PF10

Eptinezumab Reduced Migraine Hours and Severity, Which Were Accompanied by Improved HIT-6 Scores, Over Weeks 1–12: Results From the Phase 3 PROMISE-2 Trial in Chronic Migraine

Timothy Smith,[1] Laszlo Mechtler,[2] Eric Kassel,[3] David Biondi,[3] Roger Cady,[3] Suman Bhattacharya[3]

[1]StudyMetrix Research, St. Louis, MO; [2]DENT Neurologic Institute, Amherst, NY; [3]Alder BioPharmaceuticals, Inc., Bothell, WA

Introduction

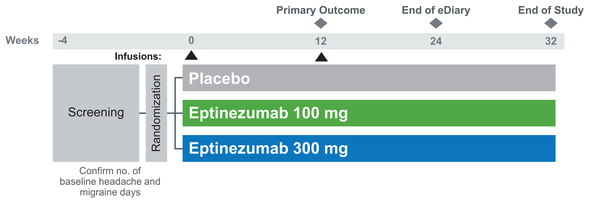
- Migraine is a highly prevalent, disabling, and costly neurologic disorder[1]
- Calcitonin gene-related peptide (CGRP) is a neuropeptide that plays an important role in migraine pathophysiology[2]
- Eptinezumab (ALD403) is an anti-CGRP IgG1 monoclonal antibody that rapidly and selectively binds to CGRP, inhibiting its biological activity[3]
  - Eptinezumab:
    - Binds the CGRP ligand with high affinity, resulting in potent and sustained inactivation of CGRP
    - Is designed for rapid onset and durability (reliable $t_{1/2}$ ~30 days)
    - Is the only anti-CGRP monoclonal antibody glycoengineered for reduced immune activation
    - Is the only anti-CGRP monoclonal antibody currently in development administered by quarterly iv infusion, allowing for 100% bioavailability within hours after infusion[3]
  - In phase 2[4,5] and phase 3[6,7] studies in episodic and chronic migraine, eptinezumab significantly reduced migraine days vs placebo, demonstrated migraine preventive efficacy, and was generally well tolerated

Objectives

- To evaluate the effects of eptinezumab on changes in migraine hours and intensity, and on Headache Impact Test-6 (HIT-6) scores with data from the phase 3 PROMISE-2 trial, which evaluated eptinezumab for migraine prevention in subjects with chronic migraine (ALD403-CLIN-011; NCT02974153)

Methods

PROMISE-2 Study Design (N=1072)



- This was a phase 3, parallel-group, double-blind, randomized, placebo-controlled trial of repeat quarterly iv infusions of eptinezumab or placebo in subjects with chronic migraine
- Inclusion criteria included:
  - Male or female aged 18–65 years
  - Diagnosis of migraine at age ≤50 years by the criteria of the 3rd Edition of the International Classification of Headache Disorders (ICHD-3) beta
  - History of migraine ≥1 year prior to screening
  - During the 28-day screening period, subjects experienced ≥15 to ≤26 headache days, of which ≥8 were migraine days
  - Prescription or over-the-counter medication for acute or prophylactic treatment of migraine had been prescribed or recommended by a healthcare professional
  - Any prophylactic use of medications for headaches was stable for ≥3 months prior to screening
- Exclusion criteria included:
  - Use of botulinum toxin within 4 months prior to screening and during the 28-day screening period
- Subjects with medication overuse headache not associated with opiates or butalbital products could be enrolled
- Subjects completed an eDiary daily from screening visit through Week 24, with 90% compliance
- Treatment included 2 iv infusions of eptinezumab or placebo administered on Days 0 and 84 (Week 12)

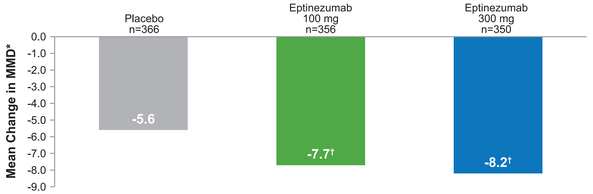
Efficacy Endpoints

Primary Endpoint	Mean change from baseline in monthly migraine days (MMD)	Weeks 1–12
Key Secondary Endpoints	Headache Impact Test (HIT-6)*	Weeks 4, 12, 16, 24, and 32†
Secondary Endpoints	Headache/migraine hours‡ Headache/migraine days with severe intensity§	12- and 24-week intervals 4-week intervals

