PF34

Baseline Population Characteristics of PROMISE-2: a Phase 3, Randomized, Double-blind, Placebo-Controlled Study of Eptinezumab for Prevention of Chronic Migraine

Egilius L.H. Spierings,[1] Arifulla Khan,[2] Roger Cady,[3] Barbara Schaeffler,[3] Suman Bhattacharya,[3] David Biondi,[3] Joe Hirman,[4] Jeff Smith[5]

[1]MedVadis Research, Watertown, MA; [2]Northwest Clinical Research Center, Bellevue, WA; [3]Alder BioPharmaceuticals, Inc., Bothell, WA; [4]Pacific Northwest Statistical Consulting, Inc., Woodinville, WA; [5]Alder BioPharmaceuticals, Ltd, Dublin, Republic of Ireland

Introduction

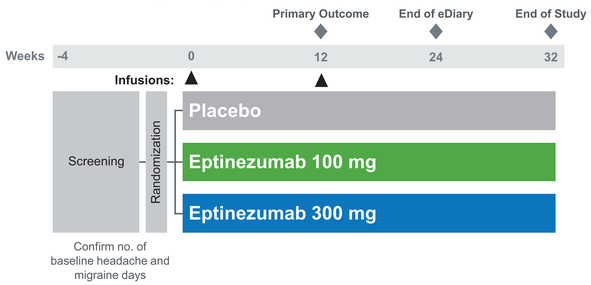
- Migraine is a highly prevalent, disabling, and costly neurologic disorder[1]
- Calcitonin gene-related peptide (CGRP) is a neuropeptide that plays an important role in migraine pathophysiology[2]
- Eptinezumab (ALD403) is an anti-CGRP IgG1 monoclonal antibody that rapidly and selectively binds to CGRP, 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 (CM), eptinezumab significantly reduced migraine days vs placebo, demonstrated migraine preventive efficacy, and was generally well tolerated

Objectives

- To examine the demographic and baseline characteristics of subjects with CM in the phase 3 PROMISE-2 trial evaluating eptinezumab for migraine prevention (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 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
  - Confounding and clinically significant pain syndromes, uncontrolled psychiatric conditions, and any active, progressive, or unstable cardiovascular, neurologic, or autoimmune disorder
  - Body mass index (BMI) ≥39 kg/m^2
- 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 migrane days (MMD)	Weeks 1–12
Key Secondary Endpoints	≥75% migraine responder rates*	Weeks 1–4
	≥50% migraine responder rates* ≥75% migraine responder rates*	Weeks 1–12
	% of subjects with a migraine	Day 1 postdose
	Headache Impact Test (HIT-6)†	Weeks 4, 12, 16, 24, and 32‡
	Headache/migraine days with triptan/ergotamine use§	Daily eDiary from time of screening to Week 24

*% of subjects with prespecified migraine response (reduction in MMD from baseline); †Measured endpoint was change from baseline in HIT-6 total score at Week 12 for 300-mg dose only; ‡4-week recall period; §Key secondary endpoint for 300 mg only; day with any triptan or ergotamine use as recorded in eDiary.

Results

Baseline Characteristics and Demographics

		Overall, N=1072
Mean age, year (SD)		41 (11)
Female, n (%)		946 (88)
Male, n (%)		126 (12)
Hispanic or Latino ethnicity, n (%)		86 (8)
Race, n (%)		
White		975 (91)
Black		82 (8)
Other*		15 (1)
Mean BMI, kg/m^2 (SD)		27 (5)
Mean age at diagnosis of migraine, year (SD)		23 (10)
Mean duration of migraine diagnosis at baseline, year (SD)		18 (12)
Mean duration of chronic migraine, year (SD)		12 (11)
Migraine started, n (%)†		
Female†	Before menarche	211 (22)
	After menarche	735 (78)
Male†	Before puberty	32 (25)
	After puberty	94 (75)
Migraine affected by hormones, n (%)†		
Menstrual cycle		297 (31)
Migraine with aura, n (%)		370 (35)
Diagnosis of medication overuse headache, n (%)		431 (40)

*Includes races not defined as white or black; †% uses number of females or males as denominator. SD, standard deviation.

Mean Monthly Migraine and Headache Days

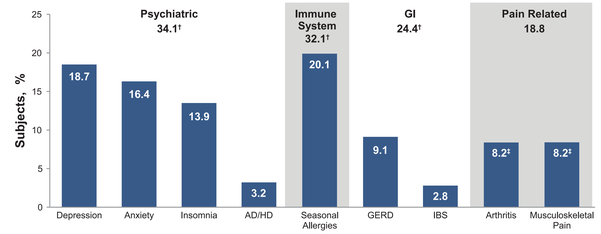
Total	Overall, N=1072
Mean MMD (SD)*	16.1 (4.6)
Mean headache days/month (SD)*	20.5 (3.1)

*Average number per 28-day period in 3 months prior to screening.

Comorbidities and Migraine Medications

- Types of comorbidities were consistent with those reported by people with migraine identified in a representative population-based sample as reported in the American Migraine Prevalence and Prevention Study[8]
  - Overall, seasonal allergy was present in 20.1% of patients, asthma in 11.3% (total n excludes subjects with >1 condition), anxiety in 16.4%, depression in 18.7%, and insomnia in 13.9%
- % of subjects using a stable dose of ≥1 prophylactic medication for migraine during the 3 months prior to screening was 44.7% (according to American Academy of Neurology/American Headache Society guidelines for migraine preventive treatment)
- Overall, 97.3% of patients were taking ≥1 acute headache medication

Psychiatric, Immune, GI, and Pain-Related Comorbidities*



*% of subjects reporting comorbidity by investigator; denominator is overall subjects; †Total % of subjects in system organ class category; ‡Total n's exclude subjects with >1 condition. AD/HD, attention-deficit/hyperactivity disorder; GERD, gastroesophageal reflux disease; GI, gastrointestinal; IBS, irritable bowel syndrome.

Medical History

- Psychiatric disorders: n=366 (34.1%); immune system disorders: n=344 (32.1%); GI disorders: n=262 (24.4%); pain-related disorders: n=202 (18.8%)

Baseline Body Mass Index Distribution

Baseline BMI, n (%)	Overall, N=1072
Underweight (<18.5 kg/m^2)	27 (2.5)
Normal weight (18.5–<25.0 kg/m^2)	444 (41.4)
Overweight (25–<30 kg/m^2)	319 (29.8)
Obese (≥30 kg/m^2)	282 (26.3)
Extreme (Class III) obesity (≥40 kg/m^2)	0

- See Lipton RB et al posters PF02 and PF110LB at this meeting for efficacy and safety results of the phase 3 PROMISE-2 trial

Conclusions

- **Baseline demographics and characteristics for the subjects included in PROMISE-2 confirm the degree to which patients with migraine are affected by their condition, both in terms of frequency of migraine, and medical and psychiatric comorbidities**
- **45% of subjects in the chronic migraine study population used prophylactic medications**
- **>50% of patients were overweight or obese**
- **Chronic migraine is a complex disease associated with significant levels of medical and psychiatric comorbidities, including medication overuse headache**

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; **8.** Lipton RB, et al. *Headache*. 2016;56:1280-6.

Acknowledgment

This study was funded by Alder BioPharmaceuticals, Inc.

Disclosures

E.L.H. Spierings: Alder, Allergan, Amgen, Teva; **A. Khan:** nothing to disclose; **R. Cady, B. Schaeffler, S. Bhattacharya, D. Biondi,** and **J. Smith:** Alder (full-time employee); **J. Hirman:** Alder (contracted service provider).

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