Efficacy and safety of erenumab in patients with episodic migraine in East Asia: Taiwan and Korea subpopulation analysis of the EMPOwER study

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INTRODUCTION

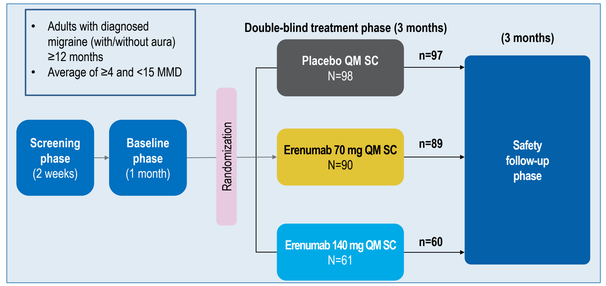
- Erenumab (erenumab-aooe in the United States) is a fully human monoclonal antibody targeting the canonical calcitonin gene-related peptide receptor[1]
- Erenumab has demonstrated efficacy and safety in episodic migraine (EM) and chronic migraine in various studies[2-5]
- Most studies were conducted in North America and Europe and there remains an unmet need for appropriate management of migraine in Asia; this represents nearly a third of the world's population
- The EMPOwER study demonstrated the efficacy and safety of erenumab in Asia, the Middle East, and Latin America
- The objective of this study was to evaluate the efficacy and safety of monthly erenumab (70 and 140 mg) in the East Asian subpopulation (Taiwan and Korea) of the EMPOwER study

METHODS

Study design

- EMPOwER (NCT03333109) was a 12-week, randomized, double-blind, placebo-controlled, Phase 3 study of erenumab in patients with EM conducted at 83 sites across 11 countries in Asia, the Middle East, and Latin America
- This subpopulation analysis presents the efficacy and safety data of erenumab in Taiwanese and Korean patients
- Patients meeting the eligibility criteria were randomized (3:3:2) to receive monthly doses of placebo, erenumab 70 mg or 140 mg every four weeks during a 12-week double-blind treatment period (DBTP) at Weeks 4, 8, and 12 (**Figure 1**)

Figure 1. Study design



Randomization was not stratified. Data was extracted for the Taiwan and Korea subpopulation. Patients who entered the safety follow-up period were those who completed the end of treatment visit and did not discontinue study at that visit. MMD, monthly migraine days; n, number of patients who entered the safety follow-up phase; N, number of randomized patients; QM, every 4 weeks; SC, subcutaneous

Outcomes

- The primary endpoint was the change from baseline in monthly migraine days (MMD) at Month 3
- Secondary endpoints assessed at Month 3 included achievement of ≥50% reduction in MMD, change from baseline in monthly acute migraine-specific medication treatment days (MSMD), change in Headache Impact Test (HIT-6^{TM}) score, and safety assessments

Statistical analysis

- The primary endpoint was analyzed using a linear mixed-effects repeated measures model based on observed monthly data during DBTP, and pairwise comparisons were conducted
- Other continuous endpoints were analyzed using a linear mixed-effects model similar to that used for the primary endpoint. The dichotomous endpoint was analyzed by the Cochran-Mantel-Haenszel test; patients who did not have MMD data at Month 3 of the DBTP were imputed as non-responders
- Treatment-emergent adverse events (AEs) and serious AEs were summarized by treatment group descriptively

RESULTS

- Of the 385 screened patients, 249 were randomized to either placebo (N=98), erenumab 70 mg (N=90), or erenumab 140 mg (N=61) (**Figure 1**)
- At baseline, the mean (standard deviation) age for the overall population was 40.4 (±10.3) years, 79.1% of patients were female; mean MMD was 7.94 (2.39) (**Table 1**)

