Efficacy of Erenumab in Chronic Migraine Patients With Acute Headache Medication Overuse: A Post Hoc Analysis Assessing Outcomes Using Different Definitions of Remission

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INTRODUCTION

- Patients with chronic migraine (CM) and medication overuse (MO) who have had lack of success with prior preventive treatment are a difficult-to-treat patient subgroup
- Erenumab (in the US, erenumab-aooe), a fully human anti–calcitonin gene-related protein (CGRP) receptor monoclonal antibody approved for migraine prevention,[1] has efficacy in patients with CM[2]
- The impact of erenumab on CM with medication overuse headache (MOH) is currently unknown; a randomized controlled trial in patients with CM-MOH (NCT03971071) is underway to evaluate the efficacy and safety of erenumab in this subgroup
- A post hoc analysis of a double-blind, placebo-controlled, 12-week study of patients with CM (NCT02066415)[2] was conducted to inform the potential benefit-risk of erenumab in CM-MOH patients

OBJECTIVE

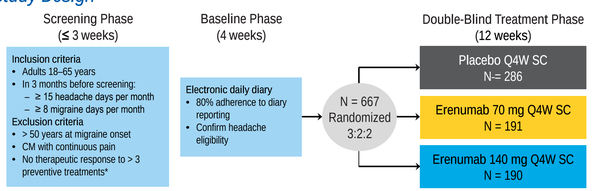
- The objective of this analysis was to evaluate the effect of erenumab on remission from MO in patients with CM who lacked success with ≥ 1 prior preventive therapy

METHODS

- Post hoc subgroup analysis of patients with CM with:
  - ≥ 14 headache days during a 28-day (4-week) baseline period
  - Observed MO (ie, ≥ 15 days of simple analgesics or ≥ 10 days of triptans, ergots, or combination therapy/month) during the 4-week baseline period
  - ≥ 1 failed prior preventive treatment category due to lack of efficacy or poor tolerability
- Preventive treatment (erenumab 70 and 140 mg subcutaneously monthly) was compared with placebo
- Using strict interpretation of ICHD-3 classification,[3] remission from MOH requires:
  - Reduction in headache days to < 15 monthly headache days (MHDs) or
  - Reduction in medication use to below MO threshold
- To adjust for a "study month" in controlled trials being 4 weeks rather than a calendar month, the guidelines of the International Headache Society[4] recommend that in clinical trials CM is defined as:
  - ≥ 14 headache days and ≥ 8 migraine days over 4 weeks
- Therefore, in this post hoc analysis we adjusted the cutoff for reduction in headache days to < 14 headache days over 4 weeks to meet the headache day criterion for remission of MOH
- Three remission definitions were defined:

- We assessed remission by all 3 definitions at weeks 9 to 12 (ie, week 12)

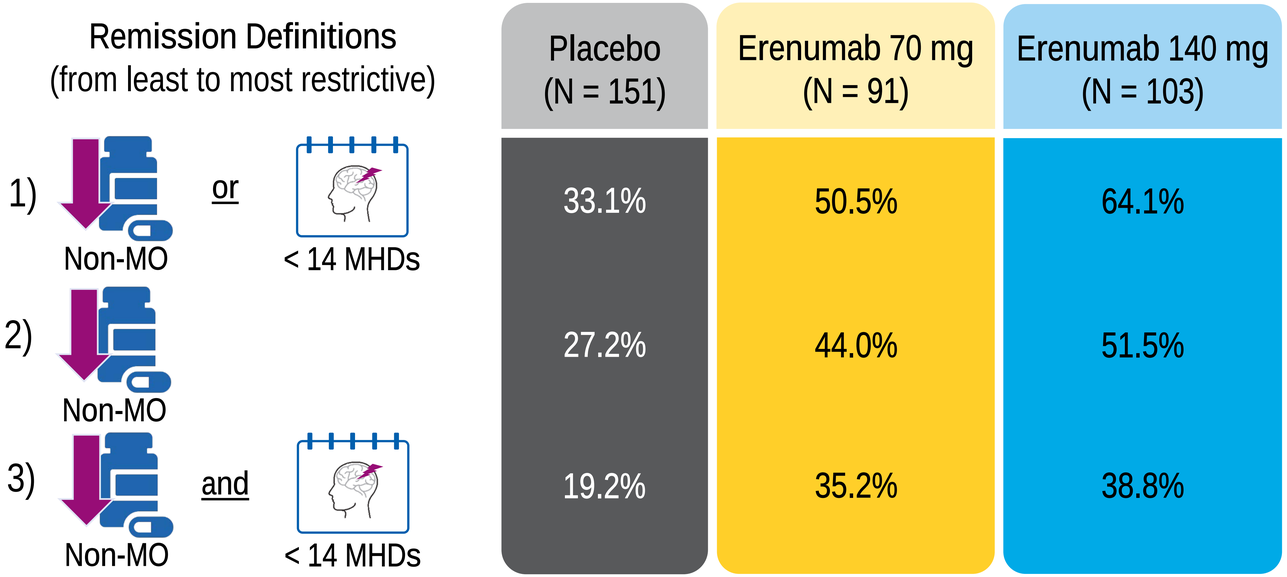
Study Design[2]



