# Safety, efficacy, and patient preference for subcutaneous zilucoplan in myasthenia gravis after switching from intravenous complement component 5 inhibitors: An interim analysis of a Phase 3b study

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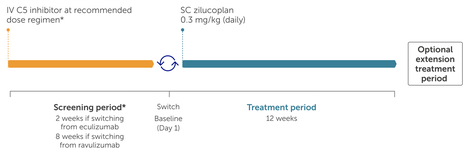
## Introduction

- Several C5 inhibitors for the treatment of gMG are administered intravenously by HCPs
- As such, there remains a need for additional therapeutic options, especially for patients who have difficulties with IV administration, or who are in underserved or rural populations where economic and logistic access to IV infusions is challenging[1]
- The peptide C5 inhibitor zilucoplan is intended for self-administration by daily SC injection, and there are data to suggest that some patients with chronic conditions may prefer this method of administration compared with administration via an IV route[1]
- The efficacy and safety of zilucoplan have been demonstrated in RAISE, a pivotal, 12-week, Phase 3, randomized, placebo-controlled study in patients with AChR Ab+ gMG[2]
  - To date, its ongoing open-label extension (RAISE-XT) has demonstrated a favorable long-term safety profile and sustained efficacy up to 96 weeks[3]
- MG0017 (NCT05514873) is an ongoing study which aims to evaluate safety, efficacy, patient satisfaction and preference after switching from IV C5 inhibitors to SC zilucoplan in adults with AChR Ab+ gMG

## Methods

- This is an interim analysis of MG0017, a Phase 3b, multicenter, 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 following a switch from an IV C5 inhibitor (**Figure 1**)
- Adults with AChR Ab+ gMG were eligible if they had clinically stable disease per the investigator's judgment, with no more than a 2-point change in MG-ADL score at baseline compared with the screening visit
  - Patients were also required to have been treated with the recommended dose regimen of IV eculizumab (for at least 3 months) or ravulizumab (for at least 4 months) and be willing to switch to zilucoplan
- The primary safety endpoint was incidence of TEAEs
- Secondary efficacy endpoints included change in MG-ADL and QMG scores from baseline to Week 12
- Patient-reported outcomes included treatment satisfaction (TSQM-9; scored from 0–100) and patient preference

**Figure 1** Study design




*The last regularly scheduled IV C5 inhibitor administration cannot occur beyond Day –14 (2 weeks) for patients receiving eculizumab or Day –56 (8 weeks) for patients receiving ravulizumab.

## Results

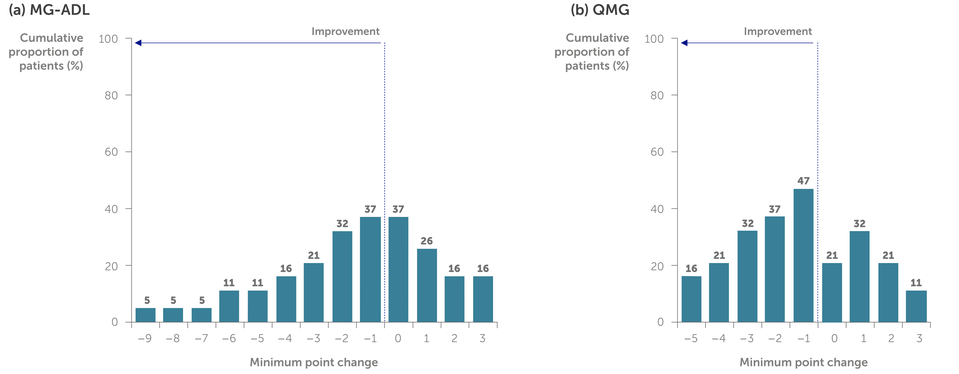
- At data cutoff (February 16, 2024), 26 patients had received zilucoplan and 18 had completed the 12-week main treatment period; three patients had discontinued
  - The safety analysis set consisted of 26 patients (**Table 1**)
  - The efficacy analysis set included the 21 patients who completed Week 12 or discontinued; of these, 15 (71.4%) were treated with eculizumab and six (28.6%) with ravulizumab, before switching to zilucoplan
- Several different reasons were cited for why patients wanted to switch from their current C5 inhibitor, including challenges with venous access, physical and logistic issues with IV infusions, and perceptions of diminishing efficacy
- Two patients discontinued due to TEAEs (fatigue and injection-site reactions in one patient, and Epstein-Barr virus infection in another patient; **Table 2**)
- At Week 12, mean (95% CI) change from baseline in MG-ADL and QMG scores was –0.84 (–2.31, 0.62) and –0.89 (–2.18, 0.39), respectively
  - MG-ADL scores were improved or unchanged in 74% of patients, and QMG scores were improved or unchanged in 68% of patients (**Figure 2**)
  - As of the cutoff date, no patients had received rescue therapy during the main treatment period
- At Week 12, TSQM-9 global satisfaction subscore had improved from baseline after switching to zilucoplan (**Figure 3a**)
- 80% (16/20) of patients preferred SC zilucoplan compared with their previous IV C5 inhibitor (**Figure 3b**)

