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LONG-TERM EFFECTIVENESS OF EPTINEZUMAB IN PATIENTS WITH MIGRAINE AND PRIOR PREVENTIVE TREATMENT FAILURES: EXTENSION OF A RANDOMIZED CONTROLLED TRIAL[1]

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VYEPTI®▼ (eptinezumab) is indicated for the prophylaxis of migraine in adults who have at least 4 migraine days per month.[2] The recommended dose is 100 mg administered by intravenous infusion every 12 weeks.[2]

CONTEXT KEY QUESTION METHODOLOGY RESULTS SAFETY LIMITATIONS CONCLUSIONS REFS PI

CONTEXT[1,3]

In the phase 3b, multicentre, multi-arm double-blind, placebo-controlled **DELIVER** study, eptinezumab reduced migraine and health-related impact compared to placebo in adults with migraine and 2–4 prior preventive treatment failures.[1,3] This is a summary of the 48-week, dose-blinded extension period of the DELIVER study. Refer to the full publication for more details.

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KEY QUESTION[1]

What is the long-term effect of eptinezumab in adult patients with documented prior preventive treatment failures arising from inadequate efficacy, tolerability, or contraindication reasons?

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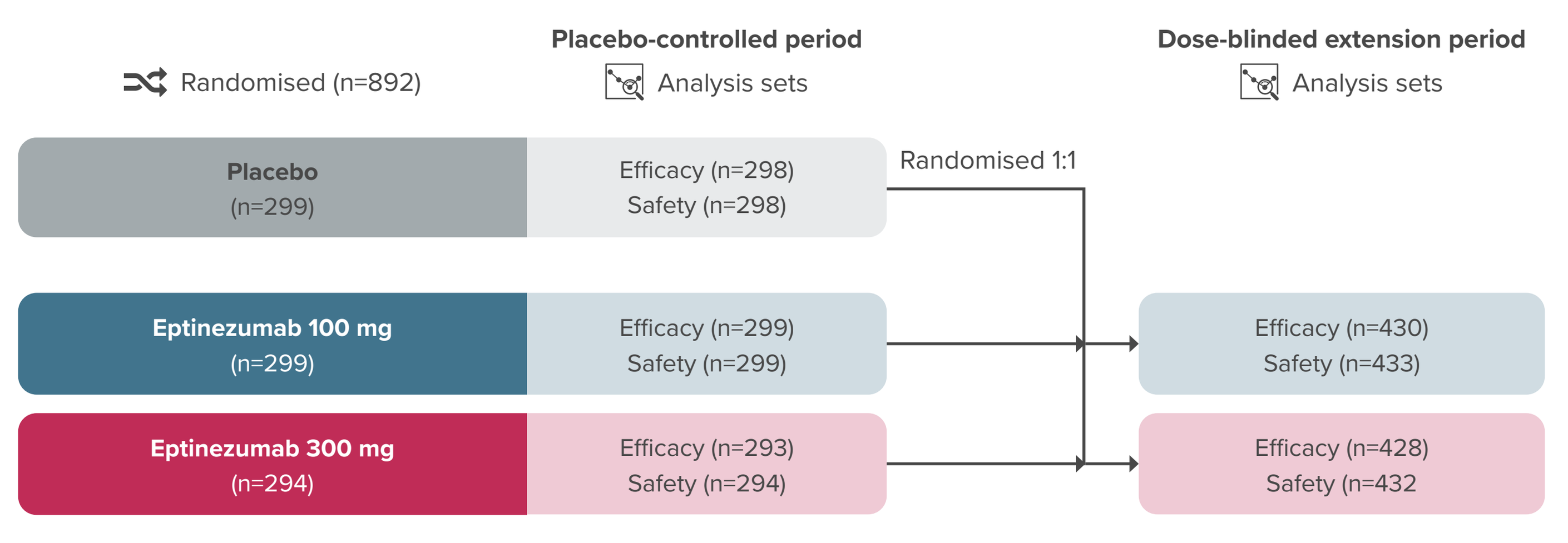
METHODOLOGY[1,3]

- Multicentre, double-blind, randomised, placebo-controlled, parallel-group, phase 3b clinical trial
- The 76-week adaptive design study comprised a 24-week placebo-controlled period and a 48-week dose-blinded extension period
- A total of 1,369 patients were screened for study inclusion and 892 were randomised to receive treatment.[1,3] 865 patients completed the placebo-controlled treatment period and enrolled in the dose-blinded extension period[1]

