Original Article

Efficacy and Tolerability of Erenumab for Prevention of Episodic Migraine in India

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Abstract

Background: EMPOwER, a 12-week, double-blind (DB), randomized, placebo-controlled study evaluated the efficacy and safety of erenumab in adult patients with episodic migraine (EM) from Asia, the Middle East, and Latin America. This study analyzes the Indian experience for the use of erunumab for prevention of episodic migraine. **Objective:** The study aimed to evaluate the efficacy and tolerability of erenumab (70 mg and 140 mg) in EM patients from India. **Methods:** Randomized patients received monthly subcutaneous injections of placebo and erenumab 70 mg or 140 mg for 3 months. The primary endpoint was a change from the baseline in monthly migraine days (MMDs) at month 3. Other endpoints included achievement of ≥50%, ≥75%, and 100% reduction in MMD; a change in monthly acute migraine-specific medication treatment days; a change in patient-reported outcomes; and safety assessment. **Results:** Of the 539 patients screened, 351 patients were randomized (erenumab, 70 mg: n = 133 and 140 mg: n = 94; placebo: n = 124). The mean (±SD) age, disease duration, and MMD were 35.1 (±8.6) years, 6.77 (±6.01) years, and 7.82 (±2.89) days, respectively. The placebo-adjusted difference in mean MMD for erenumab 70 mg was -0.88 (95% CI, -2.16, 0.39; $P = 0.174$) days, and that for erenumab 140 mg was -1.01 (-2.42, 0.41; $P = 0.164$) days versus placebo. Secondary and exploratory endpoints demonstrated consistently better results in both erenumab dosage groups versus placebo. Treatment-emergent adverse events were comparable across groups (erenumab, 70 mg: 22.7% and 140 mg: 24.5%; placebo: 25.2%). **Conclusion:** Both doses of erenumab showed numerical improvement for efficacy endpoints and were well-tolerated in the Indian population. No new safety signals were reported.

Keywords: Efficacy, erenumab, headache, Indian population, tolerability episodic migraine

Introduction

Migraine is a common disabling neurological disorder, characterized by recurrent episodes of headache.[1] It has a 1-year incidence of 14.7% in the general population and is a leading cause of disability.[2,3] A population-based study from India however has shown higher (25%) 1-year prevalence of migraine.[4] Despite the need of preventive treatment for migraine patients with ≥4 monthly migraine headache days, a recent American study showed that only around 25% patients actually receive preventive treatment.[5] This is partly because of the fact that conventional preventive medications for migraine are not specific, lack adequate efficacy, and are frequently associated with adverse effects (AEs) and poor adherence.[6] Hence, there is an unmet need to develop novel migraine-specific treatment options.

Erenumab (erenumab-aooe in the United States) is the first Food and Drug Administration (FDA)-approved monoclonal antibody (mAb)[7] for migraine prevention.[8] Previous clinical studies on erenumab from the United States, Japan, and Europe demonstrated superior efficacy compared with placebo.[9-13] Because of non-representation of migraine patients from Latin America, the Middle East, and some parts of Asia such as India, in earlier studies, EMPOwER study was conducted on episodic migraine (EM) from 2018 to 2020, and the results were published recently.[14]

This is an analysis of India-specific data from the Global EMPOwER study aimed to strengthen the evidence in the Indian population that was not adequately represented in previous clinical trials of erenumab.

Methodology

This analysis was performed for Indian EM patients who participated in a randomized, double-blind, phase 3 study [EMPOwER (NCT03333109)], which evaluated the efficacy and safety of erenumab. The study was conducted across 27 research sites in India. The methodology of the EMPOwER study has already been published in the Global publication.[14] Briefly, the details are as follows:

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Patients

Eligible patients aged 18–65 years with a documented history of migraine for 12 months according to the International Classification of Headache Disorders, third edition (ICHD-3)[15] before screening; ≥4 and <15 days/month of migraine symptoms were included. Patients >50 years old at migraine onset; no treatment response to >2 migraine-preventive therapy; use of botulinum toxin within 4 months; ergotamines or triptans on ≥10 days/month were excluded from the study.

