

Efficacy of Fremanezumab in Patients With Chronic Migraine and Comorbid Moderate to Moderately Severe Depression

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Introduction: Depression is common in chronic migraine (CM) and contributes to the already substantial burden of disease. Fremanezumab, a fully humanized monoclonal antibody (IgG2Δa) selectively targeting calcitonin gene-related peptide, has demonstrated efficacy in migraine prevention. This study evaluated fremanezumab's efficacy on migraine and headache frequency and depressive symptoms in patients with CM and comorbid moderate to moderately severe depression. **Methods:** In this Phase 3, multicenter, randomized, double-blind placebo-controlled study, eligible patients aged 18–70 with prospectively confirmed CM (≥ 15 headache days and ≥ 8 migraine days per month) were randomized 1:1:1 to receive subcutaneous injections of fremanezumab quarterly (675 mg at baseline; placebo at Weeks 4 and 8), fremanezumab monthly (675 mg at baseline; 225 mg at Weeks 4 and 8), or placebo over a 12-week treatment period. *Post hoc* analyses evaluated changes in headache and migraine frequency and depressive symptoms in patients with moderate to moderately severe depression (score of 10–19 on the nine-item Patient Health Questionnaire [PHQ-9]) at baseline. **Results:** Almost 20% (219/1130) of patients had moderate to moderately severe depression at baseline (quarterly, n=74; monthly, n=88; placebo, n=57). As in the overall study population, fremanezumab-treated patients in this subgroup had significant reductions from baseline in the mean number of monthly headache days of at least moderate severity (quarterly: -5.4 ± 0.79 ; monthly: -5.6 ± 0.75) versus those who received placebo (-2.2 ± 0.84) during the treatment period (both, $P < 0.001$), with effects observed as early as Week 4 ($P < 0.0001$). Similar treatment differences were observed for change in the mean number of migraine days ($P < 0.001$). Fremanezumab also reduced the mean PHQ-9 score from baseline to Week 12 (quarterly: -10.6 ± 0.96 ; monthly: -9.5 ± 0.90) versus placebo (-8.7 ± 1.01), but significance was not reached. **Conclusions:** Fremanezumab demonstrated efficacy in preventive treatment of CM in patients with comorbid moderate to moderately severe depression, reducing migraine and headache frequency.