Improvement in myasthenia gravis-specific outcome subdomain scores with zilucoplan: RAISE-XT 120-week *post hoc* analysis

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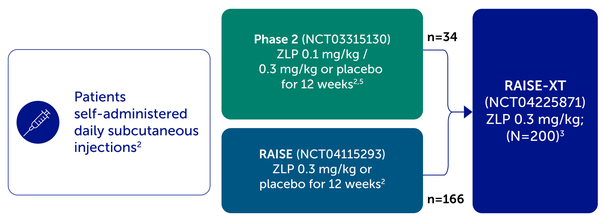
Introduction

- gMG may affect a range of muscle groups depending on the individual, and treatments may affect these muscle groups differently[1]
- In the Phase 3 RAISE study (NCT04115293), zilucoplan, a complement C5 inhibitor, demonstrated clinically meaningful improvements in MG-ADL and QMG total scores versus placebo in adults with anti-AChR Ab+ gMG[2] that were sustained in the OLE study, RAISE-XT (NCT04225871)[3,4]
- This *post hoc* analysis assessed mean CFB in MG-ADL and QMG subdomain scores up to Week 120 in patients who were experiencing those symptoms at baseline

Methods

- Patients who completed a qualifying double-blind study (NCT03315130/RAISE) could enter RAISE-XT to self-administer once-daily subcutaneous injections of zilucoplan 0.3 mg/kg (**Figure 1**)
- Mean changes from double-blind baseline to Week 120 in MG-ADL and QMG subdomain scores (ocular, bulbar, respiratory and limb/gross motor) in patients with baseline scores ≥1 in that subdomain were assessed *post hoc* (interim data cut-off: 11 November 2023) (**Figure 2**)

Figure 1 Study design



Patients who received the ZLP 0.1 mg/kg dose during the Phase 2 study were not included in this *post hoc* analysis.

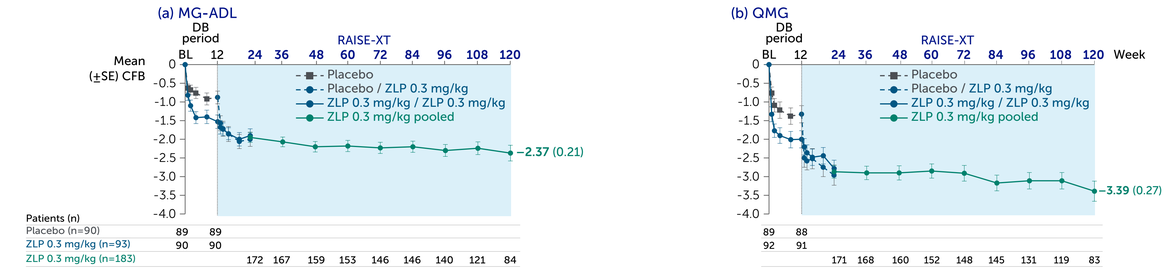
Figure 2 MG-ADL and QMG total scores each comprise four subdomain scores

Results

- Overall, 200 patients entered RAISE-XT; 183 received placebo or zilucoplan 0.3 mg/kg in the double-blind studies
- At Week 120, mean SE CFB was −7.14 (0.44; n=86) for MG-ADL and −9.84 (0.65; n=83) for QMG total scores
- Mean (SE) CFB in MG-ADL subdomain scores were: ocular, −1.37 (0.27; n=41) (**Figure 3a**); bulbar, −1.32 (0.32; n=22) (**Figure 4a**); respiratory, −0.07 (0.11; n=30) (**Figure 5a**); and limb/gross motor, −0.87 (0.17; n=39) (**Figure 6a**)
- Mean (SE) CFB in QMG subdomain scores were: ocular, −2.52 (0.30; n=52) (**Figure 3b**); bulbar, −1.00 (0.45; n=16) (**Figure 4b**); respiratory, −.06 (0.18; n=33) (**Figure 5b**); and limb/gross motor, −4.27 (0.43; n=79) (**Figure 6b**)

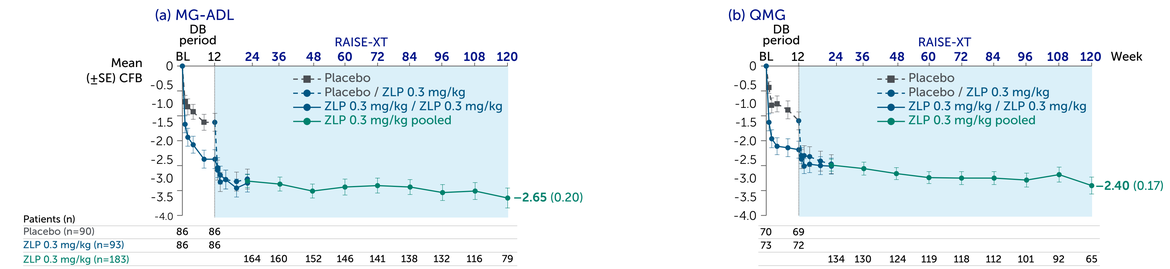
These data were previously presented at EAN 2025 (June 21–24, 2025) in Helsinki, Finland.

