Poster M2.027

Long-term safety outcomes of rozanolixizumab treatment in patients with generalized myasthenia gravis: A pooled analysis

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Introduction

- Rozanolixizumab is a humanized IgG4 mAb FcRn inhibitor, indicated for the treatment of adult patients with AChR or MuSK Ab+ gMG[1]
- In the Phase 3 MycarinG study (MG0003/NCT03971422), rozanolixizumab was associated with significant improvements in MG-specific outcomes and was well tolerated with an acceptable safety profile in adult patients with anti-AChR or anti-MuSK Ab+ gMG[2]
- The objective of this pooled analysis was to evaluate the long-term safety of rozanolixizumab in the MycarinG study and subsequent 6-week treatment cycles in the MG0007 OLE

Methods

- Data were pooled across MycarinG and MG0007 (interim analysis; data cut-off: July 8, 2022) for patients receiving ≥1 rozanolixizumab treatment cycle with a ≤8-week follow-up period. Patients were allocated to rozanolixizumab 7 mg/kg or 10 mg/kg, and were permitted to change dose at the investigator's discretion
- A predefined list of TEAEs was selected for an in-depth evaluation of safety based on: findings from nonclinical and clinical studies of rozanolixizumab; potential risks generally associated with biologic immunomodulators; and the mechanism of action of rozanolixizumab
  - Predefined TEAEs: headaches, infections, hypersensitivity, anaphylactic reactions, and gastrointestinal disorders

Results

- Overall, 188 patients received ≥1 rozanolixizumab treatment cycle (mean [SD] cycles initiated: 3.6 [2.2]). Baseline disease characteristics were balanced across both rozanolixizumab groups (**Table 1**)
- Of these 188 patients, 133 received rozanolixizumab 7 mg/kg and 131 received rozanolixizumab 10 mg/kg (patients were grouped according to the most recent dose received prior to onset of AEs; therefore, patients switching rozanolixizumab dose were allocated to both the 7 mg/kg and the 10 mg/kg treatment groups)
- TEAEs occurred in 169 of 188 patients (89.9%) (**Table 2**) and most were of mild or moderate intensity
- The incidence of predefined TEAEs was similar across repeated treatment cycles except for headaches and gastrointestinal disorders, which were more frequent in Cycle 1 (**Figure 1**)
  - Eight patients (4.3%) experienced severe headaches (rozanolixizumab 7 mg/kg, n=1; rozanolixizumab 10 mg/kg, n=7), with seven patients reporting these in Cycle 1
  - One patient in the rozanolixizumab 7 mg/kg group permanently discontinued the study due to a TEAE of headache
  - Eight patients (4.3%) experienced serious infections (rozanolixizumab 7 mg/kg, n=2; rozanolixizumab 10 mg/kg, n=6)
  - Overall, 85 patients (45.2%) reported infection (**Table 3**). The most common infections were COVID-19, upper respiratory tract infection, nasopharyngitis, and oral herpes
  - No anaphylactic or serious hypersensitivity reactions occured. No potential risk for hepatotoxicity or renal toxicity, or clinically meaningful changes in lipid or albumin levels were identified
- Three patients died due to TEAEs (COVID-19, n=1; COVID-19 pneumonia, n=1; pneumonia, n=1). All deaths were considered by investigators as not related to rozanolixizumab treatment

These data were previously presented at the European Academy of Neurology Annual Meeting in Helsinki, Finland; June 29-July 2, 2024.

Table 1 Baseline 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)
Disease duration, years, mean (SD)		7.9 (7.9)	9.0 (9.2)	8.5 (8.6)
MG-specific autoantibody status	AChR Ab+, n (%)	84 (89.4)	86 (91.5)	170 (90.4)
	MuSK Ab+, n (%)	9 (9.6)	9 (9.6)	18 (9.6)
MG-ADL score, mean (SD)		8.3 (3.7)	8.4 (2.9)	8.3 (3.4)
QMG score, mean (SD)		15.4 (3.6)	15.8 (3.6)	15.6 (3.6)

