29	33	37	41	45	49	52	60
RLZ 7 mg/kg, n	35	34	35	29	30	25	20	18	13	10	7	6	4	5	5	7
RLZ 10 mg/kg, n	35	34	32	31	30	29	24	17	14	12	10	6	7	6	3	7

RLZ 7 mg/kg baseline MG-ADL score, mean (SD): 8.4 (3.6)

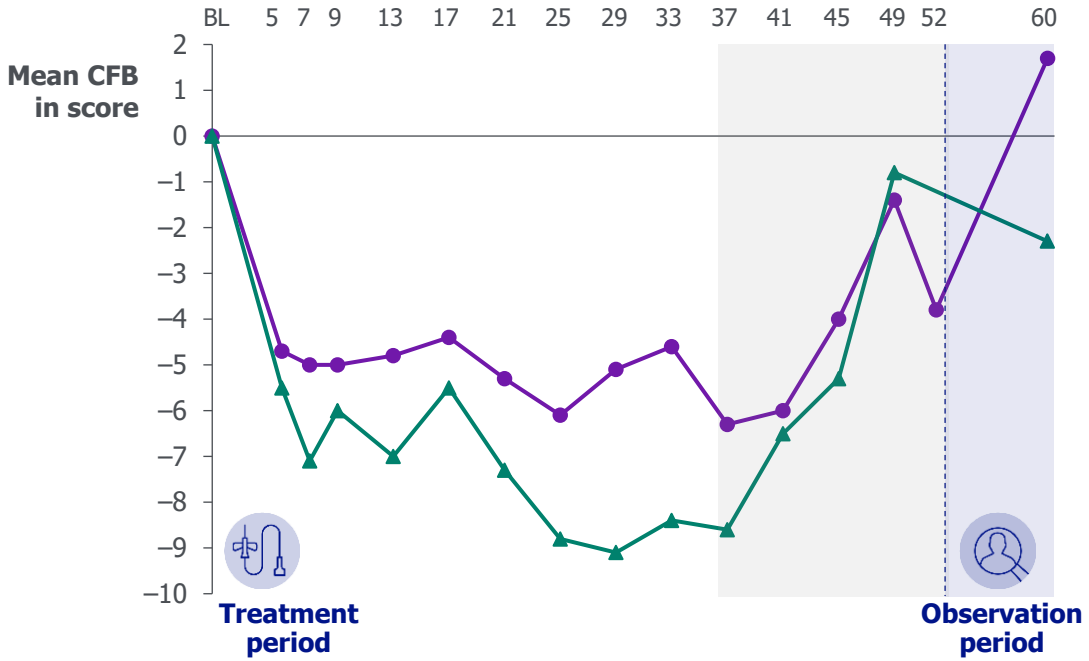
RLZ 10 mg/kg baseline MG-ADL score, mean (SD): 8.5 (3.7)

- A decrease from baseline in MG-ADL score was observed at Week 5, the earliest time of assessment
- There was a stable trend up to Week 33:
  - Mean CFB was consistently greater in the 10 mg/kg group than the 7 mg/kg group
  - Patient numbers were low after Week 33
- Maximum mean CFB up to Week 33:
  - 7 mg/kg group: **−3.1** (Week 13)
  - 10 mg/kg group: **−4.1** (Week 21)

Safety set by first dose received. The light grey area represents study visits at which patient numbers were low (≤10 per treatment group at any scheduled assessment).
BL, baseline; CFB, change from baseline; MG-ADL, Myasthenia Gravis Activities of Daily Living; RLZ, rozanolixizumab; SD, standard deviation.