**Table 1** Baseline patient characteristics

| | Zilucoplan 0.3 mg/kg (N=26) |
|---|---|
| **Age, years, mean (SD)** | **59.9** (15.9) |
| **Female, n (%)** | **13** (50.0) |
| **MGFA Disease Class*, n (%)** | |
| II | **7** (26.9) |
| III | **12** (46.2) |
| IV | **2** (7.7) |
| V | **4** (15.4) |
| Missing | **1** (3.8) |
| **MG-ADL score, mean (SD)** | **4.5** (4.1) |
| **QMG score, mean (SD)** | **10.1** (5.0) |
| **Age at onset, years, mean (SD)** | **51.2** (18.8) |
| **Duration of disease, years, mean (SD)** | **8.51** (7.83) |
| **Symptoms at onset, n (%)** | |
| Ocular | **10** (38.5) |
| Generalized | **15** (57.7) |
| Missing | **1** (3.8) |
| **Baseline gMG therapy, n (%)** | |
| Cholinesterase inhibitors | **17** (65.4) |
| Corticosteroids | **11** (42.3) |
| Azathioprine, mycophenolate mofetil | **12** (46.2) |
| **gMG treatment before switching to zilucoplan, n (%)** | |
| Eculizumab | **16** (61.5) |
| Ravulizumab | **10** (38.5) |

*At maximum intensity since gMG diagnosis.

**Figure 2** Minimum point change in (a) MG-ADL and (b) QMG scores from baseline to Week 12 (n=19)*



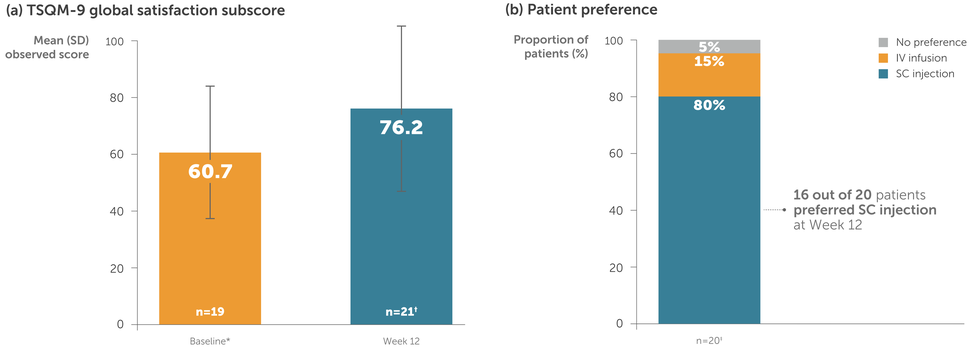

*18 patients completed Week 12; data for one patient who discontinued after Week 8 are included in the Week 12 analysis visit (next scheduled assessment following discontinuation).

