Long-term safety of repeated cycles of rozanolixizumab treatment in patients with generalized myasthenia gravis

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Introduction

- Rozanolixizumab is a humanized IgG4 monoclonal antibody FcRn inhibitor approved by the US FDA for the treatment of adults with AChR or MuSK Ab+ gMG^{1,2}
- The MycarinG (MG0003/NCT03971422) Phase 3 study demonstrated the efficacy and safety
 of one 6-week cycle of rozanolixizumab in adults with gMG¹
- Statistically significant and clinically meaningful improvements from baseline in MG-ADL scores at Day 43 were demonstrated in rozanolixizumab-treated patients when compared with patients who received placebo
- Here, we evaluate the long-term safety of repeated rozanolixizumab treatment cycles using data pooled across MycarinG and the OLE study MG0007 (NCT04650854)

Methods

- In MycarinG, patients received weekly SC rozanolixizumab or placebo
- After completing MycarinG, patients could enroll in MG0007, in which, after an initial cycle, rozanolixizumab was administered based on symptom worsening (symptom-driven cycles) (Figure 1)
- Data were pooled across MycarinG and MG0007
- Safety pool: patients with ≥ 1 treatment cycle (≥ 1 dose of rozanolixizumab in any 6-week treatment period) that was followed by a ≤ 8 -week follow-up period across MycarinG and MG0007
- Safety outcomes included the occurrence of TEAEs and TEAEs leading to discontinuation for each 6-week treatment cycle and follow-up period
- Annualized dosing rate was calculated using the number of cycles initiated divided by time in studies (years)

Results

Patients

- In total, 188 patients received ≥ 1 cycle of rozanolixizumab 7 mg/kg (Cycle 1, n=94) or 10 mg/kg (Cycle 1, n=94) over 678 cycles and were included in the safety pool
- Baseline demographics and characteristics for patients in the safety pool are reported in **Table 1**
- Median follow-up was 368.0 days (range 44–599)
- The mean annualized dosing rate was 3.4 cycles and 17.8 SC infusions per year

Safety

- In the safety pool, 89.9% (169/188) of patients experienced any TEAE (77.4% [103/133] of patients receiving 7 mg/kg and 91.6% [120/131] of patients receiving 10 mg/kg rozanolixizumab)*
- Across all TEAE categories, the incidence of TEAEs was higher in the rozanolixizumab 10 mg/kg group than the 7 mg/kg group
- Most TEAEs were mild or moderate in severity
- The overall incidence of TEAEs across all categories did not increase with repeated treatment cycles compared with Cycle 1 (Figure 2)
- Serious TEAEs occurring in >1 patient across all cycles were MG (12/188, 6.4%), MG crisis (4/188, 2.1%) and COVID-19 (3/188, 1.6%)
- Incidence of the most common TEAEs did not increase with repeated cycles of treatment (**Figure 3**)
- Headache was the most common TEAE, predominantly of mild or moderate intensity • TEAEs that resulted in permanent discontinuation in >1 patient were MG (5/188, 2.7%), MG crisis (2/188, 1.1%), decreased blood IgG (2/188, 1.1%) and a positive interferon gamma release assay result (2/188, 1.1%)
- There was no increase in the incidence of infections with repeated cycles of treatment. The most common infections were COVID-19, upper respiratory tract infection, nasopharyngitis and oral herpes
- There were no anaphylactic reactions. Most hypersensitivity-related events and injection-site reactions were of mild or moderate intensity and none led to permanent discontinuation
- Four deaths occurred during MG0007 due to: pneumonia caused by COVID-19 infection in two patients; pneumonia, acute kidney injury, acute respiratory failure, cardiac failure, and acute respiratory distress syndrome in one patient; and myocardial infarction in one patient (occurred >6 months after the last dose). All were deemed unrelated to rozanolixizumab by the investigator
- One additional death occurred after data cut-off due to circulatory failure (reported as circulatory arrest) and was deemed unrelated to rozanolixizumab
- No clinically meaningful decreases in albumin concentrations or clinically relevant trends in lipid parameters were observed (data from MG0007 only)



*When presenting data across all cycles, patients were assigned to the 7 mg/kg or 10 mg/kg dose group if they received the respective 7 mg/kg or 10 mg/kg dose at least once. Patients who received both 7 mg/kg and 10 mg/kg were included in both treatment groups, therefore the sum of the number of patients in the 7 mg/kg and 10 mg/kg groups is higher than the number of patients presented for rozanolixizumab total. Abbreviations: Ab+, autoantibody-positive; AChR, acetylcholine receptor; COVID-19, coronavirus disease 2019; FcRn, neonatal Fc receptor; FDA, Food and Drug Administration; (g)MG, (generalized) myasthenia gravis; IgG, immunoglobulin G; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK, muscle-specific tyrosine kinase; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SC, subcutaneous; SD, standard deviation; TEAE, treatment-emergent adverse even Acknowledgments: This study was funded by UCB Pharma. The authors acknowledge Emma Robinson of Ogilvy Health, London, UK, for editorial support in the form of writing, drafting tables Please use this QR code to 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 download a PDF of the poster. coordination. The authors thank the patients and their caregivers, in addition to the investigators and their teams who contributed to this study.