PATIENT DISPOSITION[1,3]



KEY INCLUSION CRITERIA[1,3]

- Adults aged 18–75 years
- Diagnosis at/before 50 years of age
- History of migraine for ≥12 months before screening
- CM or EM diagnosis per ICHD criteria
- CM criteria: Experienced ≥15 headache days and ≥8 migraine days during the 28-day screening period
- EM criteria: Experienced up to 14 headache days and ≥4 migraine days during the 28-day screening period
- Two-to-four different prior preventive migraine medication failures (i.e., propranolol/ metoprolol, topiramate, amitriptyline, flunarizine, candesartan, valproate or divalproex, or botulinum toxins A or B) in the past 10 years
- Failure due to inadequate efficacy (≥3 months), tolerability (i.e., discontinuation due to AEs), or contraindications (i.e., ineligibility due to medical reasons)

KEY EXCLUSION CRITERIA[1,3]

- Previous treatment failure of agent targeting the CGRP pathway

DELIVER PRIMARY ENDPOINT (eptinezumab vs placebo)[3]

Change from baseline in monthly migraine days (MMDs) over Weeks 1–12

PREDEFINED SECONDARY ENDPOINTS[1]

- Change from baseline in the number of MMDs during Weeks 25–36, 37–48, 49–60, and 61–72
- Percentage of patients achieving ≥50% response (≥50% reduction in MMDs) during Weeks 25–36, 37–48, 49–60, and 61–72
- Percentage of patients achieving ≥75% response during Weeks 25–36, 37–48, 49–60, and 61–72
- Change from baseline in the 6-item Headache Impact Test (HIT-6) total score at Weeks 36, 48, 60, and 72

PREDEFINED EXPLORATORY ENDPOINTS[1]

- Change from baseline in the percentage of migraine attacks of severe intensity (Weeks 25–36, 37–48, 49–60, and 61–72)
- Change from baseline in monthly acute migraine medication use
- Patient-identified most bothersome symptom (PI-MBS) score (Weeks 36, 48, 60, and 72)
- Patient Global Impression of Change (PGIC) score (Weeks 36, 48, 60, and 72)
- Change from baseline in Migraine-Specific Quality of Life questionnaire (MSQ) subscores (Weeks 36, 48, 60, and 72)
- Change from baseline in EQ-5D-5L visual analog scale (VAS) score (Weeks 36, 48, 60, and 72)
- Change from baseline in Work Productivity and Impairment, adapted for Migraine (WPAI:M) subscores for absenteeism, presenteeism, work productivity loss, and activity impairment (Weeks 36, 48, 60, and 72)

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RESULTS[1,3]

