Headache Medicine

ID: 64

Efficacy of fremanezumab in patients with migraine and comorbid depression: a systematic review and meta-analysis

Carolina Alves Corrêa[1], Gabriela Carolino[2], Yasmin Nunes[3], Amanda Rabelo[4], John Neto[5], Julia Oliveira[6]

[1]Minas Gerais School of Medical Sciences, Belo Horizonte, Minas Gerais, Brazil
[2]Juiz de Fora School of Medical and Health Sciences, Juiz de Fora, Minas Gerais, Brazil
[3]Afya School of Medical Sciences of Palmas, Palmas, Tocantins, Brazil
[4]Bauru School of Medicine, Bauru, São Paulo, Brazil
[5]Salvador University, Salvador, Bahia, Brazil
[6]Pontifical Catholic University of Minas Gerais, Belo Horizonte, Minas Gerais, Brazil

Carolina Alves Corrêa
carolalvescorrea8@gmail.com

Introduction
Migraine is the leading cause of disability among individuals under 50 years of age. Population-based studies indicate that depression is a common comorbidity in individuals living with migraine, with a bidirectional relationship in which each condition increases the risk of onset of the other. Despite the availability of preventive and acute treatments, a substantial proportion of patients remain inadequately controlled, particularly those with comorbid psychiatric conditions. Fremanezumab, a fully humanized monoclonal antibody targeting calcitonin gene-related peptide (CGRP), has emerged as a potential therapeutic strategy and has been associated with reductions in headache and migraine days.

Objective
To evaluate the efficacy of Fremanezumab in patients with migraine and depression.

Methods
We conducted a systematic review and meta-analysis following Cochrane guidelines. PubMed, Embase, and Cochrane databases were searched for randomized controlled trials (RCTs) or observational studies. Eligible studies included adult patients with chronic or episodic migraine and comorbid depression. Depressive symptoms were defined using validated diagnostic criteria or standardized assessment tools, including a Patient Health Questionnaire-9 (PHQ-9) score ≥10. The primary outcome was the change in monthly migraine days (MMD) from baseline. As a secondary outcome, changes in depressive symptom severity were assessed using the PHQ-9 score.

Results
Three randomized studies comprising 608 patients were included after screening 253 records; of these, 69 (11.3%) were male, with a median age of 42 years. Pooled analysis showed that fremanezumab significantly reduced monthly migraine days (MMD) compared with control (MD −2.68; 95% CI −3.77 to −1.59; $p < 0.0001$; $I^2=0\%$). Depressive symptom severity, assessed using the PHQ-9, showed a consistent trend toward improvement across the included studies. In the HALO CM trial, fremanezumab was associated with numerically greater reductions in PHQ-9 scores with quarterly (−10.9±1.01) and monthly dosing (−9.8±0.93) compared with placebo (−9.2). Similar findings were observed in the UNITE study, in which monthly fremanezumab also demonstrated a trend toward greater improvement in PHQ-9 scores versus placebo.

Conclusion
Fremanezumab is associated with a clinically meaningful reduction in MMD in patients with migraine and depression, with consistent trends toward improvement in depressive symptom severity as assessed by PHQ-9 scores. Further high-quality studies are warranted to better define its impact, particularly in specific subpopulations and clinical contexts.

Keywords:
Migraine
Depression
Fremanezumab
Meta-analysis

© Copyright 2025