Patient-reported outcomes during repeated cycles of rozanolixizumab treatment in patients with generalized myasthenia gravis in the Phase 3 MycarinG and open-label extension studies

MGFA Scientific Session 2023, Phoenix, AZ, USA; November 01, 2023

Ali A. Habib[1], Henry J. Kaminski[2], John Vissing[3], Asha Hareendran[4], Thomas Morel[5], Marion Boehnlein[6], Franz Woltering[6], Bernhard Greve[6], Thaïs Tarancón[7], Vera Bril[8], on behalf of the MycarinG study investigators

[1]MDA ALS and Neuromuscular Center, University of California, Irvine, Irvine, CA, USA; [2]Department of Neurology & Rehabilitation Medicine, George Washington University, Washington, DC, USA; [3]Department of Neurology, Rigshospitalet, University of Copenhagen, Copenhagen, Denmark; [4]UCB Pharma, Slough, UK; [5]UCB Pharma, Brussels, Belgium; [6]UCB Pharma, Monheim, Germany; [7]UCB Pharma, Madrid, Spain; [8]University Health Network, Toronto, ON, Canada

Introduction

- Patients living with MG experience fluctuating and variable symptoms, including muscle weakness, muscle fatigability and fatigue; each patient's experience is different[1,2]
- The MG Symptoms PRO scales were developed using items relevant to patients, to fully understand patients' experiences of the severity of specific MG symptoms, including the important symptom of physical fatigue[2]
- Rozanolixizumab is a humanized IgG4 monoclonal antibody FcRn inhibitor approved by the US FDA for the treatment of adults with AChR Ab+ or MuSK Ab+ gMG[3,4]
- In the Phase 3 MycarinG study, treatment with one 6-week cycle of rozanolixizumab resulted in significant improvements versus placebo in MG-ADL score (primary endpoint) and other MG-specific endpoints, including the MG Symptoms PRO Muscle Weakness Fatigability, Physical Fatigue and Bulbar Muscle Weakness scale scores[3]
- Here, we assessed the effect of rozanolixizumab on patient-reported MG symptom severity across the Phase 3 MycarinG (MG0003/NCT03971422)[3] study and its OLE (MG0004/NCT04124965; MG0007/NCT04650854) studies

Methods

- MycarinG enrolled patients aged ≥18 years with AChR Ab+ or MuSK Ab+ gMG, MGFA Disease Class II–IVa, MG-ADL score ≥3 (for non-ocular symptoms), and QMG score ≥11
- After completing MycarinG, in which patients were randomized to receive one cycle (six once-weekly infusions) of rozanolixizumab (7 mg/kg or 10 mg/kg) or placebo, patients could enroll in MG0004 (≤52 weeks of once-weekly rozanolixizumab) and then MG0007 (six once-weekly infusions), or in MG0007 directly (**Figure 1**)
- Data for rozanolixizumab-treated patients were pooled across MycarinG, MG0004 (first 6 weeks) and MG0007 (interim analysis; data cut-off: July 08, 2022)
  - Efficacy pool: patients with ≥2 symptom-driven treatment cycles
  - Safety pool: patients with ≥1 treatment cycle that was followed by a ≤8-week follow-up period across MycarinG and MG0007
- Outcomes included:
  - CFB to Day 43 for each cycle in MG-ADL score
  - CFB to Day 43 for each cycle in MG Symptoms PRO Muscle Weakness Fatigability, Physical Fatigue and Bulbar Muscle Weakness scores
  - Safety and tolerability

Results

Patients

- A total of 196 patients received ≥1 dose of rozanolixizumab
  - Efficacy pool: 127 (64.8%) patients
  - Safety pool: 188 (95.9%) patients
- Baseline demographics and characteristics were generally balanced between the efficacy and safety pools (**Table 1**)

