Effect of rozanolixizumab on ocular symptoms in patients with generalized myasthenia gravis: A *post hoc* item-level analysis of myasthenia gravis-specific outcomes in MycarinG

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Introduction

- Patients with gMG may experience ocular symptoms such as diplopia (double vision) and ptosis (eyelid drooping) due to ocular muscle weakness[1]
  - Ocular symptoms in MG pose a substantial burden for patients, impacting their QoL and daily activities, including driving and working[2]
  - The response of ocular signs and symptoms to therapy may vary from that of generalized muscular weakness[3]
- In the double-blind, Phase 3 MycarinG study (NCT03971422), rozanolixizumab, a humanized IgG4 mAb FcRn inhibitor, demonstrated statistically significant and clinically meaningful improvements across MG-specific outcomes versus placebo (**Figure 1**)[4]
  - Improvements in ocular subdomains across MG-specific measures, including in MG-ADL, QMG (**Figure 1**) and the MG Symptoms PRO Ocular Muscle Weakness scale have also been shown[5]
- This descriptive *post hoc* analysis aimed to investigate the effect of rozanolixizumab on ocular symptoms in patients with gMG enrolled in the MycarinG study using ocular item-level scores

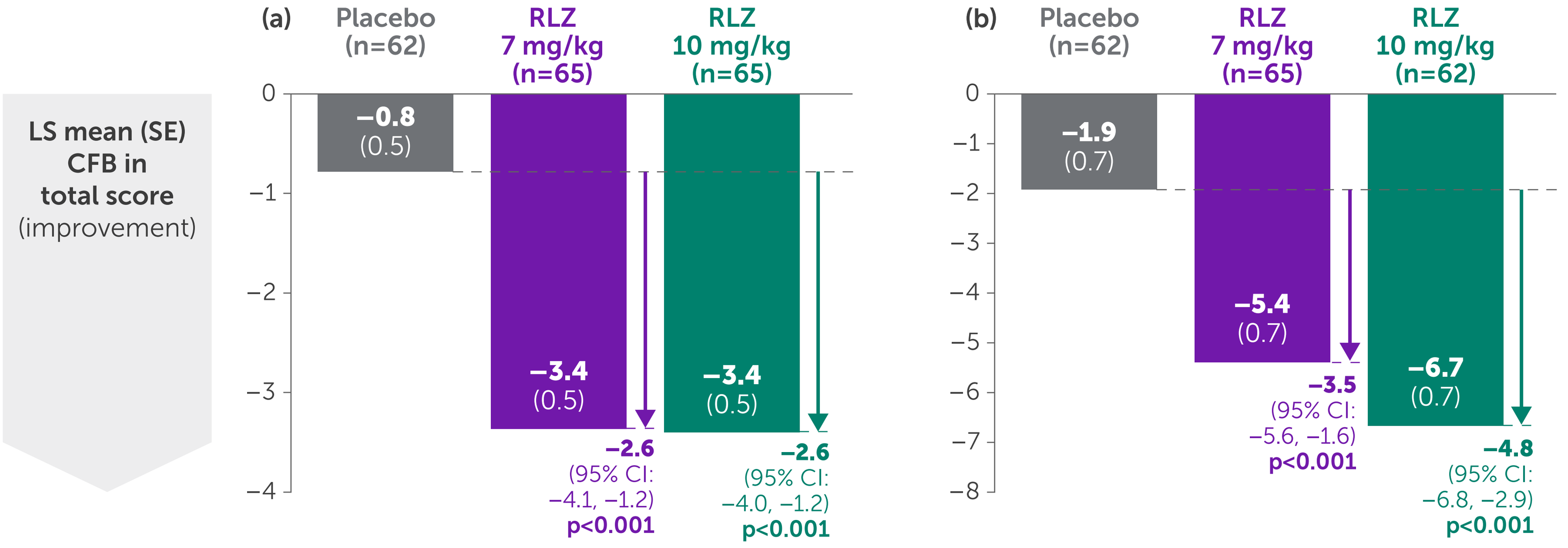
Methods

- Adults with MGFA Disease Class II–IVa anti-AChR Ab+ or anti-MuSK Ab+ gMG with an MG-ADL score ≥3 (for non-ocular symptoms) and a QMG score ≥11 were enrolled
- Patients were randomized 1:1:1 to once-weekly subcutaneous rozanolixizumab 7 mg/kg, 10 mg/kg or placebo for 6 weeks followed by an 8-week observation period
- The primary endpoint was CFB to Day 43 in MG-ADL total score; secondary endpoints included CFB to Day 43 in QMG total score
- Mean CFB in ocular item-level scores of patients with a baseline score ≥1 in each item was analyzed *post hoc*
  - MG-ADL: Double vision and eyelid droop
  - QMG: Double vision and ptosis
  - MG Symptoms PRO Ocular Muscle Weakness: Double vision and eyelid droop
- The incidence of TEAEs in the overall population was also assessed

