Effect of Erenumab on Patient-reported Outcomes in Patients With Episodic Migraine From Asia, the Middle East, and Latin America: The EMPOwER Study

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Poster session: P16 (Headache: Advances in CGRP Inhibition for Precision Medicine 4)

Poster number: 006

Poster Presentation at the 74th Annual meeting of the American Academy of Neurology (AAN) 2022, April 2-7 | Seattle

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Disclosures

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

Shuu-Jiun Wang: Received research grants from the Taiwan Minister of Technology and Science, Brain Research Center, National Yang Ming Chiao Tung University, 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; served on the advisory boards of Eli Lilly and Novartis. He has received honoraria as a moderator from Allergan, Pfizer, Eli Lilly, Bayer, and Eisai.

Artemio A Roxas Jr: Part of the advisory board and speaker of Novartis for erenumab and involved in Novartis erenumab trials for episodic migraine (EMPOwER) and chronic migraine (DRAGON).

Bibiana Saravia : None

Yi Jing Zhao: Received honoraria from Lundbeck, Teva, DKSH, and Novartis. Part of advisory board of Lundbeck, Teva, and DKSH.

Byung-Kun Kim: Consulting fees and honoraria from Center for New Health Technology Assessment, National Pension Service, Eli Lilly, Allergan, Teva, Lundbeck, Sanofi Korea, SK Pharm, Yuyu Pharma, and Ildong Pharm.

Debashish Chowdhury, Naji Riachi, Mei-Ling Sharon Tai: Funding received from Novartis for the conduct of the study.

Surat Tanprawate: Received research grants from the Faculty of Medicine, Chiang Mai University, and National Innovation Agency of Thailand; received honoraria as a lecturer from Allergan, Pfizer, Eli Lilly, Novartis, and Eisai.

Tai Ngoc Tran: Received consultation and/or honoraria/lecture fees from Abbott, Boehringer-Ingelheim, Ipsen Pharmaceuticals, Medtronic, and Novartis; and funding from Novartis for the conduct of this study.

Gabriel Paiva da Silva Lima: Employee of and stockholder in Amgen Inc.

Shaloo Pandhi, Laurent Ecochard, Michal Arkuszewski: Employees of Novartis and hold stocks in Novartis.

Subhayan Mondal: Employee of Novartis.

Funding source: This study was funded by Novartis Pharma AG, Basel, Switzerland. Erenumab is co-developed by Amgen and Novartis.

Acknowledgments: Medical writing support was provided by **Parag Betkar** and design support by **Mantosh Roy** (employees of Novartis Healthcare Pvt. Ltd., Hyderabad, India). The final responsibility for the content lies with the authors.

Background

- Erenumab is the first and only approved human monoclonal antibody targeting the canonical calcitonin gene-related peptide (CGRP) receptor[1]
- Erenumab has demonstrated efficacy and safety for the preventive treatment of episodic migraine (EM) and chronic migraine in various studies[1-6]
- The Phase 3 EMPOwER study (NCT03333109) has demonstrated the efficacy of erenumab over placebo in reducing migraine frequency over 3 months in patients with EM from Asia, the Middle East, and Latin America[7]
- The results of the primary analysis (e.g., change in monthly migraine days (MMD), change in monthly acute migraine-specific medication days, change in Headache Impact Test (HIT-6™) scores or achievement of ≥50% reduction in MMD) were reported previously[7]
- The aim of this study is to present the results of the exploratory analysis

1. Shi L, et al. *J Pharmacol Exp Ther.* 2016;356:223-31. **2.** Dodick DW, et al. *Cephalalgia.* 2018;38:1026-37. **3.** Goadsby PJ, et al. *N Engl J Med.* 2017;377:2123-32. **4.** Goadsby PJ, et al. *Cephalalgia.* 2019;39:817-26. **5.** Tepper S, et al. *Lancet Neurol.* 2017;16:425-34. **6.** Ashina M, et al. *Cephalalgia.* 2018;38:1611-21. **7.** Wang SJ, et al. *Cephalalgia.* 2021;41(13):1285-97.

