Sustained Efficacy Over 1 Year of Treatment With Erenumab: Results from the Extension Phase of the STRIVE Study in Episodic Migraine

PS108LB

Peter J. Goadsby[1], Uwe Reuter[2], Yngve Hallström[3], Gregor Broessner[4], Jo H. Bonner[5], Feng Zhang[6], Sandhya Sapra[6], Denise E. Chou[6], Jan Klatt[7], Hernan Picard[6], Robert A. Lenz[6], Daniel D. Mikol[6]

[1]NIHR-Wellcome Trust King's Clinical Research Facility, King's College Hospital, London, UK; [2]Department of Neurology, Charité Universitätsmedizin Berlin, Berlin, Germany; [3]Neuro Center, St Görans Hospital, Stockholm, Sweden; [4]Department of Neurology, Headache Outpatient Clinic, Medical University of Innsbruck, Innsbruck, Austria; [5]Mercy Research, Saint Louis, MO, USA; [6]Amgen Inc., Thousand Oaks, CA, USA; [7]Novartis Pharma AG, Basel, Switzerland

Introduction

- Erenumab is a fully human monoclonal antibody that selectively targets and blocks the canonical calcitonin gene-related peptide receptor[1], approved as a preventive treatment for migraine in adults by the US Food and Drug Administration
- The 24-week Phase 3 STRIVE study (NCT02456740; N=955) demonstrated safety and efficacy of erenumab in patients with episodic migraine[2]
- Here we report results of the 28-week dose-blinded active treatment phase (ATP) of the STRIVE study that was designed to assess sustained efficacy and long-term safety of erenumab

Objective

- To assess the efficacy and safety of erenumab in the 28-week, dose-blinded, ATP of the Phase 3 STRIVE study

Methods

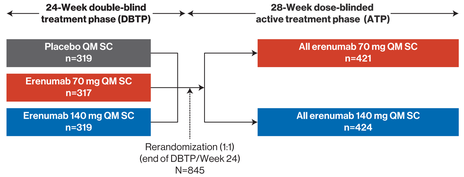
Patient population

- Adults 18 to 65 years of age with a history of episodic migraine with or without aura for ≥12 months before screening were enrolled in the trial
- 4–14 migraine days per month, with <15 headache days per month
- Patients were excluded if they had no therapeutic response (defined as no improvement in frequency, severity, or duration of migraines after ≥6 weeks of treatment at the appropriate dose) to >2 migraine preventive medication categories
- Patients with medication overuse according to ICHD-3 beta [3] criteria were excluded

Study design

- STRIVE (STudy to evaluate the efficacy and safety of erenumab in migRaIne preVEntion): Phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group study of patients with episodic migraine[2]
- 955 patients were randomized (1:1:1) during the 24-week double-blind treatment phase (DBTP) to placebo, erenumab 70 mg or 140 mg administered subcutaneously (SC) once-monthly for 24 weeks
- After completion of DBTP, 845 patients were rerandomized (1:1) to receive erenumab 70 mg (n=421) or 140 mg (n=424) SC once-monthly in a blinded fashion, stratified by treatment groups (placebo, erenumab 70 or 140 mg) assigned during the DBTP (**Figure 1**)

Figure 1. Study schema



Stratified by treatment groups assigned during the DBTP
All erenumab 70 mg: placebo (n=138), erenumab 70 mg (n=140), erenumab 140 mg (n=143)
All erenumab 140 mg: placebo (n=140), erenumab 70 mg (n=140), erenumab 140 mg (n=144)
DBTP, double-blind treatment phase; QM, once-monthly; SC, subcutaneous

- In this analysis, pre-DBTP baseline refers to the last measurement obtained before the first dose of erenumab or placebo in the DBTP
- Pre-active treatment phase (pre-ATP) baseline refers to the last measurement obtained at the end of the DBTP (i.e., at Week 24 before the first dose of erenumab in ATP)
- Change from pre-ATP baseline is the primary analytic approach, given that this is when rerandomization occurred; change from pre-DBTP baseline results are also shown, which contextualizes change from the original baseline period
- A safety follow-up was done 16 weeks after the last dose of erenumab (i.e., Week 64)

Primary endpoint

- To assess change from the baseline (pre-DBTP) to Week 52 in monthly migraine days (MMD)

