Response rates with zilucoplan in generalized myasthenia gravis: 120-week interim analysis of RAISE-XT

MDA Conference 2025, Dallas, TX, USA; March 16–19, 2025

James F. Howard Jr.[1], Miriam Freimer[2], Angela Genge[3], Channa Hewamadduma[4,5], Angelina Maniaol[6], Renato Mantegazza[7], Kimiaki Utsugisawa[8], Tuan Vu[9], Michael D. Weiss[10], Babak Boroojerdi[11], Petra W. Duda[12], Fiona Grimson[13], Mark Vanderkelen[14], and M. Isabel Leite[15], on behalf of the RAISE-XT study team

[1]Department of Neurology, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA; [2]Department of Neurology, The Ohio State University Wexner Medical Center, Columbus, OH, USA; [3]Clinical Research Unit, The Montreal Neurological Institute, Montreal, QC, Canada; [4]Academic Neuroscience Unit, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK; [5]Sheffield Institute for Translational Neurosciences (SITraN), University of Sheffield, Sheffield, UK; [6]Department of Neurology, Oslo University Hospital, Oslo, Norway; [7]Emeritus and Past Director, Department of Neuroimmunology and Neuromuscular Diseases, Fondazione IRCCS, Istituto Nazionale Neurologico Carlo Besta, Milan, Italy; [8]Department of Neurology, Hanamaki General Hospital, Hanamaki, Japan; [9]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, FL, USA; [10]Department of Neurology, University of Washington Medical Center, Seattle, WA, USA; [11]UCB, Monheim, Germany; [12]UCB, Cambridge, MA, USA (at the time of the study); [13]UCB, Slough, UK; [14]UCB, Brussels, Belgium; [15]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK.

Introduction

- Zilucoplan is a macrocyclic peptide C5 inhibitor, indicated for the treatment of adult patients with AChR Ab+ gMG[1,2]
- In the randomized, double-blind, placebo-controlled Phase 3 RAISE study (NCT04115293), patients who received zilucoplan showed significant and clinically meaningful improvements in MG-specific outcomes[1]
- In this interim analysis of the ongoing OLE RAISE-XT study (NCT04225871), we evaluate the responder rates of patients treated with zilucoplan over a 120-week follow-up

Methods

- Adult patients who completed a qualifying double-blind, placebo-controlled study (Phase 2 NCT03315130/RAISE) could enroll into RAISE-XT. Enrolled patients self-administered once-daily subcutaneous zilucoplan 0.3 mg/kg
- The primary outcome of RAISE-XT is incidence of TEAEs
- From Week 24, 12 weeks into RAISE-XT, patients who received placebo or zilucoplan 0.3 mg/kg in the qualifying studies were assessed as one pooled group
- Mean changes from double-blind study baseline to Week 120 in MG-ADL, QMG, MGC, MG-QoL 15r, and Neuro-QoL Fatigue were assessed
- The responder rates of MG-ADL, QMG, and MSE through Week 120 were also assessed
  - MG-ADL response and QMG response was a ≥3-point and ≥5-point reduction from baseline, respectively, without rescue therapy
  - MSE response was MG-ADL score of 0 or 1 without rescue therapy
- The interim data cutoff for these analyses was November 11, 2023

Results

- A total of 200 patients enrolled in RAISE-XT (**Table 1**)
  - All patients who completed RAISE enrolled into RAISE-XT
  - At the time of data cutoff, 73.0% of patients who enrolled in RAISE-XT were still enrolled, with no discontinuations reported by the investigators as being due to lack of efficacy
- At data cutoff, median (range) exposure to zilucoplan was 2.2 (0.11–5.6) years
- Zilucoplan was generally well tolerated; most TEAEs were mild or moderate in severity (**Table 2**)
  - The most common TEAEs were COVID-19, MG worsening, and headache
- In RAISE-XT, patients who received placebo in the qualifying double-blind studies saw rapid improvement in MG-ADL 1 week after switching to zilucoplan 0.3 mg/kg (Week 13; **Figure 1**)
  - Continued improvement was observed through Week 24 in both patient groups who received placebo or zilucoplan 0.3 mg/kg in the qualifying studies. This improvement was sustained through Week 120
  - Similar improvements were observed for QMG (**Figure 2**), MGC, MG-QoL 15r, and Neuro-QoL Fatigue (data not shown)
- Overall rates of MG-ADL, QMG, and MSE responders in the pooled zilucoplan 0.3 mg/kg group were high and sustained through Week 120 (**Figures 3, 4, and 5**)

