Impact of Baseline Characteristics on the Efficacy and Safety of Eptinezumab in Patients with Migraine: Subgroup Analyses of PROMISE-1 and PROMISE-2

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Introduction

- Evaluating clinical efficacy in subgroups of patients is important for determining whether a treatment effect might not be homogeneous across the entire population.[1]
- Eptinezumab is a humanized IgG1 monoclonal antibody that binds the CGRP ligand with high affinity and is approved in the United States and other countries for the preventive treatment of migraine in adults.[2,3]
- In pivotal phase 3 studies (PROMISE-1 and PROMISE-2), eptinezumab 100 mg and 300 mg significantly reduced mean monthly migraine days (MMDs) over Weeks 1–12.[4,5]
- A population pharmacokinetic analysis from 8 eptinezumab trials found that demographic characteristics and disease state had no significant effects on pharmacokinetic parameters.[6]

Objective

- This post hoc subgroup analysis of patients in the PROMISE-1 and PROMISE-2 studies assessed the clinical efficacy and safety profile of eptinezumab for the preventive treatment of migraine in subgroups defined by patient demographics, baseline clinical characteristics, and migraine history.

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Methods

Studies pooled for analysis

	PROMISE-1 (NCT02559895)	PROMISE-2 (NCT02974153)
Design	Multicenter, double-blind, randomized, placebo-controlled, phase 3 study	
Key inclusion criteria	Male or female; Diagnosed with migraine ≤50 years of age	
	Aged 18-75 years	Aged 18-65 years
	History of episodic migraine for ≥12 months	History of chronic migraine for ≥12 months
	Reported ≤14 MHDs including ≥4 MMDs in the 3 months prior to screening	Reported 15–26 MHDs including ≥8 MMDs in the 3 months prior to screening
Key secondary endpoint	≥50% reduction in MMDs (migraine responder rate) across Weeks 1–12	

Statistical analysis

Clinical efficacy definition and population	≥50% reduction in MMDs across Weeks 1–12 in all patients who received ≥1 dose of study drug, analyzed by randomized treatment
Safety analysis and population	Treatment-emergent adverse events in all patients who received ≥1 dose of study drug, analyzed by received treatment
Statistical analysis	Post hoc descriptive measures evaluated in subgroups of patients defined by demographics, baseline clinical characteristics, and migraine history

MHDs, monthly headache days; MHDs, monthly migraine days.