*Measured endpoint was change from baseline in HIT-6 total score at Week 12 for 300-mg dose only; †4-week recall period; ‡Migraine hours are sum of duration of migraines within 4-week intervals, and average 4-week duration within 12- and 24-week intervals; headache hours are similarly defined, but include all headaches; §Migraine intensity analysis based on pain severity.

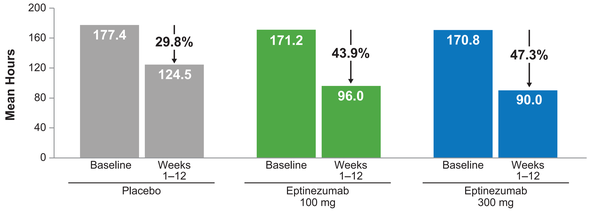
Results

Mean Change in Monthly Migraine Days: Weeks 1–12: Primary Endpoint

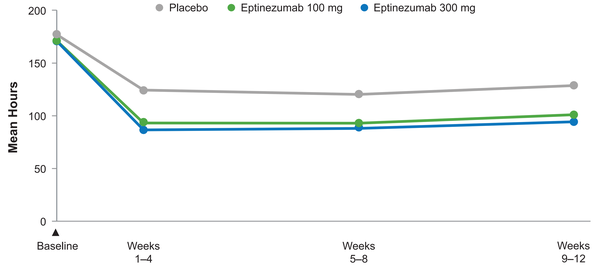


*Analysis of covariance model used to test for differences between treatment groups. †p <0.0001 vs placebo.

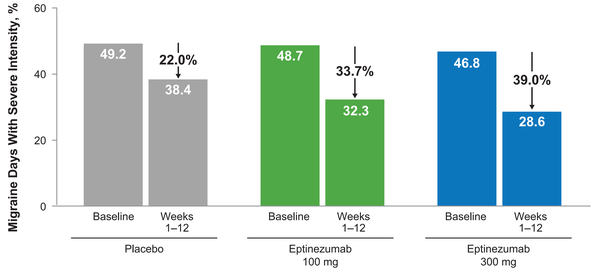
47% Decrease in Mean Monthly Migraine Hours With Eptinezumab 300 mg: Weeks 1–12



Mean Monthly Migraine Hour Reductions Sustained Through 12 Weeks

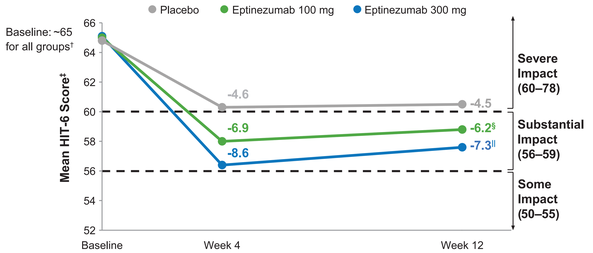


39% Decrease in Severe Migraine Days With Eptinezumab 300 mg: Weeks 1–12



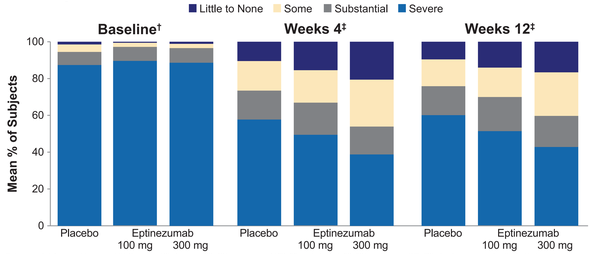
- Headache severity data collected on a 3-point scale: mild pain, moderate pain, and severe pain

Improvements in Mean HIT-6 Score Weeks 4 and 12: Key Secondary Endpoint*



*Change from baseline in total HIT-6 score for 300-mg dose only; 4-week recall period; †Baseline is last assessment collected before dosing on Day 0; ‡Life impact determined by mean HIT-6 scores: little to none (36–49), some impact (50–55), substantial (56–59), and severe (60–78); §p=0.0010 vs placebo, unadjusted; ||p <0.0001 vs placebo.