DELIVER PRIMARY ENDPOINT

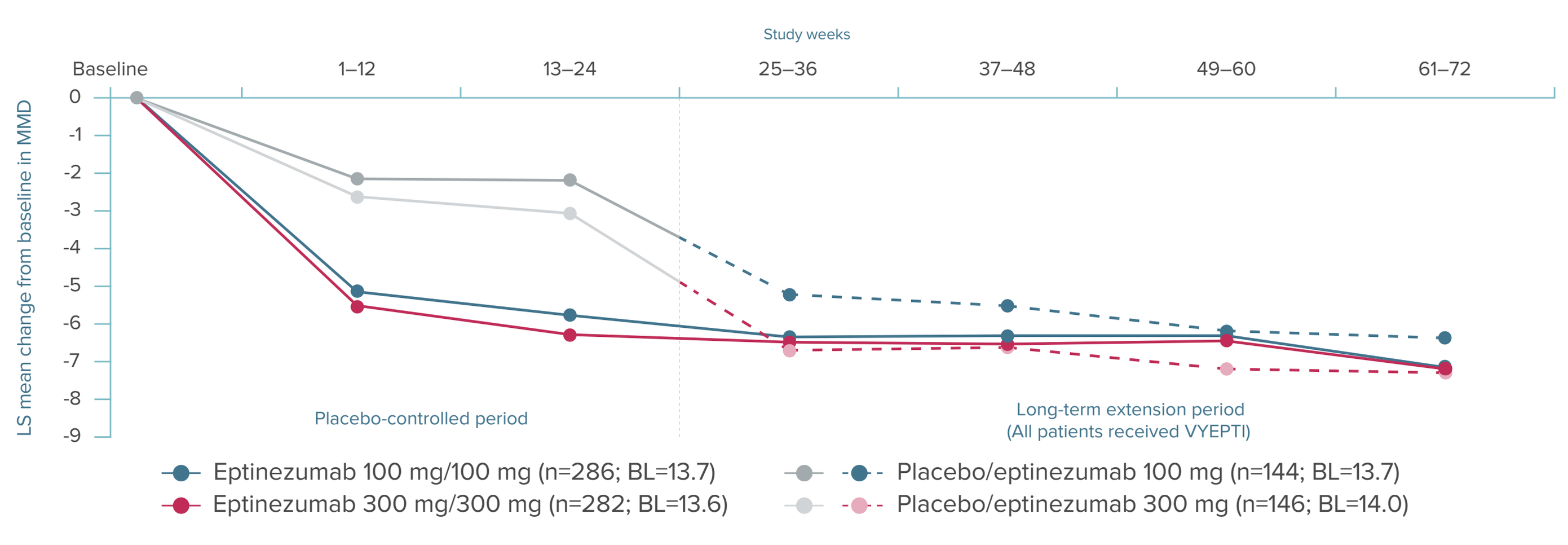
- In Weeks 1–12, eptinezumab 100 mg significantly reduced the number of MMDs compared with placebo[3]

EXTENSION PERIOD: PREDEFINED SECONDARY ENDPOINTS[1]

MIGRAINE FREQUENCY

- For patients initially randomised to placebo who started eptinezumab in the long-term extension, the first dose of eptinezumab on average resulted in a steep decrease of MMDs compared with baseline, similar to that observed with the first eptinezumab infusion in the placebo-controlled period
- In all treatment groups, mean reductions in MMDs were sustained through to the final assessment

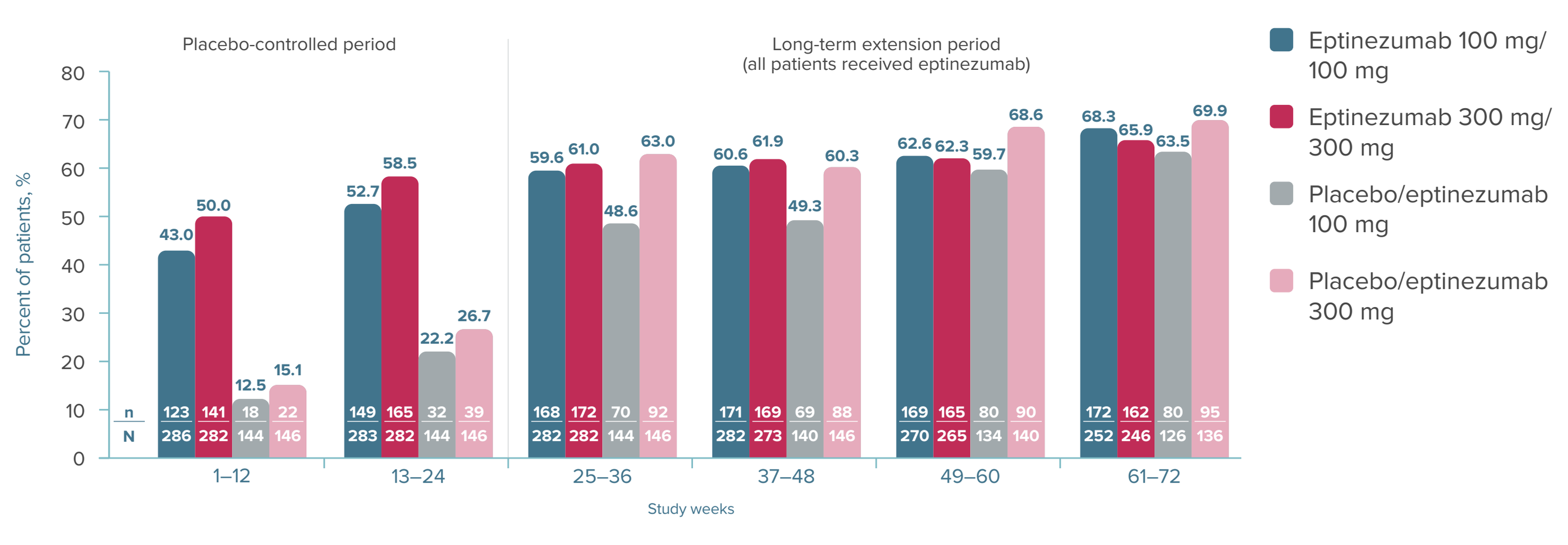
Mean change from baseline in MMDs



Adapted from Ashina M *et al. Headache Pain.* 2022.