Summary and conclusions

- Patients experienced rapid improvement of gMG symptoms, as early as 1 week after switching to zilucoplan, which were sustained through Week 120
- Improvements were consistent across multiple assessments: MG-ADL, QMG, MGC, MG-QoL 15r, and Neuro-QoL Fatigue scores
- High MG-ADL, QMG, and MSE responder rates were sustained through Week 120 of zilucoplan treatment in patients with gMG
- Zilucoplan demonstrated a favorable safety profile and was well tolerated in the long term

Table 1 Baseline characteristics

	All zilucoplan (N=200)
Age, years, mean (SD)	53.3 (15.0)
Sex, male, n (%)	90 (45.0)
MGFA Disease Class, n (%)	
IIa/b	59 (29.5)
IIIa/b	129 (64.5)
IVa/b	12 (6.0)
MG-ADL score, mean (SD)	6.3 (4.3)
QMG score, mean (SD)	14.0 (5.9)
Prior thymectomy, n (%)	96 (48.0)
Prior MG crisis, n (%)	62 (31.0)
Age at disease onset, years, mean SD	43.6 (17.9)
Duration of disease,* years, mean (SD)	9.4 (9.7)
Baseline gMG-specific medication, n (%)	
Corticosteroids	124 (62.0)
Immunosuppressants	101 (50.5)
Cholinesterase inhibitors	167 (83.5)

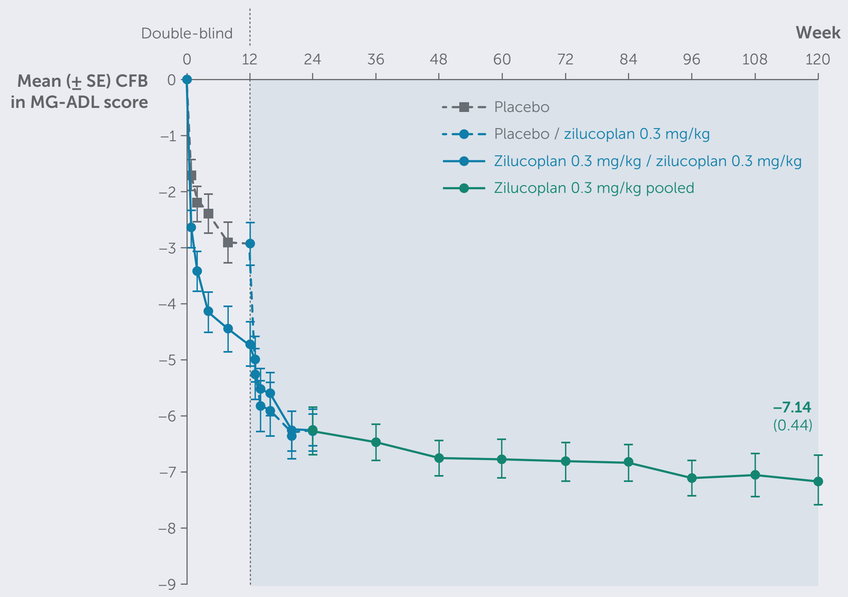
*From date of diagnosis.

Table 2 Overview of TEAEs

	All zilucoplan (N=200)
Duration of exposure, years, median (range)	2.2 (0.1–5.6)
Any TEAE, n (%)	194 (97.0)
COVID-19, n (%)	71 (35.5)
MG worsening, n (%)	59 (29.5)
Headache, n (%)	44 (22.0)
Nasopharyngitis, n (%)	42 (21.0)
Arthralgia, n (%)	36 (18.0)
Diarrhea, n (%)	34 (17.0)
URTI, n (%)	34 (17.0)
UTI, n (%)	33 (16.5)
Nausea, n (%)	32 (16.0)
Fatigue, n (%)	31 (15.5)
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 IMP,† n (%)	21 (10.5)
TEAEs leading to death,‡ n (%)	4 (2.0)

