AANEM Poster **300**
MGFA Scientific Session Poster **MG103**

Rozanolixizumab in patients aged ≥65 years with generalized myasthenia gravis: A *post hoc* analysis of the Phase 3 MycarinG study

AANEM Annual Meeting & MGFA Scientific Session; Savannah, GA, USA; October 15–18, 2024

Tuan Vu[1], Ali A. Habib[2], Robert M. Pascuzzi[3], Sabrina Sacconi[4], Fiona Grimson[5], Irene Pulido-Valdeolivas[6], Thaïs Tarancón[6], Vera Bril[7] on behalf of the MycarinG study team

[1]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, FL, USA; [2]MDA ALS & Neuromuscular Center, Department of Neurology, University of California, Irvine, Orange, CA, USA; [3]Neurology Department, Indiana University School of Medicine, Indiana University Health, Indianapolis, IN, USA; [4]Université Côte d'Azur, Peripheral Nervous System & Muscle Department, Pasteur 2 Hospital, Centre Hospitalier Universitaire de Nice, Nice, France; [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 adult patients with AChR Ab+ or MuSK Ab+ gMG[1,2]
- Patients aged ≥65 years are often underrepresented in clinical studies[3]
- This *post hoc* analysis evaluated rozanolixizumab in patients with gMG aged ≥65 years who were enrolled in the MycarinG study

Methods

- The randomized, double-blind, placebo-controlled, Phase 3 MycarinG study (NCT03971422) enrolled patients aged ≥18 years (no upper age limit) with AChR Ab+ or MuSK Ab+ gMG, MGFA Disease Class II–IVa, MG-ADL score ≥3 (for non-ocular symptoms) and QMG score ≥11[4]
- Patients were randomized 1:1:1 to once-weekly subcutaneous placebo, rozanolixizumab 7 mg/kg or rozanolixizumab 10 mg/kg for 6 weeks
- The primary endpoint was CFB at Day 43 in MG-ADL score; secondary endpoints included CFB at Day 43 in QMG score
- **Analysis of the primary and secondary endpoints was prespecified for the subgroup of age (<65 and ≥65 years); baseline characteristics and incidence of TEAEs were analyzed by age *post hoc***
- All subgroup analyses were descriptive

Results

Patients

- Overall, 200 patients received placebo (n=67), rozanolixizumab 7 mg/kg (n=66) or rozanolixizumab 10 mg/kg (n=67)
  - 151 patients were aged <65 years
  - 49 patients were aged ≥65 years
- Median (range) age at baseline was 45.0 (18–64) years in the subgroup of patients aged <65 years and 72.0 (65–89) years in the subgroup of patients aged ≥65 years
- Baseline characteristics were broadly similar between patients aged <65 years and those aged ≥65 years (**Table 1**)
  - Concomitant medications were used by 98.0% of patients aged <65 years and all patients aged ≥65 years
- Previous or ongoing comorbidities according to medical history at baseline were generally more common in patients aged ≥65 years than those aged <65 years (**Table 2**)
  - Incidence of infections was similar across both age subgroups

Efficacy

- At Day 43, greater reductions from baseline in MG-ADL scores were observed for rozanolixizumab-treated patients versus placebo-treated patients in both the <65 years and ≥65 years subgroups, with a slightly greater extent of improvement observed in the younger subgroup than the older subgroup (**Figure 1**)
- A similar trend was observed for LSM (SE) CFB in QMG scores at Day 43
  - Patients aged <65 years: placebo, −2.65 (0.76); rozanolixizumab 7 mg/kg, −5.73 (0.75); rozanolixizumab 10 mg/kg, −7.11 (0.77)
  - Patients aged ≥65 years: placebo, −1.06 (1.56); rozanolixizumab 7 mg/kg, −3.30 (1.66); rozanolixizumab 10 mg/kg, −4.36 (1.66)

