Real-World Safety and Efficacy of 156-195 U OnabotulinumtoxinA in Participants with Chronic Migraine: Results from the REPOSE Study

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Introduction

Background

- Chronic migraine (CM) is a neurological disease defined as ≥15 headache days for >3 months, with at least 8 headaches/month fulfilling criteria for migraine with or without aura[1]
- The safety and efficacy of 155-195 units (U) of onabotulinumtoxinA for the preventive treatment of CM in adults was established in the phase 3 PREEMPT clinical trials[2] and it is the licensed dosage in Canada and Europe
- Real-world evidence of the use of 156-195 U in clinical practice was needed

Objective

- To analyze the real-world safety and efficacy of 156-195 U onabotulinumtoxinA in participants with CM from the REPOSE study

Study Design

- REPOSE (NCT01686581) was a 2-year, prospective, non-interventional, observational, open-label study conducted at 78 sites across 7 European countries
- Adult (≥18 years of age) men and women prescribed onabotulinumtoxinA for CM received treatment every ~12 weeks according to their physician's discretion and guided by the Summary of Product Characteristics (SPC) and PREEMPT injection paradigm[3]
- For this analysis, participants who received ≥1 dose of onabotulinumtoxinA were stratified by treatment dose at ≥4 treatment visits into 2 groups:
  - 156-195 U dose
  - 155 U dose

Outcomes Measures

- Outcomes analyzed between dose groups across administration follow-up visits:
  - Change from baseline in participant-estimated mean frequency of headache days in the last month
  - Change from baseline in Migraine-Specific Quality of Life (MSQ) domain scores (role function restrictive, role function preventive, emotional function)
- Summary statistics including mean, standard deviation (SD), and min/max were calculated for continuous variables; frequencies and percentages in each category provided for categorical variables

Safety

- Treatment-emergent adverse events (TEAEs) were determined at each administration visit

Participant Characteristics

- 641 participants were enrolled in the REPOSE study; 633 received ≥1 onabotulinumtoxinA treatment
  - At ≥4 treatment visits, 77 participants received 156-195 U and 218 received 155 U
- Participant baseline characteristics were similar between the 2 dosage groups and consistent with the typically reported CM population (**Table 1**)
- In REPOSE, the dose and number of onabotulinumtoxinA injection sites used were similar to licensed recommendations, with the majority of sessions ranging from 155-195 U and a median of 31 injection sites at all follow-up visits

Table 1. Participant Baseline Demographic and Clinical Characteristics

	156-195U Dose[a] (N=77)[b]	155U Dose[a] (N=218)[b]
Age (years), mean (SD)	45.5 (11.3)	45.1 (11.9)
Female, n (%)	68 (88)	188 (86)
MSQ domain score, mean (SD)		
Role Function Restrictive	35.3 (16.1)	34.3 (17.6)
Role Function Preventive	50.4 (18.8)	47.0 (22.3)
Emotional Function	41.2 (24.2)	37.9 (24.9)
Monthly headache days, mean (SD)	21.5 (5.6)	21.5 (5.5)

Abbreviations: MSQ, Migraine-specific Quality of Life Questionnaire; SD, standard deviation; U, units.
[a]Participants treated with onabotulinumtoxinA dose on at least 4 administration follow-up visits.
[b]8 participants met criteria for inclusion in both dosage groups.

Results

Safety

- Treatment-emergent adverse events (TEAEs) were reported in 10/77 (13.0%) participants in the 156-195 U group and 51/218 (23.4%) participants in the 155 U group (**Table 2**)
- Serious AEs were reported by 1/77 (1.3%) in the 156-195 U group and 3/218 (1.4%) participants in the 155 U group
- No new safety signals were identified