Ethical practices

The study protocol and amendments were reviewed and approved by an Independent Ethics Committee or the Institutional Review Board at each participating site, and the study was conducted as per the ICH E6 Guidelines for Good Clinical Practice, originating in the Declaration of Helsinki and applicable regulatory requirements. Additionally, National Ethical Guidelines for Biomedical and Health Research involving Human Participants were followed, as issued by the Indian Council of Medical Research. Written informed consent was obtained from every patient prior to the initiation.

Treatment

In the double-blind treatment period (DBTP), all eligible patients were randomized (2:3:3) to receive erenumab 140 mg, erenumab 70 mg, or matching placebo once per month.

Efficacy assessments

Primary endpoint

The primary efficacy endpoint was a change from the baseline in monthly migraine days (MMDs) in the last month (month 3) of the DBTP.

Secondary endpoints

The secondary efficacy endpoints at month 3 were the achievement of ≥50%, ≥75%, and 100% reduction from the baseline in MMD; a change from the baseline in monthly acute migraine-specific medication treatment days; and a change from the baseline in the headache impact test (HIT-6™) total score.

Exploratory endpoints

The exploratory efficacy endpoints were the reduction of ≥50%, ≥75%, and 100% from the baseline in MMD in each month; a change from the baseline in monthly acute migraine-specific medication treatment days in each month; and a change from the baseline in migraine-related disability and productivity [measured by the modified Migraine Disability Assessment (MIDAS)] and Headache Impact Test- 6 (HIT-6) in each month of the DBTP.

Safety assessments

Safety was evaluated based on AEs, treatment-emergent (TE) AEs, clinical laboratory values, vital signs, and anti-erenumab antibodies.

Statistical analysis

The primary endpoint variable was evaluated using a linear mixed-effects model for repeated measures; pairwise comparisons (erenumab 70 mg versus placebo and erenumab 140 mg versus placebo) were performed subsequently. The difference of least mean squares (LSMs) versus the placebo group, the associated 95% confidence interval (CI) of the differences, and the nominal two-sided *P* values were tabulated by visit and treatment. The secondary endpoints were analyzed using a linear mixed-effects model similar to the primary endpoint. The treatment differences and odds ratio (OR) compared to placebo, nominal 95% CI, and nominal *P* values are reported without adjusting for multiplicity in this sub-group analysis, and safety endpoints were analyzed using the safety analysis set.

Results

Patient disposition

Of the 539 patients screened, 351 were randomized (erenumab 70 mg, n = 133; erenumab 140 mg, n = 94; and placebo, n = 124) in the DBTP [Figure 1].

Demographics and baseline characteristics

The baseline demographic and disease characteristics were well-balanced between the treatment groups [Table 1]. Of the 351 randomized patients, women: 78.9%; mean (±SD) age: 35.1 (±8.6) years; mean (±SD) age at the onset of a migraine: 28.4 (±9.0) years; duration: 6.77 (±6.01) years; mean (±SD) MMD: 7.82 (±2.89) days; and monthly headache days: 8.86 (±3.37) days were noted. Overall, 39.6% of patients had a history of prior prophylactic migraine treatment failure.

Prior and concomitant therapies

Overall, 317 (90.8%) patients used concomitant acute headache medication during the baseline and DBTP; the corresponding proportion of patients between the erenumab groups and placebo group was balanced. None of the patients had undergone alternative migraine therapies.

Efficacy

Primary endpoint

The difference in the adjusted means (95% CI; *P* value) in MMD was -0.88 (-2.16, 0.39; *P* = 0.174) days for erenumab 70 mg versus placebo and -1.01 (-2.42, 0.41; *P* = 0.164) days for erenumab 140 mg versus placebo at month 3 [Figure 2].