Results

- Overall, 200 patients received rozanolixizumab 7 mg/kg (n=66), 10 mg/kg (n=67) or placebo (n=67)
  - Baseline demographics and disease characteristics were generally balanced between the treatment groups
- Among patients with ocular symptoms at baseline, greater improvements from baseline to Day 43 were observed in patients treated with rozanolixizumab versus those who received placebo in all but one of the MG-ADL and QMG ocular item-level scores (**Figures 2 and 3**)
- Similarly, patients with ocular symptoms at baseline who recieved rozanolixizumab showed greater improvements from baseline to Day 43 in the MG Symptoms PRO Ocular Muscle Weakness item-level scores compared with those receiving placebo (**Figure 4**)
- Across all MG-ADL, QMG and MG Symptoms PRO Ocular Muscle Weakness ocular items, rozanolixizumab treatment resulted in a greater proportion of patients achieving a score of 0 versus placebo at Day 43 (**Table 1**)
- Overall, TEAEs occurred in 81.3% (n=52/64), 82.6% (n=57/69) and 67.2% (n=45/67) of patients treated with rozanolixizumab 7 mg/kg, 10 mg/kg and placebo, respectively; most were mild or moderate

Figure 1 Greater improvements from baseline in (a) MG-ADL and (b) QMG total scores were observed at Day 43 with rozanolixizumab versus placebo; greater improvements versus placebo were also observed in ocular subdomain scores



(a)

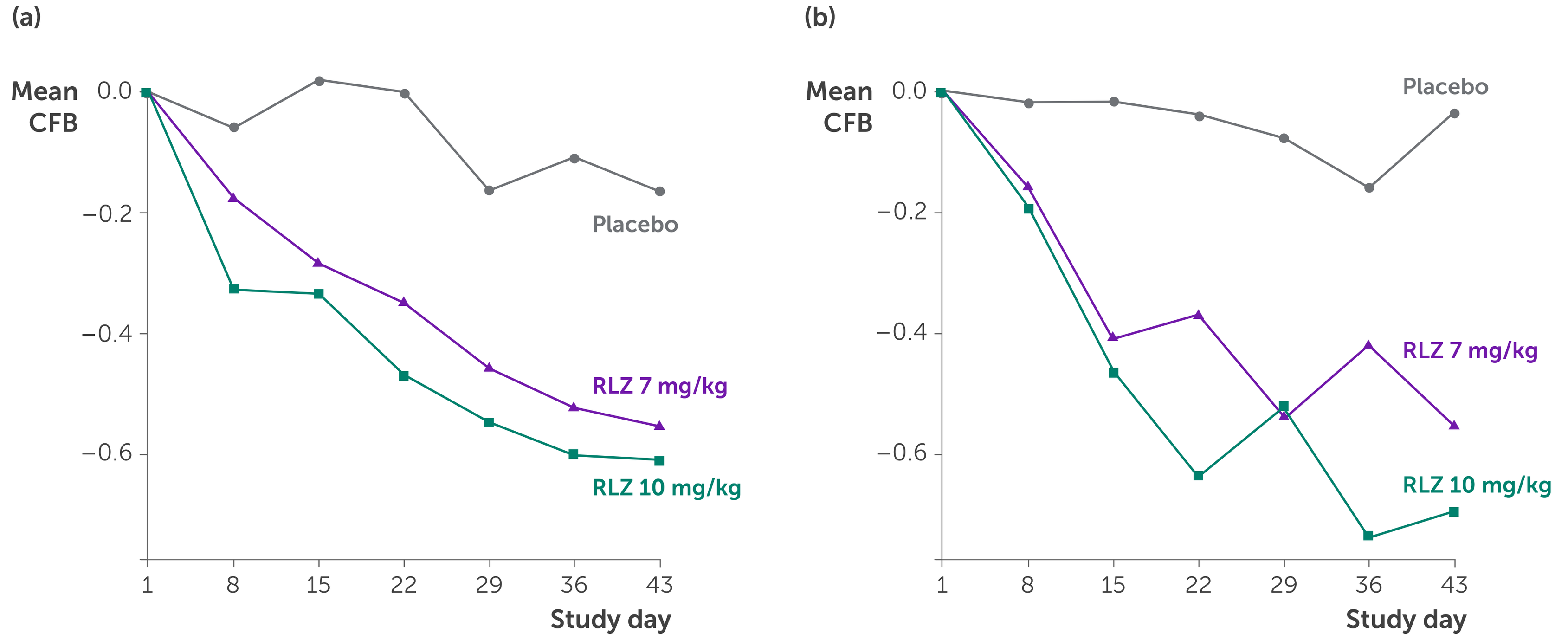
	Placebo (N=67)	RLZ 7 mg/kg (N=66)	RLZ 10 mg/kg (N=67)
Baseline score, mean (SD)	**8.4** (3.4)	**8.4** (3.8)	**8.1** (2.9)
Baseline ocular subdomain score, mean (SD)	**2.9** (1.6)	**2.6** (1.8)	**2.6** (1.7)
CFB at Day 43 in ocular subdomain score, n Mean (SD)	64 **−0.1** (0.9)	64 **−0.8** (1.3)	62 **−1.0** (1.2)

