# Two years of guideline-oriented treatment of migraine patients with Erenumab under the regulatory conditions of the healthcare system in Germany

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## Background
German regulatory guidelines demanded 5 (episodic) or 6 (chronic migraine) failed/contraindicated first-line prophylactics before covering the costs of CGRP-mABs, Valproate meanwhile was omitted. Medical guidelines[1] recommend a significant (i.e. at least 50%) treatment response as a prerequisite for sustained prescription.

## Objectives
We aimed to describe results and implications of Erenumab treatment in neurological practices under these conditions.

## Methods
Since October 2017 the headache registry of NeuroTransData network of neurologists captures demographics, headache characteristics, comorbidities, symptom load and the use and effect of acute and preventive medication via standardized webbased data entry and smartphone app. The 2-year results of up to 27 consecutive treatments with erenumab are presented.

## Results
At the time of the last analysis (01.01.21) 5355 headache patients were documented, of which 5121 met the ICHD-3 criteria for migraine (Table 1). 435 of them (8,5 %) received Erenumab at least once for up to 27 consecutive applications. Of these patients, 431 could be considered with regard to data quality at baseline (28 days before the first administration). 140 of them (32,5 %) had chronic migraine (CM). 269 (62,4 %) received Erenumab as the only prophylactic agent. 365 patients (84,7 %) started with a dose of 70 mg, half of them (183) increased the dose to 140 mg, 1 (0,2 %) reduced it from 140 to 70 mg. For two patients the dosage is unknown. 14 patients (3,2 %, 10 with 70 and 4 with 140 mg) stopped therapy due to side effects, 76 (17,6 %) due to lack of or insufficient effectiveness, 36 (8,4%) for therapy break recommended in the guidelines[1] as to be considered for cases with good response after 9 to 12 months of effective therapy. The criterion „migraine days per 28 days compared to baseline“ could be analyzed for 378 patients (Fig. 1). The response rate (at least 50% reduction of migraine days in 28 days compared to baseline) rose from 40 % after three to 48 % after six up to 65 % after 24 injections (Fig. 2). On the other hand approximately 25% of the patients had a less than 25% response accoding to this definition after two years of therapy

## Conclusion
Treatment with Erenumab under the regulatory conditions in Germany was mostly well tolerated and effective. The increasingly high rate of responders over time shows that the antibodies were mainly used in accordance with guidelines, in particular based on effectiveness. A considerable proportion of patients was treated for up to 2 years without reaching 50 %, even 25% response regarding the number of migraine days. This could indicate a good ratio between tolerability and effectiveness and point to other factors of efficacy than the number of migraine days in the evaluated sample of otherwise therapy resistant migraine patients

## References
1. Diener H.-C., May A. et al., Prophylaxe der Migräne mit monoklonalen Antikörpern gegen CGRP oder den CGRP-Rezeptor, Ergänzung der S1-Leitlinie Therapie der Migräneattacke und Prophylaxe der Migräne, 2019, in: Deutsche Gesellschaft für Neurologie (Hrsg.), Leitlinien für Diagnostik und Therapie in der Neurologie. Online: www.dgn.org/leitlinien

| Migraine with and/or without aura (ICHD-3) | 5121 |
|---|---|
| Male/Female | 799/4322 |
| Average disease duration | 19,02 Jahre (N= 4795) |
| Chronic migraine | 459 (9 %) |
| Medication overuse headache | 639 (12,5%) |
| Treatment with at least one of the CGRP-(receptor) antibodies | 538 (10,5%) |
| Erenumab | 435 (80,8%) |
| Fremanezumab | 136 (25,3%) |
| Galcanezumab | 57(10,6T%) |
| Treatment with Botox (CM) | 41<br>9 (8,2%) |
| Treatment with at least one of the other prophylactics of first choice | 2306 (45,0%) |
| Topiramate | 1355 (58,8%) |
| Amitritpyline | 1172 (50,8%) |
| Metoprolol | 1123 (48,7%) |
| Bisoprolol | 227 ( 9,8%) |
| Propranolol | 130 ( 5,6%) |
| Flunarizine | 506 (21,9%) |
| Valproate | 303 (13,1%) |

**Table 1:** *Migraine population (ICHD3) in the NTD database*

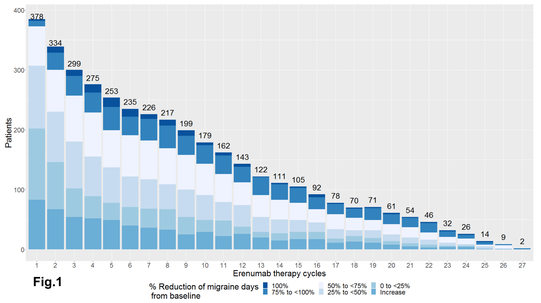


**Fig.1**

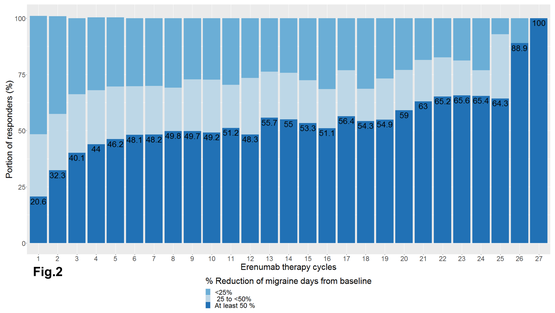


**Fig.2**

## Conflicts of interest:
Peikert A.: Novartis, TEVA , Lilly (Advisory boards, talks), Köchling M.: Janssen-Cilag, Novartis (Advisory Boards, talks), Israel- Willner H.: Novartis, TEVA, Allergan/Abbvie, Lilly (Advisory Boards und talks) Braune S: Biogen, Lilly, MedDay, Merck, Novartis, Roche; Bergmann A: Novartis, Servier. The NTD network analyzed data of its headache registry for the following companies: Novartis and TEVA.

Stühler E., Tozzi V., Dikow H., and Rossnagel F. declare that they have no potential COI.