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Clinically Meaningful Responses to Fremanezumab in Patients With Migraine and Documented Inadequate Response to 2-4 Classes of Migraine Preventive Medications in the International, Multicenter, Randomized, Placebo-controlled FOCUS Study

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CONCLUSIONS

- **Headache-related disability, based on the 6-item Headache Impact Test (HIT-6) and Migraine Disability Assessment (MIDAS) scores, was significantly improved with quarterly or monthly fremanezumab treatment compared with placebo**
- **These early improvements in HIT-6 and MIDAS scores, reflective of early improvements in headache-related disability, were observed in patients with episodic migraine (EM) and chronic migraine (CM) and documented inadequate response to 2 to 4 classes of migraine preventive medications**
- **These results support the overall benefits of fremanezumab in this population of patients with difficult-to-treat migraine**

OBJECTIVES

- Migraine is consistently a leading cause of disability worldwide, ranking as the second leading cause of years lived with disability in 2016[1]
- Fremanezumab is a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP), which is implicated in migraine pathophysiology[2,3]
- In randomized clinical trials, fremanezumab has demonstrated significant efficacy as a migraine preventive treatment in patients with EM and CM[4,5]
- The FOCUS study (ClinicalTrials.gov Identifier: NCT03308968) of fremanezumab was the first and largest study of a migraine preventive treatment in patients with EM and CM who had documented inadequate response to 2 to 4 classes of migraine preventive medications
- The impact of subcutaneous (SC) quarterly or monthly fremanezumab on headache-related disability outcomes was evaluated in the FOCUS study in patients with EM or CM and documented inadequate response to 2 to 4 classes of prior migraine preventive medications

METHODS

Patients

Table 1. Key Selection Criteria

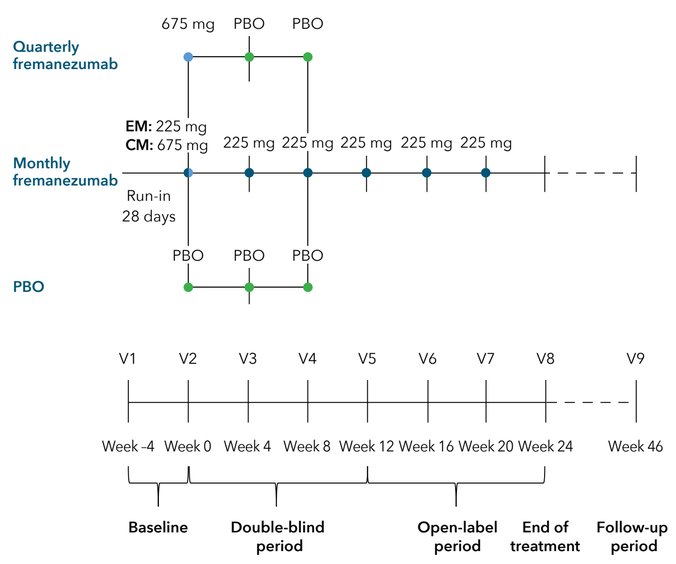
Inclusion criteria	Exclusion criteria
— Adult patients (18-70 years) with a diagnosis of migraine with onset at ≤50 years	— Any migraine preventive treatment for >5 days at screening and plan to continue treatment
— History of migraine for ≥12 months prior to screening and fulfilled criteria for EM or CM at baseline	— OnabotulinumtoxinA during the 3 months prior to screening
— Documented inadequate response (within the past 10 years) to 2-4 classes of prior migraine preventive medications: – Beta-blocker (propranolol, metoprolol, atenolol, bisoprolol) – Anticonvulsant (topiramate) – Tricyclic antidepressant (amitriptyline) – Calcium channel blocker (flunarizine) – OnabotulinumtoxinA – Valproic acid	— Opioid- or barbiturate-containing treatment on >4 days during the run-in period — Intervention/device for migraine during the 2 months prior to screening — Triptans, ergots, or nonsteroidal anti-inflammatory drugs for migraine preventive treatment — Prior exposure to a mAb targeting the CGRP pathway

EM, episodic migraine; CM, chronic migraine; mAb, monoclonal antibody; CGRP, calcitonin gene-related peptide.

Study Design

- International, multicenter, randomized, double-blind, placebo-controlled, phase 3 study
- Included a screening visit; 28-day run-in period; 12-week, double-blind, placebo-controlled treatment period; and 12-week, open-label treatment period (**Figure 1**)
  - Results of the 12-week, double-blind period are presented here
- During the double-blind period, patients were randomized (1:1:1) to SC quarterly fremanezumab, SC monthly fremanezumab, or placebo (**Figure 1**)

Figure 1. Study design and dosing for EM and CM patients.



EM, episodic migraine; CM, chronic migraine; PBO, placebo; V, visit.

