Early Onset of Efficacy With Fremanezumab in Patients With Medication Overuse and Documented Inadequate Response to 2-4 Classes of Migraine Preventive Treatments: Subgroup Analysis of the Randomized, Double-blind FOCUS Study

Zaza Katsarava,[1] Martina Machkova,[2] Verena Ramirez Campos,[3] Joshua M. Cohen,[3] Lindsay Janka,[3] Egilius L.H. Spierings[4]

[1]Department of Neurology, University of Duisburg-Essen, Essen, Germany; [2]CCR Czech Prague, Prague, Czech Republic; [3]Teva Branded Pharmaceutical Products R&D, Inc., West Chester, PA, USA; Boston Headache Institute, Waltham, MA, USA.

Conclusions

- Fremanezumab demonstrated early onset of action, with significantly greater response rates versus placebo within 1 week, in patients with medication overuse and documented inadequate response to 2 to 4 classes of migraine preventive medications
- Significantly greater reductions in weekly migraine days and headache days of at least moderate severity also occurred as early as Week 1 and were maintained through Week 3 with both fremanezumab dosing regimens versus placebo
- As patients were not counseled about medication overuse or advised to reduce acute medications, the early reductions in migraine and headache days suggest that patients with medication overuse may not need to be weaned off offending acute medications in order to obtain early and meaningful efficacy with fremanezumab

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 early efficacy in patients 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 (Month 1: 675 mg; Months 2 and 3: placebo), SC monthly fremanezumab (Month 1: EM, 225 mg; CM, 675 mg; Months 2 and 3: 225 mg), or matched monthly placebo

Study Assessments

- In patients with medication overuse at baseline, changes from baseline in weekly migraine headache days and headache days of at least moderate severity and responder rates (≥50% reduction in weekly migraine days) were evaluated at Weeks 1 to 3

Results

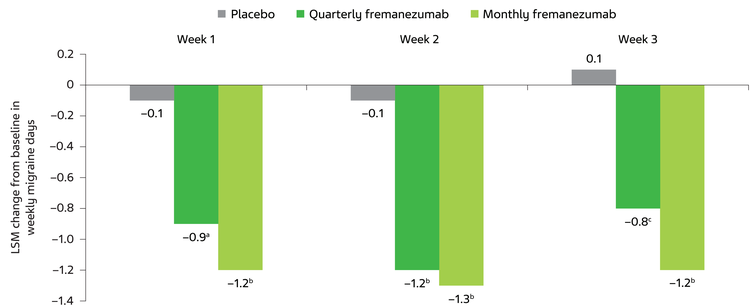
Patients

- 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 was: placebo, 17.6 days; quarterly fremanezumab, 16.6 days; monthly fremanezumab, 16.3 days

Early Efficacy in Patients With Medication Overuse

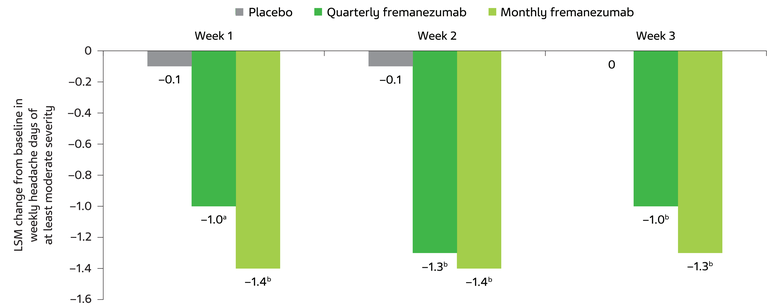
- In patients with medication overuse at baseline, both fremanezumab regimens significantly reduced the weekly average number of migraine days versus placebo (**Figure 1**)
- In patients with medication overuse at baseline, both fremanezumab regimens significantly reduced the weekly average number of headache days of at least moderate severity versus placebo (**Figure 2**)
- Significantly higher proportions of these patients with medication overuse at baseline achieved a ≥50% reduction in the weekly average number of migraine days with fremanezumab versus placebo (**Figure 3**)
  - These early responder rates were achieved by Week 1 and maintained through Week 3 and were significantly greater with fremanezumab versus placebo

Figure 1. In patients with medication overuse, change from baseline versus placebo in weekly migraine days during the first 3 weeks of fremanezumab treatment.



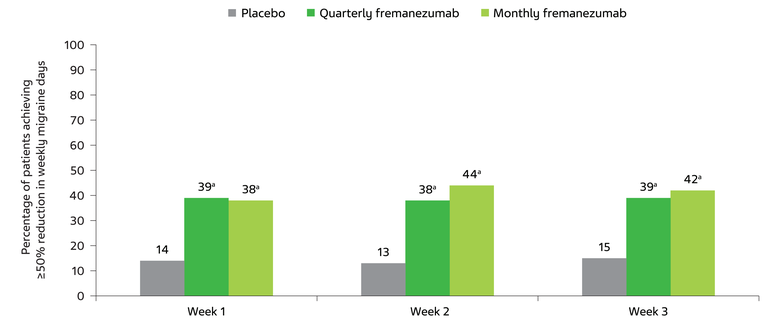
LSM, least-squares mean.
[a]*P* = 0.0018 versus placebo.
[b]*P* <0.0001 versus placebo.
[c]*P* = 0.0004 versus placebo.

Figure 2. In patients with medication overuse, change from baseline versus placebo in weekly headache days of at least moderate severity during the first 3 weeks of fremanezumab treatment.



LSM, least-squares mean.
[a]*P* = 0.0003 versus placebo.
[b]*P* ≤0.0001 versus placebo.

Figure 3. Proportion of patients achieving ≥50% reduction in weekly migraine days during the first 3 weeks of fremanezumab treatment.



[a]*P* <0.0001 versus placebo.

Presented at the PAINWeek Virtual Congress; September 11-13, 2020.

Disclosures: Z. Katsarava has served as a speaker for and received honoraria from Allergan, Novartis, Teva Pharmaceuticals, Lilly, and Merck. M. Machkova was an investigator in the study and, as such, received payment from Teva Pharmaceuticals. V. Ramirez Campos, J.M. Cohen, and L. Janka are employees and/or stockholders of Teva Pharmaceuticals. E.L.H. Spierings was an investigator in the study and, as such, received research grants from Teva Pharmaceuticals and serves on the speakers bureau for Teva Pharmaceuticals.
Acknowledgments: This study (ClinicalTrials.gov Identifier: NCT03308968) is funded by Teva Branded Pharmaceutical Products R&D, Inc. Medical writing and editorial support were provided by Alyssa Nguyen, PharmD, of MedErgy, and were funded by Teva Pharmaceuticals USA, Inc.
References: **1.** Schwedt TJ, et al. *J Headache Pain*. 2018;19(1):38. **2.** Walter S, Bigal ME. *Curr Pain Headache Rep*. 2015;19(3):6. **3.** Dodick DW, et al. *JAMA*. 2018;319(19):1999-2008. **4.** Silberstein SD, et al. *N Engl J Med*. 2017;377(22):2113-2122. **5.** Ferrari MD, et al. *Lancet*. 2019;394(10203):1030-1040.