(b)

	Placebo (N=67)	RLZ 7 mg/kg (N=66)	RLZ 10 mg/kg (N=67)
Baseline score, mean (SD)	**15.8** (3.5)	**15.4** (3.7)	**15.6** (3.7)
Baseline ocular subdomain score, mean (SD)	**3.7** (2.1)	**3.7** (2.0)	**3.9** (1.9)
CFB at Day 43 in ocular subdomain score, n Mean (SD)	64 **−0.2** (1.6)	64 **−1.1** (1.8)	62 **−1.7** (1.9)

Randomized set, which consisted of all patients who were randomized, using the treatment assigned as opposed to the actual treatment received. Total scores are pre-specified primary and secondary analyses whereas ocular subdomain scores are *post hoc* CFB values.

Figure 2 Greater improvements from baseline to Day 43 in MG-ADL (a) double vision and (b) eyelid droop scores were observed with rozanolixizumab versus placebo



(a)

	Placebo (Nsub=52)	RLZ 7 mg/kg (Nsub=47)	RLZ 10 mg/kg (Nsub=50)
Baseline item-level score, mean (SD)	**1.7** (0.7)	**1.7** (0.7)	**1.7** (0.8)
CFB to Day 43, n Mean (SD)	49 **−0.2** (0.8)	47 **−0.6** (0.9)	46 **−0.6** (0.7)

(b)

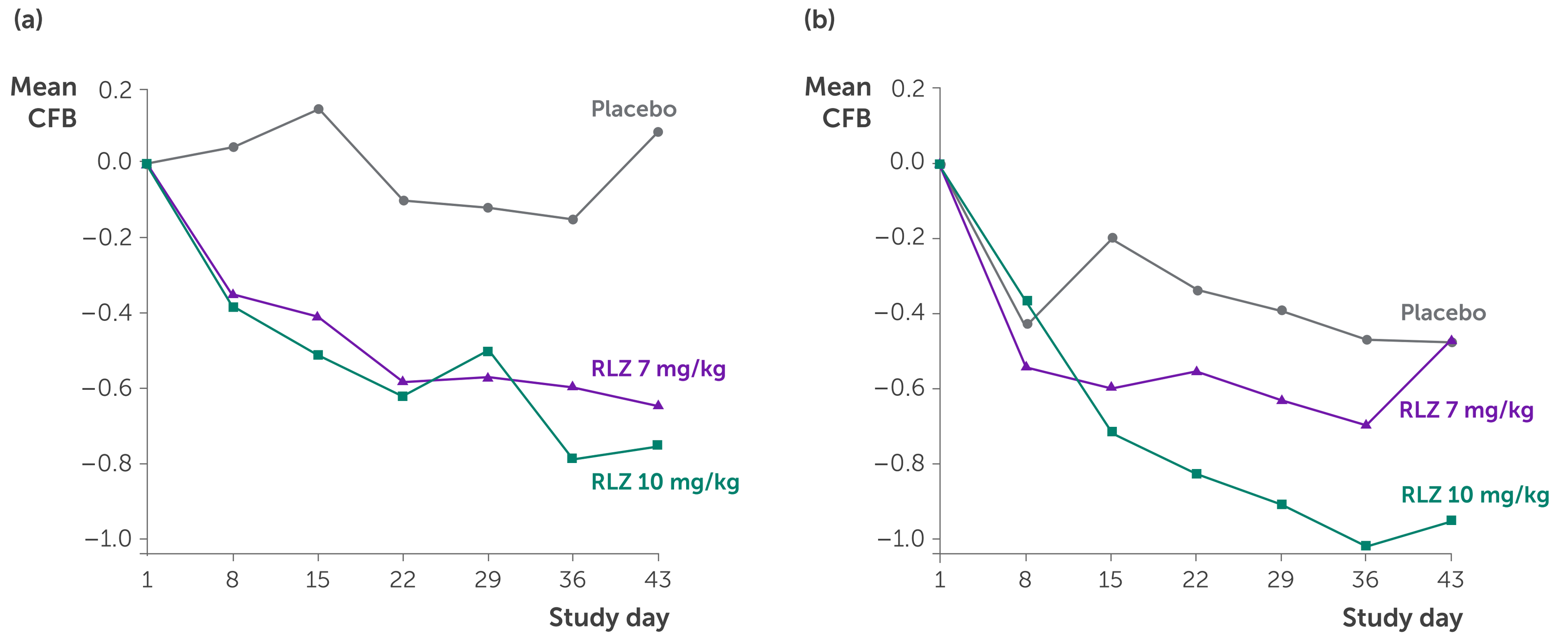
	Placebo (Nsub=54)	RLZ 7 mg/kg (Nsub=51)	RLZ 10 mg/kg (Nsub=54)
Baseline item-level score, mean (SD)	**1.9** (0.8)	**1.8** (0.8)	**1.6** (0.7)
CFB to Day 43, n Mean (SD)	53 **0.0** (0.6)	51 **−0.5** (0.9)	49 **−0.7** (0.8)