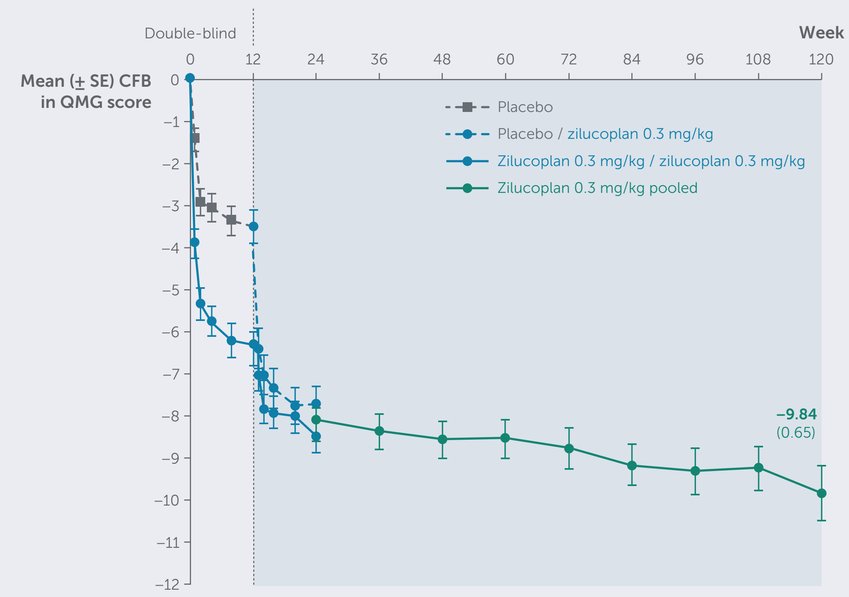
Most common TEAEs occurring in ≥15% of patients overall are reported only. *Treatment-related serious TEAEs were one (0.5%) event each of: esophagitis, injection-site infection (occurring on the right inner thigh, which is not a recommended injection site), colonic abscess and cellulitis in one patient 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).

Figure 1 Mean CFB in MG-ADL to Week 120



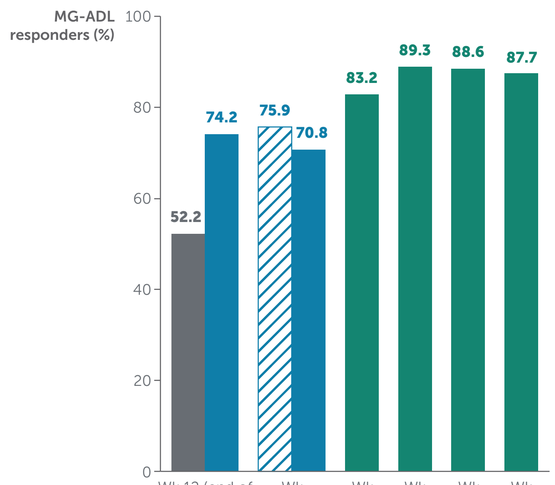
Number of patients (n)											
Placebo (n=90)	90	90	–	–	–	–	–	–	–	–	–
Zilucoplan 0.3 mg/kg (n=93)	93	93	–	–	–	–	–	–	–	–	–
Zilucoplan 0.3 mg/kg pooled (n=183)	–	–	175	170	162	156	149	148	142	123	86

Figure 2 Mean CFB in QMG to Week 120



Number of patients (n)											
Placebo (n=90)	90	89	–	–	–	–	–	–	–	–	–
Zilucoplan 0.3 mg/kg (n=93)	93	92	–	–	–	–	–	–	–	–	–
Zilucoplan 0.3 mg/kg pooled (n=183)	–	–	172	169	161	153	149	146	132	119	83

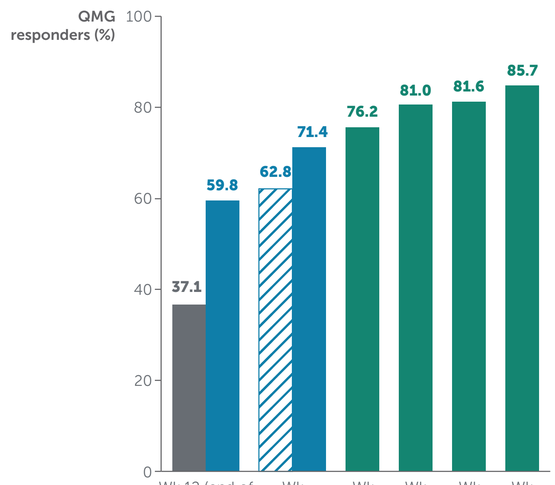
Figure 3 Mean MG-ADL responder rates to Week 120



Number of patients (n)						
Placebo / Zilucoplan 0.3 mg/kg (n=90)	90	87	–	–	–	–
Zilucoplan 0.3 mg/kg (n=93)	93	89	–	–	–	–
Zilucoplan 0.3 mg/kg pooled (n=183)	–	–	167	140	123	73

MG-ADL response was a ≥3-point reduction from baseline, without rescue therapy.