Secondary endpoints

At month 3, erenumab 70 mg: 59.4% patients (OR: 1.41 [95% CI: 0.85, 2.34; *P* = 0.179]) and erenumab 140 mg: 58.9% patients (OR: 1.38 [95% CI: 0.79, 2.42]; *P* = 0.252) versus placebo: 50.8% patients demonstrated at least a 50% reduction in MMD from the baseline [Table 2]. In the erenumab-treated groups, the change from the baseline in monthly acute migraine-specific medication days at month 3 was numerically less than the placebo group. At month 3, the difference in the adjusted means (95% CI; *P* value) was 0.05 (-0.01, 0.12; *P* = 0.116) days for erenumab 70 mg versus placebo and 0.01 (-0.06, 0.09; *P* = 0.723) days for erenumab 140 mg versus placebo [Table 3]. The reduction from the baseline in the HIT-6™ total scores at month 3 was numerically

Table 1: Demographics and baseline characteristics (randomized analysis set)

Characteristic	Erenumab 70 mg *n*=133	Erenumab 140 mg *n*=94	Placebo *n*=124	Total *n*=351
Age (years)				
Mean (±SD)	34.9 (9.2)	35.4 (7.2)	35.3 (8.9)	35.1 (8.6)
Sex - *n* (%)				
Men	31 (23.3)	16 (17.0)	27 (21.8)	74 (21.1)
Women	102 (76.7)	78 (83.0)	97 (78.2)	277 (78.9)
Weight (kg)				
Mean (±SD)	61.07 (12.24)	63.10 (10.70)	63.04 (11.65)	62.31 (11.64)
Height (cm)				
Mean (±SD)	157.73 (8.36)	157.96 (7.88)	157.83 (8.23)	157.83 (8.17)
BMI (kg/m^2)				
Mean (±SD)	24.48 (4.17)	25.33 (4.13)	25.31 (4.38)	25.00 (4.24)
Baseline Characteristics				
MMD				
Mean (±SD)	7.69 (2.67)	8.34 (3.75)	7.56 (2.27)	7.82 (2.89)
Monthly headache days				
Mean (±SD)	8.75 (2.88)	9.48 (4.67)	8.50 (2.55)	8.86 (3.37)
Monthly days of acute migraine-specific medication treatment days				
Mean (±SD)	0.20 (1.14)	0.10 (0.58)	0.20 (1.00)	0.17 (0.97)
Monthly days of acute headache-specific medication Medication treatment days				
Mean (±SD)	3.80 (2.91)	3.64 (2.53)	3.79 (2.63)	3.75 (2.70)
Age at onset of migraine (years)				
Mean (±SD)	28.1 (9.4)	28.7 (8.6)	28.4 (8.8)	28.4 (9.0)
Disease duration of migraine (years)				
Mean (±SD)	6.76 (5.96)	6.66 (6.54)	6.87 (5.69)	6.77 (6.01)
Aura status, *n* (%)				
Yes	99 (74.4)	73 (77.7)	81 (65.3)	253 (72.1)
No	34 (25.6)	21 (22.3)	43 (34.7)	98 (27.9)

Abbreviations: BMI, body mass index; MMD, monthly migraine days; SD, standard deviation

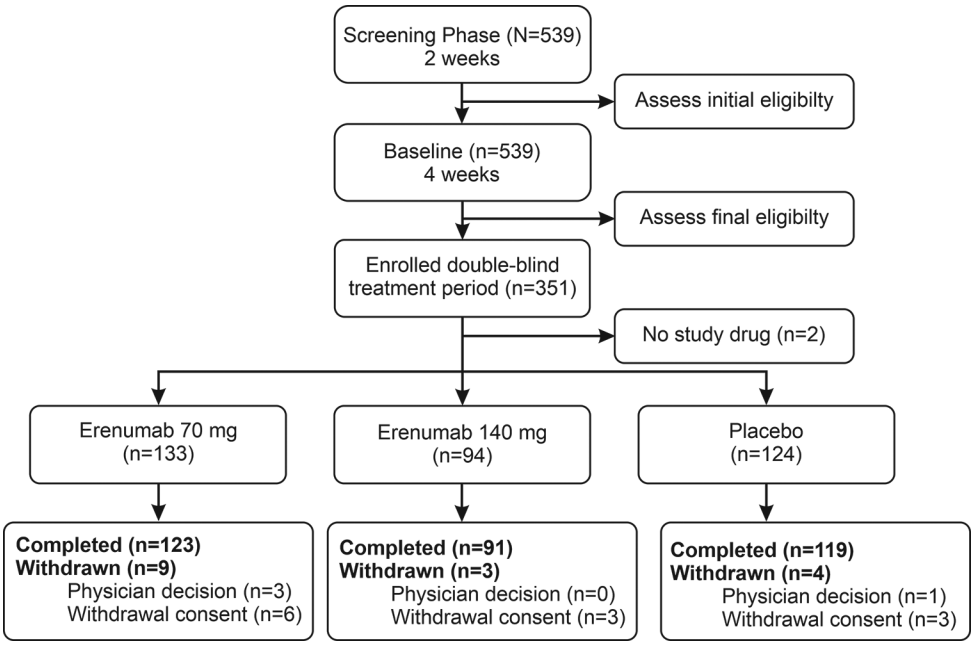

Figure 1: Study design and patient disposition (randomized analysis set)

