Non-steroidal immunosuppressant therapy changes during treatment with zilucoplan in patients with generalized myasthenia gravis: 120-week follow-up of RAISE-XT

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Introduction

- The efficacy and safety of zilucoplan in patients with acetylcholine receptor autoantibody-positive gMG were assessed in two randomized, placebo-controlled, double-blind studies (Phase 2, NCT03315130; Phase 3, NCT04115293)[1,2]
- NSISTs can be an effective strategy to reduce the symptoms of gMG, although their benefits can take a long time to take effect, and physicians and patients generally aim to reduce NSIST use where possible due to safety risks associated with long-term use[3]
- Here, we evaluate NSIST changes in patients with gMG during zilucoplan treatment in RAISE-XT

Methods

- RAISE-XT (NCT04225871) is an ongoing open-label extension study that enrolled adult patients who completed either the Phase 2 or the Phase 3 RAISE study
  - In RAISE-XT, patients self-administered once-daily subcutaneous zilucoplan 0.3 mg/kg
- During both double-blind studies and the first 12 weeks of RAISE-XT, baseline NSISTs were not permitted to be changed
  - Thereafter, NSISTs could be changed at the investigator's discretion
- In this *post hoc* analysis, we assessed the proportion of patients who changed at least one NSIST relative to double-blind baseline, and the impact this had on their MG-ADL and QMG scores at Week 120 (interim data cutoff: November 11, 2023)
  - To assess reductions in dose or discontinuation of NSISTs, we examined the population who were receiving concomitant NSIST at double-blind baseline (N=89)
  - To assess increases in dose or initiation of an NSIST, we examined the overall population (N=183)

Results

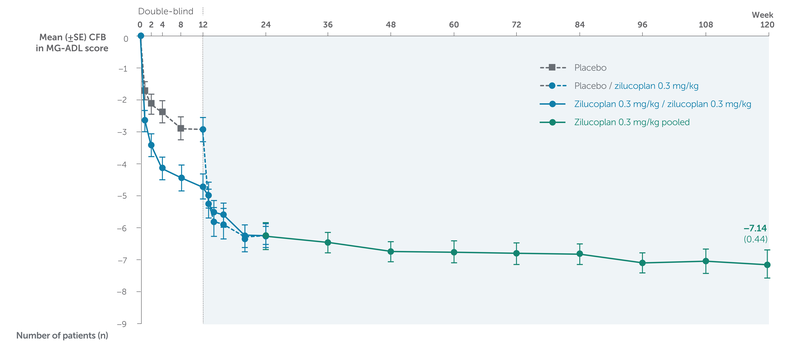
- Overall, 200 patients entered RAISE-XT, of whom 183 individuals who received 0.3 mg/kg zilucoplan were included in this analysis (**Table 1**)
  - All patients who completed RAISE opted to enroll into RAISE-XT
  - At the time of data cutoff, most patients who entered RAISE-XT (73.0%) were still enrolled, with no discontinuations reported by the investigators as being due to lack of efficacy
- Overall, improvements observed in MG-ADL score through to Week 24 were sustained through to Week 120 (**Figure 1**)
- At Week 120, approximately 30% of patients had reduced the dose of at least one of their NSISTs, including 14.9% patients who had discontinued at least one NSIST (**Figure 2a**)
- At Week 120 (N=183), only two patients (2.4%) had increased their NSIST dose, including one patient (1.2%) who had started a new NSIST – mycophenolate mofetil (**Figure 2b**)
- At Week 120, mean CFB in MG-ADL and QMG scores were similar across patients who reduced dose (**Figure 2a**), increased dose (**Figure 2b**), or had no dose changes (68.1% [n=32/47] of patients, mean [SD] CFB in MG-ADL and QMG score: –7.84 [4.22] and –10.66 [5.23], respectively)
- Over a median of 2.2 years' follow-up, TEAEs occurred in 97.0% (n=194/200) of patients (**Table 2**)

Table 1 Demographics and baseline disease characteristics

		Zilucoplan 0.3 mg/kg (N=183)
	Age, years, mean (SD)	**53.3** (15.0)
	Sex, male, n (%)	**83** (45.4)
MGFA Disease Class, n (%)	IIa/b	**54** (29.5)
	IIIa/b	**117** (63.9)
	IVa/b	**12** (6.6)
	MG-ADL score, mean (SD)	**6.4** (4.4)
	QMG score, mean (SD)	**14.1** (5.9)
	Prior thymectomy, n (%)	**88** (48.1)
	Prior MG crisis, n (%)	**59** (32.2)
	Duration of disease, years, mean (SD)	**9.4** (9.9)
	Cholinesterase inhibitor	**149** (81.4)
Baseline gMG-specific therapies, n (%)	CS	**112** (61.2)
	NSIST	**92** (50.3)

mITT population.

