PF20

Eptinezumab Reduced Migraine Frequency and Triptan/Ergotamine Use Over Weeks 1–12, and Improved HIT-6 Scores at Months 1 and 3: Results From the Phase 3 PROMISE-2 Trial in Chronic Migraine

Stephen Silberstein,[1] Egilius L.H. Spierings,[2] Gary Berman,[3] David Biondi,[4] Jeff Smith,[5] Suman Bhattacharya,[4] Roger Cady[4]

[1]Jefferson Headache Center, Philadelphia, PA; [2]MedVadis Research Corporation, Watertown, MA; [3]Clinical Research Institute, Inc., Minneapolis, MN; [4]Alder BioPharmaceuticals, Inc., Bothell, WA; [5]Alder BioPharmaceuticals, Ltd, Dublin, Republic of Ireland

Introduction

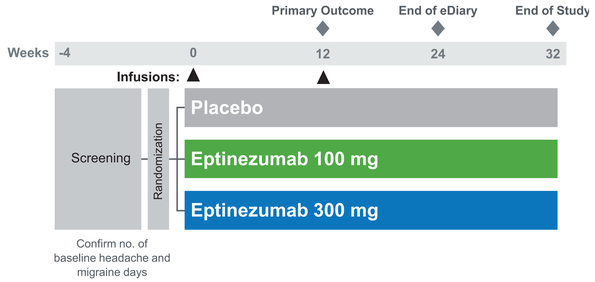
- Migraine is a highly prevalent, disabling, and costly neurologic disorder[1]
- Calcitonin gene-related peptide (CGRP) is a neuropeptide that plays an important role in migraine pathophysiology[2]
- Eptinezumab (ALD403) is an anti-CGRP IgG1 monoclonal antibody that rapidly and selectively binds to CGRP, 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

Objective

- To evaluate the effects of eptinezumab on migraine frequency and triptan/ergotamine use over Weeks 1–12, and on Headache Impact Test (HIT-6™) scores at Weeks 4 and 12 with data from the phase 3 PROMISE-2 study, 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 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†
	Headache/migraine days with triptan/ergotamine use‡	4-, 12-, and 24-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; ‡Change from baseline in triptan/ergotamine use over Weeks 1–12 for 300-mg dose only.

Results

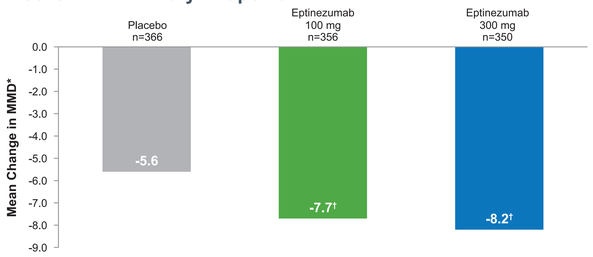
Baseline Characteristics and Demographics

	Placebo	Eptinezumab 100 mg	Eptinezumab 300 mg
Subjects, n	**366**	**356**	**350**
Mean age, year (SD)	39.6 (11.3)	41.0 (11.7)	41.0 (10.4)
Mean BMI, kg/m² (SD)	27.0 (5.6)	26.4 (5.0)	26.3 (5.0)
Female, %	89	86	90
Mean years from migraine diagnosis	17.0	18.3	19.0
Mean duration of chronic migraine, years (SD)	11.6 (10.9)	11.6 (11.7)	12.4 (11.2)
≥1 prophylactic medication, n (%)*	163 (44.5)	161 (45.2)	155 (44.3)
Mean migraine days/month (SD)	16.2 (4.6)	16.1 (4.6)	16.1 (4.8)
Mean headache days/month (SD)	20.6 (3.0)	20.4 (3.1)	20.4 (3.2)
Mean triptan/ergotamine days (SD)†	6.2 (6.7)	6.6 (6.9)	6.7 (6.5)

*According to American Academy of Neurology/American Headache Society guidelines for migraine preventive treatment (medications identified by clinical review of coded medical data); †Days with triptan or ergotamine use as recorded in eDiary averaged over 28-day screening period. BMI, body mass index; SD, standard deviation.

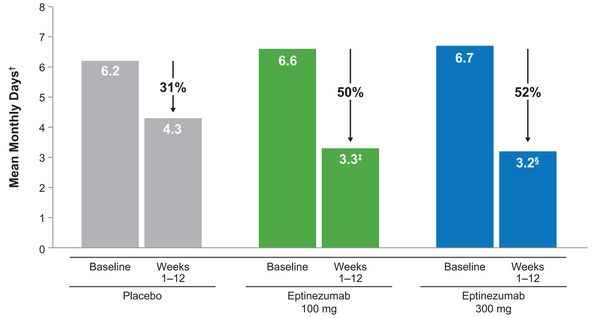
- Mean migraine days through baseline were ~16 days/month across groups
- Baseline characteristics were balanced across treatment groups

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



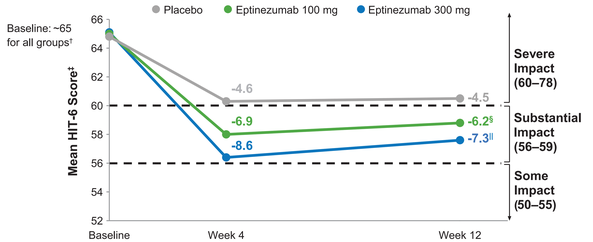
*Analysis of covariance model used to test for differences between treatment groups; †p<0.0001 vs placebo.

>50% Decrease in Days of Triptan/Ergotamine Use With Eptinezumab Weeks 1–12: Key Secondary Endpoint*



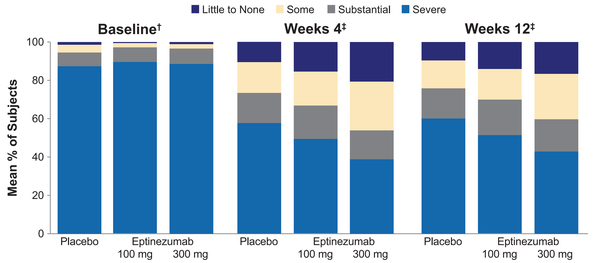
*300-mg dose only; †Analysis of covariance test; ‡p <0.0001 vs placebo, unadjusted; §p <0.0001 vs placebo.

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

- **A single infusion of eptinezumab in subjects with chronic migraine significantly reduced mean monthly migraine days over 3 months**
- **A ≥50% decrease in days of triptan/ergotamine use was observed with eptinezumab over Weeks 1–12**
- **Eptinezumab 300 mg demonstrated significant and meaningful improvements in HIT-6 scores at Week 12 and these improvements were similar to Week 4 results**
- **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.

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Disclosures

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