Effect of rozanolixizumab on bulbar and respiratory symptoms in patients with generalized myasthenia gravis: *Post hoc* item-level analysis of MycarinG

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Thomas Wallace[1], Carlo Antozzi[2], Julian Grosskreutz[3], Ali A. Habib[4], Robert M. Pascuzzi[5], Sabrina Sacconi[6], John Vissing[7], Tuan Vu[8], Fiona Grimson[9], Thaïs Tarancón[10], Vera Bril[11] on behalf of the MycarinG study team

[1]UCB, Smyrna, GA, USA; [2]Neuroimmunology and Muscle Pathology Unit, Multiple Sclerosis Center, Fondazione Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale Neurologico Carlo Besta, Milan, Italy; [3]Precision Neurology of Neuromuscular Diseases, Department of Neurology, University of Lübeck, Lübeck, Germany; [4]MDA ALS & Neuromuscular Center, Department of Neurology, University of California, Irvine, Orange, CA, USA; [5]Neurology Department, Indiana University School of Medicine, Indiana University Health, Indianapolis, IN, USA; [6]Université Côte d'Azur, Peripheral Nervous System & Muscle Department, Pasteur 2 Hospital, Centre Hospitalier Universitaire de Nice, Nice, France; [7]Department of Neurology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [8]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, FL, USA; [9]UCB, Slough, UK; [10]UCB, Madrid, Spain; [11]University Health Network, Toronto, ON, Canada

Introduction

- Fluctuating muscle weakness is the predominant manifestation of gMG, which can be life-threatening if bulbar or respiratory muscles are affected[1–3]
  - Bulbar impairment has been demonstrated in up to 80% of patients with anti-MuSK Ab+ gMG, with these patients experiencing more severe bulbar symptoms and more frequent myasthenic crises than patients with anti-AChR Ab+ gMG[3,4]
- Rozanolixizumab is a humanized IgG4 mAb FcRn inhibitor approved for the treatment of adults with anti-AChR Ab+ or anti-MuSK Ab+ gMG[5,6]
- In the double-blind, placebo-controlled, Phase 3 MycarinG study (NCT03971422), rozanolixizumab demonstrated clinically meaningful improvements in MG-ADL and QMG total scores versus placebo in patients with gMG[5]
- This *post hoc* analysis aimed to assess the effect of rozanolixizumab on bulbar and respiratory symptoms in patients with gMG in the MycarinG study

