Long-term efficacy and impact of erenumab treatment on quality of life of patients participating in the APOLLON study

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Mirja Koch is an employee of Novartis AG.

Cordula Weiss is an employee of Novartis Pharma GmbH.

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Introduction

Background

- The monoclonal antibody erenumab is an EMA and FDA approved anti-CGRP pathway treatment developed for the prevention of episodic and chronic migraine.
- Erenumab was found to be effective in the prevention of migraine in German and international studies.
- While international data support the long-term safety of erenumab, such data is still limited for the German population.
- The **APOLLON** study (**A**ssessment of **P**rolonged safety and t**OL**erability of erenumab in migraine patients in a **L**ong-term **O**pe**N**-label study) assessed long-term safety and tolerability of erenumab in migraine patients in Germany who previously participated in a 24-week, head-to-head trial comparing the tolerability of erenumab and topiramate (HER-MES, NCT03828539).

Objectives

- Assessment of long-term safety and tolerability of erenumab in migraine patients.
- Assessment of relevance, characteristics and impact of treatment discontinuation in patients previously treated with erenumab.

Methods

Study Design

The APOLLON study was an open-label study consisting of the following phases (**Figure 1**).

Screening phase: up to 2 weeks

Open-label treatment: 128 weeks

During the open-label treatment epoch, it was at the discretion of the treating physician to change the erenumab dose at each planned visit from 70 mg to 140 mg or vice versa.

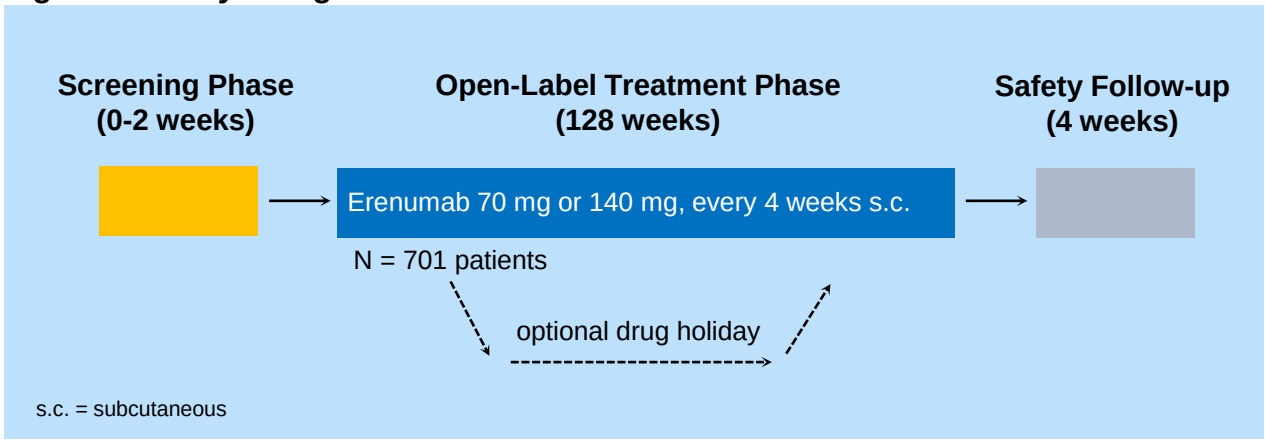
Optional drug holiday: up to 24 weeks

A drug holiday could be initiated after at least 12 weeks of treatment. Impact of treatment discontinuation on monthly migraine days was assessed 4 weeks prior to, during and 12 weeks after drug holiday.

Follow-up phase: 4 weeks

Part of routine safety monitoring

Figure 1. Study Design.



Assessments

- Headache diary
- HIT-6 (headache impact test) questionnaire
- TSQM (treatment satisfaction)

Results

Demographics, baseline disease characteristics and exposure

- In total, 701 patients at 80 participating sites in Germany were included in the APOLLON study. Baseline characteristics shown in **Tab. 1** are based on inclusion in the HER-MES study.
- Overall, patients were exposed to erenumab for about 110 weeks (**Tab. 2**) and most patients (71.6%) took 30 to 33 doses of erenumab during APOLLON (**Fig. 2**).

Table 1. Baseline characteristics.

