

Switching to subcutaneous zilucoplan from intravenous complement component 5 inhibitors in myasthenia gravis: Patient preference and satisfaction from a Phase 3b study

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Introduction

- Antibody-based complement C5 inhibitors for the treatment of gMG are administered by IV infusion by HCPs
- There remains a need for alternative therapeutic options for patients with gMG, especially for those who find IV administration challenging, or who are in underserved or rural populations where economic and logistic access to IV infusions is prohibitive
- Zilucoplan, a 15-amino acid macrocyclic peptide complement C5 inhibitor, is self-administered by daily SC injection, which some patients may prefer to IV complement C5 inhibitors
 - Zilucoplan is approved for the treatment of patients with anti-AChR Ab+ gMG in the United States¹
- Here, we report treatment satisfaction and patients' preference in adults with anti-AChR Ab+ gMG after switching to zilucoplan from IV complement C5 inhibitors

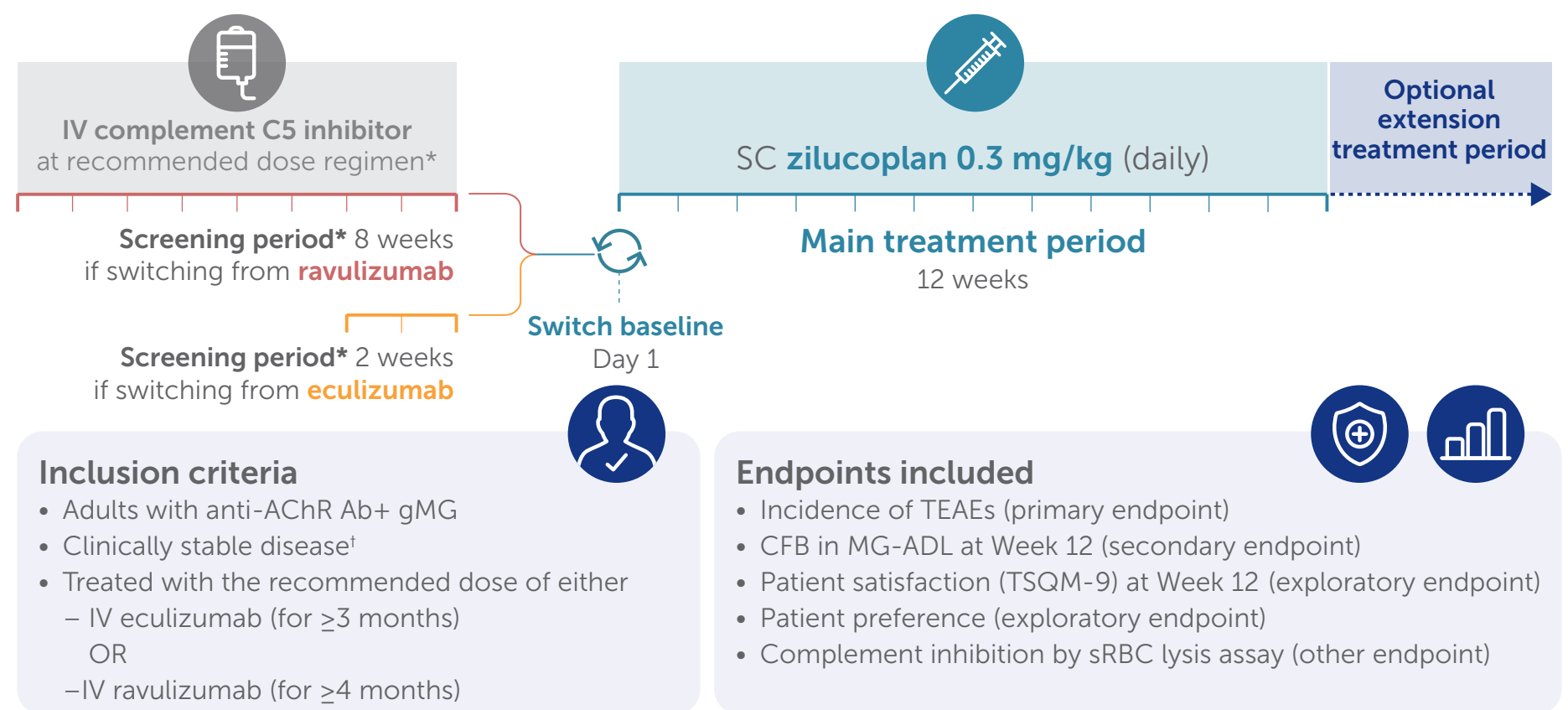
Methods

- MG0017 (NCT05514873) was a Phase 3b, open-label, single arm study with a 12-week main treatment period and an optional extension period of daily SC zilucoplan 0.3 mg/kg in patients who were willing to switch from an antibody-based, IV, complement C5 inhibitor (eculizumab or ravulizumab) (**Figure 1**)
- The primary safety endpoint was incidence of TEAEs
- Secondary efficacy endpoints included change from baseline in MG-ADL total score to Week 12
- Other patient-reported outcomes included treatment satisfaction (measured using the TSQM-9; scored from 0 to 100) and patient preference for IV or SC complement C5 inhibitors, assessed at Week 12 (both exploratory endpoints)

