Individual item-level analyses of myasthenia gravis-specific outcomes during zilucoplan treatment in RAISE and RAISE-XT

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Introduction

- Patients with gMG experience fluctuating, fatigable muscle weakness that may affect ocular, bulbar, respiratory and proximal muscles, leading to a diverse range of symptoms that can impact health-related quality of life[1,2]
- Zilucoplan is a small (15-amino acid) potent macrocyclic peptide complement C5 inhibitor approved for the treatment of adults with anti-AChR Ab+ gMG[3,4]
- In the Phase 3 RAISE study (NCT04115293), zilucoplan showed statistically significant and clinically meaningful improvements in MG-specific outcomes in patients with anti-AChR Ab+ gMG[4]
  - These improvements were sustained over 120 weeks in the ongoing Phase 3 OLE study, RAISE-XT (NCT04225871)[5]
- **This *post hoc* analysis assessed change in individual item scores for MG-ADL, QMG and MG-QoL15r**

Methods

- In RAISE, adults with MGFA Disease Class II–IV anti-AChR Ab+ gMG were randomised to self-administer once-daily subcutaneous zilucoplan 0.3 mg/kg or placebo[4]
- Adults who completed RAISE could enter RAISE-XT to receive once-daily zilucoplan 0.3 mg/kg[5]
  - The primary outcome of RAISE-XT was incidence of TEAEs
- Analyses of MG-ADL, QMG and MG-QoL15r from the RAISE and RAISE-XT (interim data cut-off: 11 November 2023) studies included:
  - The proportion of patients showing no symptoms, improvement, and no change from baseline to Week 12 (RAISE), and from double-blind baseline to Week 120 (RAISE-XT)
  - Change from double-blind baseline (CFB) to Week 120

Results

- Overall, 200 patients enrolled in RAISE-XT; 183 received either zilucoplan 0.3 mg/kg or placebo in the double-blind studies[5]
- In RAISE, treatment with zilucoplan resulted in a greater proportion of patients showing improvement or no symptoms versus placebo at Week 12 across all MG-ADL and QMG items assessed (**Table 1**)
  - Similar results were observed for MG-QoL15r
- In RAISE-XT, the proportion of patients demonstrating improvements or no symptoms further increased and was sustained through to Week 120
- The items with the highest proportion of patients showing improvement or no symptoms at Week 120 were (**Figure 1**):
  - MG-ADL items: chewing and talking (both 93.2%); swallowing and brush hair/teeth (both 87.7%)
  - QMG items: swallowing 4 oz. water (91.4%), facial muscles (85.7%) and speech following counting from 1 to 50 (94.3%)
  - MG-QoL15r items: Trouble grooming and loss of personal independence (both 76.5%); trouble eating (88.2%) and difficulty speaking (86.8%)
- TEAEs occurred in 97.0% (n=194/200, RAISE-XT) of patients
  - The two most frequently occurring TEAEs were COVID-19 (35.5% [71/200]) and MG worsening (29.5% [59/200])

Summary and conclusions

This *post hoc* analysis assessed change in item scores for MG-ADL, QMG and MG-QoL15r using data from RAISE and RAISE-XT

Treatment with zilucoplan led to improvements or no symptoms in a greater proportion of patients across individual items in MG-specific outcomes at Week 12 versus placebo

During the extension study, the proportion of patients demonstrating these improvements or no symptoms further increased and was sustained through to Week 120

These data show that long-term treatment with zilucoplan may provide benefit across a broad range of signs and symptoms of gMG

Table 1 Across all MG-ADL and QMG items assessed, zilucoplan treatment resulted in a greater proportion of patients showing improvement or no symptoms versus placebo at Week 12 (RAISE)

