Efficacy and Safety of Erenumab 70 mg in Adult Patients With Chronic Migraine: Results From a Phase 3, Randomized, Double-Blind, Placebo-Controlled DRAGON Study

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Disclosures

Shihua Wen: Employee of Novartis and holds stock in Novartis.

Shuu-Jiun Wang has received personal compensation for serving on a Scientific Advisory board for Eli-Lilly and Novartis. He has received personal compensation for serving on as a speaker or moderator for AbbVie, Biogen, Eisai, and Pfizer, Taiwan. The institution of Prof. Wang has received research support from Brain Research Center at National Yang-Ming 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, Eli-Lilly, and Novartis.

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Hebo Wang, Jiying Zhou, Qi Wan, Tingmin Yu, and Yajun Lian have declared that there is no conflict of interest.

Michal Arkuszewski, **Laurent Ecochard, and Wendy Su** are employees of and hold stocks in Novartis.

Fangfang Yin and **Zheng Li** are employees of China Novartis Institutes for Biomedical Research Co Ltd.

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Background and Methods

- DRAGON (NCT03867201)[1] is a 12-week, Phase 3, randomized, double-blind, placebo-controlled study in patients with chronic migraine (CM) from China and other Asian countries/regions that were not adequately represented in the global Phase 2 CM pivotal study[2]
- This study evaluated the efficacy and safety of once-monthly subcutaneous erenumab 70 mg (versus placebo) in adult patients with CM
- Here, we report the results from the 12-week double-blind treatment period (DBTP) of the DRAGON study

Key Inclusion Criteria

- Patients aged 18-65 years with a history of CM with or without aura for ≥12 months before screening (ICHD-3)[3]
- Patients with a history of ≥15 headache days of which ≥8 headache days meet criteria as migraine days during the baseline period