Study Assessments

- Impact of study treatment on headache-related disability was assessed based on the mean change from baseline in HIT-6 and MIDAS scores during the 4 weeks after administration of the third dose of study drug (Week 12)

RESULTS

Patients

- Efficacy analysis population, N = 837 (placebo, n = 278; quarterly fremanezumab, n = 276; monthly fremanezumab, n = 283)
- Baseline clinical characteristics were similar across treatment groups (**Table 2**)
  - Approximately 60% of patients had CM, and the mean duration of time since migraine diagnosis was approximately 24 years across all treatment groups
  - Across all treatment groups, baseline HIT-6 and MIDAS scores indicated severe disability due to headache

Table 2. Baseline Clinical Characteristics

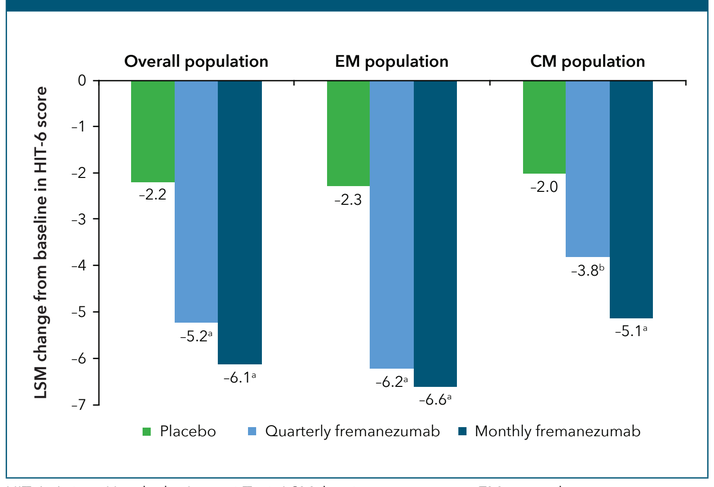
Characteristic	Placebo (n = 278)	Quarterly fremanezumab (n = 276)	Monthly fremanezumab (n = 283)
Mean (SD) years since migraine diagnosis	24.3 (13.61)	24.3 (12.83)	24.0 (13.72)
Migraine classification, n (%)			
EM	111 (40)	107 (39)	110 (39)
CM	167 (60)	169 (61)	173 (61)
Triptans/ergots during baseline, n (%)	238 (86)	235 (85)	245 (87)
Number of prior preventive medications failed, n (%)			
2	141 (51)	140 (51)	133 (47)
3	82 (29)	85 (31)	98 (35)
4	54 (19)	49 (18)	50 (18)
Baseline HIT-6 score, mean (SD)	64.1 (4.96)	64.2 (4.28)	63.9 (4.47)
Baseline MIDAS score, mean (SD)	61.6 (57.07)	61.5 (49.12)	62.3 (51.32)

SD, standard deviation; EM, episodic migraine; CM, chronic migraine; HIT-6, 6-item Headache Impact Test; MIDAS, Migraine Disability Assessment.

HIT-6 Scores

- With both fremanezumab dosing regimens in the overall population, significantly greater reductions in mean HIT-6 scores versus placebo were observed during the 4 weeks after the third dose of study treatment (all $P \leq 0.0001$; **Figure 2**)
  - Similar results were observed in the overall study population and subgroups of patients with EM and CM (**Figure 2**)

Figure 2. Reduction in disability as measured by HIT-6 score during the 4 weeks after the third dose of study drug.

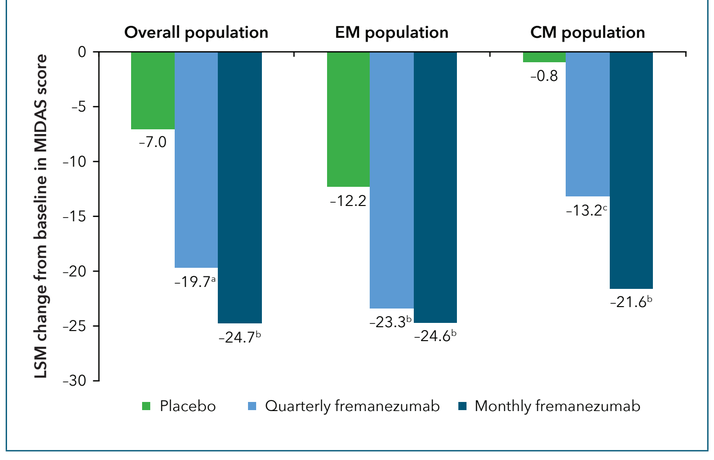


HIT-6, 6-item Headache Impact Test; LSM, least-squares mean; EM, episodic migraine; CM, chronic migraine.
[a]$P \leq 0.0001$ versus placebo.
[b]$P = 0.0068$ versus placebo.

MIDAS Scores

- With both fremanezumab dosing regimens in the overall population, significantly greater reductions in mean MIDAS scores versus placebo were observed during the 4 weeks after the third dose of study treatment (all $P \leq 0.0002$; **Figure 3**)
  - Similar results were observed in the overall study population and subgroups of patients with EM and CM (**Figure 3**)

Figure 3. Reduction in disability as measured by MIDAS score during the 4 weeks after the third dose of study drug.



MIDAS, Migraine Disability Assessment; LSM, least-squares mean; EM, episodic migraine; CM, chronic migraine.
[a]$P = 0.0002$ versus placebo.
[b]$P < 0.0001$ versus placebo.
[c]$P = 0.0162$ versus placebo.

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Disclosures

M. Ashina received personal fees from Alder BioPharmaceuticals, Allergan, Amgen, Alder, Eli Lilly, Novartis, and Teva Pharmaceuticals; participated in clinical trials as the principal investigator for Alder, Amgen, electroCore, Novartis, and Teva Pharmaceuticals trials; and has no ownership interest in nor owns stocks of any pharmaceutical company. M. Ashina serves as associate editor of *Cephalalgia* and *The Journal of Headache and Pain*. M. Ashina is president-elect of the International Headache Society and general secretary of the European Headache Federation. M.D. Ferrari was an investigator on this study for Teva Pharmaceuticals. X. Ning, M. Galic, J.M. Cohen, and R. Yang are employees of Teva Pharmaceuticals.

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