



# Early Migraine Response by Month 1 and Clinically Meaningful Improvements in Health-Related Quality of Life (HRQoL) in Patients With Migraine in Phase 3 Trials of Eptinezumab

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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<sup>2</sup>
- Migraine, especially with increasing frequency and severity, can significantly worsen an individual's health-related quality of life (HRQOL)<sup>3-5</sup>
- Calcitonin gene-related peptide (CGRP) plays an important role in migraine pathophysiology<sup>6,8</sup>
- 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<sup>9,10</sup>
- 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 at Month 3 by magnitude of migraine response by Month 1 in adults with EM or CM in clinical trials of eptinezumab

## 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
- 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 component scores to a mean of 50 and standard deviations of 10, which represents the general US population<sup>11</sup>
  - 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<sup>12-20</sup>
  - Here, we use a 3-point increase as the threshold for clinically meaningful change
- Subgroups were defined by  $\geq 50\%$ ,  $50\% < 75\%$ , or  $\geq 75\%$  migraine response by Month 1

Table 1. Descriptions of SF-36 Domain and Component Scores<sup>11</sup>

	Definition of Lowest Possible Score	Definition of Highest Possible Score
<b>Domains</b>		
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
<b>Components</b>		
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.

## CONCLUSIONS

- More than half of patients treated with eptinezumab who were  $\geq 50\%$  migraine responders achieved the  $\geq 75\%$  migraine responder threshold, with eptinezumab treatment resulting in more patients achieving either threshold vs placebo
- Patients with CM reported below normative HRQOL across all SF-36 domains and component summary scores at baseline
  - Patients achieving early and meaningful reduction in MMD frequency ( $\geq 50\%$  migraine response) experienced clinically meaningful improvements across nearly all domains and component summary scores at Month 3
- Patients with EM reported HRQOL below normative levels in relation to Bodily Pain, Physical Role Function, and Physical Component Summary scores at baseline
  - Patients achieving early and meaningful reduction in MMD frequency ( $\geq 50\%$  migraine response) experienced clinically meaningful improvements in Bodily Pain at Month 3, with mean increases in scores for Physical Role Function and Social Function moving patients toward normative levels
- The changes observed in SF-36 individual domains and component scores were proportional to the respective level of impairment at baseline, with eptinezumab-treated patients reaching normative or near-normative levels by Month 3 of treatment
- Treatment with eptinezumab generally resulted in greater changes from baseline in SF-36 scores across subgroups compared with placebo, indicating that eptinezumab treatment improves HRQOL beyond reducing monthly migraine days