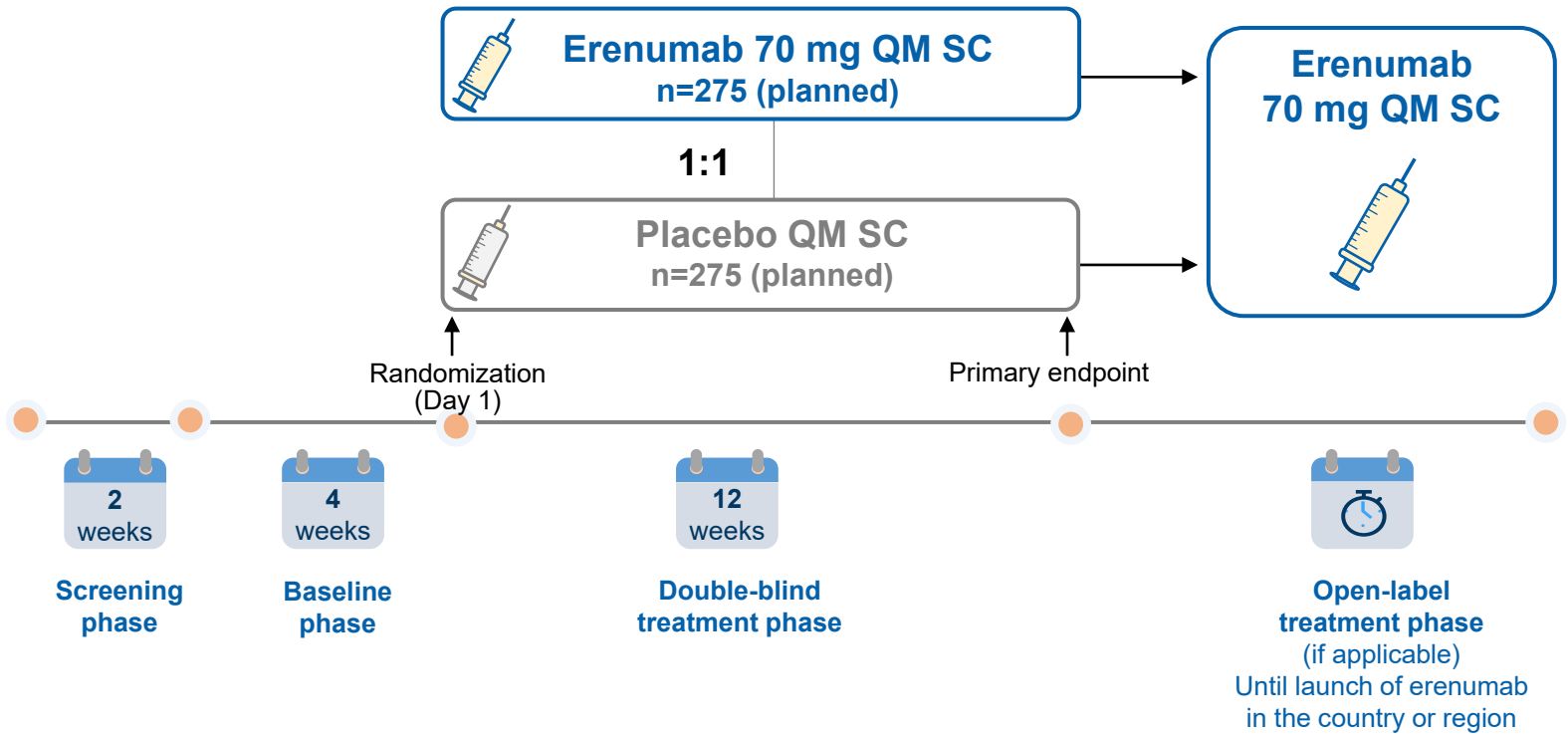
Key Exclusion Criteria

- >50 years of age at migraine onset, history of cluster or hemiplegic migraine headache, CM with continuous pain, unable to differentiate migraine from other headaches, failed >3 prior preventive treatments, pregnant or nursing women, active chronic pain syndromes (such as fibromyalgia and chronic pelvic pain), or other medical conditions

[1]ClinicalTrials.gov Identifier: NCT03867201 (https://clinicaltrials.gov/ct2/show/NCT03867201). [2]ClinicalTrials.gov Identifier: NCT02066415 (https://clinicaltrials.gov/ct2/show/NCT02066415). [3]Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018;38(1):1–211.
CM, chronic migraine; DBTP, double-blind treatment period; ICHD-3, Headache Classification Committee of the International Headache Society, 3rd edition.

Study Design

Study design



Primary endpoint

- Change from baseline in MMD

Secondary endpoints

- Proportion of patients with ≥50% reduction from baseline in MMD
- Change from baseline in monthly acute headache medication days
- Change from baseline in mMIDAS
- Safety and tolerability assessments

Note: For patients not entering the open-label treatment phase (OLTP), safety follow-up visit occurred 12 weeks after last dose of the double-blind treatment phase (DBTP). In select countries or regions, patients completing the DBTP on study drug were eligible to participate in the OLTP (until launch of erenumab in the respective country/region). The study was powered only for the primary endpoint assessed in the overall population with an alpha level of 0.05. The endpoints were assessed as change from baseline over the last 4 weeks of DBTP.

DBTP, double-blind treatment phase; MMD, monthly migraine days; mMIDAS, modified Migraine Disability Assessment; OLTP, open-label treatment phase; QM, once monthly; SC, subcutaneous.

Results: Overall Demographics and Baseline Disease Characteristics

- **Overall demographics and baseline disease characteristics were balanced between the erenumab and the placebo groups**
  - **Proportion of women was slightly higher in the placebo group as gender was not considered a stratification factor**