Secondary endpoints

- Change from the baseline (pre-DBTP) to Week 52 in mean monthly acute migraine-specific medication treatment days (MSMD)
- Proportion of patients with at least 50% reduction in MMD at Week 52
- Change from baseline (pre-DBTP) in Migraine Physical Function Impact Diary-physical impairment (MPFID-PI) to Week 52
- Change from baseline (pre-DBTP) in MPFID-everyday activities (MPFID-EA) score to Week 52

Safety

- Evaluate the safety and tolerability of erenumab

Statistical analysis

- The ATP full analysis set (FAS) included all patients who received at least one dose of erenumab in the ATP. Patients were analyzed according to their randomized treatment, regardless of the treatment received
- The ATP safety analysis set consisted of all patients who received at least one dose of erenumab in the ATP
- All the analyses were based on descriptive statistics and no statistical testing comparing treatment groups was performed

Results

- Of the 955 patients randomized into the STRIVE study, 858 completed the DBTP and 845 entered the ATP
- Of the 845 patients entering the ATP, 84.4% of patients were women, 90.2% were white, and the mean (SD) age at pre-ATP baseline was 41.6 (11.1) years (**Table 1**)

Table 1. Demographics and baseline characteristics (ATP FAS)

	Erenumab 140 mg (ATP) (N=424)	Erenumab 70 mg (ATP) (N=421)	Total (N=845)
Age, years	41.9 (10.9)	41.3 (11.3)	41.6 (11.1)
Women, n (%)	359 (84.7)	354 (84.1)	713 (84.4)
Race, white, n (%)	380 (89.6)	382 (90.7)	762 (90.2)
Treatment with migraine preventative medication, n (%)			
Naive	230 (54.2)	238 (56.5)	468 (55.4)
Prior or current use	194 (45.8)	183 (43.5)	377 (44.6)
Baseline disease characteristics			
MMD	8.23 (2.43)	8.34 (2.48)	8.28 (2.45)
Acute migraine-specific medication use, n (%)	255 (60.1)	266 (63.2)	521 (61.7)
Monthly acute migraine-specific medication use days	3.49 (3.49)	3.60 (3.41)	3.55 (3.45)
MPFID-EA	13.31 (8.60)	13.45 (8.64)	13.38 (8.61)
MPFID-PI	12.10 (9.05)	12.08 (9.31)	12.09 (9.18)

N=Number of patients in the analysis set; n=Number of patients with non-missing values; %=n/N * 100
Data specified are mean (SD) unless otherwise specified
ATP, active treatment phase; FAS, full analysis set; MMD, monthly migraine days; MPFID-EA, Migraine Physical Function Impact Diary-everyday activities; MPFID-PI, MPFID-physical impairment; SD, standard deviation

Table 2. Outcome measures (ATP FAS)

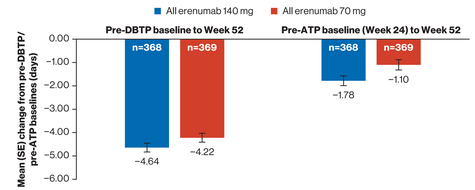
	Erenumab 140 mg (ATP) (N=424)	Erenumab 70 mg (ATP) (N=421)
MMD		
Pre-DBTP baseline MMD, mean (SD)	8.23 (2.43)	8.34 (2.48)
Change from pre-DBTP baseline to Week 52	−4.64 (0.19)	−4.22 (0.22)
Pre-ATP baseline, mean (SD)	5.34 (4.39)	5.16 (4.14)
Change from pre-ATP baseline to Week 52 (ATP)	−1.78 (0.19)	−1.10 (0.21)
Proportion of patients achieving ≥50% reduction in MMD from pre-DBTP baseline at Week 52, n (%)	239 (64.9)	225 (61.0)
Acute MSMD*		
Pre-DBTP baseline acute MSMD, mean (SD)	3.49 (3.49)	3.60 (3.41)
Change from pre-DBTP baseline to Week 52	−2.00 (0.15)	−1.75 (0.14)
Pre-ATP baseline, mean (SD)	2.52 (3.52)	2.60 (3.46)
Change from pre-ATP baseline to Week 52 (ATP)	−0.98 (0.13)	−0.72 (0.14)
MPFID-PI		
Pre-DBTP baseline MPFID-PI, mean (SD)	12.10 (9.05)	12.08 (9.31)
Change from pre-DBTP baseline to Week 52	−5.74 (0.45)	−5.42 (0.51)
Pre-ATP baseline, mean (SD)	8.11 (9.75)	8.24 (10.77)
Change from pre-ATP baseline to Week 52 (ATP)	−1.90 (0.34)	−1.28 (0.41)
MPFID-EA		
Pre-DBTP baseline MPFID-EA, mean (SD)	13.31 (8.60)	13.45 (9.64)
Change from pre-DBTP baseline to Week 52	−7.05 (0.44)	−6.94 (0.47)
Pre-ATP baseline, mean (SD)	8.30 (9.48)	8.37 (10.27)
Change from pre-ATP baseline to Week 52 (ATP)	−2.20 (0.34)	−1.62 (0.39)

