Poster **922**

Long-term zilucoplan in generalized myasthenia gravis: 96-week follow-up interim analysis of RAISE-XT

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Introduction

- Zilucoplan is a small (15 amino acid) macrocyclic peptide complement C5 inhibitor indicated for the treatment of adult patients with AChR Ab+ gMG
- In the Phase 3 RAISE study (NCT04115293), zilucoplan was associated with statistically significant and clinically meaningful improvements in MG-specific outcomes and demonstrated a favorable safety profile in patients with AChR Ab+ gMG[1]
- Long-term data from RAISE-XT (NCT04225871), an ongoing OLE study, will enhance our understanding of the safety and efficacy of zilucoplan in adults with gMG
- Here, we report responder rates for MG-ADL, QMG, and MSE over 96 weeks of zilucoplan treatment in RAISE-XT

Methods

- Patients eligible for RAISE-XT were adults with AChR Ab+ gMG who had completed a qualifying, double-blind study (Phase 2 [NCT03315130] or RAISE) and had received vaccination against *Neisseria meningitidis*
- Patients self-administered daily subcutaneous injections of zilucoplan 0.3 mg/kg
- The primary outcome is the incidence of TEAEs
- In this interim analysis, we report the mean CFB and responder rates for MG-ADL, QMG, and MSE up to 96 weeks (data cutoff date: May 11, 2023)
  - Responder rates were defined as a reduction of ≥3 points in MG-ADL score and ≥5 points in QMG score
  - MSE was defined as an MG-ADL score of 0 or 1, without rescue therapy
  - Mean change from study baseline in MGC, MG-QoL 15r, and Neuro-QoL Short Form Fatigue were also assessed

Results

- At the data cutoff, 200 patients had enrolled in RAISE-XT. Of 183 who received zilucoplan 0.3 mg/kg or placebo in the qualifying study, 93 continued zilucoplan 0.3 mg/kg and 90 switched from placebo to zilucoplan 0.3 mg/kg
- Median exposure was 1.8 years (range 0.11–5.1 years; **Table 1**)
- MG-ADL score improved rapidly in the first week after starting zilucoplan and continued to improve through to Week 24 (**Figure 1**)
  - Patients who received zilucoplan in the double-blind studies experienced rapid improvement in MG-ADL score compared with the placebo group
  - Patients who switched from placebo in the double-blind studies to zilucoplan in RAISE-XT also saw a rapid improvement in MG-ADL score from baseline following initiation of zilucoplan, with continued improvement through to Week 24
- Improvements were sustained through to Week 96 for pooled zilucoplan 0.3 mg/kg patients (**Figure 1**)
- Sustained improvements in mean CFB to Week 96 were also observed for QMG, MGC, MG-QoL 15r, and Neuro-Qol Short Form Fatigue scores (**Figure 2**)
- Responder rates for MG-ADL and QMG increased up to Week 24 and were sustained through to Week 96 in the zilucoplan group (**Figure 3**)
  - The placebo-switch group experienced a rapid increase in responder rates within one week after switching to zilucoplan
- MSE responder rates (i.e., percentage of patients with MG-ADL scores of 0 or 1 at a given time point) continued to improve through to Week 96 (**Figure 3**)
- TEAEs occurred in 191 of 200 patients (95.5%). The three most common TEAEs were COVID-19, MG, and headache (**Table 1**)
- Overall, 71 patients (35.5%) reported serious TEAEs, of which four were considered to be treatment related (**Table 1**)

Summary and conclusions

RAISE-XT is an ongoing OLE study evaluating the long-term safety and efficacy of zilucoplan in patients with AChR Ab+ gMG

Zilucoplan was associated with a rapid improvement of symptoms, which was sustained through to Week 96; improvements in symptoms were consistent across MG-ADL, QMG, MGC, MG-QoL 15r, and Neuro-QoL Short Form Fatigue scores

High MG-ADL and QMG responder rates were sustained, and MSE responder rate increased through to Week 96

Zilucoplan had a favorable safety profile and was well tolerated in the long term