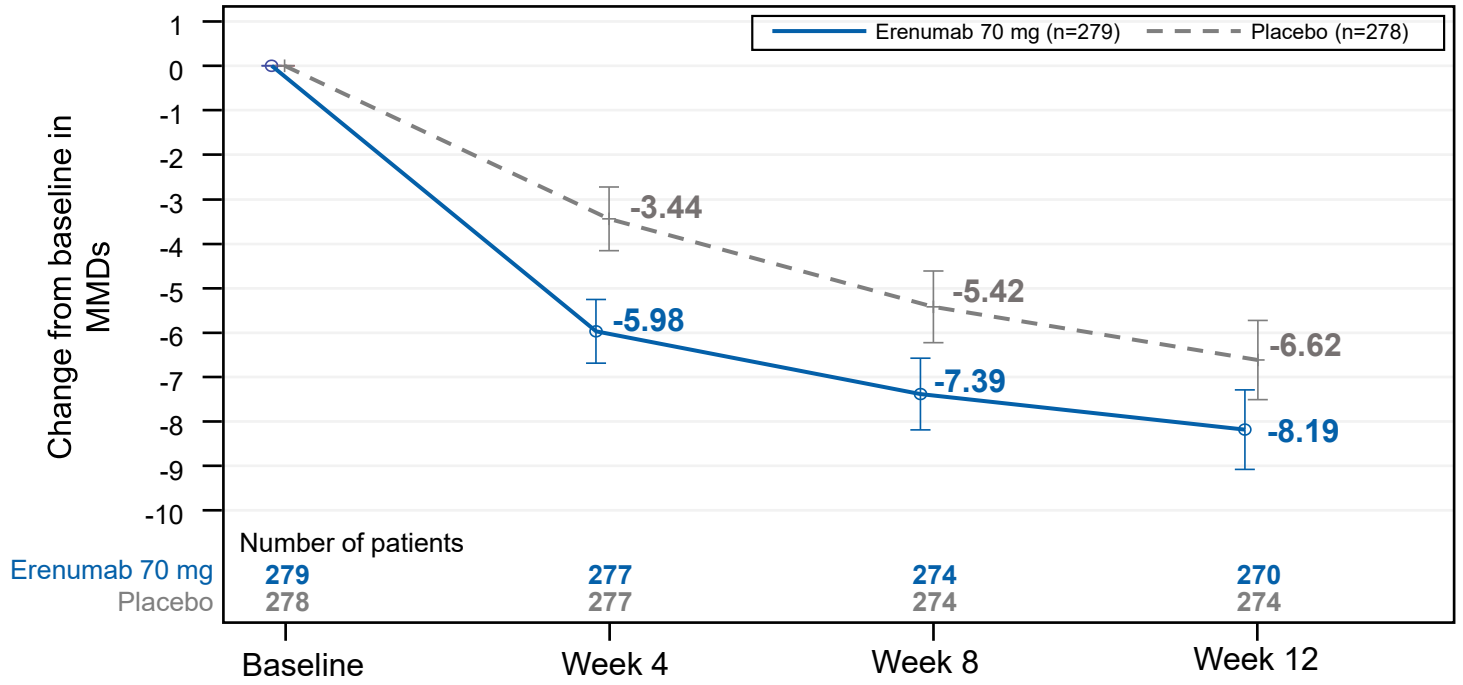
Patient demographics and baseline disease characteristics (FAS)	Erenumab 70 mg N=279	Placebo N=278	All patients N=557
Age (years), mean (±SD)	41.4 (10.9)	41.9 (10.9)	41.7 (10.9)
Men, n (%)	62 (22.2)	41 (14.7)	103 (18.5)
Women, n (%)	217 (77.8)	237 (85.3)	454 (81.5)
BMI (kg/m²), mean (±SD)	23.3 (4.0)*	23.1 (4.0)	23.2 (4.0)
Monthly migraine days, mean (±SD)	19.1 (5.3)	19.3 (5.6)	19.2 (5.4)
Monthly headache days, mean (±SD)	21.7 (4.2)	22.1 (4.3)	21.9 (4.3)
Monthly moderate and severe headache days, mean (±SD)	16.8 (6.3)	17.2 (6.4)	17.0 (6.4)
Monthly acute headache medication use, days, mean (±SD)	14.1 (8.3)	14.6 (8.2)	14.3 (8.2)
Age at onset of migraine (years), mean (±SD)	23.3 (10.0)	24.2 (9.6)	23.7 (9.8)
Disease duration of migraine with/without aura (years), mean (±SD)	18.2 (11.9)	17.8 (11.4)	18.0 (11.6)

Note: The baseline period for efficacy endpoints is defined as the period between Week −4 and the day prior to study Day 1. *Data for BMI missing for one patient.
BMI, body mass index; FAS, full analysis set; SD, standard deviation.

