# Response over time with zilucoplan in generalized myasthenia gravis: *Post hoc* analysis of RAISE-XT 60-week follow up

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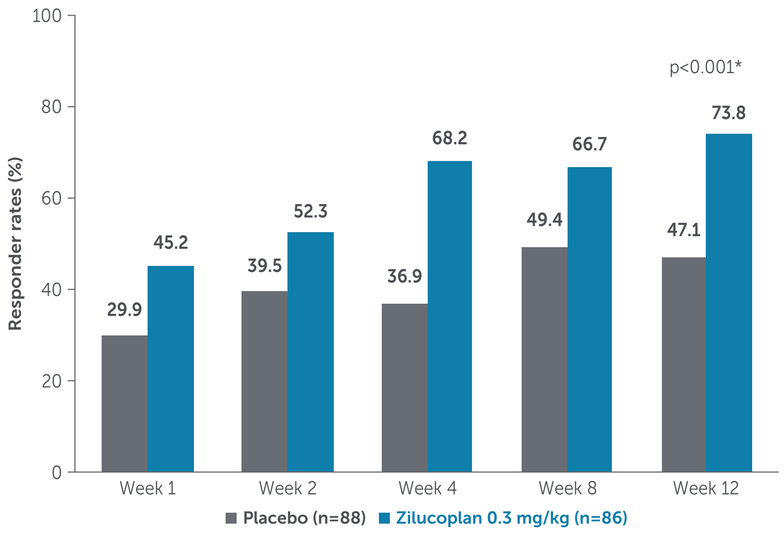
## Introduction

- Zilucoplan is a macrocyclic peptide C5 inhibitor, indicated for the treatment of adult patients with AChR Ab+ gMG[1,2]
- In the Phase 3 RAISE study (NCT04115293) and interim analysis of the Phase 3 ongoing OLE study RAISE-XT (NCT04225871), patients with AChR Ab+ gMG treated with zilucoplan showed clinically meaningful improvements in MG-specific outcomes[1,3]
- At Week 12 in the RAISE study, significantly more patients in the zilucoplan group were MG-ADL responders (≥3-point improvement from baseline) compared with the placebo group (**Figure 1**)
- Here, we assess the response to treatment with zilucoplan up to Week 60 of the ongoing RAISE-XT study

## Methods

- Adults with AChR Ab+ gMG who completed qualifying double-blind placebo-controlled studies (Phase 2 NCT03315130 or RAISE) could enroll into RAISE-XT. During the trial, patients self-administered once-daily subcutaneous zilucoplan 0.3 mg/kg
- The primary outcome of RAISE-XT is incidence of TEAEs
- In this *post hoc* analysis, MG-ADL and QMG responder rates were assessed up to Week 60 in patients who received zilucoplan 0.3 mg/kg in the two qualifying studies and continued zilucoplan in RAISE-XT
- MG-ADL responders and QMG responders were defined as achieving a ≥3-point and ≥5-point improvement from baseline, respectively, without rescue medication
- The interim data cut-off was September 8, 2022

**Figure 1** MG-ADL responders to Week 12 in RAISE




*P-value was calculated based on the Chi-squared statistic, serving as exploratory analysis. MG-ADL responders achieved ≥3-point reductions from baseline without rescue therapy.

**Table 1** Overview of TEAEs

| | **All zilucoplan** N=200 |
|---|---|
| **Duration of zilucoplan exposure, years, median (range)** | 1.2 (0.11–4.45) |
| **Any TEAE, n (%)** | 188 (94.0) |
| Myasthenia gravis, n (%) | 52 (26.0) |
| COVID-19, n (%) | 49 (24.5) |
| Headache, n (%) | 35 (17.5) |
| Diarrhea, n (%) | 30 (15.0) |
| Nasopharyngitis, n (%) | 30 (15.0) |
| **Serious TEAE,* n (%)** | 64 (32.0) |
| Serious treatment-related TEAE, n (%) | 2 (1.0) |
| **TEAE resulting in permanent withdrawal from IMP, n (%)** | 17 (8.5) |
| **Treatment-related TEAE, n (%)** | 67 (33.5) |
| **Severe TEAE, n (%)** | 57 (28.5) |
| **TEAEs leading to deaths,† n (%)** | 4 (2.0) |

The most common TEAEs occurring in ≥15% of patients overall are reported only. *The most common serious TEAEs were myasthenia gravis worsening (n=15, 7.5%) and COVID-19 pneumonia (n=4, 2.0%); †TEAEs leading to death included cardiac arrest (n=2) and accidental head injury (n=1) in the zilucoplan 0.3 mg/kg/0.3 mg/kg group, and death from an unknown cause (n=1) in the placebo/zilucoplan 0.3 mg/kg group.