Table 2. Adverse Drug Reactions

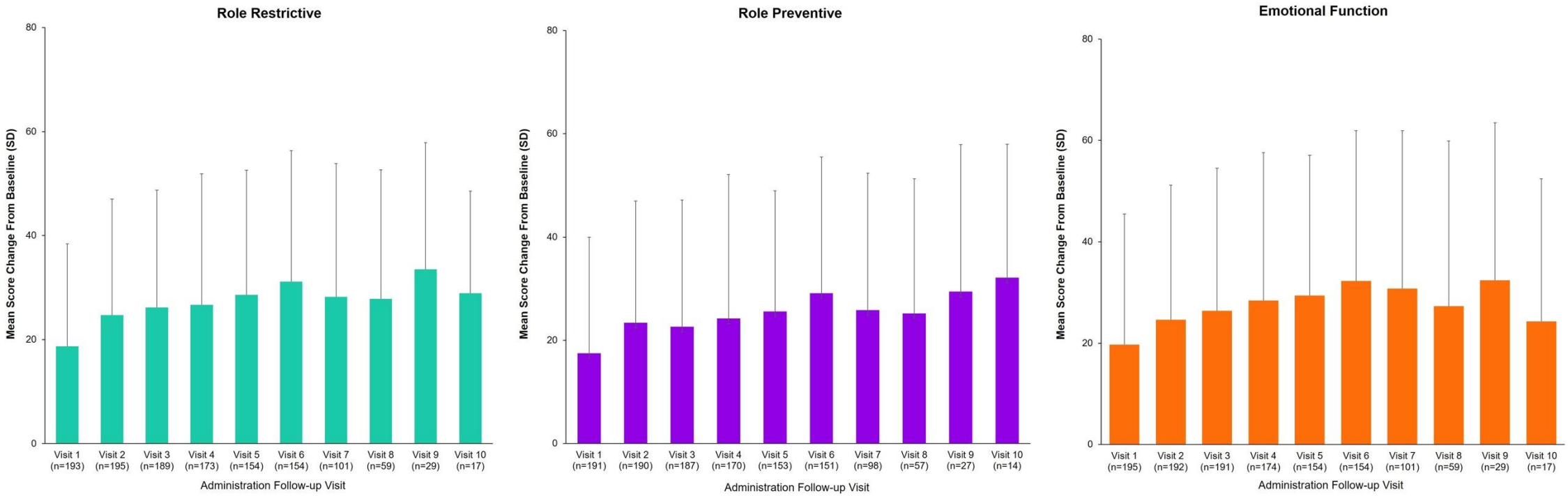
	156-195U Dose[a] (N=77)[b]	155U Dose[a] (N=218)[b]
Any TEAE, n (%)	10 (13.0)	51 (23.4)
Mild	5 (6.5)	24 (11.0)
Moderate	3 (3.9)	18 (8.3)
Severe	2 (2.6)	9 (4.1)
Serious AE, n (%)	1 (1.3)	3 (1.4)

Abbreviations: AE, adverse event; TEAE, treatment-emergent adverse event; U, units.
[a]Participants treated with onabotulinumtoxinA dose on at least 4 administration follow-up visits.
[b]8 participants met criteria for inclusion in both dosage groups.

Migraine-Specific Quality of Life (MSQ)

