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Effect of zilucoplan on fatigue in patients with generalized myasthenia gravis: RAISE-XT 120-week follow-up

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Introduction

- Fatigue is a debilitating symptom that negatively impacts the quality of life of many patients with gMG[1]
- Zilucoplan is a potent complement C5 inhibitor that rapidly and completely blocks complement activity, resulting in statistically significant and clinically meaningful improvements in gMG symptoms compared with placebo at Week 12 of the pivotal Phase 3, double-blind, 12-week RAISE study (NCT04115293)[2]
- In RAISE, treatment with zilucoplan resulted in clinically meaningful and nominally significant improvement in fatigue versus placebo in patients with anti-AChR Ab+ gMG, as measured by the Neuro-QoL Short Form Fatigue scale[1]
  - These improvements were sustained in the ongoing, Phase 3, OLE study RAISE-XT (NCT04225871) up to 60 weeks[1]
- Here, we assessed the long-term effect of zilucoplan on fatigue in patients with gMG in RAISE-XT up to Week 120

Methods

- Adults with anti-AChR Ab+ gMG who completed the Phase 2 study or RAISE could enter RAISE-XT and self-administer daily subcutaneous zilucoplan 0.3 mg/kg injections[3]
  - This analysis only included patients from RAISE, as Neuro-QoL Short Form Fatigue was not assessed in the Phase 2 study
  - The primary outcome of RAISE-XT was incidence of TEAEs[3]
- Neuro-QoL Short Form Fatigue raw scores can be converted into T-scores to apply thresholds for clinical meaningfulness and fatigue severity[4,5]
- In this *post hoc* analysis, we report:
  - CFB in Neuro-QoL Short Form Fatigue T-scores over time
  - The proportion of patients who had clinically meaningful change in fatigue severity levels
  - Fatigue severity level transition from RAISE baseline to Week 120
- The interim data cutoff date for RAISE-XT was November 11, 2023

Results

- Overall, 200 patients enrolled in RAISE-XT, 166 of whom entered from RAISE
- Rapid improvements (within 1 week) were observed in Neuro-QoL Short Form Fatigue T-scores versus RAISE baseline, and increased to Week 12
  - During RAISE-XT, T-scores further improved to Week 24 and these improvements were sustained through to Week 120 (**Figure 1**)
- Of patients with available data at baseline and Week 120, 77.0% (n=47/61) showed clinically meaningful improvement (≥3.5-point decrease[5]) in their T-score at Week 120 compared with baseline (**Figure 2**)
- In total, 60.7% (n=37/61) of patients improved by at least one fatigue severity level at Week 120 (**Figure 3**)
  - At Week 120, 60.7% (n=37/61) of patients had mild or no fatigue compared with 19.7% (n=12/61) at baseline
  - 1.6% (n=1/61) of patients had severe fatigue at Week 120, compared with 26.2% (n=16/61) of patients at baseline
- With a median exposure of 2.2 (range 0.1–5.6) years in RAISE-XT, TEAEs occurred in 97.0% (n=194/200) of patients
  - Overall, 40.5% (n=81/200) of patients experienced a serious TEAE, of whom 2.5% (n=5/200) experienced a serious treatment-related TEAE

Summary and conclusions

In this *post hoc* analysis, we assessed the long-term effect of zilucoplan on fatigue in patients with gMG in RAISE-XT