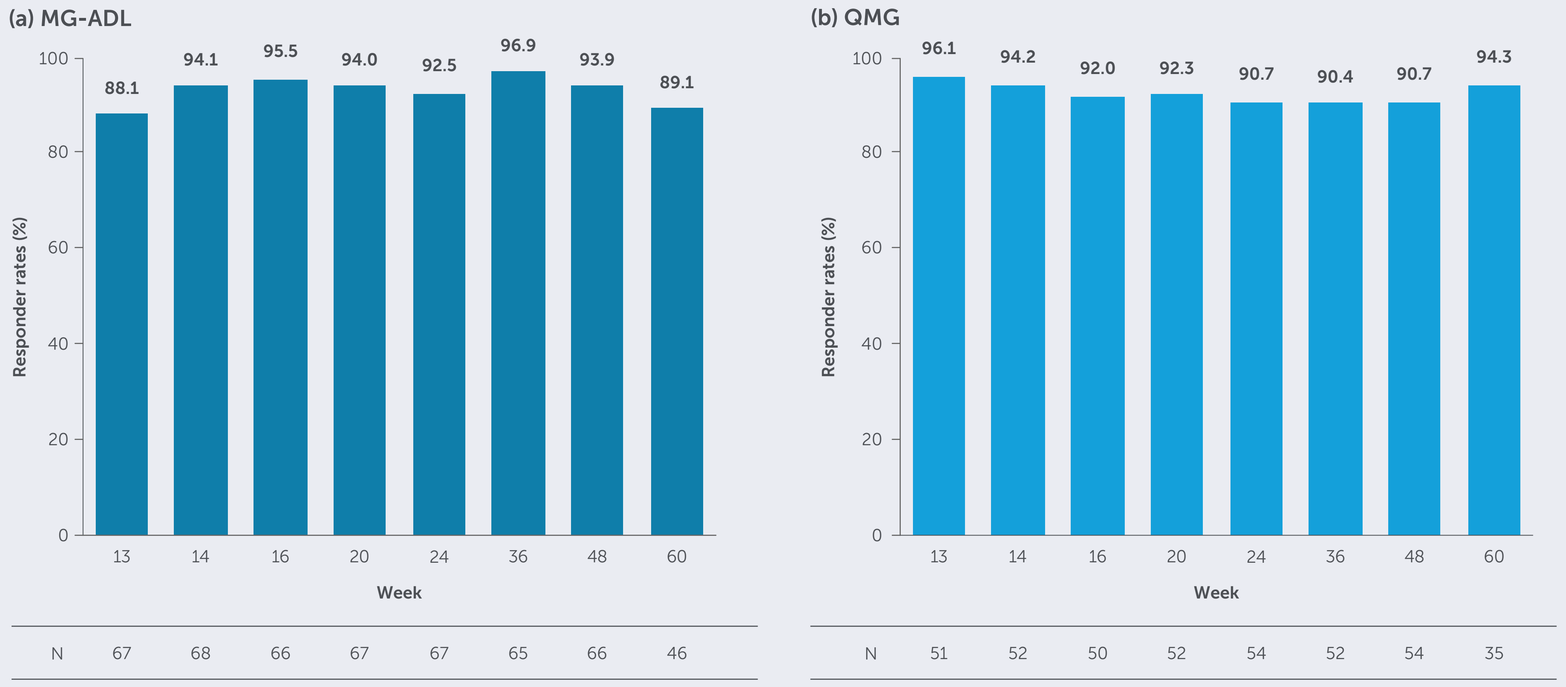
## Results

- In total, 200 patients enrolled in RAISE-XT, of whom 93 had received zilucoplan 0.3 mg/kg in the qualifying double-blind studies
- Of these 93 patients, 74.2% (n=69) were MG-ADL responders and 59.8% (n=55) were QMG responders at Week 12
  - Among the MG-ADL and QMG responders at Week 12, responder rates remained high throughout the OLE up to Week 60 (**Figure 2**)
- At Week 12, 25.8% (n=24) were MG-ADL non-responders and 40.2% (n=37) were QMG non-responders
  - Approximately half of Week 12 non-responders were responders two weeks into the extension study at Week 14 for both MG-ADL and QMG (**Figure 3**)
- Zilucoplan was generally well tolerated; most TEAEs were mild or moderate in severity (**Table 1**)
  - The most common TEAEs were MG and COVID-19

