# Erenumab versus topiramate for the prevention of migraine: Results of a post-hoc efficacy analysis

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# Disclosures

- **Uwe Reuter received honoraria for consulting and lectures within the past 3 years from Abbvie, Amgen, PharmAllergan, Eli Lilly, Lundbeck, Novartis Pharma, Hormosan Pharma, electroCore, Medscape, Novartis, Pfizer, StreaMedUp, Teva**; holds no stocks of pharmaceutical companies or medical device companies
- Marc Ehrlich, Monika Maier-Peuschel, Christian Sieder, and Christian Hentschke are employees of Novartis


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# Background

Migraine is a leading cause of disability worldwide[1]

Erenumab (erenumab-aooe in the United States), a fully human monoclonal antibody targeting calcitonin gene-related peptide (CGRP) pathway, was approved in 2018 by the US Food and Drug Administration and European Medicines Agency as the first medication specifically developed for migraine prevention[2,3]

The HER-MES trial is the first and only head-to-head, randomized, controlled study comparing a CGRP pathway treatment (erenumab) with a standard of care therapy (topiramate) for migraine prevention

HER-MES was designed to compare treatment effectiveness (a combination of tolerability and efficacy), taking into account the potential impact of a treatment's tolerability on its efficacy in migraine prevention

The HER-MES study demonstrated a **significantly superior tolerability and effectiveness** of erenumab compared with topiramate[4]

Treatment efficacy amongst adherent patients is an important factor when it comes to treatment decision-making in migraine prevention. Thus, we will address the following question through a post-hoc analysis:

**Does erenumab show a higher efficacy than topiramate amongst those patients who completed the HER-MES trial on study drug?**

**1**. Steiner TJ, et al. *J Headache Pain*. 2020;21(1):137; **2**. Aimovig (erenumab-aooe). Full Prescribing Information, Amgen Inc, Thousand Oaks, CA, 2021; **3**. Aimovig. Summary of Product Characteristics, Novartis Europharm Limited, Dublin, Ireland, 2021; **4**. Reuter U, et al. Cephalalgia. 2021: doi:10.1177/03331024211053571

