# Real-World Evidence for Control of Patients With Chronic Migraine Who Received Calcitonin Gene–Related Peptide Monoclonal Antibody Therapy Added to OnabotulinumtoxinA Treatment

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# Disclosures

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Introduction

## Background

- A multimodal management approach layering treatments that target different pathways in migraine pathophysiology may improve outcomes in people with chronic migraine (CM)
- Combination treatment with mechanistically distinct preventive therapies could be additive or synergistic in preventive treatment of migraine[1]
- Preclinical studies suggest that onabotulinumtoxinA and calcitonin gene–related peptide monoclonal antibodies (CGRP mAbs) prevent activation of different types of pain fibers[1-4]
- Several clinical reports of adding CGRP mAb therapy to onabotulinumtoxinA treatment in real-world settings support a potential additive effect of combination treatment[5-8]

## Objective

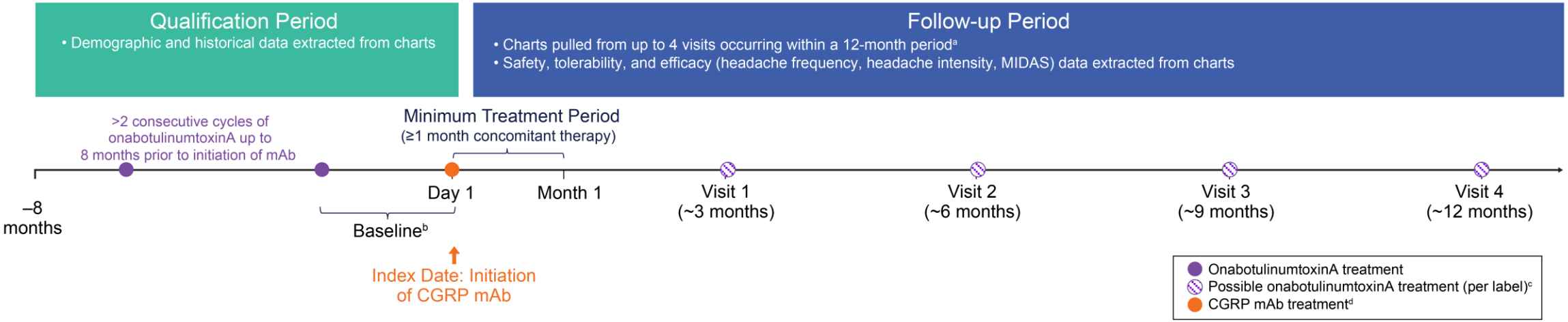
- To collect real-world data to gain improved understanding of the safety, tolerability, and potential benefits of adding a CGRP-targeted mAb to onabotulinumtoxinA treatment in patients with CM

1. Pellesi L, et al. *Headache*. 2020;60:1056-65. 2. Melo-Carrillo A, et al. *J Neurosci*. 2017;37:10587-96. 3. Melo-Carrillo A, et al. *Cephalalgia*. 2019;39:1358-65. 4. Burstein R, et al. *Headache*. 2020;60:1259-72. 5. Armanious M, et al. Poster presented at the *61st Annual Scientific Meeting of the American Headache Society (AHS)*; July 11–14, 2019; Philadelphia, PA, USA. 6. Boudreau GP. *Anesth Pain Res*. 2020;4:1-4. 7. Cohen F, et al. Poster presented at the *2020 American Headache Society (AHS) Virtual Annual Scientific Meeting*. 8. Singh S, et al. *Neurology*. 2020;94(15 suppl):5257.

# Study Design

- Retrospective, longitudinal chart review (October 2018–November 2019) in adults with CM treated at 1 clinical site with ≥2 consecutive cycles of onabotulinumtoxinA and ≥1 month of subsequent combination treatment with a CGRP mAb and onabotulinumtoxinA
- Outcomes were also evaluated in patients who completed approximately 12 months of onabotulinumtoxinA treatment (4 visits) after initiation of CGRP mAb (completers cohort)

## Study Design




CGRP, calcitonin gene–related peptide; mAb, monoclonal antibody; MIDAS, Migraine Disability Assessment Scale.
[a]Not all patients had 4 visits or 12 months of data. [b]Baseline assessments for outcome measures (eg, headache day frequency, headache intensity, disability) were collected from the visit at which the CGRP mAb was prescribed and reflect patient assessments during approximately 1–3 months prior to initiation of the CGRP mAb. [c]OnabotulinumtoxinA treatment is not always administered per label. [d]CGRP mAbs were self-administered by subcutaneous injection. Per label, erenumab and galcanezumab are administered once monthly, and fremanezumab is administered once every 3 months.

