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

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Introduction

- Rozanolixizumab is a humanized IgG4 mAb FcRn inhibitor approved by the US FDA for the treatment of adults with AChR Ab+ or MuSK Ab+ gMG[1,2]
- In the Phase 3, randomized, placebo-controlled MycarinG study (MG0003/NCT03971422), weekly SC rozanolixizumab 7 mg/kg or 10 mg/kg for a single 6-week cycle was generally well tolerated and provided clinically meaningful improvements in MG-specific outcomes in patients with gMG[1]
- Patients from MycarinG who completed the study or required rescue therapy during the observation period could enroll in MG0004 (NCT04124965), a Phase 3, multicenter, randomized, OLE study of weekly rozanolixizumab for up to 52 weeks

Methods

- Patients enrolled in MycarinG were aged ≥18 years with AChR Ab+ or MuSK Ab+ gMG[1]
  - Patients could enroll in MG0004 if they either completed MycarinG or required rescue therapy (IVIg or PLEX) during the observation period and opted to enter MG0004 and receive rozanolixizumab instead
- In MG0004, patients were re-randomized (1:1) to receive up to 52 once-weekly SC infusions of rozanolixizumab 7 mg/kg or 10 mg/kg, followed by an 8-week observation period (**Figure 1**)
  - Patients could switch dose at the investigator's discretion
  - After ≥6 visits, patients could roll over into MG0007 (NCT04650854), an OLE study of cyclic rozanolixizumab[3–5]
- Efficacy outcomes included CFB up to Week 60 in MG-ADL, MGC and QMG scores, CFB in total IgG and use of rescue therapy; analyses are presented by first dose received
- Safety variables were assessed for patients who received ≥1 rozanolixizumab dose; TEAEs are presented by most recent dose

Results

Patients

- A total of 71 patients were re-randomized in MG0004, of whom 70 received ≥1 dose of rozanolixizumab 7 mg/kg (n=35) or 10 mg/kg (n=35)
- Baseline characteristics were generally balanced between dose groups (**Table 1**)
- Mean (SD) duration of rozanolixizumab treatment and number of infusions were:
  - 7 mg/kg: 22.9 (14.6) weeks; 21.7 (13.0) infusions
  - 10 mg/kg: 23.7 (14.6) weeks; 21.6 (12.3) infusions
- After Week 6, patients could transition to the MG0007 study; 17 (24.3%) patients remained iMnG0004 at Week 33 and 8 (11.4%) patients completed 52 weeks of chronic weekly treatment
- In the 7 mg/kg group, 5/35 patients switched to 10 mg/kg, of whom 3 remained on the higher dose; in the 10 mg/kg group, 14/35 patients switched to 7 mg/kg, of whom 12 remained on the lower dose

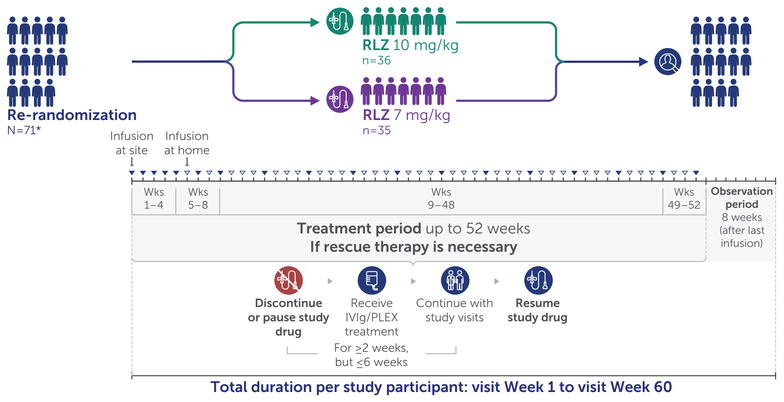
Safety

- Overall, 85.7% (60/70) of patients reported ≥1 TEAE, with similar incidences across 7 mg/kg and 10 mg/kg (76.0% [38/50] and 78.6% [33/42], respectively) (**Table 2**)
  - The most common TEAEs were headache, diarrhea, decreased blood IgG, nausea, pyrexia and UTI
  - Most TEAEs were mild or moderate, with severe TEAEs reported in 24.0% of patients in the 7 mg/kg group and 11.9% in the 10 mg/kg group
- Serious TEAEs were reported in 14.0% (7/50) of patients in the 7 mg/kg group and 4.8% (2/42) in the 10 mg/kg group
  - The only serious TEAE reported in >1 patient was MG worsening (3 cases in 7 mg/kg; 1 case in 10 mg/kg)
  - No serious TEAEs were considered to be related to rozanolixizumab
- TEAEs leading to discontinuation of rozanolixizumab were reported in 6.0% (3/50) of patients in the 7 mg/kg group (MG [n=2] and congestive cardiac failure [n=1]) and no patients in the 10 mg/kg group
- Infections were reported in 26.0% (13/50) of patients in the 7 mg/kg group and 21.4% (9/42) of patients in the 10 mg/kg group
  - There were no serious, severe or opportunistic infections, and no infections led to study discontinuation
- No clinically relevant reductions in albumin were observed and no patients reported TEAEs related to albumin reductions
- There were no deaths

