Patient-reported and quality-of-life outcomes from MycarinG, a randomized, placebo-controlled, double-blind, Phase 3 trial of rozanolixizumab in generalized myasthenia gravis

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Summary

gMG is a chronic autoimmune disease that can unpredictably impair patients' routine daily activities

MycarinG assessed the efficacy and safety of the FcRn inhibitor rozanolixizumab in patients with gMG

The MG Symptoms PRO measure is a novel PRO measure developed specifically for use in MG, including a detailed assessment of physical fatigue

Compared to placebo, rozanolixizumab improved multiple patient-reported outcomes, including fatigue

Rozanolixizumab improved the symptoms of patients with MG as well as their ability to carry out daily activities

Objective

- To assess the effect of rozanolixizumab on patient-reported outcomes (PROs) in patients with gMG

Introduction

- gMG is a rare, chronic, heterogeneous and unpredictable autoimmune disease that can impair patients' ability to carry out routine daily activities and negatively impact quality of life[1–3]
- PROs are important tools for understanding the impact of symptoms of a disease on a patient's life and for showing that the effects of a treatment translate into a clinical benefit that is meaningful to patients[4]
  - The MG Symptoms PRO measure is a novel PRO measure developed specifically for use in MG, which aims to provide a more granular and detailed measurement of MG severity than existing measures, including a detailed assessment of physical fatigue that is not included in other measures[4]
- Rozanolixizumab is a humanized IgG4 mAb that inhibits FcRn, reducing IgG autoantibody serum levels[5]
- Here we report the results of rozanolixizumab on PROs of patients with gMG, including the MG Symptoms PRO measure

Methods

- The MycarinG study (MG0003/NCT03971422) was a randomized, double-blind, placebo-controlled, Phase 3 trial
- Adults with MGFA Class II–IVa, AChR or MuSK autoantibody-positive gMG with an MG-ADL score of ≥3 and a QMG score of ≥11, who were considered for treatment with additional therapy such as IVIg or plasma exchange and had a body weight of ≥35 kg, were enrolled
- Patients were randomized 1:1:1 to weekly subcutaneous rozanolixizumab 7 mg/kg, 10 mg/kg or placebo for 6 weeks (**Figure 1**)
- The primary endpoint was CFB to Day 43 in MG-ADL
- Secondary PRO endpoints included MG Symptoms PRO Muscle Weakness Fatigability, Physical Fatigue and Bulbar Muscle Weakness. Other PRO endpoints included MGII, MG-QoL 15r and EQ-5D-5L (a generic quality-of-life scale that is not MG-specific)

Results

Patients

- A total of 200 patients were randomized (66 to rozanolixizumab 7 mg/kg, 67 to rozanolixizumab 10 mg/kg and 67 to placebo), with 43 patients completing the study in both the rozanolixizumab 7 mg/kg and 10 mg/kg groups and 42 completing the study in the placebo group (**Figure 1**)
- Baseline demographic and disease characteristics were balanced between treatment groups (**Table 1**)

Efficacy

- MG-ADL CFB to Day 43 (primary endpoint) in both rozanolixizumab 7 mg/kg and rozanolixizumab 10 mg/kg groups was clinically meaningfully and highly statistically significantly improved compared with placebo (p<0.001 for both doses; **Figure 2**)
- Greater improvements in Muscle Weakness Fatigability, Physical Fatigue, and Bulbar Muscle Weakness were reported by patients treated with rozanolixizumab than with placebo at Day 43, as assessed by the MG Symptoms PRO (p<0.001 for Muscle Weakness Fatigability and Bulbar Muscle Weakness, both doses; p=0.012 for Physical Fatigue, rozanolixizumab 7 mg/kg; and p<0.001 for Physical Fatigue, rozanolixizumab 10 mg/kg; **Figure 3**)
- Improvement in CFB to Day 43 in MGII was greater in both rozanolixizumab groups than in the placebo group (**Figure 4**)
- Improvements in CFB to Day 43 in MG-QoL 15r and EQ-5D-5L scores were greater in both rozanolixizumab groups than in the placebo group (**Figure 5**)

Safety

- A higher proportion of TEAEs occurred in the rozanolixizumab 7 mg/kg (81.3%) and 10 mg/kg (82.6%) arms than in the placebo arm (67.2%)
  - The majority of TEAEs were mild or moderate in severity with rozanolixizumab 7 mg/kg, 10 mg/kg or placebo
  - The most frequently reported TEAEs were headache, diarrhoea, pyrexia and nausea