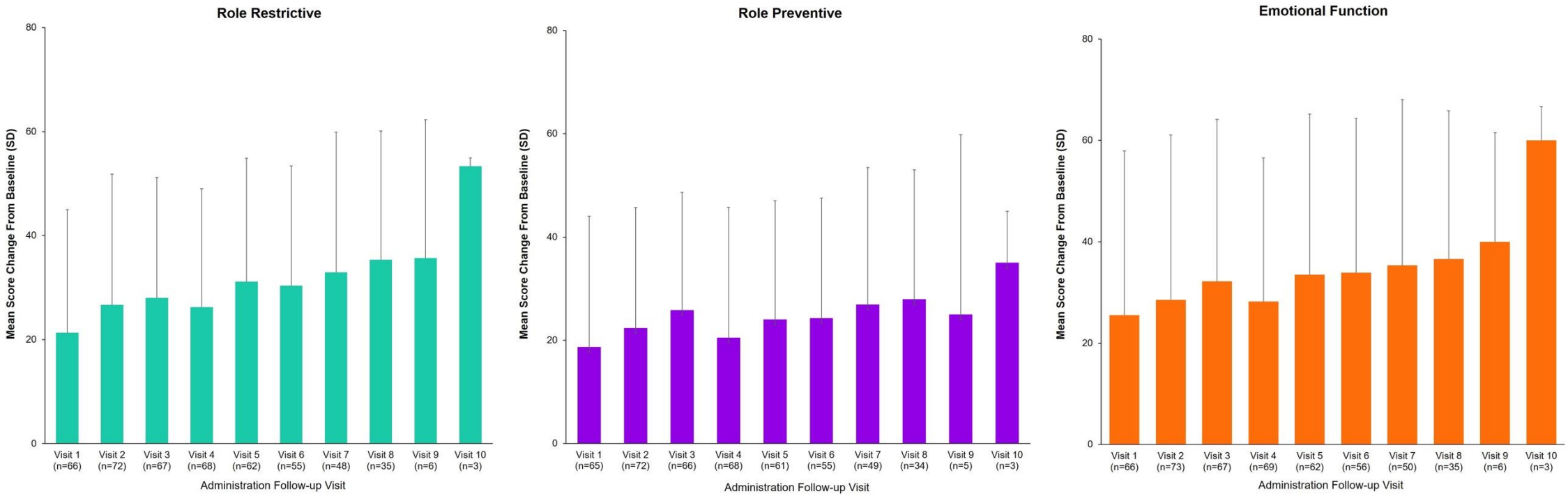
- The MSQ is a 14-item questionnaire designed to measure how migraine affects and/or limits daily functioning across 3 domains, with higher scores indicating better quality of life[4]
  - Role restrictive: 7 items assess how migraine limits one's daily social and work-related activities
  - Role preventive: 4 items assess how migraine prevents these activities
  - Emotional function: 3 items assess the emotions associated with migraine
- In REPOSE, treatment with both 155 U (**Figure 1a**) and 156-195 U (**Figure 1b**) onabotulinumtoxinA resulted in increased MSQ scores across all role function domains at all study visits compared with baseline

Figure 1a. Improvements in Migraine-Specific Quality of Life with 155 U OnabotulinumtoxinA[a]



[a]Participants treated with onabotulinumtoxinA dose at 4 or more visits.

Figure 1b. Improvements in Migraine-Specific Quality of Life with 156-195 U OnabotulinumtoxinA[a]