higher in the erenumab-treated versus placebo group. Higher the reduction, better is the improvement. The difference in the adjusted means (95% CI; *P* value) was determined as -2.32 (-4.43, -0.20; *P* = 0.032) days for erenumab 70 mg

Table 2: Proportion of patients displaying a reduction of at least 50%, 75%, and 100% in MMD (full analysis set)

Week (Month)	Reduction (%)	Treatment group	*n**/M† (%)	Comparison	OR 95% CI	*P*
Week 4	≥50	Placebo	48/118 (40.7)			
(Month 1)		Erenumab 70 mg	63/128 (49.2)	Erenumab 70 mg vs. placebo	1.41 (0.85, 2.34)	0.180
		Erenumab 140 mg	47/90 (52.2)	Erenumab 140 mg vs. placebo	1.59 (0.92, 2.75)	0.099
	≥75	Placebo	32/118 (27.1)			
		Erenumab 70 mg	32/128 (25.0)	Erenumab 70 mg vs. placebo	0.90 (0.51, 1.58)	0.705
		Erenumab 140 mg	31/90 (34.4)	Erenumab 140 mg vs. placebo	1.41 (0.78, 2.56)	0.259
	100	Placebo	19/118 (16.1)			
		Erenumab 70 mg	15/128 (11.7)	Erenumab 70 mg vs. placebo	0.69 (0.33, 1.43)	0.322
		Erenumab 140 mg	12/90 (13.3)	Erenumab 140 mg vs. placebo	0.80 (0.37, 1.75)	0.577
Week 8	50	Placebo	57/118 (48.3)			
(Month 2)		Erenumab 70 mg	76/128 (59.4)	Erenumab 70 mg vs. placebo	1.57 (0.94, 2.60)	0.082
		Erenumab 140 mg	47/90 (52.2)	Erenumab 140 mg vs. placebo	1.17 (0.67, 2.02)	0.582
	75	Placebo	38/118 (32.2)			
		Erenumab 70 mg	46/128 (35.9)	Erenumab 70 mg vs. placebo	1.18 (0.70, 2.01)	0.539
		Erenumab 140 mg	31/90 (34.4)	Erenumab 140 mg vs. placebo	1.10 (0.62, 1.98)	0.739
	100	Placebo	23/118 (19.5)			
		Erenumab 70 mg	23/128 (18.0)	Erenumab 70 mg vs. placebo	0.90 (0.47, 1.72)	0.758
		Erenumab 140 mg	19/90 (21.1)	Erenumab 140 mg vs. placebo	1.10 (0.56, 2.18)	0.779
Week 12	50	Placebo	60/118 (50.8)			
(Month 3)		Erenumab 70 mg	76/128 (59.4)	Erenumab 70 mg vs. placebo	1.41 (0.85, 2.34)	0.179
		Erenumab 140 mg	53/90 (58.9)	Erenumab 140 mg vs. placebo	1.38 (0.79, 2.42)	0.252
	75	Placebo	39/118 (33.1)			
		Erenumab 70 mg	58/128 (45.3)	Erenumab 70 mg vs. placebo	1.69 (1.00, 2.84)	0.049
		Erenumab 140 mg	39/90 (43.3)	Erenumab 140 mg vs. placebo	1.55 (0.88, 2.74)	0.131
	100	Placebo	25/118 (21.2)			
		Erenumab 70 mg	41/128 (32.0)	Erenumab 70 mg vs. placebo	1.76 (0.99, 3.14)	0.056
		Erenumab 140 mg	24/90 (26.7)	Erenumab 140 mg vs. placebo	1.35 (0.71, 2.58)	0.361

