Effect of rozanolixizumab on myasthenia gravis-specific outcome subdomain scores: *Post hoc* analyses from the Phase 3 MycarinG study

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Robert M. Pascuzzi[1], Ali A. Habib[2], John Vissing[3], Tuan Vu[4], Asha Hareendran[5], Francesca Pannullo[5], Thaïs Tarancón[6], Vera Bril[7] on behalf of the MycarinG study team

[1]Neurology Department, Indiana University School of Medicine, Indiana University Health, Indianapolis, IN, USA; [2]MDA ALS & Neuromuscular Center, Department of Neurology, University of California, Irvine, Orange, CA, USA; [3]Department of Neurology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [4]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, FL, USA; [5]UCB, Slough, UK; [6]UCB, Madrid, Spain; [7]University Health Network, Toronto, ON, Canada

Introduction

- Rozanolixizumab is a humanized IgG4 mAb FcRn inhibitor approved for the treatment of adults with AChR Ab+ or MuSK Ab+ gMG[1,2]
- In the randomized, double-blind, placebo-controlled, Phase 3, MycarinG study (NCT03971422), one 6-week cycle of rozanolixizumab significantly improved MG-specific outcomes versus placebo in patients with gMG (**Figure 1**)[1]
- Treatment for gMG may have differential effects across the different muscle groups affected by the disease[3–5]
  - These differential effects have been evaluated using the subdomain scores of MG-ADL and QMG[5–7]
  - This *post hoc* analysis aimed to evaluate the effect of rozanolixizumab treatment on MG-ADL and QMG subdomain scores assessing ocular, bulbar, respiratory and limb weakness/gross motor muscle groups

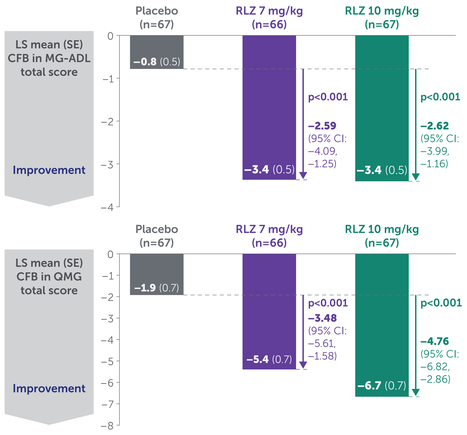
Methods

- Patients enrolled in MycarinG were aged ≥18 years with AChR Ab+ or MuSK Ab+ gMG, MGFA Disease Class II–IVa, with an MG-ADL score ≥3 (for non-ocular symptoms) and a QMG score ≥11[1]
- Patients were randomized 1:1:1 to receive weekly subcutaneous rozanolixizumab 7 mg/kg, rozanolixizumab 10 mg/kg, or placebo for 6 weeks, followed by an 8-week observation period[1]
- The primary endpoint was CFB to Day 43 in MG-ADL total score; secondary endpoints included CFB to Day 43 in QMG total score[1]
- MG-ADL and QMG subdomain scores were derived by grouping individual items into muscle groups (**Table 1**)[8,9]
- The CFB to Day 43 in MG-ADL and QMG subdomains was analyzed *post hoc*
  - All *post hoc* analyses were descriptive

Results

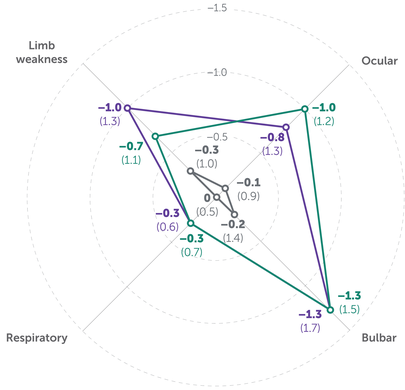
- Overall, 200 patients received rozanolixizumab 7 mg/kg (n=66), 10 mg/kg (n=67), or placebo (n=67)
- Baseline demographics and disease characteristics were generally balanced between the treatment groups (**Table 2**)
- Mean CFB at Day 43 across all MG-ADL subdomain scores was higher for the rozanolixizumab treatment groups compared with the placebo group (**Figure 2**)
  - In rozanolixizumab-treated patients, mean CFB was highest in the bulbar subdomain score
- Mean CFB at Day 43 across all QMG subdomain scores was also higher for the rozanolixizumab treatment groups compared with the placebo group (**Figure 3**)
  - In rozanolixizumab-treated patients, mean CFB was highest in the gross motor subdomain score
- In all patients, mean CFB was lowest in the respiratory subdomain score for both MG-ADL and QMG. However, mean respiratory subdomain scores at baseline were low (**Figure 2** and **3**); patients with severe respiratory or oropharyngeal muscle weakness (MGFA Disease Class IVb/V) were excluded from the study
- Rozanolixizumab treatment was generally well tolerated, and most adverse events were mild or moderate (**Table 3**)
  - The most frequent TEAEs in rozanolixizumab-treated patients were headache (41.4%), diarrhea (20.3%), pyrexia (16.5%), and nausea (9.8%)

Figure 1 CFB in MG-ADL and QMG total scores at Day 43



Randomized set.

