Eptinezumab Reduces Migraine Frequency Within the First Month After Treatment in Patients with Episodic or Chronic Migraine

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BACKGROUND

- Migraine is a disabling and costly neurological disorder and is estimated to affect more than 1.3 billion individuals worldwide, resulting in more than 47 million person-years lived with disability[1,2]
- Determining the success of preventive treatment for migraine is patient-centric and based on multiple factors in addition to migraine frequency, including migraine severity, attack duration, and improvement in patient-reported outcomes of health-related quality of life and daily functioning[3]
- Calcitonin gene-related peptide (CGRP) plays an important role in migraine pathophysiology[4-6]
- Eptinezumab (ALD403) is a humanized IgG1 anti-CGRP monoclonal antibody that: binds the CGRP ligand with high affinity resulting in potent and sustained inactivation of CGRP, is designed for rapid onset and durability ($t_{1/2}$ of 27 days), and is administered quarterly by intravenous (IV) infusion, allowing for 100% bioavailability with immediate C_{max} at the end of infusion[7-9]
- In phase 3 clinical trials in patients with episodic migraine (EM; NCT02559895) and chronic migraine (CM; NCT02974153), eptinezumab demonstrated significant reductions in mean monthly migraine days

OBJECTIVE

- To evaluate migraine responder rates (MRRs) in patients with episodic migraine (EM) and chronic migraine (CM) over the first month after treatment with eptinezumab vs placebo

METHODS

- PROMISE-1 (Figure 1) and PROMISE-2 (Figure 2) were phase 3, parallel-group, double-blind, randomized, placebo-controlled trials of eptinezumab for the preventive treatment of migraine
  - PROMISE-1 evaluated up to 4 quarterly IV infusions of eptinezumab or placebo in patients with EM
  - PROMISE-2 evaluated up to 2 quarterly IV infusions of eptinezumab or placebo in patients with CM

Figure 1. PROMISE-1 Study Design

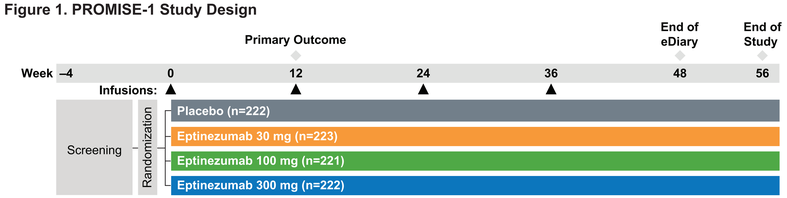
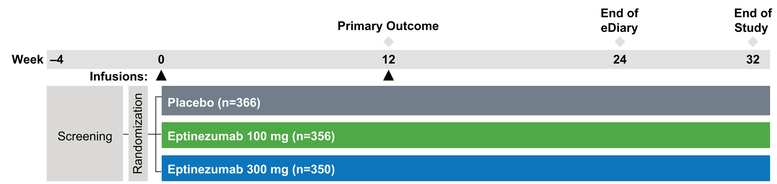


Figure 2. PROMISE-2 Study Design



- The primary efficacy endpoint for both studies was the mean change from baseline in monthly migraine days (MMDs) over Months 1–3 (Weeks 1–12)
- ≥50% MRRs over Months 1–3 and ≥75% MRRs over Month 1 and Months 1–3 were key secondary endpoints
- Post hoc analyses were conducted to calculate quartile MRRs of <25%, 25%–<50%, 50%–<75%, and 75%–<100% migraine response at Month 1

CONCLUSIONS

- Eptinezumab treatment resulted in a rapid, robust onset of preventive benefit, with over half of patients with EM or CM experiencing a meaningful reduction in MMDs within the first month after the first infusion
- Responder rates were consistent across PROMISE-1 and PROMISE-2
  - Approximately 75% of eptinezumab-treated patients experienced ≥25% migraine response
  - Of eptinezumab-treated patients achieving ≥50% migraine response, over half achieved ≥75% reduction in migraines
- Achieving ≥25% reduction in monthly migraine frequency can be clinically meaningful to patients with migraine, especially those with CM
  - Previous post hoc analyses of PROMISE-2 data indicated that patients with 25%–<50% migraine response experienced meaningful improvements in health-related quality of life and disability over the first infusion period similar to that of patients achieving 50%–<75% migraine response[10]

RESULTS

- Results for the primary and key secondary efficacy endpoints are presented in Podium Presentation 003 (PROMISE-1) and Poster 10-006 (PROMISE-2)

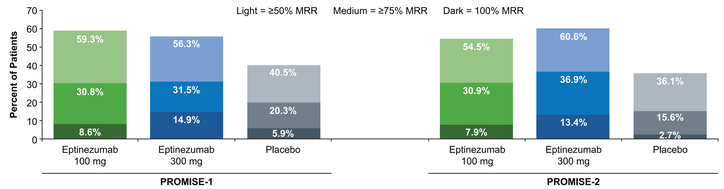
Table 1. Baseline Demographics and Disease Characteristics (Safety Population)