Figure 1 Study design

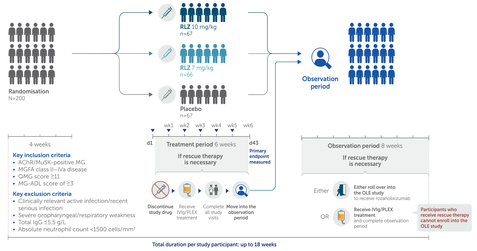


Table 1 Demographic and baseline characteristics

		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)
MGFA class at baseline, n (%)	Class II	23 (34.3)	29 (43.9)	26 (38.8)
	Class III	41 (61.2)	34 (51.5)	39 (58.2)
	Class IVa/b	3 (4.5)	3 (4.5)	2 (3.0)
Geographic region, n (%)	North America	21 (31.3)	21 (31.8)	18 (26.9)
	Europe	41 (61.2)	36 (54.5)	43 (64.2)
	Asia (inc. Japan)	5 (7.5)	9 (13.7)	6 (9.0)
Race, n (%)	Asian	5 (7.5)	9 (13.6)	7 (10.4)
	Black	1 (1.5)	0	4 (6.0)
	White	46 (68.7)	41 (62.1)	49 (73.1)
	Missing*	14 (20.9)	16 (24.2)	7 (10.4)
Baseline medications, n (%)	Corticosteroids for systemic use	38 (56.7)	43 (65.2)	48 (71.6)
	Immunosuppressants	33 (49.3)	32 (48.5)	38 (56.7)
	Parasympathomimetics	60 (89.6)	55 (83.3)	57 (85.1)
Duration of disease, years, mean (SD)		9.4 (9.3)	6.9 (6.8)	9.6 (9.9)
MG-ADL score at baseline, mean (SD)		8.4 (3.4)	8.4 (3.8)	8.1 (2.9)
QMG score at baseline, mean (SD)		15.8 (3.5)	15.4 (3.7)	15.6 (3.7)

*Data on race were not permitted to be collected in certain countries.

Figure 2 LSM CFB to Day 43 in MG-ADL (primary outcome)

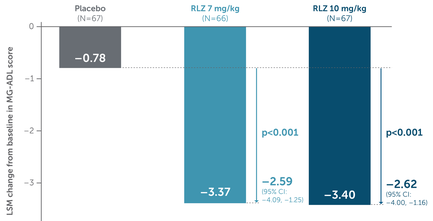
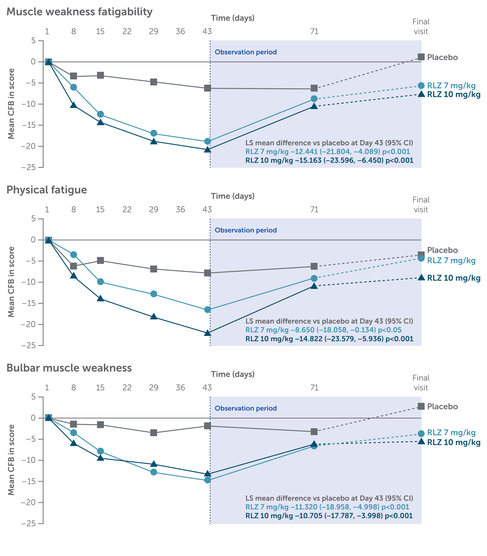
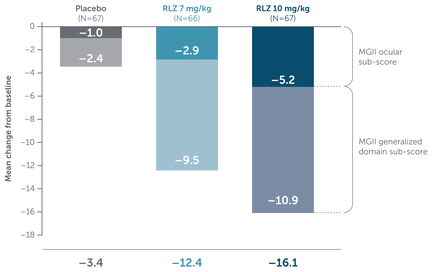


Figure 3 MG Symptoms PRO mean CFB over time



Final visit could occur on any day up to Day 99.

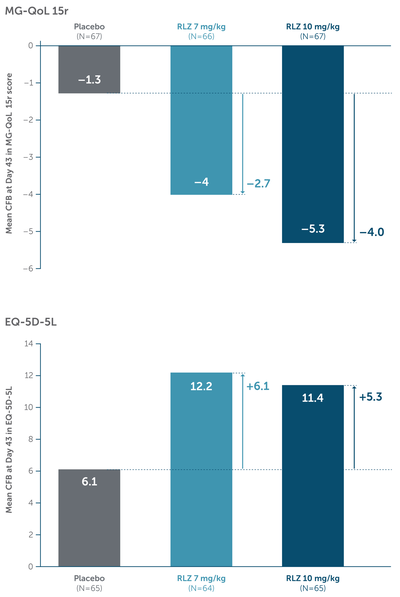
Figure 4 Mean CFB in MGII scores and sub-scores at Day 43



Conclusions

- Both rozanolixizumab 7 mg/kg and 10 mg/kg improved patients' symptoms and their ability to undertake daily activities, as demonstrated by MG-ADL, MG Symptoms PRO scales, MG-QoL 15r and EQ-5D-5L, with an acceptable safety profile
- The MG Symptoms PRO used in this study provides a more granular and detailed assessment of muscle weakness and muscle weakness fatigability symptoms than currently available PRO measures and also includes fatigue, a key concern to people with MG[4]
- Further validation of the MG Symptoms PRO measure is ongoing
- Primary efficacy and safety outcomes from MycarinG are presented at this congress in Poster 25

Figure 5 Mean CFB at Day 43 in MG-QoL 15r and EQ-5D-5L



Rozanolixizumab is not approved for treatment of MG by any health authority.