Results

- Patient demographics and baseline disease characteristics are presented in **Table 1**
- 26 patients enrolled in MG0017 and received zilucoplan

Figure 1 Study design



*The last dose of IV complement C5 inhibitor administration could not occur beyond the screening visit (Day -14 ±3 days for patients receiving eculizumab or Day -56 ±3 days for patients receiving ravulizumab), to ensure approximately 2 weeks' or 8 weeks' interval, respectively, before the first SC zilucoplan administration. ¹Per investigator's judgment, with <2-point change in MG-ADL score at baseline compared with screening visit. Complement inhibition at baseline and Week 12 was assessed using a sheep red blood cell lysis assay

Table 1 Demographics and baseline disease characteristics

	Zilucoplan 0.3 mg/kg (N=26)
Female, n (%)	13 (50.0)
Age at initial diagnosis, years, mean (min, max)	51.7 (7, 73)
Duration of disease from diagnosis, years, mean (min, max)	8.4 (0.8, 31.0)
MG-ADL score at baseline, mean (min, max)	4.5 (0, 13)
QMG score at baseline, mean (min, max)	10.1 (2, 23)
Baseline gMG therapy, n (%)	
Cholinesterase inhibitors	19 (73.1)
Corticosteroids	12 (46.2)
Azathioprine, mycophenolate mofetil	13 (50.0)
Prior IV complement C5 inhibitor treatment before switching to ZLP, n (%)	
Ecuzumab	16 (61.5)
Ravulizumab	10 (38.5)

Table 2 Overview of TEAEs

	Zilucoplan 0.3 mg/kg (N=26)
Any TEAE,* n (%)	19 (73.1)
Any increase	3 (11.5)
Diarrhea	2 (7.7)
Injection-site pain	2 (7.7)
Lipase increase	2 (7.7)
Nausea	2 (7.7)
Pain	2 (7.7)
Sinusitis	2 (7.7)
Serious TEAE, n (%)	1 (3.8) [†]
Treatment-related TEAE, n (%)	6 (23.1)
TEAE resulting in permanent withdrawal from zilucoplan, n (%)	2 (7.7) [†]
Severe TEAE, n (%)	3 (11.5)

Safety set. Data are presented as n (%), where n=number of patients with TEAE. *Specific TEAEs listed are those occurring in ≥5% of patients. [†]Diverticulitis and pyelonephritis (both in the same patient), considered to be unrelated to zilucoplan by the investigator. [‡]Injection-site pain, injection-site discoloration, pain, anxiety and fatigue (n=1) and reactivation of Epstein-Barr virus (n=1); the TEAEs of injection-site pain and discoloration that resulted in permanent withdrawal were deemed treatment-related by the investigator.

Abbreviations: Ab+, antibody positive; AChR, acetylcholine receptor; BL, baseline; C5, component 5; CFB, change from baseline; CI, confidence interval; gMG, generalized myasthenia gravis; HCP, healthcare professional; IV, intravenous; LS, least squares; MG, myasthenia gravis; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis; SC, subcutaneous; sRBC, sheep red blood cell; TEAE, treatment-emergent adverse event; TSQM-9, 9-item Treatment Satisfaction Questionnaire for Medication; ZLP, zilucoplan.