	PROMISE-1			PROMISE-2		
	Eptinezumab 100 mg n=223	Eptinezumab 300 mg n=224	Placebo n=222	Eptinezumab 100 mg n=356	Eptinezumab 300 mg n=350	Placebo n=366
Age (years), mean (SD)	40.0 (10.66)	40.2 (11.72)	39.9 (11.67)	41.0 (11.72)	41.0 (10.36)	39.6 (11.28)
Sex, n (%)						
Male	44 (19.7%)	25 (11.2%)	36 (16.2%)	49 (13.8%)	36 (10.3%)	41 (11.2%)
Female	179 (80.3%)	199 (88.8%)	186 (83.8%)	307 (86.2%)	314 (89.7%)	325 (88.8%)
Race, n (%)						
White	196 (87.9%)	187 (83.5%)	181 (81.5%)	332 (93.3%)	322 (92.0%)	321 (87.7%)
Black or African American	17 (7.6%)	27 (12.1%)	30 (13.5%)	21 (5.9%)	23 (6.6%)	38 (10.4%)
Other*	10 (4.5%)	10 (4.4%)	11 (5.0%)	3 (0.8%)	5 (1.4%)	7 (1.9%)
BMI (kg/m^2), mean (SD)	29.4 (7.66)	28.9 (7.14)	29.6 (7.28)	26.4 (4.98)	26.3 (5.04)	27.0 (5.56)
Age at migraine diagnosis (years), mean (SD)	22.5 (10.77)	22.0 (9.87)	23.1 (10.87)	22.8 (10.64)	22.0 (9.30)	22.6 (9.98)
Duration of migraine diagnosis (years), mean (SD)	17.4 (11.18)	18.2 (11.75)	16.9 (11.23)	18.3 (12.22)	19.0 (11.50)	17.0 (11.63)
Duration of chronic migraines (years), mean (SD)	—	—	—	11.6 (11.72)	12.3 (11.15)	11.6 (10.90)
Number of migraine days, mean (SD)†	8.7 (2.85)	8.6 (2.87)	8.4 (2.68)	16.1 (4.61)	16.1 (4.77)	16.2 (4.55)
Medication-overuse headache diagnosis, n (%)§	—	—	—	139 (39.0%)	147 (42.0%)	145 (39.6%)

BMI, body mass index; SD, standard deviation; SF-36, 36-item Short-Form Health Survey (v2.0). *Other includes Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, multiple races, and other. †As reported by the eDiary in the in the 28-day screening period. §Based on 3rd edition of the International Classification of Headache Disorders (beta).

- Baseline demographics and disease characteristics were generally balanced across treatment arms and across studies (Table 1)
  - Patients with EM experienced ~8.6 migraine days/month, and patients with CM experienced ~16.1 migraine days/month at baseline
  - Approximately 40% of patients in PROMISE-2 had a dual diagnosis of CM and medication-overuse headache

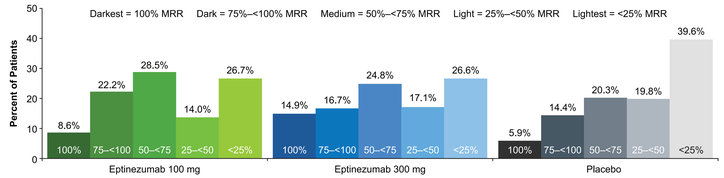
Figure 3. PROMISE-1 and PROMISE-2 ≥50%, ≥75%, and 100% Migraine Responder Rates at Month 1



The ≥75% migraine responder rate at Month 1 was a prespecified key secondary endpoint, with both eptinezumab 100 mg and 300 mg achieving clinical significance vs placebo, in both trials.

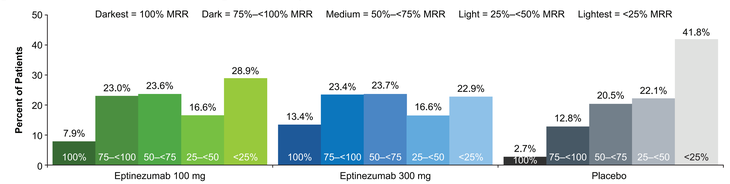
- In PROMISE-1, more patients treated with eptinezumab experienced ≥50% migraine response over Month 1 than with placebo, including ≥75% and 100% migraine response (Figure 3)
- Similar results were observed in eptinezumab-treated patients in the PROMISE-2 trial, demonstrating a consistency across trials in reducing migraine frequency
  - A smaller proportion of placebo-treated patients achieved ≥50%, ≥75% or 100% response

Figure 4. PROMISE-1 Quartile Migraine Responder Rates at Month 1



- In PROMISE-1, eptinezumab treatment resulted in meaningful reductions in migraine frequency over Month 1 vs placebo across quartile responder thresholds (Figure 4)
- About a quarter (~25%) of eptinezumab-treated patients experienced <25% migraine response compared with ~40% of placebo patients during the first month
  - Complete non-response was experienced by 17.2% (100 mg) and 15.8% (300 mg) of eptinezumab-treated patients compared with 26.6% of placebo patients
- Of the eptinezumab-treated patients experiencing ≥25% migraine response (~75% of the total population), 81% (100 mg) and 77% (300 mg) achieved ≥50% response and 42% (100 mg) and 43% (300 mg) achieved ≥75% response
  - Of the placebo patients experiencing ≥25% migraine response (~60% of the total population), 67% achieved ≥50% response and 34% achieved ≥75% response

Figure 5. PROMISE-2 Quartile Migraine Responder Rates at Month 1



- In PROMISE-2, eptinezumab treatment resulted in meaningful reductions in migraine frequency over Month 1 vs placebo across quartile responder thresholds (Figure 5)
- About a quarter (~25%) of eptinezumab-treated patients experienced <25% migraine response compared with ~40% of placebo patients during the first month
  - Complete non-response was experienced by 14.3% (100 mg) and 11.7% (300 mg) of eptinezumab-treated patients compared with 24.6% of placebo patients
- Of the eptinezumab-treated patients experiencing ≥25% migraine response (~75% of the total population), 77% (100 mg) and 78% (300 mg) achieved ≥50% response and 43% (100 mg) and 48% (300 mg) achieved ≥75% response
  - Of the placebo patients experiencing ≥25% migraine response (~60% of the total population), 62% achieved ≥50% response and 27% achieved ≥75% response

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