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Safety and tolerability of rozanolixizumab in the randomized Phase 3 MycarinG study

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Rozanolixizumab is an investigational new product and has not been approved by any authority.

Disclosures

Tuan Vu is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion, Argenx, Ra/UCB Pharma, Horizon/Viela Bio, Janssen/Momenta, Sanofi, Regeneron and Cartesian Therapeutics, and receives speaking and consulting honoraria from Alexion, Argenx and UCB Pharma.

Henry Kaminski is a Consultant for Roche, Cabeletta 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.

Artur Drużdż has nothing to disclose.

Julian Grosskreutz has served as a Consultant for Biogen, Alexion and UCB Pharma, and his institution has received research support from the Boris Canessa 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.

Sabrina Sacconi has nothing to disclose.

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 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 Pharma, Alexion Pharmaceuticals, Stealth Biotherapeutics, UCB Pharma, Genethon, ML Biopharma, Reneo Pharma, Pharnext, Janssen Pharmaceuticals, Khondrion, Regeneron and Dynacure.

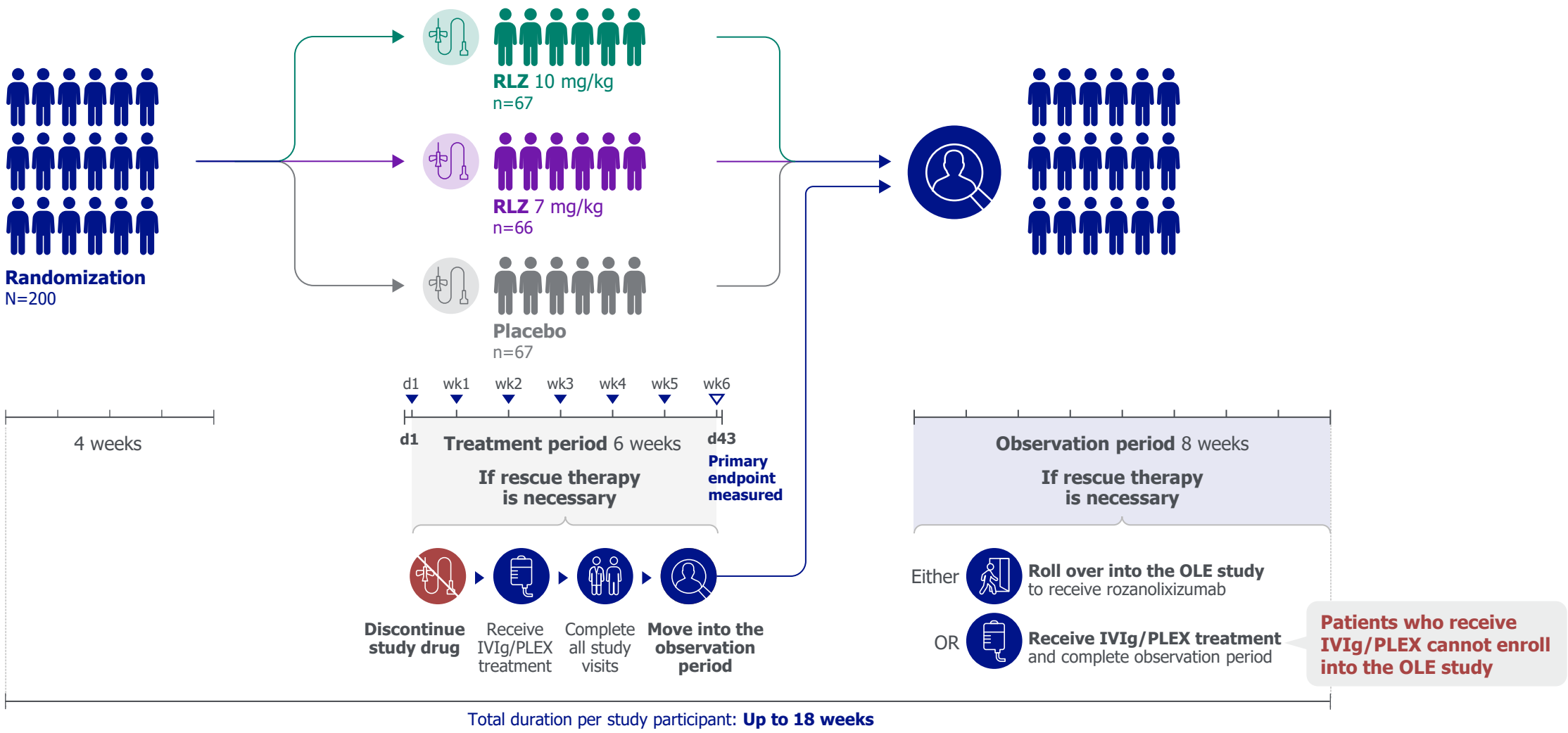
Marion Boehnlein, Maryam Gayfieva and Bernhard Greve are employees and shareholders of UCB Pharma.