Objective

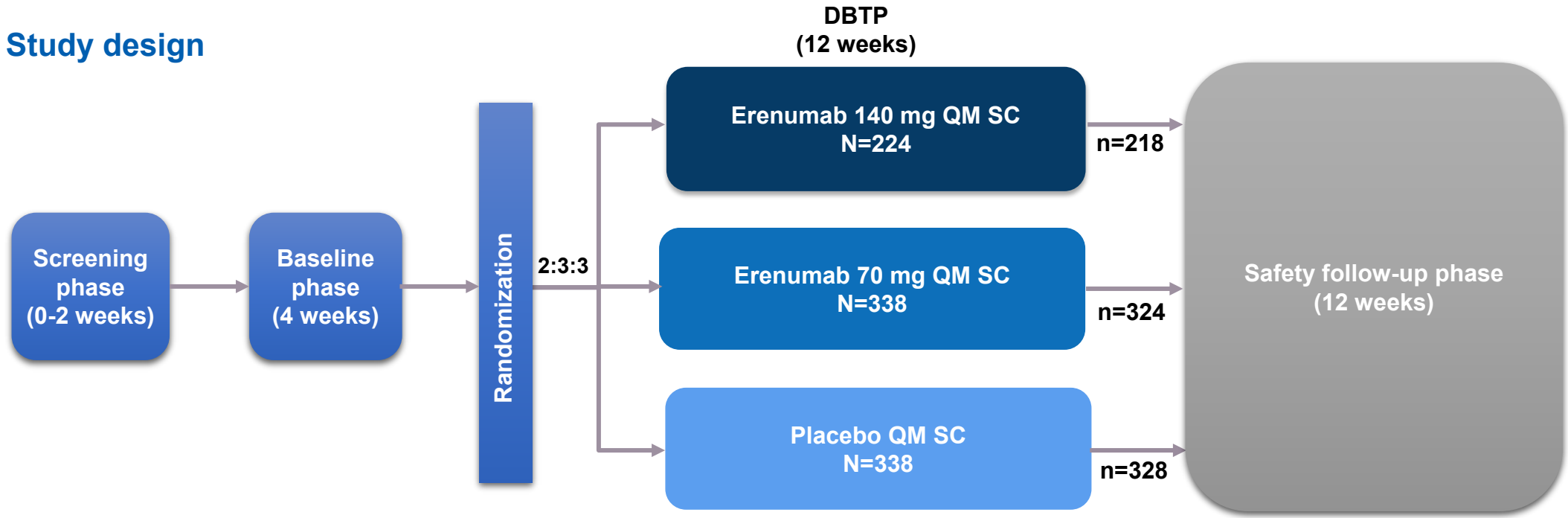
The objective of this exploratory analysis was to evaluate the effect of erenumab (140 mg and 70 mg QM) on patient-reported outcomes (PROs), assessing the function and quality of life (QoL) outcomes after 3 months of treatment in patients with EM from Asia, the Middle East, and Latin America

EM, episodic migraine; QM, every 4 weeks.

Methods

EMPOwER was a randomized, double-blind, placebo-controlled, parallel-group, Phase 3 study conducted at 83 sites across 11 countries in Asia, the Middle East, and Latin America (**Figure 1**)

Figure 1. Study design



DBTP, double-blind treatment phase; N, number of randomized patients; n, number of patients who entered safety follow-up phase; QM, every 4 weeks; SC, subcutaneous.

Methods (Cont'd)

- Main inclusion criteria:
  - Adults aged 18 to 65 years, with a diagnosis of migraine according to ICHD-3
  - An average of ≥4 to <15 MMDs and <15 monthly headache days (MHDs)
- Main exclusion criteria:
  - Age >50 years at migraine onset
  - No therapeutic response to >2 prophylactic treatments of migraine
- Exploratory PROs assessed over 3 months:
  - Adjusted mean change from baseline in HIT-6™, modified Migraine Disability Assessment (mMIDAS), Migraine Physical Function Impact Diary (MPFID), and EuroQoL 5-dimension 5-level scale (EQ-5D-5L)
- Statistical analysis:
  - The exploratory PROs: Pairwise comparisons versus placebo using linear mixed-effects repeated measures model based on observed monthly data
  - The p-values reported for the exploratory outcomes are intended only as a descriptive measure and should be interpreted with caution

HIT-6, Headache Impact Test; ICHD-3, International Classification of Headache Disorders-3 beta; MMD, monthly migraine day, PRO, patent-reported outcome.