Primary Endpoint (Change in MMD)
Overall Population

At Week 12, statistically significant reduction from baseline in MMD for erenumab 70 mg (adjusted mean change −8.19 [SE 0.46], difference: −1.57; P=0.015) compared with placebo (adjusted mean change −6.62 [0.45]) was noted

Change from baseline in MMD by treatment and visit for overall population (FAS)



TD versus placebo (95% CI): −1.57 (−2.83, −0.30; P=0.015)

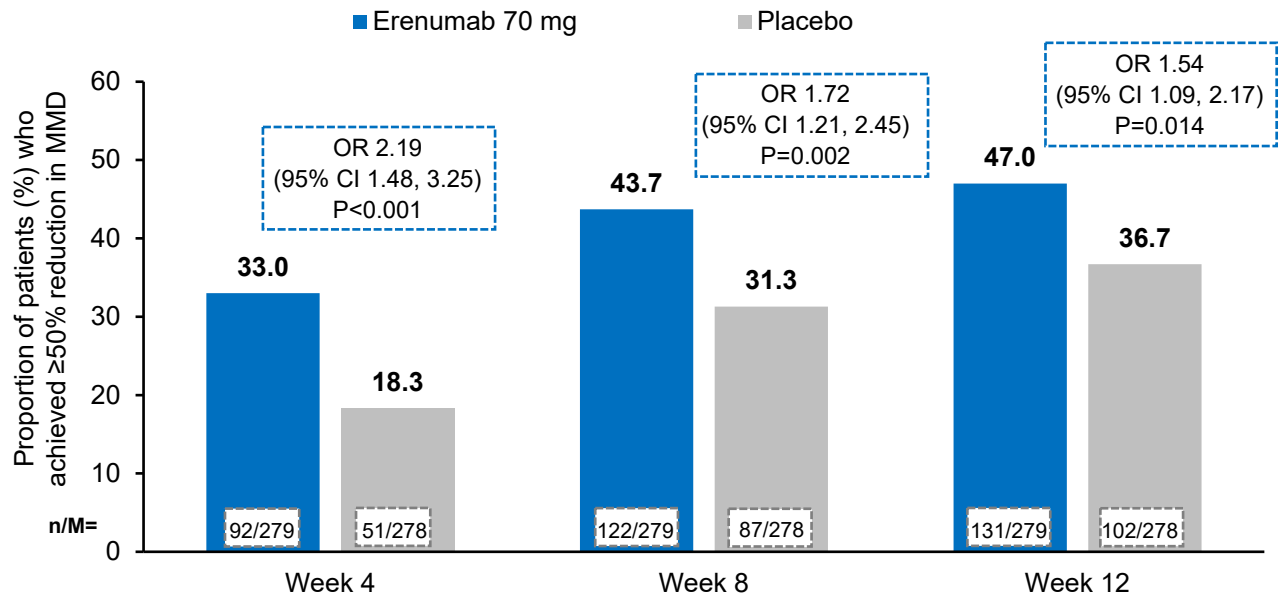
Adjusted least squares means and 95% CIs from the primary analysis model are presented.
Note: The primary efficacy endpoint (change from baseline in MMD) was analyzed using a generalized linear mixed effects repeated measures model based on observed monthly data during the treatment period.
CI, confidence interval; FAS, full analysis set; MMD, monthly migraine days; SE, standard error; TD, treatment difference.