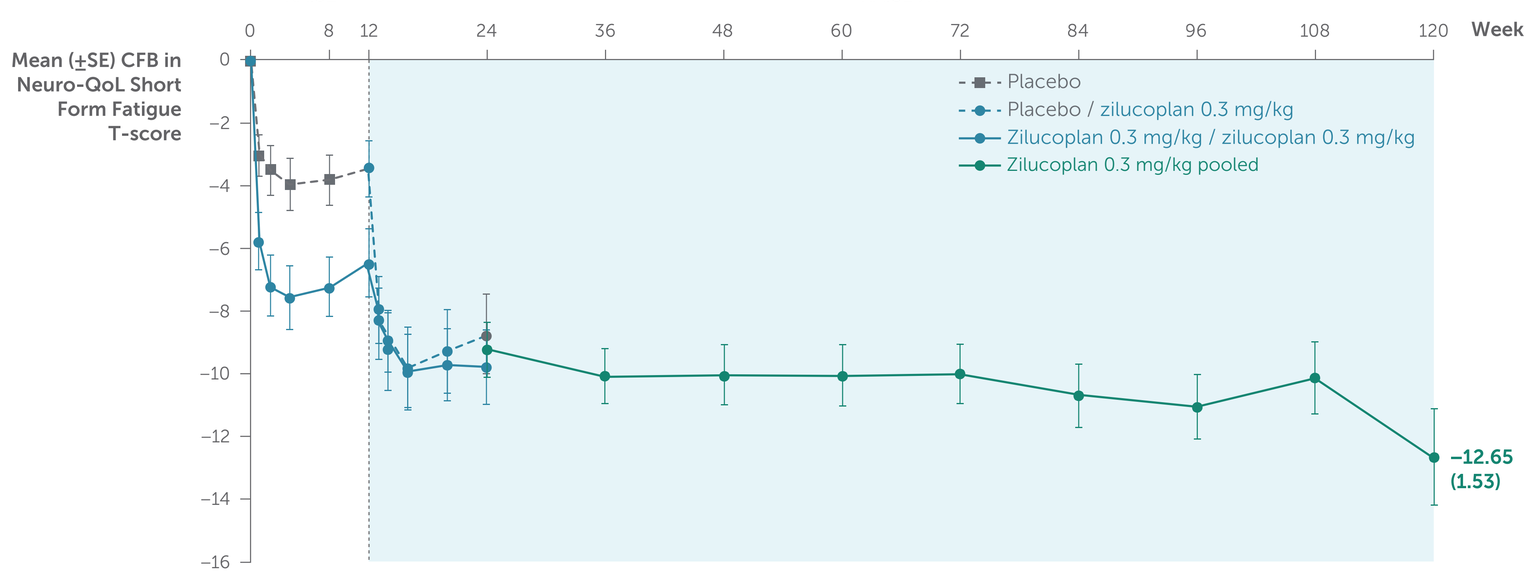
Rapid and sustained reduction in fatigue was observed through to Week 120 with zilucoplan treatment

More than three-quarters of patients showed clinically meaningful improvements in fatigue at Week 120 compared with baseline

At Week 120, over 60% of patients had mild or no fatigue, and only 1 patient out of 61 had severe fatigue

These data demonstrate that long-term treatment with zilucoplan resulted in sustained and clinically relevant reduction in fatigue in patients with gMG

Figure 1 Improvements in Neuro-QoL Short Form Fatigue T-scores were sustained through to Week 120



