Erenumab discontinuation in migraine patients: interim analysis of the APOLLON study population

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Introduction

- Erenumab is the first EMA and FDA approved anti-CGRP pathway treatment specifically developed for migraine prevention in adults.
- Current international guidelines and German national regulations suggest discontinuation of therapy after 9-12 months of continuous treatment with erenumab.
- However, comprehensive data on treatment discontinuation and the impact on the course of migraine disease is still limited.
- Here we present data from an interim analysis of the APOLLON study.

Objective

- To assess the relevance and characteristics of a drug holiday (DH) in patients
  previously treated with erenumab.
- To investigate the impact of therapy discontinuation on disease outcome.

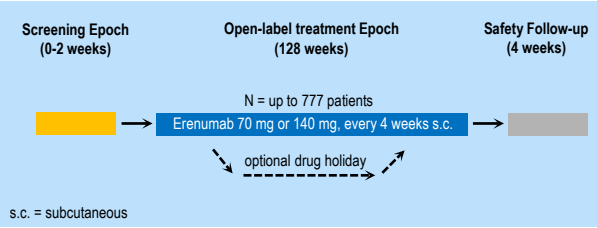
Methods

- 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), is a 128-week open-label study assessing the 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).
- The patients were allowed to discontinue treatment once at any time during the study after 12 weeks of continuous treatment with erenumab.
- Impact of treatment discontinuation on monthly migraine days (MMD) was assessed 4 weeks prior to, during and 12 weeks after the medication free epoch.

Study Design

- The APOLLON study consists of three epochs **(Figure 1)**:
  - **Screening epoch** lasting up to two weeks
  - **Open-label treatment epoch** lasting 128 weeks
    During the open-label treatment epoch, it is 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.
    In addition, an optional drug holiday lasting up to 24 weeks can be initiated after at least twelve weeks of treatment.
  - **Follow-up epoch** lasting four weeks
    This epoch is part of routine safety monitoring.

Figure 1. Study design



Results

Demographics and baseline disease characteristics

In total, 701 patients at 80 participating sites in Germany were included in the APOLLON study. Demographics and baseline characteristics from 107 patients from an interim analysis with cut-off date 14th of February 2021 are shown; baseline characteristics are based on inclusion in the HER-MES study **(Table 1)**.

- Patients included in the interim analysis (n=107) represent 15.3% of total patients in the study (n=701).
- Mean age is 40.5 ±13 years
- There are more female (85%) than male patients (15%)

Table 1: Demographic and baseline disease characteristics

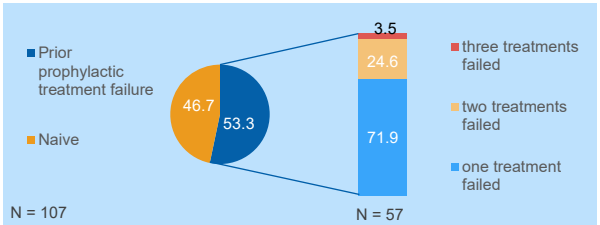
Baseline characteristics	Patients (N=107)
Age (years) ±SD	40.5 ±13.0
Gender	
female, n (%)	91 (85.0)
male, n (%)	16 (15.0)
Weight (kg) ±SD	68.3 ± 15.5
Disease duration (years) ±SD	20.0 ± 13.0
Aura	
present, n (%)	73 (68.2)
not present , n (%)	34 (31.8)
Monthly headache days* (days)*SD	11.5 ± 4.5
Monthly migraine days* (days)±SD	10.5 ± 4.2
Monthly migraine days – stratification factor**, n (%)	
4-7 monthly migraine days, n (%)	29 (27.1)
8-14 monthly migraine days, n (%)	70 (65.4)
≥ 15 monthly migraine days, n (%)	8 (7.5)

*Normalized to 28 days
**Differs from Monthly migraine days categories due to protocol deviations

Treatment

- Of the 57 (53.3%) patients who had prior prophylactic treatment failures 71.9% failed one, 24.6% failed two, and 3.5% failed three prior treatments **(Figure 2)**
- Patients were eligible for HER-MES if they had not received prior prophylactic migraine treatment (naive) or, due to lack of efficacy or tolerability, had failed or had not been suitable for up to three previous prophylactic treatments