Efficacy

- Clinically relevant improvements in MG-ADL score were observed with rozanolixizumab treatment (**Figure 2a**)
  - CFB in MG-ADL score showed a stable trend up to Week 33, after which patient numbers were lower (≤10 per treatment group at any scheduled assessment); mean CFB was consistently greater in the 10 mg/kg group compared with the 7 mg/kg group up to Week 33
  - The maximum mean reduction from baseline up to Week 33 was –3.1 (Week 13) for the 7 mg/kg group and –4.1 (Week 21) for the 10 mg/kg group
  - A rapid decrease from baseline in MG-ADL score was observed at Week 5, the earliest time of assessment following treatment initiation, with a mean CFB of –2.7 in the 7 mg/kg group and –3.2 in the 10 mg/kg group
- Similar trends were observed in the CFB of MGC (**Figure 2b**) and QMG scores (**Figure 2c**)
- A rapid median decrease from baseline in total IgG of 48.0% in the 7 mg/kg group and 47.9% in the 10 mg/kg group was observed at Week 2
  - The median maximum reduction from baseline was 75.6% (n=32) and 79.9% (n=33), respectively
- Use of rescue therapy up to Week 60 was reported in 4 (11.4%) patients in the 7 mg/kg group (2 each during the treatment and observation periods) and no patients in the 10 mg/kg group; all received IVIg

Figure 1 MG0004 study design



*Patients could switch dose from 10 mg/kg to 7 mg/kg and vice versa at the investigator's discretion.

Table 1 Baseline demographic and patient characteristics

		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)
Geographic region, n (%)	North America	**16** (45.7)	**11** (30.6)	**27** (38.0)
	Europe	**15** (42.9)	**21** (58.3)	**36** (50.7)
	Asia (excl. Japan)	**0**	**2** (5.6)	**2** (2.8)
	Japan	**4** (11.4)	**2** (5.6)	**6** (8.5)
Race, n (%)	Asian	**4** (11.4)	**4** (11.1)	**8** (11.3)
	Black	**2** (5.7)	**3** (8.3)	**5** (7.0)
	White	**17** (48.6)	**19** (52.8)	**36** (50.7)
	Missing*	**12** (34.3)	**10** (27.8)	**22** (31.0)
Thymectomy, yes, n (%)		**14** (40.0)	**15** (41.7)	**29** (40.8)
Historical anti-AChR Ab+, n (%)		**30** (85.7)	**32** (88.9)	**62** (87.3)
Historical anti-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 for systemic use	**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)

Randomized set; 1 patient was not treated and was not included in the safety set.
*Data on race were not permitted to be collected in France and Canada.
†Data obtained at MG0003 baseline.

Summary and conclusions

MG0004 was a Phase 3, multicenter, randomized, OLE study of chronic weekly rozanolixizumab treatment for up to 52 weeks in patients with gMG

Chronic weekly rozanolixizumab was generally well tolerated, with a safety profile similar to repeated cycles of rozanolixizumab treatment[5]

