Long-term safety, tolerability, and efficacy of fremanezumab in migraine
A randomized study

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Study question
Is fremanezumab a safe, tolerable, and effective long-term preventive treatment for migraine?

What is known and what this paper adds
Two 12-week phase 3 trials provided evidence for the safety and efficacy of fremanezumab as a preventive treatment for migraine. This trial’s results provide evidence for its safety and efficacy over 12 months.

Methods
This double-blind, parallel-group, phase 3 trial included 1,110 patients with chronic migraine (CM) and 780 patients with episodic migraine (EM) at 135 sites in the United States, Canada, the European Union, Russia, and Israel. Participants had previously completed a placebo-controlled trial of fremanezumab (HALO) or were newly enrolled. Trial procedures occurred between March 2016 and December 2018. Participants were randomized to groups receiving fremanezumab monthly (559 patients with CM and 386 patients with EM) or quarterly (551 patients with CM and 394 patients with EM) administered as subcutaneous injections. Over 12 months, the investigators recorded adverse events, monthly migraine days, and monthly headache days. Prespecified exploratory efficacy outcomes were the from-baseline changes in monthly migraine days and headache days over 12 months.

Results and study limitations
The most common adverse events were injection-site reactions, including induration (33%), pain (31%), and erythema (26%). Serious AEs occurred in 5%–7% of patients and were similar across treatment groups. Patients with CM and patients with EM receiving either dosing regimen (quarterly or monthly) experienced from-baseline reductions in monthly migraine days and in monthly headache days of at least moderate severity. These findings provide Class IV evidence for fremanezumab being safe, well tolerated, and effective over 12 months. The present study’s limitations include the lack of a placebo group and that the study was not powered to detect between-group differences in efficacy outcomes. Further, the exclusion of patients with continuous headache or ineffective therapy with ≥2 preventive drug classes may limit generalizability.

Table  Efficacy outcomes for each fremanezumab treatment group

<table>
<thead>
<tr>
<th>Treatment group</th>
<th>Mean 12-month from-baseline change in:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Monthly migraine days</td>
<td>Monthly headache days</td>
</tr>
<tr>
<td>CM quarterly</td>
<td>−7.2 ± 0.3</td>
<td>−6.4 ± 0.3</td>
</tr>
<tr>
<td>CM monthly</td>
<td>−8.0 ± 0.3</td>
<td>−6.8 ± 0.3</td>
</tr>
<tr>
<td>EM quarterly</td>
<td>−5.2 ± 0.2</td>
<td>−4.4 ± 0.2</td>
</tr>
<tr>
<td>EM monthly</td>
<td>−5.1 ± 0.2</td>
<td>−4.2 ± 0.2</td>
</tr>
</tbody>
</table>

Registration, study funding, and competing interests
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