Effect of Eptinezumab on Utility Scores in Patients With Migraine: Results From the DELIVER Study

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KEY POINTS

- An eptinezumab treatment effect (*P*<0.001) can be added to the base-case regression model evaluating the relationship between MMDs and MSQ-derived utility scores.
- On average, patients treated with eptinezumab in DELIVER had higher utility scores than did placebo patients, which is partially driven by the larger MMD reduction with eptinezumab treatment.
- Patients treated with eptinezumab had higher quality of life scores (as measured by utilities) beyond the significant reduction in MMDs.

CONCLUSIONS

- These results suggest that there is an eptinezumab-specific impact on utility scores, in addition to the impact of reduction in MMDs.
- Changes in migraine severity, related symptoms, and patients' most bothersome symptom may contribute substantially to improvement in quality of life and should be explored as additional drivers of utility scores in future work.

Introduction

- Cost-utility modeling informs reimbursement decisions and is based on the premise that health outcome improvements can be expressed as disease-independent utility scores.[1,2]
- Previous cost-utility analyses of anti-calcitonin gene-related peptide (anti-CGRP) therapy expressed the utility gain as a function of monthly migraine days (MMDs).[3]
- The EQ-5D instrument is a generic and commonly used measure of obtaining utilities for health economics modeling. For a disorder such as migraine—which is defined by recurring acute events such as MMDs—utility scores derived from disease-specific patient-reported outcomes such as the Migraine-Specific Quality of Life Questionnaire (MSQ) are often preferred.[3-5]
- MSQ scores can then be used to derive utility scores using a previously published, basic mapping algorithm[2] that has been accepted by the National Institute for Health and Care Excellence (NICE).[6]
- Exploring the presence of an additional treatment effect on utility after controlling for MMDs can be insightful for policymakers and clinicians.

Objective

- This post hoc analysis of the DELIVER clinical trial for the preventive treatment of migraine aims to estimate the impact of eptinezumab treatment on utility scores, including the impact beyond MMD reduction.

Methods

- DELIVER was a randomized, double-blind, placebo-controlled phase 3b clinical study (NCT04418765) that investigated the efficacy and safety of eptinezumab treatment in patients with migraine (episodic or chronic) and documented evidence of 2–4 prior preventive treatment failures.[7]
  - The full analysis set, consisting of 890 adults, received ≥1 dose of eptinezumab (100 mg or 300 mg) or placebo—administered intravenously over 30–45 minutes every 12 weeks for up to 2 doses—and had a valid baseline assessment and ≥1 valid 4-week assessment of MMDs during Weeks 1–12.[7]
  - The primary efficacy endpoint was the change from baseline in the mean number of MMDs during Weeks 1–12.[7]
- MSQ scores were mapped to EQ-5D-3L utilities.[2]
- In the base-case model, a linear mixed model, the impact of MMDs on utilities at Baseline, Week 12, and Week 24 was evaluated (Model 1a – using MSQ-derived utilities) (**Table 1**). In addition to MMDs, a treatment effect was added to MMDs as independent variables (Models 1b and 1c).
  - Model 1c used a pooled treatment effect across 100-mg and 300-mg doses.
  - To capture the potential treatment impact on utilities, baseline data were not included in Models 1b and 1c.
- The overall treatment effect of eptinezumab on utility scores was estimated using a mixed model for repeated utility measures with month (Weeks 12 and 24), treatment, and country as factors and with baseline score as a continuous covariate (**Table 2**).