**Table 2** Overview of TEAEs during the main treatment period

| | Zilucoplan 0.3 mg/kg (N=26) |
|---|---|
| **Any TEAE, n (%)** | **15** (57.7) |
| **Serious TEAE, n (%)** | **0** |
| **Treatment-related TEAEs, n (%)** | **5** (19.2) |
| **Severe TEAEs, n (%)** | **2** (7.7) |
| Lipase increase* | **1** (3.8) |
| Injection-site pain | **1**† (3.8) |
| Pain† | **1**† (3.8) |
| **TEAE resulting in permanent withdrawal from zilucoplan, n (%)** | **2** (7.7) |
| Injection-site pain | **1**† (3.8) |
| Injection-site discoloration | **1**† (3.8) |
| Fatigue | **1**† (3.8) |
| Epstein-Barr virus infection | **1** (3.8) |
| **TEAEs leading to death, n (%)** | **0** |

Data are presented as n (%), where n=number of patients with TEAE. Preferred terms are reported according to MedDRA 26.1.
*Lipase increase was considered treatment-related and was resolved within 18 days with no action taken with zilucoplan. †Occurred in the same patient. †Reported as worsening pain. Not treatment-related, resolved in 1 day with no action taken with zilucoplan.

**Figure 3** (a) Patient satisfaction with treatment at baseline and Week 12, and (b) patient preference at Week 12

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## Summary and conclusions

This ongoing study is evaluating safety, clinical outcomes, and patient preferences following a treatment switch from IV eculizumab or ravulizumab to SC zilucoplan

In this interim analysis, zilucoplan demonstrated a favorable safety profile and did not raise any safety concerns

MG symptoms remained stable or improved in the majority of patients after switching from an IV C5 inhibitor to SC zilucoplan

Patients reported higher treatment satisfaction and 80% of patients had a preference for SC treatment after a switch from IV treatment

These interim data provide information that may be valuable for physicians and patients evaluating the potential use of a C5 inhibitor for the treatment of gMG; final data will be presented at future congresses

**Abbreviations:** AChR Ab+, positive for autoantibodies against the acetylcholine receptor; C5, complement component 5; CI, confidence interval; gMG, generalized myasthenia gravis; HCP, healthcare professional; IV, intravenous; MedDRA, Medical Dictionary for Regulatory Activities; MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America; QMG, Quantitative Myasthenia Gravis; SC, subcutaneous; SD, standard deviation; TEAE, treatment-emergent adverse event; TSQM-9, 9-item Treatment Satisfaction Questionnaire for Medication.

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**References:** 1. Overton PM, et al. Patient-Prefer Adherence. 2021;15:811–834 2. Howard JF, Jr., et al. Lancet Neurol. 2023;22(5):395–406. 3. Howard JF, Jr., et al. Long-term safety and efficacy of zilucoplan in myasthenia gravis: additional interim analyses of RAISE-XT [oral]. AAN 2024. Presentation S15.002.