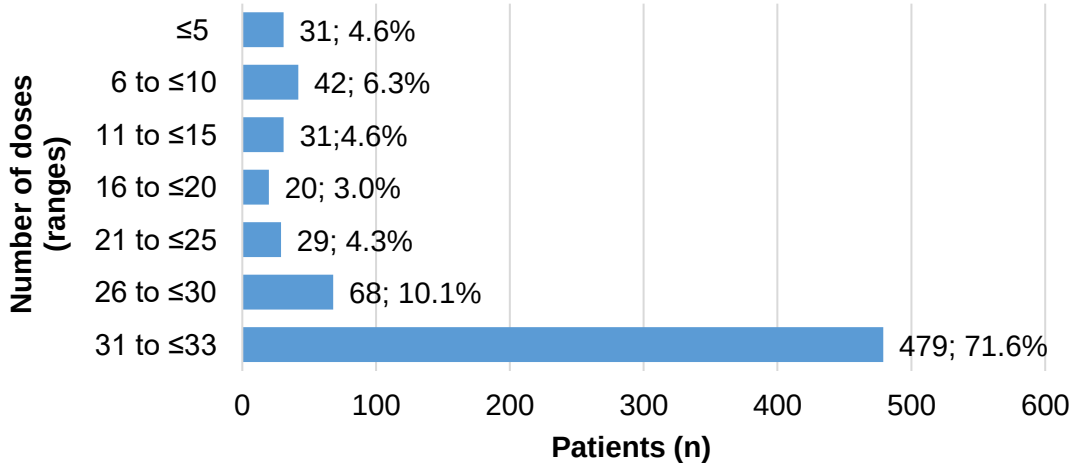
Baseline characteristics (HER-MES)	Patients (N=701)
Age, years±SD	41.8±12.3
Female, n (%)	608 (86.7)
Disease duration, years±SD	22±12
Aura present, n (%)	463 (66.0)
Monthly headache days[a], days±SD	11.5±4.1
Monthly migraine days[a], days±SD	10.4±3.8
Monthly migraine days categories – stratification factor[b]	
4-7 monthly migraine days, n (%)	165 (23.6)
8-14 monthly migraine days, n (%)	470 (67.1)
≥15 monthly migraine days, n (%)	65 (9.3)
Any acute headache medication, n (%)	681 (97.1)
Migraine specific medication, n (%)	571 (81.6)
Non-migraine specific medication, n (%)	109 (15.5)

[a]Normalized to 28 days.
[b]Differs from monthly migraine days categories due to protocol deviations; n=700 due to protocol deviations.

Table 2. Exposure to erenumab.

Exposure (APOLLON)	Patients (N=701)
Duration of exposure incl. drug holidays, weeks±SD	111.4±35.3
Duration of exposure excl. drug holidays, weeks±SD	108.4±39.2

Figure 2. Doses (ranges) of erenumab taken by patients[c].



[c]One patient (not included) received 34 doses by mistake; n=700.

Results

Long-term tolerability and safety

- 29 patients (out of 155 early discontinuations) discontinued the study due to adverse events (AEs) (**Fig. 3**), mostly due to nervous system, gastrointestinal or skin and subcutaneous disorders (**Fig. 4**).
- **Tab. 3** shows the exposure adjusted incidence rate (EAIR) of adverse events per 100 subject years by subgroup.

Figure 3. Treatment discontinuation (n=155) due to adverse events (AEs).

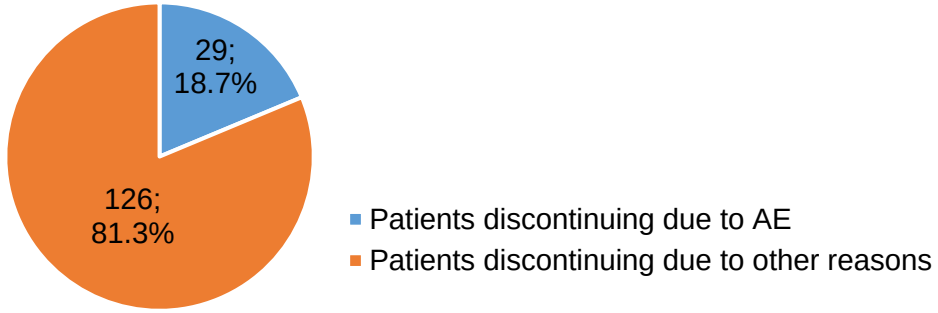


Figure 4. AEs leading to treatment discontinuation (n=29).