Results

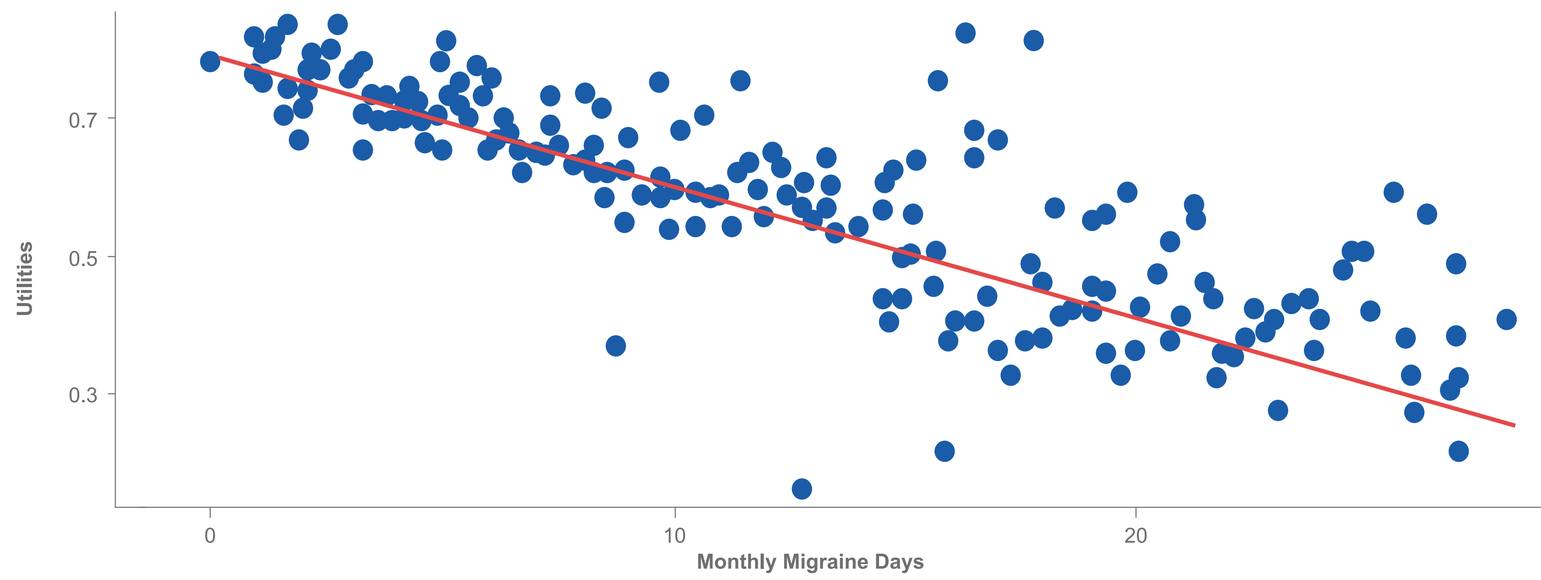
- The base-case model for the relationship between MSQ-derived utility scores and MMDs is presented in **Figure 1**, which shows the results of the linear mixed model plotted along with the average utility scores calculated for every given MMD value in DELIVER.
  - For every increase of 1 MMD, the mean utility score decreased, on average, by 0.0189 (MSQ, 95% CI: -0.0198, -0.0180) (*P*<0.001) (**Table 1**, Model 1a), as captured in the slope of the trend line.
- The utility scores were generally higher for the eptinezumab treatment arm compared to the placebo arm (**Figure 2**), providing justification for the addition of a treatment effect to the base-case linear mixed model (ie, Models 1b and 1c).
- Score improvements were similar for eptinezumab 100 mg and 300 mg (**Table 1**, Model 1b).
- After pooling both doses and controlling for number of MMDs, eptinezumab patients had an additional utility increment of 0.056 (95% CI: 0.0382, 0.0742) relative to placebo patients (**Table 1**, Model 1c).
- Analysis of patients' change from baseline in utility (Weeks 12 and 24) revealed that a strong eptinezumab treatment effect relative to placebo was observed, with the combined impact resulting in a gain of 0.092 utility points for eptinezumab compared to placebo (*P*<0.001) (**Table 2**).

Table 1. Estimates of health utilities in relation to monthly migraine days, with and without a specific treatment effect

Model	Variable	Utility Estimate*	Standard Error	95% Confidence Interval	*P*-value
1a. No treatment effect (base-case model)	Intercept[a]	0.7938	0.0063	(0.7815, 0.8061)	<0.001
	Monthly migraine days	–0.0189	0.0004	(–0.0198, –0.0180)	<0.001
1b. By treatment arm	Intercept[a]	0.7294	0.0095	(0.7108, 0.7480)	<0.001
	Monthly migraine days	–0.0132	0.0005	(–0.0143, –0.0121)	<0.001
	Eptinezumab 100 mg	0.0553	0.0106	(0.0346, 0.0760)	<0.001
	Eptinezumab 300 mg	0.0571	0.0106	(0.0363, 0.0780)	<0.001
1c. Pooled treatment effect	Intercept[a]	0.7294	0.0095	(0.7108, 0.7481)	<0.001
	Monthly migraine days	–0.0132	0.0005	(–0.0143, –0.0121)	<0.001
	Eptinezumab	0.0562	0.0092	(0.0382, 0.0742)	<0.001