Results

Demographic and baseline characteristics

- Of 900 randomized patients, 865 (96.1%) patients completed DBTP, and 840 (93.3%) patients completed the study. The main reason for discontinuing the study drug in DBTP (20 [2.2%]) and discontinuing the study in the safety follow-up period (21 [2.3%]) was patient decision
- At baseline, the mean (SD) age of the patients treated in the study was 37.5 (9.9) years and the majority (81.9%) were female. The mean (SD) MMD was 8.23 (2.81) days and the mean (SD) MHD was 9.28 (3.06)
- At baseline, the PRO scores were well balanced between the treatment groups

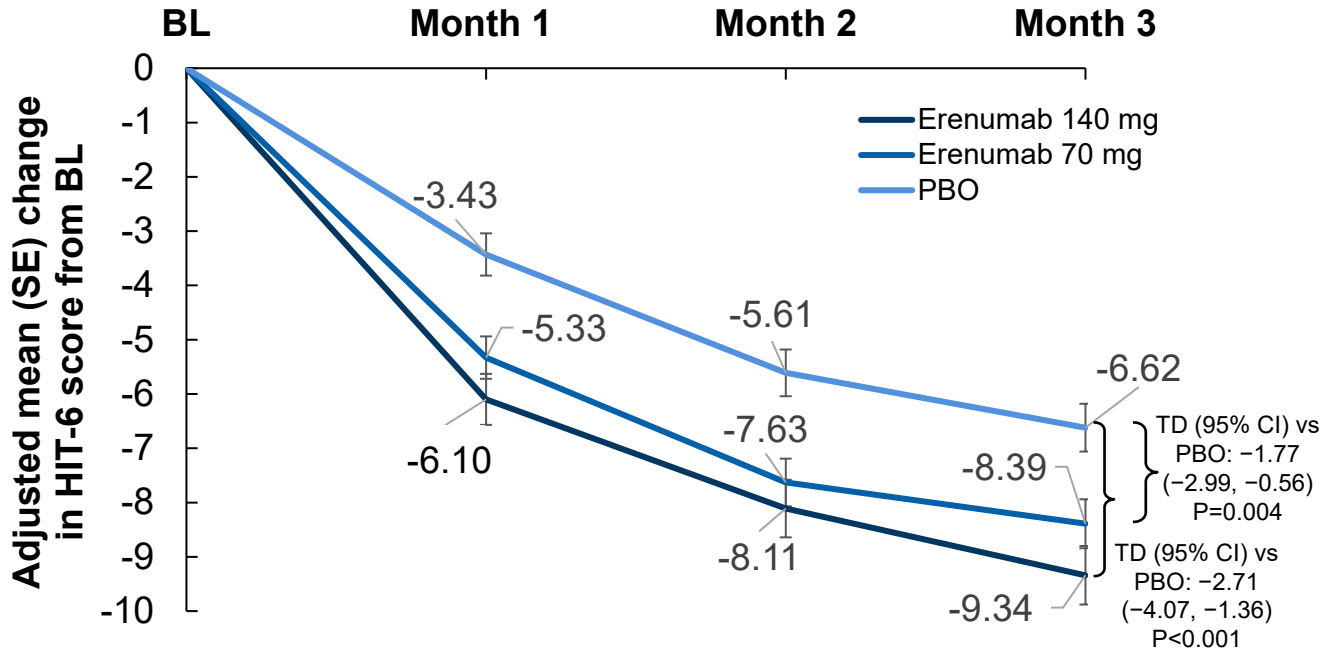
DBTP, double-blind treatment phase; MHD, monthly headache days; MMD, monthly migraine day; PRO, patient-reported outcome; SD, standard deviation.

Results (Cont'd)

HIT-6 score – Change from baseline to Month 3

- At Month 3, there was a statistically significant reduction from baseline in HIT-6 total score for erenumab 140 mg (−9.34, difference: −2.71, P<0.001) and 70 mg (−8.39, difference: −1.77, P=0.004) compared with placebo (−6.62) (**Figure 2**)

Figure 2: Adjusted mean change from baseline in HIT-6 total score by visit (FAS)



BL, baseline; CI, confidence interval; FAS, full analysis set; HIT-6, Headache Impact Test; PBO, placebo; SE, standard error; TD, treatment difference; vs, versus.