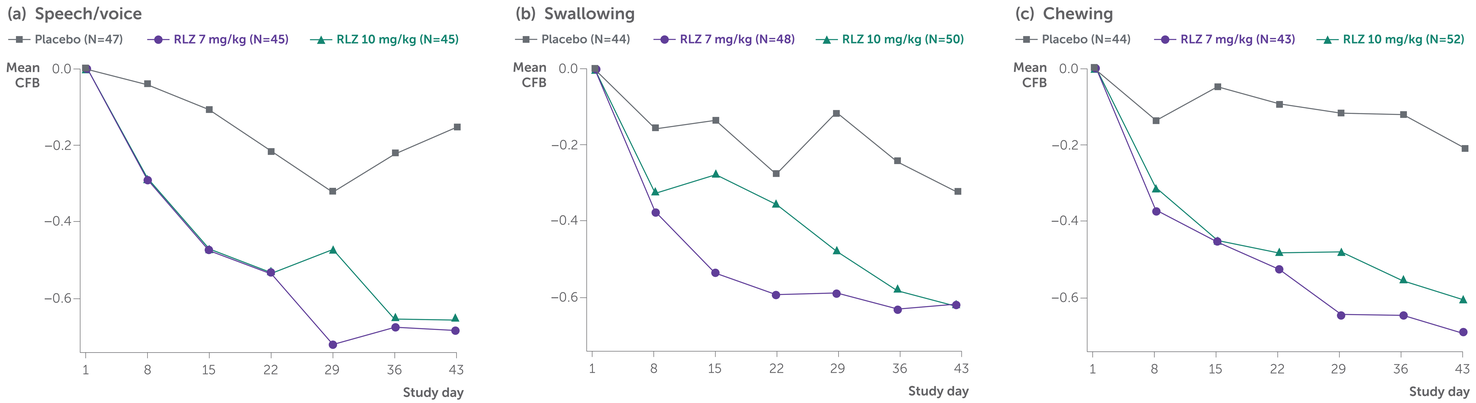
Methods

- 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[5]
- Patients were randomized 1:1:1 to once-weekly subcutaneous infusions of rozanolixizumab 7 mg/kg, 10 mg/kg or placebo for 6 weeks (Day 43), followed by an 8-week observation period[5]
- The primary endpoint was CFB at Day 43 in MG-ADL total score; secondary endpoints included CFB at Day 43 in QMG total score[5]
- Mean CFB at Day 43 in MG-ADL and QMG bulbar and respiratory item-level scores was assessed *post hoc* for patients with a baseline score of ≥1 in each item
- 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
  - Patients included adults with moderate-to-severe anti-AChR Ab+ (n=179) or anti-MuSK Ab+ (n=21) gMG
- LS mean (SE) CFB in MG-ADL total score at Day 43 in the rozanolixizumab 7 mg/kg, 10 mg/kg and placebo groups was: –3.4 (0.5), –3.4 (0.5) and –0.8 (0.5), respectively (p-value for difference versus placebo: p<0.001 for both)
  - LS mean (SE) CFB in QMG total score at Day 43 was: –5.4 (0.7), –6.7 (0.7) and –1.9 (0.7), respectively (p-value for difference versus placebo: p<0.001 for both)
- Patients treated with rozanolixizumab showed greater improvements from baseline to Day 43 in MG-ADL and QMG bulbar item-level scores than those who received placebo (**Figures 1 and 2**)
  - Similarly, greater improvements were observed from baseline to Day 43 in MG-ADL and QMG respiratory item-level scores in rozanolixizumab-treated patients compared with placebo-treated patients (**Figure 3**)
  - Numerical separation from placebo was observed as early as Day 8 for the majority of items
- Rozanolixizumab treatment resulted in a higher percentage of patients achieving a score of 0 versus placebo at Day 43 in all but one of the MG-ADL and QMG bulbar and respiratory items (**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 Mean CFB in MG-ADL bulbar item-level scores: (a) speech/voice, (b) swallowing and (c) chewing for patients with baseline score ≥1 in that item



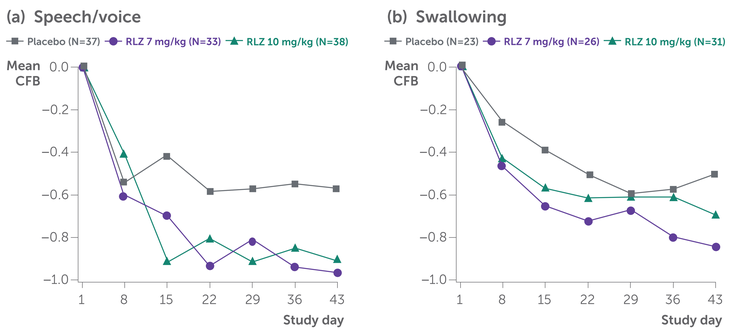
	Placebo (N=47)	RLZ 7 mg/kg (N=45)	RLZ 10 mg/kg (N=45)
Baseline item-level score, mean (SD)	**1.2** (0.4)	**1.3** (0.5)	**1.2** (0.5)
CFB to Day 43, n/N* Mean (SD)	**46/47** **–0.2** (0.6)	**44/45** **–0.7** (0.7)	**41/45** **–0.7** (0.7)

	Placebo (N=44)	RLZ 7 mg/kg (N=48)	RLZ 10 mg/kg (N=50)
Baseline item-level score, mean (SD)	**1.2** (0.4)	**1.2** (0.4)	**1.2** (0.4)
CFB to Day 43, n/N* Mean (SD)	**43/44** **–0.3** (0.7)	**47/48** **–0.6** (0.6)	**45/50** **–0.6** (0.6)

	Placebo (N=44)	RLZ 7 mg/kg (N=43)	RLZ 10 mg/kg (N=52)
Baseline item-level score, mean (SD)	**1.2** (0.4)	**1.3** (0.4)	**1.2** (0.4)
CFB to Day 43, n/N* Mean (SD)	**43/44** **–0.2** (0.5)	**43/43** **–0.7** (0.7)	**48/52** **–0.6** (0.6)

Randomized set, which consisted of all patients who were randomized, using the treatment assigned instead of the actual treatment received. Data reported in the tables have been rounded to one decimal place. *CFB to Day 43 was calculated for patients with baseline and Day 43 data.