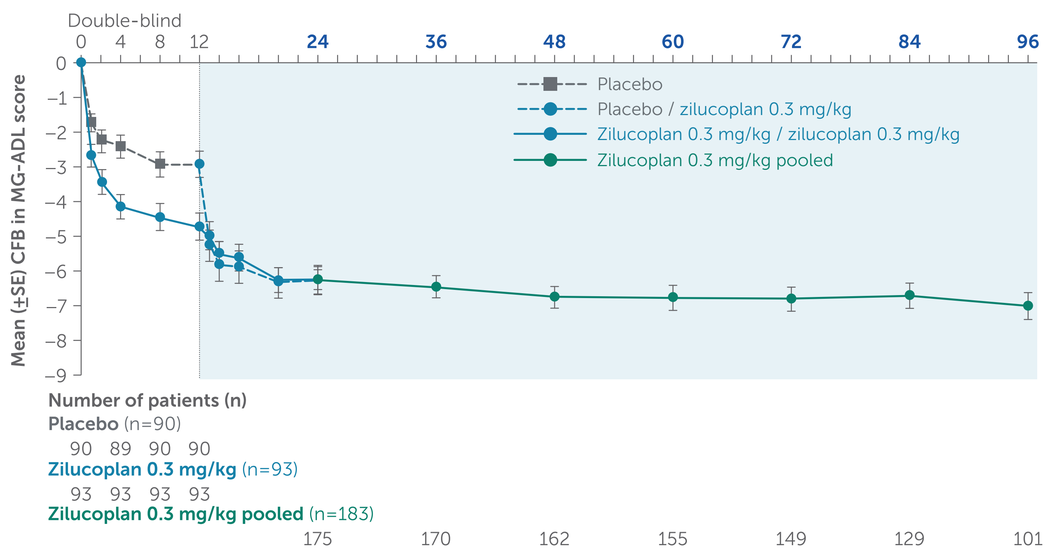
In RAISE-XT, zilucoplan treatment was well tolerated and efficacy was sustained for up to 96 weeks, supporting long-term use in patients with AChR Ab+ gMG

Table 1 Duration of exposure and TEAEs

	All zilucoplan (N=200)
Duration of zilucoplan exposure, years, median (range)	1.8 (0.11–5.1)
Any TEAE, n (%)	191 (95.5)
COVID-19	64 (32.0)
MG	58 (29.0)
Headache	40 (20.0)
Nasopharyngitis	39 (19.5)
Diarrhea	33 (16.5)
Nausea	32 (16.0)
Arthralgia	32 (16.0)
URTI	32 (16.0)
Fatigue	30 (15.0)
Serious TEAE, n (%)	71 (35.5)
Treatment-related serious TEAE,* n (%)	4 (2.0)
TEAE resulting in permanent withdrawal from IMP,† n (%)	19 (9.5)
Treatment-related TEAE, n (%)	70 (35.0)
Severe TEAE, n (%)	64 (32.0)
TEAEs leading to death,‡ n (%)	4 (2.0)

*Treatment-related serious TEAEs were: one (1.1%) event of esophagitis and one (1.1%) event of injection-site infection (occurring on the right inner thigh, which is not a recommended injection site) in the zilucoplan 0.3 mg/kg / 0.3 mg/kg group; one (8.3%) event of colonic abscess in the zilucoplan 0.1 mg/kg / 0.1 mg/kg / 0.3 mg/kg group; and one (1.1%) event of headache in the placebo / zilucoplan 0.3 mg/kg group. †Includes all deaths. ‡No deaths were considered treatment related. 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. Most common TEAEs occurring in ≥15% of patients overall are reported only.

Figure 1 CFB in MG-ADL



Patients received zilucoplan for up to 96 weeks.