Randomized set. Nsub is the number of patients with a baseline score of ≥1 in each item.

Summary and conclusions

- This *post hoc* analysis evaluated the effect of rozanolixizumab versus placebo on ocular symptoms in patients with gMG enrolled in the randomized, double-blind, placebo-controlled Phase 3 MycarinG study
- Ocular symptoms in MG pose a substantial burden for patients, impacting QoL and daily activities
- Overall, greater improvements in ocular item-level scores across MG-specific outcomes were observed with rozanolixizumab than placebo, suggesting a benefit for patients with gMG who experience ocular signs and symptoms

Figure 3 In general, greater improvements from baseline to Day 43 in QMG (a) double vision and (b) ptosis were observed with rozanolixizumab versus placebo



(a)

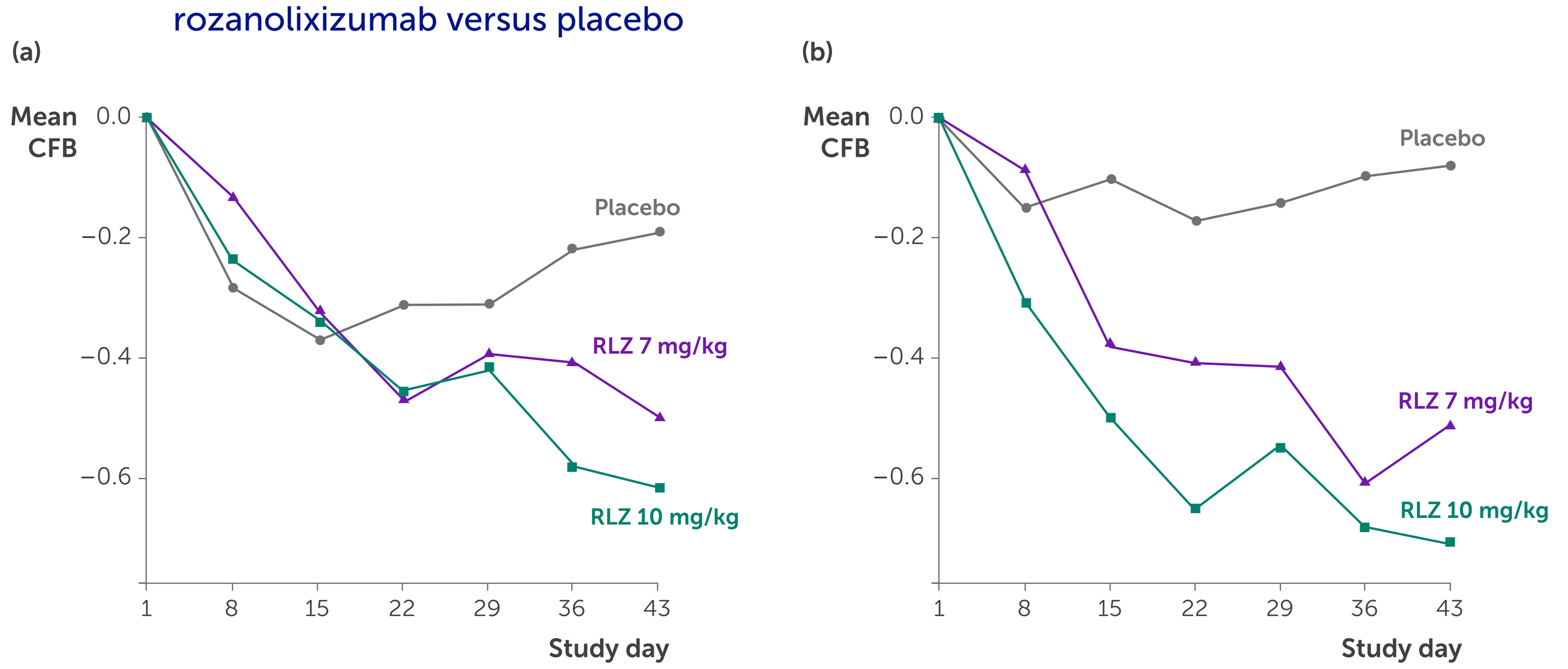
	Placebo (Nsub=51)	RLZ 7 mg/kg (Nsub=46)	RLZ 10 mg/kg (Nsub=53)
Baseline item-level score, mean (SD)	**1.9** (0.9)	**2.1** (0.8)	**2.0** (0.8)
CFB to Day 43, n Mean (SD)	50 **0.1** (1.1)	45 **−0.6** (1.1)	48 **−0.8** (1.1)