Similar trends were observed in MGC and QMG scores with rozanolixizumab treatment

MGC

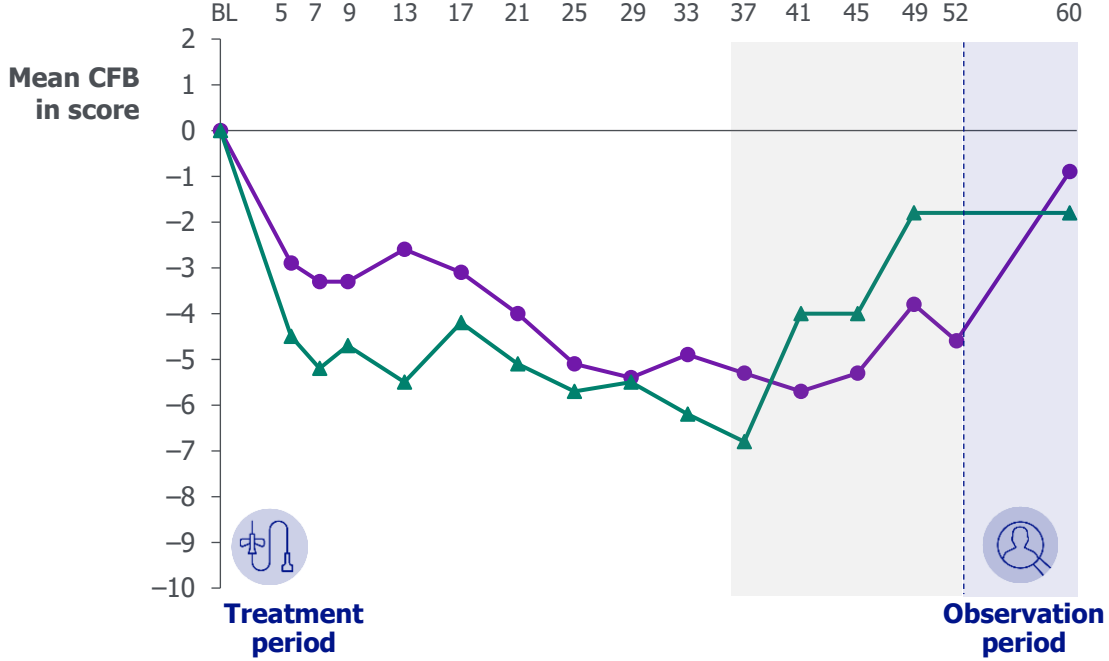


Visit (Week)	BL	5	7	9	13	17	21	25	29	33	37	41	45	49	52	60
RLZ 7 mg/kg, n	35	34	35	29	30	25	20	18	13	9	7	6	4	5	5	7
RLZ 10 mg/kg, n	35	35	33	30	30	29	24	17	14	12	10	6	7	6	2	7

RLZ 7 mg/kg baseline MGC score, mean (SD): 15.0 (7.3)

RLZ 10 mg/kg baseline MGC score, mean (SD): 15.8 (7.5)

QMG



Visit (Week)	BL	5	7	9	13	17	21	25	29	33	37	41	45	49	52	60
RLZ 7 mg/kg, n	35	34	35	28	30	25	20	18	13	10	7	6	4	5	5	7
RLZ 10 mg/kg, n	35	34	32	30	29	28	23	16	13	11	9	5	6	5	2	6

RLZ 7 mg/kg baseline QMG score, mean (SD): 15.2 (5.1)

RLZ 10 mg/kg baseline QMG score, mean (SD): 15.3 (5.6)

Safety set by first dose received. The light grey area represents study visits at which patient numbers were low (≤10 per treatment group at any scheduled assessment).
BL, baseline; CFB, change from baseline; MGC, Myasthenia Gravis Composite; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation.

Conclusions

MG0004 was a Phase 3, multicentre, randomised, OLE study of chronic weekly rozanolixizumab treatment for up to 52 infusions in patients with gMG

Chronic weekly rozanolixizumab was generally well tolerated with a safety profile similar to repeated cycles of rozanolixizumab treatment[1]

Clinically relevant mean improvements were maintained across MG-specific outcomes up to Week 33; patient numbers were low after Week 33

The MG0004 study further supports the long-term safety, tolerability and efficacy of rozanolixizumab in patients with AChR Ab+ or MuSK Ab+ gMG

AChR Ab+, acetylcholine receptor autoantibody positive; (g)MG, (generalised) myasthenia gravis; MuSK Ab+, muscle-specific tyrosine kinase autoantibody positive; OLE, open-label extension.

1. Vu T, et al. Long-term safety of repeated cycles of rozanolixizumab treatment in patients with generalized myasthenia gravis [poster]. AANEM 2023. Poster 269.