# Analysis Populations

- Of the 300 charts reviewed, 257 patients met eligibility criteria for the primary analysis cohort
  - 103 patients (40.1%) completed 4 visits after initiation of CGRP mAb (completers cohort)
- The average headache frequency was 21–22 monthly headache days (MHDs) before initiation of onabotulinumtoxinA and 12 MHDs before starting CGRP mAb as add-on therapy

## Demographics and Headache and Disability Characteristics

| Parameter | Primary Analysis Cohort (n=257) | | Completers Cohort (n=103) | |
|---|---|---|---|---|
| Female, n (%) | 211 (82.1) | | 89 (86.4) | |
| Age, y, mean (SD) | 50.2 (12.3)[a] | | 49.8 (11.3)[b] | |
| Years since migraine diagnosis, mean (SD) | 5.0 (5.2)[c] | | 4.5 (3.9)[d] | |
| Years since initiation of onabotA, mean (SD) | 3.8 (3.1)[e] | | 3.5 (2.7)[b] | |
| Index CGRP mAb treatment, n (%) | | | | |
| Erenumab[f] | 200 (77.8) | | 87 (84.5) | |
| 70 mg | 136 (52.9) | | 58 (56.3) | |
| 140 mg | 62 (24.1) | | 29 (28.2) | |
| Galcanezumab 240 mg[g] | 42 (16.3) | | 11 (10.7) | |
| Fremanezumab | 15 (5.8) | | 5 (4.9) | |
| 225 mg | 8 (3.1) | | 2 (1.9) | |
| 675 mg | 7 (2.7) | | 3 (2.9) | |
| **Headache and disability characteristics** | **Before onabotA** | **Baseline (before mAb)** | **Before onabotA** | **Baseline (before mAb)** |
| Headache frequency, days/month, mean (SD) | 21 (8)[h] | 12 (8)[c] | 22 (8)[i] | 12 (9)[j] |
| Change from pre-onabotA, mean (95% CI) | — | -9 (-11, -8) | — | -10 (-12, -7) |
| Headache intensity,[k] mean (SD) | NA | 6.5 (3.6)[l] | NA | 6.1 (1.9)[m] |
| MIDAS score, mean (SD) | NA | 43.7 (43.4)[n] | NA | 42.8 (41.9)[o] |
| Moderate to very severe disability, n (%) | NA | 179 (83.3)[n] | NA | 76 (86.4)[o] |

CGRP, calcitonin gene–related peptide; mAb, monoclonal antibody; MIDAS, Migraine Disability Assessment Scale; NA, not available; onabotA, onabotulinumtoxinA.
[a]n=220. [b]n=86. [c]n=246. [d]n=102. [e]n=218. [f]Erenumab dose was not reported in 2 patients in the primary cohort. [g]Galcanezumab is administered as a 240 mg loading dose, followed by monthly doses of 120 mg. [h]n=241. [i]n=92. [j]n=100. [k]Headache intensity rated on a 0–10 scale. [l]n=232. [m]n=93. [n]n=215. [o]n=88.

# Safety and Tolerability

- In the primary analysis cohort, 62 (25.3%) of 245 patients with ≥1 follow-up visit discontinued onabotulinumtoxinA and/or CGRP mAb at any time post-baseline
- Patients discontinued CGRP mAb ~7-fold more often than onabotulinumtoxinA (23.3% vs 3.3%)
- In the completers cohort, 10 (9.7%) of 103 patients discontinued CGRP mAb; no patient discontinued onabotulinumtoxinA
- Adverse event (AE) rates were similar in the primary analysis and completers cohorts
  - The most common AEs were constipation and nausea
  - Constipation occurred most frequently with erenumab (primary: 18/21; completers 9/9)

