Compliance to daily self-administered subcutaneous zilucoplan in patients with generalized myasthenia gravis: A *post hoc* analysis of the RAISE-XT study

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Katherine Ruzhansky[1], Miriam Freimer[2], M. Isabel Leite[3], Angelina Maniaol[4], Renato Mantegazza[5], Kimiaki Utsugisawa[6], Tuan Vu[7], Michael D. Weiss[8], Babak Boroojerdi[9], Fiona Grimson[10], Natasa Savic[11], James F. Howard Jr.[12], on behalf of the RAISE-XT study team

[1]Department of Neurology, Medical University of South Carolina, Charleston, SC, USA; [2]Department of Neurology, The Ohio State University Wexner Medical Center, Columbus, OH, USA; [3]Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK; [4]Department of Neurology, Oslo University Hospital, Oslo, Norway; [5]Department of Neuroimmunology and Neuromuscular Diseases, Fondazione IRCCS, Istituto Nazionale Neurologico Carlo Besta, Milan, Italy; [6]Department of Neurology, Hanamaki General Hospital, Hanamaki, Japan; [7]Department of Neurology, University of South Florida Morsani College of Medicine, Tampa, FL, USA; [8]Department of Neurology, University of Washington Medical Center, Seattle, WA, USA; [9]UCB, Monheim, Germany; [10]UCB, Slough, UK; [11]UCB, Bulle, Switzerland; [12]Department of Neurology, The University of North Carolina at Chapel Hill, Chapel Hill, NC, USA

Introduction

- Zilucoplan is a small, 15-amino-acid macrocyclic peptide complement C5 inhibitor[1]
  - It is the first and only complement C5 inhibitor approved for the treatment of adults with AChR Ab+ gMG that is self-administered as a once-daily SC injection,[1,2] which may provide a preferable alternative to IV-infused antibody-based complement C5 inhibitors for some patients[3]
- In the randomized, double-blind, placebo-controlled Phase 3 RAISE study (NCT04115293), zilucoplan demonstrated significant and clinically meaningful improvements in MG-specific outcomes in patients with gMG, with improvements sustained in RAISE-XT (NCT04225871), an ongoing OLE study[4,5]
- Here, we evaluated compliance to self-administered, once-daily SC injections of zilucoplan among patients with gMG in RAISE-XT

Methods

- Patients completing either the qualifying double-blind Phase 2 (NCT03315130) or the Phase 3 RAISE study could enter RAISE-XT
  - In RAISE-XT, patients administered SC zilucoplan 0.3 mg/kg once daily by self-injection
- The primary safety endpoint of RAISE-XT was the incidence of TEAEs
- Compliance to zilucoplan treatment was based on patient-reported syringe use
- The percentage of medication reported to be taken was analyzed *post hoc* in the overall population and in the following subgroups:

Age (<65 years and ≥65 years)

Disease duration (<median and ≥median)

Sex (male and female)

Baseline MG-ADL score (≤9 and ≥10)

- Additional assessments included the duration of exposure to zilucoplan
- The interim data cutoff for these analyses was November 11, 2023
- All analyses were descriptive

Results

- In total, 200 patients entered RAISE-XT (**Table 1**)
- Compliance data were analyzed for 199 patients
  - One patient was excluded from the compliance analysis as they discontinued the qualifying Phase 2 study before entering RAISE-XT
- Over a median (range) exposure to zilucoplan of 2.2 (0.1–5.6) years, 95.0% (189/199) of patients reported that they had taken >95% of their medication
- Overall, patients reported taking a mean percentage of 99.2% of their medication (**Figure 1**)
  - There was no relevant impact of age, sex, disease duration or baseline MG-ADL score on compliance; mean percentage of medication taken was ≥98.4% of doses for all subgroups (**Figure 1**)

