Eptinezumab Meaningfully Improves Quality of Life (QoL) in Patients With Episodic or Chronic Migraine Within 1 Month After Treatment

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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]
- Migraine, especially with increasing frequency and severity, can significantly worsen an individual's health-related quality of life (HRQOL)[3-5]
- Calcitonin gene-related peptide (CGRP) plays an important role in migraine pathophysiology[6-8]
- 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[9,10]
- 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 changes in HRQOL after treatment with a single IV infusion of eptinezumab or placebo in patients with EM or CM, stratified by baseline HRQOL

METHODS

- PROMISE-1 and PROMISE-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
  - After a 28-day screening period, infusions of eptinezumab or placebo were administered on Day 0 and at Weeks 12, 24, and 36, with an end-of-study visit occurring at Week 56
- PROMISE-2 evaluated up to 2 quarterly IV infusions of eptinezumab or placebo in patients with CM
  - After a 28-day screening period, infusions of eptinezumab or placebo were administered on Day 0 and at Weeks 12, with an end-of-study visit occurring at Week 32

Table 1. Descriptions of SF-36 Domain and Component Scores[11]

	Definition of Lowest Possible Score	Definition of Highest Possible Score
Domains		
Physical function (10 items)	Very limited in performing all physical activities, including bathing or dressing	Performs all types of physical activities including the most vigorous without limitations due to health
Physical role function (4 items)	Problems with work or other daily activities as a result of physical health	No problems with work or other daily activities
Bodily pain (2 items)	Very severe and extremely limiting pain	No pain or limitations due to pain
General health (5 items)	Evaluates personal health as poor and believes it is likely to get worse	Evaluates personal health as excellent
Mental health (5 items)	Feelings of nervousness and depression all of the time	Feels peaceful, happy, and calm all of the time
Emotional role function (3 items)	Problems with work or other daily activities as a result of emotional problems	No problems with work or other daily activities
Social function (2 items)	Extreme and frequent interference with normal social activities due to physical and emotional problems	Performs normal social activities without interference due to physical or emotional problems
Vitality (4 items)	Feels tired and worn out all of the time	Feels full of pep and energy all of the time
Components		
Physical component summary (PCS)*	Limitations in self-care, physical, social, and role activities, severe bodily pain, frequent tiredness, health rated "poor"	No physical limitations, disabilities, or decrements in well-being, high energy level, health rated "excellent"
Mental component summary (MCS)*	Frequent psychological distress, social and role disability due to emotional problems, health rated "poor"	Frequent positive affect, absence of psychological distress and limitations in usual social/role activities due to emotional problems, health rated "excellent"

*Each domain score contributes to the component scores; however, the first 4 domains listed contribute the most to the PCS score and the latter 4 contribute the most to the MCS score.

- HRQOL was evaluated descriptively using the Short-Form Health Survey (SF-36, v2.0)—a robust measure of general health (Table 1)—which was administered at the baseline, Month 1, and Month 3 visits in both studies
- The SF-36 was scored using norm-based scoring, which is the standardization of mean scores and standard deviations for all SF-36 domains and components scores to a mean of 50 and standard deviations of 10, representing the general US population[11]
  - Norm-based scoring provides a basis for comparisons across scales and more clearly reflects the impact of a disease or treatment
  - When a scale score is below 50, health status is below average, and each point is 1/10 of a standard deviation
- Clinically meaningful change in SF-36 scores is estimated between 2.5 and 5 points, which varies across disease states[12-20]
  - Here, we use a 3-point increase as the threshold for clinically meaningful change
- Subgroups were defined by baseline SF-36 scores (<35, 35-39, 40-44, 45-49, ≥50) for each respective domain and component summary
  - Stratification was based on multiples of half of the norm-based standard deviation (5 points), with a score of 35 representing 1.5 standard deviations below the mean

CONCLUSIONS

- Patients with lower SF-36 scores, indicating higher impairment of HRQOL, experienced greater improvements throughout the quarterly infusion period compared with patients that scored closer to the normative value at baseline
  - Patients with a higher SF-36 score at baseline generally maintained normative population scores at Month 1 and through the quarterly infusion period
- Treatment with eptinezumab generally resulted in greater changes from baseline in SF-36 scores across subgroups compared with placebo, with patients most diminished at baseline experiencing substantial improvements towards normalizing HRQOL
- Eptinezumab demonstrated early clinically meaningful improvements in SF-36 domain and component summary scores within the first month after initial infusion in patients with migraine and diminished HRQOL, with changes maintained or further increased through 3 months

RESULTS

- Primary and key secondary results are presented in Podium Presentation 003 (PROMISE-1) and Poster 10-006 (PROMISE-2)