Safety

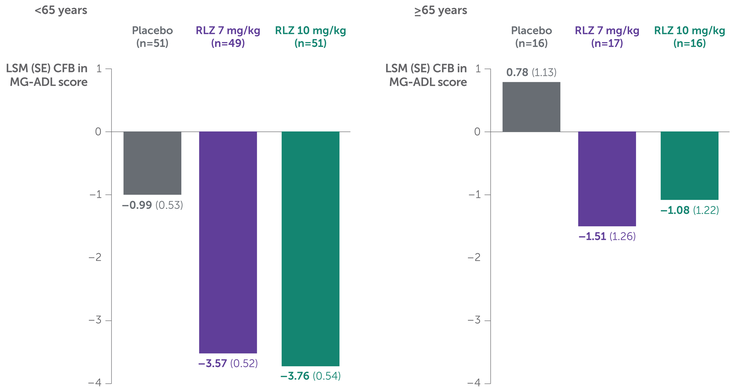
- TEAEs occurred in 60.8–85.4% of patients aged <65 years and 68.8–87.5% of patients aged ≥65 years (**Table 3**)
  - The most common TEAE overall in the MycarinG study was headache, which was experienced by a higher proportion of patients aged <65 years than ≥65 years
  - The most frequent TEAE among all patients aged ≥65 years was diarrhea; most events were mild or moderate
- Incidence of infections was comparable between older and younger rozanolixizumab-treated patients
  - Patients aged <65 years: placebo, 15.7%; rozanolixizumab 7 mg/kg, 14.6%; rozanolixizumab 10 mg/kg, 30.8%
  - Patients aged ≥65 years: placebo, 31.3%; rozanolixizumab 7 mg/kg, 18.8%; rozanolixizumab 10 mg/kg, 29.4%; incidence was lowest in the rozanolixizumab 7 mg/kg group and comparable between the placebo and rozanolixizumab 10 mg/kg groups

Table 1 Baseline characteristics

		<65 years			≥65 years		
		Placebo n=51	RLZ 7 mg/kg n=49	RLZ 10 mg/kg n=51	Placebo n=16	RLZ 7 mg/kg n=17	RLZ 10 mg/kg n=16
Age, years, median (range)		**41.0** (18–64)	**46.0** (22–64)	**47.0** (19–64)	**71.5** (68–85)	**71.0** (65–89)	**72.5** (65–81)
Age at initial MG diagnosis, years, mean (SD)		**33.4** (13.7)	**40.0** (12.1)	**34.8** (14.9)	**66.8** (8.4)	**65.6** (9.2)	**67.1** (4.7)
Sex, female, n (%)		**38** (74.5)	**33** (67.3)	**32** (62.7)	**9** (56.3)	**6** (35.3)	**3** (18.8)
MGFA Disease Class, n (%)	IIa/b	**16** (31.4)	**21** (42.9)	**20** (39.2)	**7** (43.8)	**8** (47.1)	**6** (37.5)
	IIIa/b	**32** (62.7)	**26** (53.1)	**29** (56.9)	**9** (56.3)	**8** (47.1)	**10** (62.5)
	IVa/b	**3** (5.9)	**2** (4.1)	**2** (3.9)	**0**	**1** (5.9)	**0**
Thymectomy, yes, n (%)		**29** (56.9)	**29** (59.2)	**19** (37.3)	**2** (12.5)	**3** (17.6)	**1** (6.3)
MG-ADL score, mean (SD)		**9.0** (3.4)	**8.2** (3.9)	**8.2** (2.8)	**6.6** (2.5)	**9.0** (3.7)	**7.8** (3.0)
QMG score, mean (SD)		**16.3** (3.8)	**15.6** (3.6)	**15.5** (3.9)	**14.5** (2.2)	**15.1** (4.1)	**16.1** (3.0)
Duration of disease, years, mean (SD)		**10.1** (10.1)	**7.0** (7.2)	**10.7** (10.8)	**7.3** (6.0)	**6.6** (5.8)	**5.9** (4.7)
Prior MG crisis, n (%)		**16** (31.4)	**13** (26.5)	**14** (27.5)	**7** (43.8)	**6** (35.3)	**3** (18.8)
Baseline medication, n (%)	MuSK Ab+ gMG, n (%)*	**7** (13.7)	**5** (10.2)	**7** (13.7)	**1** (6.3)	**0**	**1** (6.3)
	AChR Ab+ gMG, n (%)*	**44** (86.3)	**43** (87.8)	**45** (88.2)	**15** (93.8)	**17** (100.0)	**15** (93.8)
	Any AChEI	**46** (90.2)	**41** (83.7)	**42** (82.4)	**13** (81.3)	**14** (82.4)	**15** (93.8)
	Any CS	**26** (51.0)	**33** (67.3)	**38** (74.5)	**12** (75.0)	**9** (52.9)	**10** (62.5)
	Any NSIST	**24** (47.1)	**23** (46.9)	**28** (54.9)	**8** (50.0)	**8** (47.1)	**9** (56.3)