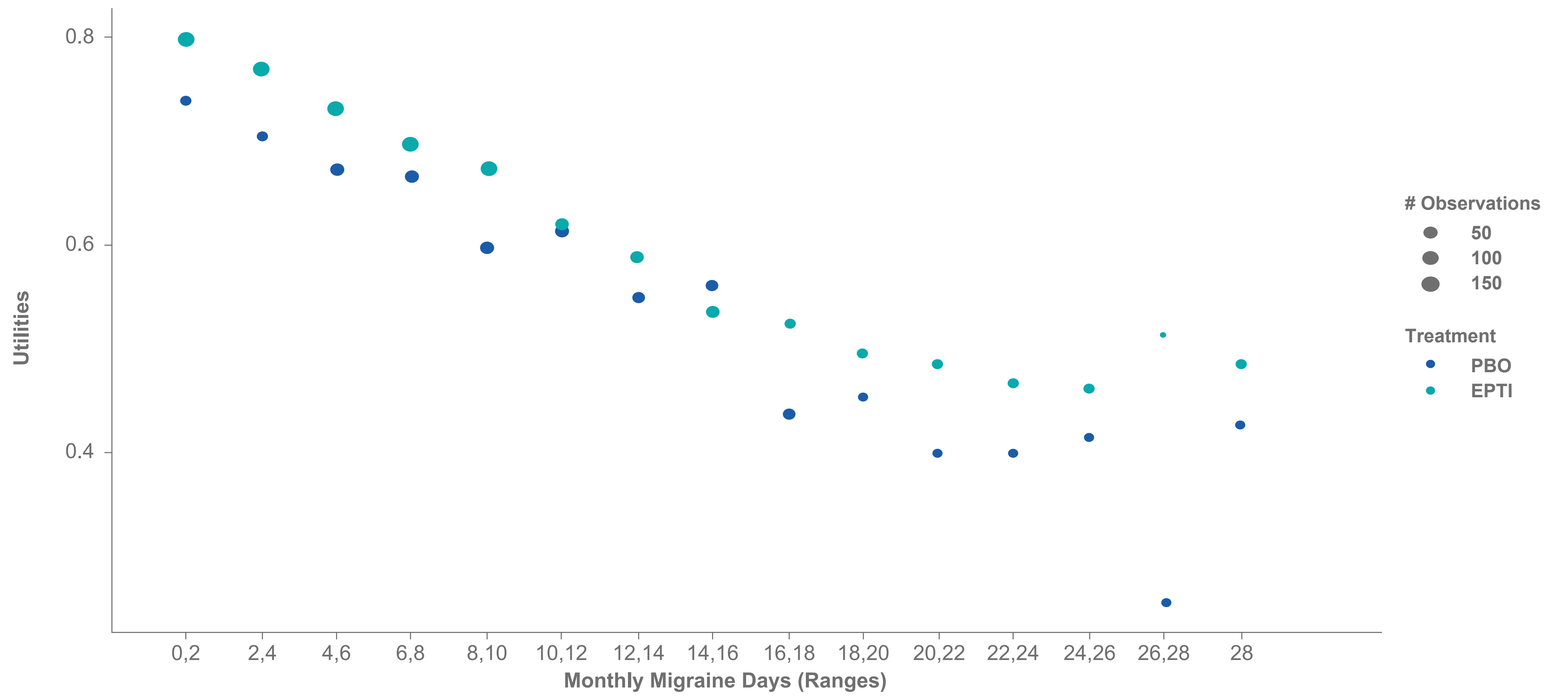
[a]The intercept is the utility experienced by DELIVER patients at 0 MMDs. *Increase in utility scores. MMDs, monthly migraine days; MSQ, Migraine-Specific Quality of Life Questionnaire.

Figure 1. Comparison of the average utilities for given MMDs, with the predicted utility trend line from the base-case model*



*Each point represents the average MSQ-derived utility score for a given MMD value. Each patient could contribute up to 3 observations. The red trend line represents the base-case, linear mixed model. Higher utilities mean better quality of life. MMD, monthly migraine days.

Figure 2. Average utility score per post-baseline MMD by treatment arms*



*Each pair of numbers corresponds to a range of MMDs. Each patient could contribute up to 2 observations. EPTI, eptinezumab; MMDs, monthly migraine days; PBO, placebo.

Table 2. Change from baseline in utility scores for patients treated with eptinezumab or placebo for Weeks 1–24

Treatment Group	Change From Baseline		Comparison to Placebo				
	Mean	SE	Difference	SE	Lower	Upper	*P*-value
Placebo	0.082	0.011	—				
Eptinezumab 100 mg	0.171	0.011	0.089	0.010	0.068	0.109	<0.001
Eptinezumab 300 mg	0.178	0.011	0.095	0.010	0.075	0.115	<0.001
Eptinezumab pooled	0.174	0.010	0.092	0.009	0.075	0.110	<0.001
Eptinezumab ≥50% responders vs. placebo (Weeks 1–12 only)*	0.238	0.011	0.151	0.010	0.132	0.171	<0.001

*≥50% responders are patients who reported an average MMD frequency over Weeks 1–12 that was ≥50% below their baseline frequency. MMRM with month (Weeks 12 and 24) and treatment as factors, and with baseline score as a continuous covariate. MMD, monthly migraine day; MMRM, mixed model for repeated measures; SE, standard error.

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