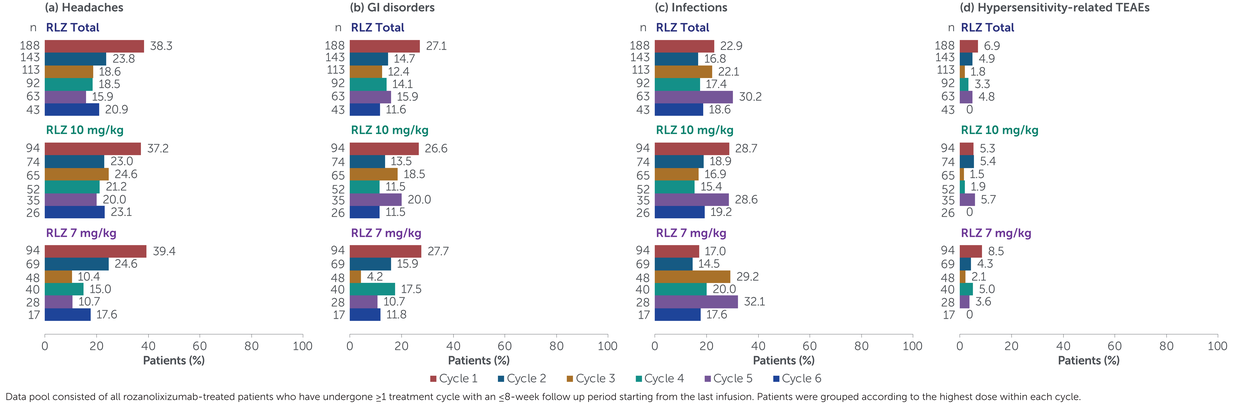
Data pool consisted of all rozanolixizumab-treated patients who have undergone ≥1 treatment cycle with an ≤8-week follow-up period starting from the last infusion. Patients were allocated to the 7 mg/kg and 10 mg/kg treatment groups according to their first rozanolixizumab treatment cycle.

Table 2 Overview of TEAEs

	Over all cycles		
	RLZ 7 mg/kg (n=133)	RLZ 10 mg/kg (n=131)	RLZ total (N=188)
Any TEAE	103 (77.4)	120 (91.6)	169 (89.9)
Serious TEAEs	14 (10.5)	29 (22.1)	42 (22.3)
Permanent discontinuation of study drug due to TEAEs	8 (6.0)	19 (14.5)	27 (14.4)
Treatment-related TEAEs	57 (42.9)	81 (61.8)	111 (59.0)
Severe TEAEs	12 (9.0)	39 (29.8)	50 (26.6)
TEAEs leading to death	1 (0.8)	2 (1.5)	3 (1.6)

Data are presented as n (%). Data pool consisted of all rozanolixizumab-treated patients who have undergone ≥1 treatment cycle with an ≤8-week follow-up period starting from the last infusion. Patients switching rozanolixizumab dose were allocated to both the 7 mg/kg and the 10 mg/kg treatment groups.

Figure 1 Incidence of predefined TEAEs



Data pool consisted of all rozanolixizumab-treated patients who have undergone ≥1 treatment cycle with an ≤8-week follow up period starting from the last infusion. Patients were grouped according to the highest dose within each cycle.

Table 3 Incidence of predefined TEAEs

	Over all cycles		
	RLZ 7 mg/kg (n=133)	RLZ 10 mg/kg (n=131)	RLZ total (N=188)
Headaches	55 (41.4)	56 (42.7)	89 (47.3)
Infections	43 (32.3)	54 (41.2)	85 (45.2)
Hypersensitivity-related TEAEs	14 (10.5)	11 (8.4)	25 (13.3)
Anaphylactic reaction	0	0	0
Injection-site reaction	13 (9.8)	12 (9.2)	23 (12.2)
Any GI disorder	38 (28.6)	48 (36.6)	73 (38.8)
Hepatic events	2 (1.5)	7 (5.3)	9 (4.8)
Lipid-related events	3 (2.3)	5 (3.8)	8 (4.3)
Kidney-related events	0	3 (2.3)	3 (1.6)
Albumin-related events	0	0	0

Data are presented as n (%). Data pool consisted of all rozanolixizumab-treated patients who have undergone ≥1 treatment cycle with an ≤8-week follow up period starting from the last infusion. For the entire study summary, patients were grouped according to the most recent dose received prior to onset of AEs; therefore, patients switching rozanolixizumab dose were allocated to both the 7 mg/kg and the 10 mg/kg treatment groups.

Summary and conclusions

- Incidence of predefined TEAEs, including headaches, infections, hypersensitivity, and gastrointestinal disorders, did not increase with subsequent cycles of rozanolixizumab treatment
- There were no clinically meaningful changes in albumin or lipid levels and no potential risk for hepatotoxicity or renal toxicity
- The majority of TEAEs were of mild or moderate intensity and nonserious. No anaphylactic or serious hypersensitivity reactions occured
- Across all cycles, rozanolixizumab was generally well tolerated and demonstrated an acceptable long-term safety profile at both doses

Abbreviations: Ab+, antibody positive; AChR, acetylcholine receptor; AE, adverse event; COVID-19, coronavirus disease 2019; FcRn, neonatal Fc receptor; GI, gastrointestinal; gMG, generalized myasthenia gravis; IgG, immunoglobulin G; mAb, monoclonal antibody; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MuSK, muscle-specific tyrosine kinase; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation; TEAE, treatment-emergent adverse event.

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