Early Impact of Eptinezumab on the Health-Related Quality of Life (HRQoL) of Patients with Episodic or Chronic Migraine: SF-36 Analysis Across the Spectrum of Migraine

Merle L. Diamond,[1] Richard Lipton,[2] Ruslan Horblyuk,[3] Joe Hirman,[4] Roger Cady,[5] Eric Kassel[5]

[1]Diamond Headache Clinic, Chicago, IL, United States; [2]Albert Einstein College of Medicine, Bronx, NY, United States; [3]AESARA, Inc., Chapel Hill, NC, United States; [4]Pacific Northwest Statistical Consulting, Inc., Woodinville, WA, United States; [5]Alder BioPharmaceuticals, Inc., Bothell, WA, United States

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10-025

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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, which often presents 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[9-11]
- 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 (MMDs)

OBJECTIVE

- To evaluate the impact of eptinezumab on HRQOL across the spectrum of migraine frequency

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[12]

	Definition of Lowest Possible Score	Definition of Highest Possible Score
Domains		
Physical function (PF; 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 (RP; 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 (BP; 2 items)	Very severe and extremely limiting pain	No pain or limitations due to pain
General health (GH; 5 items)	Evaluates personal health as poor and believes it is likely to get worse	Evaluates personal health as excellent
Mental health (MH; 5 items)	Feelings of nervousness and depression all of the time	Feels peaceful, happy, and calm all of the time
Emotional role function (RE; 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 (SF; 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 (V; 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, which represents the general US population[12]
  - 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[13-21]
  - Here, we use a 3-point increase as the threshold for clinically meaningful change
- Subgroups were defined by baseline MMDs (<7, 7-9, 10-11, 12-14, 15-18, 19-22, ≥23)

CONCLUSIONS

- Higher migraine frequency at baseline was indicative of greater impairments in HRQOL, as measured by domain and component scores of the SF-36
- In EM and CM patients with diminished HRQOL, eptinezumab treatment demonstrated clinically meaningful improvements in SF-36 scores beginning as early as 1 month
- Greater improvements in HRQOL were observed among patients with higher MMD frequency at baseline
- Eptinezumab generally demonstrated greater improvements in SF-36 scores than placebo
- Patients with a summary score at 50 or above were maintained at the normative line for HRQOL
- In the component summary scores, in general, improvements observed after the first month of treatment were sustained through the end of the infusion period (Month 3)

RESULTS

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

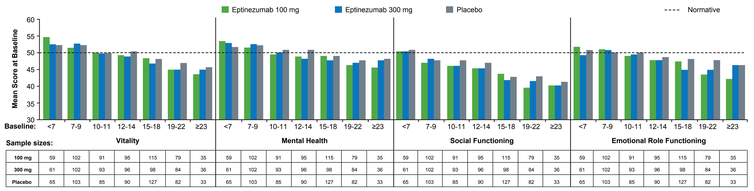
Table 2. Baseline Demographics and Disease Characteristics (Safety Population)

	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

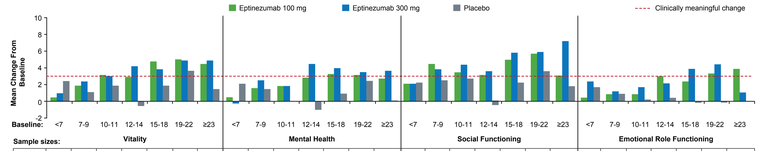
Figure 1. Baseline Scores for Domains Contributing the Most to the Mental Component Summary Score



Sample sizes:	<7	7-9	10-11	12-14	15-18	19-22	≥23
Vitality							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33
Mental Health							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33
Social Functioning							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33
Emotional Role Functioning							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33

- Baseline scores for the domains contributing most to the MCS were balanced across treatment groups and indicated greater impairment as the frequency of MMDs increased (Figure 1)
- The impairments were observed in patients with ≥12 MMDs, although patients with ≥7 MMDs demonstrated impairments in Social Functioning

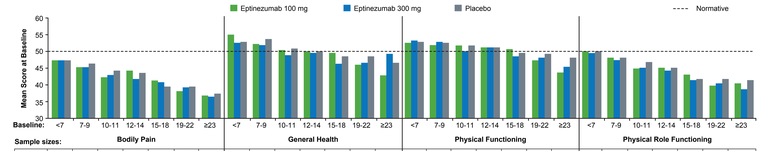
Figure 2. Change From Baseline to Month 1 in Scores for Domains Contributing the Most to the Mental Component Summary Score



Sample sizes:	<7	7-9	10-11	12-14	15-18	19-22	≥23
Vitality							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34
Mental Health							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34
Social Functioning							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34
Emotional Role Functioning							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34

