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(REVIEW ARTICLE)

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A Comparison of Fremanezumab and Eptinezumab in the Prevention of Chronic Episodic Migraine

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Abstract

Chronic migraine is a disorder that affects millions worldwide. Research indicates that people suffering from chronic migraine respond well to monoclonal antibody treatment aimed at characteristic immune cell markers. By targeting immune cell markers, the immune system is subsequently suppressed in a way such that disease activity is decreased. Monoclonal antibody treatments targeted towards a variety of immune cell markers have historically been shown to result in decreases in chronic migraine disease activity. Many studies have assessed disease activity with monoclonal antibody treatments, but few have compared different treatments.

A systematic review of a study that assessed the migraine activity using mean monthly migraine days (MMDs) for those taking fremanezumab was then compared to the findings of another study which assessed the MMDs with those taking eptinezumab

The patients treated with fremanezumab had significantly decreased MMDs when compared with other matched controls. Those who were treated with fresolimumab had significantly decreased MMDs when compared with other matched controls. However, those who were treated with eptinezumab had a greater reduction of MMDs as compared to control groups than did those who were treated with fremanezumab.

Monoclonal antibody treatments for chronic migraine are widespread. It is critical that these treatments are compared in order to find those with the greatest efficacy. For this review, eptinezumab seemed to have a greater reduction of disease activity than did fremanezumab. Further studies with greater sample sizes are needed to conclude which has greater efficacy.

Keywords: Chronic Migraine; Fremanezumab; Eptinezumab; Monoclonal Antibody Therapy; CGRP

1. Introduction

There is sufficient information to suggest that persons suffering from chronic migraine respond well to monoclonal antibody therapy (1). Two prominent monoclonal antibody treatments for the treatment of chronic migraine are the anti-calcitonin gene-related peptide agents such as fremanezumab and eptinezumab(1,2).

Anti-calcitonin gene-related peptide agents are fully humanized monoclonal antibodies that bind to both isoforms of the calcitonin gene-related peptide ligand (1). Calcitonin gene-related peptide is a neuropeptide that is implicated in central and peripheral pathophysiological events that occur in migraine (1).

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It is well known that both of these monoclonal antibody therapies could have effects in reducing mean monthly migraine days (MMDs) for those with chronic migraine, but little has been done to compare their efficacies (1,2). This is especially important to know such that a physician can prescribe the best pharmacological intervention to treat a patient with chronic migraine

2. Methods

For the study conducted using fremanezumab (1):

Study participants were aged 18 to 70 years with episodic migraine (6-14 headache days, with at least 4 migraine days, during 28-day pretreatment period)..Patients were randomized 1:1:1 to receive subcutaneous monthly dosing of fremanezumab (n = 290; 225 mg at baseline, week 4, and week 8); a single higher dose of fremanezumab, as intended to support a quarterly dose regimen (n = 291; 675 mg of fremanezumab at baseline; placebo at weeks 4 and 8); or placebo (n = 294; at baseline, week 4, and week 8).The primary endpoint was mean change in mean number of monthly migraine days during the 12-week period after the first dose.

For the study conducted using eptinezumab (2):

This was a phase 3, double-blind, randomized, placebo-controlled, parallel-group, efficacy, and safety study. Adults 18 to 65 years of age (inclusive) with a diagnosis of migraine at or before 50 years of age were eligible for participation if they had a history of CM for ≥12 months before screening, completed the headache electronic diary (eDiary) on ≥24 of the 28 days after screening visit and before randomization (the screening period), and experienced ≥15 to ≤26 headache days and ≥8 migraine days during the 28-day screening period. Patients used an eDiary to document headaches and migraines for 4 weeks after the screening visit to confirm eligibility criteria and to establish baseline values. Eligible patients were then randomly assigned to receive eptinezumab 100 mg, eptinezumab 300 mg, or placebo in a 1:1:1 ratio. Randomization was stratified by the number of migraine days recorded during the screening period (≤17 vs >17 days) and preventive medication use during the 3 months before screening (use vs no use). The total duration of the study was 32 weeks, with 10 scheduled visits (screening, day 0, and weeks 2, 4, 8, 12, 16, 20, 24, and 32). After the last patient completed the week 12 visit, the analysis of the primary endpoint was performed

3. Results

For the study conducted using fremanezumab (1):

The 875 patients who were randomized (mean age, 41.8 [SD, 12.1] years; 742 women [85%]), 791 (90.4%) completed the trial. From baseline to 12 weeks, mean migraine days per month decreased from 8.9 days to 4.9 days in the fremanezumab monthly dosing group, from 9.2 days to 5.3 days in the fremanezumab single-higher-dose group, and from 9.1 days to 6.5 days in the placebo group. This resulted in a difference with monthly dosing vs placebo of −1.5 days (95% CI, −2.01 to −0.93 days; P < .001) and with single higher dosing vs placebo of −1.3 days (95% CI, −1.79 to −0.72 days; P < .001).

For the study conducted using eptinezumab (2):

Both 100 and 300 mg of eptinezumab demonstrated statistically significant reductions in MMDs during weeks 1 to 12 (p < 0.0001; figure 3 and table 2). MMDs decreased from 16.1 to 8.5 days in the eptinezumab 100 mg group, from 16.1 to 7.9 days in the eptinezumab 300 mg group, and from 16.2 to 10.5 days in the placebo group. Relative to placebo, eptinezumab reduced mean (95% confidence interval) MMDs from baseline (during the 28-day screening period) by −2.0 (−2.9 to −1.2) days for the 100 mg dose and −2.6 (−3.4 to −1.7) days for the 300 mg dose.

Table 1 MMD Results of Each Treatment

Treatment Group	Difference in MMD	p-value
Eptinezumab 100mg	-2.0	p < 0.0001
Eptinezumab 300mg	-2.6	p < 0.0001
Fremanezumab (monthly)	-1.5	p < 0.0001

Fremanezumab (single higher dose)	-1.3	$p < 0.0001$

The above (**Table 1**) depicts the differences in MMD that each treatment had when compared to the respective control groups. The difference in MMD was statistically significant for all treatment groups when compared to the control groups.

4. Conclusion

Our analysis suggests that while both fremanezumab and eptinezumab are likely effective in reducing MMDs, both eptinezumab groups were able to reduce MMDs more than either fremanezumab-treated groups. This also indicates that eptinezumab likely targets the calcitonin gene-related peptide ligand more specifically and with a higher affinity than does fremanezumab. The analyses are limited in the sense that they both couldn't accurately control for the severity of chronic migraine and comorbidities. Additionally, the length of both research studies could not be controlled. There is also the likelihood that there is another immune marker that may be even more implicated in the pathogenesis of chronic migraine than calcitonin gene-related peptide. Also, further studies must be conducted with larger sample sizes controlling for age and other demographic factors. While eptinezumab shows promising results, there is plenty more investigation that must be conducted to find the most effective monoclonal antibody treatment for chronic migraine.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

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