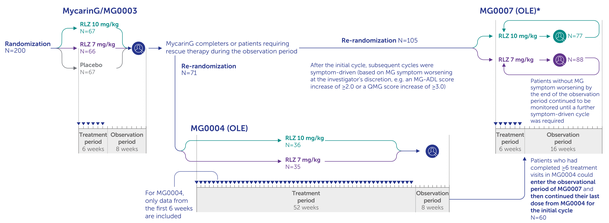
Efficacy

- A clinically meaningful improvement from baseline to Day 43 in MG-ADL score was observed in Cycle 1, with a consistent profile across repeated cycles[5]
- MG Symptoms PRO scale scores showed improvement from baseline to the end of the first treatment cycle, with broadly consistent improvement observed across repeated cycles (**Figure 2**)

Safety

- Across all cycles, 169 (89.9%) patients experienced a TEAE by most recent dose (rozanolixizumab 7 mg/kg: 77.4% [n=103/133]; rozanolixizumab 10 mg/kg: 91.6% [n=120/131])
- The incidence of TEAEs did not increase with repeated cycles of treatment compared with Cycle 1
- Rozanolixizumab was well tolerated over repeated treatment cycles; TEAEs leading to permanent discontinuation from the study occurred in 15.5% (n=29/188) of patients
- Pooled safety data have been presented previously[5] and additional data will be presented at AANEM 2023 (Poster 269)

Figure 1 MycarinG and OLE study design



*After the initial cycle, dose modifications from 10 mg/kg to 7 mg/kg and *vice versa* were permitted at the beginning of each treatment cycle provided the benefit–risk ratio remained favorable for the patient.

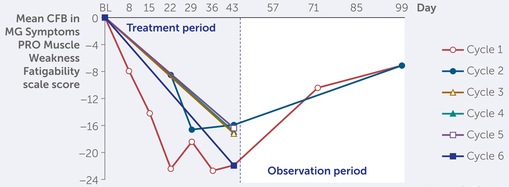
Table 1 Baseline demographics and characteristics

		Efficacy pool RLZ total (N=127)	Safety pool RLZ total (N=188)
Age, years, mean (SD)		**50.6** (16.2)	**52.5** (16.3)
Sex, female, n (%)		**76** (59.8)	**111** (59.0)
Geographic region, n (%)	North America	**28** (22.0)	**54** (28.7)
	Europe	**84** (66.1)	**114** (60.6)
	Asia (excl. Japan)	**3** (2.4)	**7** (3.7)
	Japan	**12** (9.4)	**13** (6.9)
Race, n (%)	Asian	**15** (11.8)	**21** (11.2)
	Black	**1** (0.8)	**4** (2.1)
	White	**83** (65.4)	**127** (67.6)
	Native Hawaiian or other Pacific Islander	**0**	**1** (0.5)
	Missing*	**28** (22.0)	**35** (18.6)
Thymectomy at baseline, yes, n (%)†		**55** (43.3)	**75** (39.9)
AChR Ab+, n (%)†		**115** (90.6)	**170** (90.4)
MuSK Ab+, n (%)†		**12** (9.4)	**18** (9.6)
MG-ADL score at baseline, mean (SD)		**8.8** (3.4)	**8.3** (3.4)
QMG score at baseline, mean (SD)		**16.0** (3.8)	**15.6** (3.6)
Duration of disease, years, mean (SD)		**8.2** (8.6)	**8.5** (8.6)

*Data on race were not permitted to be collected in certain countries. No patients were American Indian/Alaska native or other/mixed.
†Captured from historical data case report form.

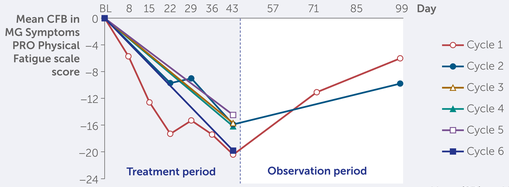
Figure 2 Mean CFB in key MG Symptoms PRO scale scores over time for repeated cycles of rozanolixizumab