## Table 2. Adverse Events

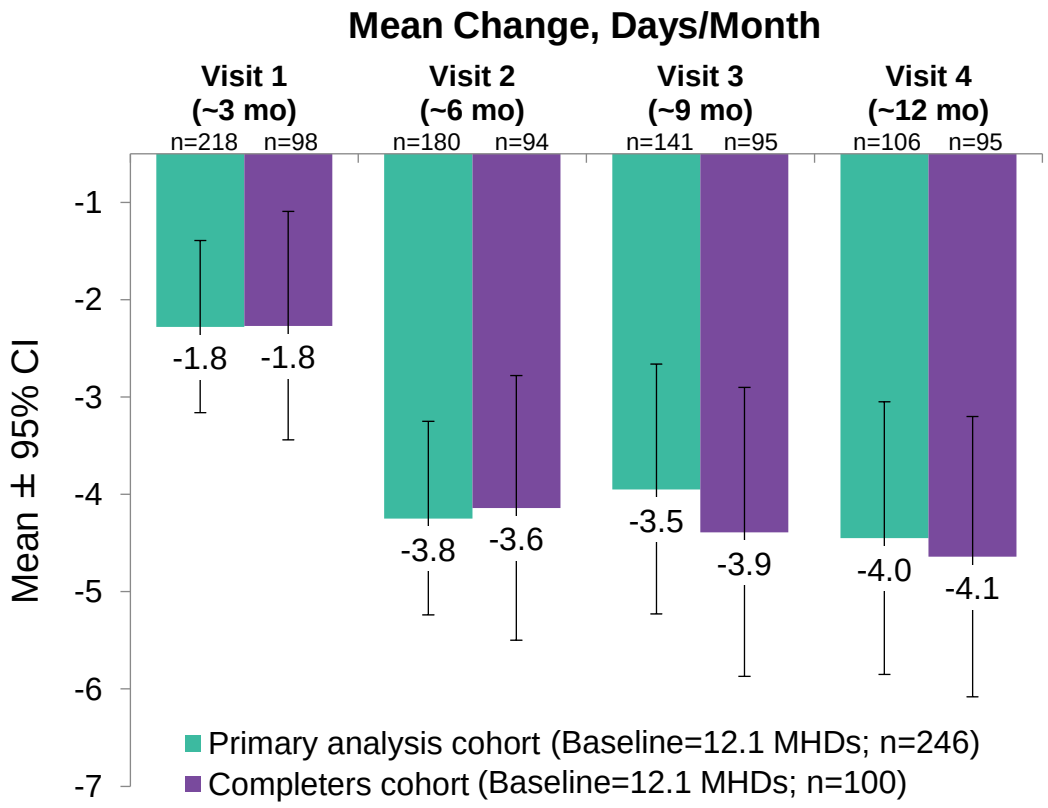
| AEs in >2 patients, n (%) | Primary Analysis Cohort[a] (n=245) | Completers Cohort (n=103) |
|---|---|---|
| Any AE | 68 (27.8) | 31 (30.1) |
| Constipation | 21 (8.6) | 9 (8.7) |
| Nausea | 8 (3.3) | 5 (4.9) |
| Neck pain | 6 (2.4) | 5 (4.9) |
| Musculoskeletal pain | 6 (2.4) | 2 (1.9) |
| Headache worsening | 5 (2.0) | 1 (1.0) |
| Migraine worsening | 4 (1.6) | 2 (1.9) |
| Erythema | 3 (1.2) | 2 (1.9) |
| Neuropathy | 3 (1.2) | 1 (1.0) |
| Injection site pain | 3 (1.2) | 0 |