Randomized set. *Captured from historical case report form.

Figure 1 Mean CFB to Day 43 in MG-ADL score by age subgroup and treatment group



LSM difference vs placebo (97.5% CI)	
RLZ 7 mg/kg	**−2.58** (−3.96, −1.20)
RLZ 10 mg/kg	**−2.77** (−4.13, −1.40)

LSM difference vs placebo (97.5% CI)	
RLZ 7 mg/kg	**−2.29** (−5.19, 0.61)
RLZ 10 mg/kg	**−1.85** (−4.69, 0.98)

Randomized set.

Summary and conclusions

This *post hoc* analysis evaluated rozanolixizumab treatment in patients with gMG aged ≥65 years who were enrolled in the Phase 3 MycarinG study

At baseline, previous or ongoing comorbidities were more frequent in patients aged ≥65 years than those aged <65 years, with all patients aged ≥65 years receiving concomitant medications

Treatment with rozanolixizumab was efficacious and generally well tolerated regardless of age subgroup, with slightly greater improvements from baseline in MG-ADL score observed in patients aged <65 years than those aged ≥65 years, and comparable safety profiles

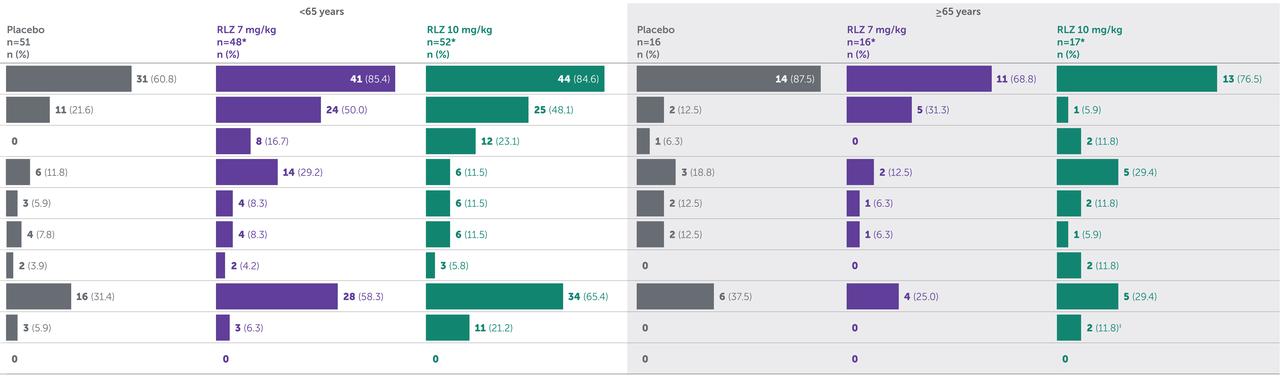
Overall, the findings of this *post hoc* analysis support the use of rozanolixizumab in patients with gMG aged ≥65 years, an underrepresented group in clinical studies

Table 2 Previous or ongoing conditions according to medical history at baseline by age subgroup