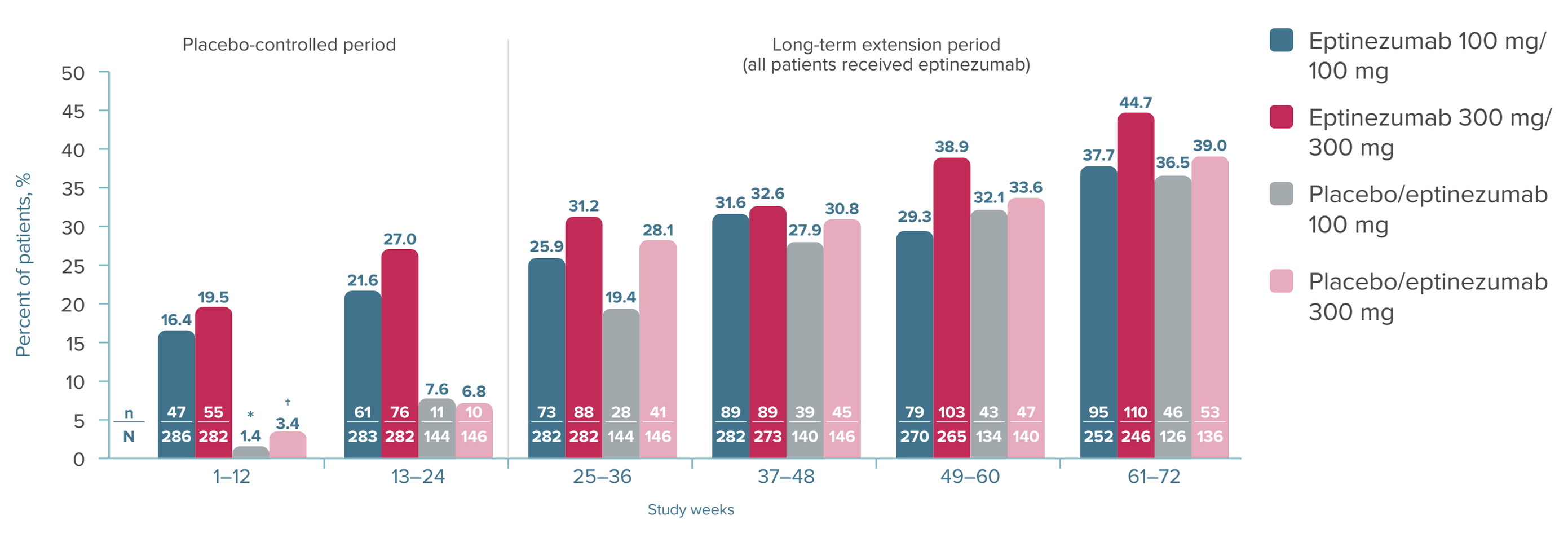
- For patients who switched from placebo to eptinezumab, the first eptinezumab dose (Weeks 25–36) resulted in a more than doubling of ≥50% responder rates and approximate tripling of ≥75% responder rates compared with the preceding dosing interval (Weeks 13–24)

Patients achieving ≥50% reduction in MMDs



Adapted from Ashina M *et al. Headache Pain.* 2022.

