ePoster #568

Three-year efficacy and safety of erenumab in participants with episodic migraine and 2–4 prior preventive treatment failures: Results from the LIBERTY study

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BACKGROUND

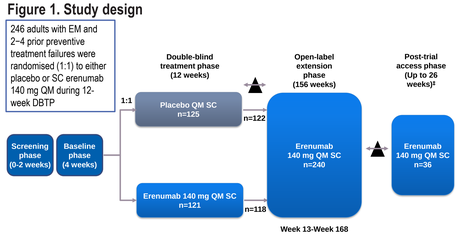
- Erenumab (erenumab-aooe in the United States) is a fully human monoclonal antibody targeting the canonical calcitonin gene-related peptide receptor[1]
- Erenumab has been shown to reduce the frequency of monthly migraine days (MMD) and achieve other clinically meaningful responses in pivotal clinical trials in patients with episodic migraine (EM)[2-4] or chronic migraine[5-6]
- The results of the double-blind treatment phase (DBTP) of the LIBERTY study (NCT03096834) demonstrated the efficacy of erenumab 140 mg in patients with EM for whom 2−4 prior preventive treatments had failed[7]
- Interim analyses demonstrated that efficacy was maintained throughout the first[8] and second[9] years of the open-label extension phase (OLEP)
- Here, we present the efficacy and safety of erenumab 140 mg at the completion of the LIBERTY study (3 years of OLEP and 6 months of post-trial access phase [PTA])

METHODS

Study design

- LIBERTY was a multicentre, randomised, double-blind, placebo-controlled, parallel-group, Phase 3b study conducted across Europe and Australia in patients with EM for whom 2–4 prior preventive treatments had failed (**Figure 1**)
- Patients completing the DBTP (N=240) were enrolled into the OLEP and received once-monthly subcutaneous erenumab 140 mg for up to an additional 3 years. A subset of patients (N=36) then entered PTA phase for up to 6 months

Figure 1. Study design



•▲• Follow-up phase 16 weeks after the last dose of the study drug. ‡Post-trial access phase was for a subset of patients. DBTP, double-blind treatment phase; EM, episodic migraine; n, number of patients; OLEP, open-label extension phase; QM, once monthly; SC, subcutaneous.

Outcomes

- Achievement of at least 30%, 50%, 75%, and 100% reduction in MMD compared with DBTP baseline (BL)
- Change from DBTP BL in MMD, headache impact test (HIT-6™) total score, migraine physical function impact diary (MPFID) Everyday Activities (EA) and Physical Impairment (PI) scores, and safety

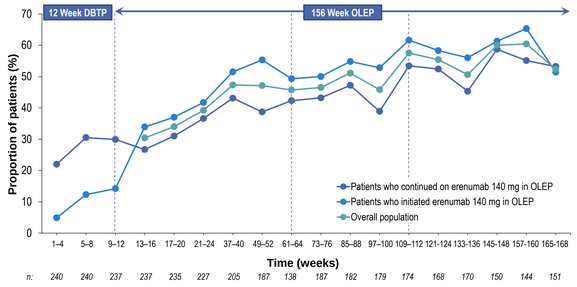
Statistical analysis

- Descriptive statistics were used to summarise continuous endpoints by each treatment group at each visit; for categorical endpoints, the number and percentage of patients were used
- Treatment-emergent adverse events (AEs) and serious AEs were monitored

RESULTS

- Overall, 240 (97.6%) of the 246 randomised patients entered the OLEP (118 continuing erenumab, 122 switching from placebo); 169 (70.4%) patients completed the 3-year OLEP; all 36 patients completed PTA
- Discontinuations were mainly due to lack of efficacy in 30 (12.5%) patients, patient decision in 26 (10.8%), and AEs in 11 (4.6%, single case per AE)
- The baseline demographic characteristics were collected at the start of the DBTP and were generally well-balanced between treatment groups[8]
- The proportion of patients who achieved ≥50% reduction in MMD from DBTP baseline increased through the first year; the improvement was sustained through the end of the 3 years of the OLEP across all treatment groups (**Figure 2**)

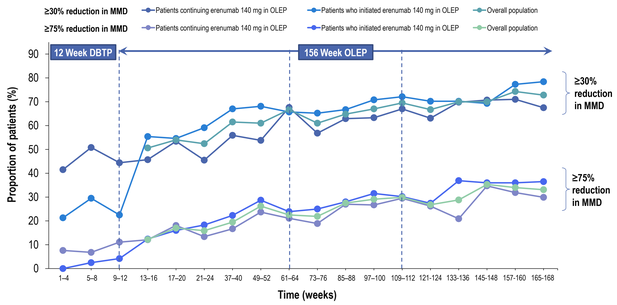
Figure 2. Proportion of patients with ≥50% reduction in MMD from DBTP baseline



DBTP, double-blind treatment phase; MMD, monthly migraine days; n: the total number of patients in the treatment group with response variable defined in respective visit; OLEP, open-label extension phase

- The proportion of patients achieving ≥30% and ≥75% reduction from baseline in MMD increased from DBTP through to Week 168, showing sustained improvement during the 3 years of the OLEP (**Figure 3**)
  - Similarly, the proportion of patients achieving 100% reduction from baseline in MMD were 12.3%, 16.1%, and 13.2% at Week 64, Week 112, and Week 168, respectively