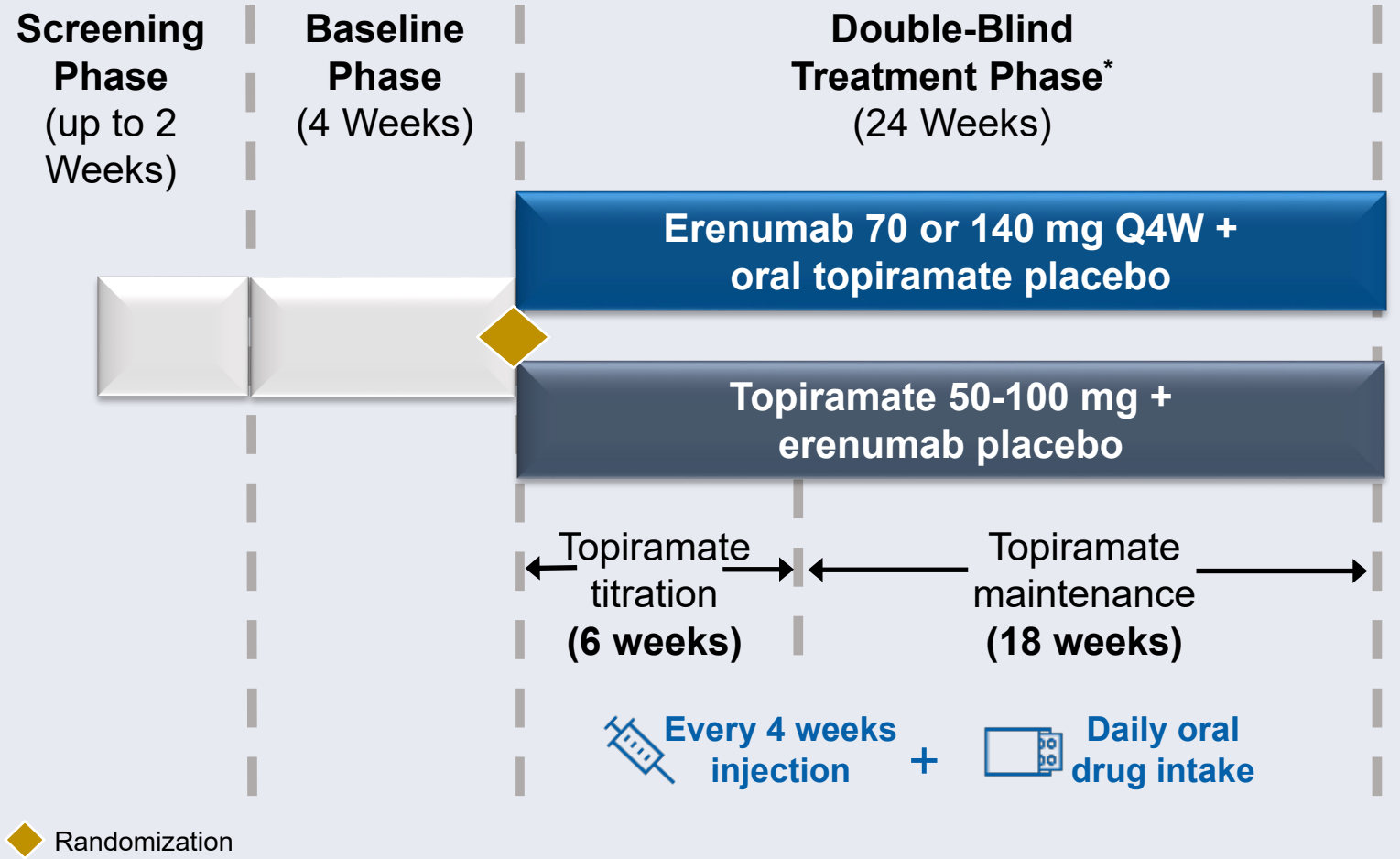
# Methods

- The presented sensitivity analysis displays a hypothetical scenario to evaluate the efficacy of erenumab vs topiramate as if all patients had tolerated their randomized treatment (ie, erenumab or topiramate)

- Missing efficacy values from patients who discontinued study treatment were added through multiple imputation based on the observed on-treatment responses in this trial

- This intention-to-treat analysis was performed in the population of the full analysis set and preserves the randomization of the clinical trial

# Study Design



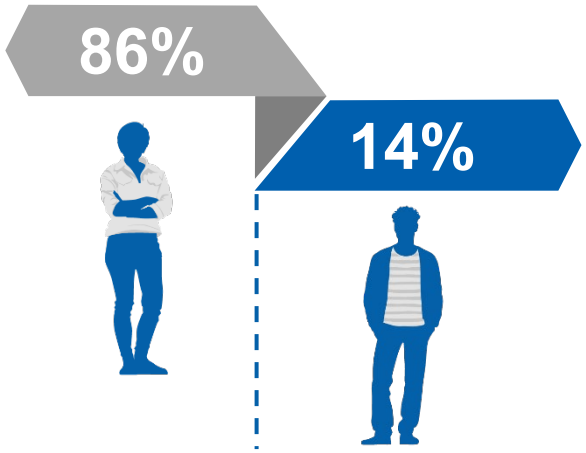

- Adult patients with at least four monthly migraine days (MMD) at baseline
- Endpoints: Percentage of patients achieving ≥ 50% reduction from baseline in MMD (50% responder rate) and the change from baseline in MMD over months 4 through 6 using a multiple imputation model

Stratification factor for randomization: monthly migraine day frequency. *The 24-week double-blind treatment phase comprised an up-titration phase of 6 weeks with weekly visits followed by a maintenance phase with visits at weeks 8, 12, 16, 20 and 24.[4] Q4W, every 4 week.

