Efficacy of repeated cycles of rozanolixizumab treatment in subgroups of patients with generalized myasthenia gravis: A pooled analysis of a Phase 3 study and two Phase 3 open-label extension studies

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Robert M. Pascuzzi[1], Renato Mantegazza[2], Artur Drużdż[3], Marion Boehnlein[4], Bernhard Greve[4], Franz Woltering[4], Maryam Gayfieva[5], Vera Bril[6], on behalf of the MycarinG study investigators

[1]Department of Neurology, Indiana University School of Medicine, Indiana University Health, Indianapolis, IN, USA; [2]Fondazione Istituto di Ricovero e Cura a Carattere Scientifico, Istituto Nazionale Neurologico Carlo Besta, Milan, Italy; [3]Department of Neurology, Municipal Hospital Poznań, Poznań, Poland; [4]UCB Pharma, Monheim, Germany; [5]UCB Pharma, Slough, UK; [6]University Health Network, Toronto, ON, Canada

Introduction

- Rozanolixizumab is a humanized IgG4 mAb that targets the IgG-binding region of FcRn, accelerating lysosomal degradation of IgG, including pathogenic autoantibodies[1], approved by the US FDA for the treatment of adults with AChR or MuSK Ab+ gMG[2]
- The double-blind, placebo-controlled Phase 3 MycarinG study (MG0003/NCT03971422) demonstrated efficacy of a single 6-week cycle of rozanolixizumab in patients with gMG[3]
- After MycarinG, patients could enroll in two OLE studies, which provide data on additional cycles of rozanolixizumab treatment
- Here, we conducted a subgroup analysis of rozanolixizumab efficacy over repeated cycles of treatment in patients with gMG

Methods

- MycarinG included patients aged ≥18 years with AChR Ab+ or MuSK Ab+ gMG, who were being considered for treatment with additional therapy such as IVIg or plasma exchange
- Patients who completed MycarinG or who required rescue therapy during the observation period could enroll into MG0004 (NCT04124965) then MG0007 (NCT04650854), or directly into MG0007 (**Figure 1**)
- Pooled data are reported across MycarinG, MG0004 (the first 6 weeks only) and MG0007 (interim analysis; data cut-off: July 08, 2022)
- CFB in MG-ADL, QMG and MGC to Day 43 are reported in patients who had received ≥2 symptom-driven treatment cycles (efficacy pool [up to 4 cycles]) for the following prespecified subgroups:
  - Autoantibody status (AChR Ab+/MuSK Ab+)
  - Duration of disease (<5.4 years/≥5.4 years)
  - Age (18–<65 years/≥65 years)
  - Thymectomy (yes/no)
  - Baseline MG-ADL score (<5/≥5)
- TEAEs are reported for patients who had received ≥1 treatment cycle (≥1 dose of rozanolixizumab in any 6-week treatment period followed by an [up to] 8-week follow-up period across MycarinG and MG0007 [safety pool])

Results

Patients

- 127 patients received ≥2 symptom-driven cycles of rozanolixizumab at data cut-off
  - At data cut-off, 152 and 109 patients had undergone at least 6 and 12 months of study duration, respectively
- Baseline characteristics for the efficacy and safety pools are provided in **Table 1**. Between respective subgroups, results were generally similar (data not shown)

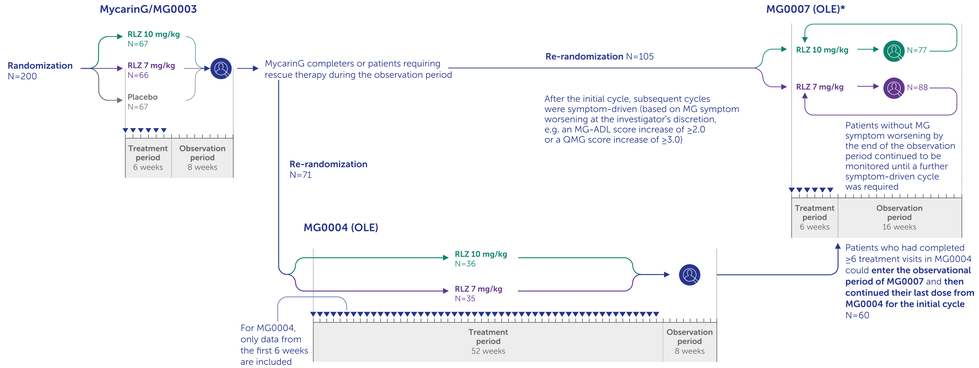
Efficacy

- Efficacy of rozanolixizumab, including mean CFB in MG-ADL, MGC and QMG scores, was maintained over repeated cycles of treatment in the overall population[4]
- Improvements from baseline in MG-ADL scores at Day 43 were consistent between the overall study population and prespecified subgroups, across repeated cycles of rozanolixizumab (**Figures 2–6**)
- Improvements in MGC and QMG score from baseline for the different subgroups were consistent with the overall population

Safety

- Overall, 169/188 (89.9%) patients in the safety pool reported ≥1 TEAE
- In general, the incidence of TEAEs across all categories was similar across subgroups (**Table 2**)
  - The majority of TEAEs were of mild or moderate severity

Figure 1 MycarinG and OLE study design



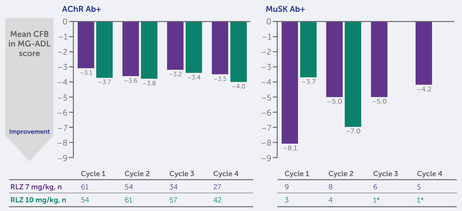
*After the initial cycle, dose modifications from 10 mg/kg to 7 mg/kg and *vice versa* were permitted at the beginning of each treatment cycle and provided the benefit–risk ratio remained favorable for the patient.

