MG-ADL and QMG scores over time in patients with generalized myasthenia gravis: *Post-hoc* analysis of MycarinG and open-label studies

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Disclosures

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).

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Tuan Vu is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion Pharmaceuticals, argenx, Ra Pharmaceuticals (now UCB Pharma), Viela Bio (now Horizon Therapeutics), Momenta (now Johnson and Johnson), Regeneron Pharmaceuticals, Immunovant and Cartesian Therapeutics, and has received speaking and/or consulting honoraria from Alexion Pharmaceuticals, argenx and UCB Pharma.

Thaïs Tarancón, Fiona Grimson and Pauline Payen are employees and shareholders of UCB Pharma.

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 Pharmaceuticals, UCB Pharma, Arvinas, ML Biopharma and Horizon Therapeutics. 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, Viela Bio (now Horizon Therapeutics), argenx, Novartis, Alexion Pharmaceuticals, Stealth Biotherapeutics, UCB Pharma, Genethon, ML Biopharma, Reneo Pharma, Pharnext, Janssen Pharmaceuticals, Khondrion, Regeneron Pharmaceuticals and Dynacure.

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AChR Ab+, positive for autoantibodies against the acetylcholine receptor; FDA, Food and Drug Administration; gMG, generalized myasthenia gravis; MuSK Ab+, positive for autoantibodies against muscle-specific tyrosine kinase.
Rozanolixizumab is approved by the US FDA for the treatment of adults with AChR Ab+ or MuSK Ab+ gMG.

Background

Rozanolixizumab, a humanized IgG4 mAb FcRn inhibitor, is approved by the US FDA for the treatment of adults with AChR Ab+ or MuSK Ab+ gMG[1]

MycarinG (MG0003/NCT03971422) was a randomized, double-blind, placebo-controlled, Phase 3 study of six weekly doses of rozanolixizumab 7 mg/kg or 10 mg/kg in adults with gMG[2]

Rozanolixizumab demonstrated statistically significant and clinically meaningful efficacy with multiple MG-specific endpoints; both doses were well tolerated[2]

Following MycarinG, patients could enroll in two OLE studies (MG0004/NCT04124965 or MG0007/NCT04650854)[3,4]

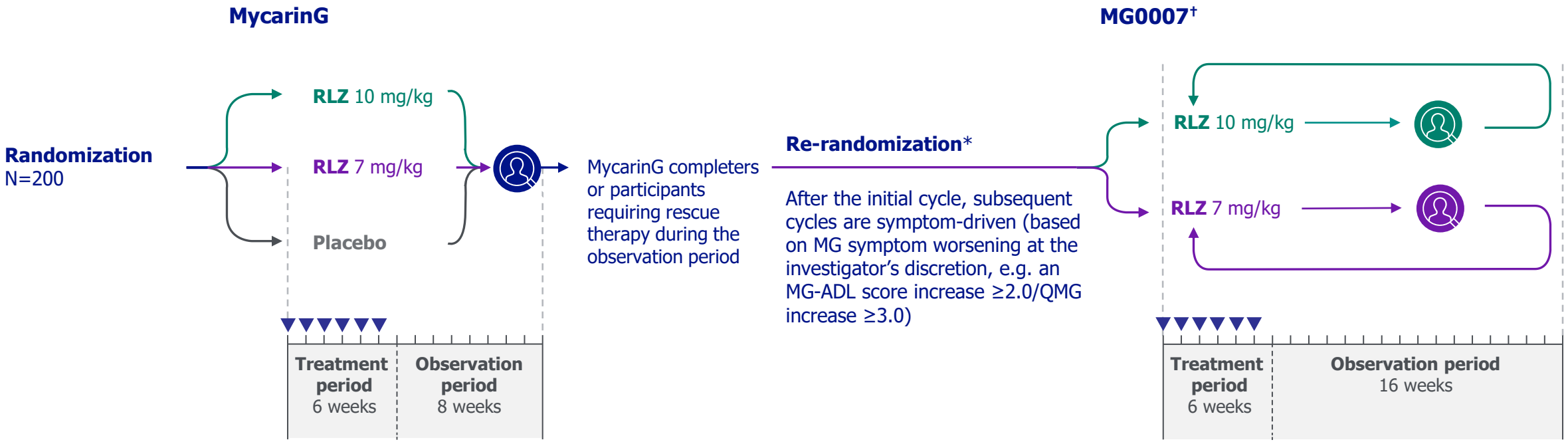
Objective: A *post-hoc* analysis was conducted in patients with ≥2 consecutive symptom-driven cycles to evaluate MG-specific outcomes over time for the cohort across rozanolixizumab cycles

AChR Ab+, positive for autoantibodies against the acetylcholine receptor; FcRn, neonatal Fc receptor; FDA, Food and Drug Administration; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; mAb, monoclonal antibody; MuSK Ab+, positive for autoantibodies against muscle-specific tyrosine kinase; OLE, open-label extension.