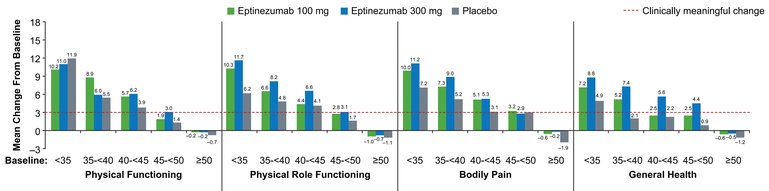
Table 2. Baseline Demographics and Disease Characteristics (Safety Population)

	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/m²), 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 2)
  - 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

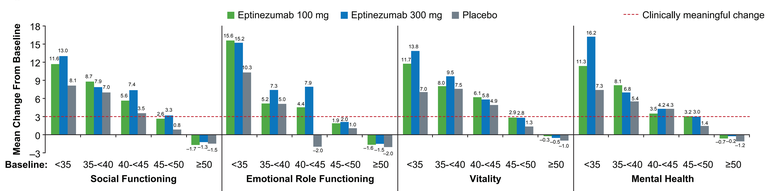
Figure 1. Change From Baseline to Month 1 in PCS Domain Scores



Sample size:	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50
100 mg	40	22	47	108	346	112	114	55	79	203	172	103	62	75	151	68	53	48	76	318
300 mg	39	26	59	94	347	112	111	68	76	198	174	101	63	86	141	69	46	78	79	293
Placebo	25	23	52	119	356	94	111	86	77	207	159	108	68	81	159	48	45	72	80	330

- Within the first month of treatment, there was a consistent trend in patients with worse HRQOL at baseline (as indicated by baseline SF-36 scores) to achieve greater increases in SF-36 scores across PCS domains (Figure 1)
- Eptinezumab treatment generally demonstrated greater improvements in PCS domain scores compared with placebo treatment, achieving clinically meaningful increases in SF-36 scores across nearly all subgroups with diminished HRQOL (ie, baseline SF-36 scores <50)
  - Patients who had normative or near-normative (ie, 45–<50) SF-36 scores generally remained at those levels
  - In patients with below normative levels, eptinezumab treatment provided substantial improvement towards normative scores
- Improvements were maintained or further increased at Month 3

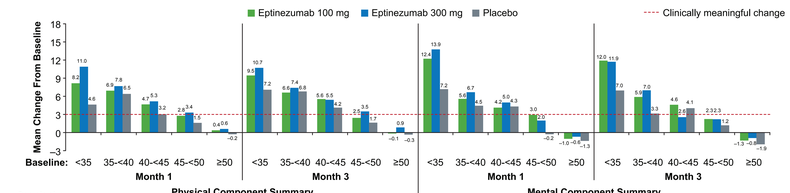
Figure 2. Change From Baseline to Month 1 in MCS Domain Scores



Sample size:	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50
100 mg	103	86	73	105	196	58	77	30	100	298	69	35	88	115	256	66	55	39	78	325
300 mg	108	84	65	96	212	71	77	15	79	323	71	38	82	110	264	65	44	53	63	340
Placebo	95	75	71	96	238	53	67	21	93	341	46	43	93	121	272	48	51	59	57	360

- There was a general trend in patients with worse HRQOL at baseline (as indicated by baseline SF-36 scores) to achieve greater increases in SF-36 scores across MCS domains within the first month of treatment; though sample sizes vary across subgroups (Figure 2)
- Eptinezumab treatment consistently demonstrated greater improvements in MCS domain scores compared with placebo, achieving clinically meaningful increases in SF-36 scores across nearly all subgroups with diminished HRQOL (ie, baseline SF-36 scores <50)
  - Patients who had normative or near-normative (ie, 45–<50) SF-36 scores generally remained at those levels
  - In patients with below normative levels, eptinezumab treatment provided substantial improvement towards normative scores
- Improvements were maintained or further increased at Month 3

Figure 3. Change From Baseline to Months 1 and 3 in Component Summary Scores



Sample size:	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50	<35	35–<40	40–<45	45–<50	≥50
100 mg	40	81	113	130	199	40	80	112	126	194	77	56	52	78	300	76	55	54	75	292
300 mg	57	73	120	114	201	55	72	117	111	195	82	49	52	59	323	80	49	50	54	317
Placebo	44	75	113	129	214	42	72	108	120	205	61	48	61	70	335	58	43	59	65	322

- As observed with the changes from baseline in SF-36 domain scores, patients with worse baseline SF-36 scores achieved greater improvements in SF-36 Physical and Mental Component Summary scores within the first month of treatment (Figure 3)
- Improvements that were achieved by the first month were sustained or further increased through Month 3
- Generally, eptinezumab treatment demonstrated greater improvements in Physical and Mental Component Summary scores compared with placebo

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