(a) Muscle Weakness Fatigability



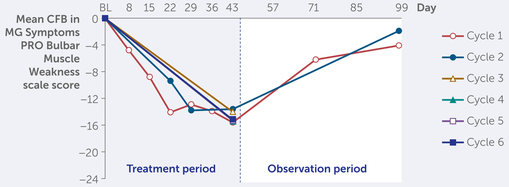
	BL	8	15	22	29	36	43	57	71	85	99	Mean (SD) BL score	Mean (SD) CFB at Day 43
Cycle 1, n	127	91	88	59	94	43	125	–	73	–	92	**49.6** (24.9)	**−21.9** (23.3)
Cycle 2, n	126	–	–	37	14	1	123	–	–	–	16	**44.2** (23.7)	**−15.9** (19.9)
Cycle 3, n	98	–	–	–	–	–	98	–	–	–	–	**46.0** (23.5)	**−17.2** (19.5)
Cycle 4, n	75	–	–	–	–	–	74	–	–	–	–	**47.0** (22.8)	**−16.9** (18.6)
Cycle 5, n	51	–	–	–	–	–	51	–	–	–	–	**44.1** (21.6)	**−16.4** (17.9)
Cycle 6, n	31	–	–	–	–	–	31	–	–	–	–	**45.7** (23.2)	**−21.9** (19.7)

(b) Physical Fatigue



	BL	8	15	22	29	36	43	57	71	85	99	Mean (SD) BL score	Mean (SD) CFB at Day 43
Cycle 1, n	127	91	88	59	94	43	125	–	73	–	92	**52.3** (26.9)	**−20.4** (20.9)
Cycle 2, n	126	–	–	37	13	1	123	–	–	–	16	**47.3** (25.5)	**−15.9** (19.1)
Cycle 3, n	98	–	–	–	–	–	98	–	–	–	–	**49.4** (26.3)	**−15.7** (18.9)
Cycle 4, n	75	–	–	–	–	–	74	–	–	–	–	**50.0** (24.0)	**−16.2** (20.6)
Cycle 5, n	51	–	–	–	–	–	51	–	–	–	–	**47.5** (23.1)	**−14.5** (20.2)
Cycle 6, n	31	–	–	–	–	–	31	–	–	–	–	**48.5** (24.8)	**−19.8** (22.9)

(c) Bulbar Muscle Weakness



	BL	8	15	22	29	36	43	57	71	85	99	Mean (SD) BL score	Mean (SD) CFB at Day 43
Cycle 1, n	127	91	88	59	94	43	125	–	73	–	92	**29.0** (22.5)	**−15.6** (19.1)
Cycle 2, n	126	–	–	37	14	1	123	–	–	–	16	**27.6** (22.8)	**−13.6** (19.7)
Cycle 3, n	98	–	–	–	–	–	98	–	–	–	–	**28.1** (23.3)	**−14.0** (16.8)
Cycle 4, n	75	–	–	–	–	–	74	–	–	–	–	**30.1** (22.8)	**−15.3** (19.8)
Cycle 5, n	51	–	–	–	–	–	51	–	–	–	–	**29.1** (26.0)	**−15.3** (21.4)
Cycle 6, n	31	–	–	–	–	–	31	–	–	–	–	**26.8** (22.8)	**−15.2** (19.1)

Efficacy pool. Efficacy data collected at or after rescue use are excluded with no imputation of missing data for the respective cycle. Data are presented for total rozanolixizumab (7 mg/kg and 10 mg/kg dose groups combined). Higher scores in the MG Symptoms PRO scales (0–100) represent more severe symptoms.

Summary and conclusions

The MG Symptoms PRO scales were developed to collect detailed information about patients' individual experiences of weakness across different muscle groups

In addition, the scales evaluate patients' experiences of muscle weakness fatigability and physical fatigue, which are not commonly evaluated by other MG-specific measures[2]

Data from the MG Symptoms PRO Muscle Weakness Fatigability, Physical Fatigue and Bulbar Muscle Weakness scale scores showed improvement from baseline to the end of the first symptom-driven cycle; consistent improvement was observed in subsequent treatment cycles

Rozanolixizumab was well tolerated over repeated cycles of treatment

Rozanolixizumab consistently improved MG symptoms of most relevance to patients across repeated treatment cycles

Abbreviations: AANEM, American Association of Neuromuscular & Electrodiagnostic Medicine; AChR Ab+, positive for autoantibodies against the acetylcholine receptor; BL, baseline; CFB, change from baseline; FcRn, neonatal Fc receptor; FDA, Food and Drug Administration; gMG, (generalized) myasthenia gravis; IgG, immunoglobulin G; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK Ab+, positive for autoantibodies against muscle-specific kinase; OLE, open-label extension; PRO, patient-reported outcome; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation; TEAE, treatment-emergent adverse event; US, United States.