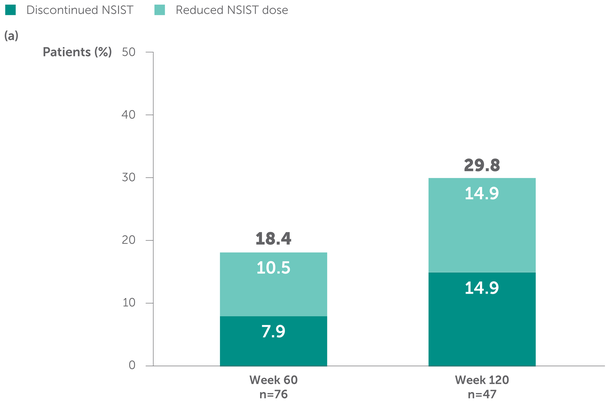
Figure 1 Mean CFB in MG-ADL score to Week 120



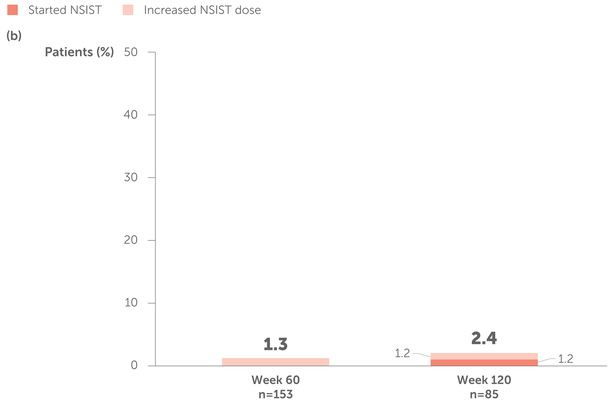
Number of patients (n)													
Placebo (n=90)	90	–	–	90	–	–	–	–	–	–	–	–	–
Zilucoplan 0.3 mg/kg (n=93)	93	–	–	93	–	–	–	–	–	–	–	–	–
Zilucoplan 0.3 mg/kg pooled (n=183)	–	–	–	–	175	170	162	156	149	148	142	123	86

mITT population.

Figure 2 Proportion of patients who had changed NSIST dose at Weeks 60 and 120 of treatment with zilucoplan 0.3 mg/kg



	Week 60 n=76	Week 120 n=47
n (%)	**14** (18.4)	**14** (29.8)
Mean (SD) CFB in MG-ADL score	**–7.64** (4.75)	**–7.57** (4.69)
Mean (SD) CFB in QMG score	**–10.86** (6.88)	**–12.14** (6.29)



	Week 60 n=153	Week 120 n=85
n (%)	**2** (1.3)	**2** (2.4)
Mean (SD) CFB in MG-ADL score	**–8.00** (5.66)	**–6.50** (4.95)
Mean (SD) CFB in QMG score	**–10.50** (2.12)	**–11.50** (0.71)

mITT population.

Summary and conclusions

This *post hoc* analysis investigated changes in concomitant NSIST among patients receiving zilucoplan in the RAISE-XT OLE study

At Week 120, nearly 30% of patients had reduced NSIST dose or discontinued NSIST, whereas only one patient had started a new NSIST

Sustained efficacy for up to 120 weeks with zilucoplan treatment allowed for discontinuation or dose reduction of concomitant NSIST, which may be beneficial for managing the safety risks associated with long-term NSIST use

For data on CS tapering in RAISE-XT, see poster MG28

For detailed safety and efficacy results of RAISE-XT, see poster MG40

Table 2 Overview of TEAEs

	All zilucoplan (N=200)
Duration of exposure, years, median (range)	**2.2** (0.11–5.6)
Any TEAE,* n (%)	**194** (97.0)
COVID-19, n (%)	**71** (35.5)
MG worsening, n (%)	**59** (29.5)
Serious TEAE,† n (%)	**81** (40.5)
Treatment-related serious TEAE, n (%)	**5** (2.5)
Treatment-related TEAE, n (%)	**73** (36.5)
TEAE resulting in permanent withdrawal from IMP,‡ n (%)	**21** (10.5)
Severe TEAE, n (%)	**72** (36.0)
TEAEs leading to deaths,§ n (%)	**4** (2.0)

Safety set. *Specific TEAEs listed are the two most commonly occurring. †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).

Abbreviations: CFB, change from baseline; COVID-19, coronavirus disease 2019; CS, corticosteroid; gMG, generalized myasthenia gravis; IMP, investigational medicinal product; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; mITT, modified intent-to-treat; NSIST, non-steroidal immunosuppressant therapy; OLE, open-label extension study; QMG, Quantitative Myasthenia Gravis; SD, standard deviation; SE, standard error; TEAE, treatment-emergent adverse event.

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