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Impact of Fremanezumab on Migraine-associated Symptoms in Patients With 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

- **In patients with migraine and documented inadequate response to 2 to 4 classes of prior migraine preventive medications, quarterly and monthly fremanezumab significantly reduced migraine-related symptoms (nausea or vomiting; photophobia and phonophobia) versus placebo**
  - **These reductions in migraine-related symptoms were observed as early as at 4 weeks and were maintained through 12 weeks of double-blind treatment**
- **These results further support the clinical efficacy of fremanezumab in this population with difficult-to-treat episodic migraine (EM) and chronic migraine (CM)**

INTRODUCTION

- One goal of migraine preventive treatment is to reduce headache-related symptoms,[1] including nausea or vomiting and photophobia and phonophobia[2]
- Fremanezumab is a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP)
  - Approved for the preventive treatment of migraine in adults[3]
- The FOCUS study 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

OBJECTIVE

- To evaluate the impact of subcutaneous (SC) quarterly or monthly fremanezumab on migraine-related symptoms (nausea or vomiting and photophobia and phonophobia) in EM or CM patients with documented inadequate response to 2 to 4 classes of migraine preventive medications

METHODS

Patients

Table 1. Key Selection Criteria

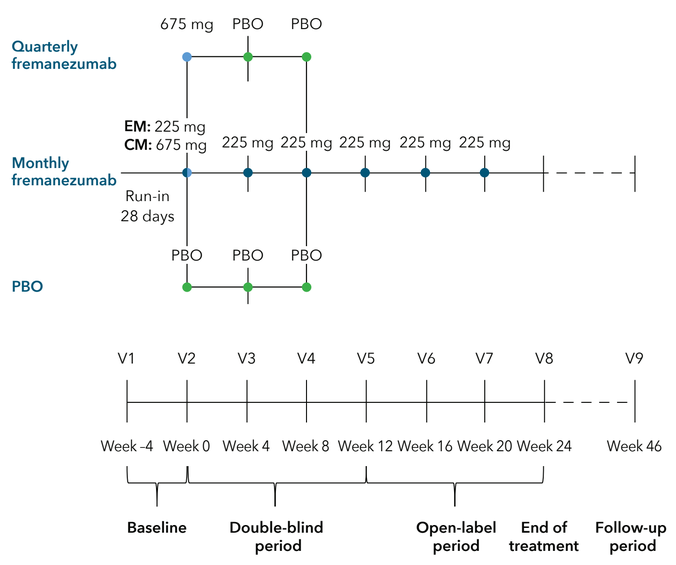
Inclusion criteria	Exclusion criteria
— Adult patients (18-70 years) with a diagnosis of migraine with onset at ≤50 years	— Any migraine preventive treatment use for >5 days at screening and plan to continue treatment
— History of migraine for ≥12 months prior to screening and fulfilled criteria for 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

- Exploratory endpoints: mean changes from baseline in the monthly average number of days with migraine-related nonheadache symptoms during 12 weeks
  - Nausea or vomiting
  - Photophobia and phonophobia

RESULTS

Patients

- Efficacy analysis population, N = 837 (placebo, n = 278; quarterly fremanezumab, n = 276; monthly fremanezumab, n = 283)
- Demographic and baseline characteristics were well balanced across treatment groups (**Table 2**)

Table 2. Demographic and Baseline Characteristics[a]

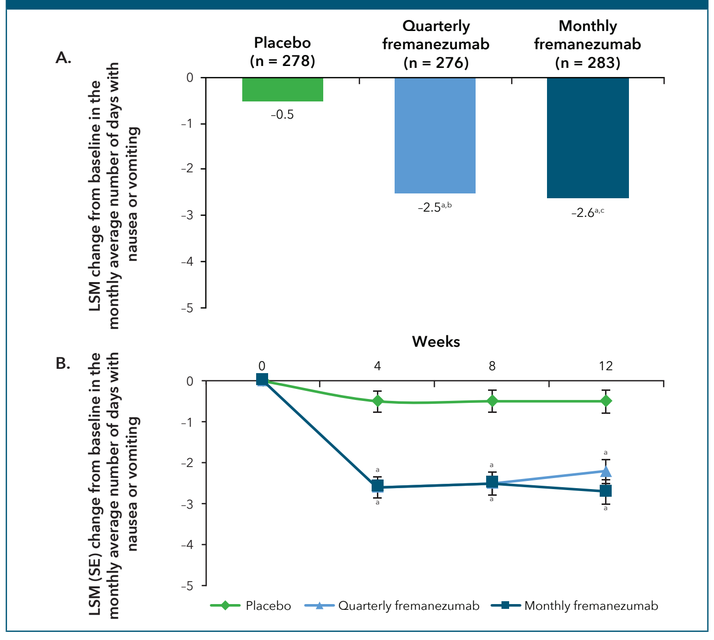
Characteristic	Placebo (n = 278)	Quarterly fremanezumab (n = 276)	Monthly fremanezumab (n = 283)
Age, years	46.8 (11.11)	45.8 (10.97)	45.9 (11.05)
Age category, years, n (%)			
18-45	120 (43)	125 (45)	128 (45)
>45	158 (57)	151 (55)	155 (55)
Sex, n (%)			
Male	46 (17)	47 (17)	45 (16)
Female	232 (83)	229 (83)	238 (84)
Migraine classification, n (%)			
Episodic	111 (40)	107 (39)	110 (39)
Chronic	167 (60)	169 (61)	173 (61)
Baseline number of days with nausea or vomiting	6.5 (6.01)[b]	6.6 (5.85)	6.6 (5.94)
Baseline number of days with photophobia and phonophobia	9.8 (7.71)[b]	9.4 (6.83)	9.3 (6.83)