Abbreviations: AChR, acetylcholine receptor; CFB, change from baseline; CI, confidence interval; d, day; EQ-5D-5L, European Quality of Life 5 Dimensions 5 Levels; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; IVIg, intravenous immunoglobulin; LSM, least-squares mean; mAb, monoclonal antibody; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MGII, Myasthenia Gravis Impairment Index; MG-QoL 15r, Myasthenia Gravis Quality of Life 15-item scale revised; MuSK, muscle-specific kinase; OLE, open-label extension; PLEX, plasma exchange; PRO, patient-reported outcome; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation; TEAE, treatment-emergent adverse event; wk, week.

References: 1. Gilhus NI, *et al. Nat Rev Dis Primers* 2019;5:30. 2. Nowak R. *Neurol Rev (Suppl)* 2018 March;1:1. 3. Twork S, *et al. Health Qual Life Outcomes* 2010;8:129. 4. Cleanthous S, *et al. Orphanet J Rare Dis* 2021;16:457. 5. Smith B, *et al. MAbs* 2018;10:1111–20. **Author disclosure:** Vera Bril is a Consultant for Grifols, CSL, UCB, Argenx, Takeda, Alnylam, Octapharma, Pfizer, Powell Mansfield, Akcea, Ionis, Immunovant, Sanofi, Momenta (now Jb3), Roche, Janssen, Alexion and NovoNordisk. She has received research support from Alexion, Grifols, CSL, UCB Pharma, Argenx, Takeda, Octapharma, Akcea, Momenta, Immunovant, Ionis and Viela Bio (now Horizon). Julian Grosskreutz has served as a Consultant for Biogen, Alexion and UCB, and his institution has received research support from the Boris Canesisa Foundation. Ali A. Habib has received research support from Argenx, Alexion, Viela Bio, UCB Pharma, Genentech, Regeneron and Sanofi. He has received consulting fees/honoraria from Argenx, Alexion and UCB Pharma. Renato Mantegazza has received funding for travel and meeting attendance or advisory board participation from Alexion, Argenx, Biomarin, Catalyst, Sanofi, Regeneron and UCB Pharma. Kimiaki Utsugisawa has served as a paid Consultant for UCB Pharma, Argenx, Janssen Pharma, Viela Bio, Chugai Pharma, Hanall BioPharma and Mitsubishi Tanabe Pharma, and has received speaker honoraria from Argenx, Alexion, Pharmaceuticals and the Japan Blood Products Organization. John Vissing has been a Consultant on advisory boards for Sanofi Genzyme, Sarepta Therapeutics, Viela Bio, Novartis Pharma AG, Fulcrum Therapeutics, Stealth Biotherapeutics, Roche, Biogen, Lupin, Genethon, Amicus Therapeutics, Zogenix, Regeneron, UCB Biopharma, Arvinas, ML Biopharma, Horizon Therapeutics and Lundbeck Pharma. He has received research, travel support, and/or speaker honoraria from Sanofi Genzyme, Argenx, Alexion Pharmaceuticals, Biogen, Lupin, Stealth Biotherapeutics, Edgewise Therapeutics, Fulcrum Therapeutics and UCB Pharma. He is a principal investigator in clinical trials for Sanofi Genzyme, Roche, Horizon Therapeutics, Argenx, Novartis Pharma, Alexion Pharmaceuticals, Stealth Biotherapeutics, UCB Biopharma, Genethon, ML Biopharma, Reneo Pharma, Pharnext, Janssen Pharmaceuticals, Khondrion, Regeneron and Dynacure. Tuan Vu is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion, Argenx, RaVUCB, Horizon/Viela Bio, Janssen/Momenta, Sanofi, Regeneron and Cartesian Therapeutics, and receives speaking and consulting honoraria from Alexion, Argenx and UCB. Henry Kaminski is a Consultant for Roche, Cabaletta Bio, Lincoln Therapeutics, Takeda and UCB Pharmaceuticals, and is CEO and CMO of ARC Biotechnology, LLC based on US Patent 8,961,98. He is Principal Investigator of the Rare Disease Network for Myasthenia Gravis (RGNet) National Institute of Neurological Disorders & Stroke, U54 NS115054 and Targeted Therapy for Myasthenia Gravis. He has received R41 NS103131-01 to ARC Biotechnology. Marion Boehnlein, Ali Bozorg, Maryam Gayfieva, Thomas Morel and Franz Woltering are employees and shareholders of UCB Pharma. Artur Drużdż and Sabrina Sacconi have nothing to disclose. **Acknowledgements.** The authors thank the patients and their caregivers, in addition to the investigators and their teams who contributed to this study. This study was funded by UCB Pharma. The authors acknowledge Luke Worley, Ogilvy Health, London, UK, for editorial assistance, which was funded by UCB. The authors also acknowledge Veronica Porkess, PhD, of UCB Pharma, Slough, UK, for publication coordination.

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