Results (Cont'd)

mMIDAS and converted MIDAS* – Change from baseline to Month 3

- At Month 3, both erenumab groups had a statistically significant reduction from baseline in mMIDAS scores (140 mg: −8.99, difference: −2.40 [P<0.001], 70 mg: −8.11, difference: −1.52 [P=0.011]) compared to placebo (−6.59) (**Figure 3a**). The responder rate as per the MIDAS disability category were 52.0% for 140 mg, 55.1% for 70 mg, and 38.0% for placebo group (**Figure 3b**). The responder rate refers to the proportion of patients with an improvement in the MIDAS disability category

Figure 3a. Adjusted mean change from baseline in mMIDAS by visit (FAS)

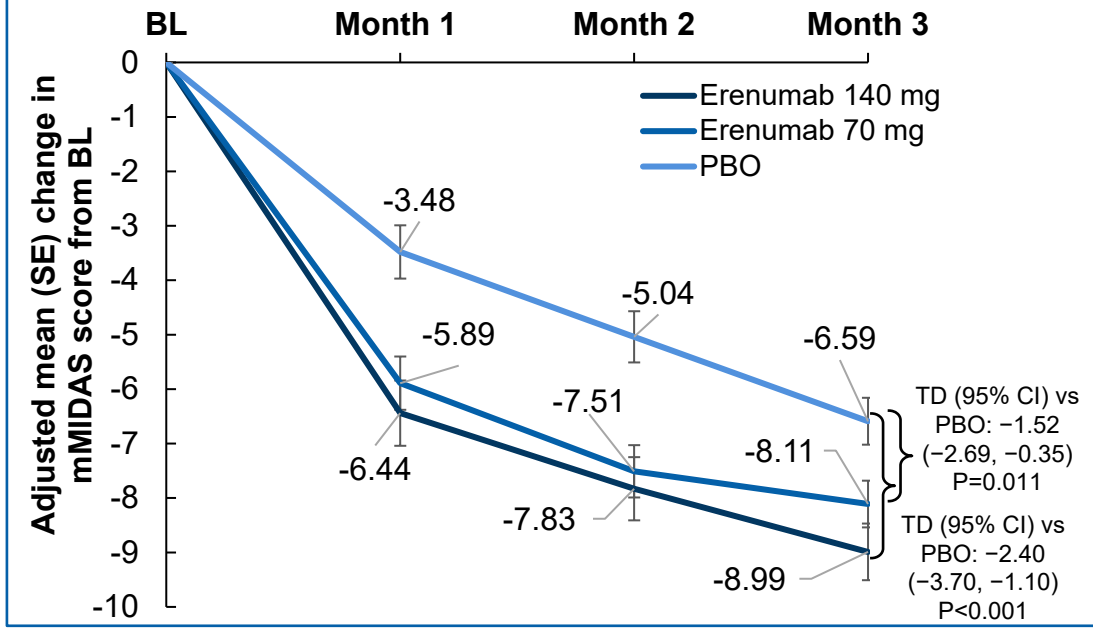
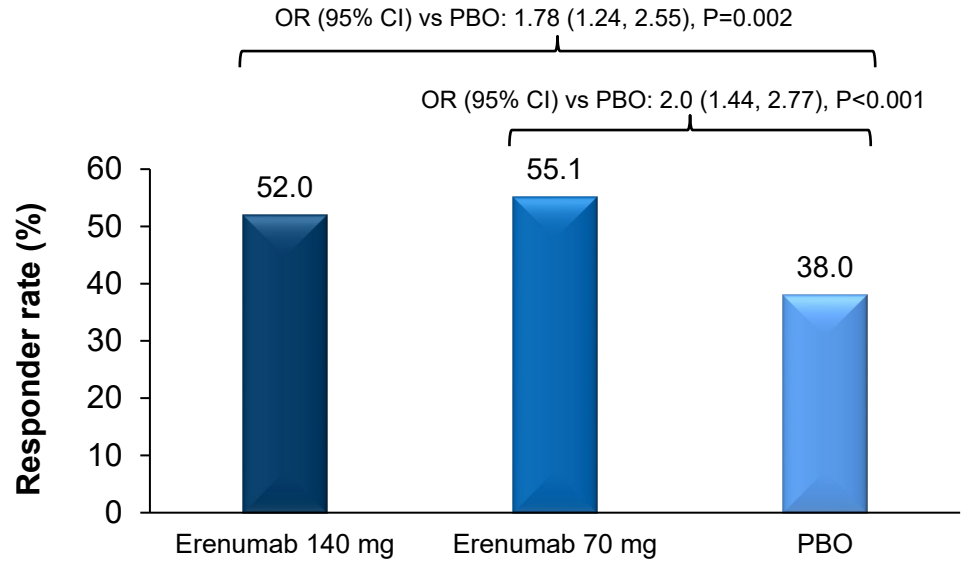