Vera Bril is a Consultant for Grifols, CSL, UCB Pharma, Argenx, Takeda, Alnylam, Octapharma, Pfizer, Powell Mansfield, Akcea, Ionis, Immunovant, Sanofi, Momenta (now J&J), 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).

Statistical analysis was conducted by UCB Pharma.

This study was funded by UCB Pharma.

MycarinG: A multicenter, double-blind, placebo-controlled, Phase 3 study



d, day; IVIg, intravenous immunoglobulin; OLE, open-label extension; PLEX, plasma exchange; RLZ, rozanolixizumab; wk, week.

ClinicalTrials.gov. NCT03971422. https://clinicaltrials.gov/ct2/show/NCT03971422. Accessed on 21 July 2022.

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Patient demographics and baseline characteristics

Baseline demographics and disease characteristics were generally balanced between treatment groups

		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)
Geographic region, n (%)	Europe	41 (61.2)	36 (54.5)	43 (64.2)
	North America	21 (31.3)	21 (31.8)	18 (26.9)
	Asia (inc. Japan)	5 (7.5)	9 (13.6)	6 (9.0)
Autoantibody status, n (%)*	AChR Ab+	59 (88.1)	60 (90.9)	60 (89.6)
	MuSK Ab+	8 (11.9)	5 (7.6)	8 (11.9)
Thymectomy, n (%)		31 (46.3)	32 (48.5)	20 (29.9)
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)
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 (AChEIs)	60 (89.6)	55 (83.3)	57 (85.1)
MGFA disease class at baseline, n (%)	Class IIa/b	23 (34.3)	29 (43.9)	26 (38.8)
	Class IIIa/b	41 (61.2)	34 (51.5)	39 (58.2)
	Class IVa/b†	3 (4.5)	3 (4.5)	2 (3.0)

*2 patients were positive for both AChR and MuSK autoantibodies, and 2 had unknown status.
†Only 1 patient, who was randomized to the placebo group, had Class IVb disease.
AChEI, acetylcholinesterase inhibitor; AChR Ab+, positive for autoantibodies against the acetylcholine receptor; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MuSK Ab+, positive for autoantibodies against muscle-specific kinase; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation.