# Results

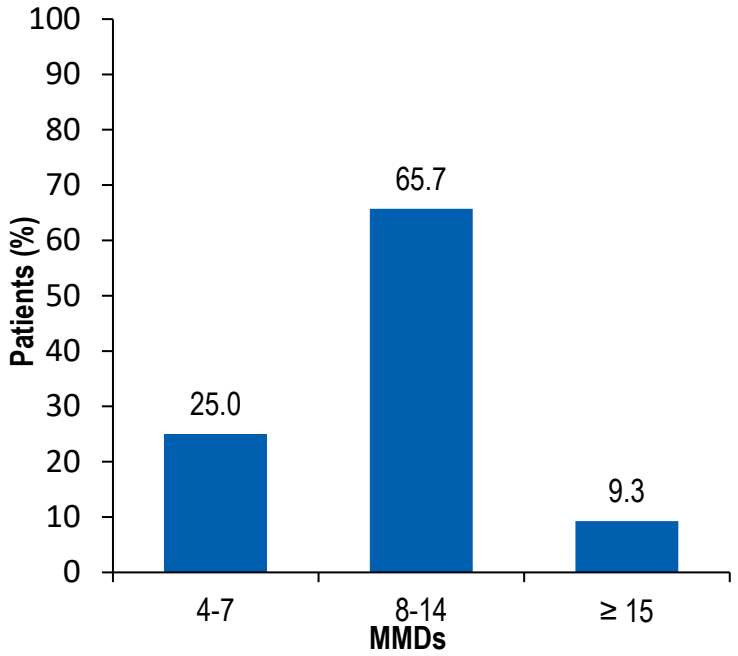
## Patient characteristics at baseline

### 777 Patients were randomized

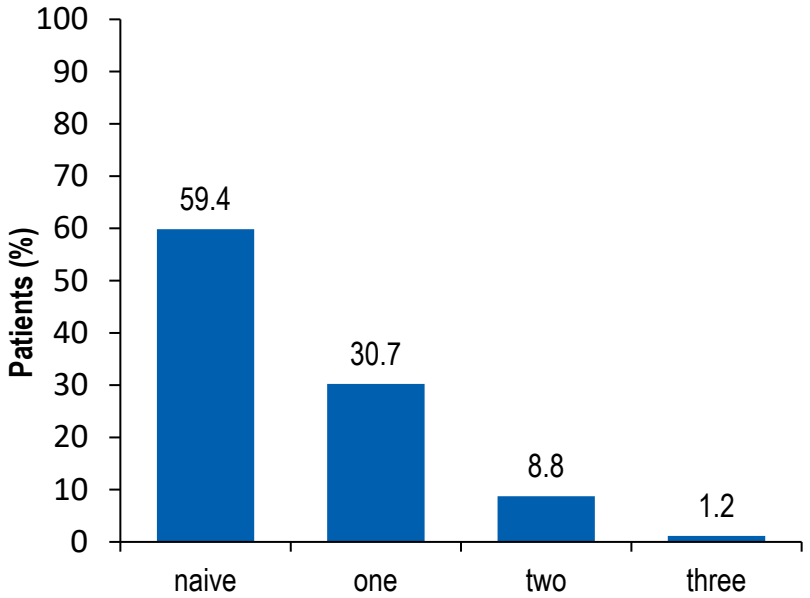



- Ø 41 years old
- Ø 22 years since disease onset
- Ø 10.4 MMDs

### Stratification




### Prior prophylactic treatment failure*




*Out of metoprolol/propranolol, amitriptyline, flunarizine.

MMD, monthly migraine days.