Figure 2: Prior prophylactic treatment failure status*

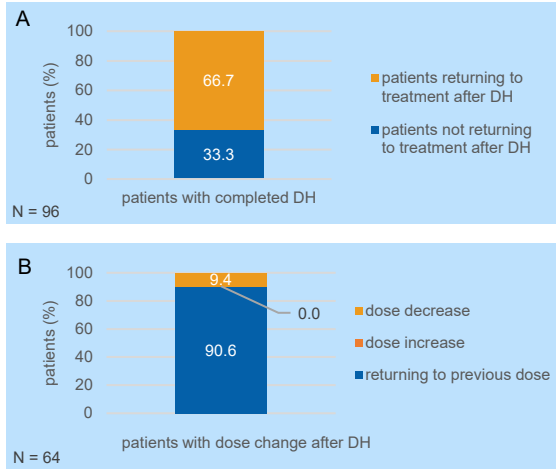


*Prior treatment failure of propranolol/metoprolol, amitriptyline, flunarizine

Drug holidays

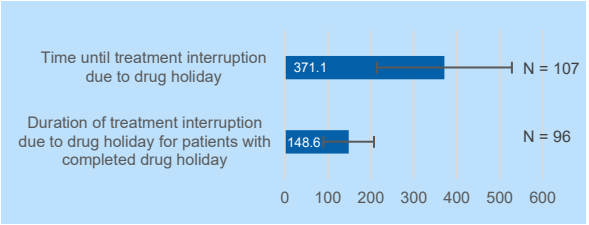
- All patients had planned and started DH, 96 (89.7%) patients completed DH, whereof 64 (66.7%) returned to treatment after DH **(Figure 3A)**
- 58 patients with completed DH returned to previous dose after DH (90.6%) and 6 (9.4%) changed dose after DH (all of which were dose decrease) **(Figure 3B)**

Figure 3: Proportion of patients returning to treatment after drug holiday



- The mean time until treatment interruption was 371.1±157.0 days, and the mean duration of treatment interruption due to DH was 148.6±58.7 days for the 96 patients with completed DH **(Figure 4)**

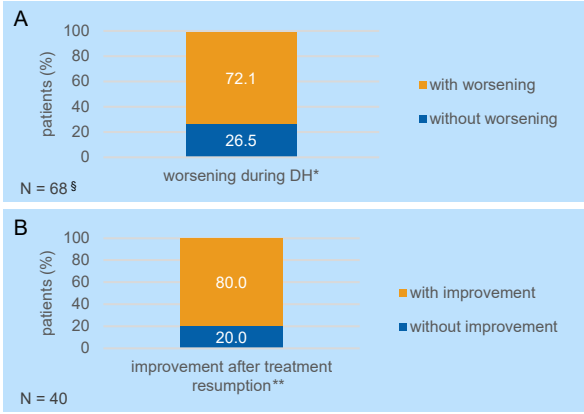
Figure 4: Time (mean days ±SD) until treatment interruption and duration



Migraine evolution during and after drug holiday

- At drug holiday initiation, the baseline MMDs were recorded to be 7.01±7.72
- Patients with or without worsening in MMDs during DH or with and without improvement after treatment resumption are shown in **Figure 5A and B**.

Figure 5: Patients with or without worsening (A) in MMDs during DH or improvement after treatment resumption (B)



*A significant worsening in MMD during drug holiday is defined as an increase in MMD during DH of at least 30% compared to MMD in the period of 4 weeks before DH
**A significant improvement in MMD after treatment resumption is defined as a decrease of at least 30% in MMD in the period of 12 weeks after DH compared to MMD in the period of DH.
§ Only patients included with at least one monthly interval with = 14 diary days each during DH initiation and during DH

Conclusion

- This analysis provides preliminary insights into the patients´ response after erenumab treatment discontinuation and contributes data that can further elucidate whether treatment discontinuation should be performed as currently recommended
- The majority of patients reported worsening of monthly migraine days after a drug holiday and an improvement after treatment resumption. Most of them returned to their previous dose.
- Thus, the discontinuation of migraine prevention was associated with a progressive worsening of migraine over time.
- A discontinuation attempt should be carefully discussed with patients on an individual basis.
- Future studies are needed to support these findings and also to identify predictors for successful treatment discontinuation.

Disclosures

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