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

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INTRODUCTION

- Migraine is one of the most common causes of disability worldwide and the third-leading cause of health loss of 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 migraine therapies are frequently discontinued due to a low tolerability or insufficient efficacy of the drugs[4]
- Erenumab (erenumab-aooe in the U.S.) is a monoclonal antibody targeting the calcitonin gene-related peptide (CGRP) receptor
- In 2018, the FDA and EMA approved erenumab as the first medication specifically developed for migraine prevention
- For the first time, erenumab will be directly compared to one of the most commonly used migraine prophylactic drugs in a randomized, controlled trial

OBJECTIVE

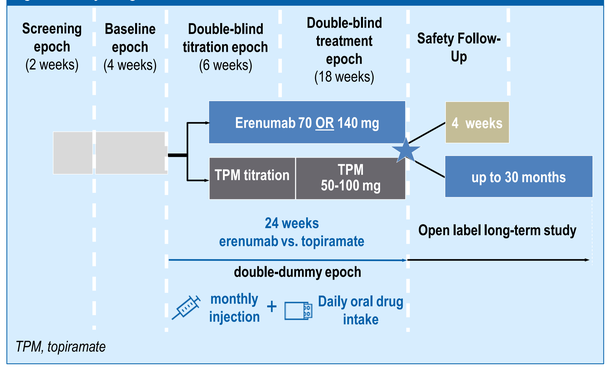
- HER-MES (Head-to-head study of erenumab against topiramate – Migraine study to assess tolerability and efficacy in a patient-centered setting) is the first head-to-head trial comparing the tolerability and efficacy of erenumab to topiramate in a German cohort of 777 adult migraine patients with at least four monthly migraine days (MMD).

METHODS

STUDYDESIGN

- HER-MES comprised a 24-week double-blind, double-dummy treatment epoch (DBTE; **Figure 1**) in which patients received
  (1) either 70 mg or 140 mg subcutaneous erenumab (investigator's choice) and an oral placebo or
  (2) a subcutaneous placebo and the maximally tolerated dose of oral topiramate (50-100 mg/daily; control group).

Figure 1. Study design



TPM, topiramate

- 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, flunarizine)
- 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.

RESULTS

- 777 randomized patients were randomized at 82 sites in Germany (erenumab: 389 patients | topiramate group: 389 patients);
- Data was available for analysis from 776 patients (one randomized patient did not receive study medication and was excluded).
- Demographic / baseline characteristics were similar between groups (**Table 1**).

Table 1. 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

- Both, primary and secondary endpoints were met, showing a significant difference between erenumab and topiramate.
  – 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), **Figure 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), **Figure 3 & Table 2**.

Figure 2. Treatment discontinuation due to adverse events

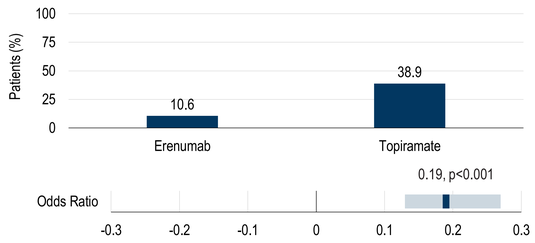
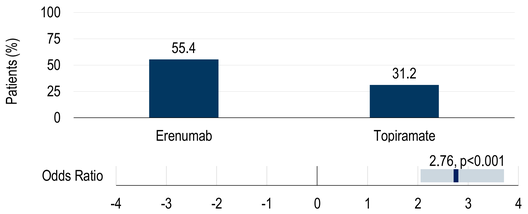


Figure 3. At least 50% reduction of MMD over the last three months*



**month 4 to 6*

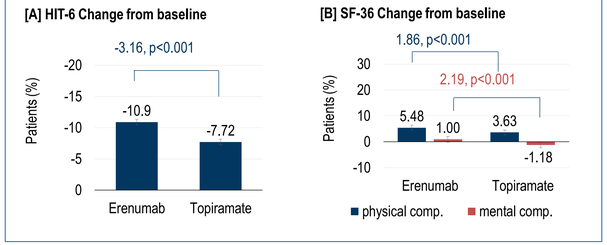
Table 2. Adverse events reported during the double-blind treatment epoch

	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.

- Exploratory analysis of quality of life as assessed by patient reported outcomes, i.e. SF-36 (36-Item Short Form Health Survey) and HIT-6 (Headache Impact Test -6™) revealed higher improvements for Erenumab vs topiramate (**Figure 4**).
  – 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
  – Difference of change of SF-6 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)

Figure 4. Quality of life assessed by HIT-6 [A] and SF-36 [B]



CONCLUSIONS

- Erenumab showed favorable 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.

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CONFLICTS OF INTERESTS

Uwe Reuter received personal compensation from Allergan, Amgen, Eli Lilly, Medscape, StreaMedUp, Novartis, and Teva for scientific presentations and participation in advisory board meetings. Astrid Gendolla received personal compensation from Novartis for scientific presentations and participation in advisory board meetings and is owner/founder of Praxis Gendolla. Axel Heinze received honoraria for lectures and consulting fees from Novartis for membership on advisory boards and a steering committee. Marc Ehrlich, Jan Klatt, Shihua Wen, Peggy Hours-Zesiger, Jacqueline Nickisch, Christian Sieder, Christian Hentschke, Monika Maier-Peuschel are employees of Novartis and as such, may be eligible for Novartis stock and stock options.

FUNDING

This study was funded by Novartis Pharma GmbH, Nuremberg, Germany and Novartis Pharma AG, Basel, Switzerland. Erenumab is co-developed by Amgen and Novartis.

ACKNOWLEDGMENTS

This study was conducted at several sites in Germany who have contributed to this work through their commitment to science and patients. Also, Dr. Renate Handrock and Martina Gogeissl where involved in scientific discussions regarding study set up. Cross-functional teams at Novartis were responsible for correct study conduct.

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MLR Id (128609)

Poster presented at the 63rd American Headache Society (AHS), Virtual Annual Scientific Meeting, June 3-6, 2021