Figure 2 Mean CFB in QMG bulbar item-level scores: (a) speech/voice and (b) swallowing for patients with baseline score ≥1 in that item

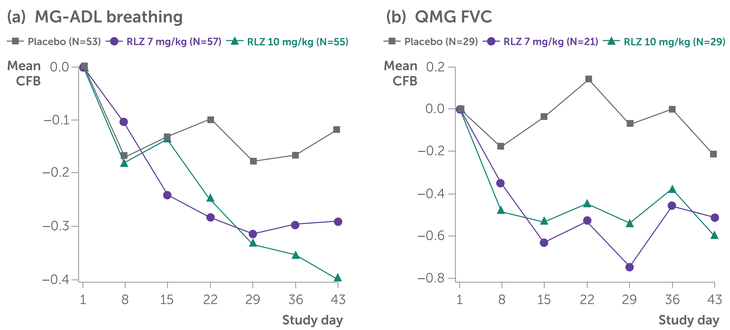


	Placebo (N=37)	RLZ 7 mg/kg (N=33)	RLZ 10 mg/kg (N=38)
Baseline item-level score, mean (SD)	**1.9** (0.7)	**1.6** (0.7)	**1.8** (0.8)
CFB to Day 43, n/N* Mean (SD)	**35/37** **–0.6** (0.9)	**32/33** **–1.0** (0.8)	**34/38** **–0.9** (1.0)

	Placebo (N=23)	RLZ 7 mg/kg (N=26)	RLZ 10 mg/kg (N=31)
Baseline item-level score, mean (SD)	**1.2** (0.4)	**1.1** (0.3)	**1.1** (0.3)
CFB to Day 43, n/N* Mean (SD)	**22/23** **–0.5** (0.6)	**25/26** **–0.8** (0.5)	**29/31** **–0.7** (0.7)

Randomized set. Data reported in the tables have been rounded to one decimal place. *CFB to Day 43 was calculated for patients with baseline and Day 43 data.

Figure 3 Mean CFB in MG-ADL and QMG respiratory item-level scores: (a) MG-ADL breathing and (b) QMG FVC for patients with baseline score ≥1 in that item



	Placebo (N=53)	RLZ 7 mg/kg (N=57)	RLZ 10 mg/kg (N=55)
Baseline item-level score, mean (SD)	**1.2** (0.4)	**1.2** (0.4)	**1.1** (0.3)
CFB to Day 43, n/N* Mean (SD)	**51/53** **–0.1** (0.5)	**55/57** **–0.3** (0.6)	**50/55** **–0.4** (0.7)

	Placebo (N=29)	RLZ 7 mg/kg (N=21)	RLZ 10 mg/kg (N=29)
Baseline item-level score, mean (SD)	**1.4** (0.7)	**1.7** (0.8)	**1.7** (0.8)
CFB to Day 43, n/N* Mean (SD)	**27/29** **–0.2** (0.6)	**21/21** **–0.5** (0.7)	**25/29** **–0.6** (0.9)

Randomized set. Data reported in the tables have been rounded to one decimal place. *CFB to Day 43 was calculated for patients with baseline and Day 43 data.

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; FVC, forced vital capacity; gMG, 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; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event.

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Summary and conclusions

In the Phase 3 MycarinG study, rozanolixizumab treatment resulted in clinically meaningful and statistically significant improvements in MG-ADL and QMG total scores from baseline compared with placebo

Patients receiving rozanolixizumab also showed greater improvements from baseline to Day 43 in all MG-ADL and QMG bulbar and respiratory item-level scores than those receiving placebo

A greater proportion of patients receiving rozanolixizumab acheived an item-level score of 0 at Day 43 in all but one of the MG-ADL and QMG bulbar and resipiratory items versus those receiving placebo

These data support the efficacy of treatment with rozanolixizumab for patients with gMG exhibiting bulbar and/or respiratory symptoms, which can be life-threatening[3]

Table 1 Proportion of patients achieving a score of 0 in MG-ADL and QMG respiratory and bulbar items

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 bulbar, % (n/Nsub)			
Speech/voice	**21.3** (10/47)	**51.1** (23/45)	**51.1** (23/45)
Swallowing	**31.8** (14/44)	**47.9** (23/48)	**42.0** (21/50)
Chewing	**13.6** (6/44)	**48.8** (21/43)	**40.4** (21/52)
MG-ADL respiratory, % (n/Nsub)			
Breathing	**13.2** (7/53)	**24.6** (14/57)	**38.2** (21/55)
QMG bulbar, % (n/Nsub)			
Speech/voice	**24.3** (9/37)	**54.5** (18/33)	**39.5** (15/38)
Swallowing	**34.8** (8/23)	**69.2** (18/26)	**51.6 (16/31)**
QMG respiratory, % (n/Nsub)			
FVC	**20.7** (6/29)	**33.3** (7/21)	**20.7** (6/29)

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

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