Figure 3 Improvements in MG-ADL and QMG ocular subdomain scores were sustained through to Week 120*



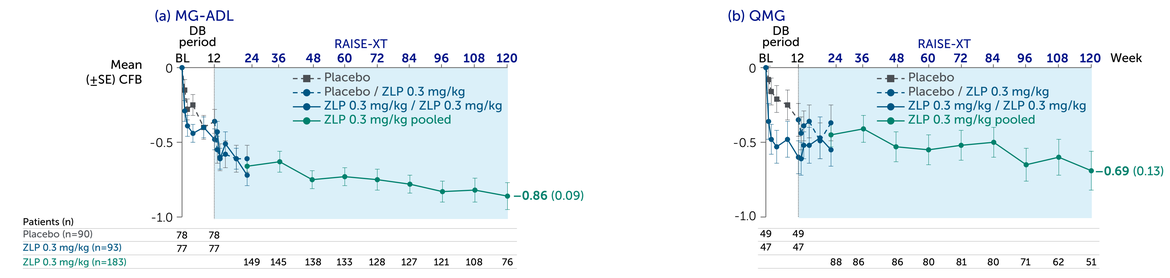
mITT population, which included all patients enrolled in RAISE-XT who received at least one dose of zilucoplan and had at least one post-dosing MG-ADL score. Baseline is defined as the baseline of the parent double-blind study.

Figure 4 Improvements in MG-ADL and QMG bulbar subdomain scores were sustained through to Week 120*



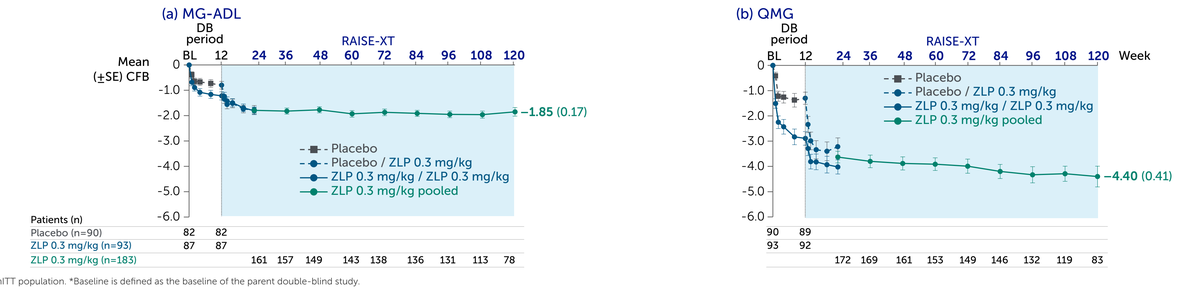
mITT population. *Baseline is defined as the baseline of the parent double-blind study.

Figure 5 Improvements in MG-ADL and QMG respiratory subdomain scores were sustained through to Week 120*



mITT population. *Baseline is defined as the baseline of the parent double-blind study.

Figure 6 Improvements in MG-ADL and QMG limb/gross motor subdomain scores were sustained through to Week 120*



mITT population. *Baseline is defined as the baseline of the parent double-blind study.

Summary and conclusions

- gMG may affect a range of muscle groups depending on the individual, and treatments may affect these muscle groups differently[1]
- In this *post hoc* analysis, zilucoplan led to improvements in all MG-ADL and QMG subdomain scores, which were sustained for up to 120 weeks of treatment
- Zilucoplan demonstrated a favourable safety profile and was well tolerated
- These data support zilucoplan as a long-term treatment option for patients with gMG across a broad range of symptom patterns

Table 1 Most TEAEs were mild or moderate in severity

	All zilucoplan (N=200)
Duration of exposure, years, median (range)	2.2 (0.1–5.6)
Any TEAE, n (%)	194 (97.0)
Treatment-related TEAE, n (%)	73 (36.5)
Serious TEAE, n (%)	81 (40.5)
Treatment-related serious TEAE,* n (%)	5 (2.5)
Severe TEAE, n (%)	72 (36.0)
TEAE resulting in permanent withdrawal from study drug,† n (%)	21 (10.5)
TEAEs leading to death,‡ n (%)	4 (2.0)

Most common TEAEs, n (%)	**All zilucoplan** (N=200)
COVID-19	71 (35.5)
MG worsening	59 (29.5)
Headache	44 (22.0)
Nasopharyngitis	42 (21.0)
Arthralgia	36 (18.0)
Diarrhoea	34 (17.0)
URTI	34 (17.0)
UTI	33 (16.5)
Nausea	32 (16.0)
Fatigue	31 (15.5)

Safety set, which included all patients who received at least one dose of the study drug in RAISE-XT. The individual most common TEAEs reported are those occurring in ≥15% of patients overall. *Treatment-related serious TEAEs were one event each of oesophagitis, injection-site infection (occurring on the right inner thigh, which is not a recommended injection site), colonic abscess and cellulitis in one patient each and headache and photophobia in the same patient. †Includes all deaths. ‡No deaths were considered treatment related. TEAEs leading to death included cardiac arrest (n=2), accidental head injury (n=1) and death from an unknown cause (n=1).

Abbreviations: Ab+, antibody positive; AChR, acetylcholine receptor; BL, baseline; C5, component 5; CFB, change from baseline; COVID-19, coronavirus disease 2019; DB, double-blind; gMG, generalised myasthenia gravis; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; mITT, modified intent-to-treat; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; SE, standard error; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection; ZLP, zilucoplan.

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