Figure 3b. Proportion of patients with improvement in MIDAS disability categories



. *Since mMIDAS scoring is based on 1-month recall period, the original MIDAS disability categories were based on converted mMIDAS scores, calculated as a sum of all three-monthly assessments, representing 3-months recall period. Change to lower disability category after baseline is considered an improvement. BL, baseline; CI, confidence interval; FAS, full analysis set; MIDAS, Migraine Disability Assessment; mMIDAS, modified MIDAS; OR, odds ratio; PBO, placebo; SE, standard error; TD, treatment difference; vs, versus

Results (Cont'd)

MPFID scores – Change from baseline to Month 3

- At Month 3, there was a statistically significant improvement in the MPFID scores compared with placebo (MPFID-PI: 140 mg: −4.27, difference: −1.96 [P=0.014], 70 mg: −3.95, difference: −1.64 [P=0.021], placebo: −2.31 (**Figure 4a**); MPFID-EA: 140 mg: −5.61, difference: −2.42 [P=0.002], 70 mg: −4.94, difference: −1.75 [P=0.011], placebo: −3.19) (**Figure 4b**)

Figure 4a. Adjusted mean change from baseline in MPFID-PI by visit (FAS)

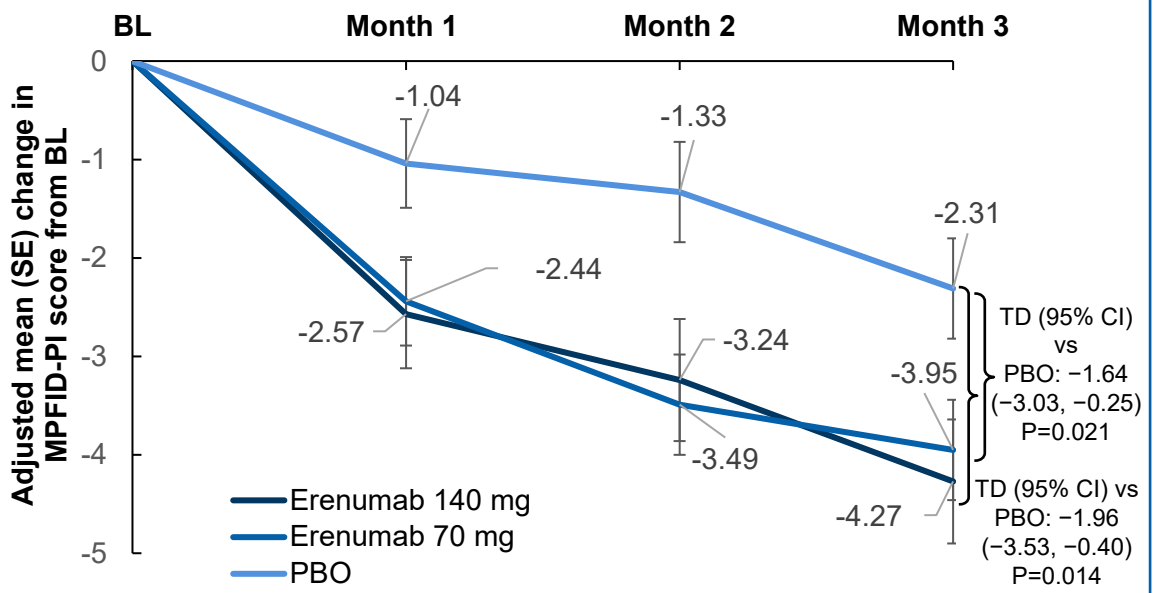
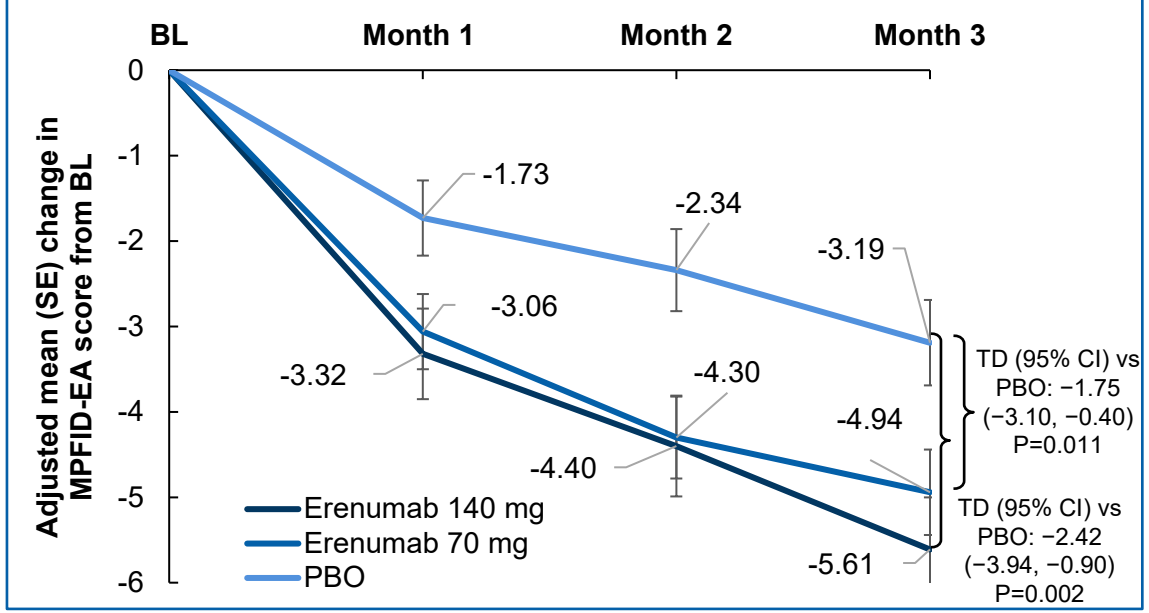