Abbreviations: CI, confidence interval; MMD, monthly migraine days; OR, odds ratio. *The number of patients who responded. †The total number of patients in the treatment group with the response variable defined

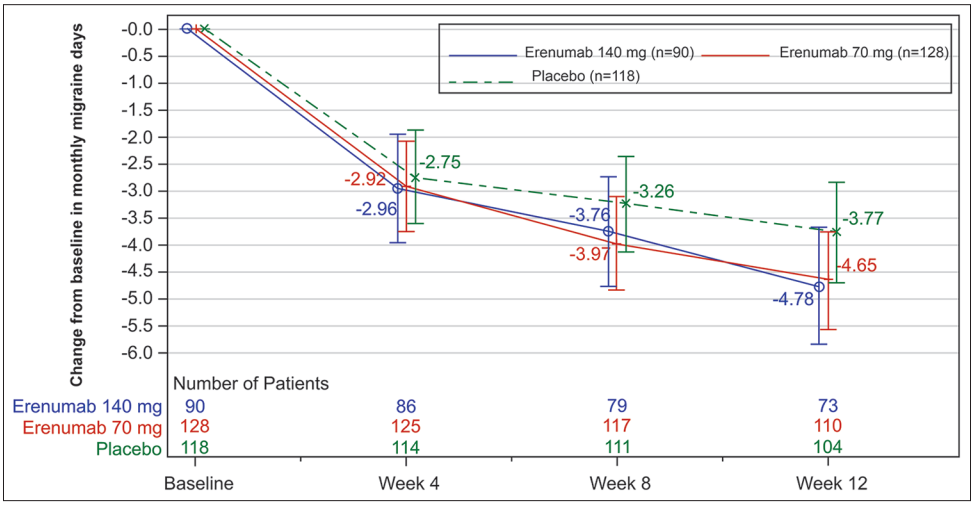

Figure 2: Change from the baseline in MMD in the Indian sub-population (full analysis set)

versus placebo and -2.06 (-4.35, 0.23; $P = 0.078$) days for erenumab 140 mg versus placebo [Table 3].

Exploratory endpoints

The proportion of patients with ≥50%, ≥75%, or 100% reduction from the baseline in MMD at each month was higher in erenumab groups versus placebo [Table 2]. The erenumab-treated groups demonstrated a larger decrease in the modified MIDAS scores versus the placebo group [Table 3].

Safety

During the DBTP, no serious AEs (SAEs) were observed in the erenumab-treated groups; however, one patient in the placebo group reported two SAEs. The incidence of TEAEs

Table 3: Change from the baseline in monthly acute migraine-specific medication days, HIT-6™ total scores, and migraine-related disability and productivity

