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Efficacy and safety of erenumab in patients with episodic migraine from the EMPOwER study

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Background and Methods

Background

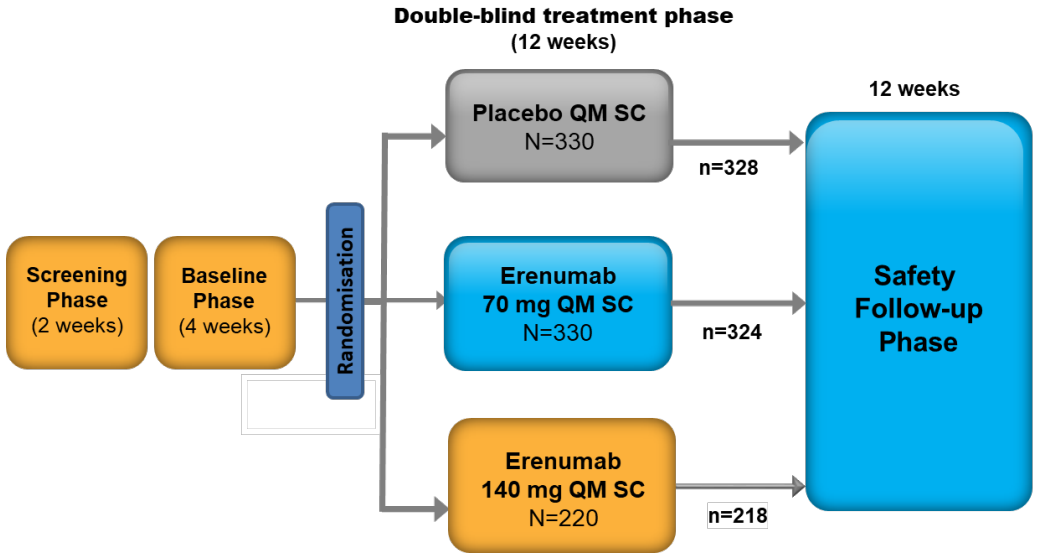
- Erenumab is a fully human monoclonal antibody that selectively blocks the canonical calcitonin gene-related peptide receptor[1]
- EMPOwER (NCT03333109) was a 12-week, double-blind, randomised erenumab study in patients with episodic migraine (EM) from Asia, Middle East and Latin America
- Previous clinical trials of erenumab have not included patients with migraine from these regions

Objective

- To evaluate the efficacy and safety of erenumab (70 mg and 140 mg once monthly [QM]) in adult patients with EM

Figure 1. Study design

Eligibility criteria
- Adults aged 18–65 years, with a prior diagnosis of migraine according to the ICHD-3 beta[2] for ≥12 months before screening
- Average of ≥4 and <15 MMD and <15 MHD across the 3-month period before screening and during a 4-week baseline phase



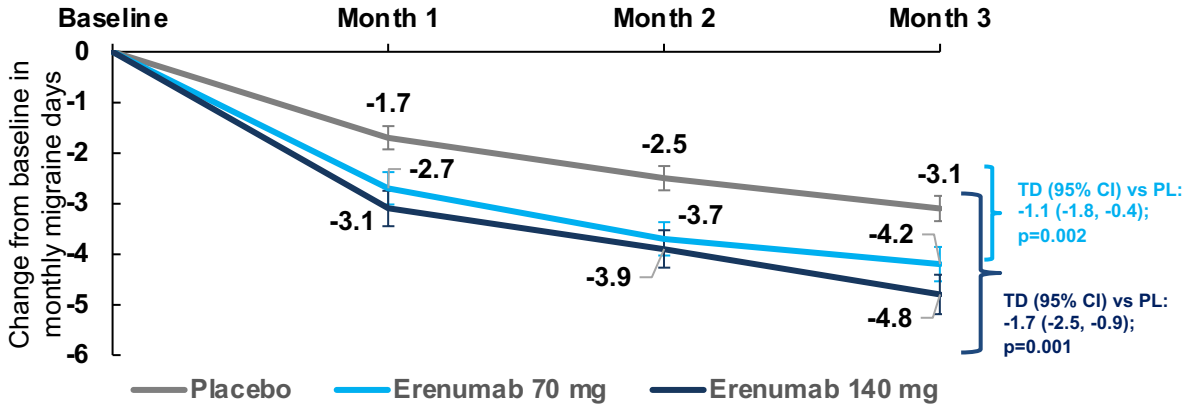
Study endpoints
- The primary endpoint was the change from baseline in MMD at Month 3
- Secondary endpoints assessed achievement of ≥50% reduction in MMD, change in HIT-6™, change in MSMD and safety/tolerability at Month 3

n, patients who entered the safety follow-up phase; HIT-6™, headache impact test; ICHD, International Headache Society Classification International Classification Headache Disorders; MHD, monthly headache days; MMD, monthly migraine days; MSMD; monthly acute migraine-specific medication days, SC, subcutaneous; QM, once monthly

1. Shi L, et al. *J Pharmacol Exp Ther*. 2016;356:223–31; 2. Headache Classification Committee of the International Headache Society (IHS). 2013;33:629–808

Results

Figure 2. Change from baseline in MMD by treatment and visit (mITT analysis set)