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Figure 1

Randomization N=200

Data presented within this poster are fro
*Patients entering MG0007 from MG00
permitted at the beginning of each treat
MG symptom worsening at the investiga
observation period continued to be mor

Tab	le 1	

Geogra	phic
region,	n (%)

Race, n (%)

Safety pool.





n MycarinG and MG0007 only

4 continued their last dose from MG0004 for the initial cycle. †After the initial cycle, dose modifications from 10 mg/kg to 7 mg/kg and vice versa were nent cycle provided the benefit—risk ratio remained favorable for the patient. After the initial cycle, subsequent cycles were symptom-driven (based o cor's discretion, e.g. an MG-ADL score increase of \geq 2.0 or a QMG score increase of \geq 3.0). Patients without MG symptom worsening by the end of the itored until a further symptom-driven cycle was required

Baseline demographics and characteristics*

		RLZ 7 mg/kg (n=94)	RLZ 10 mg/kg (n=94)	RLZ total (N=188)
	Age, years, mean (SD)	53.1 (14.9)	52.0 (17.6)	52.5 (16.3)
	Sex, female, n (%)	56 (59.6)	55 (58.5)	111 (59.0)
Geographic	Europe	52 (55.3)	62 (66.0)	114 (60.6)
	North America	30 (31.9)	24 (25.5)	54 (28.7)
region, n (%)	Japan	8 (8.5) 5 (5.3)	5 (5.3)	13 (6.9)
	Asia (excl. Japan)	4 (4.3)	3 (3.2)	7 (3.7)
	White	58 (61.7)	69 (73.4)	127 (67.6)
	Missing [†]	24 (25.5)	11 (11.7)	35 (18.6)
Race, n (%)	Asian	12 (12.8)	9 (9.6)	21 (11.2)
	Black	0	4 (4.3)	4 (2.1)
	Native Hawaiian or other Pacific Islander	0	1 (1.1)	1 (0.5)
	MG-ADL score, mean (SD)	8.3 (3.7)	8.4 (2.9)	8.3 (3.4)

*The allocation of patients to treatment group was based on the maximum dose received during the first rozanolixizumab treatment cycle, although patients may have switched rozanolixizumab doses within subsequent cycles. [†]Data on race were not permitted to be collected in France and Canada.

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Figure 3 Most common TEAEs by treatment cycle

Cycle 1	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total
Cycle 2	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total
Cycle 3	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total
Cycle 4	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total
Cycle 5	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total
Cycle 6	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total







Tuan Vu¹, Julian Grosskreutz², Maryam Gayfieva³, Marion Boehnlein⁴, Irene Pulido-Valdeolivas⁵, Franz Woltering⁴, Vera Bril⁶

¹Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, FL, USA; ²Precision Neurology, Department of Neurology, University of Lübeck, Lübeck, Germany; ³UCB Pharma, Slough, UK; ⁴UCB Pharma, Monheim, Germany; ⁵UCB Pharma, Madrid, Spain; ⁶University Health Network, Toronto, Canada.

Incidence of TEAE (%)		Art	hralgia							1	ncidenc	e of TE/	AE (%)
40 45 50		0	5	10	15	20	25	3()	35	40	45	50
	Cycle 1	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total	5.3 5.3 5.3 5.3		I							I	
	Cycle 2	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total	1.4 4.1 2.8										
	Cycle 3	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total	2.1 1.5 1.8										
	Cycle 4	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total	5.0 6	7.7 .5									
	Cycle 5	RLZ 7 mg/kg 0 RLZ 10 mg/kg 0 RLZ total 0											
	Cycle 6	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total	5.9 3.8 4.7)									
Incidence of TEAE (%)		CC	VID-19							1	ncidenc	e of TE/	AE (%)
40 45 50		0	5	10	15	20	25	30)	35	40	45	50
	Cycle 1	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total	3.2 1.1 2.1	I	I					-	I	I	
	Cycle 2	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total	5.8	8.1 7.0									
	Cycle 3	RLZ 7 mg/kg RLZ 10 mg/kg RLZ total	6. 3.1 4.4	3									
	Cycle 4	RLZ 7 mg/kg 0 RLZ 10 mg/kg RLZ total	4.3	7.7									
	Cycle 5	RLZ 7 mg/kg	3.6		Cycle	2	1	_	2	3	4	5	6
		RLZ total	1.6		RLZ	- 7 ma/ka	. n 🤉)4	69	48	40	28	17
	Cycle 6	RLZ 7 mg/kg 0			RLZ	10 ma/k	(q , n)4	74	65	52	35	26
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