Acknowledgments: This study was funded by UCB Pharma. The authors acknowledge Beatrix Poulton, BSc, and Mary Berrington, PhD, of Ogilvy Health, London, UK, for editorial support in the form of writing, drafting tables and figures, collating author comments, and editorial assistance, which was funded by UCB Pharma. The authors acknowledge Veronica Porkess, PhD, of UCB Pharma, Slough, UK, for publication coordination. The authors thank the patients and their caregivers, in addition to the investigators and their teams who contributed to this study.

Author disclosures: Ali A. Habib has received research support from Alexion Pharmaceuticals, argenx, Cabaletta Bio, Genentech, Regeneron, UCB Pharma, and Viela Bio (now Horizon Therapeutics). He has received consulting fees/honoraria from Alexion Pharmaceuticals, argenx, Genentech/Roche, Immunovant, and UCB Pharma. Henry J. Kaminski is a Consultant for Roche, Cabaletta Bio, Lincoln Therapeutics, Takeda, and UCB Pharma 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 (MGNet) National Institute of Neurological Disorders & Stroke; U54 NS115054, and Targeted Therapy for Myasthenia Gravis. He has received R41 NS110331-01 to ARC Biotechnology. John Vissing has been a Consultant on advisory boards for Sanofi Genzyme, Sarepta Therapeutics, Viela Bio (now Horizon Therapeutics), Novartis, Fulcrum Therapeutics, Stealth Biotherapeutics, Roche, Biogen, Lupin, Genethon, Amicus Therapeutics, Zogenix, Regeneron, UCB Pharma, 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, Alexion Pharmaceuticals, Stealth Biotherapeutics, UCB Pharma, Genethon, ML Biopharma, Reneo Pharma, Pharnext, Janssen Pharmaceuticals, Khondrion, Regeneron, and Dynacure. Asha Hareendran, Thomas Morel, Marion Boehnlein, Franz Woltering, Bernhard Greve, and Thaïs Tarancón are employees and shareholders of UCB Pharma. Vera Bril is a Consultant for Akcea, Alexion Pharmaceuticals, Alnylam, argenx, CSL, Grifols, Ionis, Immunovant, Janssen Pharmaceuticals, Momenta (now Johnson and Johnson), Novo Nordisk, Octapharma, Pfizer, Powell Mansfield, Sanofi, Takeda, Roche and UCB Pharma. She has received research support from Akcea, Alexion Pharmaceuticals, argenx, CSL, Grifols, Immunovant, Ionis, Momenta (now Johnson and Johnson), Octapharma, Takeda, UCB Pharma and Viela Bio (now Horizon Therapeutics).

References: 1. Barnett C, et al. Neurol Clin. 2018;36(2):339–353. 2. Cleanthous S, et al. Orphanet J Rare Dis. 2021;16(1):457. 3. Bril V, et al. Lancet Neurol. 2023;22(5):383–394. 4. Rystiggo® US PI. https://www.ucb-usa.com/RYSTIGGO-prescribing-information.pdf. Accessed on October 2023.5. Bril V, et al. Long-term efficacy and safety of symptom-driven cyclical rozanolixizumab treatment in patients with generalized myasthenia gravis: a pooled analysis of a Phase 3 study and two open-label extension studies [poster]. AAN 2023. Poster P1-5-012.

For more information on MG Symptoms PRO Scales visit: https://eprovide.mapi-trust.org/instruments/myasthenia-gravis-symptoms-patient-reported-outcome-scales

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