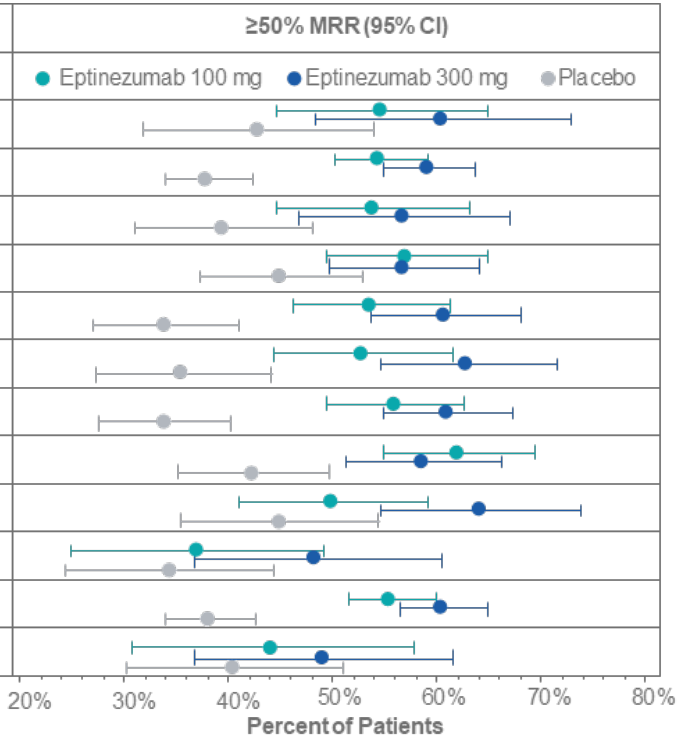
Demographics

	Eptinezumab 100 mg (N=577)	Eptinezumab 300 mg (N=572)	Placebo (N=588)
Age (years), mean (SD)	40.6 (11.30)	40.7 (10.92)	39.7 (11.42)
Sex, n (%)			
Male	93 (16.1%)	61 (10.7%)	77 (13.1%)
Female	484 (83.9%)	511 (89.3%)	511 (86.9%)
Race, n (%)			
White	525 (91.0%)	509 (89.0%)	502 (85.4%)
Other[a]	52 (9.0%)	62 (11.0%)	86 (14.6%)
Body mass index (kg/m^2), mean (SD)	27.5 (6.28)	27.3 (6.07)	28.0 (6.38)
Age at migraine diagnosis (years), mean (SD)	22.6 (10.65)	22.0 (9.50)	22.8 (10.32)
Duration of migraine diagnosis (years), mean (SD)	17.9 (11.84)	18.7 (11.60)	17.0 (11.45)
Episodic or chronic migraine, n (%)			
Episodic	221 (38.3%)	222 (38.8%)	222 (37.8%)
Chronic	356 (61.7%)	350 (61.2%)	366 (62.2%)
Duration of chronic migraine (years), mean (SD)[b]	11.6 (11.71)	12.4 (11.14)	11.6 (10.89)
Medication-overuse headache diagnosis, n (%)[c]	139 (24.1%)	147 (25.7%)	145 (24.7%)
Baseline headache days, mean (SD)	16.4 (5.90)	16.4 (5.93)	16.6 (5.94)
Baseline migraine days, mean (SD)	13.3 (5.41)	13.2 (5.50)	13.3 (5.49)

[a]Other includes Black or African American, Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander, multiple races, and other. [b]Only captured in PROMISE-2; [c]Only captured in PROMISE-2; percentage is out of total population for both treatment arms and placebo (PROMISE-1 and PROMISE-2). SD, standard deviation.

≥50% MRR Over Weeks 1–12 in Subgroups Defined by Baseline Demographics

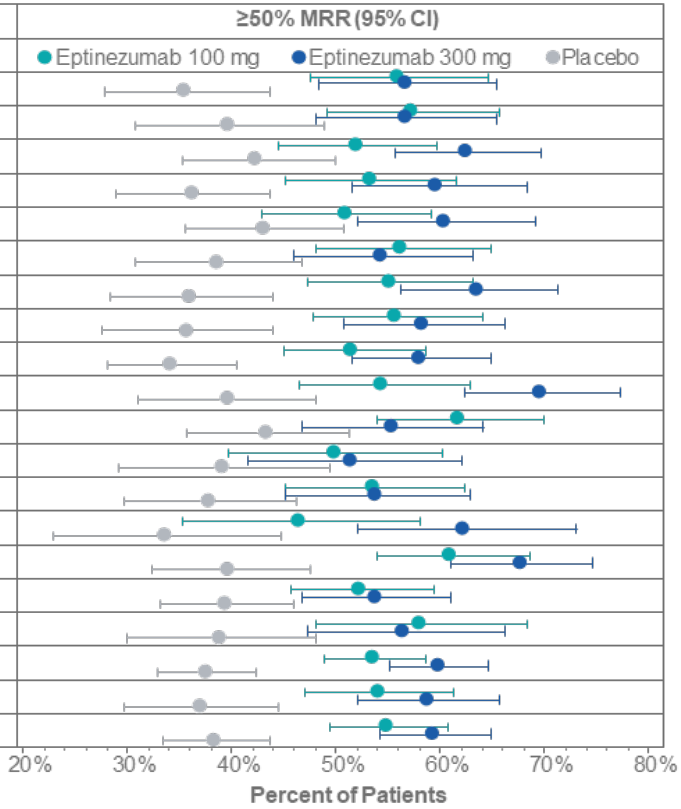
		100 mg	300 mg	Placebo
Sex	Male	54.8% (n=93)	60.7% (n=61)	42.9% (n=77)
	Female	54.5% (n=484)	59.3% (n=511)	38.0% (n=511)
Age at screening	18–29 years	53.9% (n=115)	57.0% (n=93)	39.5% (n=124)
	30–39 years	57.2% (n=159)	56.9% (n=181)	45.1% (n=162)
	40–49 years	53.8% (n=171)	60.8% (n=171)	34.1% (n=176)
	≥50 years	53.0% (n=132)	63.0% (n=127)	35.7% (n=126)
BMI group	Underweight/normal (≤24.9 kg/m²)	56.1% (n=223)	61.1% (n=244)	34.0% (n=215)
	Overweight (25–29.9 kg/m²)	62.1% (n=174)	58.8% (n=165)	42.4% (n=177)
	Obese, Class I (30–35.0kg/m²)	50.0% (n=118)	64.2% (n=95)	45.0% (n=109)
	Obese, Class II (>35.0kg/m²)	37.1% (n=62)	48.5% (n=68)	34.5% (n=87)
Race	White	55.6% (n=525)	60.7% (n=509)	38.2% (n=502)
	Non-white	44.2% (n=52)	49.2% (n=63)	40.7% (n=86)



MRR, migraine responder rate (ie, reduction in monthly migraine day frequency).