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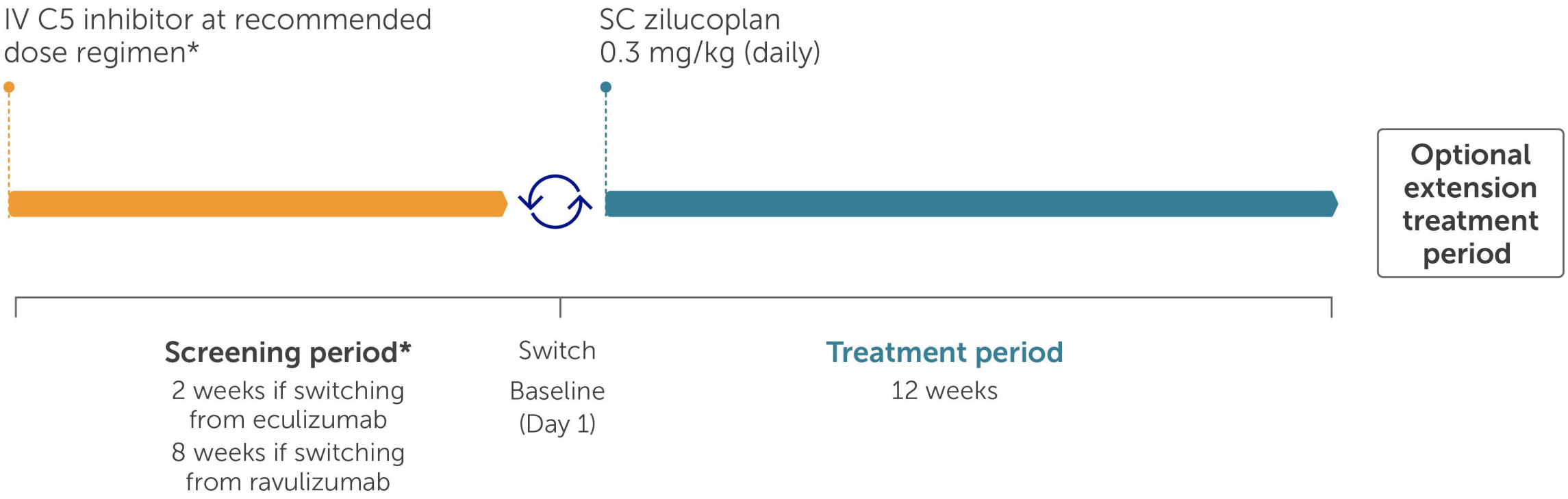


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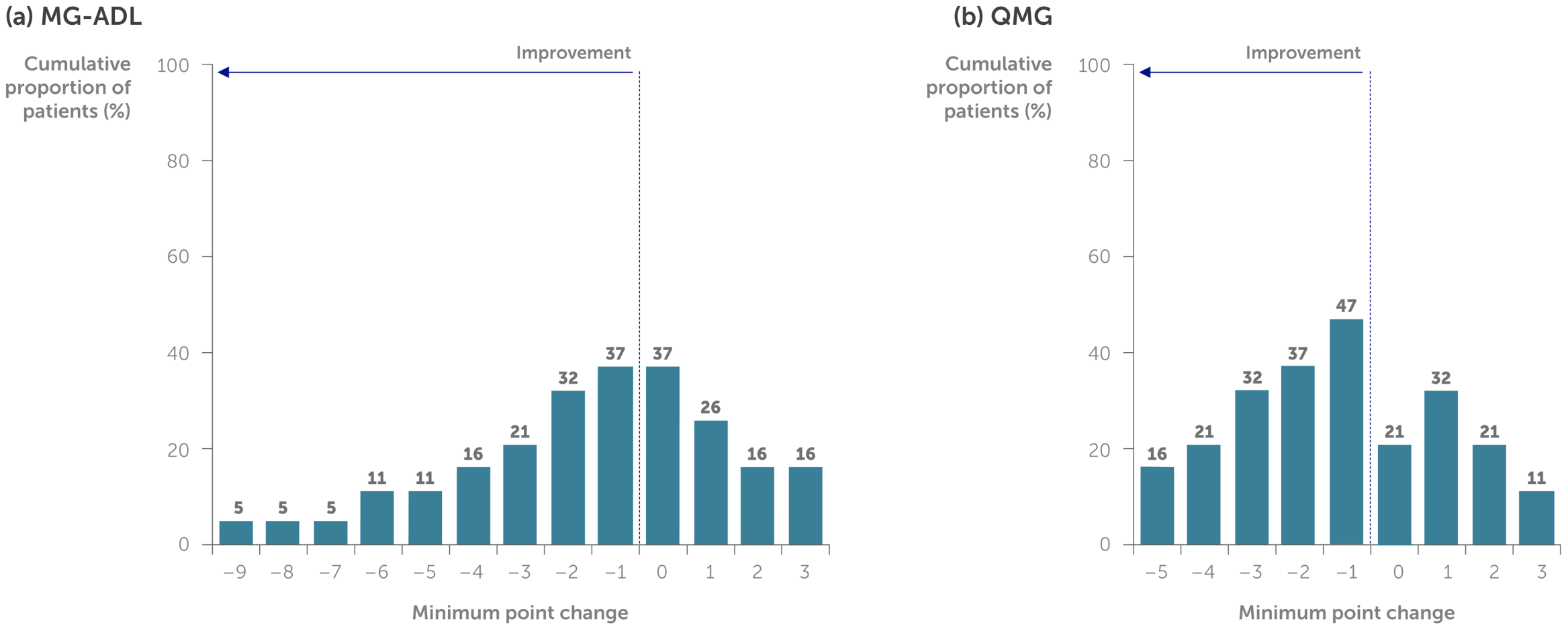