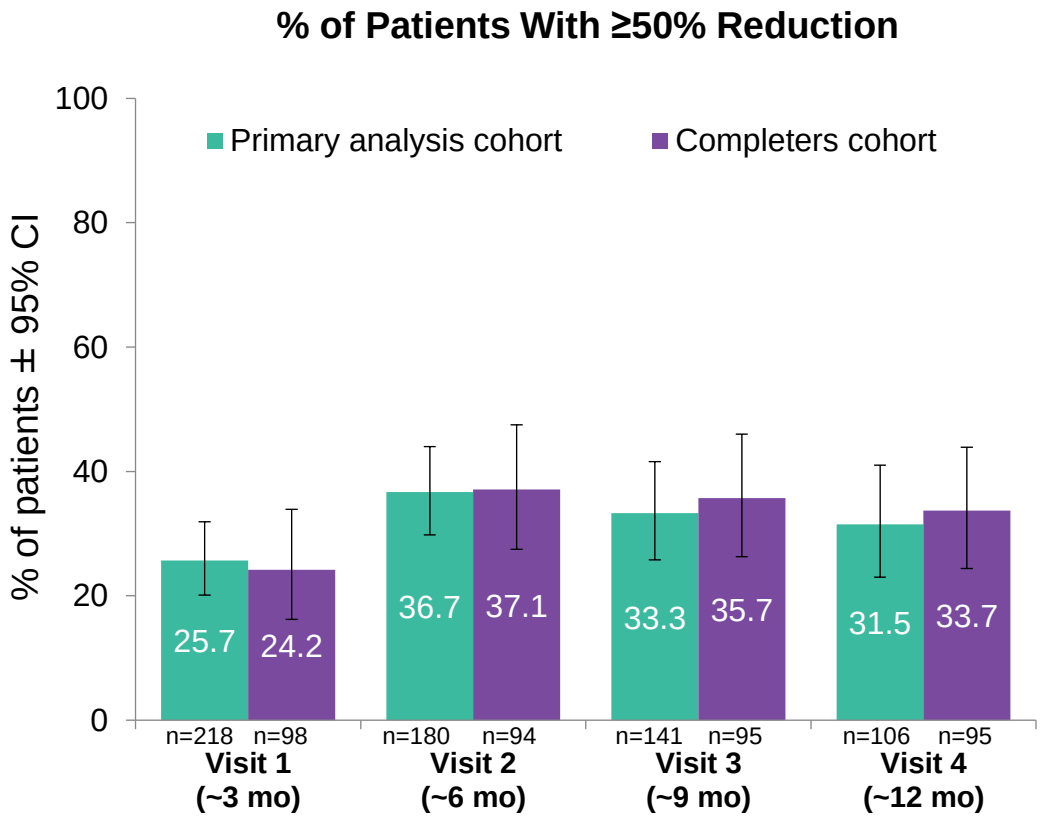
AE, adverse event.
[a]Patients with ≥1 follow-up visit.

# Efficacy

- At baseline, onabotulinumtoxinA treatment alone had resulted in mean reductions of 9 and 10 MHDs in the primary and completer cohorts, respectively
- Compared with onabotulinumtoxinA treatment alone (baseline), adding a CGRP mAb resulted in statistically significant[a] and clinically meaningful reductions in mean MHDs at all visits in both cohorts

## Change From Baseline in Headache Frequency (MHDs)



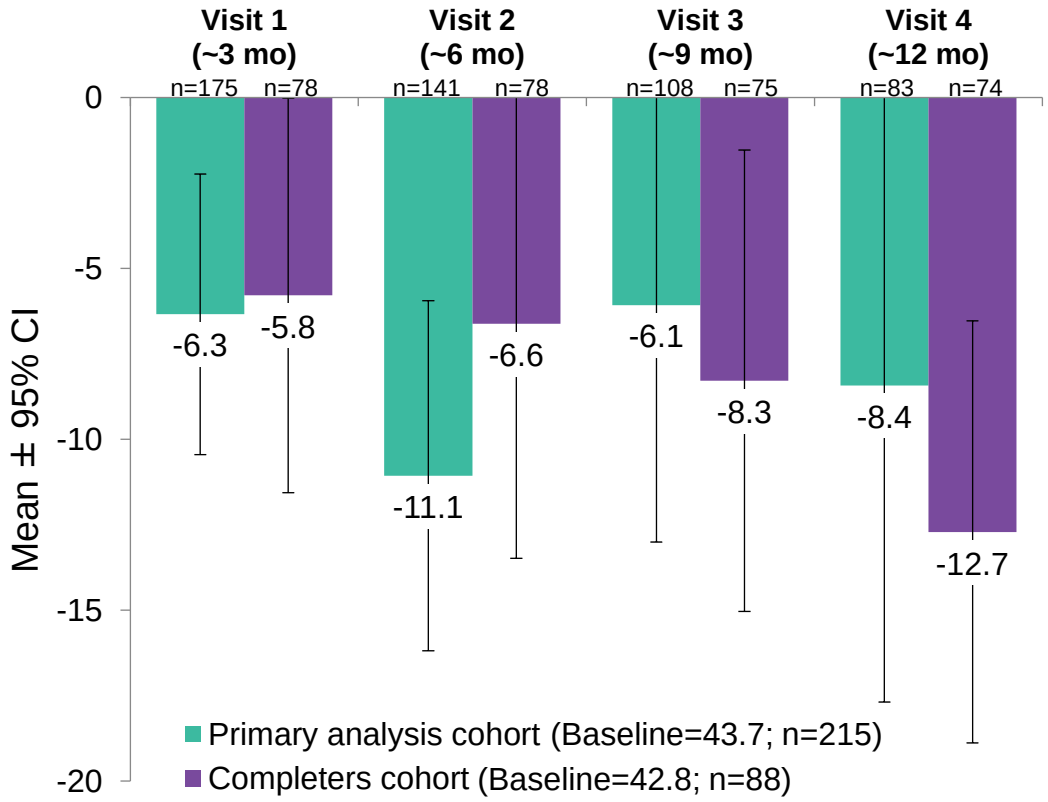

MHDs, monthly headache days.
[a]95% CIs did not include 0.