1. Rystiggo® US PI. https://www.ucb-usa.com/RYSTIGGO-prescribing-information.pdf. Accessed September 2023; 2. Bril V, et al. Lancet Neurol. 2023;22(5):383–394; 3. ClinicalTrials.gov. NCT04124965. https://clinicaltrials.gov/ct2/show/study/NCT04124965. Accessed September 2023; 4. ClinicalTrials.gov. NCT04650854. https://clinicaltrials.gov/ct2/show/study/NCT04650854. Accessed September 2023.

MycarinG and MG0007 study design

- For this *post-hoc* analysis, rozanolixizumab data were pooled across MycarinG and MG0007 (interim analysis; data cut-off: July 08, 2022)
- Mean change from baseline in MG-ADL and QMG scores over time was assessed in patients with ≥2 consecutive symptom-driven cycles*



*As the MG0004 study did not employ a 6-week repeated cycle treatment regimen with follow-up, the *post-hoc* efficacy pool and safety pool did not utilize data from MG0004.
†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. 60 patients enrolled in MG0007 from MG0004 who are not depicted separately on this diagram because the MG0004 study was not included in this *post-hoc* analysis.
MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab.

Exposure to rozanolixizumab

A total of **196 patients** received ≥1 dose of rozanolixizumab

- 110/196 (56.1%) received **≥2 consecutive symptom-driven cycles** (*post-hoc* efficacy pool)
- 188/196 (95.9%) patients received **≥1 cycle** (safety pool)

For all patients with available follow-up (n=188), the **mean annualized dosing rate*** was **3.4 cycles** and **17.8 infusions** per year

The *post-hoc* analysis pool includes data from MycarinG and MG0007.
*Annualized dosing rate was calculated using the number of cycles initiated divided by time in studies (years).

Baseline patient characteristics

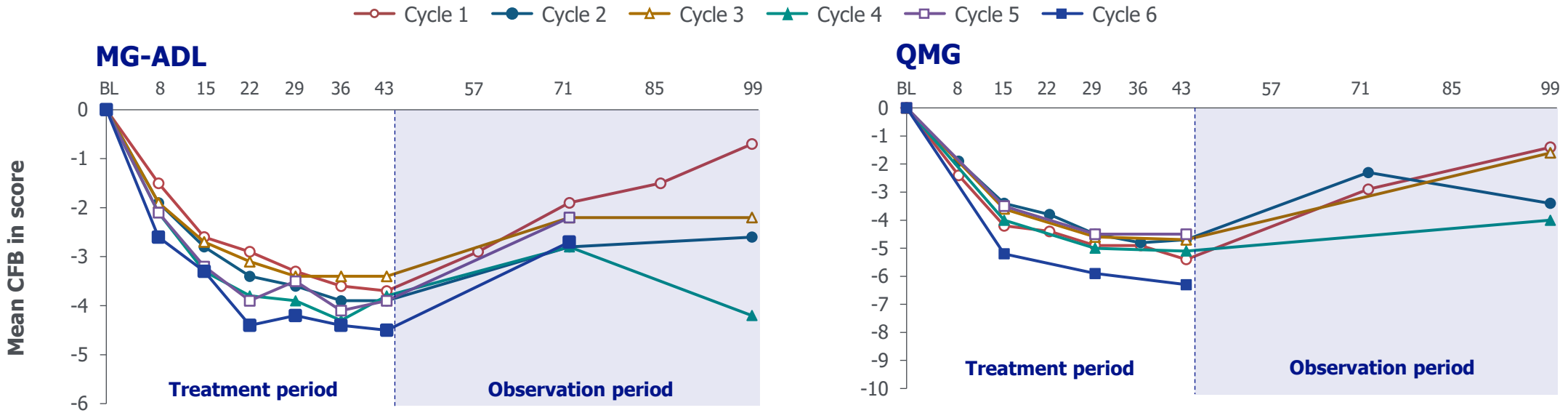
- Baseline characteristics reflected a population with moderate-to-severe gMG

		***Post-hoc* efficacy pool**	**Safety pool**
		RLZ total (N=110)	**RLZ total** (N=188)
Age, years, mean (SD)		50.8 (16.5)	52.5 (16.3)
Sex, female, n (%)		67 (60.9)	111 (59.0)
Thymectomy at MycarinG baseline, yes, n (%)*		48 (43.6)	75 (39.9)
AChR Ab+, n (%)*		99 (90.0)	170 (90.4)
MuSK Ab+, n (%)*		11 (10.0)	18 (9.6)
MG-ADL score at baseline, mean (SD)		9.1 (3.3)	8.3 (3.4)
QMG score at baseline, mean (SD)		16.2 (3.7)	15.6 (3.6)
Duration of disease, years, mean (SD)		8.6 (8.7)	8.5 (8.6)
Baseline gMG medication, n (%)	Corticosteroids for systemic use	67 (60.9)	120 (63.8)
	Immunosuppressants	55 (50.0)	97 (51.6)
	Parasympathomimetics	96 (87.3)	162 (86.2)

*Captured from historic data case report forms.
AChR Ab+, positive for autoantibodies against the acetylcholine receptor; gMG, generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK Ab+, positive for autoantibodies against muscle-specific tyrosine kinase; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation.