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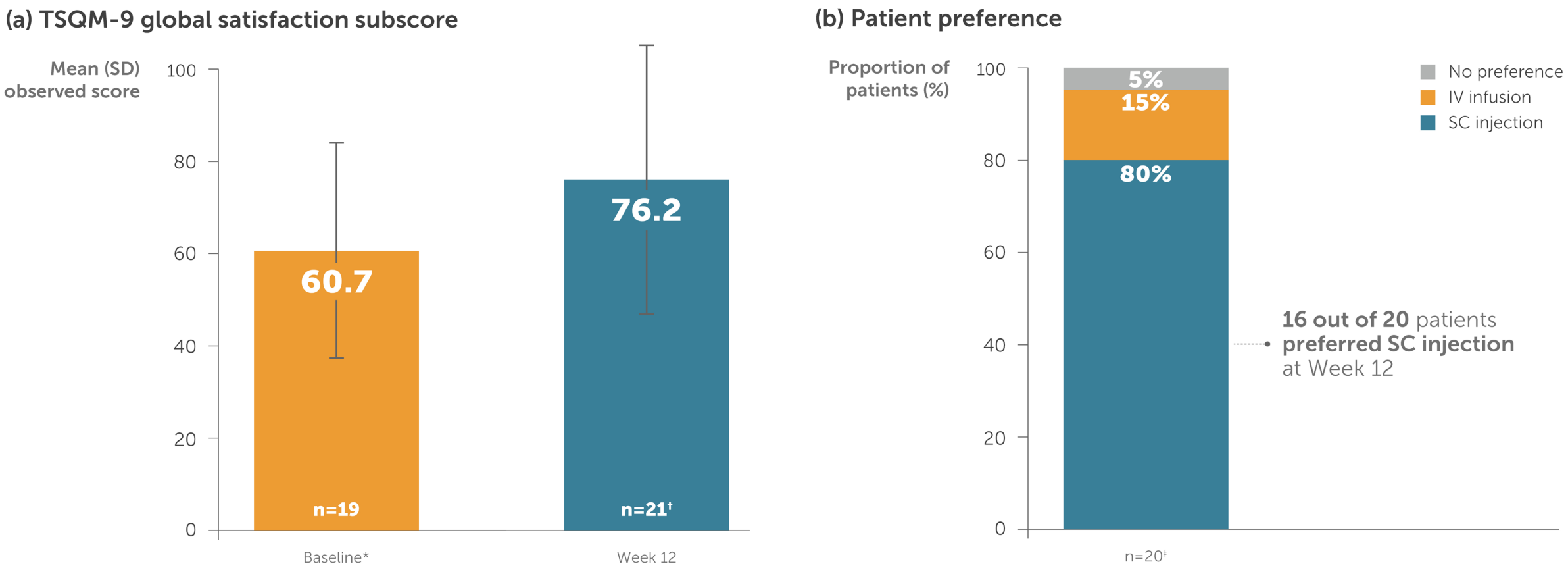


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