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

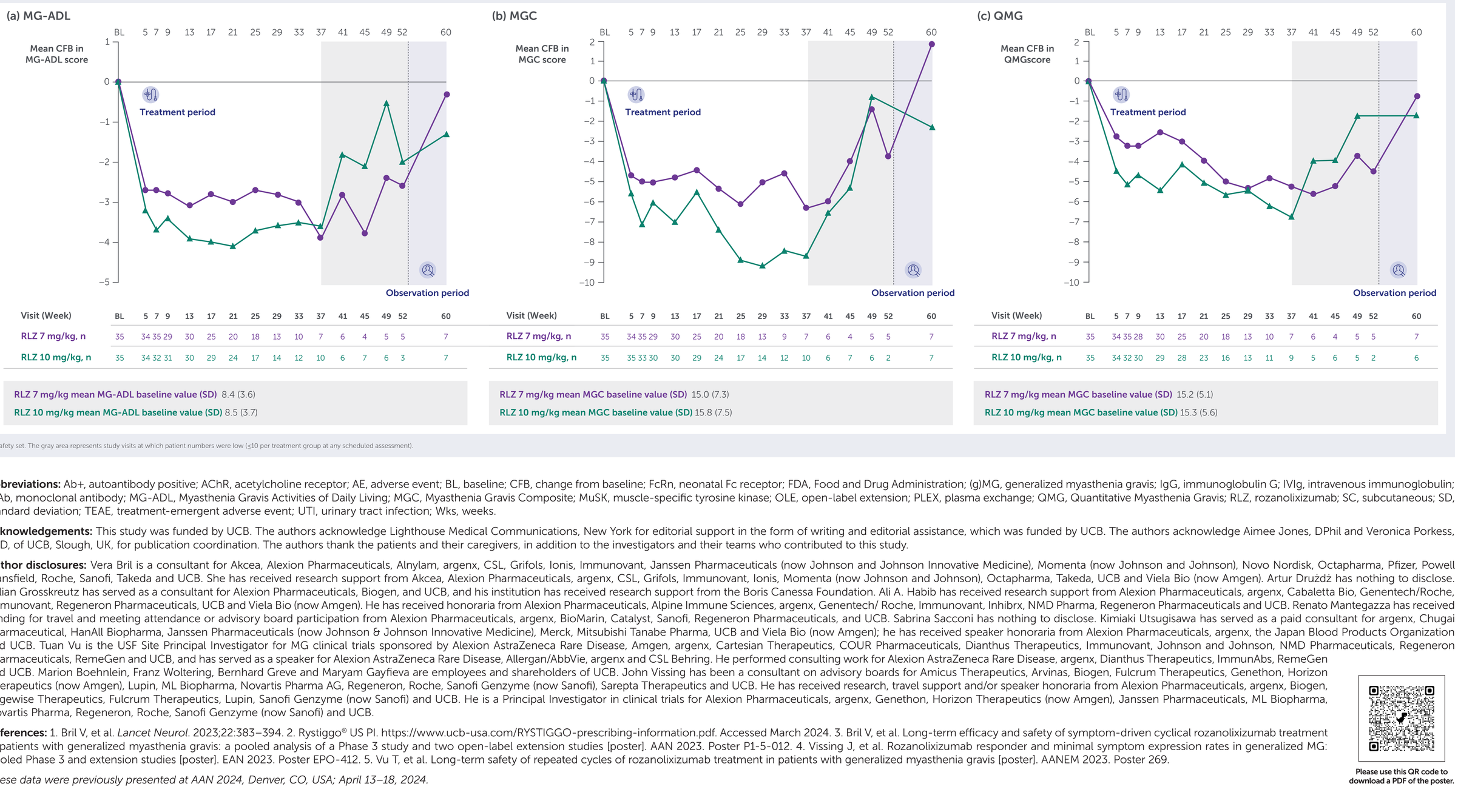
The MG0004 study further supports the long-term safety, tolerability and efficacy of rozanolixizumab in patients with AChR Ab+ or MuSK Ab+ gMG

Table 2 Overview of TEAEs

	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)
Diarrhea	**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)
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.
*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.
‡MG (n=2) and congestive cardiac failure (n=1).
§Specific severe TEAEs listed are those occurring in >1 patient overall.

Figure 2 Mean CFB in MG-ADL, MGC, and QMG scores



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 mean MG-ADL baseline value (SD) 8.4 (3.6)
RLZ 10 mg/kg mean MG-ADL baseline value (SD) 8.5 (3.7)

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 mean MGC baseline value (SD) 15.0 (7.3)
RLZ 10 mg/kg mean MGC baseline value (SD) 15.8 (7.5)

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 mean MGC baseline value (SD) 15.2 (5.1)
RLZ 10 mg/kg mean MGC baseline value (SD) 15.3 (5.6)

Safety set. The gray area represents study visits at which patient numbers were low (≤10 per treatment group at any scheduled assessment).

Abbreviations: Ab+, autoantibody positive; AChR, acetylcholine receptor; AE, adverse event; BL, baseline; CFB, change from baseline; FcRn, neonatal Fc receptor; FDA, Food and Drug Administration; (g)MG, generalized myasthenia gravis; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; mAb, monoclonal antibody; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGC, Myasthenia Gravis Composite; MuSK, muscle-specific tyrosine kinase; OLE, open-label extension; PLEX, plasma exchange; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SC, subcutaneous; SD, standard deviation; TEAE, treatment-emergent adverse event; UTI, urinary tract infection; Wks, weeks.

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