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Eptinezumab for Prevention of Chronic Migraine: Results of 2 Quarterly Intravenous Infusions in the Phase 3 PROMISE-2 (PRevention Of Migraine via Intravenous eptinezumab Safety and Efficacy–2) Trial

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Introduction

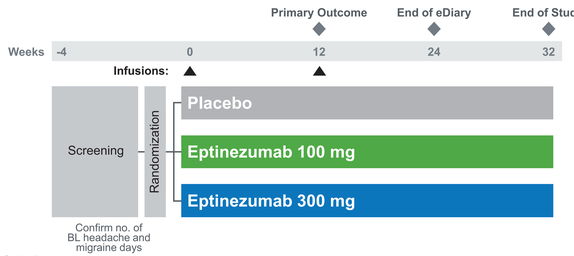
- Migraine is a highly prevalent, disabling, and costly neurologic disorder[1]
- Calcitonin gene-related peptide (CGRP) is a neuropeptide that plays an important role in migraine pathophysiology[2]
- Eptinezumab (ALD403) is an anti-CGRP IgG1 monoclonal antibody that rapidly and selectively binds to CGRP, 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 studies in episodic and chronic migraine (CM),[4,5] and a phase 3 study in episodic migraine,[6] eptinezumab significantly reduced migraine days vs placebo, demonstrated migraine preventive efficacy, and was generally well tolerated
  - Here we present the findings of the phase 3 PROMISE-2 trial (ALD403-CLIN-011: NCT02974153) in patients with CM

Objectives

- To evaluate the efficacy and safety of 2 quarterly iv infusions of eptinezumab for the prevention of migraine in adult patients with CM

Methods

PROMISE-2 Study Design (N=1072)



BL, baseline.

- 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 CM
- 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 BL in monthly migraine days (MMD)	Weeks 1–12
Key Secondary Endpoints	≥75% migraine responder rate*	Weeks 1–4
	≥50% migraine responder rate*	Weeks 1–12
	≥75% migraine responder rate*	
Secondary Endpoints	100% migraine responder rate†	Weeks 1–12

*% of subjects with migraine response (prespecified reduction from BL in MMD); †% of subjects who were migraine-free for each 4-week interval on average over Weeks 1–12.

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/m^2 (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 CM, year (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.

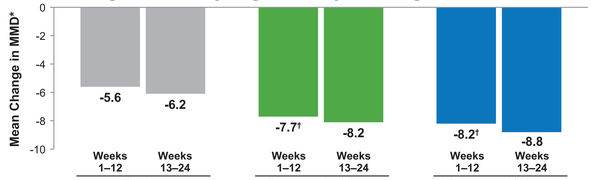
- Mean BL migraine days were ~16 days/month across groups
- BL characteristics were balanced across treatment groups

Subject Disposition

Randomized Subjects, n (%)	Placebo n=375	Eptinezumab 100 mg n=372	Eptinezumab 300 mg n=374	Overall N=1121*
Full analysis population†	366 (98)	356 (96)	350 (94)	1072 (96)
Week 12‡	356 (95)	349 (94)	344 (92)	1049 (94)
Week 24‡	336 (90)	333 (90)	331 (89)	1000 (89)
Discontinued treatment early§	24 (7)	16 (5)	15 (4)	55 (5)
TEAE	3 (<1)	3 (<1)	8 (2)	14 (1)
Subject consent withdrawal or lost to follow-up	19 (2)	10 (1)	7 (1)	36 (3)
Other	2 (<1)	3 (<1)	0	5 (<1)

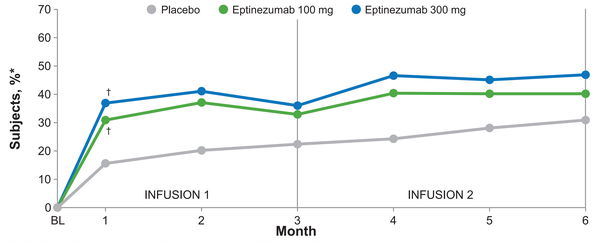
*All randomized: N=1121; all randomized and dosed: n=1072; all randomized, dosed, and captured at Week 12: n=1049; †Includes all randomized subjects who received eptinezumab or placebo; ‡Subjects by visit; §% based on all randomized subjects; ‖% based on full analysis population. TEAE, treatment-emergent adverse event.

Mean Change in Monthly Migraine Days Through 2 Dose Intervals



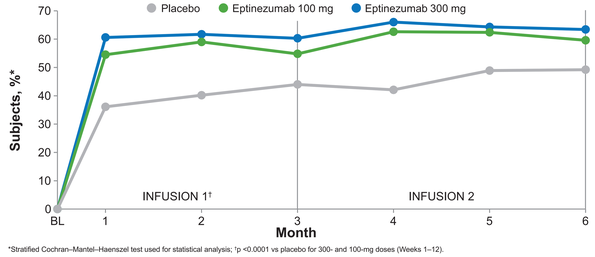
*Analysis of covariance model used to test for difference between treatment arms; †p <0.0001 vs placebo (Weeks 1–12).

≥75% Migraine Responder Rate Through 2 Dose Intervals



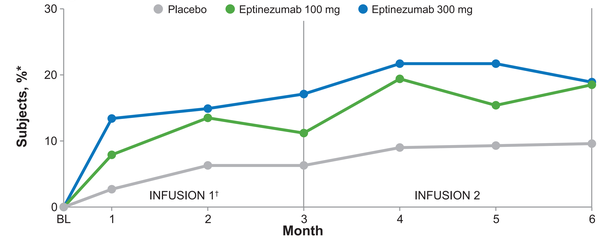
*Stratified Cochran–Mantel–Haenszel test used for statistical analysis; †p <0.0001 vs placebo (Weeks 1–4).

≥50% Migraine Responder Rate Through 2 Dose Intervals



*Stratified Cochran–Mantel–Haenszel test used for statistical analysis; †p <0.0001 vs placebo for 300- and 100-mg doses (Weeks 1–12).

Monthly Migraine Freedom—100% Responder Rate—Through 2 Dose Intervals



*Stratified Cochran–Mantel–Haenszel test used for statistical analysis; %s of subjects with mean monthly freedom from migraine averaged over 3 months; †p <0.0001 vs placebo for 300- and 100 mg doses (Weeks 1–12/unadjusted).

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 TEAEs reported unrelated to study drug; ‡≥2% in any active treatment group.

Conclusions

- **Eptinezumab subjects with CM showed significant reductions in monthly migraine activity across the primary and all key secondary endpoints**
- **33% of subjects treated with eptinezumab 300 mg experienced ≥75% reduction in MMD over Weeks 1–12, which increased to 43% of subjects after the 2nd infusion**
- **61% of subjects sustained a ≥50% reduction in MMD over Weeks 1–12, which increased to 64% of subjects after the 2nd infusion**
- **Subjects experiencing monthly migraine freedom increased from ~15% to 20% from the 1st to 2nd infusion**
- **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.

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Disclosures

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