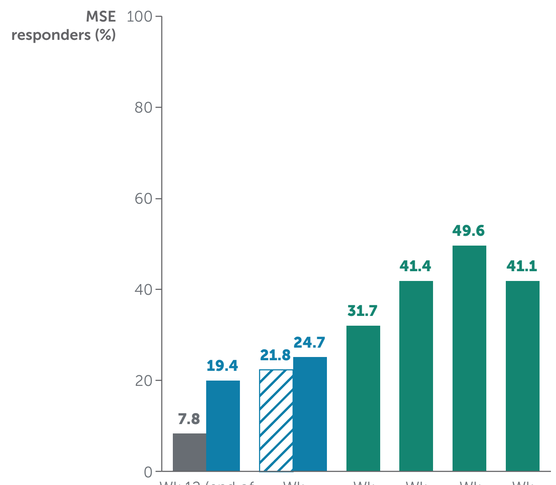
Figure 4 Mean QMG responder rates to Week 120



Number of patients (n)						
Placebo / Zilucoplan 0.3 mg/kg (n=90)	89	86	–	–	–	–
Zilucoplan 0.3 mg/kg (n=93)	92	84	–	–	–	–
Zilucoplan 0.3 mg/kg pooled (n=183)	–	–	164	137	114	70

QMG response was a ≥5-point reduction from baseline, without rescue therapy.

Figure 5 Mean MSE responder rates to Week 120



Number of patients (n)						
Placebo / Zilucoplan 0.3 mg/kg (n=90)	90	87	–	–	–	–
Zilucoplan 0.3 mg/kg (n=93)	93	89	–	–	–	–
Zilucoplan 0.3 mg/kg pooled (n=183)	–	–	167	140	123	73

MSE response was MG-ADL score of 0 or 1 without rescue therapy.

Placebo (n=90) | Placebo / zilucoplan 0.3 mg/kg (n=90) | Zilucoplan 0.3 mg/kg / zilucoplan 0.3 mg/kg (n=93) | Zilucoplan 0.3 mg/kg pooled (n=183)

Abbreviations: Ab+, autoantibody positive; AChR, acetylcholine receptor; C5, complement component 5; CFB, change from baseline; 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; MGC, Myasthenia Gravis Composite; MGFA, Myasthenia Gravis Foundation of America; MG-QoL 15r, Myasthenia Gravis Quality of Life 15-item revised; MSE, minimal symptom expression; Neuro-QoL, Quality of Life in Neurological Disorders; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection; UTI, urinary tract infection.

Acknowledgements: This study was funded by UCB. The authors acknowledge Lighthouse Medical Communications, New York, US, for editorial support in the form of writing and editorial assistance, which was funded by UCB. The authors acknowledge Aimee Jones, DPhil, and Veronica Porkess, PhD, of UCB, Slough, UK, for publication coordination. The authors thank the patients and their caregivers, in addition to the investigators and their teams who contributed to this study.