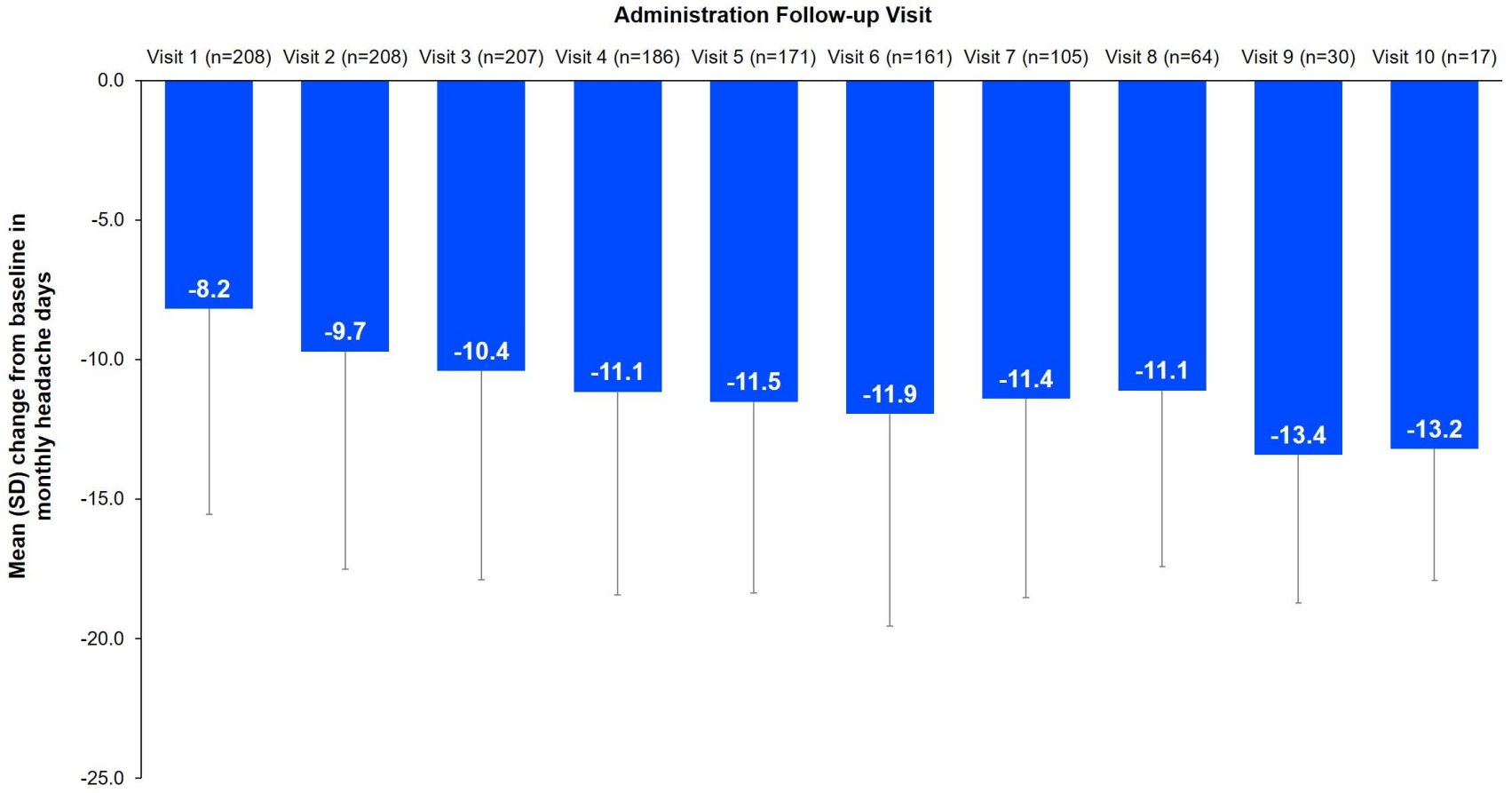
[a]Participants treated with onabotulinumtoxinA dose at 4 or more visits.

Results

Headache Day Frequency

- At baseline, participants in the 155 U group reported a mean (SD) of 21.5 (5.5) headache days/month, which decreased by a range of 8.2 to 13.4 days/month with onabotulinumtoxinA across all time points (**Figure 2a**)

Figure 2a. Reduction in Headache Day Frequency with 155 U OnabotulinumtoxinA[a]

