Minimal symptom expression in generalized myasthenia gravis: A *post hoc* analysis of MycarinG and open-label studies

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Introduction

- Rozanolixizumab is a humanized IgG4 mAb FcRn inhibitor approved for the treatment of adults with AChR Ab+ or MuSK Ab+ gMG[1]
- In the Phase 3 MycarinG study (NCT03971422), reductions in MG-ADL score from baseline were significantly greater in the rozanolixizumab 7mg/kg group (LS mean CFB: -3.37) and rozanolixizumab 10 mg/kg group (-3.40) compared with placebo (-0.78; p<0.001 for both rozanolixizumab doses)[2]
- Attainment of MSE (MG-ADL score: 0 or 1) is a stringent measure of therapeutic efficacy and a treatment goal in MG[3,4]
- This *post hoc* analysis used pooled data from the MycarinG study[2] and its OLE studies to assess MSE response across subsequent rozanolixizumab treatment cycles for patients who achieved MSE in Cycle 1

Methods

- In the Phase 3 MycarinG study, patients were randomized 1:1:1 to receive a weekly subcutaneous infusion of rozanolixizumab 7 mg/kg, 10 mg/kg or placebo for a 6-week cycle, followed by an 8-week observation period
- Patients who either completed MycarinG or required rescue therapy during the observation period could enroll in one of two OLE studies: MG0004 (NCT04124965) then MG0007 (NCT04650854); or MG0007 directly (**Figure 1**)
- Data from patients who had ≥2 symptom-driven treatment cycles were pooled across MycarinG, MG0004 (first 6 weeks), and MG0007 (interim analysis; data cutoff: July 8, 2022)
- Efficacy outcomes included proportion of patients who achieved MSE at Cycle 1, proportion of patients who achieved MSE at subsequent cycles (Cycles 2, 3, and 4), and change in MG-ADL score during each cycle for individual patients who achieved MSE

Results

- **Patients**
  - The efficacy pool included 127 patients treated with either rozanolixizumab 7 mg/kg or 10 mg/kg who had ≥2 symptom-driven cycles; baseline characteristics were generally representative of a population with moderate-to-severe gMG (**Table 1**)
  - The safety pool included 188 patients with ≥1 cycle and ≤8-week follow-up period across MycarinG and MG0007; baseline demographics and characteristics were similar to those in the efficacy pool[5]
- **Efficacy**
  - More than a quarter of patients achieved MSE in Cycle 1 and over 64% of these patients continued to achieve MSE in subsequent treatment cycles (**Figure 2**)
  - Up to 21% of patients who did not achieve MSE in treatment Cycle 1 went on to achieve MSE in subsequent treatment cycles (**Figure 2**)
  - Almost all patients who achieved MSE did so within 6 weeks of starting the treatment cycle, irrespective of MG-ADL score at the start of the treatment cycle (**Figure 3**)
    - In the first four treatment cycles, some patients achieved MSE as early as 1 week after rozanolixizumab infusion
- **Safety**
  - Across all cycles, 89.9% of patients (n=169) experienced a TEAE, with the most frequent TEAEs being headache (46.3%), diarrhea (28.7%), pyrexia (18.1%), nausea (14.9%), COVID-19 infection (13.8%), and arthralgia (11.2%)[6]
  - In general, the incidence of TEAEs did not increase with repeated cycles of treatment compared with Cycle 1[7]

