Efficacy and safety of eptinezumab in patients with chronic migraine

PROMISE-2

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Study objective and summary result
This trial evaluated the efficacy of eptinezumab as a preventive treatment for chronic migraine (CM), and the results showed that eptinezumab reduces migraine frequency in patients with CM.

Classification of evidence
Class I.

What is known and what this paper adds
Several monoclonal antibodies that target calcitonin gene–related peptide (CGRP) have received regulatory approval as preventive treatments for CM. Eptinezumab is the first intravenous CGRP-targeting monoclonal antibody for migraine, and this trial’s results provide evidence for efficacy and safety of eptinezumab in prevention of chronic migraine.

Participants and setting
For the Prevention of Migraine via Intravenous ALD403 Safety and Efficacy–2 (PROMISE-2) trial, the investigators recruited 1,072 adults with ≥12-month histories of CM through 128 sites in 13 countries. Each participant experienced 15–26 headache days and ≥8 migraine days during a 28-day screening period. The trial began on November 30, 2016, and ended on April 20, 2018.

Design, size, and duration
In this double-blind phase 3 trial, the investigators randomized the participants 1:1:1 to groups that received IV administrations of placebo (n = 366), 100 mg of eptinezumab (n = 356), or 300 mg of eptinezumab (n = 350) at baseline and in week 12. The participants recorded their headaches in daily electronic diary entries for 24 weeks.

Primary outcome measures
The primary outcome was changes from-baseline in monthly migraine days (MMDs) in weeks 1 through 12 (or month 1 through 3).

Main results and the role of chance
The eptinezumab groups’ from-baseline MMD reductions were greater than those of the placebo group (p < 0.0001).

Harms
The placebo and eptinezumab groups had similar rates of treatment-emergent adverse events.

Bias, confounding, and other reasons for caution
The overall response to placebo was strong, so may have inflated the observed absolute drug efficacy.

Generalizability to other populations
The presence of serious comorbidities was an exclusion criterion for the PROMISE-2 trial. This may limit the generalizability of the trial’s results to patients with serious comorbidities.

Study funding/potential competing interests
This study was funded by H. Lundbeck A/S. Some authors report receiving honoraria, consulting fees, committee appointments, and funding from various healthcare companies, science publishers, foundations, and scholarly societies, including Lundbeck Seattle BioPharmaceuticals and the American Academy of Neurology; receiving employment from healthcare companies, including Lundbeck Seattle BioPharmaceuticals; and owning stock in healthcare companies, including Lundbeck Seattle BioPharmaceuticals. Go to Neurology.org/N for full disclosures.

Trial registration number
NCT02974153 on ClinicalTrials.gov.
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