Table 1. Baseline demographic and clinical characteristics

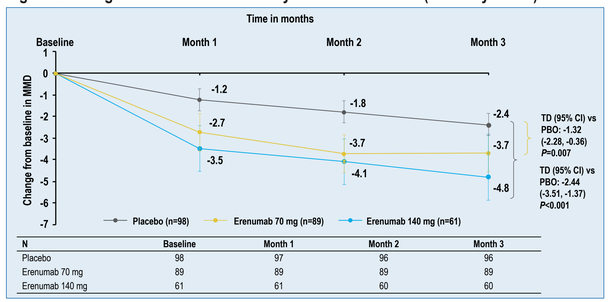
	Placebo (N=98)	Erenumab 70 mg (N=90)	Erenumab 140 mg (N=61)
Age, years	41.5 (9.6)	39.6 (10.3)	39.9 (11.4)
Female, n (%)	81 (82.7)	72 (80.0)	44 (72.1)
Body mass index, kg/m^2	23.2 (3.7)	23.4 (3.7)	23.8 (4.4)
Age at onset of migraine, years	27.4 (10.0)	27.5 (9.8)	25.8 (10.4)
Migraine duration, years	14.2 (9.5)	12.0 (9.4)	14.1 (9.8)
Aura, n (%)			
Present	66 (67.3)	65 (72.2)	46 (75.4)
Absent	32 (32.7)	25 (27.8)	15 (24.6)
Number of prior preventive treatment failure, n (%)			
0	70 (71.4)	69 (76.7)	43 (70.5)
1	20 (20.4)	14 (15.6)	13 (21.3)
2	4 (4.1)	6 (6.7)	4 (6.6)
3	3 (3.1)	0	0
4	1 (1.0)	1 (1.1)	0
>4	0	0	1 (1.6)
MMD	8.1 (2.6)	7.9 (2.2)	7.8 (2.4)
MHD	9.1 (2.4)	9.0 (2.3)	8.8 (2.6)
Monthly acute MSMD	4.0 (3.3)	4.1 (3.1)	4.3 (3.0)
Monthly acute headache-specific medication days	5.7 (3.1)	5.7 (2.3)	5.5 (2.5)

Data are mean (standard deviation) unless specified. MHD, monthly headache days; MMD, monthly migraine days, MSMD, migraine-specific medication days

Efficacy results

- At Month 3, there was a statistically significant greater reduction from baseline in mean MMD for erenumab 70 mg (−3.68 days, *P*=0.007) and 140 mg (−4.81 days, *P*<0.001) compared with placebo (−2.37 days) (**Figure 2**)
- A higher proportion of patients achieved ≥50% reduction in MMD with erenumab 70 mg (52.8%, *P*=0.011) and 140 mg (67.2%, *P*<0.001) compared with placebo (33.7%) (**Table 2**)
- There was a greater reduction in MSMD with erenumab 70 mg (−1.5, P=0.007) and 140 mg (−2.36, P<0.001) compared with placebo (−0.54). Similarly, a greater reduction in the HIT-6^{TM} score with erenumab 70 mg (−7.59, P=0.007), and 140 mg (−7.98, P=0.006) compared with placebo (−4.77) was reported

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



N	Baseline	Month 1	Month 2	Month 3
Placebo	98	97	96	96
Erenumab 70 mg	89	89	89	89
Erenumab 140 mg	61	61	60	60

Error bars represent the standard error; *P*<0.05 was considered as statistically significant. A linear mixed-effects model included treatment group, baseline value, stratification factor, scheduled visit, and the interaction of the treatment group with scheduled visit. Unstructured covariance matrix assumed. Adjusted LSMs and 95% CIs from the primary analysis model are presented. 95% CI are presented for the month 3 data.
CI, confidence interval; MMD, monthly migraine days; N, number of patients included in the analysis set; PBO, placebo; TD, treatment difference

Table 2. Change from baseline in secondary endpoints at Month 3 (full analysis set)

	Placebo	Erenumab 70 mg	Erenumab 140 mg
≥50% reduction in MMD			
m/M (%)	33/98 (33.7)	47/89 (52.8)	41/61 (67.2)
Odds ratio (95% CI)	-	2.14 (1.18, 3.85)	3.93 (2.00, 7.69)
p-value	-	0.011	<0.001
MSMD*			
Mean change (SE)	−0.54 (0.25)	−1.50 (0.26)	−2.36 (0.31)
Mean difference (95% CI)	-	−0.95 (−1.64, −0.27)	−1.81 (−2.58, −1.05)
p-value	-	0.007	<0.001
HIT-6^{TM} score*			
Mean change (SE)	−4.77 (0.74)	−7.59 (0.79)	−7.98 (0.93)
Mean difference (95% CI)	-	−2.82 (−4.86, −0.78)	−3.21 (−5.49, −0.92)
p-value	-	0.007	0.006

