ASSESSMENT OF THE LONG-TERM SAFETY AND EFFICACY OF ERENUMAB DURING OPEN-LABEL TREATMENT IN PATIENTS WITH CHRONIC MIGRAINE

10-016

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INTRODUCTION

- Erenumab, a fully human monoclonal antibody specific to the calcitonin gene-related peptide (CGRP) receptor complex, is approved in the United States for prevention of episodic migraine (EM) and chronic migraine (CM) at subcutaneous (SC) doses of 70 mg or 140 mg monthly[1]
- The short-term efficacy and safety of erenumab in CM was confirmed in a pivotal 12-week, placebo-controlled study (NCT02066415)[2]
- The current study aimed to assess the long-term safety and efficacy in CM over 1 year of open-label treatment with erenumab (NCT02174861)

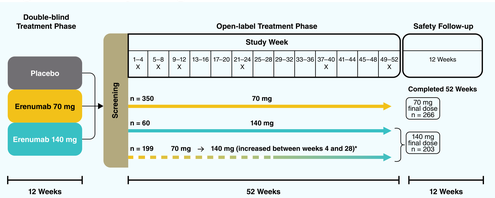
CONCLUSIONS

- Erenumab was safe and well tolerated in patients with CM, with no new safety events and no dose-dependent AEs reported
- Erenumab treatment resulted in sustained efficacy at 1 year

METHODS

- In the pivotal study, patients with CM received placebo or SC erenumab 70 or 140 mg once-monthly during the double-blind treatment phase (DBTP)[2]
- Patients who completed the 12-week DBTP[2] could enroll into the 52-week open-label treatment phase (OLTP; **Figure 1**), wherein patients initially received erenumab 70 mg monthly. Following a protocol amendment:
  - Erenumab was started at 140 mg for patients enrolled post-amendment
  - Erenumab 70 mg was continued for patients who had completed the week 28 visit
  - The dose was increased from 70 to 140 mg for patients who had not completed the week 28 visit

Figure 1. *Study Design*



X Efficacy evaluation
*By week 40, any patient who had the dose increased to 140 mg at or before week 28 had received 140 mg for ≥ 12 weeks and therefore had reached steady-state

Endpoints

- Primary endpoint assessed the long-term safety of erenumab treatment, as measured by the subject incidence of adverse events (AEs)
- Secondary endpoints assessed long-term efficacy of erenumab, including:
  - Change from baseline to week 52 in monthly migraine days (MMD)
  - Proportion of patients achieving ≥ 50% reduction in MMD at week 52
  - Change from baseline to week 52 in monthly acute migraine–specific medication (AMSM) use days

Analyses

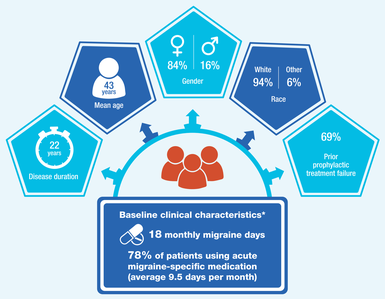
- No formal statistical tests were performed
- A post hoc analysis of efficacy data, based on the last dose received, was conducted for patients who completed the 52-week OLTP
- Week 40 was selected as an analysis point, because by week 40, any patient who had the dose increased to 140 mg at or before week 28 had received 140 mg for ≥ 12 weeks and therefore had reached steady-state

RESULTS

Baseline Demographics and Clinical Characteristics

- Almost three-quarters (74.1%; n = 451) of the 609 enrolled patients completed the study
  - The primary reason for discontinuation (20.4% of 158 patients) was withdrawal of consent
- Baseline characteristics were representative of a typical cohort of patients with CM (**Figure 2**)

Figure 2. *Baseline Patient Characteristics*

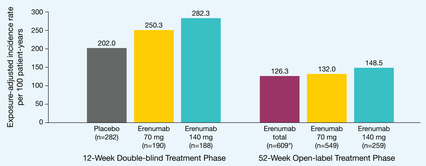


Full analysis set. Data are mean.
*Based on 605 patients in the efficacy analysis set.