Patients achieving ≥75% reduction in MMDs

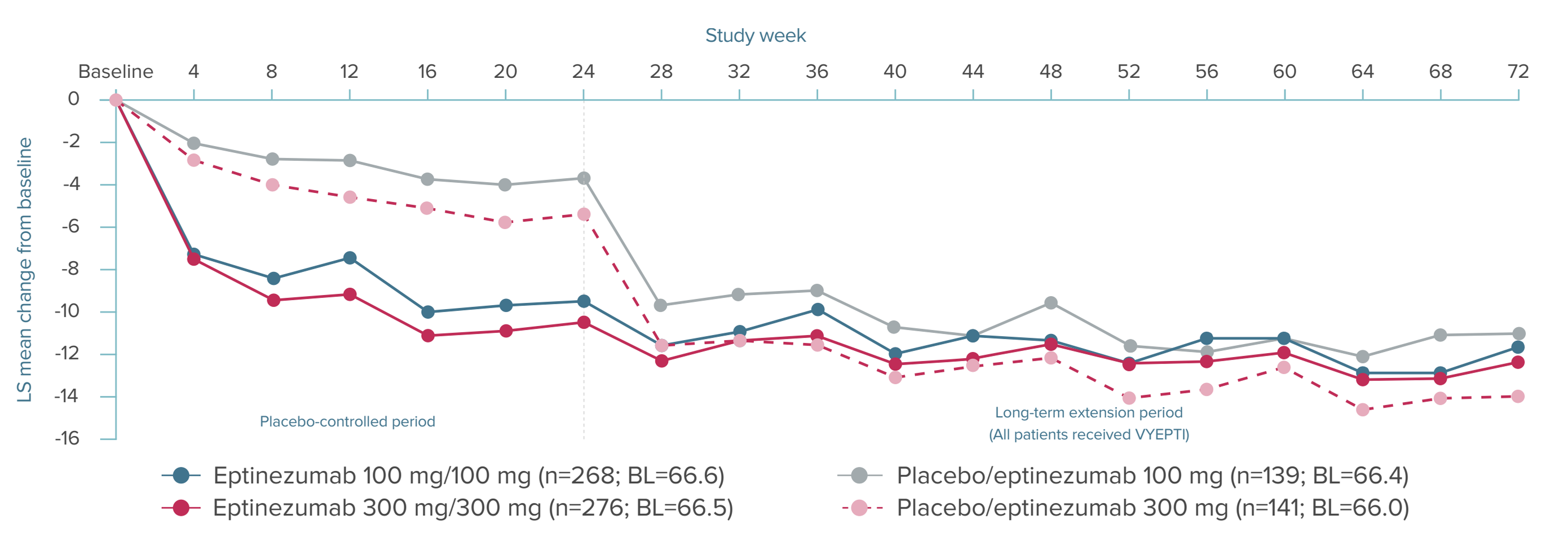


*n/N = 2/144; †n/N = 5/146.
Adapted from Ashina M *et al. Headache Pain.* 2022.

HEADACHE IMPACT

- By the end of the extension period, mean HIT-6 total scores were reduced by −11.0 to −14.0 points across groups; this represents a change in headache-related life impact from severe impact at baseline to some impact

Mean change from baseline in HIT-6 total score



Adapted from Ashina M *et al. Headache Pain.* 2022.

EXTENSION PERIOD: PREDEFINED EXPLORATORY ENDPOINTS

- Mean acute medication use was reduced to below ICHD-3 thresholds for acute medication overuse, and remained at similarly reduced levels for the remainder of treatment

BY THE END OF THE STUDY:

- Mean PI-MBS and PGIC scores reflected "much improvement" in patients' most bothersome symptom and disease status, respectively
- Mean MSQ role functioning-restrictive subscores improved by 32–40 points, role function-preventive and emotional function subscores by 26–33 points each, and mean EQ-5D-5L scores improved by 6–9 points
- Working patients reported 3.5–7.4 fewer days missed (WPAI:M absenteeism)

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SAFETY & TOLERABILITY[1,3]

- Safety and tolerability for the placebo-controlled period have previously been described in full in the primary DELIVER publication[3]

IN THE EXTENSION PERIOD:[1]

- Treatment-emergent adverse events (TEAEs) were reported with similar frequency across treatment groups
- The most commonly reported TEAEs were COVID-19, nasopharyngitis, and upper respiratory chest infection
- The proportions of patients with serious adverse events (SAEs), TEAEs leading to withdrawal, and TEAEs leading to infusion interruption were low