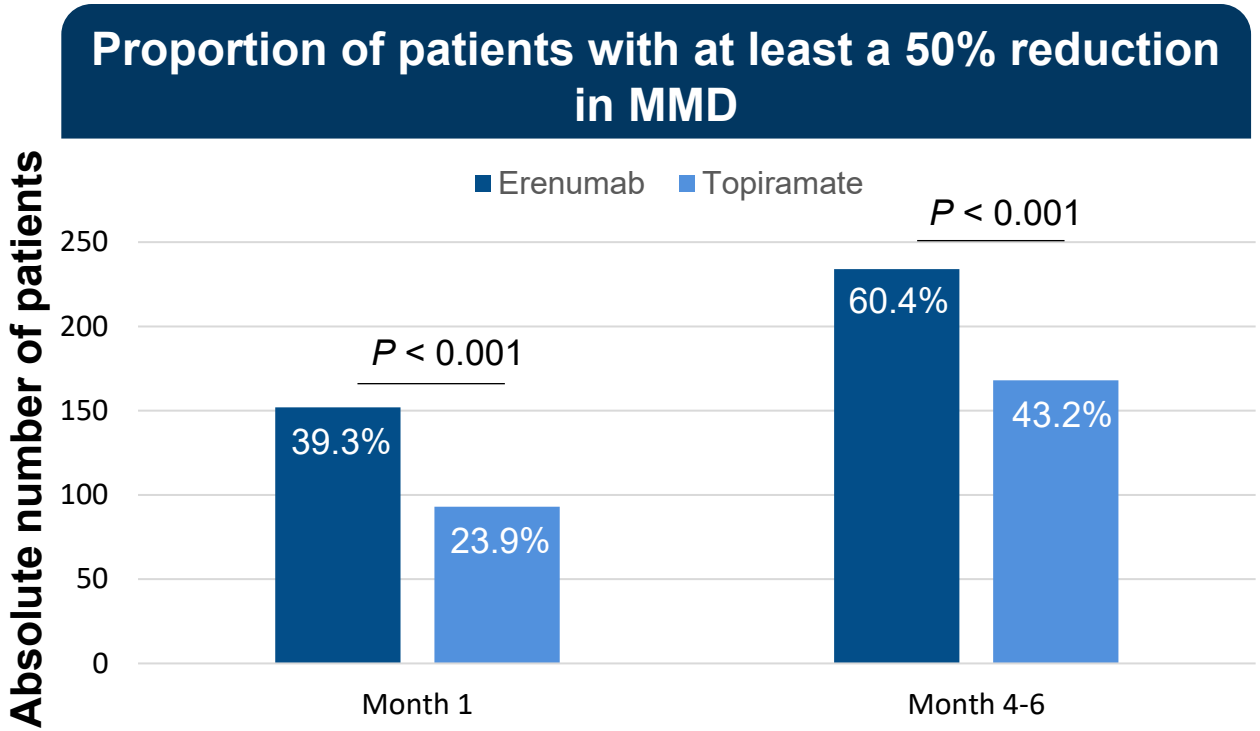
# Results

**Proportion of patients who discontinued study medication during the 24-weeks double-blind treatment phase**

| Category | Erenumab (N = 389) | Topiramate (N = 388) |
|---|---|---|
| Patients who completed double blind treatment, n (%) | 334 (85.9) | 231 (59.5) |
| Patients who discontinued double blind treatment, n (%) | 55 (14.1) | 157 (40.5) |
| **Reason for discontinuation, n (%)** | | |
| Adverse events | 41 (10.6) | 151 (38.9) |
| Lack of efficacy | 1 (0.3) | - |
| Lost to follow up | 4 (1.0) | 1 (0.3) |
| Withdrawal of informed consent | 1 (0.3) | - |
| Patient/guardian decision | 4 (1.0) | 3 (0.8) |
| Physician decision | 1 (0.3) | - |
| Protocol deviation | 3* (0.8) | 1 (0.3) |
| Pregnancy | - | 1 (0.3) |

*One patient did not receive erenumab.