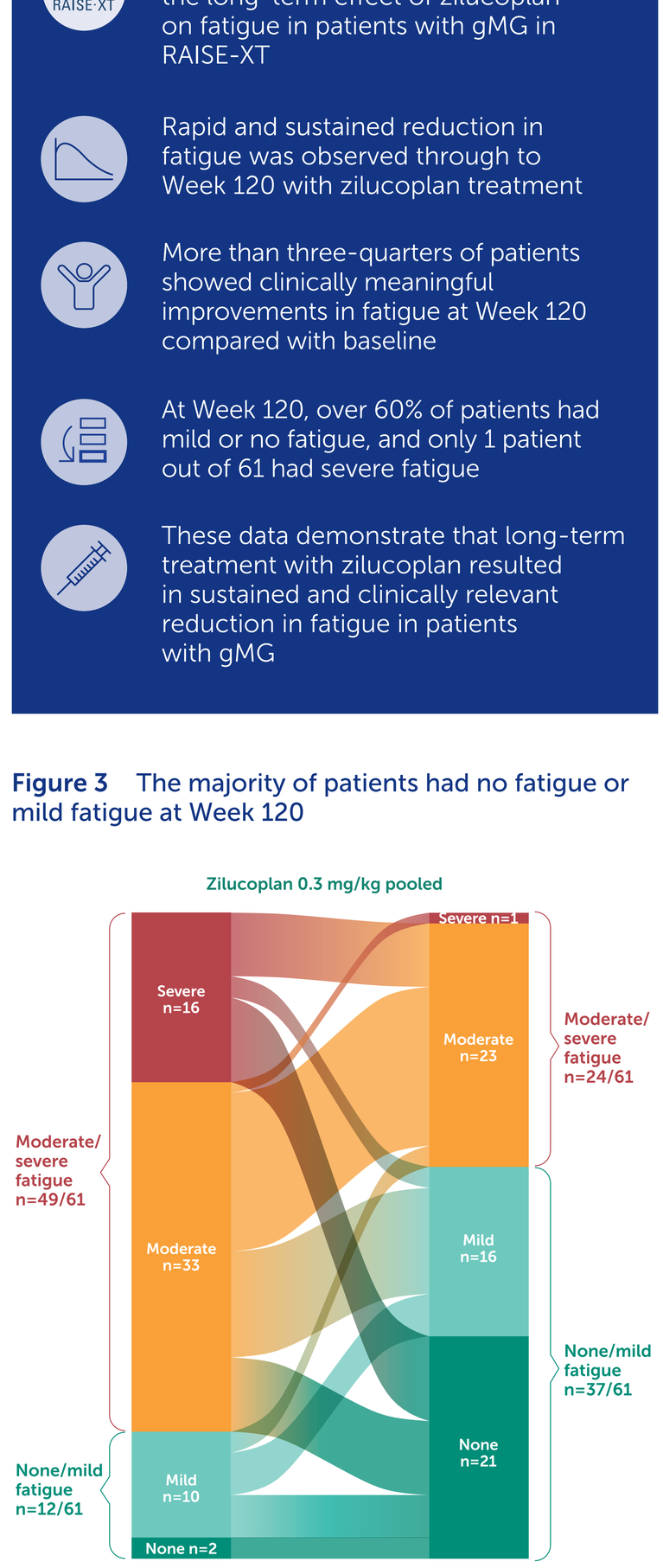
Number of patients (n)												
Placebo (n=84)	81	80	–	–	–	–	–	–	–	–	–	–
Zilucoplan 0.3 mg/kg (n=82)	74	72	–	–	–	–	–	–	–	–	–	–
Zilucoplan 0.3 mg/kg pooled (n=166)	–	–	–	143	142	133	127	123	122	110	99	61

mITT population, which included all patients who received at least one dose of zilucoplan and had at least one post-dosing MG-ADL score.

Figure 2 Most patients showed a clinically meaningful improvement in their Neuro-QoL Short Form Fatigue T-score at Week 120 compared with baseline

mITT population. Each dot represents 1 patient.

Figure 3 The majority of patients had no fatigue or mild fatigue at Week 120



mITT population. The fatigue severity level thresholds for Neuro-QoL Short Form Fatigue T-scores were defined as: no fatigue ("none"), <45; mild fatigue, 45–55; moderate fatigue, 56–65; and severe fatigue, >65.[4]

Abbreviations: Ab+, antibody positive; AChR, acetylcholine receptor; C5, component 5; CFB, change from baseline; gMG,generalized myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; mITT, modified intention-to-treat; Neuro-QoL, Quality of Life in Neurological Disorders; OLE, open-label extension; SE, standard error; TEAE, treatment-emergent adverse event.

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References: 1. Weiss MD, et al. J Neurol. 2024;271(5):2758–2767. 2. Howard JF Jr., et al. Lancet Neurol. 2023;22(5):395–406. 3. Howard JF Jr., et al. Ther Adv Neurol Dis. 2024;17:17562864241243186. 4. Cook KF, et al. Qual Life Res. 2015;24(3):575–589. 5. Cook KF, et al. Qual Life Res. 2017;26(11):2961–2971.

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