Safety

- Total exposure during the DBTP was 43.1 patient-years for both 70 mg and 140 mg doses and 63.7 patient-years for placebo; total exposure during the OLTP (70 and 140 mg) was 527.0 patient-years
- Exposure-adjusted incidence rates of treatment-emergent AEs are reported in **Figure 3** and **Table 1;** no new safety events and no dose-dependent AEs were reported
- Most AEs were grade 1 or 2 in severity; no grade 4 or fatal AEs were reported

Figure 3. *Exposure-Adjusted Incidence Rates of Treatment-Emergent AEs (Summarized Based on the Dose Received When the AE Occurred)*



Safety analysis set
*The numbers for the 2 dose groups (n = 549, n = 259) are not additive to the total (N = 609); 199 patients who were exposed to both doses are also included in these columns; grading categories determined using CTCAE v4.03

Table 1. *Exposure-Adjusted Incidence Rates of Treatment-Emergent AEs (Summarized Based on the Dose Received When the AE Occurred)*

	12-week DBTP, n (r)			52-week OLTP, n (r)		
	Placebo	Erenumab		Erenumab		Total
	n = 282	70 mg n = 190	140 mg n = 188	70 mg n = 549	140 mg n = 259	N = 609*
Any AE	110 (202.0)	83 (250.3)	88 (282.3)	311 (132.0)	157 (148.5)	398 (126.3)
Grade ≥ 3	13 (18.0)	11 (22.6)	4 (8.3)	28 (6.6)	8 (3.7)	34 (5.4)
Serious AEs	7 (9.5)	6 (12.1)	2 (4.1)	14 (3.3)	10 (4.7)	24 (3.8)
AE leading to discontinuation of erenumab	2 (2.7)	0	2 (4.1)	9 (2.1)	7 (3.3)	16 (2.5)
Most frequent AEs†						
Viral upper respiratory tract infection	14 (19.3)	6 (12.2)	3 (6.1)	68 (17.1)	35 (17.8)	96 (16.4)
Upper respiratory tract infection	4 (5.4)	5 (10.1)	6 (12.5)	33 (7.8)	13 (6.2)	45 (7.2)
Sinusitis	6 (8.1)	3 (6.0)	2 (4.1)	31 (7.5)	14 (6.7)	44 (7.1)
Arthralgia	3 (4.0)	2 (4.0)	1 (2.1)	16 (3.8)	11 (5.2)	27 (4.2)

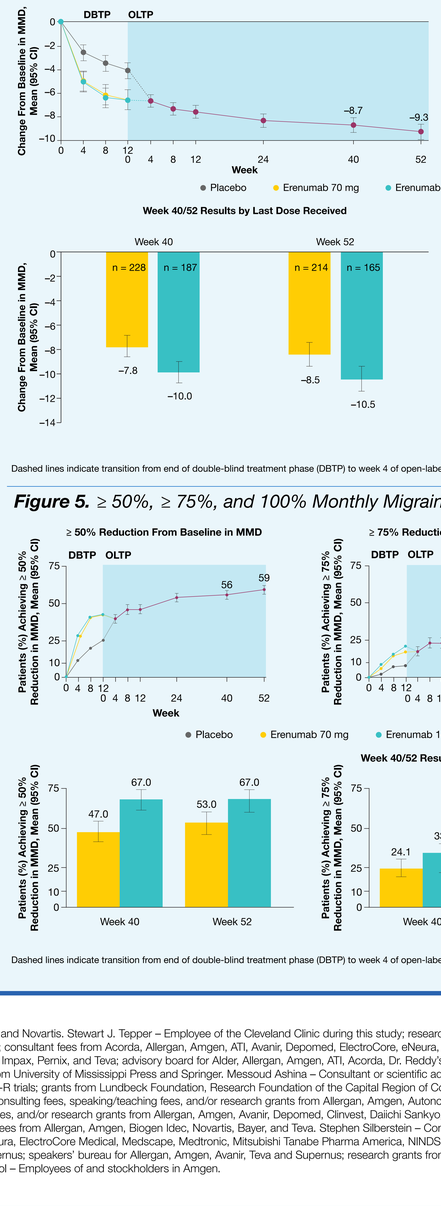
Safety analysis set
*The numbers for the 2 dose groups (n = 549, n = 259) are not additive to the total (N = 609); 199 patients who were exposed to both doses are also included in these columns; grading categories determined using CTCAE v4.03
†≥ 4.2 patients per 100 patient-years in the total erenumab group during OLTP; coded in MedDRA v20.0
DBTP, double-blind treatment phase; OLTP, open-label treatment phase; r, exposure-adjusted patient rate per 100 patient-years (r/e*100)