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- 16 patients switched from eculizumab and 10 switched from ravulizumab
- Patients wanted to switch for a variety of reasons, including logistical challenges, lengthy infusion times and challenges with venous access (**Figure 2**)
- 23 patients completed the main treatment period and three had discontinued (two due to TEAEs [Table 2], the third due to non-compliance with study protocol)
- TEAEs were mostly mild in severity (**Table 2**)
- In the total population, there was a nominally significant improvement in MG-ADL score (**Figure 3**)
 - Clinically meaningful and nominally significant improvements were observed in MG-ADL scores in patients who switched from ravulizumab (**Figure 3**)
- At Week 12, MG symptoms were improved or unchanged in approximately 75% of patients (data not shown)²
- Over three-quarters of the study population preferred SC treatment
 - Of those who preferred SC treatment, about half were from the prior eculizumab subgroup and half from the prior ravulizumab subgroup (**Figure 4**)
- Mean TSQM-9 Global Satisfaction, Effectiveness and Convenience subscores all showed clinically meaningful increases from baseline at Week 12, except the Effectiveness subscore for prior eculizumab subgroup (**Figure 5**)
- In patients with both baseline and Week 12 TSQM-9 scores available, the mean percentage increases in score from baseline in the **prior eculizumab**, **prior ravulizumab** and the **total population** were
 - Global Satisfaction: **41.6% (n=13)**, **53.9% (n=10)** and **47.0% (n=23)**
 - Effectiveness: **15.3% (n=12)**, **49.6% (n=10)** and **30.9% (n=22)**
 - Convenience: **60.3% (n=13)**, **32.4% (n=10)** and **48.2% (n=23)**
- Complement inhibition increased from 93.5% at baseline to 98.5% at Week 12 with zilucoplan treatment in the total population
 - The increase in complement inhibition was particularly pronounced in the subgroup of patients who switched from ravulizumab (87.3% to 98.9%)

Figure 2 Reasons patients wanted to switch from IV complement C5 inhibitors

	Patients switching from eculizumab n=16	Patients switching from ravulizumab n=10	Total N=26
Logistical challenges, including travel and time spent at a hospital	7 (43.8)	1 (10.0)	8 (30.8)
Challenges with venous access	2 (12.5)	2 (20.0)	4 (15.4)
Lengthy intravenous infusion	3 (18.8)	0	3 (11.5)
Other	4 (25.0)	7 (70.0)	11 (42.3)

“ Eculizumab, other reasons for switching (n=4) ”

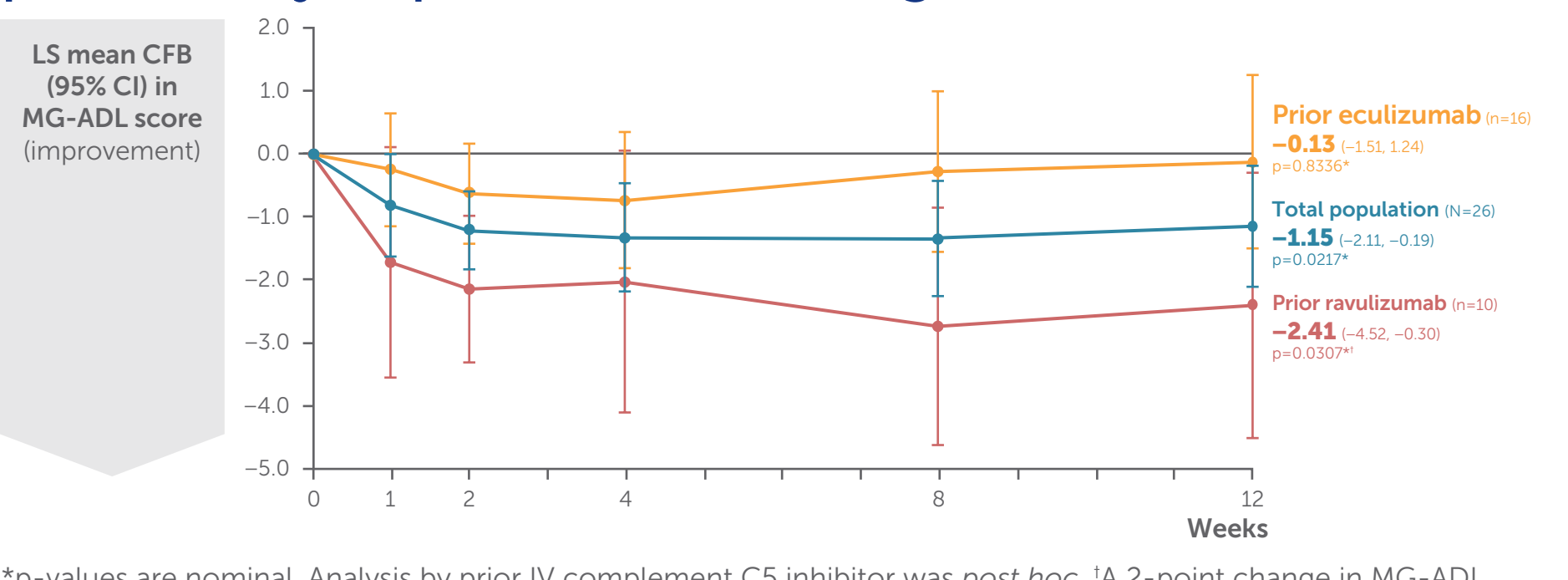
Wearing off
Loss of hair
Sick after infusions and would like to try a different treatment
Happy with current treatment, but would like to participate in a research study to help science