Comparison	Week (Month)	Erenumab, *n* (Adjusted mean [SE])	Placebo, *n* (Adjusted mean [SE])	Difference Adjusted Mean (SE)	95% CI	*P*
Monthly acute migraine-specific medication days						
Erenumab 70 mg vs. placebo	Week 4 (Month 1)	125 (-0.13 [0.02])	114 (-0.15 [0.02])	0.01 (0.03)	-0.04, 0.07	0.582
	Week 8 (Month 2)	117 (-0.10 [0.03])	111 (-0.18 [0.03])	0.08 (0.04)	0.01, 0.16	0.032
	Week 12 (Month 3)	110 (-0.13 [0.02])	104 (-0.18 [0.02])	0.05 (0.03)	-0.01, 0.12	0.116
Erenumab 140 mg vs. placebo	Week 4 (Month 1)	86 (-0.15 [0.02])	114 (-0.15 [0.02])	-0.01 (0.03)	-0.06, 0.05	0.827
	Week 8 (Month 2)	79 (-0.18 [0.03])	111 (-0.18 [0.03])	-0.00 (0.04)	-0.08, 0.08	0.975
	Week 12 (Month 3)	73 (-0.17 [0.03])	104 (-0.18 [0.02])	0.01 (0.04)	-0.06, 0.09	0.723
HIT-6™ Total Scores						
Erenumab 70 mg vs. placebo	Week 4 (Month 1)	116 (-5.72 [0.67])	111 (-3.69 [0.69])	-2.03 (0.96)	-3.92, -0.14	0.035
	Week 8 (Month 2)	113 (-8.28 [0.74])	109 (-5.91 [0.75])	-2.37 (1.05)	-4.43, -0.30	0.025
	Week 12 (Month 3)	105 (-9.65 [0.76])	103 (-7.34 [0.77])	-2.32 (1.08)	-4.43, -0.20	0.032
Erenumab 140 mg vs. placebo	Week 4 (Month 1)	84 (-5.24 [0.79])	111 (-3.69 [0.69])	-1.55 (1.04)	-3.61, 0.50	0.137
	Week 8 (Month 2)	85 (-8.10 [0.85])	109 (-5.91 [0.75])	-2.19 (1.13)	-4.42, 0.04	0.054
	Week 12 (Month 3)	78 (-9.40 [0.88])	103 (-7.34 [0.77])	-2.06 (1.16)	-4.35, 0.23	0.078
Migraine-Related Disability and Productivity						
Erenumab 70 mg vs. placebo	Week 4 (Month 1)	116 (-6.15 [0.84])	111 (-2.87 [0.86])	-3.29 (1.20)	-5.64, -0.93	0.006
	Week 8 (Month 2)	113 (-7.65 [0.74])	109 (-5.69 [0.76])	-1.96 (1.06)	-4.03, 0.12	0.065
	Week 12 (Month 3)	104 (-8.71 [0.56])	103 (-7.81 [0.57])	-0.90 (0.79)	-2.46, 0.66	0.257
Erenumab 140 mg vs. placebo	Week 4 (Month 1)	84 (-5.18 [0.98])	111 (-2.87 [0.86])	-2.31 (1.30)	-4.88, 0.25	0.077
	Week 8 (Month 2)	85 (-7.86 [0.86])	109 (-5.69 [0.76])	-2.17 (1.14)	-4.41, 0.07	0.057
	Week 12 (Month 3)	78 (-9.47 [0.65])	103 (-7.81 [0.57])	-1.67 (0.86)	-3.36, 0.02	0.053

Abbreviations: CI, confidence interval; HIT-6, Headache Impact Test-6; SE, standard error

was well-balanced between erenumab and placebo groups and was consistent with previous studies on erenumab with no new safety signals.[14] Pyrexia (5.7%), nasopharyngitis (2.9%), constipation (2.3%), and cough (1.7%) were the most frequently occurring TEAEs among all patients [Table 4]. Nasopharyngitis and cough were reported more frequently in the erenumab 140 mg group (6.4% and 3.2%, respectively) versus erenumab 70 mg (0.8% and 0.8%, respectively) and placebo (2.4% and 1.6%, respectively) groups. In general, the type and pattern of TEAEs observed in the Indian sub-population and the Global EMPoWER study were similar.[14] The majority of AEs reported across treatment groups were observed to be grades 1/2; only one patient in the erenumab 70 mg group reported grade 3 AE, which was unrelated to study treatment. Notable changes in the sitting systolic blood pressure (low or high) were higher in the placebo group (10%) versus erenumab groups (70 mg: 7.8%; 140 mg: 5.4%). However, the elevated sitting systolic and diastolic blood pressures were higher in both erenumab groups (70 mg: 4.7% and 6.3%; 140 mg: 4.3% and 6.5%) versus the placebo group (2.5% each).

Immunogenicity

During DBTP, overall, 5.5% of the patients developed binding antibodies against erenumab. One patient developed neutralizing antibodies in the erenumab 70 mg-treated group. None of the patients reported immune disorder-related TEAEs. The observed results in Indian EM patients were consistent with those reported by the Global study.[14]

Discussion

EMPOwER is the first randomized DB study conducted to evaluate the efficacy and safety of erenumab in patients with EM from India. Two different doses (70 mg and 140 mg) of erenumab were administered subcutaneously once monthly, and both these dose groups demonstrated numerically higher mean reduction in MMD change from the baseline to month 3 versus the placebo group. The study however was not powered for demonstration of the statistically significant difference between the test drug and placebo (which was demonstrated by the Global study).[14] The study also demonstrated that both erenumab doses were more efficacious (numerical superiority) in secondary and exploratory endpoints versus placebo.