TEAEs in the open-label extension period (safety analysis set)

	n (%)			
	Eptinezumab 100 mg/100 mg (n=288)	Eptinezumab 300 mg/300 mg (n=284)	Placebo/eptinezumab 100 mg (n=145)	Placebo/eptinezumab 300 mg (n=148)
Any TEAE	159 (55.2)	148 (52.1)	72 (49.7)	81 (54.7)
Any SAE	9 (3.1)	9 (3.2)	2 (1.4)	7 (4.7)
TEAE leading to withdrawal	3 (1.0)	6 (2.1)	0	3 (2.0)
TEAE leading to infusion interruption/termination	1 (0.3)	1 (0.4)	0	0
Death	0	0	0	0
TEAEs in ≥1.5% of patients				
COVID-19	63 (21.9)	63 (22.2)	25 (17.2)	31 (20.9)
Nasopharyngitis	19 (6.6)	27 (9.5)	7 (4.8)	13 (8.8)
Upper respiratory tract infection	13 (4.5)	8 (2.8)	4 (2.8)	6 (4.1)
Arthralgia	6 (2.1)	6 (2.1)	1 (0.7)	2 (1.4)
Pruritus	2 (0.7)	6 (2.1)	1 (0.7)	0
Dyspepsia	1 (0.3)	5 (1.8)	0	1 (0.7)
Gastroenteritis	3 (1.0)	5 (1.8)	0	1 (0.7)
Post-vaccine syndrome	0	5 (1.8)	1 (0.7)	1 (0.7)
Sinusitis	4 (1.4)	5 (1.8)	2 (1.4)	2 (1.4)
Urinary tract infection	3 (1.0)	5 (1.8)	3 (2.1)	4 (2.7)
Pharyngitis	3 (1.0)	4 (1.4)	0	3 (2.0)
Upper abdominal pain	4 (1.4)	3 (1.1)	1 (0.7)	3 (2.0)
Bronchitis	4 (1.4)	3 (1.1)	1 (0.7)	3 (2.0)
Cystitis	1 (0.3)	3 (1.1)	0	5 (3.4)
Migraine	7 (2.4)	3 (1.1)	0	1 (0.7)
Nausea	2 (0.7)	3 (1.1)	1 (0.7)	5 (3.4)
Back pain	8 (2.8)	2 (0.7)	1 (0.7)	2 (1.4)
Fatigue	5 (1.7)	2 (0.7)	0	1 (0.7)
Hypertension	3 (1.0)	2 (0.7)	3 (2.1)	0
Menopause	1 (0.3)	0	1 (0.7)	3 (2.0)

Adapted from Ashina M *et al. Headache Pain.* 2022.

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LIMITATIONS[1]

- The extension phase of DELIVER lacked a placebo or active comparator arm, which may limit the interpretation of the results
- Enrolled patients were predominantly White and female, limiting their generalisability to the broader population
- The methodology did not allow for dose escalation or reduction; therefore, the effects of changing dose levels during long-term treatment cannot be evaluated

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CONCLUSIONS[1]

- This long-term extension study highlights eptinezumab as an effective and well-tolerated long-term preventive migraine treatment option for adults with a history of 2–4 prior preventive treatment failures
- Benefits were sustained for up to 18 months across migraine endpoints, including reductions in frequency and severity of migraine, reductions in acute medication use, high responder rates, and patient-reported improvements in functioning, disease status, and health-related quality of life
- The long-term safety and tolerability of eptinezumab was demonstrated by a 90.4% completion rate and a safety profile comparable to that reported in prior studies

CONTEXT KEY QUESTION METHODOLOGY RESULTS SAFETY LIMITATIONS CONCLUSIONS REFS PI

REFERENCES & ABBREVIATIONS

1. Ashina M, *et al. J Headache Pain.* 2023;24(1):155.
2. Lundbeck. VYEPTI. Summary of Product Characteristics.
3. Ashina M, *et al. Lancet Neurol.* 2022;21(7):597–607.

AE, adverse event; **BL,** baseline; **CGPR,** calcitonin gene-related peptide; **CM,** chronic migraine; **EM,** episodic migraine; **EQ-5D-5L,** European Quality of Life 5-Dimension 5-Level; **HIT-6,** 6-item Headache Impact Test; **ICHD,** International Classification of Headache Disorders; **LS,** least squares; **MMDs,** monthly migraine days; **MSQ,** migraine-specific quality of life; **PGIC,** Patient's Global Impression of Change; **PI-MBS,** patient-identified most bothersome symptom; **TEAE,** treatment-emergent adverse event; **WPAI:M,** Work Productivity and Activity Impairment: Migraine.

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