# Disability

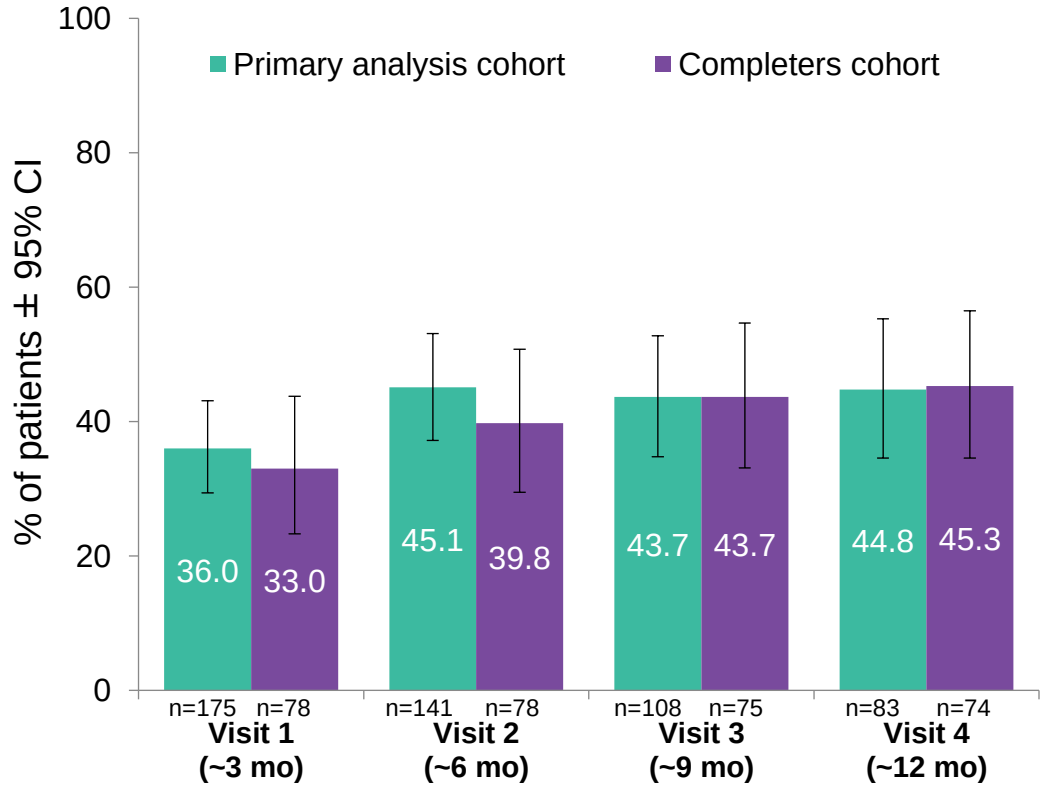
- Compared with onabotulinumtoxinA treatment alone (baseline), adding a CGRP mAb resulted in clinically meaningful improvements in disability (≥5-point decrease in MIDAS) at all visits

## Change From Baseline in Migraine-Related Disability (MIDAS Score)

### Mean Change in MIDAS Score




### % of Patients With ≥5-Point Reduction




CGRP, calcitonin gene–related peptide; mAb, monoclonal antibody; MIDAS, Migraine Disability Assessment Scale.

# Conclusions

In this retrospective, real-world study of 257 patients receiving onabotulinumtoxinA and either erenumab, galcanezumab, or fremanezumab, combination treatment was well tolerated, and no new safety signals were identified

Patients in this study had clinically meaningful responses to onabotulinumtoxinA prior to initiating a CGRP mAb. Combining onabotulinumtoxinA with CGRP mAb was associated with additional clinically meaningful improvements in headache frequency and migraine-related disability compared with onabotulinumtoxinA without a CGRP mAb

Additional real-world and controlled trials should be considered to further assess safety and the potential benefit of this treatment paradigm for people with CM

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