Summary and conclusions

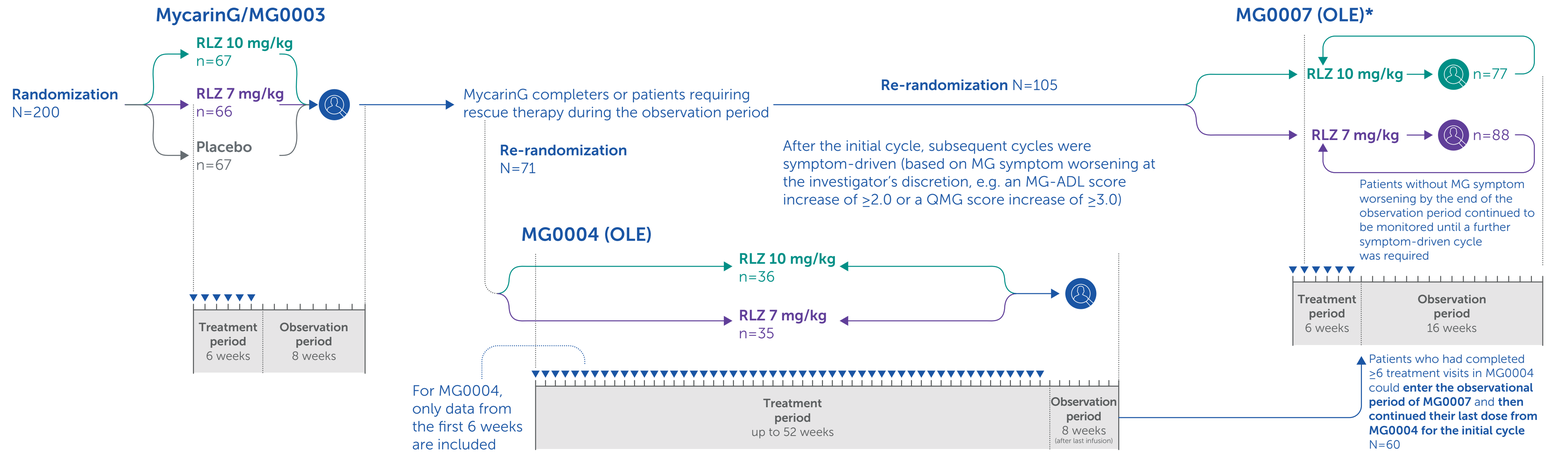
MSE is a strong, clinically meaningful endpoint and a stringent measure of therapeutic efficacy; attainment of MSE is a therapeutic goal in the treatment of gMG

Among patients who achieved MSE in Cycle 1 of rozanolixizumab, >64% continued to achieve MSE in Cycles 2–4

All except two patients who achieved MSE did so within the first 6 weeks of starting the rozanolixizumab treatment cycle, and some patients achieved MSE as early as 1 week into the treatment cycle

Patients receiving rozanolixizumab who achieved MSE in the first treatment cycle demonstrated a consistent response rate over subsequent cycles, while up to 21% of initial non-achievers were able to achieve MSE with subsequent rozanolixizumab treatment cycles

Figure 1 MycarinG and OLE study design

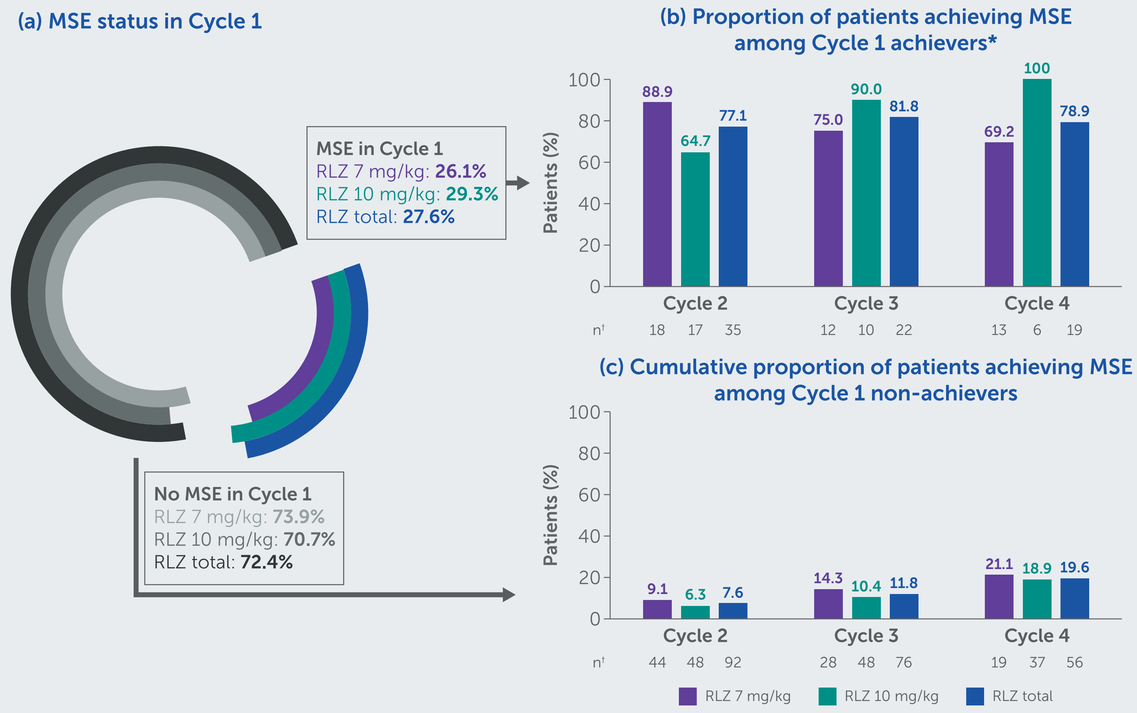


*After the initial cycle, dose modifications from 10 mg/kg to 7 mg/kg and *vice versa* were permitted at the beginning of each treatment cycle provided the benefit–risk ratio remained favorable for the patient.

