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Early Onset of Response to Fremanezumab in Migraine Patients With 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

- **Fremanezumab demonstrated early onset of efficacy in migraine patients with inadequate response to 2 to 4 classes of migraine preventive medications and moderate to severe depression**
- **Significantly greater reductions from baseline in the weekly number of migraine days and headache days of at least moderate severity were achieved as early as Week 1 with fremanezumab versus placebo**
- **These results showing rapid onset of efficacy may be relevant for physicians treating 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

OBJECTIVE

- To evaluate early efficacy (first 3 weeks) of fremanezumab in patients with 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[5]

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

Study Assessments

- In patients with comorbid depression, changes from baseline in the weekly average number of migraine days by Week 1 and through Week 3 were evaluated
- Changes from baseline in the weekly average number of headache days of at least moderate severity by Week 1 and through Week 3 were also evaluated in this population

RESULTS

Patients

Table 1. Patients With Comorbid Depression: Baseline Weekly Average Migraine Days and Headache Days of at Least Moderate Severity

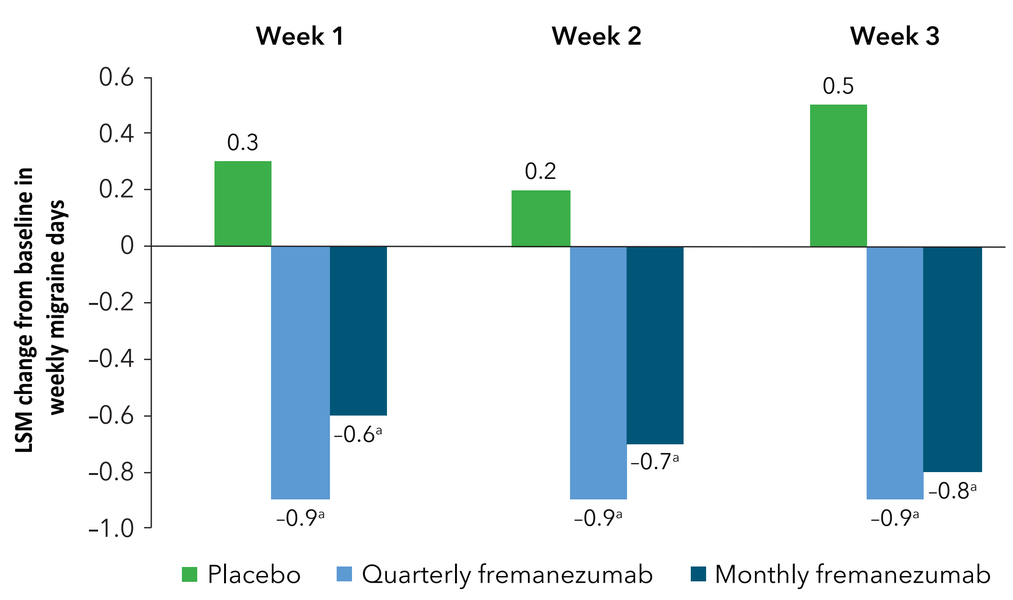
Baseline values, mean (SD)	Placebo (n = 48)	Quarterly fremanezumab (n = 62)	Monthly fremanezumab (n = 44)
Weekly average migraine days	4.5 (1.4)	4.3 (1.4)	4.2 (1.6)
Weekly average headache days of at least moderate severity	3.9 (1.4)	3.9 (1.6)	3.6 (1.5)

SD, standard deviation.

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

Efficacy in Patients With Comorbid Depression

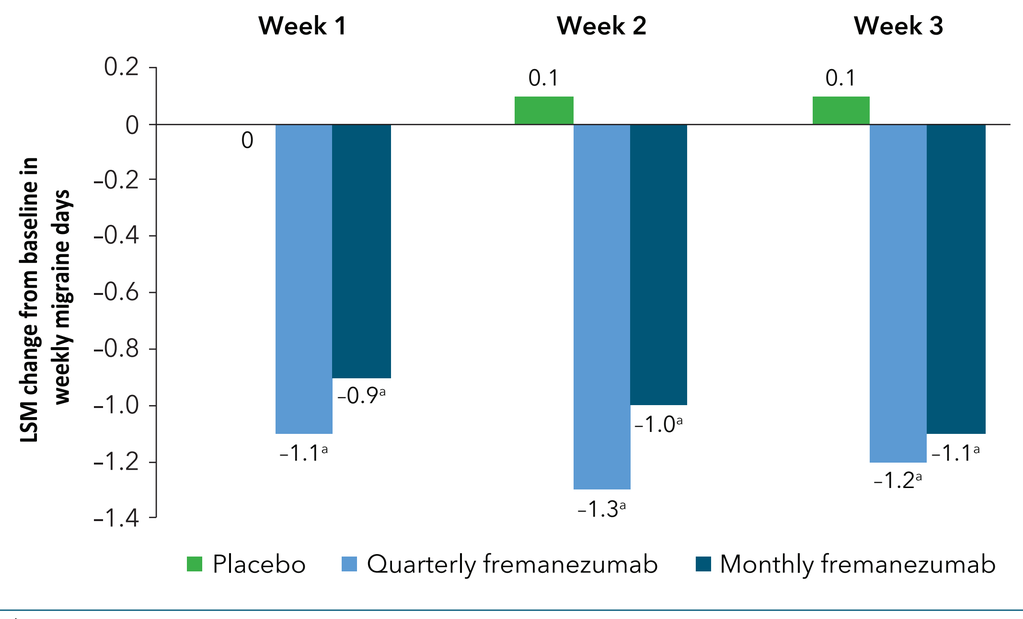
Figure 1. Change from baseline versus placebo in the weekly average number of migraine days during the first 3 weeks of treatment.



LSM, least-squares mean.
[a]*P* <0.05 versus placebo.

- Reductions from baseline in the weekly average number of migraine days (**Figure 1**) and weekly average number of headache days of at least moderate severity (**Figure 2**) were significantly greater with both dosing regimens of fremanezumab versus placebo at each weekly time point for the first 3 weeks of double-blind treatment

Figure 2. Change from baseline versus placebo in the weekly number of headache days of at least moderate severity during the first 3 weeks of treatment.



LSM, least-squares mean.
[a]*P* ≤0.05 versus placebo.

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Disclosures

A. Blumenfeld has no conflicts of interest to disclose. R. Yang, J.M. Cohen, and V. Ramirez-Campos are employees of Teva Pharmaceuticals. P. Pozo-Rosich has received honoraria as a consultant and speaker for Allergan, Almirall, Chiesi, Eli Lilly, Novartis, and Teva Pharmaceuticals. P. Pozo-Rosich's research group has received research grants from Allergan and has received funding for clinical trials from Alder, electroCore, Eli Lilly, Novartis, and Teva Pharmaceuticals. P. Pozo-Rosich does not own stocks from any pharmaceutical company.

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