Figure 4b. Adjusted mean change from baseline in MPFID-EA by visit (FAS)



BL, baseline; CI, confidence interval; EA, Everyday Activity; FAS, full analysis set; MPFID, Migraine Physical Function Impact Diary; PBO, placebo; PI, Physical Impairment; SE, standard error; TD, treatment difference; vs, versus.

Results (Cont'd)

EQ-5D-5L – Change from baseline to Month 3

- A greater improvement in the EQ-5D-5L QoL visual analog scale (VAS) score with erenumab 140 mg (8.13, difference: 2.91, P=0.017) and 70 mg (7.08, difference: 1.86, P=0.088) compared with placebo (5.22) was noted (**Figure 5a**). No meaningful differences between erenumab groups and placebo group were noted in the index values (**Figure 5b**)

Figure 5a. Adjusted mean change from baseline in EQ-5D-5L QoL VAS score by visit (FAS)

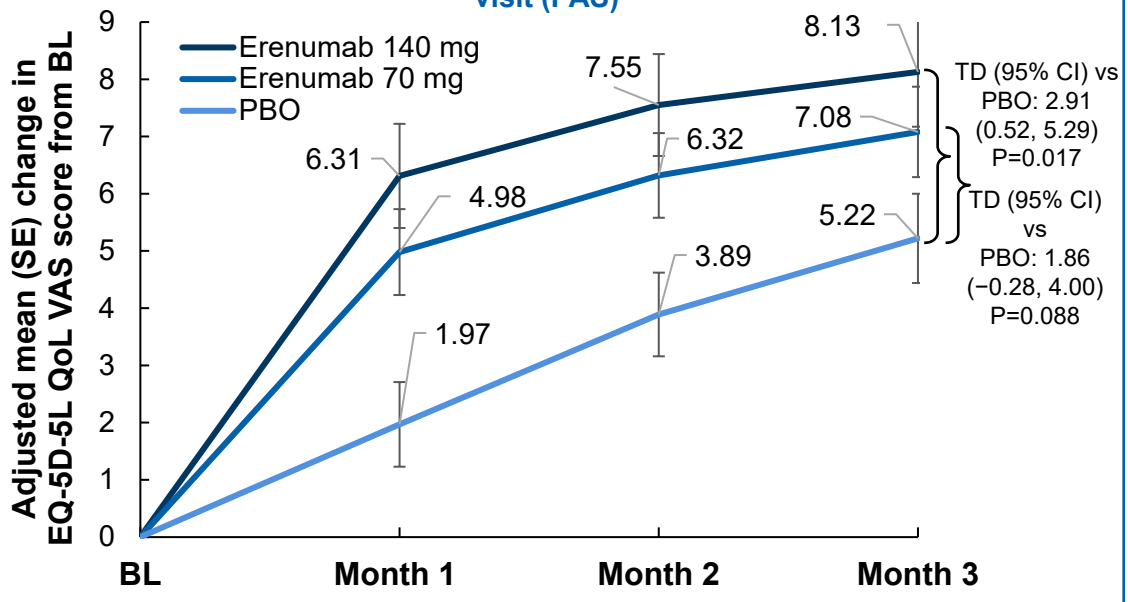
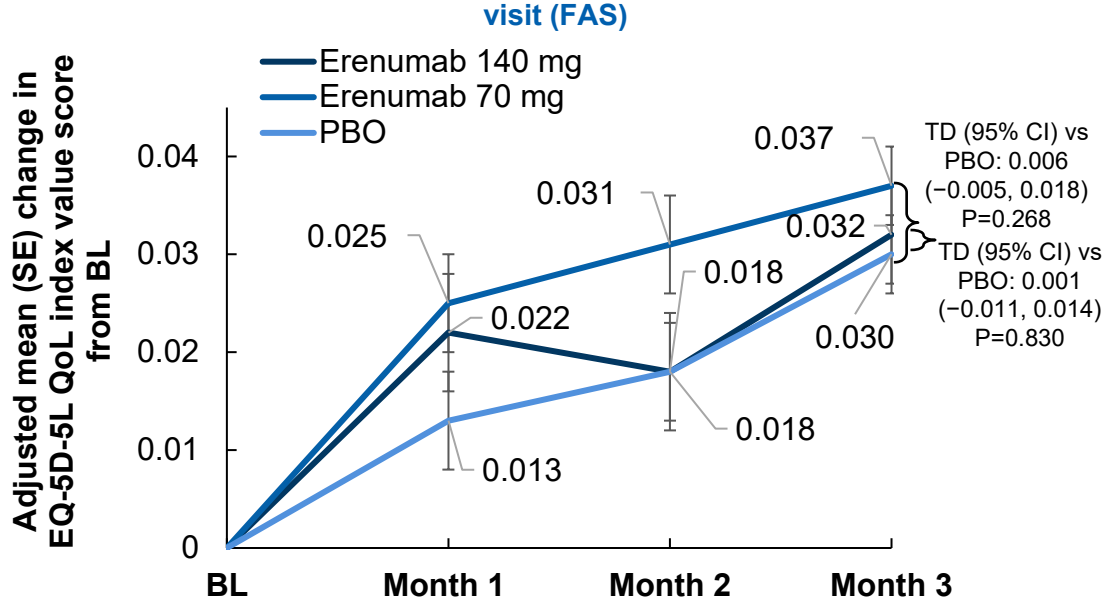


Figure 5b. Adjusted mean change from baseline in EQ-5D-5L QoL index value by visit (FAS)



BL, baseline; CI, confidence interval; EQ-5D-5L, EuroQoL 5-dimension 5-level scale; FAS, full analysis set; PBO, placebo; QoL, quality of life; SE, standard error; TD, treatment difference; VAS, visual analog scale; vs, versus.

Conclusions

- This exploratory analysis of the EMPOwER study demonstrated that erenumab had clinically meaningful improvement versus placebo on the physical functioning and other aspects of daily activities impacted by headache, as assessed by the PRO scales measured in patients with EM from Asia, the Middle East, and Latin America
- Overall, complementary to the primary/secondary efficacy and safety results (previously reported)[1], the PRO results reinforce the benefits of erenumab as an effective therapy for the prevention of migraine in patients with EM

EM, episodic migraine; PRO, patient-reported outcome.

1. Wang SJ, et al. *Cephalalgia*, 2021;41(13):1285-97.