≥50% MRR Over Weeks 1–12 in Subgroups Defined by Baseline Disease Characteristics

		100 mg	300 mg	Placebo
Age at migraine diagnosis*	<15 years	56.2% (n=130)	56.9% (n=130)	35.7% (n=143)
	15–<20 years	57.5% (n=134)	56.8% (n=125)	39.8% (n=113)
	20–<30 years	52.1% (n=165)	62.7% (n=185)	42.4% (n=172)
	30–<40 years	53.4% (n=148)	59.8% (n=132)	36.3% (n=160)
Duration of migraine diagnosis*	<9 years	51.0% (n=147)	60.5% (n=124)	43.1% (n=160)
	9–<16 years	56.4% (n=133)	54.5% (n=132)	38.7% (n=142)
	16–<26 years	55.2% (n=154)	63.7% (n=157)	36.2% (n=149)
	≥26 years	55.9% (n=143)	58.5% (n=159)	35.8% (n=137)
Baseline monthly migraine days	<10 days/month	51.7% (n=207)	58.3% (n=211)	34.2% (n=219)
	10–14 days/month	54.6% (n=141)	69.7% (n=142)	39.7% (n=126)
	15–19 days/month	61.9% (n=139)	55.5% (n=128)	43.5% (n=154)
	≥20 days/month	50.0% (n=90)	51.6% (n=91)	39.3% (n=89)
Baseline monthly headache days	<10 days/month	53.8% (n=132)	54.0% (n=124)	38.1% (n=134)
	10–14 days/month	46.6% (n=73)	62.5% (n=80)	33.8% (n=74)
	15–19 days/month	61.2% (n=170)	67.8% (n=177)	39.9% (n=158)
	≥20 days/month	52.5% (n=202)	53.9% (n=191)	39.6% (n=222)
Migraine onset relative to menarche (females only)	Pre-menarche	58.2% (n=91)	56.7% (n=104)	39.1% (n=110)
	Post-menarche	53.7% (n=393)	60.0% (n=407)	37.7% (n=401)
Menstrual trigger (females only)	Yes	54.2% (n=190)	58.9% (n=202)	37.1% (n=170)
	No	55.1% (n=292)	59.5% (n=309)	38.5% (n=340)



*Subgroups defined based the interquartile range of the full population pooled across studies and treatment groups.
MRR, migraine responder rate (ie, reduction in monthly migraine day frequency).

Treatment-Emergent Adverse Events (TEAEs) in the Total Pooled Population

Patients, n (%)	Epti 100 mg (N=579)	Epti 300 mg (N=574)	Placebo (N=588)
Any TEAE	296 (51.1)	311 (54.2)	303 (51.5)
Any grade 3 or higher TEAE	10 (1.7)	15 (2.6)	18 (3.1)
Any study drug–related TEAE	68 (11.7)	85 (14.8)	48 (8.2)
Any TEAE leading to study drug discontinuation	9 (1.6)	13 (2.3)	8 (1.4)
Any TEAE leading to study drug infusion interruption	9 (1.6)	9 (1.6)	6 (1.0)
Any serious TEAE	7 (1.2)	7 (1.2)	9 (1.5)

Patients, n (%)	Epti 100 mg (N=579)	Epti 300 mg (N=574)	Placebo (N=588)
TEAEs in ≥2% of any eptinezumab group and with greater incidence than placebo			
Arthralgia	10 (1.7)	14 (2.4)	9 (1.5)
Back pain	14 (2.4)	9 (1.6)	13 (2.2)
Cough	10 (1.7)	12 (2.1)	7 (1.2)
Dizziness	15 (2.6)	13 (2.3)	12 (2.0)
Fatigue	16 (2.8)	14 (2.4)	8 (1.4)
Influenza	5 (0.9)	18 (3.1)	14 (2.4)
Nasopharyngitis	36 (6.2)	47 (8.2)	34 (5.8)
Nausea	11 (1.9)	17 (3.0)	15 (2.6)
Upper respiratory tract infection	37 (6.4)	42 (7.3)	36 (6.1)
Urinary tract infection	11 (1.9)	16 (2.8)	9 (1.5)

Epti, eptinezumab.

Key Points

- This post hoc analysis evaluated clinical response with eptinezumab vs placebo in patients with migraine across several subgroups of patients.
- For each of the 64 subgroup evaluations of clinical response, ≥50% MRRs were numerically higher for each eptinezumab treatment group compared to placebo.
- There was a ≥10%-point difference in ≥50% MRRs, favoring both doses of eptinezumab, for all subgroups defined by sex, age, baseline monthly headache days, baseline monthly migraine days, and menstruation-related migraine characteristics.
- Incidence of TEAEs was similar across dose levels and by classes of baseline demographic and disease characteristics, with a safety profile similar to that observed in the primary trial reports.

Conclusions

- **Eptinezumab demonstrated a consistent efficacy and safety profile in the phase 3 pivotal PROMISE-1 and PROMISE-2 clinical trials that was not generally impacted by demographic and baseline migraine disease characteristics.**
- **This post hoc analysis suggests that most patient characteristics—as captured in the PROMISE-1 and PROMISE-2 trials—did not meaningfully impact the efficacy (≥50% migraine responder rates) or safety (TEAEs) profiles of eptinezumab in the preventive treatment of migraine.**