Mean MG-ADL and QMG change from baseline per treatment cycle

- Consistent clinical improvements were observed across MG-specific outcomes including MG-ADL and QMG scores following repeated cycles of rozanolixizumab treatment



Cycle	BL	8	15	22	29	36	43	57	71	85	99
Cycle 1, n	127	120	117	118	123	117	127	80	85	57	94
Cycle 2, n	127	108	112	110	125	112	127	-	66	-	39
Cycle 3, n	98	94	95	97	97	95	98	-	48	-	21
Cycle 4, n	75	75	74	70	72	73	75	-	30	-	5
Cycle 5, n	51	48	49	50	48	48	51	-	13	-	1
Cycle 6, n	32	30	32	30	32	32	32	-	7	-	-

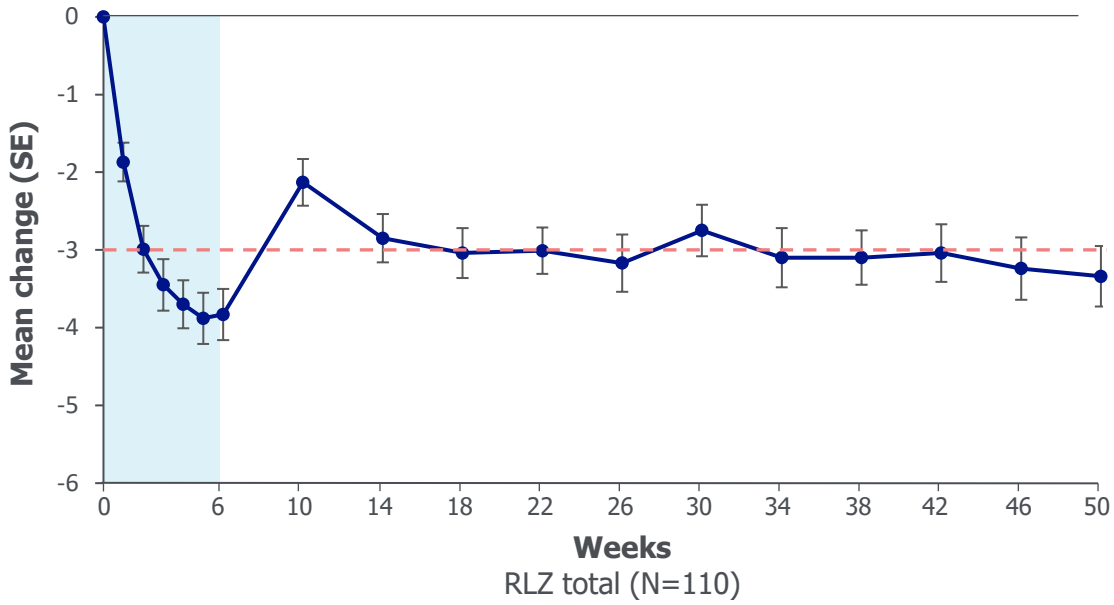
BL	8	15	22	29	36	43	57	71	85	99
127	107	117	106	107	101	127	-	74	-	93
126	37	106	36	84	39	125	-	19	-	38
98	1	83	-	82	-	97	-	-	-	19
75	-	60	-	59	1	74	-	-	-	5
51	-	38	-	37	-	51	-	-	-	-
32	-	25	-	24	-	32	-	-	-	-

These data are from a prespecified pooled analysis of MycarinG, MG0004 and MG0007 including 127 patients who received ≥2 symptom-driven cycles.
BL, baseline; CFB, change from baseline; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis.
Bril V, et al. AAN 2023. Poster P1–5–012.

