Effects of Erenumab on Non-pain Symptoms in Patients with Chronic Migraine

Stewart J Tepper,[1] Uwe Reuter,[2] Messoud Ashina,[3] Jan L Brandes,[4] Feng Zhang,[5] Nan Sun,[6] Xiangyi Meng,[6] Ahmad Abdrabboh,[6] Ronald Zielman,[7] Denise E Chou,[5] Paul Winner[8]

[1]Geisel School of Medicine at Dartmouth, Hanover, NH, CA, USA; [2]Dept Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany; [3]Dept Neurology, Danish Headache Center, Rigshospitalet Glostrup, Faculty of Health and Medical Sciences, University of Copenhagen, Denmark; [4]Nashville Neuroscience Group and Vanderbilt University Department of Neurology, Nashville, TN, USA; [5]Amgen Inc., Thousand Oaks, CA, USA; [6]Novartis Pharmaceuticals Corporation, East Hanover, NJ, USA; [7]Novartis Pharma AG, Basel, Switzerland; [8]Premiere Research Institute, Nova Southeastern University, West Palm Beach, FL, USA

Introduction

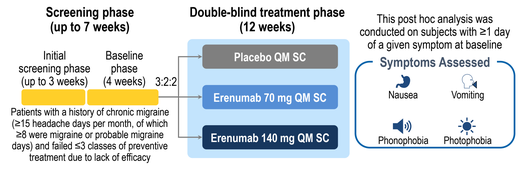
- Migraine is a major cause of pain and disability, afflicting 14.4% of individuals worldwide[1]
- Chronic migraine (CM), which is defined as headaches occurring on ≥15 days/month for >3 months, which, on at least 8 days/month, have features of migraine headache, affects approximately 1–2% of the global population[2,3]
- Erenumab (erenumab-aooe in the U.S.) is a fully human monoclonal antibody that inhibits the calcitonin gene-related peptide receptor and is indicated for the preventive treatment of migraine in adults
- In a Phase 2 pivotal study of adults with chronic migraine (NCT02066415), erenumab treatment (both 70 mg and 140 mg) led to a greater reduction from baseline in mean monthly migraine days (MMDs) compared to placebo [-2.5 days, 95% CI (-3.5, -1.4), p<0.001][4]
- Non-pain symptoms are frequently cited by patients as their most bothersome migraine-associated symptoms and are often disabling[5]
- However, changes in non-pain migraine symptoms are inconsistently assessed in migraine prevention trials, resulting in a paucity of evidence to inform clinical practice

Objective

The objective of this post hoc analysis was to assess effects of erenumab on migraine-associated non-pain symptoms

Methods

Study design



Analysis of patient-reported non-pain symptoms in people living with CM

Symptom Collection & Severity Scoring

Severity of non-pain symptoms was collected on days where patients reported a headache, and was assessed using a categorical scale:

0	1	2	3
Symptom-free	Mild	Moderate	Severe

Endpoints

Change from baseline in:
- Number of monthly non-pain symptom days
- Cumulative monthly symptom severity[a]
- Monthly average symptom severity[b]

Analyses

- The ANCOVA model was applied to all analyses
- Treatment effects at Week 12 were reported as differences [least-squares mean (95% CI)] in changes from baseline relative to placebo; *p* values are nominal without multiplicity adjustment

[a]Defined as the sum of patient-reported daily worst symptom score per monthly interval.
[b]Defined as the sum of the severity of corresponding migraine symptom between each monthly dose divided by the total number of observed qualified migraine days in that interval. For monthly average severity of symptoms at baseline, data collected from week -4 through the day prior to study day 1 were utilized.

Preventive treatment with erenumab in CM may reduce days with migraine-associated non-pain symptoms, including light/sound sensitivity, nausea, and vomiting, highlighting the potential benefit of erenumab therapy in improving disease burden beyond migraine headache frequency.

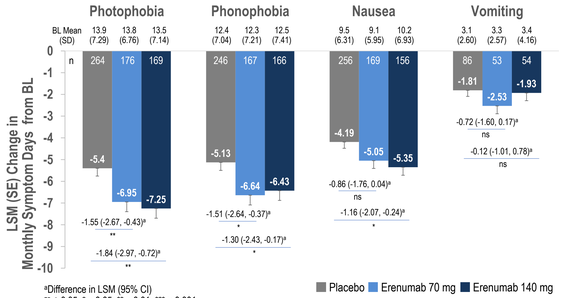
Table 1. Baseline and clinical characteristics

Baseline characteristics	Placebo (N=281)	Erenumab 70 mg (N=188)	Erenumab 140 mg (N=187)
Mean age, years (SD)	42.1 (11.4)	41.2 (11.3)	43.1 (11.1)
Female gender, n (%)	224 (79.7)	165 (87.8)	159 (85.0)
White race, n (%)	263 (93.6)	173 (92.0)	181 (96.8)
MMDs, mean (SD)	18.2 (4.7)	17.9 (4.4)	17.8 (4.7)
Prior prophylactic topiramate use, n (%)	150 (53.4)	87 (46.3)	97 (51.9)
Prior onabotulinum toxin use, n (%)	65 (23.1)	48 (25.5)	43 (23.0)
Subjects with photophobia, n (%) Days with photophobia, mean (SD)[a]	264 (94.0) 13.9 (7.3)	176 (93.6) 13.8 (6.8)	169 (90.4) 13.5 (7.1)
Subjects with phonophobia, n (%) Days with phonophobia, mean (SD)[a]	246 (87.5) 12.4 (7.0)	167 (88.8) 12.3 (7.2)	166 (88.8) 12.5 (7.4)
Subjects with nausea, n (%) Days with nausea, mean (SD)[a]	256 (91.1) 9.5 (6.3)	169 (89.9) 9.1 (6.0)	156 (83.4) 10.2 (6.9)
Subjects with vomiting, n (%) Days with vomiting, mean (SD)[a]	86 (30.6) 3.1 (2.6)	53 (28.2) 3.3 (2.6)	54 (28.9) 3.4 (4.2)

N=number of patients in the efficacy analysis set; n=number of patients analyzed.
[a]Mean and SD were computed based on the n experiencing indicated symptom at baseline.