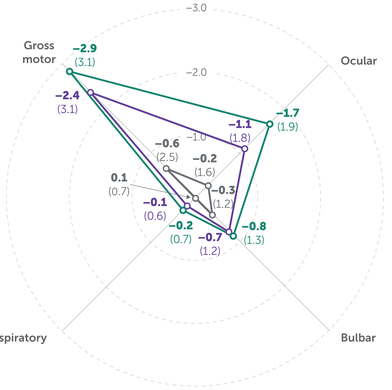
Figure 2 Mean (SD) CFB in MD-ADL subdomain scores at Day 43



Mean (SD) baseline subdomain scores	Ocular	Bulbar	Limb weakness	Respiratory
Placebo (n=67)	2.9 (1.6)	2.4 (1.6)	2.2 (1.2)	1.0 (0.6)
RLZ 7 mg/kg (n=66)	2.6 (1.8)	2.5 (1.7)	2.2 (1.5)	1.0 (0.5)
RLZ 10 mg/kg (n=67)	2.6 (1.7)	2.6 (1.6)	2.0 (1.2)	0.9 (0.5)

Randomized set. Patients with MGFA Disease Class IVb/V disease were excluded from MycarinG.

Figure 3 Mean (SD) CFB in QMG subdomain scores at Day 43



Mean (SD) baseline subdomain scores	Ocular	Bulbar	Gross motor	Respiratory
Placebo (n=67)	3.7 (2.1)	1.5 (1.5)	10.0 (2.5)	0.6 (0.9)
RLZ 7 mg/kg (n=66)	3.7 (2.0)	1.2 (1.2)	10.0 (2.7)	0.5 (0.9)
RLZ 10 mg/kg (n=67)	3.9 (1.9)	1.5 (1.3)	9.4 (2.9)	0.7 (1.0)

Randomized set. Patients with MGFA Disease Class IVb/V disease were excluded from MycarinG.

Summary and conclusions

In the Phase 3 MycarinG study, one 6-week cycle of rozanolixizumab treatment significantly improved MG-ADL and QMG total scores versus placebo in patients with gMG

Compared with placebo, rozanolixizumab treatment led to improvements at Day 43 across ocular, bulbar, respiratory and limb weakness/gross motor muscle groups evaluated by MG-ADL and QMG subdomain scores

The findings from *post hoc* analyses support the efficacy of rozanolixizumab across a broad range of signs and symptoms experienced by patients with gMG, including those with ocular and bulbar symptoms

Table 1 MG-ADL and QMG items comprising the muscle group for each subdomain score

Muscle group	MG-ADL*	QMG†
Ocular	• Double vision • Eyelid droop	• Double vision • Ptosis (upward gaze) • Facial muscles
Bulbar	• Talking • Chewing • Swallowing	• Speech • Swallowing
Respiratory	• Breathing	• Forced vital capacity
Limb weakness/gross motor	• Impairment of ability to brush teeth or comb hair • Impairment of ability to arise from a chair	• Right arm outstretched • Left arm outstretched • Right hand grip • Left hand grip • Head lift • Right leg outstretched • Left leg outstretched

*The total MG-ADL score ranges from 0 to 24, with a higher score indicating more severe disability.
†The total QMG score ranges from 0 to 39, with a higher score indicating more severe disability.

Table 2 Baseline demographic and disease characteristics

		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)
AChR Ab+, n (%)		**59** (88.1)	**60** (90.9)	**60** (89.6)
MuSK Ab+, n (%)		**8** (11.9)	**5** (7.6)	**8** (11.9)
Duration of disease, years, mean (SD)		**9.4** (9.3)	**6.9** (6.8)	**9.6** (9.9)
MG-ADL score, mean (SD)		**8.4** (3.4)	**8.4** (3.8)	**8.1** (2.9)
QMG score, mean (SD)		**15.8** (3.5)	**15.4** (3.7)	**15.6** (3.7)
MGFA Disease Class, n (%)	IIa/b	**23** (34.3)	**29** (43.9)	**26** (38.8)
	IIIa/b	**41** (61.2)	**34** (51.5)	**39** (58.2)
	IVa/b*	**3** (4.5)	**3** (4.5)	**2** (3.0)

Randomized set.
*Only one patient, who was randomized to the placebo group, had Class IVb disease.

Table 3 Overview of TEAEs

Preferred term	Placebo (n=67), % (n)	RLZ 7 mg/kg (n=64), % (n)*	RLZ 10 mg/kg (n=69), % (n)*
Any TEAE	**67.2** (45)	**81.3** (52)	**82.6** (57)
Serious TEAEs	**9.0** (6)	**7.8** (5)	**10.1** (7)
Patient withdrawal from study due to TEAEs	**3.0** (2)	**3.1** (2)	**7.2** (5)
Treatment-related TEAEs†	**32.8** (22)	**50.0** (32)	**56.5** (39)
Severe TEAEs	**4.5** (3)	**4.7** (3)	**18.8** (13)
All deaths (AEs leading to death)	**0**	**0**	**0**

Safety set.
*Two patients in the rozanolixizumab 7 mg/kg group who incorrectly received 10 mg/kg were analyzed in the 10 mg/kg group for safety analyses.
†Treatment-related TEAEs as assessed by investigators.

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

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