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Efficacy With Fremanezumab in Migraine Patients With Comorbid Moderate to Severe Depression and Documented Inadequate Response to 2-4 Classes of Migraine Preventive Treatments: Subgroup Analysis of the Randomized, Placebo-controlled FOCUS Study

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CONCLUSIONS

- **In patients with migraine, moderate to severe depression, and inadequate response to 2 to 4 classes of migraine preventive medications, significant reductions in monthly migraine days were observed with fremanezumab treatment versus placebo**
- **Significant reductions in monthly headache days of at least moderate severity were also observed with fremanezumab treatment versus placebo in this population**
- **These results demonstrate that fremanezumab is effective in migraine patients who have failed 2 to 4 prior preventive medications and have moderate to severe depression, which may be relevant for clinical decision making for patients with difficult-to-treat migraine and comorbid depression**

INTRODUCTION

- Up to 30% of patients with episodic migraine (EM) and up to 57% of patients with chronic migraine (CM) have comorbid depression[1]
- Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) that selectively targets calcitonin gene-related peptide (CGRP),[2] has proven efficacy for preventive treatment of migraine in adults[3,4]
- The FOCUS study (ClinicalTrials.gov Identifier: NCT03308968) of fremanezumab was the first and largest study of a migraine preventive treatment in a population of adults with difficult-to-treat EM and CM and documented inadequate response to 2 to 4 classes of migraine preventive medications[5]

OBJECTIVE

- To evaluate efficacy of fremanezumab in patients with comorbid moderate to severe depression

METHODS

Patients

- This subgroup analysis included migraine patients with moderate to severe comorbid depression (**Box 1**)

Box 1. Subgroup Analysis Population

Comorbid Moderate to Severe Depression

- Identified based on PHQ-9 score ≥10
- PHQ-9 is a 9-item questionnaire used to screen for and measure depression severity[6]

PHQ-9, Patient Health Questionnaire-9.

- Patients with significant psychiatric issues (eg, major depression) that, in the investigator's opinion, would compromise the patient's ability to participate in the study were excluded

Study Design

- International, multicenter, randomized, double-blind, placebo-controlled phase 3 study
- During the double-blind period, patients were randomized (1:1:1) to subcutaneous (SC) quarterly fremanezumab (Months 1, 2, 3: 675 mg, placebo, placebo), SC monthly fremanezumab (Months 1, 2, 3: 225 mg [EM]/675 mg [CM], 225 mg, 225 mg), or matched monthly placebo
- This study was approved by institutional review boards, and all patients provided written informed consent prior to participation in the study

Statistical Analysis

- Efficacy analyses were conducted in the modified intention-to-treat population in this subgroup of patients with comorbid moderate to severe depression using a mixed-effects model for repeated measures

Study Assessments

- In patients with comorbid depression, changes from baseline in the monthly average number of migraine days in the first 4 weeks and during 12 weeks of double-blind treatment were evaluated
- Changes from baseline in the monthly average number of headache days of at least moderate severity in the first 4 weeks and during 12 weeks of double-blind treatment were also evaluated in this population

RESULTS

Patients

Table 1. Patients With Comorbid Depression: Demographics and Baseline Characteristics