Author disclosures: James F Howard Jr. has received research support (paid to his institution) from Ad Scientiam, Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, the Centers for Disease Control and Prevention (Atlanta, GA, USA), the Myasthenia Gravis Foundation of America, the Muscular Dystrophy Association, the National Institutes of Health (including the National Institute of Neurological Disorders and Stroke and the National Institute of Arthritis and Musculoskeletal and Skin Diseases), NMD Pharma, PCORI, and UCB; he has received honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, Amgen, argenx, Biohaven Ltd, Biologix Pharma, CheckRare CME, Curie.Bio, F. Hoffmann-La Roche, Medscape CME, Merck EMD Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB, and Zai Labs; and non-financial support from Alexion AstraZeneca Rare Disease, argenx, Biohaven Ltd, Cartesian Therapeutics, Toleranzia AB, UCB, and Zai Labs. Miriam Freimer has served as a paid consultant for Alexion Pharmaceuticals, argenx, and UCB. She receives research support from Alnylam Pharmaceuticals, Avidity Biosciences, Fulcrum Therapeutics, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), the NIH, and UCB. Angela Genge has served as a paid consultant for Alexion Pharmaceuticals, ALS Pharmaceuticals, Amicus Therapeutics, Amylyx Pharmaceuticals, Anelixis Pharmaceuticals, Annexon Biosciences, Apellis Pharmaceuticals, Atlantic Research Group, Biogen, Calico, Cytokinetics, Eli Lilly, Ionis Pharmaceuticals, Medtronic, Mitsubishi Tanabe Pharma, Orion, QurAlis, Ra Pharmaceuticals (now UCB), Roche, Sanofi Genzyme (now Sanofi), UCB, and Wave Life Sciences. Channa Hewamadduma has received funding for consultancy on scientific or educational advisory boards for argenx, Biogen, Lupin, Roche, and UCB; and has received an investigator-led research grant from UCB. His study activities were supported by Sheffield NIHR BRC UK Centre grant. He is a trustee of the myasthenia gravis patient organization Myaware. Angelina Maniaol has received payment for travel, meeting attendance, consulting honoraria, or advisory board participation from argenx, Biogen, CSL Behring, Novartis, and UCB. Renato Mantegazza has received funding for travel and meeting attendance or advisory board participation from Alexion Pharmaceuticals, argenx, BioMarin, Catalyst, Sanofi, Regeneron Pharmaceuticals, and UCB. Kimiaki Utsugisawa has served as a paid consultant for argenx, Chugai Pharmaceutical, HanAll Biopharma, Janssen Pharmaceuticals (now Johnson & Johnson Innovative Medicine), Merck, Mitsubishi Tanabe Pharma, UCB, and Viela Bio (now Amgen); he has received speaker honoraria from Alexion Pharmaceuticals, argenx, the Japan Blood Products Organization, and UCB. Tuan Vu is the USF Site Principal Investigator for MG clinical trials sponsored by Alexion AstraZeneca Rare Disease, Amgen, argenx, Cartesian Therapeutics, COUR Pharmaceuticals, Dianthus Therapeutics, Immunovant, Johnson & Johnson, Regeneron Pharmaceuticals, RemeGen, and UCB, and has served as a speaker for Alexion AstraZeneca Rare Disease, Allergan/AbbVie, argenx, and CSL Behring. He performed consulting work for Alexion AstraZeneca Rare Disease, argenx, Dianthus Therapeutics, ImmunAbs, RemeGen, and UCB. Michael D. Weiss has received honoraria for serving on scientific advisory boards for Alexion Pharmaceuticals, Amylyx, argenx, Biogen, Immunovant, Mitsubishi Tanabe Pharma, and Ra Pharmaceuticals (now UCB); consulting honoraria from CSL Behring and Cytokinetics; and speaker honoraria from Soleo Health. He also serves as a special government employee for the US Food and Drug Administration. Babak Boroojerdi, Petra W. Duda, Fiona Grimson, and Mark Vanderkelen are employees and shareholders of UCB. M. Isabel Leite is funded by the NHS (Myasthenia and Related Disorders Service and National Specialised Commissioning Group for Neuromyelitis Optica, UK) and by the University of Oxford, UK. She has been awarded research grants from UK associations for patients with myasthenia and with muscular disorders (Myaware and Muscular Dystrophy UK, respectively) and the University of Oxford. She has received speaker honoraria or travel grants from Biogen, the Guthy-Jackson Charitable Foundation, Novartis, and UCB. She serves on scientific or educational advisory boards for argenx, Horizon Therapeutics (now Amgen), and UCB.

References: 1. Howard JF Jr., et al. *Lancet Neurol.* 2023;22(5):395–406. 2. Zilucoplan US PI. www.accessdata.fda.gov/drugsatfda_docs/label/2024/216834s001lbl.pdf. Last updated April 2024. Accessed January 2025.

These data were previously presented at the International Congress on Neuromuscular Disease in Perth, Australia; October 25–29, 2024 and AANEM Annual Meeting & MGFA Scientific Session in Savannah, GA; October 15–18, 2024.

Please use this QR code to download a PDF of the poster.