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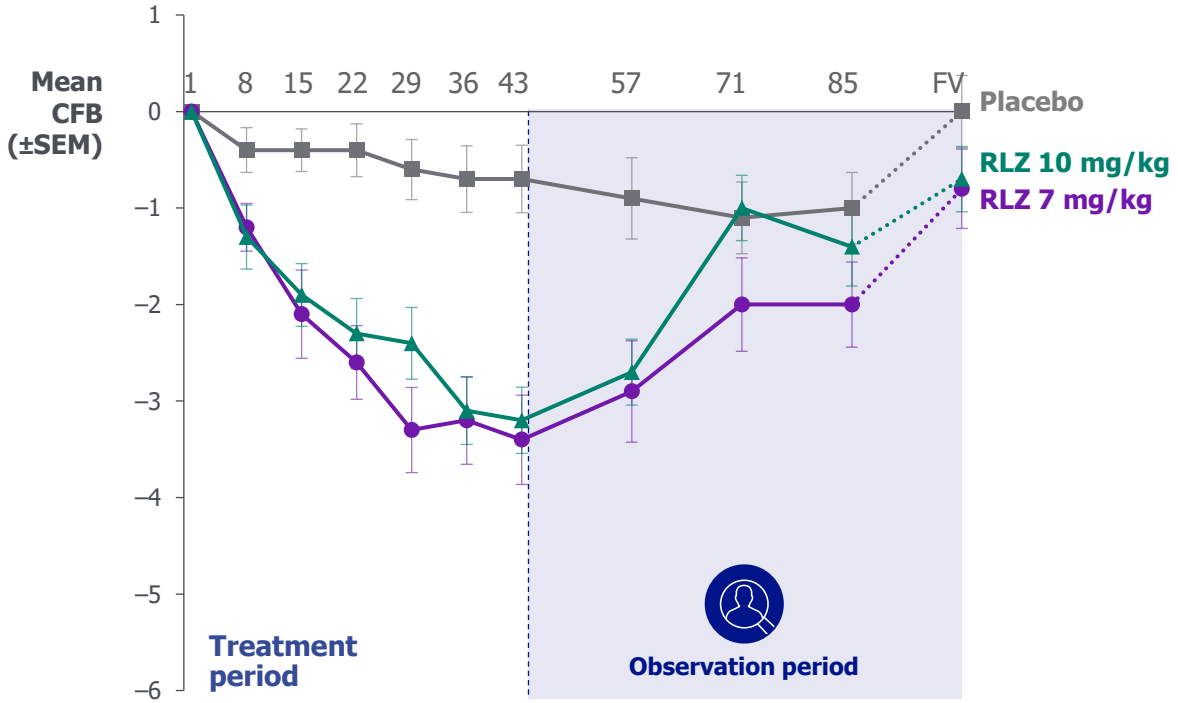
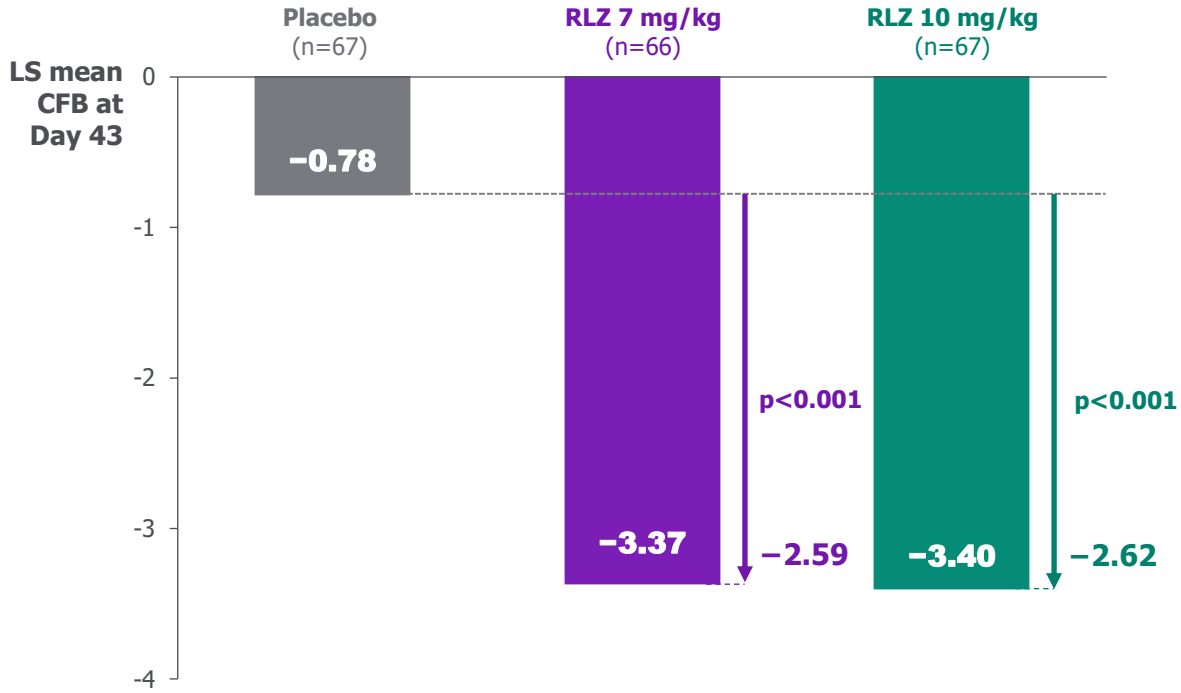
Change from baseline in MG-ADL