## Summary and conclusions

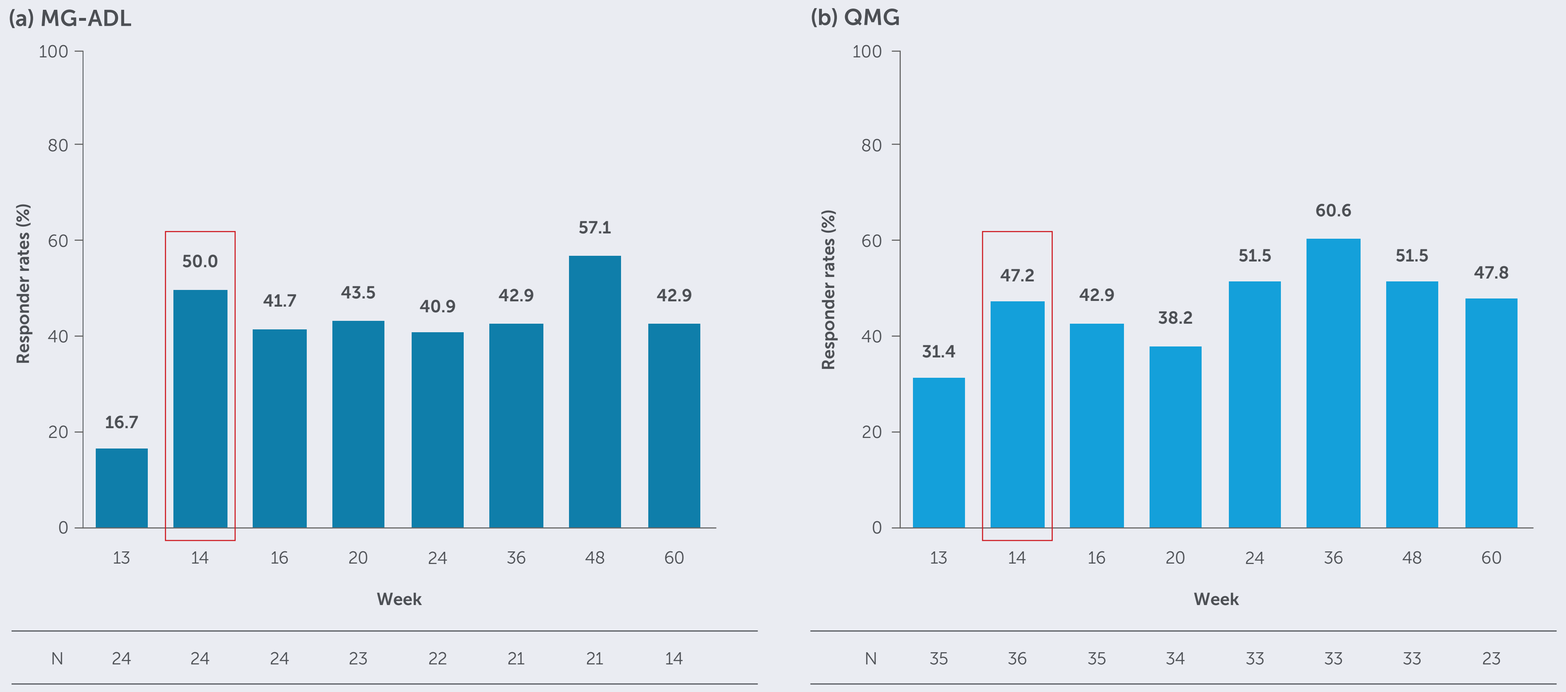
- The majority of patients who received zilucoplan were MG-ADL and QMG responders at Week 12 of the double-blind studies
- Among the Week 12 responders, responder rates were maintained at approximately 90% for MG-ADL and QMG throughout the OLE, up to Week 60
- Of patients who were non-responders at Week 12, approximately half became MG-ADL and QMG responders as early as the second week of RAISE-XT (Week 14)
- Zilucoplan had a favorable safety profile and was well tolerated in the long term
- These data demonstrate the benefit of long-term zilucoplan treatment

**Figure 2** Responder rates in Week 12 responders for (a) MG-ADL and (b) QMG




MG-ADL and QMG responders achieved ≥3-point and ≥5-point reductions from double-blind baseline without rescue therapy, respectively.

**Figure 3** Responder rates in Week 12 non-responders for (a) MG-ADL and (b) QMG




MG-ADL and QMG responders achieved ≥3-point and ≥5-point reductions from double-blind baseline without rescue therapy, respectively.

**Abbreviations:** Ab+, autoantibody positive; AChR, acetylcholine receptor; C5(a,b), complement component 5(a,b); CME, continuing medical education; COVID-19, coronavirus disease 2019; (g)MG, (generalized) myasthenia gravis; IMP, investigational medicinal product; MG-ADL, Myasthenia Gravis Activities of Daily Living; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; TEAE, treatment-emergent adverse event.

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*These data were previously presented at the Congress of European Academy of Neurology in Helsinki, Finland; June 29–July 2, 2024.*

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