Table 1 Baseline demographic and disease characteristics

		Efficacy pool			Safety pool
		RLZ 7 mg/kg (n=69)	RLZ 10 mg/kg (n=58)	RLZ total (N=127)	RLZ total (N=188)
Age, years, mean (SD)		**52.0** (14.3)	**48.9** (18.3)	**50.6** (16.2)	**52.5** (16.3)
Sex, female, n (%)		**40** (58.0)	**36** (62.1)	**76** (59.8)	**111** (59.0)
Geographic region, n (%)	North America	**19** (27.5)	**9** (15.5)	**28** (22.0)	**54** (28.7)
	Europe	**40** (58.0)	**44** (75.9)	**84** (66.1)	**114** (60.6)
	Asia (excl. Japan)	**2** (2.9)	**1** (1.7)	**3** (2.4)	**7** (3.7)
	Japan	**8** (11.6)	**4** (6.9)	**12** (9.4)	**13** (6.9)
Race, n (%)	Asian	**10** (14.5)	**5** (8.6)	**15** (11.8)	**21** (11.2)
	Black	**0**	**1** (1.7)	**1** (0.8)	**4** (2.1)
	Native Hawaiian or other Pacific Islander	**0**	**0**	**0**	**1** (0.5)
	White	**41** (59.4)	**42** (72.4)	**83** (65.4)	**127** (67.6)
	Missing*	**18** (26.1)	**10** (17.2)	**28** (22.0)	**35** (18.6)
Thymectomy at MycarinG baseline, yes, n (%)†		**33** (47.8)	**22** (37.9)	**55** (43.3)	**75** (39.9)
Anti-AChR autoantibody positive, n (%)†		**61** (88.4)	**54** (93.1)	**115** (90.6)	**170** (90.4)
Anti-MuSK autoantibody positive, n (%)†		**9** (13.0)	**3** (5.2)	**12** (9.4)	**18** (9.6)
MG-ADL score at baseline, mean (SD)		**9.1** (3.8)	**8.4** (2.9)	**8.8** (3.4)	**8.3** (3.4)
QMG score at baseline, mean (SD)		**16.0** (3.8)	**16.0** (3.7)	**16.0** (3.8)	**15.6** (3.6)
Duration of disease, years, mean (SD)		**7.9** (8.4)	**8.5** (8.9)	**8.2** (8.6)	**8.5** (8.6)
Baseline gMG medication, n (%)	Corticosteroids for systemic use	**41** (59.4)	**38** (65.5)	**79** (62.2)	**120** (63.8)
	Immunosuppressants	**35** (50.7)	**30** (51.7)	**65** (51.2)	**97** (51.6)
	Parasympathomimetics	**59** (85.5)	**52** (89.7)	**111** (87.4)	**162** (86.2)

Treatment groups are according to the first symptom-driven cycle of RLZ.
*Data on race were not permitted to be collected in some countries. No patients were American Indian/Alaska native, or other/mixed.
†Captured from historical case report form.

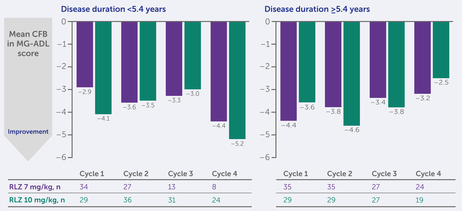
Figure 2 Mean MG-ADL CFB at Day 43 for MuSK Ab+ and AChR Ab+ populations



	AChR Ab+				MuSK Ab+			
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 1	Cycle 2	Cycle 3	Cycle 4
RLZ 7 mg/kg, n	61	54	34	27	9	8	6	5
RLZ 10 mg/kg, n	54	61	57	42	3	4	1*	1*

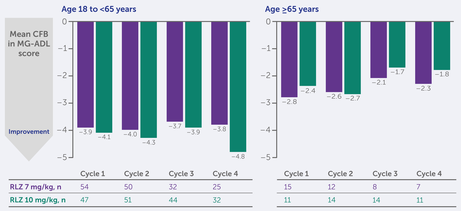
*Mean CFB in MG-ADL score could not be calculated for n=1.