Improvements from baseline with rozanolixizumab 7 mg/kg and 10 mg/kg were both clinically meaningfully and highly statistically significantly different compared with placebo at Day 43 (p<0.001 for both doses).



Day of visit	1	8	15	22	29	36	43	57	71	85	FV
Placebo, n	67	67	66	65	64	61	64	54	49	46	64
RLZ 7 mg/kg, n	66	66	62	62	63	63	64	55	52	43	64
RLZ 10 mg/kg, n	67	66	64	64	61	60	62	63	59	47	64



LS mean difference vs placebo (95% CI)	
RLZ 7 mg/kg	**−2.59** (−4.09, −1.25)
RLZ 10 mg/kg	**−2.62** (−3.99, −1.16)

CFB, change from baseline; CI, confidence interval; FV, final visit (could occur up to Day 99); LS, least squares; MG-ADL, Myasthenia Gravis Activities of Daily Living; RLZ, rozanolixizumab; SEM, standard error of the mean.

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Overview of TEAEs

Most TEAEs were mild to moderate in severity

Preferred term	Placebo (n=67) % (n)	RLZ 7 mg/kg (n=64) % (n)*	RLZ 10 mg/kg (n=69) % (n)*
Any TEAE	**67.2** (45)	**81.3** (52)	**82.6** (57)
Serious TEAEs	**9.0** (6)	**7.8** (5)	**10.1** (7)
Treatment withdrawal due to TEAEs	**3.0** (2)	**3.1** (2)	**5.8** (4)
Treatment-related TEAEs†	**32.8** (22)	**50.0** (32)	**56.5** (39)
Severe TEAEs	**4.5** (3)	**4.7** (3)	**18.8** (13)
All deaths (AEs leading to death)	**0**	**0**	**0**

- In the placebo group, one patient discontinued due to a TEAE of MG, and one patient discontinued due to a TEAE of MG crisis
- In the 7 mg/kg rozanolixizumab group, the two withdrawals were due to arthralgia and headache
- In the 10 mg/kg rozanolixizumab group, one patient discontinued due to diarrhea; one patient withdrew due to upper abdominal pain and vomiting; one patient withdrew due to oral herpes, MSCC, and DVT; and one patient discontinued due to pruritus

*Two patients in the 7 mg/kg group who incorrectly received 10 mg/kg were analyzed in the 10 mg/kg group for PK/PD and safety analyses.
†Treatment-related TEAEs as assessed by investigators. Assessed in the safety set.
AE, adverse event; DVT, deep vein thrombosis; MG, myasthenia gravis; MSCC, metastatic squamous cell carcinoma; PK/PD, pharmacokinetics/pharmacodynamics; RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event.