SOC	<65 years N=151 n (%)	≥65 years N=49 n (%)
Any*	**151** (100.0)	**49** (100.0)
Nervous system disorders	**151** (100.0)	**49** (100.0)
Metabolism and nutrition disorders†	**45** (29.8)	**32** (65.3)
Musculoskeletal and connective tissue disorders†	**38** (25.2)	**28** (57.1)
Vascular disorders†	**41** (27.2)	**27** (55.1)
Respiratory, thoracic and mediastinal disorders†	**31** (20.5)	**22** (44.9)
GI disorders	**43** (28.5)	**20** (40.8)
Eye disorders†	**21** (13.9)	**19** (38.8)
Cardiac disorders†	**19** (12.6)	**18** (36.7)
Endocrine disorders	**25** (16.6)	**15** (30.6)
Reproductive system and breast disorders	**17** (11.3)	**14** (28.6)
Infections and infestations	**35** (23.2)	**11** (22.4)
Psychiatric disorders	**30** (19.9)	**11** (22.4)
Renal and urinary disorders	**22** (14.6)	**11** (22.4)
Immune system disorders	**15** (9.9)	**10** (20.4)
Neoplasms benign, malignant and unspecified (including cysts and polyps)	**27** (17.9)	**10** (20.4)
Surgical and medical procedures	**33** (21.9)	**5** (10.2)

Randomized set. *Specific SOCs listed are those that occurred in ≥20% of patients in either age subgroup. †More common in patients aged ≥65 years than those aged <65 years by ≥20 percentage points.

Table 3 Overview of TEAEs and most frequent TEAEs by age subgroup and treatment group



Safety set. Bars represent the percentage of patients. *Two patients in the 7 mg/kg group (n=1 for each age subgroup) who incorrectly received 10 mg/kg were analyzed in the 10 mg/kg group for safety analyses. ‡Specific TEAEs listed are those that occurred in ≥10% of patients across both RLZ treatment groups in either age subgroup. †Diarrhea (n=1) and acute respiratory insufficiency and tracheal prosthesis dislocation (n=1).

Abbreviations: AE, adverse event; AChEI, acetylcholinesterase inhibitor; AChR Ab+, positive for autoantibodies against the acetylcholine receptor; CFB, change from baseline; CI, confidence interval; CS, corticosteroid; FcRn, neonatal Fc receptor; GI, gastrointestinal; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; LSM, least squares mean; mAb, monoclonal antibody; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK Ab+, positive for autoantibodies against muscle-specific tyrosine kinase; NSIST, non-steroidal immunosuppressive therapy; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation; SE, standard error; SOC, system organ class; TEAE, treatment-emergent adverse event.

Acknowledgments: This study was funded by UCB. The authors acknowledge Beatrix Poulton, BSc, of Ogilvy Health, London, UK, for editorial assistance, which was funded by UCB. The authors thank Veronica Porkess, PhD, of UCB for publication and editorial support. The authors thank the patients and their caregivers, in addition to the investigators and their teams who contributed to this study.

Author disclosures: 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 Pharmaceuticals, 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. 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. Robert M. Pascuzzi is Professor Emeritus of Neurology at Indiana University and receives compensation for his professional work from Indiana University Health. He has no financial relationship with any pharmaceutical company and receives no compensation from any pharmaceutical company (present or past). Robert M. Pascuzzi speaks at educational seminars on a broad variety of general neurology topics for primary care physicians through the organization Medical Education Resources (an educational organization with no links or ties to any pharmaceutical or healthcare business company). Therefore, Robert M. Pascuzzi has no conflicts of interest related to this research, manuscript, presentation, or publication. Sabrina Sacconi has nothing to disclose. Fiona Grimson, Irene Pulido-Valdeolivas, and Thaïs Tarancón are employees and shareholders of UCB. Vera Bril is a Consultant for Alexea, Alexion Pharmaceuticals, Almylam, 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 Alexea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson & Johnson), Octapharma, Takeda Pharmaceuticals, UCB and Viela Bio (now Amgen).

References: 1. Smith B, et al. mAbs. 2018;10(7):1111–1130. 2. Rozanolixizumab US PI. https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761286s000lbl.pdf. Accessed August 2024. 3. van Marum RJ. Br J Clin Pharmacol. 2020;86(10):2014–2016. 4. Bril V, et al. Lancet Neurol. 2023;22(5):383–394.

Please use this QR code to download a PDF of the poster.