“ Ravulizumab, other reasons for switching (n=7) ”

Wearing off, less effective
Experiencing symptoms about 1.5 weeks prior to next infusion
Lack of efficacy
Would like to try a new treatment to see if this would improve MG symptoms
Would like to try an alternative treatment
Recommended by doctor, hates poking
Easier administration

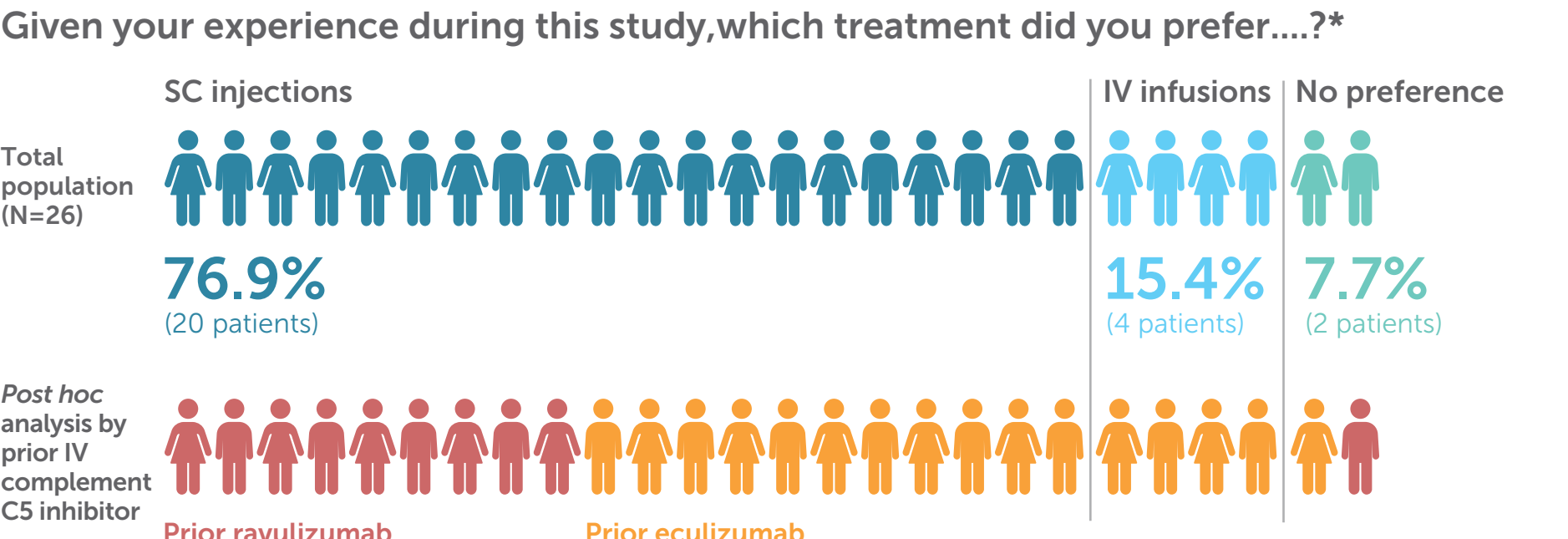
Data are presented as n (%). 'Other' was an option for investigators to write free text. Answers here are written verbatim.

Figure 3 MG-ADL score improved to Week 12, particularly in patients switching from ravulizumab



*p-values are nominal. Analysis by prior IV complement C5 inhibitor was post hoc. [†]A 2-point change in MG-ADL score is considered clinically meaningful.³