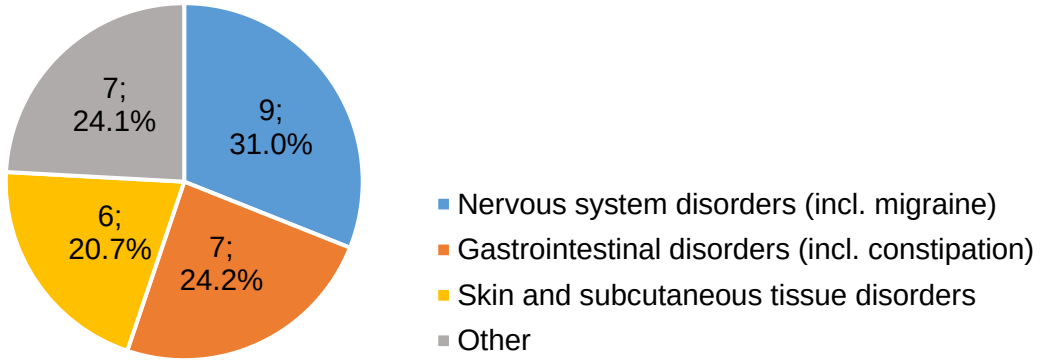


Table 3. Exposure adjusted incidence rate (EAIR) of adverse events per 100 subject years.

Variable	n	EAIR [CI]
All patients	580	98.16 [88.58; 107.73]
Gender		
Female	508	101.21 [90.61; 111.81]
Male	72	80.93 [59.05; 102.81]
Monthly migraine days categories[a]		
4-7 monthly migraine days	138	92.57 [74.66; 110.47]
8-14 monthly migraine days	388	97.59 [85.90; 109.28]
≥15 monthly migraine days	53	120.44 [78.96; 161.92]
Starting dose		
70 mg	195	98.31 [80.90; 115.73]
140 mg	385	98.08 [86.64; 109.51]
Prior prophylactic treatment failure		
Treatment naive	327	95.80 [83.14; 108.47]
Treatment failure (1-3 treatments)	253	101.37 [86.74; 116.00]

[a]Stratified; differs from monthly migraine days categories due to protocol deviations.
n:number of patients in analysis. CI: confidence interval.

Results

Long-term efficacy, tolerability and impact on quality of life

- HIT-6 (Headache Impact Test) data show an improvement of the average HIT-6 scores by nearly 6 points to a stable level within the first six months (mean±SD: 57.4±7.4 to 51.8±8.0) (**Fig. 4**).
- TSQM-II (Treatment Satisfaction Questionnaire for Medication) scores (**Fig. 5**) improved under erenumab treatment compared to baseline values (based on previous prophylactic therapy).

Figure 4. HIT-6 scores at baseline, 6 months (6M) and end of study (30M).