Figure 3 Mean MG-ADL CFB at Day 43 by duration of disease



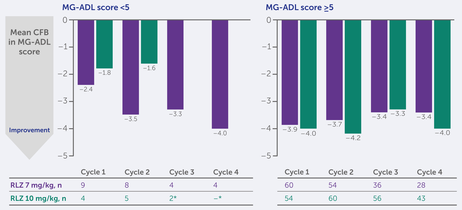
	Disease duration <5.4 years				Disease duration ≥5.4 years			
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 1	Cycle 2	Cycle 3	Cycle 4
RLZ 7 mg/kg, n	34	27	13	8	35	35	27	24
RLZ 10 mg/kg, n	29	36	31	24	29	29	27	19

Figure 4 Mean MG-ADL CFB at Day 43 by age



	Age 18 to <65 years				Age ≥65 years			
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 1	Cycle 2	Cycle 3	Cycle 4
RLZ 7 mg/kg, n	54	50	32	25	15	12	8	7
RLZ 10 mg/kg, n	47	51	44	32	11	14	14	11

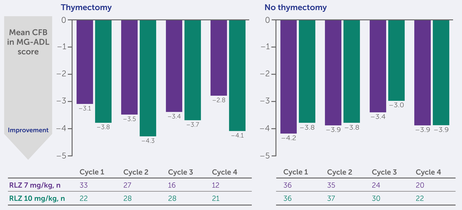
Figure 5 Mean MG-ADL CFB at Day 43 by baseline MG-ADL score



	MG-ADL score <5				MG-ADL score ≥5			
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 1	Cycle 2	Cycle 3	Cycle 4
RLZ 7 mg/kg, n	9	8	4	4	60	54	36	28
RLZ 10 mg/kg, n	4	5	2*	–*	54	60	56	43

*Mean CFB in MG-ADL score was not calculated for n=2.
For Figures 2–6, dose groups are based on respective cycle.

Figure 6 Mean MG-ADL CFB at Day 43 by thymectomy status at baseline



	Thymectomy				No thymectomy			
	Cycle 1	Cycle 2	Cycle 3	Cycle 4	Cycle 1	Cycle 2	Cycle 3	Cycle 4
RLZ 7 mg/kg, n	33	27	16	12	36	35	24	20
RLZ 10 mg/kg, n	22	28	28	21	36	37	30	22

Table 2 Overview of TEAEs in all cycles* by subgroup (safety pool)

	Autoantibody status		Duration of disease (years)		Age (years)		MG-ADL score		Thymectomy status		
	MuSK Ab+ (n=18)	AChR Ab+ (n=170)	<5.4 (n=89)	≥5.4 (n=99)	18–65 (n=140)	≥65 (n=48)	<5 (n=24)	≥5 (n=164)	Yes (n=75)	No (n=113)	All (N=188)
Any TEAE	**14** (77.8)	**154** (90.6)	**81** (91.0)	**88** (88.9)	**127** (90.7)	**42** (87.5)	**21** (87.5)	**148** (90.2)	**68** (90.7)	**101** (89.4)	**169** (89.9)
Serious TEAEs	**2** (11.1)	**40** (23.5)	**22** (24.7)	**20** (20.2)	**29** (20.7)	**13** (27.1)	**9** (37.5)	**33** (20.1)	**17** (22.2)	**25** (22.1)	**42** (22.3)
Permanent discontinuations from study drug due to TEAE	**3** (16.7)	**24** (14.1)	**12** (13.5)	**15** (15.2)	**19** (13.6)	**8** (16.7)	**6** (25.0)	**21** (12.8)	**11** (14.7)	**16** (14.2)	**27** (14.4)
Treatment-related TEAEs	**11** (61.1)	**101** (59.4)	**53** (59.6)	**58** (58.6)	**87** (62.1)	**24** (50.0)	**12** (50.0)	**99** (60.4)	**52** (69.3)	**59** (52.2)	**111** (59.0)
Severe TEAEs	**2** (11.1)	**48** (28.2)	**23** (25.8)	**27** (27.3)	**34** (24.3)	**16** (33.3)	**7** (29.2)	**43** (26.2)	**18** (24.0)	**32** (28.3)	**50** (26.6)
All deaths (TEAEs leading to death)	**0**	**3** (1.8)	**0**	**3** (3.0)	**2** (1.4)	**1** (2.1)	**1** (4.2)	**2** (1.2)	**1** (1.3)	**2** (1.8)	**3** (1.6)

Data are presented as n (%), where n is the number of patients reporting at least one TEAE within the category.
*Data are derived from a 'most recent dose' analysis.

Summary and conclusions

This pooled analysis assessed the long-term efficacy and safety of repeated cycles of rozanolixizumab treatment across prespecified subgroups

Improvement from baseline in MG-ADL to Day 43 was maintained over repeated cycles of treatment in the overall population and in prespecified subgroup populations of autoantibody status, duration of disease, age, baseline MG-ADL and thymectomy status

No relevant differences were observed in safety profile between different subgroups

Rozanolixizumab efficacy was maintained across multiple treatment cycles in a broad population with gMG

Abbreviations: Ab, autoantibody; AChR, acetylcholine receptor; CFB, change from baseline; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; mAb, monoclonal antibody; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGC, Myasthenia Gravis Composite; MuSK, muscle-specific kinase; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event.
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