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EPTINEZUMAB IN EPISODIC MIGRAINE: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY (PROMISE-1)[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]

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CONTEXT[1]

This is a summary of a phase 3, multicentre, double-blind, placebo-controlled, parallel-group clinical study, which was the first to investigate the efficacy, safety and tolerability of intravenous (IV) eptinezumab in patients with episodic migraine. Refer to the full publication for more details.

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KEY QUESTION[1]

Is eptinezumab (vs placebo) an effective and generally well tolerated preventive treatment in adults with episodic migraine?

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METHODOLOGY[1]

- Randomised, phase 3, multicentre, double-blind, placebo-controlled, parallel-group study
- A total of 2,413 patients were screened for study inclusion, 898 were randomised to receive treatment
- A total of 888 patients received treatment and were included in the efficacy analysis
- Patients received treatment for 60 weeks on Day 0, 4, 8, 12, 16, 20, 24, 28, 36, 48 and 56

PATIENT DISPOSITION

Randomised (n=898)	Analysis sets	Completed Week 12
Placebo (n=225)	Efficacy (n=222) Safety (n=222)	n=205 (91.1%)
Eptinezumab 30 mg (n=224)	Efficacy (n=223) Safety (n=219)	n=205 (91.5%)
Eptinezumab 100 mg (n=225)	Efficacy (n=221) Safety (n=213)	n=212 (94.2%)
Eptinezumab 300 mg (n=224)	Efficacy (n=222) Safety (n=224)	n=213 (95.1%)

VYEPTI 30 mg is not licensed in the UK. VYEPTI 300 mg is not available in the UK.

PRIMARY ENDPOINT (eptinezumab vs placebo)

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

SECONDARY ENDPOINTS (eptinezumab vs placebo)

- Proportion of patients with ≥75% reduction in migraines from baseline (≥75% migraine responder rate) over Weeks 1–4
- Proportion of patients with ≥75% reduction in migraines from baseline (≥75% migraine responder rate) over Weeks 1–12
- Proportion of patients with ≥50% reduction in migraines from baseline (≥50% migraine responder rate) over Weeks 1–12
- Percentage of patients with a migraine on the day after dosing

KEY INCLUSION CRITERIA

- Adults aged 18–75 years
- Diagnosis at/before 50 years of age
- History of migraine for ≥12 months with ≤14 headache days per month (including ≥4 migraine days in the 3 months prior to screening)
- Acute migraine medication ≤14 days per 28-day period in the 3 months prior to screening

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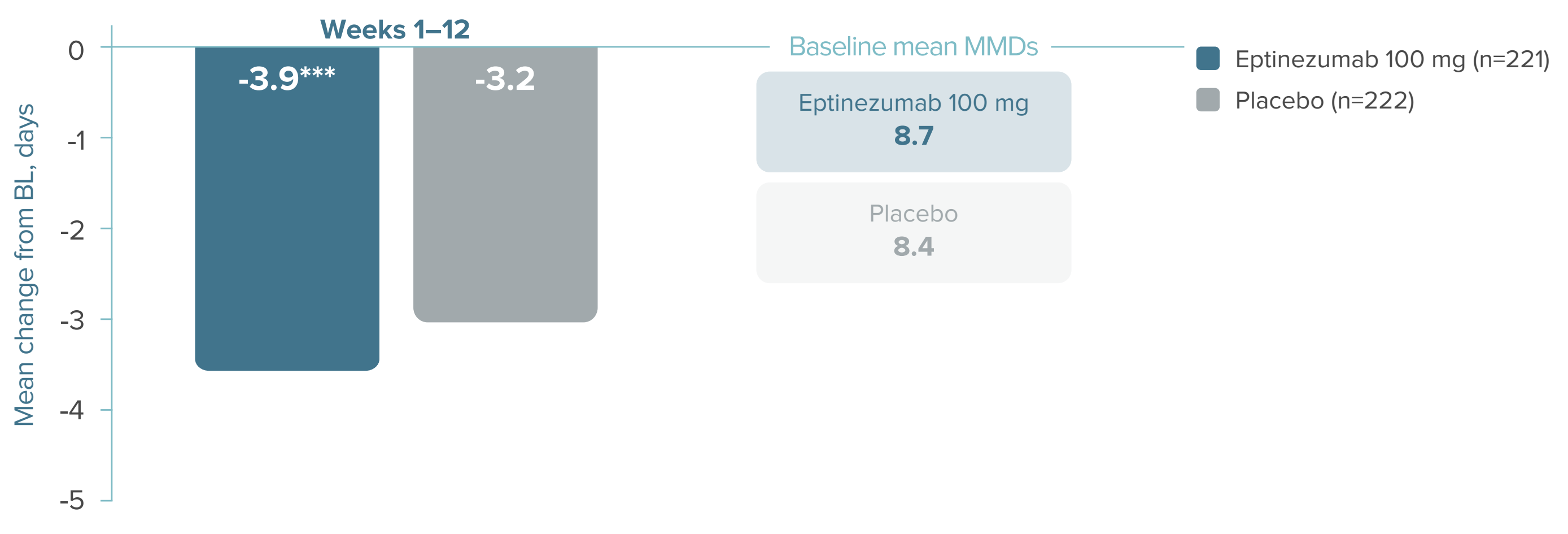
RESULTS[1]