Secondary Endpoints (Other Efficacy Outcomes)

≥50% Reduction in MMD, Monthly Acute Headache Medication Days, and mMIDAS Scores

- A significantly higher percent of patients receiving erenumab achieved ≥50% reduction in MMD from baseline compared to those receiving placebo (OR: 1.54; 95% CI: 1.09, 2.17; P=0.014) at Week 12
- Higher reduction in monthly acute headache medication days and mMIDAS scores were observed with erenumab group compared to the placebo group

Proportion of patients achieving ≥50% reduction from baseline in MMD (FAS)



Change From Baseline at Week 12 in Monthly Acute Headache Medication Days

	Erenumab n=270	Placebo n=274
Adjusted mean change (SE)	−5.34 (0.39)	−4.66 (0.39)
Difference (95% CI)	−0.67 (−1.76, 0.41)	P=NS

Change From Baseline in Migraine-related Disability and Productivity (mMIDAS score)

	Erenumab n=263	Placebo n=268
Adjusted mean change (SE)	−14.67 (1.20)	−12.93 (1.19)
Difference (95% CI)	−1.74 (−5.06, 1.58)	P=NS

The p-values reported for the secondary endpoints are nominal and should be interpreted with caution. Statistical analysis for the proportion of patients with ≥50% reduction from baseline in MMD was done using Cochran-Mantel-Haenszel test adjusting for stratification factor after missing data were imputed (NRI). Monthly acute headache medication days and mMIDAS were analyzed using a generalized linear mixed effects repeated measures model similar to the primary endpoint.

CI, confidence interval; FAS, full analysis set; M, total number of patients in the treatment group with response variable defined; MMD, monthly migraine days; mMIDAS, modified Migraine Disability Assessment; n, number of patients who achieved ≥50% reduction in MMD; NRI, non-responder imputation; NS, not statistically significant; OR, odds ratio; SE, standard error.

Safety
Overall Population

Overall, the safety and tolerability profile of erenumab 70 mg was similar to placebo, with the exception of constipation, which is a known adverse event with erenumab 70 mg

Summary of treatment-emergent adverse events (TEAEs) during the double-blind treatment phase (Safety Analysis Set)

	Erenumab 70 mg N=279 n (%)	Placebo N=278 n (%)
Any AE (at least one AE)	127 (45.5)	132 (47.5)
Any treatment-related AE	36 (12.9)	37 (13.3)
AEs leading to study treatment discontinuation	2 (0.7)	2 (0.7)
SAEs	7 (2.5)	7 (2.5)
Deaths	0	0
TEAEs (at least 1.5% in erenumab 70-mg group) by preferred term		
Constipation	24 (8.6)	9 (3.2)
Upper respiratory tract infection	15 (5.4)	20 (7.2)
Nasopharyngitis	10 (3.6)	5 (1.8)
Dizziness	5 (1.8)	12 (4.3)
Pain in extremity	5 (1.8)	1 (0.4)

Preferred terms are sorted in descending order of frequency in erenumab 70-mg column and then alphabetically. A patient with multiple occurrences of an AE under one treatment is counted only once in this AE category for that treatment. A patient with multiple AEs is counted only once in the “at least one AE" row. N, number of patients in the analysis set; n, number of patients reporting at least one occurrence of an adverse event in that class. MedDRA Version 24.0 has been used for the reporting of AEs.

AE, adverse event; SAE, serious adverse event.

Conclusions

The DRAGON study demonstrated the efficacy and safety of erenumab 70 mg in adult patients with CM from China and other Asian countries/regions. These results are consistent with findings of erenumab pivotal studies

- Erenumab demonstrated a statistically significant reduction in MMDs as compared with placebo
- Significantly higher percent of patients receiving erenumab achieved ≥50% reduction in MMD from baseline as compared to those receiving placebo
- Although not powered to demonstrate significance, a higher reduction in the acute headache medication days and mMIDAS scores was observed with erenumab when compared to placebo, which is consistent with pivotal studies
- No new safety findings were observed; the safety/tolerability was consistent with pivotal studies

CM, chronic migraine; MMD, monthly migraine days; mMIDAS, modified Migraine Disability Assessment.

Thank you!

We thank all the investigators and patients for their contribution to the study.