Table 1 Patient demographics and baseline disease characteristics for patients who had ≥2 symptom-driven cycles

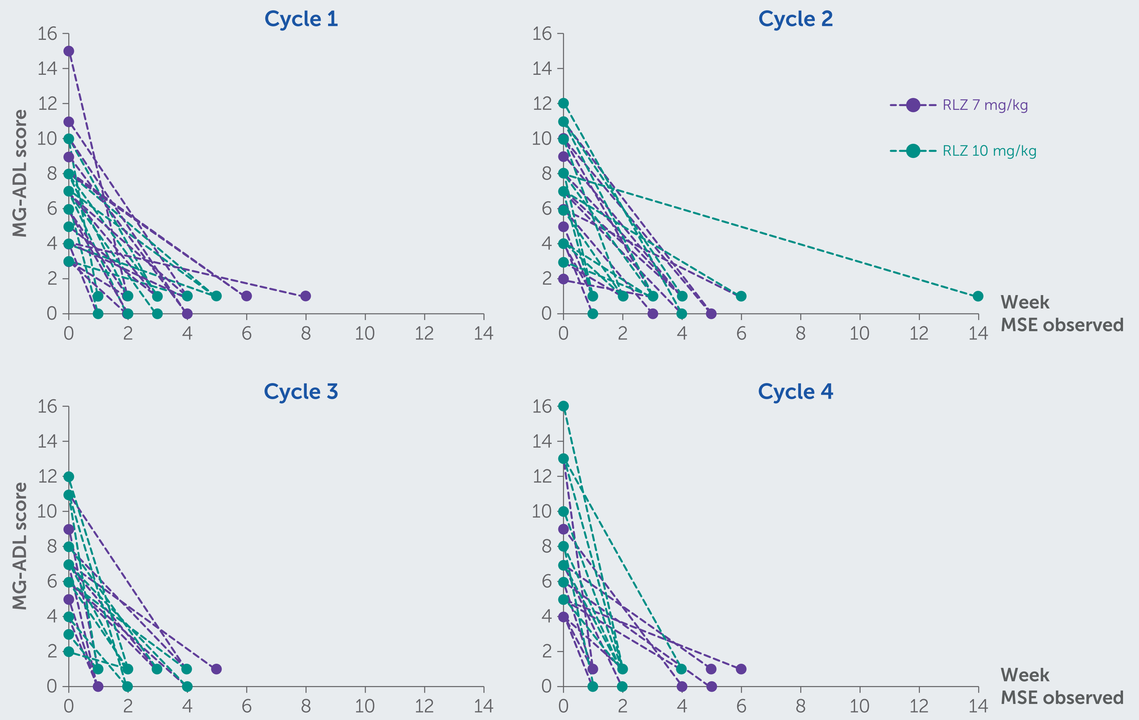
	RLZ 7 mg/kg (n=69)	RLZ 10 mg/kg (n=58)	RLZ total (N=127)
Age, years, mean (SD)	52.0 (14.3)	48.9 (18.3)	50.6 (16.2)
Sex, female, n (%)	40 (58.0)	36 (62.1)	76 (59.8)
AChR Ab+, n (%)	61 (88.4)	54 (93.1)	115 (90.6)
MuSK Ab+, n (%)	9 (13.0)	3 (5.2)	12 (9.4)
MG-ADL score at baseline, mean (SD)	9.1 (3.8)	8.4 (2.9)	8.8 (3.4)
QMG score at baseline, mean (SD)	16.0 (3.8)	16.0 (3.7)	16.0 (3.8)
Duration of disease, years, mean (SD)	7.9 (8.4)	8.5 (8.9)	8.2 (8.6)

Figure 2 MSE achievers and non-achievers per cycle



Efficacy pool, patients with ≥2 symptom-driven cycles.
*Response per cycle; †Number of patients who completed a post-baseline MG-ADL assessment, and who completed at least 2, 3 and 4 treatment cycles, respectively.

Figure 3 MG-ADL scores over the treatment cycle for individual patients who achieved MSE, by cycle



Efficacy pool, patients with ≥2 symptom-driven cycles.

Abbreviations: Ab+, antibody-positive; AChR, acetylcholine receptor; CFB, change from baseline; FcRn, neonatal Fc receptor; gMG, generalized myasthenia gravis; IgG4, immunoglobulin G4; LS, least squares; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MSE, minimal symptom expression; MuSK, muscle-specific kinase; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; RLZ, rozanolixizumab; SD, standard deviation.

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