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RESEARCH SUBMISSIONS

Long-term (48 weeks) effectiveness, safety, and tolerability of erenumab in the prevention of high-frequency episodic and chronic migraine in a real world: Results of the EARLY 2 study

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Abstract

Objective: To evaluate the long-term effectiveness, safety, and tolerability of erenumab in a real-world migraine population, looking for putative predictors of responsiveness.

Background: Erenumab proved to be effective, safe, and well tolerated in the prevention of episodic migraine (EM) and chronic migraine (CM) in long-term extension studies of double-blind, placebo-controlled trials in patients with no more than two (EM) or three (CM) prior preventive treatment failures.

Methods: A 48-week, multicenter, longitudinal cohort real-life study was conducted at 15 headache centers across eight Italian regions between December 20, 2018 and July 31, 2020. We considered all consecutive patients with high-frequency episodic migraine (HFEM) or CM aged 18–65 years. Each patient was treated with erenumab 70 mg, administered monthly. The dose was switched to 140 mg in nonresponders and in responders who had become nonresponders for at least 4 weeks. Change in monthly migraine days (MMDs) or monthly headache days (MHDs) at Weeks 45–48 compared with baseline was the primary efficacy endpoint. Secondary endpoints encompassed variation in monthly analgesic intake, achievement of a ≥50%, ≥75%, or 100% reduction in migraine or headache days, and any change in the Visual Analogue Scale (VAS) and Headache Impact Test-6 scores (HIT-6) during the same time interval.

Results: A total of 242 patients with migraine received at least one dose of erenumab 70 mg and were considered for safety analysis, whereas 221 received a monthly erenumab dose for ≥48 weeks and were included in the effectiveness and safety analysis set. All patients had previously been treated unsuccessfully with ≥3 migraine-preventive medication classes. From baseline to Weeks 45–48, erenumab treatment reduced MMD by 4.3 ± 5.3 (mean ± SD) in patients with HFEM, and MHD by

Abbreviations: AE, adverse event; CGRP, calcitonin gene-related peptide; CM, chronic migraine; EARLY, ErenumAb in Real Life in Italy; HFEM, high-frequency episodic migraine; HIT-6, Headache Impact Test-6; mAbs, monoclonal antibodies; MHDs, monthly headache days; MMDs, monthly migraine days; VAS, Visual Analogue Scale.

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12.8 ± 8.9 (mean ± SD) in subjects with CM. VAS and HIT-6 scores were decreased by 1.8 ± 1.9 (mean ± SD) and 12.3 ± 11 (mean ± SD) in HFEM, and by 3.0 ± 2.2 (mean ± SD) and 13.1 ± 11.2 (mean ± SD) in CM. Median monthly analgesic intake passed from 11.0 (interquartile range [IQR] 10.0–13.0) to 5 (IQR 2.0–8.0) in HFEM and from 20.0 (IQR 15.0–30.0) to 6.0 (IQR 3.8–10.0) in CM. The ≥50% responders were 56.1% (32/57) in HFEM and 75.6% (124/164) in CM; ≥75% responders were 31.6% (18/57) and 44.5% (73/164); and 100% responders were 8.8% (5/57) and 1.2% (2/164), respectively. At Week 48, 83.6% (137/164) of patients with CM had reverted to EM. Erenumab was safe and well tolerated. Responsiveness to erenumab was positively associated with cutaneous allodynia (OR: 5.44, 95% CI: 1.52–19.41; $p = 0.009$) in HFEM. In patients with CM, ≥50% responsiveness was positively associated with male sex (OR: 2.99, 95% CI: 1.03–8.7; $p = 0.044$) and baseline migraine frequency (OR: 1.12, 95% CI: 1.05–1.20; $p = 0.001$) and negatively associated with psychiatric comorbidities (OR: 0.37, 95% CI: 0.15–0.87; $p = 0.023$) and prior treatment failures (OR: 0.77, 95% CI: 0.64–0.92; $p = 0.004$).

Conclusions: Long-term (48-week) erenumab treatment provides sustained effectiveness, safety, and tolerability in real-life patients with HFEM or CM with ≥3 prior preventive treatment failures. The dose of 140 mg was required in most patients along the study and should be taken into consideration as the starting dose. Allodynia (in HFEM), male sex, and baseline migraine frequency (in CM) might represent positive responsiveness predictors. Conversely, psychiatric comorbidities and multiple prior preventive treatment failures could be negative predictors in patients with CM.

KEYWORDS
allodynia, calcitonin gene-related peptide, erenumab, long-term treatment, migraine, sex

INTRODUCTION

Migraine is a chronic, evolutive, neurological disease with paroxysmal manifestations that warrants an appropriate preventive treatment in patients with frequent (≥4 migraine days/month) or disabling episodes inadequately managed by acute medications.[1–3] However, migraine prophylaxis is underutilized and often hampered to date by the lack of effectiveness, poor tolerability, and low treatment adherence of standard pharmacological therapies, characterized by a 16- to 24-week discontinuation rate ranging from 23% with propranolol to 43.1% with topiramate to 45.1% with amitriptyline.[4,5] Effective and well-tolerated migraine prevention improves quality of life by reducing attack frequency and interictal disability, which reduces migraine-related stress, cephalalgiophobia, and avoidant behaviors.[6–8]

A valuable possibility of improving migraine prophylaxis is now offered by monoclonal antibodies (mAbs) to the calcitonin gene-related peptide (CGRP) or to its receptor, characterized by a favorable efficacy–tolerability ratio, which allows to extend the treatment for more than 3–6 months, the duration of usual migraine prevention.[9,10] CGRP mAbs demonstrated sustained efficacy with good safety and tolerability in long-term, open-label extension studies of 12- or 24-week, double-blind treatment phases.[11–15] These findings led the European Headache Federation to suggest a prolonged CGRP mAb use (up to12 months) in both episodic migraine (EM) and chronic migraine (CM).[16]

In the 12-week, real-life, EARLY (ErenumAb in Real Life in Italy) study, we documented a high effectiveness and tolerability of erenumab in 373 patients with migraine affected by high-frequency episodic migraine (HFEM: ≥8 migraine days/month) or CM with multiple (≥3) prior therapeutic failures.[17] Here, we describe the results of the long-term EARLY 2 study, a 48-week, multicenter, prospective, cohort study involving 242 patients affected by HFEM or CM, aimed at verifying whether long-term erenumab treatment results in sustained efficacy, safety, and tolerability in the real world. We hypothesized that the long-term treatment with erenumab is effective, safe, and well tolerated in a real-life setting.

METHODS

EARLY 2 is a 48-week, multicenter, longitudinal, cohort, real world, evidence study conducted at 15 headache centers across eight Italian regions (Lombardy, Piedmont, Liguria, Emilia-Romagna, Latium, Campania, Basilicata, and Calabria) from December 20, 2018 to July 31, 2020.