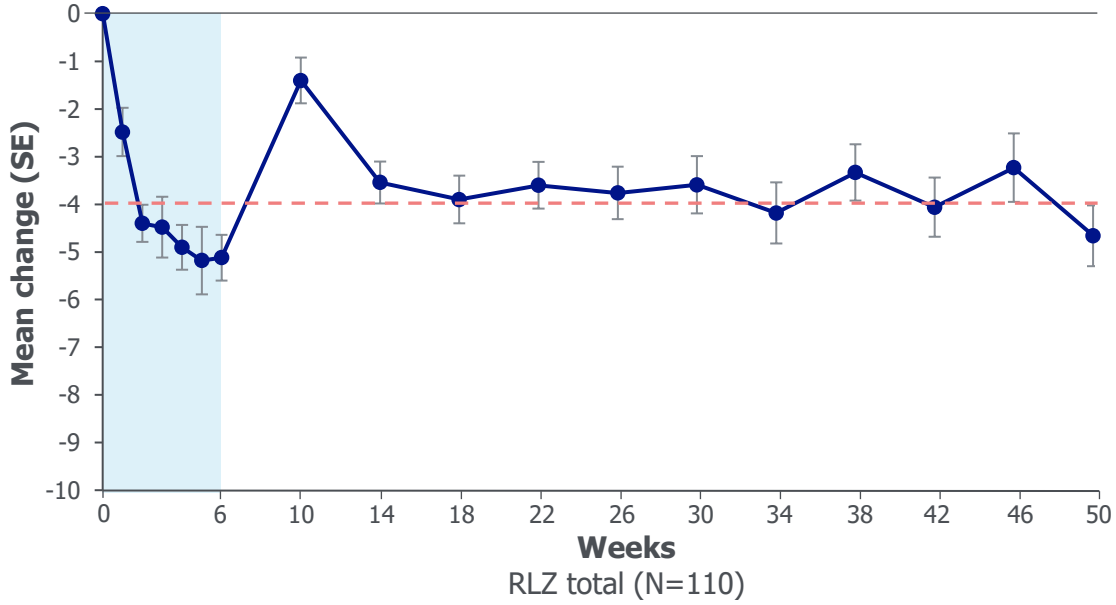
Mean MG-ADL and QMG change from baseline over time (*post-hoc* efficacy pool)

- Mean MG-ADL and QMG improvements were maintained over time for the cohort across rozanolixizumab cycles, while individual patients moved through consecutive treatment cycles
- Cohort mean MG-ADL and QMG scores stabilized around a 3- and 4-point improvement, respectively, compared to study baseline scores

MG-ADL



QMG



The blue shading denotes the first 6-week treatment cycle. The pink dashed line denotes where score improvement stabilized.
MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SE, standard error.

Overview of TEAEs by cycle number (safety pool)

- In general, the incidence of TEAEs across all categories did not increase with repeated cycles of treatment compared with Cycle 1

Patients experiencing TEAEs, RLZ total, n (%)

	All cycles* (N=188)	Cycle 1 (N=188)	Cycle 2 (N=143)	Cycle 3 (N=113)	Cycle 4 (N=92)	Cycle 5 (N=63)	Cycle 6 (N=43)
Any TEAE	**169** (89.9)	**147** (78.2)	**100** (69.9)	**67** (59.3)	**53** (57.6)	**46** (73.0)	**28** (65.1)
Serious TEAEs	**42** (22.3)	**20** (10.6)	**9** (6.3)	**5** (4.4)	**5** (5.4)	**6** (9.5)	**0**
Permanent discontinuation from study due to TEAEs	**29** (15.4)	**13** (6.9)	**8** (5.6)	**3** (2.7)	**4** (4.3)	**1** (1.6)	**0**
Permanent discontinuation of study drug due to TEAEs	**27** (14.4)	**12** (6.4)	**8** (5.6)	**2** (1.8)	**4** (4.3)	**1** (1.6)	**0**
Treatment-related TEAEs	**111** (59.0)	**94** (50.0)	**51** (35.7)	**26** (23.0)	**28** (30.4)	**22** (34.9)	**18** (41.9)
Severe TEAEs	**50** (26.6)	**23** (12.2)	**9** (6.3)	**6** (5.3)	**8** (8.7)	**8** (12.7)	**2** (4.7)
TEAEs leading to death	**3** (1.6)	**0**	**2** (1.4)	**1** (0.9)	**0**	**0**	**0**

All Cycles data are derived from a 'most recent dose' analysis. Data for each individual Cycle are derived from a 'by Cycle' analysis.
*Includes data up to Cycle 9 where available.
RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event.

For further information on safety, see Poster 269, Vu T et al., AANEM 2023

Conclusions

Rozanolixizumab consistently improved MG-specific outcomes across repeated cycles of treatment[1]

This *post-hoc* analysis demonstrated that the clinically meaningful improvements in gMG symptoms were maintained over time for the cohort across rozanolixizumab cycles, while individual patients moved through consecutive treatment cycles

Rozanolixizumab had an acceptable safety profile that was maintained across repeated treatment cycles, consistent with previous studies of rozanolixizumab[2,3]

gMG, generalized myasthenia gravis.
1. Bril V, et al. AAN 2023. Poster P1-5-012; 2. Bril V, et al. Neurol. 2021;96(6):e853–e865; 3. Bril V, et al. Lancet Neurol. 2023;22(5):383–394.