*A linear mixed-effects model included treatment group, baseline value, stratification factor, scheduled visit, and the interaction of the treatment group with scheduled visit. Unstructured covariance matrix assumed
Statistical analysis utilizes a Cochran-Mantel-Haenszel (CMH) test adjusting for stratification factor after missing data are imputed as non-response (NRI)
CI, confidence interval; HIT-6^{TM}, headache impact test score; M, the total number of patients in the treatment group with a response variable defined; m, the number of patients who responded; MMD, monthly migraine days; MSMD, monthly acute migraine-specific medication treatment days; SE, standard error

Safety results

- In general, the safety profile of erenumab was in line with that of the global population; there were no newly emergent safety signals
- Treatment-emergent AEs were reported in 39/98 (39.8%) patients receiving placebo, 30/89 (33.7%) patients receiving erenumab 70 mg, and 25/61 (41.0%) patients receiving erenumab 140 mg
- The most frequent treatment-emergent AEs were constipation, dizziness, nasopharyngitis, and injection site erythema (**Table 3**)
- During the DBTP, no serious AEs (SAEs) were reported in patients receiving erenumab. One patient receiving placebo reported one SAE (abortion) and this was suspected to be related to the study treatment by the investigator
- Two patients discontinued the placebo during the DBTP due to AEs (diplopia in one patient, and pain in extremity and hypoesthesia in another patient)

CONCLUSIONS

- The EMPOwER study demonstrated the efficacy and safety of monthly erenumab (70 and 140 mg) in adults with EM from Taiwan and Korea, consistent with the results from the global population
- A consistent benefit was observed with erenumab (70 mg and 140 mg) versus placebo across all efficacy endpoints

Table 3. Summary of treatment-emergent AEs, during the DBTP (safety analysis set)

Events	Placebo N=98, n (%)	Erenumab 70 mg N=89, n (%)	Erenumab 140 mg N=61, n (%)
At least one AE	39 (39.8)	30 (33.7)	25 (41.0)
Any SAEs	1 (1.0)	0	0
Any AE leading to treatment discontinuation	2 (0.6)	0	0
Most frequent treatment-emergent AEs (≥3% in any group) by preferred term			
Constipation	1 (1.0)	4 (4.5)	4 (6.6)
Dizziness	2 (2.0)	1 (1.1)	3 (4.9)
Back pain	0	0	2 (3.3)
Cystitis	0	0	2 (3.3)
Nasopharyngitis	4 (4.1)	1 (1.1)	2 (3.3)
Pruritus	0	1 (1.1)	2 (3.3)
Diarrhea	3 (3.1)	0	0
Upper respiratory tract infection	1 (1.0)	3 (3.4)	1 (1.6)
Injection site erythema	4 (4.1)	2 (2.2)	0
Migraine	1 (1.0)	3 (3.4)	0

Preferred terms are sorted by descending frequency of AEs in the erenumab 140 mg column and then alphabetically. A patient with multiple AEs is counted only once in the "at least one AE" row. A patient with multiple AEs with the same preferred term is counted only once for that preferred term. MedDRA Version 22.0 was used for the reporting of AEs. AE, adverse event.

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CONFLICTS OF INTERESTS

Shuu-Jiun Wang served on the advisory boards of Eli Lilly and Novartis, Taiwan. He has received honoraria as a moderator from AbbVie, Pfizer, Eli Lilly, Bayer, and Eisai. He has received research grants from the Taiwan Ministry of Technology and Science, Brain Research Center, National Yang Ming Chiao Tung University from The Featured Areas Research Center Program within the framework of the Higher Education Sprout Project by the Ministry of Education (MOE) in Taiwan, Taipei Veterans General Hospital, and Taiwan Headache Society. **Byung-Kun Kim** received personal compensation for speaking, serving on a scientific advisory board, or consulting from Eli Lilly, Teva Korea, Allergan Korea, Lundbeck Korea, YuYu Pharm, and SK Chemical. **Gabriel Paiva Da Silva Lima** is an employee and owns stocks in Amgen Inc. **Shaloo Pandhi, Shihua Wen, Peggy Hours-Zesiger** are employees and own stocks in Novartis. **Subhayan Mondal** is an employee of Novartis.

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