OPR-200

Erenumab versus topiramate for the prevention of migraine: Results of a randomized active-controlled double-dummy trial (HER-MES)

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Disclosures

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Marc Ehrlich, Jan Klatt, Shihua Wen, Peggy Hours-Zesiger, Jacqueline Nickisch, Christian Sieder, Christian Hentschke, and Monika Maier-Peuschel are employees of Novartis and as such, may be eligible for Novartis stock and stock options.

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Background and Objective

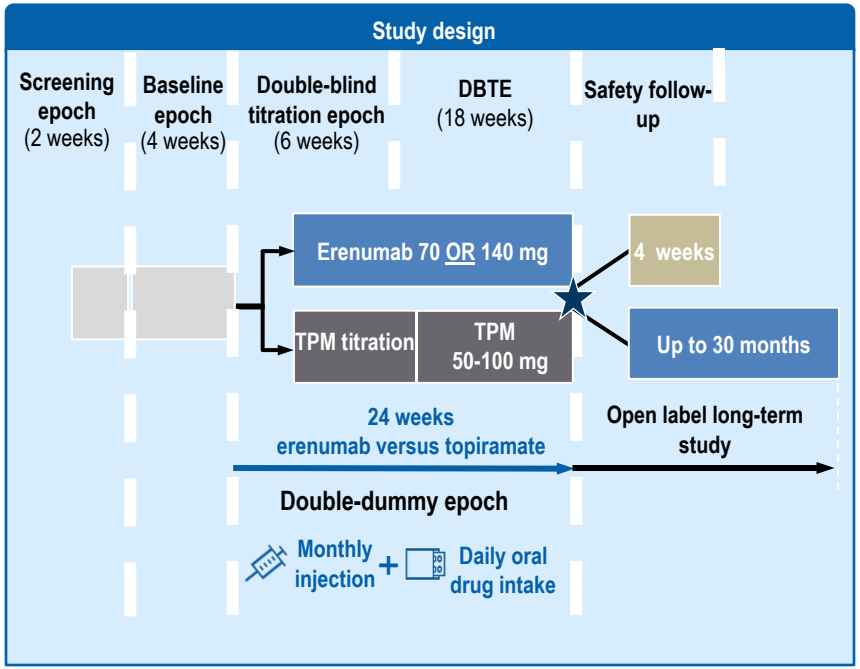
- Migraine is one of the most common causes of disability worldwide and the third-leading cause of health loss in men and women less than 50 years old[1]
- Only about 12% of the population with episodic migraine, or migraine which occurs less than 15 days per month, are using a preventative treatment[2]
- Health resources and costs are substantially occupied, directly by health care and indirectly by a reduced working capability[3]
- Current preventative oral migraine therapies are frequently discontinued, largely due to tolerability issues and/or perceived lack of efficacy of the drugs[4]
- Erenumab is a monoclonal antibody targeting the CGRP receptor
- In 2018, the FDA and EMA approved erenumab as the first medication specifically developed for migraine prevention
- For the first time, erenumab has been directly compared to one of the most commonly used migraine prophylactic drugs in a randomised, double-blinded, double-dummy controlled trial

Objective: HER-MES is the first head-to-head trial comparing the tolerability and efficacy of erenumab to topiramate in a German cohort of 777 adult migraine patients with at least four monthly migraine days

1. Vos T, et al. *Lancet*, 2016; 388(10053):1545–602; **2.** Lipton RB, et al. *Neurology*, 2007;68(5):343–9; **3.** Stokes M, et al. *Headache*, 2011; 51(7):1058–77; **4.** Blumenfeld AM, et al. *Headache*, 2013; 53(4):644–55.
CGRP, calcitonin gene-related peptide; EMA, European Medicines Agency; FDA, Food and Drug Administration.