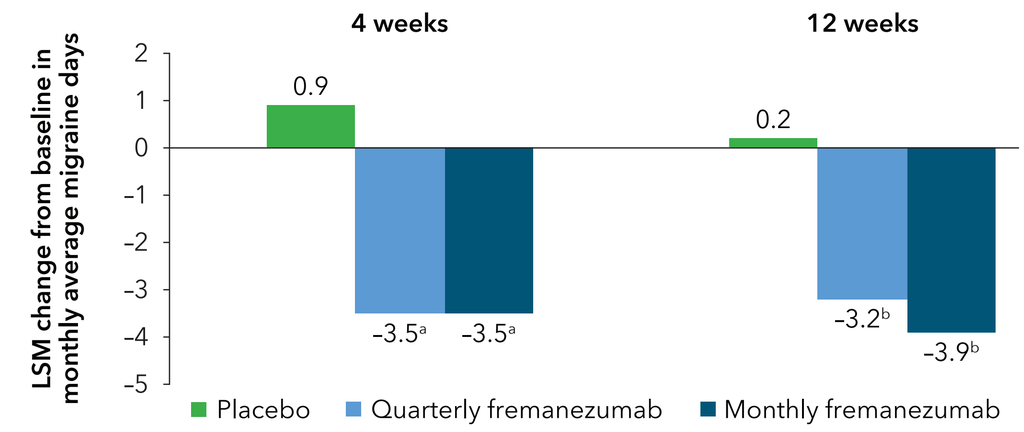
Baseline values	Placebo (n = 48)	Quarterly fremanezumab (n = 62)	Monthly fremanezumab (n = 44)
Age (years), mean (SD)	47.8 (11.19)	47.0 (11.19)	44.7 (12.69)
Female sex, n (%)	44 (92)	49 (79)	38 (86)
Monthly average migraine days, mean (SD)	18.0 (5.4)	17.2 (5.4)	16.7 (6.3)
Monthly average headache days of at least moderate severity, mean (SD)	15.5 (5.6)	15.8 (6.3)	14.5 (6.1)
PHQ-9 scores, mean (SD)	14.6 (3.41)	14.2 (3.51)	14.5 (3.66)

SD, standard deviation; PHQ-9, Patient Health Questionnaire-9.

- For this subgroup analysis population (patients with moderate to severe depression; n = 154), baseline monthly average numbers of migraine days and headache days of at least moderate severity are summarized in **Table 1**

Efficacy in Patients With Comorbid Depression

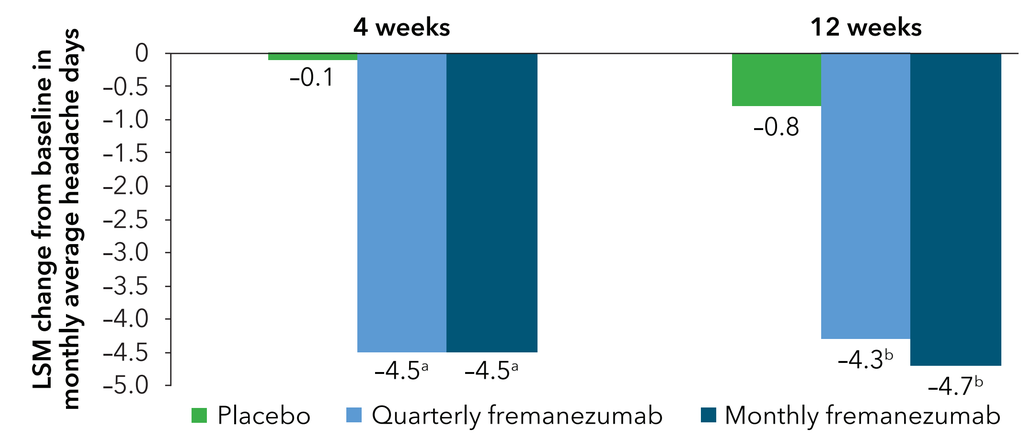
Figure 1. In patients with comorbid depression, change from baseline versus placebo in the monthly average number of migraine days at 4 weeks and at 12 weeks of treatment.



LSM, least-squares mean.
[a]*P* = 0.0003 versus placebo.
[b]*P* <0.01 versus placebo.

- In patients with comorbid depression, reductions from baseline in the monthly average number of migraine days were significantly greater with both quarterly and monthly fremanezumab versus placebo at 4 weeks and at 12 weeks of treatment (**Figure 1**)

Figure 2. In patients with comorbid depression, change from baseline versus placebo in the monthly average number of headache days of at least moderate severity at 4 weeks and at 12 weeks of treatment.



LSM, least-squares mean.
[a]*P* ≤0.001 versus placebo.
[b]*P* ≤0.0074 versus placebo.

- In patients with comorbid depression, reductions from baseline in the monthly average number of headache days of at least moderate severity were also significantly greater with both fremanezumab dosing regimens versus placebo at 4 weeks and at 12 weeks of treatment (**Figure 2**)

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