>50% Reductions in Severe and Substantial Life Impact Scores With Eptinezumab as Measured by HIT-6*



*Life impact determined by mean HIT-6 scores: little to none (36–49), some impact (50–55), substantial (56–59), and severe (60–78); †Last assessment collected before dosing on Day 0; ‡4-week recall period.

Safety Profile Through Week 32*

Subjects, n (%)	Placebo n=366	Eptinezumab 100 mg n=356	Eptinezumab 300 mg n=350
Any TEAE	171 (47)	155 (44)	182 (52)
Any serious TEAE†	3 (<1)	3 (<1)	4 (1)
Any TEAE leading to drug withdrawal	2 (<1)	3 (<1)	8 (2)
Most frequent TEAEs‡			
Nasopharyngitis	22 (6)	19 (5)	33 (9)
Upper respiratory tract infection	20 (6)	15 (4)	19 (5)
Nausea	7 (2)	6 (2)	12 (3)
Urinary tract infection	6 (2)	8 (2)	12 (3)
Arthralgia	3 (<1)	5 (1)	11 (3)
Influenza	9 (3)	1 (<1)	10 (3)
Dizziness	4 (1)	5 (1)	9 (3)
Sinusitis	15 (4)	7 (2)	9 (3)
Migraine	16 (4)	6 (2)	8 (2)
Anxiety	1 (<1)	4 (1)	7 (2)
Fatigue	7 (2)	8 (2)	6 (2)
Back pain	6 (2)	7 (2)	6 (2)
Bronchitis	8 (2)	7 (2)	4 (1)

*Safety profile represents safety population; †All serious treatment-emergent adverse events (TEAEs) reported unrelated to study drug; ‡≥2% in any active treatment group.

Conclusions

- **Eptinezumab significantly reduced monthly migraine days over Weeks 1–12 after a single iv infusion in subjects with chronic migraine**
- **Eptinezumab 300 mg reduced migraine hours by 47% over Weeks 1–12**
  - **Similar reductions were obtained over each 4-week interval**
- **Eptinezumab 300 mg reduced migraines with severe intensity by 39% over Weeks 1–12**
- **Decreases in migraine hours and intensity at Weeks 4 and 12 were associated with meaningful reductions in the impact of migraine on subjects' lives as measured by HIT-6 scores (>50% reductions)**
- **Overall TEAE rates for eptinezumab were similar to placebo and the safety profile was consistent with previous eptinezumab studies**

References

1. Lipton RB, Silberstein SD. *Headache.* 2015;55:103-22; **2.** Ho TE, et al. *Nat Rev Neurol.* 2010;6:573-82; **3.** Baker B, et al. *Cephalalgia.* 2017;37(suppl):109; **4.** Dodick DW, et al. *Lancet Neurol.* 2014;13:1100-7; **5.** Dodick D, et al. *Neurology.* 2017;88(suppl 16):S52.003; **6.** Saper J, et al. *Cephalalgia.* 2017;37(suppl):319-74; **7.** Lipton RB, et al. *Neurology.* 2018;90(suppl 15):S32.

Acknowledgment

This study was funded by Alder BioPharmaceuticals, Inc.

Disclosures

T. Smith: Alder; Amgen; Avanir; Dr Reddy's Laboratories, Guidepoint, Lilly, Novartis, Pharmalyte, Promius, Zosano; **L. Mechtler:** No conflicts reported; **E. Kassel, D. Biondi, R. Cady,** and **S. Bhattacharya:** Alder (full-time employee).

ALDER BIOPHARMACEUTICALS

QR

Presented at AHS 60th Annual Meeting, June 28–July 1, San Francisco, CA

© 2018 Alder Biopharmaceuticals, Inc. All rights reserved.