Figure 4 Zilucoplan SC injections were preferred by the majority of patients



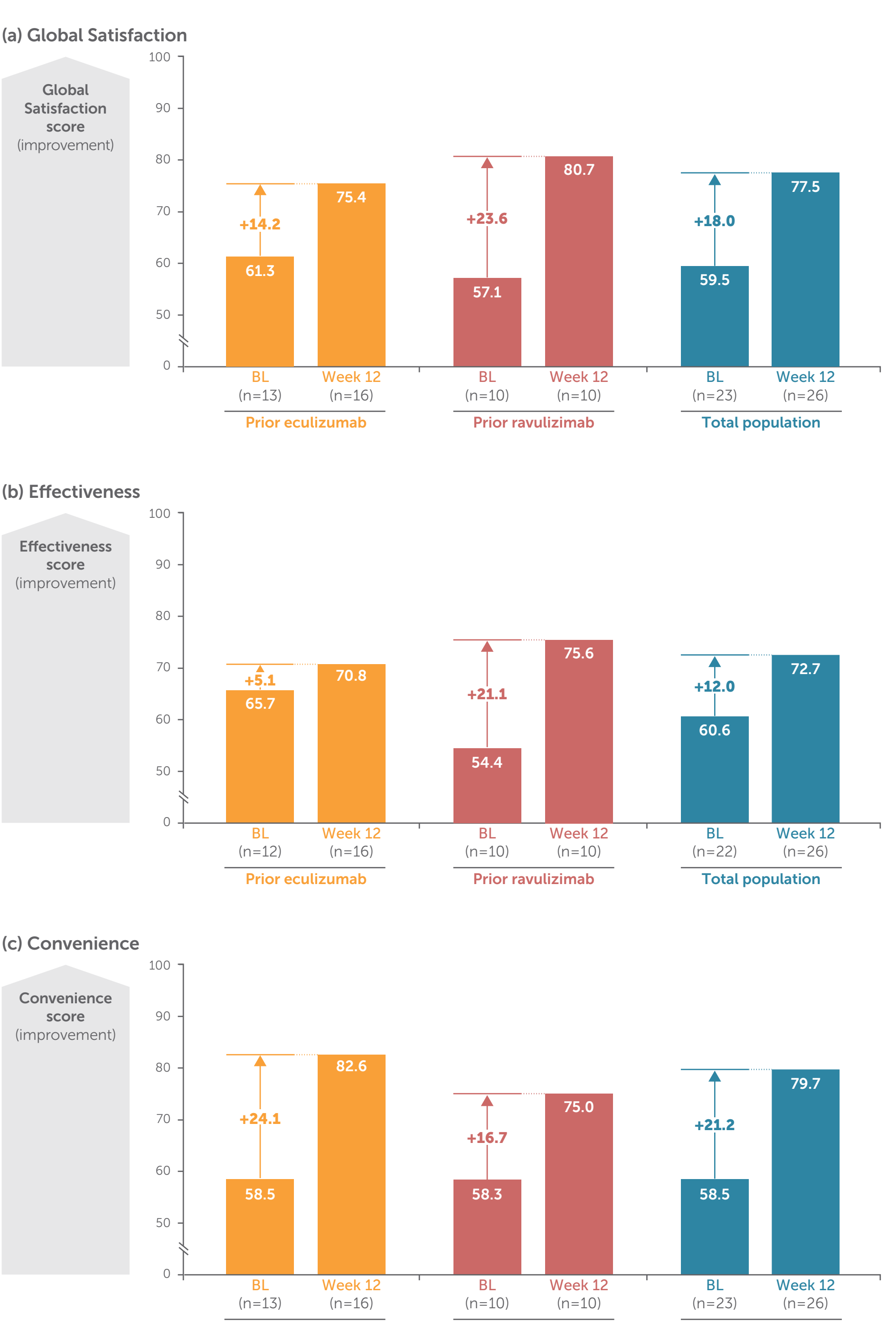
*The verbatim question asked at the end of the study was "Think about your experience of the subcutaneous treatment you received during the clinical trial compared with your previous intravenous treatment. All things considered, which treatment did you prefer? (please select one answer): Intravenous infusion/subcutaneous injection/ no preference."

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Summary and conclusions

- Switching from IV complement C5 inhibitors (eculizumab or ravulizumab) to SC zilucoplan was well tolerated
- Following a treatment switch from IV eculizumab or ravulizumab to zilucoplan, MG-ADL total score improved, and this was clinically meaningful for patients switching from ravulizumab
- Overall treatment satisfaction increased after switching from IV complement C5 inhibitors to SC zilucoplan
 - In the Effectiveness subdomain of TSQM-9, patients switching from ravulizumab showed the greatest improvement
 - In the Convenience subdomain, patients switching from eculizumab showed the greatest improvement
- More than three-quarters of patients preferred SC to IV treatment
- For HCPs and their patients who are considering self-administered daily SC injections, switching to zilucoplan from IV complement C5 inhibitors is feasible

Figure 5 Clinically meaningful improvements in TSQM-9 scores⁴ for a) Global Satisfaction, b) Effectiveness and c) Convenience were observed at Week 12



The Global Satisfaction, Effectiveness and Convenience domains and scoring in TSQM-9 are the same as those used in TSQM v1.4, therefore use of the published meaningful change thresholds for TSQM v1.4 is considered appropriate here.⁴ The published meaningful change thresholds for Global Satisfaction, Effectiveness and Convenience are 12.24, 9.99 and 10.81, respectively.⁴ Numerical discrepancies in this figure are due to rounding of data.

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