Percentage of patients showing improvement or no symptoms

0 to <20%	20 to <40%	40 to <60%	60 to <80%	80 to 100%

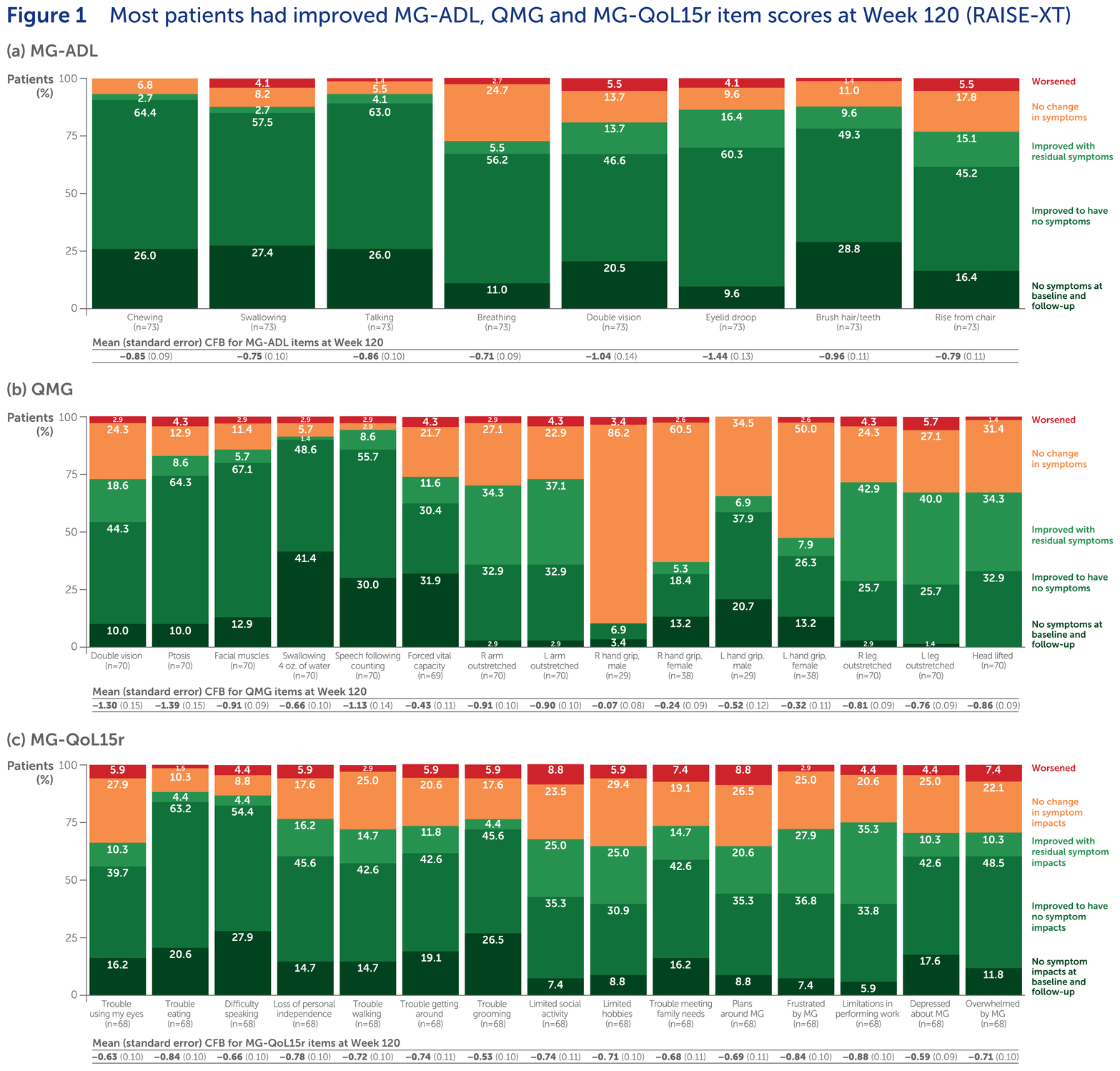
(a) MG-ADL

MG-ADL item, % (n)	Placebo N=85	Zilucoplan 0.3 mg/kg N=84
Chewing	**49.4** (42)	**71.4** (60)
Swallowing	**55.3** (47)	**71.4** (60)
Talking	**57.6** (49)	**73.8** (62)
Breathing	**38.8** (33)	**52.4** (44)
Double vision	**50.6** (43)	**66.7** (56)
Eyelid droop	**48.2** (41)	**65.5** (55)
Brush hair/teeth	**52.9** (45)	**58.3** (49)
Rise from chair	**43.5** (37)	**63.1** (53)

(b) QMG

QMG item, % (n)	Placebo N=88	Zilucoplan 0.3 mg/kg N=86
Double vision	**35.7** (30)	**51.8** (43)
Ptosis	**50.0** (42)	**65.1** (54)
Facial muscles	**58.3** (49)	**66.3** (55)
Swallowing 4 oz. water	**76.2** (64)	**83.1** (69)
Speech following counting	**72.6** (61)	**79.5** (66)
Forced vital capacity	**63.1** (53)	**74.7** (62)
R arm outstretched	**26.2** (22)	**43.4** (36)
L arm outstretched	**25.0** (21)	**41.0** (34)
R hand grip (male)	**19.0** (8)	**27.3** (9)
R hand grip (female)	**19.0** (8)	**26.0** (13)
L hand grip (male)	**40.5** (17)	**54.5** (18)
L hand grip (female)	**30.1** (13)	**46.0** (23)
R leg outstretched	**22.6** (19)	**45.8** (38)
L leg outstretched	**22.6** (19)	**47.0** (39)
Head lifted	**34.5** (29)	**54.2** (45)

Figure 1 Most patients had improved MG-ADL, QMG and MG-QoL15r item scores at Week 120 (RAISE-XT)



No patients had worsened scores for chewing (MG-ADL) and L hand grip (male; QMG). MG-ADL and QMG item severity scores range from 0 to 3 and MG-QoL15r items range from 0 to 2. Higher scores correspond to more severe impairment. A decrease from baseline indicates improvement.

Abbreviations: anti-AChR Ab+, anti-acetylcholine receptor antibody-positive; C5, component 5; CFB, change from baseline; gMG, generalised myasthenia gravis; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; MG-QoL15r, Myasthenia Gravis Quality of Life 15-item revised; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; TEAE, treatment-emergent adverse event.

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