*As only ~60% of patients were taking acute migraine-specific medications (MSMs) during pre-DBTP baseline, the effect shown here for the overall population is less than that observed in patients using MSMs during pre-DBTP baseline
Data are presented as mean (SE) unless specified
Results for change from pre-ATP baseline to Week 52 are highlighted
ATP, active treatment phase; FAS, full analysis set; MMD, monthly migraine days; MPFID-EA, Migraine Physical Function Impact Diary-everyday activities; MPFID-PI, MPFID-physical impairment; MSMD, migraine-specific medication treatment days; SE, standard error; SD, standard deviation

Primary endpoint

- The mean (SE) change in MMD from pre-DBTP baseline/pre-ATP baseline is presented in **Figure 2**

Figure 2. Change from pre-DBTP baseline/pre-ATP baseline in MMD (ATP FAS)



Error bars represent SE
ATP, active-treatment phase; DBTP, double-blind treatment phase; FAS, full analysis set; MMD, monthly migraine days; SE, standard error

- In addition to the ATP 70 mg and 140 mg analyses described above, efficacy in patients either staying on 70 mg or increasing dose from 70 mg to 140 mg was assessed, compared to pre-ATP baseline; similarly, efficacy in patients either staying on 140 mg or decreasing dose to 70 mg was assessed
  - 140 mg → 70 mg: mean (SE) change from pre-ATP baseline to Week 52 in MMD of −0.07 (0.31)
  - 140 mg → 140 mg: mean (SE) change from pre-ATP baseline to Week 52 in MMD of −0.63 (0.28)
  - 70 mg → 70 mg: mean (SE) change from pre-ATP baseline to Week 52 in MMD of −1.08 (0.35)
  - 70 mg → 140 mg: mean (SE) change from pre-ATP baseline to Week 52 in MMD −1.82 (0.32)
- Finally, efficacy in the placebo → 70 mg and placebo → 140 mg switchers was assessed, compared to pre-ATP baseline, and results recapitulated the *numerically* greater efficacy observed for 140 mg versus 70 mg in the DBTP:
  - placebo → 70 mg: mean (SE) change from pre-ATP baseline to Week 52 in MMD of −2.18 (0.43)
  - placebo → 140 mg: mean (SE) change from pre-ATP baseline to Week 52 in MMD of −2.86 (0.37)

Secondary endpoints

- At Week 52, the proportion of patients who achieved ≥50% reduction in MMD from pre-DBTP baseline was 61.0% in the erenumab 70 mg group and 64.9% in the 140 mg group (**Table 2**)
- In the ATP, the mean (SE) change in monthly acute MSMD from pre-ATP baseline to Week 52 was −0.72 (0.14) days in the 70 mg group and −0.98 (0.13) days in the 140 mg group
- The mean (SE) change in monthly average MPFID-PI scores from pre-ATP baseline to Week 52 was −1.28 (0.41) in the erenumab 70 mg group and −1.90 (0.34) in the 140 mg group during the ATP
- From pre-ATP baseline to Week 52, the mean (SE) change in MPFID-EA scores was −1.62 (0.39) in the 70 mg group and −2.20 (0.34) in the 140 mg group during the ATP

Safety

- Overall during the ATP, treatment-emergent adverse events (TEAEs) were reported in 241 (57.2%) and 233 (55.0%) patients in erenumab 70 mg and 140 mg groups, respectively (**Table 3**)