Methods

- HER-MES comprised a 24-week double blind period in which patients received:
  - either 70 mg or 140 mg subcutaneous erenumab (investigator's choice) and an oral placebo or
  - a subcutaneous placebo and the maximally tolerated dose of oral topiramate (50–100 mg/daily; control group)
- Main inclusion criteria were:
  - treatment naïve OR not eligible for up to three different prophylactic treatments OR treatment failure of up to three prophylactic treatments (including metoprolol/propranolol, amitriptyline and flunarizine, excluding topiramate)
- **The primary endpoint** of tolerability was assessed by the rate of treatment discontinuation due to adverse events
- **The secondary endpoint** addressing efficacy was assessed by the proportion of patients achieving at least a 50% reduction from baseline MMD over months 4, 5 and 6 of the DBTE



DBTE, double-blind treatment epoch; MMD, monthly migraine day; TPM, topiramate.

Results

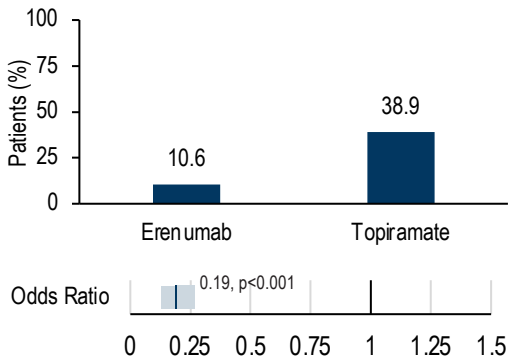
Demographics and baseline characteristics	Erenumab (N = 388)	Topiramate (N = 388)	Total (N = 776)
Age, years (mean±SD | range)	40.8±12.4 (18–66)	40.7±12.4 (18–65)	40.7±12.4 (18–66)
Gender, female (no [%])	331 (85.3)	335 (86.3)	666 (85.8)
Ethnicity, Caucasian (no [%])	383 (98.7)	387 (99.7)	770 (99.2)
Weight†, kg (mean±SD)	73.3±17.9	72.7±17.5	73.0±17.7
BMI† (mean±SD)	25.6±5.6	25.3±5.6	25.5±5.6
Disease duration, years (mean±SD)	21.8±12.5	21.9±12.4	21.9±12.4
Monthly headache days‡, no. (mean±SD)	11.4±4.2	11.5±4.1	11.5±4.2
Monthly migraine days, no.‡ (mean±SD) | categories (no [%])	10.3±4.0	10.5±3.8	10.4±3.9
4 to 7 days	97 (25.0)	97 (25.0)	194 (25.0)
8 to 14 days	255 (65.7)	255 (65.7)	510 (65.7)
≥ 15 days	36 (9.3)	36 (9.3)	72 (9.3)
Acute headache medication use, (no [%])			
Migraine-specific	304 (78.4)	320 (82.5)	624 (80.4)
Non-migraine-specific	74 (19.1)	58 (14.9)	132 (17.0)
Prior prophylactic treatment attempts§, (no [%])			
None (naïve)	232 (59.8)	229 (59.0)	461 (59.4)
1 failed	115 (29.6)	123 (31.7)	238 (30.7)
2 failed	37 (9.5)	31 (8.0)	68 (8.8)
3 failed	4 (1.0)	5 (1.3)	9 (1.2)

†n = 387 in the topiramate group; ‡n= 387 in the erenumab group; §Out of propranolol/metoprolol, amitriptyline, flunarizine
BMI, body mass index; SD, standard deviation.

