Impact of Fremanezumab on Any Acute Headache Medication Use in Migraine Patients With Medication Overuse and Documented Inadequate Response to 2-4 Migraine Preventive Medications in the Multicenter, Randomized, Placebo-controlled FOCUS Study

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Conclusions

- Fremanezumab provided early and consistent reductions in the use of acute headache medication versus placebo in patients with medication overuse at baseline and documented inadequate response to 2 to 4 classes of migraine preventive medications
- These results demonstrate that, even in this population of patients with difficult-to-treat migraine, fremanezumab treatment reduces the need for acute headache medication, potentially reducing the risk of medication overuse

Introduction

- Patients who overuse acute medications for migraine generally experience more migraine days, greater migraine severity, and more severe pain intensity[1]
  - Given the increased disease burden for patients with migraine and acute medication overuse, there is a need for effective preventive medications in this population
- 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 migraine and documented inadequate response to 2 to 4 classes of migraine preventive medications[5]

Objective

- A subgroup analysis evaluated changes in the days of use of any acute headache medication in patients from the FOCUS study with medication overuse (use of any acute medication on ≥15 days/month or triptans/ergots/combination medications on ≥10 days/month) at baseline

Methods

Patients

- This study included adult patients with episodic migraine (EM) or chronic migraine (CM) with documented inadequate response to 2 to 4 classes of prior migraine preventive medications
- This subgroup analysis included patients with medication overuse at baseline (**Box 1**)
- Patients in this subgroup analysis were not detoxified or educated/counseled about the risk of medication overuse

Box 1. Definition of Medication Overuse

≥ 15 days/month using any acute medication

≥ 10 days/month using triptans/ergots/combination medications

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
- 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 medication overuse at baseline, changes from baseline in the monthly average number of days of use of any acute headache medication at 4 and 8 weeks and during the 12 weeks after the first dose
  - Differences between groups were compared using an analysis of covariance

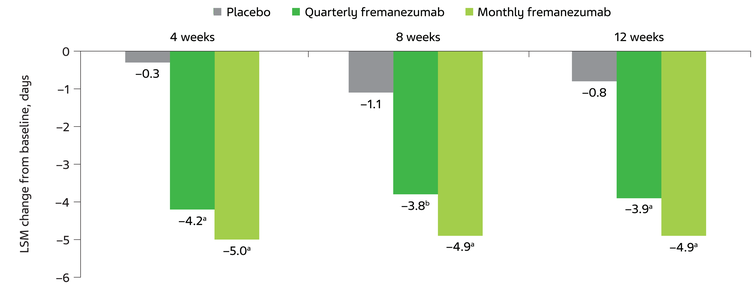
Results

Patients

- Efficacy analysis population (patients with medication overuse), n = 435 (placebo, n = 134; quarterly fremanezumab, n = 152; monthly fremanezumab, n = 149)
- In this subgroup of patients with medication overuse, the monthly average number of migraine days at baseline was: placebo, 17.6 days; quarterly fremanezumab, 16.6 days; monthly fremanezumab, 16.3 days
  - The monthly average number of days of acute headache medication use at baseline for this subgroup was: placebo, 17.3 days; quarterly fremanezumab, 17.1 days; monthly fremanezumab, 16.4 days

Efficacy in Patients With Medication Overuse

Figure 1. In patients with medication overuse, change from baseline in the monthly average number of days of use of any acute headache medication at Weeks 4 and 8 and during 12 weeks.



LSM, least-squares mean.
[a]*P* <0.0001 versus placebo.
[b]*P* = 0.0016 versus placebo.

- In patients with medication overuse at baseline, both fremanezumab regimens significantly reduced the monthly average number of days with any acute headache medication use at 4 and 8 weeks and during the 12 weeks after the first dose versus placebo (**Figure 1**)

Table 1. In Patients With Medication Overuse, LSM Change From Baseline and LSMD Versus Placebo in the Monthly Average Number of Days of Use of Any Acute Headache Medication Over Time

Change from baseline and difference versus placebo	Placebo (n = 134)	Quarterly fremanezumab (n = 152)	Monthly fremanezumab (n = 149)
Week 4			
LSM (SE) change from baseline	−0.3 (0.60)	−4.2 (0.60)[a]	−5.0 (0.54)[a]
LSMD (SE) versus placebo	–	−3.9 (0.70)	−4.7 (0.67)
Week 8			
LSM (SE) change from baseline	−1.1 (0.71)	−3.8 (0.70)[b]	−4.9 (0.63)[a]
LSMD (SE) versus placebo	–	−2.7 (0.87)	−3.8 (0.83)
Week 12			
LSM (SE) change from baseline	−0.8 (0.61)	−3.9 (0.61)[a]	−4.9 (0.55)[a]
LSMD (SE) versus placebo	–	−3.1 (0.72)	−4.1 (0.69)

LSM, least-squares mean; LSMD, least-squares mean difference; SE, standard error.
[a]*P* <0.0001 versus placebo.
[b]*P* = 0.0016 versus placebo.

- Placebo-subtracted reductions in the monthly average number of days with any acute headache medication use were significantly greater with fremanezumab versus placebo at 4 and 8 weeks and during the 12 weeks after the first dose (**Table 1**)

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