- At Month 1, changes from baseline in MCS domain scores were generally greater among patients with the higher MMD frequency at baseline (Figure 2)
- Clinically meaningful improvements for patients with ≥15 MMDs were observed across all domains
- Numerical increases observed in MCS domains were indicative of patients approaching the normative levels
- In patients with ≥7 MMDs at baseline, improvements were consistently greater with eptinezumab treatment than placebo

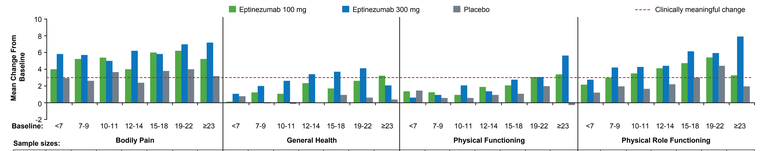
Figure 3. Baseline Scores for Domains Contributing the Most to the Physical Component Summary Score



Sample sizes:	<7	7-9	10-11	12-14	15-18	19-22	≥23
Bodily Pain							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33
General Health							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33
Physical Functioning							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33
Physical Role Functioning							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33

- Baseline scores for the domains contributing most to the PCS were balanced across treatment groups and indicated greater impairment as the frequency of MMDs increased (Figure 3)
- The most noticeable impairments were observed in all patients for Bodily Pain and in patients with ≥7 MMDs in Physical Role Functioning

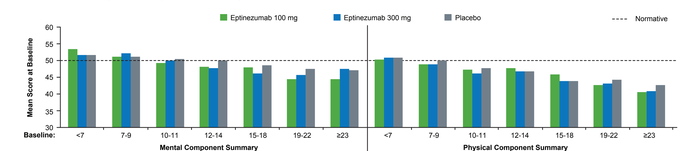
Figure 4. Change From Baseline to Month 1 in Scores for Domains Contributing the Most to the Physical Component Summary Score



Sample sizes:	<7	7-9	10-11	12-14	15-18	19-22	≥23
Bodily Pain							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34
General Health							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34
Physical Functioning							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34
Physical Role Functioning							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34

- At Month 1, changes from baseline in PCS domain scores were generally greater among patients with the higher MMD frequency at baseline (Figure 4)
- In general, the lower the domain score, the greater the improvement seen in the treatment groups
- Patient improvement in PCS domain scores increased, shifting patients toward the normative line
- The greatest improvements were observed in Bodily Pain and Physical Role Functioning, which were the most impacted of the PCS domains at baseline
- Improvements across domains were consistently greater with eptinezumab treatment than placebo

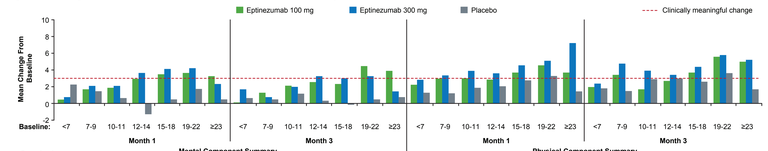
Figure 5. Baseline Mental and Physical Component Summary Scores



Sample sizes:	<7	7-9	10-11	12-14	15-18	19-22	≥23
Mental Component Summary							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33
Physical Component Summary							
100 mg	59	102	91	95	115	79	35
300 mg	61	102	93	96	98	84	36
Placebo	65	103	85	90	127	82	33

- Baseline scores for the MCS and PCS were balanced across treatment groups and indicated greater impairment as the frequency of MMDs increased (Figure 5)
- Impairments at baseline for in PCS started at ≥7 MMDs and in MCS at ≥12 MMDs

Figure 6. Change From Baseline to Months 1 and 3 in Mental and Physical Component Summary Scores



Sample sizes:	<7	7-9	10-11	12-14	15-18	19-22	≥23
Mental Component Summary – Month 1							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34
Mental Component Summary – Month 3							
100 mg	57	98	89	90	111	77	32
300 mg	57	98	89	94	96	84	32
Placebo	59	101	78	81	118	81	29
Physical Component Summary – Month 1							
100 mg	56	98	91	94	114	77	33
300 mg	59	103	91	96	97	84	35
Placebo	63	102	83	87	124	82	34
Physical Component Summary – Month 3							
100 mg	57	98	89	90	111	77	32
300 mg	57	98	89	94	96	84	32
Placebo	59	101	78	81	118	81	29

- Improvements in MCS and PCS scores observed at Month 1 were maintained at Month 3 (Figure 6)
- Clinically meaningful improvements were observed and maintained across nearly all subgroups for the PCS scores and subgroups of with ≥12 baseline MMDs for the MCS scores
- Improvements across MCS and PCS were greater with eptinezumab treatment than placebo

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