Most common TEAEs

Preferred term	Placebo (n=67) % (n)	RLZ 7 mg/kg (n=64) % (n)*	RLZ 10 mg/kg (n=69) % (n)*
Any TEAE	**67.2** (45)	**81.3** (52)	**82.6** (57)
Headache†	**19.4** (13)	**45.3** (29)	**37.7** (26)
Diarrhea	**13.4** (9)	**25.0** (16)	**15.9** (11)
Pyrexia	**1.5** (1)	**12.5** (8)	**20.3** (14)
Nausea	**7.5** (5)	**7.8** (5)	**11.6** (8)
Arthralgia	**3** (2)	**6.3** (4)	**7.2** (5)
Nasopharyngitis	**4.5** (3)	**1.6** (1)	**7.2** (5)
Myalgia	**1.5** (1)	**3.1** (2)	**5.8** (4)
Vomiting	**1.5** (1)	**3.1** (2)	**5.8** (4)
Hypertension	**0**	**7.8** (5)	**0**
Urinary tract infection	**6** (4)	**3.1** (2)	**2.9** (2)

- No patients experienced TEAEs related to effects on lipids or reduction in albumin

*Two patients in the 7 mg/kg group who incorrectly received 10 mg/kg were analyzed in the 10 mg/kg group for PK/PD and safety analyses.
†There were no requirements for analgesic headache prophylaxis in the study protocol.
PK/PD, pharmacokinetic/pharmacodynamic; RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event.
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MycarinG selected adverse events of focus

AEOF category	Placebo (n=67) % (n)	RLZ 7 mg/kg (n=64) % (n)*	RLZ 10 mg/kg (n=69) % (n)*
Any headache	19.4 (13)	45.3 (29)	37.7 (26)
Serious headache	0	0	1.4 (1)
Severe headache	0	1.6 (1)	8.7 (6)
Anaphylactic/serious hypersensitivity reactions	0	0	0
Any infection or infestation	19.4 (13)	15.6 (10)	30.4 (21)
Nasopharyngitis	4.5 (3)	1 (1.6)	7.2 (5)
Oral herpes	0	0	4.3 (3)
Urinary tract infections	6.0 (4)	3.1 (2)	2.9 (2)
URTI	1.5 (1)	3.1 (2)	1.4 (1)
Serious infection or infestation	1.5 (1)	0	0
Any injection-site reaction	3.0 (2)	6.3 (4)	5.8 (4)
Serious injection-site reaction	0	0	0

- Most cases were mild or moderate
- Headaches occurred most frequently after the first infusion
- No patients in MycarinG experienced a recurrence of severe headaches
- Generally, severe headache was well managed with non-opioid analgesics
- One patient in the 7mg/kg group discontinued the study due to headaches

- No TEAEs suggestive of anaphylactic or serious hypersensitivity reactions

- Infections were mainly mild or moderate
  - Nasopharyngitis, oral herpes, and URTI were the most frequent infections in RLZ groups with incidence higher than in placebo
  - No severe or serious infections in rozanolixizumab groups

- The incidence of injection-site reactions was low and similar in all groups, with no serious injection-site reactions

*Two patients in the 7 mg/kg group who incorrectly received 10 mg/kg were analyzed in the 10 mg/kg group for PK/PD and safety analyses.
AEOF, adverse events of focus; PK/PD, pharmacokinetic/pharmacodynamic; RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infections.
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Summary and conclusions

- The results of MycarinG indicate that rozanolixizumab has an acceptable safety profile and is generally well tolerated in patients with gMG
- The incidence of TEAEs and treatment-related TEAEs was higher in the rozanolixizumab groups than in the placebo group, but comparable between the rozanolixizumab groups
    - Most TEAEs were mild to moderate in severity
- The most frequently reported TEAEs were headache, pyrexia, diarrhea and nausea
    - A higher incidence of headache was reported in the rozanolixizumab groups versus placebo, with most cases mild to moderate; generally, severe cases were well managed with non-opioid analgesics
- There were no severe or serious infections in the rozanolixizumab groups
    - Nasopharyngitis, oral herpes, and upper respiratory tract infections were reported more frequently in the rozanolixizumab groups than in the placebo group
- Treatment withdrawal due to TEAEs was low; the rate was similar in the rozanolixizumab 7 mg/kg and placebo groups and higher in the rozanolixizumab 10 mg/kg group

gMG, generalized myasthenia gravis; TEAE, treatment-emergent adverse event.

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