- During the OLTP, anti-erenumab binding antibodies and neutralizing antibodies were observed in 34 (5.8%) and 3 (0.5%) patients, respectively
  - 17 and 2 patients, respectively, had negative results at the final visit

Efficacy

- Erenumab demonstrated sustained efficacy over 52 weeks of treatment
- Patients who completed the 52-week OLTP showed a numerically greater benefit with erenumab 140 mg versus 70 mg at weeks 40 and 52 for:
  - change from DBTP baseline in MMD (**Figure 4**)
  - MMD responder rates (a ≥ 50%, ≥ 75%, and 100% reduction from DBTP baseline) (**Figure 5**)
  - change from DBTP baseline in monthly AMSM use days (in AMSM users at baseline) (**Figure 6**)

Figure 4. *Change From DBTP Baseline in Monthly Migraine Days (MMD)*



Dashed lines indicate transition from end of double-blind treatment phase (DBTP) to week 4 of open-label treatment phase (OLTP)

Figure 6. *Change From DBTP Baseline in Monthly Acute Migraine–Specific Medication (AMSM) Use Days (in AMSM Users at Baseline)*

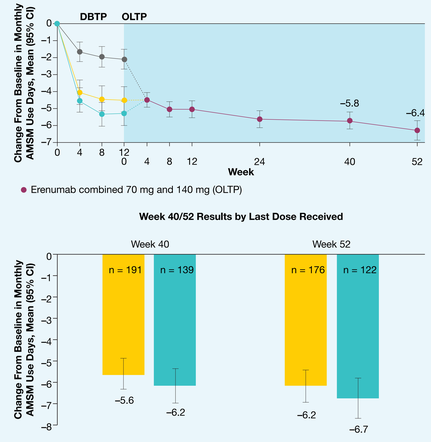
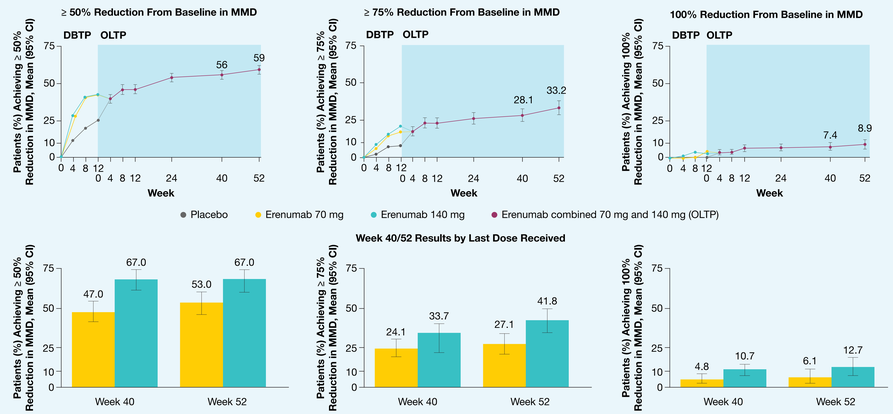


Figure 5. *≥ 50%, ≥ 75%, and 100% Monthly Migraine Days (MMD) Responder Rates*



Dashed lines indicate transition from end of double-blind treatment phase (DBTP) to week 4 of open-label treatment phase (OLTP)

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1. Aimovig® (erenumab-aooe) Prescribing Information, 2019.
2. Tepper S, et al. *Lancet Neurol.* 2017;16:425-34.

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The final responsibility of the content lies with the authors.

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