Figure 2 CFB in QMG, MGC, MG-QoL 15r, and Neuro-QoL Short Form Fatigue

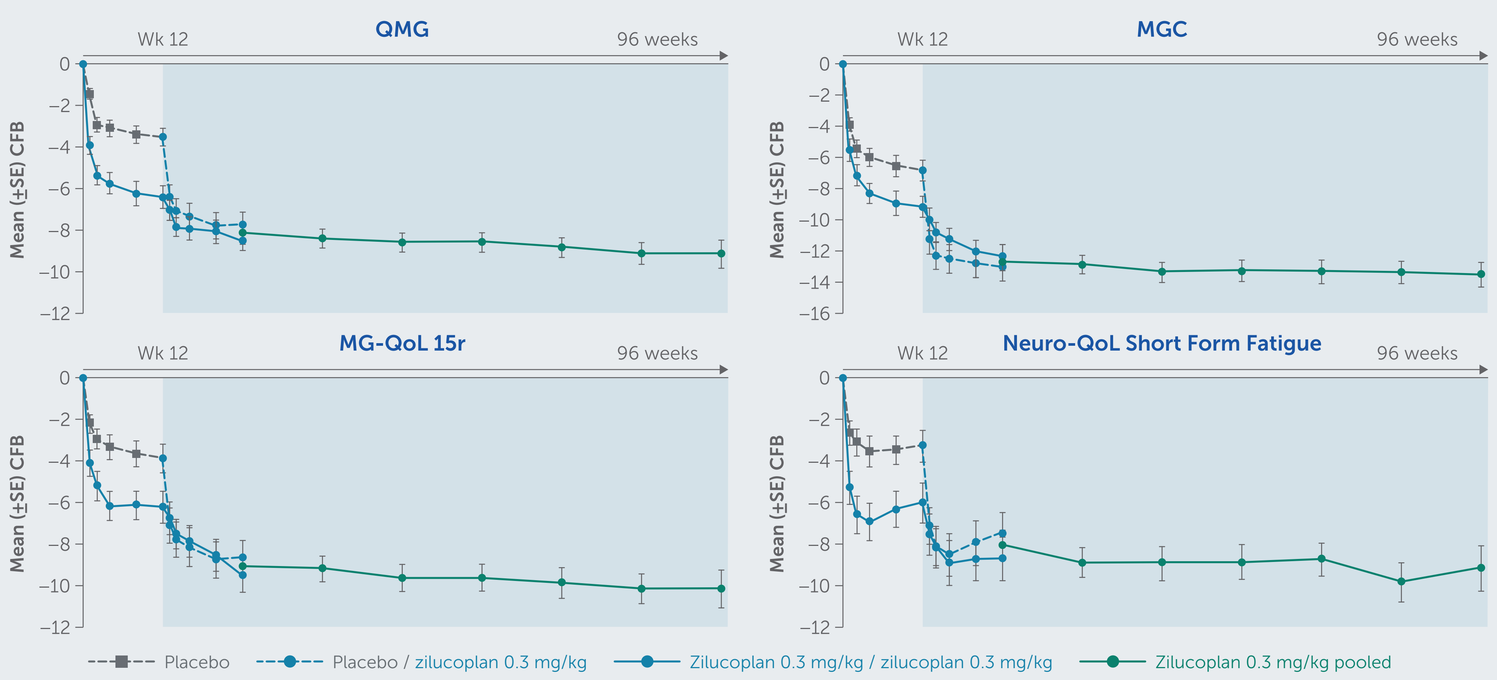
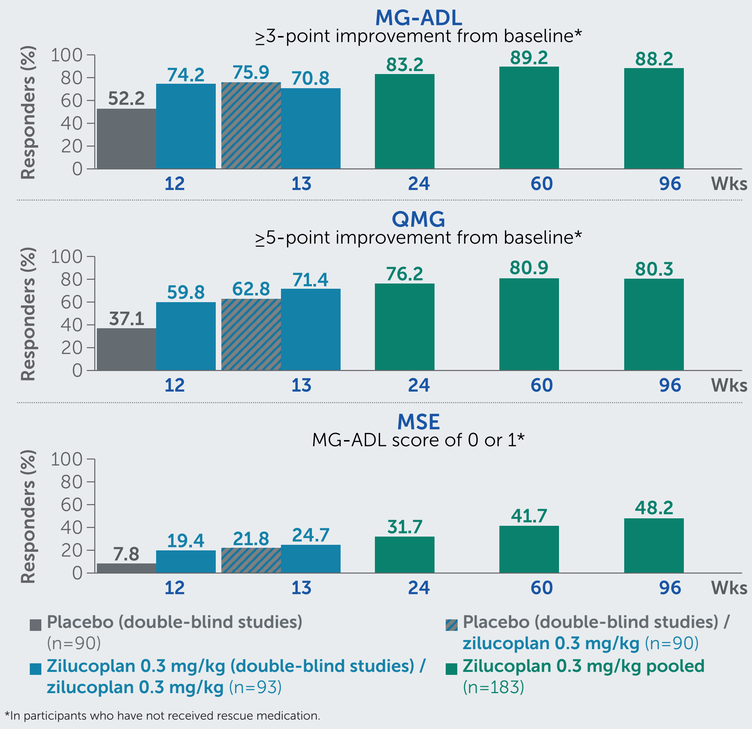


Figure 3 Responder rates



*In participants who have not received rescue medication.

Abbreviations: Ab+, antibody-positive; AChR, acetylcholine receptor; C5, component 5; CFB, change from baseline; COVID-19, coronavirus disease 2019; gMG, generalized myasthenia gravis; IMP, investigational medicinal product; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGC, Myasthenia Gravis Composite; MG-QoL 15r, Myasthenia Gravis Quality of Life 15-item revised; MSE, minimal symptom expression; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; QoL, quality of life; SE, standard error; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection; Wk, week.

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References: 1. Howard JF Jr., et al. *Lancet Neurol.* 2023;22(5):395–406.

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