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P4-091

Eptinezumab Reduced Migraine Frequency, Hours, and Pain Intensity Through Week 24: Results From the Phase 3 PROMISE-1 Trial

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Introduction

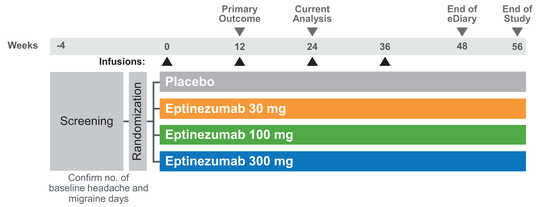
- Migraine is a highly prevalent, disabling, and costly neurologic disorder[1]
- Calcitonin gene-related peptide (CGRP) is a neuropeptide that plays an important role in migraine pathophysiology[2]
- Eptinezumab (ALD403) is a humanized, anti-CGRP monoclonal antibody that selectively and potently inhibits CGRP biological activity[3]
  - Eptinezumab binds the CGRP ligand with high affinity, resulting in rapid and durable inactivation of CGRP
  - Eptinezumab is the only anti-CGRP monoclonal antibody currently in development that is administered by quarterly iv infusion, allowing for 100% bioavailability at the time of infusion
  - In phase 3 studies in episodic migraine and chronic migraine (see Saper J et al[4] and Lipton R et al[5] oral presentations at this meeting), and a phase 2 study in episodic migraine,[6] eptinezumab significantly reduced migraine days vs placebo, demonstrated migraine preventive efficacy, and was well tolerated
  - In a phase 2b study in chronic migraine, a single iv infusion of eptinezumab rapidly decreased migraine frequency, duration, and intensity, and was well tolerated[7]

Objective

- To evaluate the effect of eptinezumab on duration and severity of migraine in an exploratory analysis of data from the PROMISE-1 trial evaluating eptinezumab (2 quarterly infusions) for migraine prevention in subjects with episodic migraine (ALD403-CLIN-006; NCT02559895)

Methods

PROMISE-1 Study Design (N=888)



- This was a phase 3, parallel-group, double-blind, randomized, placebo-controlled trial of repeat quarterly infusions of eptinezumab or placebo in subjects with episodic migraine
- Eligibility criteria included:
  - Male or female aged 18–75 years
  - Diagnosis of migraine at age ≤50 years by the criteria of the 2nd edition of the International Classification of Headache Disorders (ICHD-2)
  - History of migraine ≥12 months
    - 4–14 headache days/month, of which ≥4 met ICHD-2 criteria for migraine
    - During the 28-day screening period, subjects experienced ≤14 headache days, of which ≥4 were migraine days
  - No use of botulinum toxin and preventive migraine/headache medications prior to (4 and 2 months, respectively) and during the 28-day screening period
  - Subjects completed an eDiary daily from screening visit through Week 48
- Eligible subjects were randomized into 1 of 3 eptinezumab dose levels (30, 100, or 300 mg) or placebo
- Eligible subjects returned to the site on Day 0 for the 1st infusion, which occurred after the 28-day screening (baseline) period

Statistical Hierarchy

- PROMISE-1 was a 4-arm study in which subjects were randomized to eptinezumab 30, 100, or 300 mg, or placebo in a 1:1:1:1 ratio
- A formal inferential testing algorithm was used to control statistical multiplicity, which tested the primary and all key secondary endpoints in a fixed sequence
- Due to a nonsignificant p-value for the 100-mg group vs placebo for the 75% migraine responder rate (Weeks 1–12) secondary endpoint, the primary endpoint and key secondary endpoints were not statistically significant for the 30-mg group

Endpoints

Primary Endpoint	Mean change from baseline in monthly migraine days	Weeks 1–12
Key Secondary Endpoints	≥75% migraine responder rates	Weeks 1–4
	≥50% migraine responder rates ≥75% migraine responder rates	Weeks 1–12

Results

Baseline Characteristics and Demographics

	Placebo	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg
Safety population, n	**222**	**219**	**223**	**224**
Mean age, year	39.9	39.1	40.0	40.2
Mean weight, kg	82.4	82.0	82.4	80.2
Female, %	84	85	80	89
Mean years from migraine diagnosis	16.9	17.0	17.4	18.2
Subjects with ≥1 prophylactic medication, n (%)	10 (5)	14 (6)	9 (4)	8 (4)
Efficacy population, n	**222**	**223**	**221**	**222**
Mean migraine days/month	8.4	8.7	8.7	8.6
Mean headache days/month	9.9	10.2	10.0	10.1
Mean triptan/ergotamine days*	1.5	1.4	1.5	1.6

*Days with triptan or ergotamine use as recorded in eDiary averaged over 28-day screening period.