The findings of this study are consistent with the results of the Global study and two previous studies of erenumab versus placebo in patients with EM.[10,12,14] The Global study demonstrated a substantial benefit with erenumab 70 mg and 140 mg over placebo in reducing the MMDs per month [–1.1 days (70 mg) and –1.7 days (140 mg)] at month 3.[14] STRIVE, a phase III randomized study, similarly showed a relative decrease in migraine days per month of –1.4 (erenumab 70 mg) and –1.9 (erenumab 140 mg) throughout the final 3 months of the 6-month DBTP.[12] In a randomized phase II study in Japanese patients with EM, a greater reduction in MMD was observed for erenumab versus

Table 4: TEAEs during the DBTP (safety analysis set)

Preferred term	Erenumab 70 mg *n*=132 *n* (%)	Erenumab 140 mg *n*=94 *n* (%)	Placebo *n*=123 *n* (%)
Number of patients with at least one TEAE	30 (22.7)	23 (24.5)	31 (25.2)
Nasopharyngitis	1 (0.8)	6 (6.4)	3 (2.4)
Constipation	3 (2.3)	4 (4.3)	1 (0.8)
Cough	1 (0.8)	3 (3.2)	2 (1.6)
Pyrexia	5 (3.8)	3 (3.2)	12 (9.8)
Blood glucose increased	1 (0.8)	2 (2.1)	1 (0.8)
Abdominal pain upper	0	1 (1.1)	1 (0.8)
Acarodermatitis	0	1 (1.1)	0
Arthropod bite	0	1 (1.1)	0
Blood triglycerides abnormal	0	1 (1.1)	0
Blood triglycerides increased	2 (1.5)	1 (1.1)	0
Burning sensation	0	1 (1.1)	0
Headache	0	1 (1.1)	0
Hyperlipidemia	2 (1.5)	1 (1.1)	0
Muscle spasms	0	1 (1.1)	0
Nausea	0	1 (1.1)	1 (0.8)
Pain	0	1 (1.1)	1 (0.8)
Palpitations	0	1 (1.1)	0
Sneezing	0	1 (1.1)	0
Upper respiratory tract infection	2 (1.5)	1 (1.1)	1 (0.8)
Urinary tract infection	0	1 (1.1)	0
Vertigo	1 (0.8)	1 (1.1)	0
Vomiting	1 (0.8)	1 (1.1)	1 (0.8)
Blood creatine phosphokinase increased	1 (0.8)	0	2 (1.6)
Diarrhea	3 (2.3)	0	0
Hypertriglyceridemia	1 (0.8)	0	2 (1.6)
Injection site swelling	0	0	2 (1.6)
Pruritus	2 (1.5)	0	2 (1.6)

Abbreviations: DBTP, double-blind treatment period; TEAEs, treatment-emergent adverse events

placebo, with differences of –2.31 and –1.89 days for erenumab 70 and 140 mg, respectively.[13]

The mean age of patients (35.1 years) in the present study was similar to the Global population (37.5 years)[14] but slightly lower than the age of patients included in the STRIVE (40.9 years),[12] the ARISE study (42.1 years),[10] the LIBERTY study (44.4 years),[16] and the Japanese study (44.3 years).[13] The study population comprised predominantly of women, which is consistent with previous studies on erenumab.[10,12,13,16] A majority of the patients (72.1%) at the baseline had migraine with aura consistent with the Global study (70%).[14] However, the ARISE (51.0%) and LIBERTY (35.0%) studies demonstrated a smaller number of patients with aura at the baseline.[10,16] The baseline aura status in the EMPOwER study was self-reported using an electronic diary, and patients might have confused prodromal symptoms with aura symptoms. Although over 85.8% of patients took acute headache medication, only a very small proportion (4.3%) utilized migraine-specific acute medication in contrast to other studies [Global (36.8%),[14] STRIVE (58.8%),[12] and ARISE (61%)].[10] Another contrasting finding was a higher placebo response observed in the Global (-3.1 MMD)[14] and Indian population-based EMPOwER study (-3.8 MMD) as compared to the STRIVE (-1.8 MMD)[12] and ARISE studies (-1.8 MMD).[10] The diverse placebo response rate across studies could be because of variations in the study design (inclusion/exclusion criteria, number of treatment arms, trial duration), enrolled patient population (age, gender, prior treatments, medical history), and geographical areas (across multi-national trials).[17]