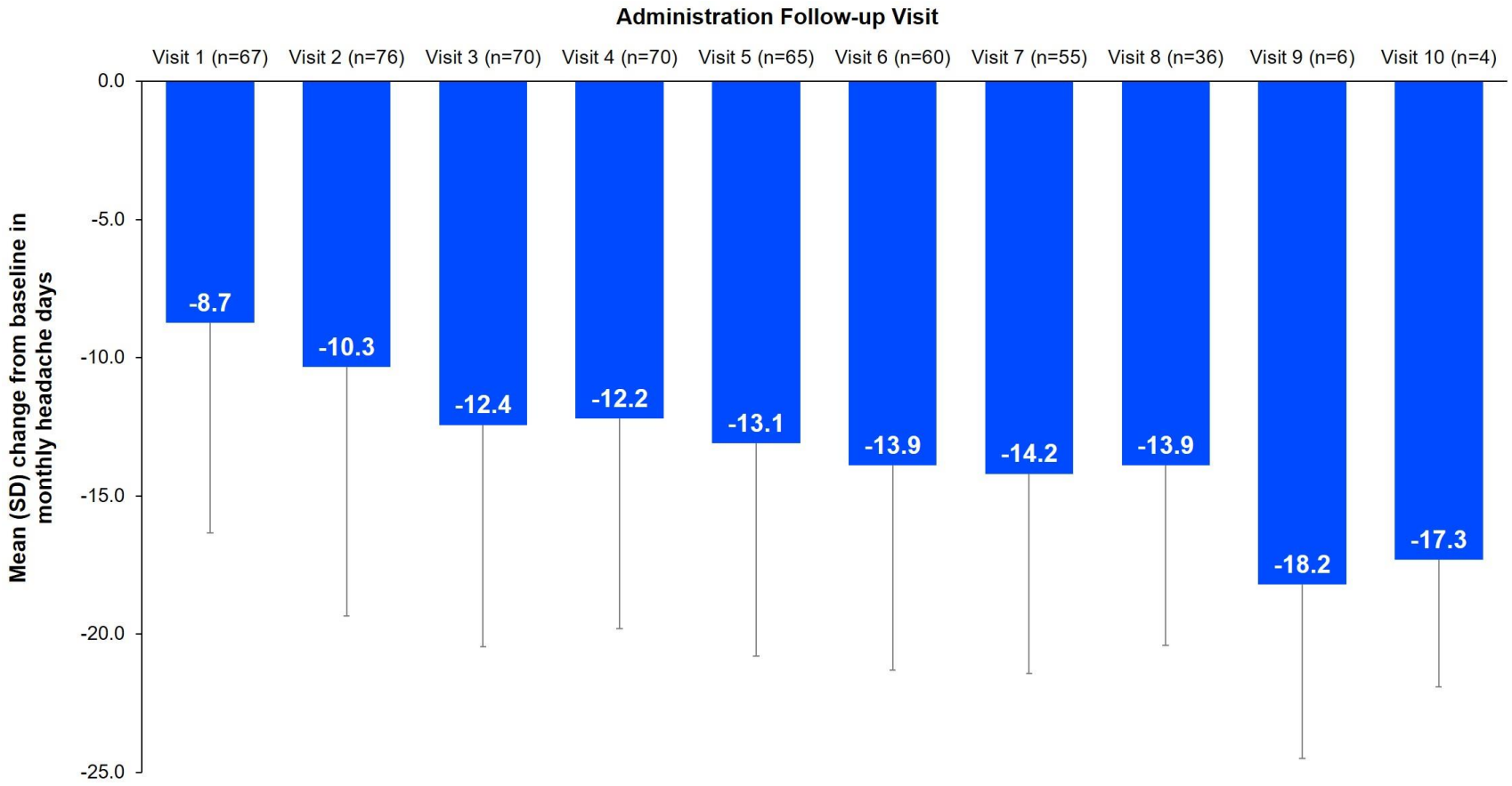


[a]Participants treated with 155 U onabotulinumtoxinA at 4 or more visits.

Headache Day Frequency (cont'd)

- Participants in the 156-195 U group reported a mean (SD) of 21.5 (5.6) headache days/month at baseline; treatment with onabotulinumtoxinA resulted in 8.7 to 18.2 fewer headache days/month across all time points (**Figure 2b**)

Figure 2b. Reduction in Headache Day Frequency with 156-196 U OnabotulinumtoxinA[a]



[a]Participants treated with 156-195 U onabotulinumtoxinA at 4 or more visits.

Summary and Limitations

- Participant-reported outcomes are based on participant recollection, which may result in incomplete and/or missing data
- To understand real-world treatment practices, this observational study did not use any formal protocol requirements or exclusion criteria
- There were no clinically meaningful differences in baseline characteristics, reductions in headache frequency, or MSQ domain scores between participants treated with 156-195 U and 155 U doses
- These real-world findings confirm that the 156-195 U dose is efficacious and safe, consistent with findings from the PREEMPT clinical trials

Conclusions

Treatment with 156-195 U onabotulinumtoxinA was safe and well tolerated in REPOSE

Similar rates of treatment-emergent adverse events were reported between the 2 dosage groups

These real-world findings confirm that 156-195 U is a safe and efficacious dose for chronic migraine

References

References

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