# Results



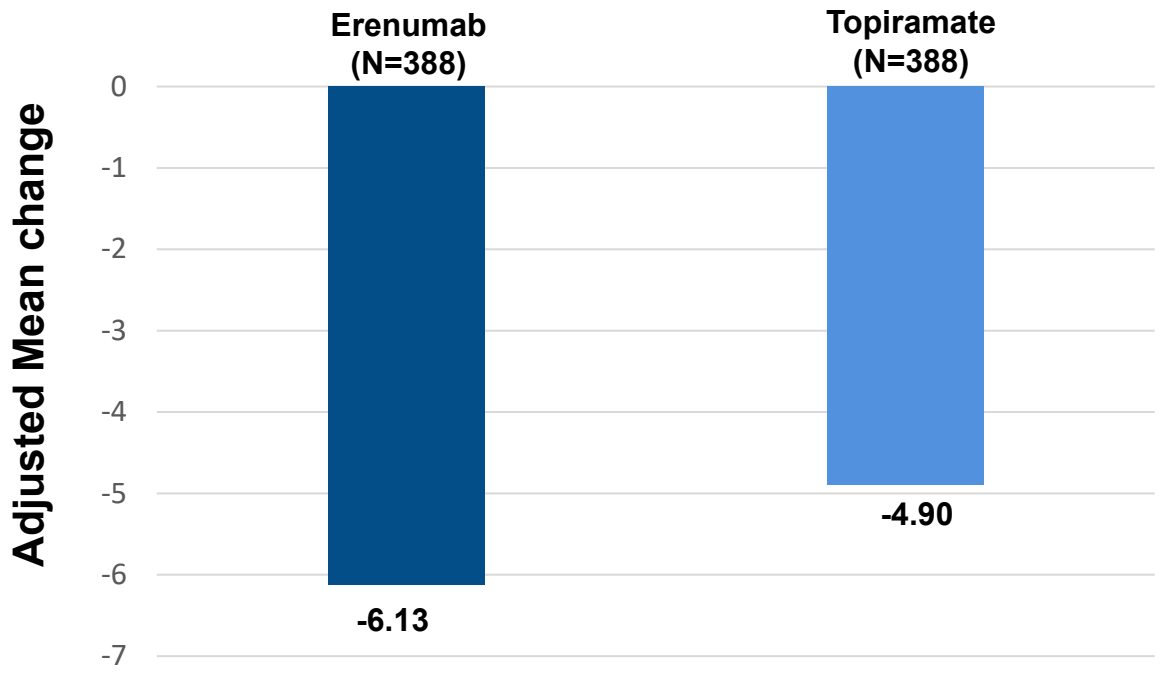

| | | |
|---|---|---|
| OR | 2.06 | 2.02 |
| 95% CI | 1.49–2.84 | 1.48–2.76 |

- Patients were **2-fold (OR=2) more likely to reduce their MMDs by 50%** or more with erenumab versus topiramate.
- This effect was observed starting from month 1 and confirmed in months 4-6.

CI, confidence interval; MMD, monthly migraine days; OR, odds ratio.

# Results

## Change from baseline in MMD over last three months (month 4, 5, 6)




**Erenumab vs topiramate (difference): −1.24**
**95% CI: −1.87, −0.61; P<0.001**

Patients receiving **erenumab** reported a **significantly larger reduction in MMD** versus topiramate.

CI, confidence interval; MMD, monthly migraine days.

# Conclusions

- The HER-MES post-hoc sensitivity analysis confirmed the good efficacy of topiramate for migraine prevention, but also demonstrated that erenumab is an even more efficient therapy for migraine prophylaxis than is topiramate regarding the following:
    - Achieving a ≥ 50% reduction in MMD
    - The numeric reduction of MMD from baseline
    - Early onset of action (significant superiority starting from month 1)
- The post-hoc sensitivity analysis of the HER-MES trial further supports the initially published[4] superior effectiveness results of erenumab compared with topiramate in the prevention of migraine across a broad patient population

**4**. Reuter U, et al. *Cephalalgia.* 2021: doi:10.1177/03331024211053571