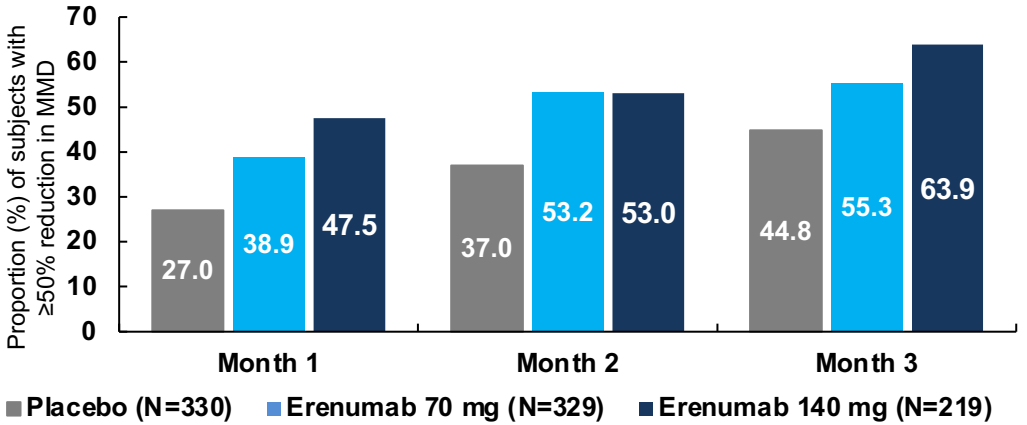


N values	Baseline	Month 1	Month 2	Month 3
Placebo	330	324	318	310
Erenumab 70 mg	329	325	316	306
Erenumab 140 mg	219	214	205	199

The error bars represent the standard error

- Change in MMD from baseline at Month 3 was −3.1 for placebo, −4.2 and −4.8 for erenumab 70 mg and 140 mg, respectively, and achieved statistical significance versus placebo (p=0.002 [70 mg] and <0.001 [140 mg])

Figure 3. Proportion of patients with ≥50% reduction from baseline in MMD (mITT analysis set)



OR (95% CI) vs placebo	Erenumab 70 mg	Erenumab 140 mg
Month 1	1.7 (1.2, 2.4); p=0.001	2.5 (1.7, 3.5); p<0.001
Month 2	1.9 (1.4, 2.7); p<0.001	1.9 (1.4, 2.7); p<0.001
Month 3	1.5 (1.1, 2.1); p=0.007	2.2 (1.6, 3.2); p<0.001

Statistical analysis utilises a Cochran-Mantel-Haenszel test adjusting for stratification factor after missing data are imputed as non-response

- Proportion of patients achieving ≥50% reduction in MMD at Month 3 was statistically significant in erenumab 70 mg and 140 mg versus placebo (55% and 64% vs 45%; p=0.007 [70 mg] and <0.001 [140 mg])

The mITT analysis set consists of all patients who started study medication and had completed at least one post-baseline efficacy measurement during the double-blind treatment phase

CI, confidence interval; ITT, intention-to-treat analysis set.; MMD, monthly migraine days; OR, odds ratio; PL, placebo; TD, treatment difference

Results and Conclusions

Table 1: Change from baseline to Month 3 in secondary outcomes-MSMD and HIT-6™ scores (mITT analysis set)

		Adjusted mean change (SE)		Mean difference, (95%CI); p value
		Erenumab	Placebo	
MSMD	Erenumab 70 mg (N*=123) vs placebo (N*=127)	−1.84 (0.26)	−0.49 (0.26)	−1.36, (−2.07, −0.64); <0.001
	Erenumab 140 mg (N*=80) vs placebo (N*=127)	−2.39 (0.33)	−0.49 (0.26)	−1.90, (−2.71, −1.09); <0.001
HIT-6™	Erenumab 70 mg (N=329) vs placebo (N=330)	−8.39 (0.45)	−6.62 (0.44)	−1.77, (−2.99, −0.56); 0.004
	Erenumab 140 mg (N=219) vs placebo (N=330)	−9.34 (0.54)	−6.62 (0.44)	−2.71, (−4.07, −1.36); <0.001

N, the number of patients included in the mITT analysis set. N*, the number of patients in mITT analysis set who had at least one migraine specific medication during baseline

Safety

- In general, safety and tolerability profiles of erenumab 70 mg or 140 mg were comparable with placebo, and there were no newly emergent safety signals
- Six serious adverse events were reported in 5 patients (3 [0.9%] in erenumab 70 mg and 2 [0.6%] in placebo groups) and none were treatment related except asthenia in placebo group. No deaths were reported during the study
- None of the patients in the erenumab groups, while 2 (0.6%) patients from the placebo group discontinued the study treatment due to adverse events
- The most frequent treatment-emergent adverse events (≥2% in any treatment group) were constipation (4%), nasopharyngitis (2%), pyrexia (3.4%) and upper respiratory tract infection (2.2%). Most adverse events observed were mild or moderate in severity. Injection site pain was reported only in 7 (0.8%) patients (4 [1.2%] in erenumab 140 mg; 3 [1.3%] in erenumab 70 mg and none in placebo

Conclusion

- **The EMPOwER study confirms the efficacy and safety of erenumab 70 mg and 140 mg in adult patients with EM from the regions of Asia, Middle East, and Latin America not adequately represented in the previous erenumab trials**
- **Consistent with the previous pivotal studies of erenumab in patients with EM, an efficacy related dose response was observed and no apparent dose-response pattern was observed across the most common treatment-emergent adverse events[1,2]**

The mITT analysis set consists of all patients who started study medication and had completed at least one post-baseline efficacy measurement during the double-blind treatment phase
CI, confidence interval; EM, episodic migraine; HIT-6™, headache impact test; MSMD; monthly acute migraine-specific medication days; SE, standard error

1. Goadsby PJ, et al. *N Engl J Med* 2017;377: 2123–32; 2. Sakai F, et al. *Headache* 2019;59:1731–42