(b)

	Placebo (Nsub=51)	RLZ 7 mg/kg (Nsub=48)	RLZ 10 mg/kg (Nsub=49)
Baseline item-level score, mean (SD)	**1.9** (0.9)	**1.8** (0.9)	**1.8** (0.9)
CFB to Day 43, n Mean (SD)	50 **−0.5** (0.9)	47 **−0.5** (1.0)	44 **−1.0** (1.1)

Randomized set. Nsub is the number of patients with a baseline score of ≥1 in each item.

Figure 4 Greater improvements from baseline to Day 43 in MG Symptoms PRO Ocular Muscle Weakness (a) double vision and (b) eyelid drooping scores were observed with rozanolixizumab versus placebo



(a)

	Placebo (Nsub=49)	RLZ 7 mg/kg (Nsub=44)	RLZ 10 mg/kg (Nsub=51)
Baseline item-level score, mean (SD)	**1.8** (0.7)	**1.6** (0.7)	**1.5** (0.8)
CFB to Day 43, n Mean (SD)	46 **−0.2** (1.0)	44 **−0.5** (0.8)	47 **−0.6** (0.7)

(b)

	Placebo (Nsub=51)	RLZ 7 mg/kg (Nsub=49)	RLZ 10 mg/kg (Nsub=50)
Baseline item-level score, mean (SD)	**1.8** (0.8)	**1.6** (0.7)	**1.5** (0.7)
CFB to Day 43, n Mean (SD)	50 **−0.1** (0.7)	49 **−0.5** (0.7)	45 **−0.7** (0.7)

Randomized set. Nsub is the number of patients with a baseline score of ≥1 in each item.

Table 1 Across all ocular items assessed, rozanolixizumab treatment resulted in a greater proportion of patients achieving a score of 0 versus placebo at Day 43

Legend: 0–<10% | 10–<20% | 20–<30% | 30–<40% | 40–<50% | 50–100%

	Placebo N=67	RLZ 7 mg/kg N=66	RLZ 10 mg/kg N=67
MG-ADL ocular, % (n/Nsub)			
Double vision	**13.5** (7/52)	**31.9** (15/47)	**34.0** (17/50)
Eyelid droop	**7.4** (4/54)	**31.4** (16/51)	**46.3** (25/54)
QMG ocular, % (n/Nsub)			
Double vision	**9.8** (5/51)	**26.1** (12/46)	**32.1** (17/53)
Ptosis	**15.7** (8/51)	**31.3** (15/48)	**46.9** (23/49)
MG Symptoms PRO Ocular Muscle Weakness, % (n/Nsub)			
Double vision	**14.3** (7/49)	**29.5** (13/44)	**35.3** (18/51)
Eyelid drooping	**9.8** (5/51)	**26.5** (13/49)	**42.0** (21/50)

Randomized set. Nsub is the number of patients with a baseline score of ≥1 in each item.

Abbreviations: Anti-AChR Ab+, anti-acetylcholine receptor antibody positive; anti-MuSK Ab+, anti-muscle-specific tyrosine kinase antibody positive; CFB, change from baseline; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG4, immunoglobulin G4; LS, least squares; mAb, monoclonal antibody; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; PRO, patient-reported outcome; QoL, quality of life; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event.

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