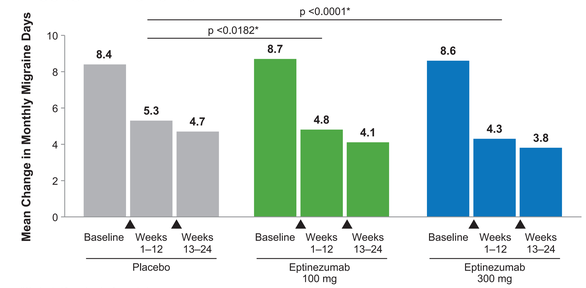
- Mean baseline migraine days were ~8.5 days/month across groups
- Baseline characteristics were balanced across treatment groups

Disposition

Subjects, n (%)	Placebo	Eptinezumab 30 mg	Eptinezumab 100 mg	Eptinezumab 300 mg	Overall
Full analysis population*	222 (99)	223 (100)	221 (98)	222 (99)	888 (99)
Week 12†	205 (91)	205 (92)	212 (94)	213 (95)	835 (93)
Week 24†	186 (83)	194 (87)	193 (86)	198 (88)	771 (86)
Discontinued treatment early‡	54 (24)	51 (23)	45 (20)	43 (19)	193 (22)
Adverse event	6 (3)	11 (5)	5 (2)	5 (2)	27 (3)
Subject consent withdrawal/ lost to follow-up	45 (20)	30 (13)	32 (14)	34 (15)	141 (16)
Other	3 (1)	8 (4)	7 (3)	3 (1)	21 (2)

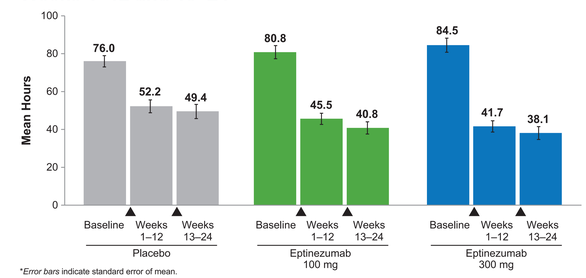
*Includes all subjects who received eptinezumab or placebo; % based on all randomized subjects; †Subjects who attended each visit; ‡% based on full analysis population.

Eptinezumab Decreased Mean Monthly Migraine Days Through 2 Dose Intervals
Weeks 1–12 and 13–24



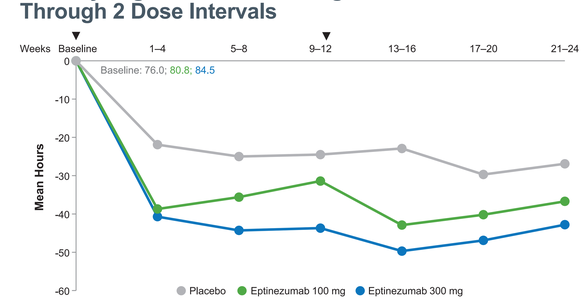
*Weeks 1–12 vs placebo for each dose.

Monthly Migraine Hours Through 2 Dose Intervals*
Weeks 1–12 and 13–24



**Error bars* indicate standard error of mean.

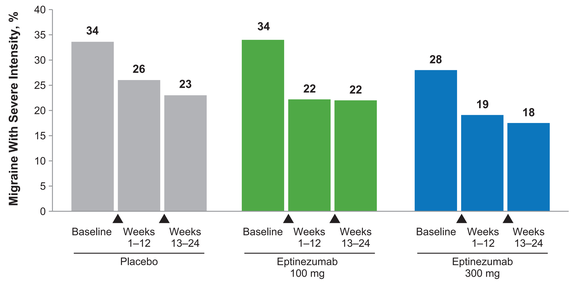
Monthly Migraine Hours: Changes From Baseline Through 2 Dose Intervals



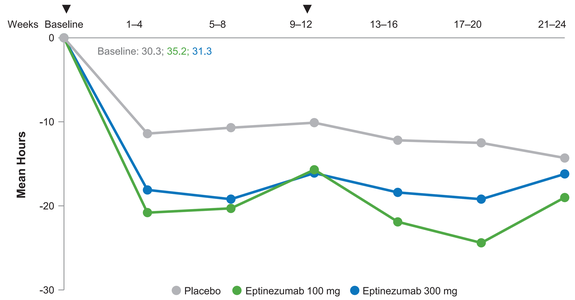
Lengths of Migraine Attacks

- Mean migraine attack average hours at baseline were 13.83, 15.34, and 12.87 with eptinezumab 100 and 300 mg, and placebo, respectively
- Corresponding mean migraine attack average hours over Weeks 1-4 were 11.96, 11.71, and 12.87
- Corresponding mean migraine attack average hours over Weeks 21–24 were 13.34, 12.46, and 14.52
- Corresponding changes in average lengths of migraine attacks from baseline were -1.9, -3.6, and 0 hours over Weeks 1–4, and -0.5, -2.9, and +1.7 hours over Weeks 21–24

Percentages of Migraine With Severe Intensity Through 2 Dose Intervals
Weeks 1–12 and 13–24



Hours of Migraine With Severe Intensity: Changes From Baseline Through 2 Dose Intervals*



*Post-hoc analysis.

Conclusions

- **Eptinezumab 300 and 100 mg demonstrated significant efficacy vs placebo for migraine prevention in patients with episodic migraine**
- **Repeated quarterly iv infusion of eptinezumab reduced migraine days and hours by ~50% over 6 months**
- **Migraine frequency, average hours of migraine, and migraine intensity were reduced by eptinezumab, and the reductions were maintained for 6 months after 2 quarterly infusions**

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. AAN 2017, abstr P2.155; **4.** Saper J, et al. AAN, 2018, abstr 1356; **5.** Lipton R, et al. AAN 2018, Emerging Science; **6.** Dodick DW, et al. *Lancet Neurol*. 2014;13:1100-7; **7.** Smith J, et al. AAN 2017, abstr S52.033.

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Disclosures

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