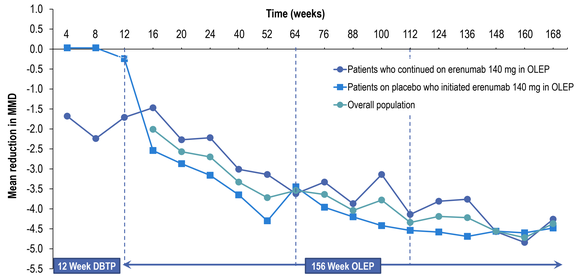
Figure 3. Proportion of patients with ≥30% and ≥75% reduction in MMD from DBTP baseline



DBTP, double-blind treatment phase; MMD, monthly migraine days; OLEP, open-label extension phase

- The mean reduction in MMD from DBTP baseline showed sustained improvement over 3 years across all treatment groups in the OLEP (**Figure 4**)

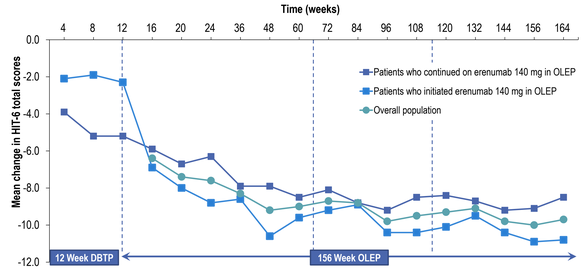
Figure 4. Change in MMD from DBTP baseline until Week 168 of the OLEP



DBTP, double-blind treatment phase; MMD, monthly migraine days; OLEP, open-label extension phase

- Mean (SD) change in HIT-6 total score from DBTP baseline decreased through year one and the improvement was then maintained through year 3; HIT-6 score was −9.7 (8.9) at Week 164 (**Figure 5**)

Figure 5. Change in HIT-6 total score from DBTP baseline until Week 164 of the OLEP



DBTP, double-blind treatment phase; HIT-6 - Headache Impact Test; OLEP, open-label extension phase

- Mean (SD) change from DBTP baseline at 3-year completion was −6.1 (8.2) for MPFID-EA and −5.1 (7.6) for MPFID-PI scores (**Table 1**), showing a similar trend in improvement as the HIT-6 scores

Table 1. Patient-reported outcomes after 3 years of the OLEP (open-label analysis set)

Outcomes	Patients continuing erenumab 140 mg, N=118		Patients switching to erenumab 140 mg, N=122		Overall population entering OLEP, N=240	
Change from DBTP BL in	m	Mean (SD)	m	Mean (SD)	m	Mean (SD)
MPFID-PI	77	−5.5 (6.7)	74	−4.6 (8.5)	151	−5.1 (7.6)
MPFID-EA	77	−6.8 (7.0)	74	−5.3 (9.3)	151	−6.1 (8.2)

Change from baseline = post-baseline−BL. The BL period is defined as the period between Week-4 visit and the day prior to first dose. The BL value is the prorated number to 28-day equivalents during BL period. At each time point, only patients with a value at both BL and that time point are included; BL, baseline; DBTP, double-blind treatment phase; EA, everyday activities; m, the total number of patients in the treatment group with observed data at Week 168; MPFID; Migraine Physical Function Impact Diary; N, number of patients included in the analysis set; OLEP, open-label extension phase; PI, physical impairment.

RESULTS (Continued)

- During the OLEP and PTA, the most common treatment-emergent AEs were nasopharyngitis, influenza, and back pain
- The incidence of AEs of special interest remained low throughout the trial (**Table 2**)

Table 2. Summary of treatment-emergent AEs in the OLEP+PTA (safety analysis set)

Events	OLEP, overall population, N=240 % (rate per 100 patient-years)		
	Year 1	Year 1+2	Year 1+2+3+PTA
Any AE	80.8% (242.9)	86.3% (198.0)	89.6% (176.2)
Any SAE	6.7% (7.2)	10.4% (6.3)	14.2% (6.0)
AE leading to discontinuation of treatment	1.7% (1.7)	3.8% (2.1)	5.0% (1.9)
Any treatment-related AE	23.8% (30.1)	27.5% (19.8)	30.4% (15.4)
Most frequent AEs and AEs of interest in the OLEP, by preferred term			
Nasopharyngitis	30.8% (41.4)	41.3% (33.9)	47.1% (28.8)
Influenza	12.9% (14.6)	16.3% (10.3)	17.1% (7.5)
Back pain	7.5% (8.2)	10.8% (6.6)	13.8% (5.8)
Hypertension	2.9% (3.1)	5.8% (3.4)	9.6% (3.9)
Constipation	2.5% (2.7)	5.4% (3.1)	6.7% (2.7)

Time at risk during OLEP is time from start of OLEP to onset of first event in OLEP or minimum (end of study date, last investigational product dose date+112 days). MedDRA Version 23.1 was used for reporting of AEs. Year 1+2+3+PTA overall population are cumulative of data from all 3 years of OLEP and post-trial access. AE, adverse event; N, number of patients in analysis set; OLEP, open-label extension phase; PTA, post-trial access; SAE, serious adverse event.

CONCLUSIONS

- The LIBERTY 3-year study represents a long-term follow-up of the efficacy and tolerability of erenumab in patients with difficult-to-treat EM in whom 2–4 prior migraine preventive treatments had failed
- No new safety signals were reported after long-term exposure; the exposure-adjusted rate of overall and most frequently reported AEs remained low during the open-label extension phase + post-trial access phase
- Efficacy was sustained over the 3 years of the OLEP, and the high retention rate (70.4%) illustrates that erenumab was well tolerated in these patients, in line with previous studies

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