Erenumab treatment led to significantly greater reductions in photophobia and phonophobia days and improvements in MMDs relative to placebo at Week 12

Figure 1. Change from baseline in monthly non-pain symptom days



[a]Difference in LSM (95% CI)
n≥0.05, *p<0.05, **p<0.01, ***p<0.001

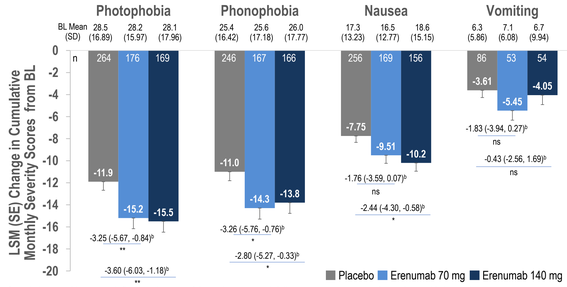
Table 2. Outcomes at Week 12 in subjects with ≥1 non-pain symptom at baseline

Week 12	Placebo (N=263)	Erenumab 70 mg (N=175)	Erenumab 140 mg (N=178)
MMDs, mean (SD)	14.05 (7.1)	11.17 (7.5)	11.26 (7.5)
Change from baseline, days (SE)	-4.20 (0.39)	-6.85 (0.47)	-6.70 (0.47)
Placebo-adjusted difference, days	-	-2.64	-2.49
95% CI	-	-3.84, -1.45	-3.68, -1.30
p-value	-	< 0.001	< 0.001
Subjects with photophobia, n (%)	256 (97.3)	162 (92.6)	160 (89.9)
Days with photophobia, mean (SD)[a]	8.4 (7.2)	7.0 (7.3)	6.5 (6.8)
Subjects with phonophobia, n (%)	237 (90.1)	153 (87.4)	158 (88.8)
Days with phonophobia, mean (SD)[a]	7.3 (7.2)	5.8 (6.9)	6.1 (6.9)
Subjects with nausea, n (%)	246 (93.5)	157 (89.7)	149 (83.7)
Days with nausea, mean (SD)[a]	5.4 (5.9)	4.3 (5.0)	4.7 (5.9)
Subjects with vomiting, n (%)	85 (32.3)	48 (27.4)	49 (27.5)
Days with vomiting, mean (SD)[a]	1.3 (2.9)	0.7(1.1)	1.3 (3.9)

[a]Mean and SD were computed based on the n experiencing indicated symptom at Week 12.

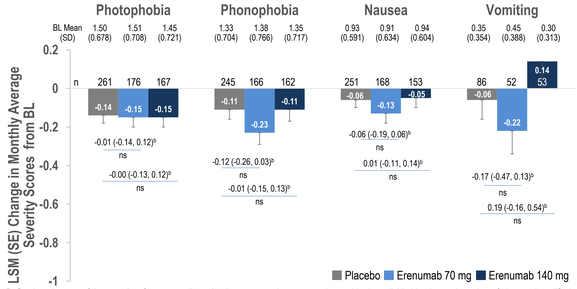
At Week 12, erenumab treatment led to a significantly greater reduction from baseline in cumulative monthly photophobia and phonophobia severity relative to placebo; monthly average non-pain symptom severity was similar between treatment groups

Figure 2. Changes in cumulative monthly non-pain symptom severity[a]



[a]Cumulative monthly scores defined as the sum of the patient-reported daily worst symptom score for each monthly interval.
[b]Difference in LSM (95% CI).
n≥0.05, *p<0.05, **p<0.01, ***p<0.001

Figure 3. Changes in monthly average non-pain symptom severity[a]



[a]Defined as the sum of the severity of corresponding migraine symptom between each monthly dose divided by the total number of observed qualified migraine days in that interval
[b]Difference in LSM (95% CI).
n≥0.05

Results

- Baseline characteristics, including MMDs, of subjects in the overall study (efficacy analysis set) were generally similar between treatment groups (**Table 1**)
- Treatment with erenumab led to significant reductions from baseline in both the number of days with photophobia and the number of days with phonophobia relative to placebo (**Fig. 1**)
- In patients with ≥1 non-pain symptom at baseline, treatment with erenumab led to a significant reduction in MMDs relative to placebo at Week 12, consistent with the overall study (**Table 2**)
- Relative to placebo, erenumab treatment led to a reduction from baseline in cumulative monthly symptom severity of both photophobia and phonophobia (**Fig. 2**)
- Change from baseline in monthly average non-pain symptom severity was largely similar between treatment groups (**Fig. 3**)

Disclosures

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Abbreviations: BL, Baseline; CI, confidence interval; CM, chronic migraine; LSM, least-squares mean; MMDs, monthly migraine days; ns, not significant; QM, once monthly; SC, subcutaneous; SD, standard deviation; SE, standard error.

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Corresponding author email address: sitepper@gmail.com
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