Results

Both primary and secondary endpoints were met, showing a significant difference between erenumab and topiramate

Treatment discontinuation due to adverse events

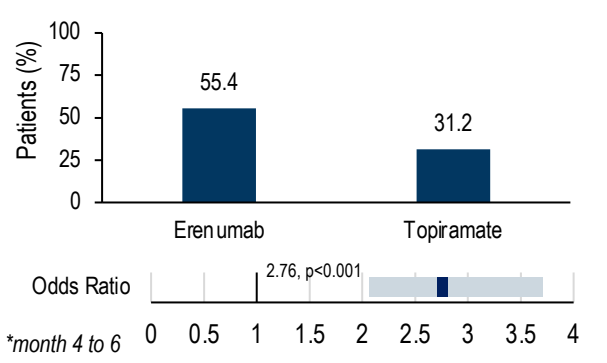


Adverse events reported during the double-blind treatment epoch

	Erenumab (N = 388)	Topiramate (N = 388)
Study treatment-related adverse event	215 (55.4)	315 (81.2)
Study treatment-related serious adverse event	1 (0.3)	2 (0.5)
Adverse event leading to treatment discontinuation†	41 (10.6)	151 (38.9)

†Number of patients with at least one event leading to treatment discontinuation. One patient could report multiple adverse events leading to treatment discontinuation.

At least 50% reduction of MMD over the last three months*



1 During the DBTE 10.6% of patients in the erenumab group vs. 38.9% of patients in the topiramate group discontinued medication due to adverse events (primary endpoint; odds ratio 0.19, 95% CI: 0.13 to 0.27, p<0.001)

2 More patients in the erenumab vs. topiramate group achieved a ≥50% reduction in MMD from baseline (secondary endpoint; 55.4% vs. 31.2%; odds ratio, 2.76; 95% CI: 2.06 to 3.71; p<0.001)

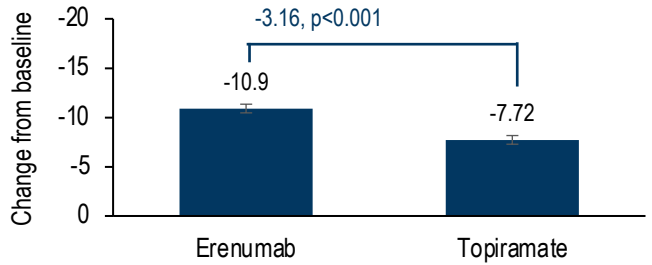
CI, confidence interval; DBTE, double blind treatment epoch; MMD, monthly migraine day.

Results

Exploratory analysis of quality of life as assessed by patient-reported outcomes, i.e., SF-36 and HIT-6 revealed greater improvements for erenumab vs. topiramate

Quality of life assessed by HIT-6

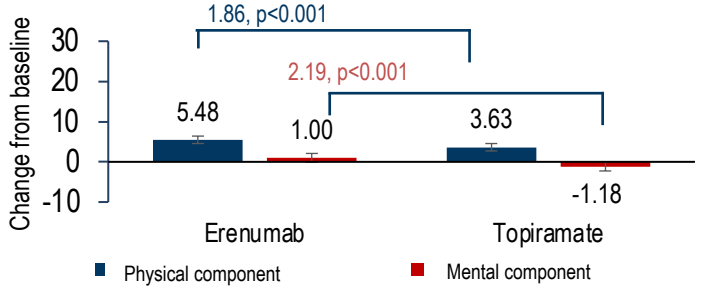
HIT-6 change from baseline to Week 24



Difference of change in HIT-6 score from baseline between erenumab vs. topiramate group was −3.16, 95% CI −4.26 to −2.06, p<0.001

Quality of life assessed by SF-36

SF-36 change from baseline to Week 24



Difference of change in SF-36 from baseline between erenumab vs. topiramate was 1.86, 95% CI 0.96 to 2.75, p<0.001 (physical component) and 2.19, 95% CI 1.04 to 3.33, p<0.001 (mental component)

HIT-6, Headache Impact Test-6™; SF-36, 36-Item Short Form Health Survey.

Conclusions

Erenumab showed favourable tolerability and efficacy vs. topiramate

The results of this first head-to-head trial of a therapy targeting the CGRP pathway compared to a prophylactic standard-of-care therapy will provide guidance to inform clinical decision-making for the preventive treatment of migraine

CGRP, calcitonin gene-related peptide.