PRIMARY ENDPOINT

- Eptinezumab 100 mg demonstrated statistically significant reduction from baseline in the frequency of migraine days over Weeks 1–12 (compared with placebo)

Change from baseline to Week 12 in mean MMDs



***p=0.0182 vs placebo.
Adapted from Ashina M, *et al. Cephalalgia.* 2020.

SECONDARY ENDPOINTS

- Patients treated with eptinezumab 100 mg were more likely to achieve ≥75% reduction in migraine from baseline during Weeks 1–4 vs placebo, and during Weeks 1–12 vs placebo
- Patients treated with eptinezumab 100 mg were more likely to achieve ≥50% reduction in migraine from baseline during Weeks 1–12 vs placebo **(Not statistically significant per the testing hierarchy; unadjusted *p*-value presented)**
- An observed migraine-preventive effect of eptinezumab 100 mg was observed on the first day after dosing

Summary of selected secondary endpoints

		Eptinezumab 100 mg (n=221)	Placebo (n=222)
≥75% migraine responder rate, Weeks 1–4	Patients, n (%)	68 (30.8)	45 (20.3)
	p-value vs placebo	0.0112	
	OR vs placebo	1.752	
≥75% migraine responder rate, Weeks 1–12	Patients, n (%)	49 (22.2)	36 (16.2)
	p-value vs placebo	0.1126	
	OR vs placebo	1.470	
≥50% migraine responder rate, Weeks 1–12	Patients, n (%)	110 (49.8)	83 (37.4)
	p-value vs placebo	0.0085 Not statistically significant*	
	OR vs placebo	1.662	
Percentage of patients with a migraine, Day 1	Baseline percentage†	31.0%	29.8%
	Day 1 percentage	14.8%	22.5%
	p-value vs placebo	0.0312 Not statistically significant*	

***Not statistically significant per the testing hierarchy; unadjusted *p*-value presented.**
†Baseline is the daily average over the 28-day screening period prior to achieving treatment.
Adapted from Ashina M, *et al. Cephalalgia.* 2020.

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SAFETY & TOLERABILITY[1]

- The incidence of adverse events was generally balanced among treatment groups
- Most events were mild or moderate in severity
- TEAEs leading to study drug withdrawal occurred in 6 patients in the eptinezumab 100 mg group (2.7%) and 6 patients in the placebo group (2.7%)

Adverse events reported in ≥2% of patients in any treatment group*

	Eptinezumab 100 mg (n=223)	Placebo (n=222)
Any event	141 (63.2)	132 (59.5)
Upper respiratory tract infection	22 (9.9)	16 (7.2)
Nasopharyngitis	17 (7.6)	12 (5.4)
Sinusitis	6 (2.7)	14 (6.3)
Dizziness	10 (4.5)	8 (3.6)
Nausea	5 (2.2)	8 (3.6)
Bronchitis	6 (2.7)	8 (3.6)
Cough	8 (3.6)	7 (3.2)
Fatigue	8 (3.6)	1 (<1)
Back pain	7 (3.1)	7 (3.2)
Influenza	4 (1.8)	5 (2.3)
Diarrhoea	3 (1.3)	3 (1.4)

*Including treatment groups for doses unlicensed and/or unavailable in the UK (not reported).
Adapted from Ashina M, *et al. Cephalalgia.* 2020.

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LIMITATIONS[1]

- Study sites were only in two countries, limiting geographic diversity
- Low numbers of non-Caucasians and men
- Overall response to placebo was high

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CONCLUSIONS[1]

These results demonstrate a clinically meaningful migraine preventive effect of eptinezumab 100 mg in patients with episodic migraine over Weeks 1–12 following first IV infusion.

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REFERENCES & ABBREVIATIONS

1. Ashina M, *et al. Cephalalgia.* 2020;40(3):241–54.
2. Lundbeck. VYEPTI. Summary of Product Characteristics.

IV, intravenous; MMDs, monthly migraine days; **OR,** odds ratio; **TEAE,** treatment-emergent adverse event.

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