SD, standard deviation.
[a]Mean (SD) unless otherwise specified.
[b]n = 279.

Migraine-related Symptoms

- Fremanezumab significantly reduced the monthly average number of days with nausea or vomiting during 12 weeks versus placebo (both *P* <0.0001; **Figure 2A**)
  - Significant reductions were observed as early as Week 4 and were maintained through Week 12 (all *P* <0.0001; **Figure 2B**)

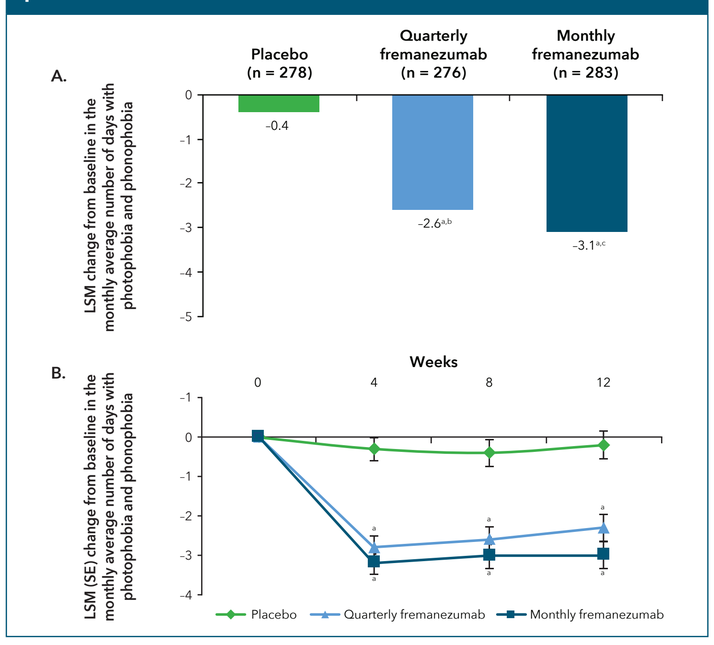
Figure 2. Change from baseline in the monthly average number of days with nausea or vomiting (A) during the 12-week, double-blind treatment period and (B) at 4, 8, and 12 weeks in patients with a documented inadequate response to 2 to 4 classes of migraine preventive medications.



LSM, least-squares mean; SE, standard error; LSMD, least-squares mean difference.
[a]*P* <0.0001 versus placebo.
[b]LSMD (SE) versus placebo: –1.9 (0.29).
[c]LSMD (SE) versus placebo: –2.1 (0.29).

- Similarly, fremanezumab significantly reduced the monthly average number of days with photophobia and phonophobia versus placebo during 12 weeks (both *P* <0.0001; **Figure 3A**)
  - Significant reductions were observed as early as Week 4 and were maintained through Week 12 (all *P* <0.0001; **Figure 3B**)

Figure 3. Change from baseline in the monthly average number of days with photophobia and phonophobia (A) during the 12-week, double-blind treatment period and (B) at 4, 8, and 12 weeks in patients with a documented inadequate response to 2 to 4 classes of migraine preventive medications.



LSM, least-squares mean; SE, standard error; LSMD, least-squares mean difference.
[a]*P* <0.0001 versus placebo.
[b]LSMD (SE) versus placebo: –2.2 (0.34).
[c]LSMD (SE) versus placebo: –2.8 (0.34).

References

1. American Headache Society. *Headache*. 2019;59(1):1-18.
2. Headache Classification Committee of the International Headache Society. *Cephalalgia*. 2018;38(1):1-211.
3. AJOVY® (fremanezumab-vfrm) injection, for subcutaneous use [prescribing information]. Teva Pharmaceuticals USA, Inc.: North Wales, PA; 2019.

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