*No reduction in frequency, duration or severity of headache after ≥ 6 weeks of treatment at generally accepted doses of the preventive treatment
CM = chronic migraine; Q4W = once every 4 weeks; SC = subcutaneous

RESULTS

Remission was Achieved More Frequently In Erenumab Patients Than In Placebo Patients at Week 12



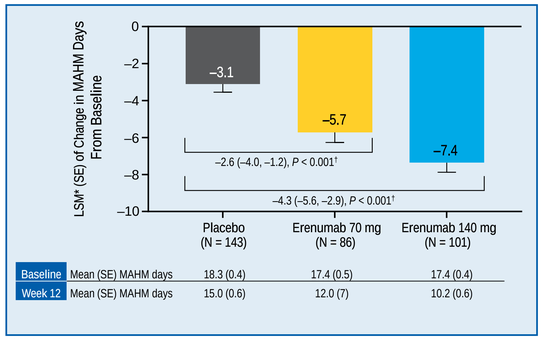
MHD = monthly headache days; MO = medication overuse

Patient Demographics and Baseline Characteristics in CM Patients With MO who Had Lack of Success With Prior Preventive Treatment (N = 349)

	Age, Female, White	Monthly Headache Days*	Monthly Acute Headache Medication Days	Monthly Acute Migraine-Specific Medication Days	Triptan Overuse†
Placebo (N = 153)	44.0 y, 78.4%, 96.1%	16.3	18.3	13.2	71.9%
Erenumab 70 mg (N = 92)	43.3 y, 89.1%, 96.7%	16.7	17.4	12.5	75.0%
Erenumab 140 mg (N = 104)	44.3 y, 88.5%, 99.0%	16.4	17.3	13.0	76.0%

Data represent mean unless otherwise indicated
*Moderate to severe
†Patients with ≥ 10 days of triptan use at baseline

Erenumab 70 and 140 mg Significantly Reduced Monthly Acute Headache Medication Days Compared With Placebo at Week 12



*LSM (SE) is estimated from a generalized linear mixed model adjusting for treatment, visit, treatment by visit interaction, stratification factor region, and baseline value
†Difference in LSM (95% CI) for erenumab versus placebo; nominal *p*-values
CI = confidence interval; LSM = least squares mean; MAHM = monthly acute headache medication; SE = standard error

CONCLUSIONS

- Erenumab significantly reduced monthly acute headache medication days compared with placebo in CM patients with MO who had lack of success with prior preventive treatment
- Across all definitions of remission from medication overuse, erenumab 140 mg consistently demonstrated numerically better outcomes than erenumab 70 mg
- The follow-up study underway to confirm the efficacy of erenumab in patients with MOH applies the strict ICHD-3 interpretation for MOH remission assessed over 3 months

LIMITATIONS

- This was a post hoc analysis; therefore, results must be interpreted with caution
- Medication overuse status was based on overuse during a 4-week baseline period, and not the > 3-month period used for the ICHD-3 diagnosis of MOH[3]
- As the concomitant diagnosis of MOH was not systematically collected during screening it is unknown how many of the patients included in this post hoc analysis had MOH
- The double-blind treatment phase was 12 weeks, precluding assessment of the long-term effectiveness of erenumab compared with placebo in patients with MO beyond this point

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