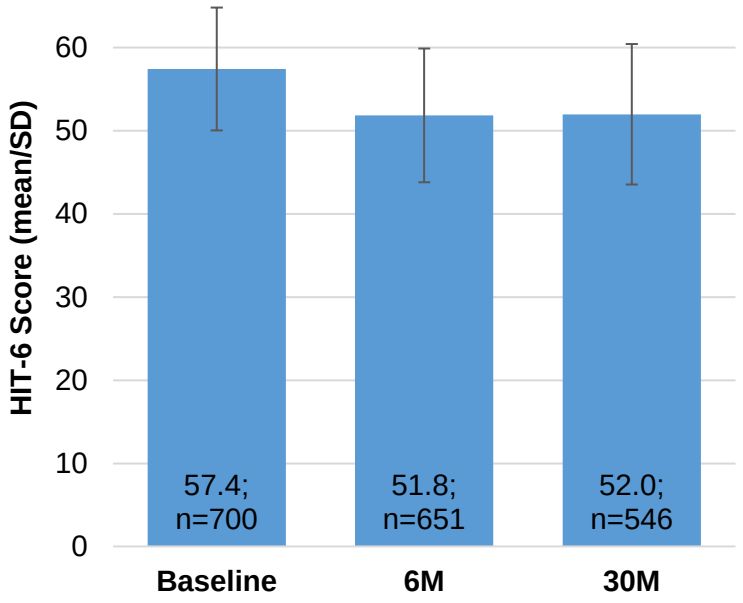
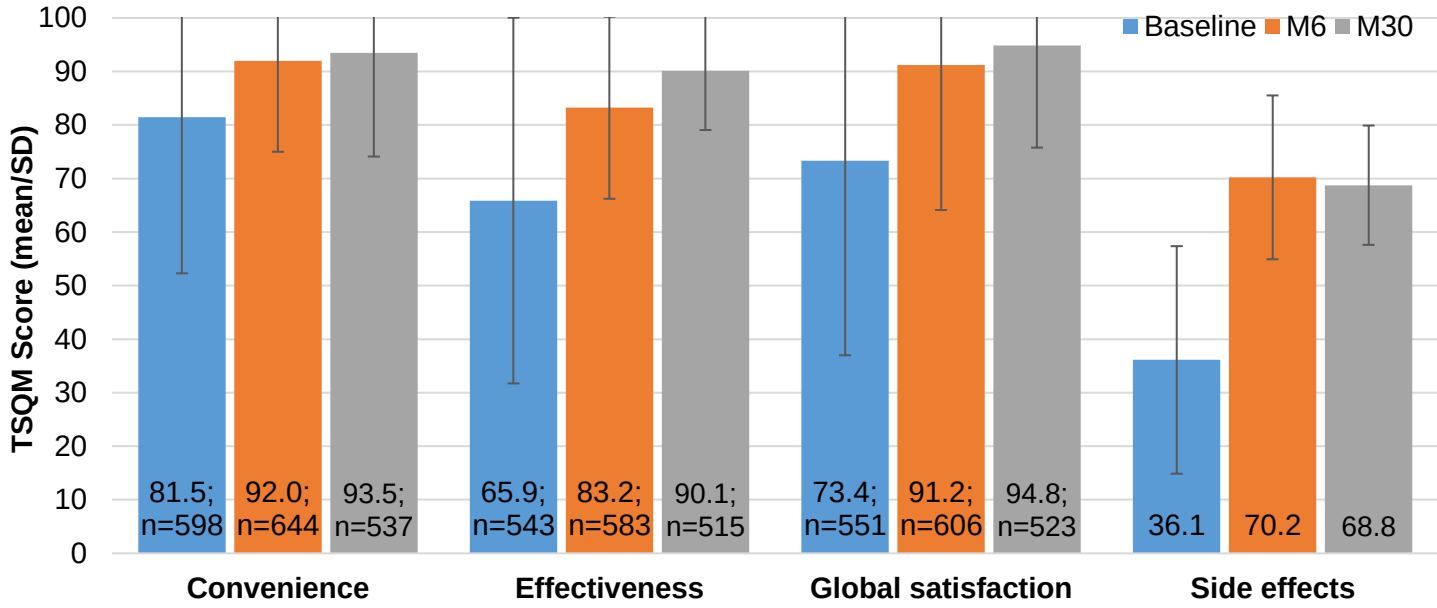


Figure 5. TSQM-II scores (convenience, effectiveness, global satisfaction, side effects) at baseline, 6 months (6M) and end of study (30M).



Conclusions

- On average, patients were exposed to erenumab for about 110 weeks.
- 155 patients discontinued the study early. Out of these, 29 patients discontinued due to adverse events. The adverse events given as reasons for discontinuation were most often related to nervous system, gastrointestinal or skin and subcutaneous disorders.
- A comparison of EAIR of adverse events per 100 subject years shows a slightly higher value for patients who suffered from a higher number of MMDs at baseline and patients who had at least one prophylactic treatment failure before starting erenumab treatment. Male patients have a lower EAIR compared to female patients.
- The HIT-6 score improved by nearly 6 points within the first 6 months of the study.
- During the study, treatment satisfaction increased in all observed areas: convenience, effectiveness, global satisfaction and side effects.

The results provide additional data and insights regarding the long-term efficacy, tolerability and safety as well as the impact on quality of life of erenumab-treated migraine patients in Germany. Thus, the results add to the understanding of monoclonal antibody-based migraine prophylaxis.