In our study, both erenumab groups had a greater proportion of patients achieving 50% or greater reduction from the baseline in the mean number of MMD versus the placebo group, which is in line with previously published studies such as ARISE and LIBERTY.[10,16] Erenumab was also considerably more effective than placebo for reductions in migraine frequency, acute medication usage, increased achievement of ≥75% and 100% reduction in MMD, and functional outcomes (secondary endpoints). These results are consistent with Global EMPOwER and other studies on erenumab.[14,16]

The assessment of the effect of migraine therapies on physical functioning, quality of life, and disability outcomes is gaining importance.[10,12,18,19] This study demonstrated greater reduction in the modified MIDAS scores and reduction in HIT-6™ total scores from the baseline in both the erenumab dosage groups versus the placebo group. Previous studies have also shown

significant improvement in functional outcomes in migraine patients on erenumab than on placebo.[10,20,21] These results thus highlight the significance of the treatment response in improving headache disability and reducing headache impact, respectively.

Overall, the incidence of TEAEs was similar across the treatment groups during the DBTP. Findings for hematology and clinical chemistry were comparable across all treatment groups. Neutralizing antibodies developed in four patients; no immune disorder-related TEAEs or deaths were reported throughout the study. Elevated sitting systolic and diastolic blood pressures was reported in both erenumab groups and placebo; however, no such changes were observed in earlier studies.[9,18] The overall safety profile seen in this study was in line with the Global EMPOwER study.[14] Erenumab was found to be well-tolerated with a favorable tolerability profile in Indian patients with EM.

Propranolol, topiramate, divalproex, and amitriptyline are commonly used conventional migraine preventive drugs around the world, including India.[1,22-24] However, the rates of adherence to oral preventive medication are poor in clinical practice.[6,25] Most of the conventional preventive drugs are non-specific, and exact mechanisms of action in migraine are uncertain. Additionally, they display considerable adverse effects. A monthly injection of erenumab may overcome the necessity of daily oral preventive drugs and help increase treatment adherence. Further, erenumab has a definite migraine-specific mechanism of action and highly favorable tolerability profile which has been demonstrated in this study and in Global randomized clinical trials (RCTs). Therefore, the results of this study provide evidence for an alternative efficacious and well-tolerated treatment option for migraine prevention in Indian episodic migraine patients.

The limitation of the current study is the short 12-week DBTP study assessment, and hence a long-term study in the Indian population is warranted to understand more about sustained efficacy and tolerability of erenumab. Further, the study did not include CM patients. Erenumab has also shown good efficacy in CM patients in a recent Global study.[11] Nevertheless, importantly, EMPOwER is the first study of a migraine-specific drug (a monoclonal antibody to the CGRP receptor) to be conducted in Indian patients with EM, which demonstrated better efficacy and tolerability versus placebo. A low number of dropouts because of AEs in the Indian sub-study further substantiates improved adherence because of a favorable safety profile.

Conclusion

Based on the findings, once-monthly subcutaneous injection of erenumab was found to be effective in reducing the frequency of migraine episodes along with improvement in headache impact and disability in the Indian EM pateints. The effectiveness of erenumab demonstrated consistently better outcomes in both erenumab dose groups versus placebo. No new safety signals were observed for erenumab in the Indian EM pateints.

Clinical implications

1. Erenumab is a fully human monoclonal antibody designed to specifically target and antagonize the canonical Calcitonin gene-related peptide (CGRP) receptor.
2. Erenumab treatment resulted in numerically greater reductions in MMDs, with an increase in the proportion of patients achieving at least a 50% reduction from the baseline in MMDs along with improvement in patient-reported outcomes in Indian EM patients.
3. This phase 3 study provides evidence that once-monthly subcutaneous injection of erenumab is a potential new preventive treatment in Indian EM patients.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient (s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

Debashish Chowdhury, Jaydip Ray Chaudhuri, Pahari Ghosh, Rahul Kulkarni are the principal investigators for Novartis sponsored trials.

Sumit Singh has attended advisory boards and is a speaker in Novartis sponsored meetings.

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