Safety

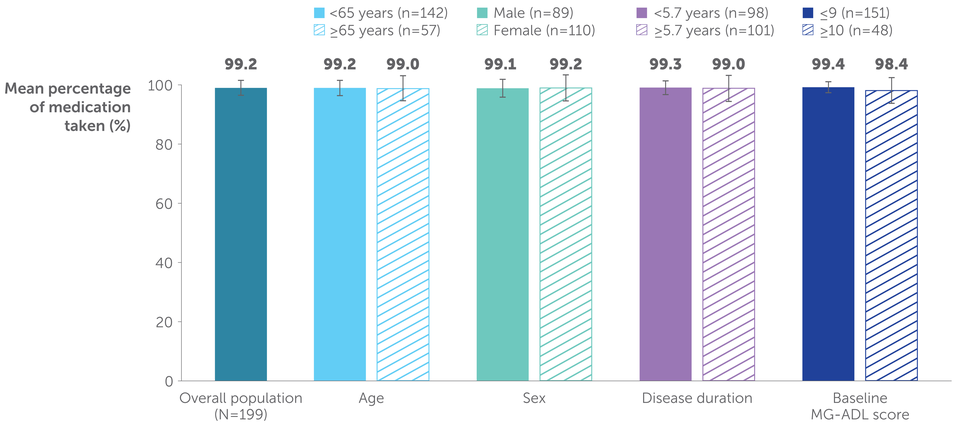
- In RAISE-XT, TEAEs occurred in 97.0% (194/200) of patients
  - The two most frequently reported TEAEs were COVID-19 (35.5% [71/200] patients) and MG worsening (29.5% [59/200] patients)
- In total, 10.5% (21/200) of patients experienced a TEAE resulting in permanent withdrawal of zilucoplan, including 2.0% (4/200) of patients who experienced TEAEs leading to death
  - No deaths were considered treatment related
- Injection site reactions were experienced by 23.5% (47/200) of patients
  - Of these, injection site pain was reported by 5.5% (11/200) of patients

Table 1 Demographics and baseline disease characteristics

		All zilucoplan (N=200)
Age, years, mean (SD)		**53.3** (15.0)
Age, years, n (%)	<65 years	**143** (71.5)
	≥65 years	**57** (28.5)
Sex, n (%)	Female	**110** (55.0)
	Male	**90** (45.0)
MGFA Disease Class, n (%)	IIa/b	**59** (29.5)
	IIIa/b	**129** (64.5)
	IVa/b	**12** (6.0)
Disease duration, years, median (range)		**5.7** (0.2–51.9)
Disease duration, n (%)	<5.7 years	**95** (47.5)
	≥5.7 years	**105** (52.5)
MG-ADL score, mean (SD)		**6.3** (4.3)
Baseline MG-ADL score, n (%)	≤9	**151** (75.5)
	≥10	**49** (24.5)
QMG score, mean (SD)		**14.0** (5.9)
Prior thymectomy, n (%)		**96** (48.0)
Prior MG crisis, n (%)		**62** (31.0)

ITT population.

Figure 1 Compliance to daily zilucoplan self-injection by subgroup



Compliance set. Compliance data were analyzed for 199 patients.

Summary and conclusions

This *post hoc* analysis investigated compliance to self-administered, once-daily SC injection of zilucoplan in the RAISE-XT OLE study

Overall, patients reported taking a mean percentage of 99.2% of their medication over a maximum exposure to zilucoplan of 5.6 years

Irrespective of age, sex, disease duration and baseline MG-ADL score, compliance to zilucoplan daily injection was high

Long-term compliance to self-administered, daily injection with zilucoplan was high, suggesting high patient satisfaction

Abbreviations: AChR Ab+, positive for autoantibodies against the acetylcholine receptor; C5, component 5; gMG, generalized myasthenia gravis; ITT, intention to treat; IV, intravenous; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; OLE, open-label extension; QMG, Quantitative Myasthenia Gravis; SC, subcutaneous; SD, standard deviation; TEAE, treatment-emergent adverse event.

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