Table 3. Adverse events during the ATP

	Erenumab 140 mg (ATP)			Erenumab 70 mg (ATP)		
	Placebo (N=140) n (%)	Erenumab 70 mg (N=140) n (%)	Erenumab 140 mg (N=144) n (%)	Placebo (N=138) n (%)	Erenumab 70 mg (N=140) n (%)	Erenumab 140 mg (N=143) n (%)
All TEAEs	76 (54.3)	74 (52.9)	83 (57.6)	85 (61.6)	81 (57.9)	75 (52.4)
Severity						
Grade ≥2	42 (30.0)	51 (36.4)	54 (37.5)	62 (44.9)	49 (35.0)	51 (35.7)
Grade ≥3	4 (2.9)	8 (5.7)	8 (5.6)	8 (5.8)	12 (8.6)	6 (4.2)
Grade ≥4	0	1 (0.7)	2 (1.4)	0	0	0
Serious adverse events	3 (2.1)	6 (4.3)	5 (3.5)	3 (2.2)	7 (5.0)	4 (2.8)
Leading to discontinuation of erenumab	2 (1.4)	4 (2.9)	4 (2.8)	0	5 (3.6)	1 (0.7)
Fatal adverse events	0	1 (0.7)*	0	0	0	0

*One patient who switched from DBTP 70 mg to 140 mg in ATP died due to arrhythmogenic right ventricular dysplasia. A postmortem genetic assessment revealed the patient was heterozygous for a frameshift variant consistent with a genetic form of arrhythmia/cardiomyopathy
ATP, active treatment phase; DBTP, double-blind treatment phase; TEAEs, treatment-emergent adverse events

- Safety data from this analysis were comparable to those reported for the patient population[2] and were comparable to placebo as observed in prior studies

Conclusions

- Over 52 weeks, erenumab provided sustained efficacy in prevention of episodic migraine, and tolerability profile comparable to placebo as observed in prior studies
- In the overall population, change in MMD, change in monthly acute MSMD, and change in MPFID-EA was >50% reduced from baseline for both the 70 mg and 140 mg dose groups (almost 50% for MPFID-PI, both dose groups)
- At Week 52, the proportion of patients who achieved ≥50% reduction in MMD in the erenumab 70 mg and 140 mg treatment groups sustained over 24 weeks from pre-DBTP baseline and further improved over 28 weeks ATP
- Across all endpoints, compared to pre-ATP baseline, *numerically* greater efficacy was observed for patients receiving erenumab 140 mg versus 70 mg during the dose-blinded ATP:
  - For patients switching from placebo to 140 mg or 70 mg
  - For patients who increased dose from 70 mg to 140 mg, compared to those treated with 70 mg during the DBTP and remained on 70 mg
  - For patients treated with 140 mg during the DBTP and remained on 140 mg during the ATP, compared to those who decreased dose to 70 mg

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Acknowledgments

The authors acknowledge the following Novartis employees: **Rohita Gattoju** for medical writing support and coordinating author reviews and **Edward Kattekola** for design assistance. The final responsibility for the content lies with the authors.

Disclosures

This study was supported by Amgen Inc.

Erenumab is co-developed by Amgen and Novartis.

Peter J. Goadsby — grants and personal fees from Amgen and Eli Lilly and Company and personal fees from Alder Biopharmaceuticals, Allergan, Autonomic Technologies Inc., Dr Reddy's Laboratories, Electrocore LLC, eNeura, Novartis, Scion, Teva Pharmaceuticals, and Trigemina Inc., and personal fee from MedicoLegal work, Journal Watch, Up-to-Date, Oxford University Press, Massachusetts Medical Society, and Wolters Kluwer; and a patent Magnetic stimulation for headache assigned to eNeura without fee. **Uwe Reuter** — consulting fee, speaking/teaching fee, and/or research grants: Allergan, Amgen, Autonomic Technologies, CoLucid, ElectroCore, Novartis, Pharm Allergan, Eli Lilly, and TEVA. **Yngve Hallström** — advisory board: Amgen and Sanofi. **Gregor Broessner** — consulting fees: Novartis, Pfizer, Allergan, Reckitt Benkiser; Speakers bureau: Novartis, Pfizer, Allergan, Reckitt Benkiser, Linde AG; research grants: Novartis, Amgen. **Jo H. Bonner** — has nothing to disclose. **Feng Zhang, Sandhya Sapra, Denise E. Chou, Hernan Picard, Robert A. Lenz and Daniel D. Mikol** — employees and stock: Amgen. **Jan Klatt** — employee and stock: Novartis.

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Poster presented at the 60th Annual Scientific Meeting of the American Headache Society (AHS), San Francisco, CA, USA, June 28–July 1, 2018.

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