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EPTINEZUMAB DEMONSTRATED EFFICACY IN SUSTAINED PREVENTION OF EPISODIC AND CHRONIC MIGRAINE BEGINNING ON DAY 1 AFTER DOSING[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[1,3]

The PROMISE-1 and PROMISE-2 trials had previously demonstrated the efficacy and safety of eptinezumab in patients with episodic migraine (EM) and chronic migraine (CM), respectively.[3,4] Those trials reported benefits from day 1, but questions remained as to whether this represented onset of benefit or a transient benefit.[1] This is a summary of a post hoc analysis that investigated the timing of treatment onset.[1] Refer to the full publication for further details.

KEY QUESTION[1]

Does day 1 after infusion represent the point at which the preventive benefit of eptinezumab is established in patients with EM and CM, and is this benefit sustained over 12 weeks?

METHODOLOGY[1]

- A post hoc closed testing analysis of PROMISE-1 and PROMISE-2: randomised, double-blind, parallel-group, and placebo-controlled trials of eptinezumab for the preventive treatment of migraine[1,3,4]
  - In PROMISE-1, a total of 898 patients with EM were randomised, 888 received treatment, and 665 patients were included in this analysis (eptinezumab 30 mg was not included)[3]
  - In PROMISE-2, a total of 1,121 patients with CM were randomised and 1,072 received treatment

PATIENT DISPOSITION[3,4]

Randomised → Full analysis population

PROMISE-1 (n=898)[3]	Placebo (n=222)	Eptinezumab 100 mg (n=221)	Eptinezumab 300 mg (n=222)
PROMISE-2 (n=1,121)[4]	Placebo (n=366)	Eptinezumab 100 mg (n=356)	Eptinezumab 300 mg (n=350)

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

- The primary efficacy endpoint in both PROMISE-1 and PROMISE-2 was the mean change from baseline in monthly migraine days over Weeks 1–12 (Days 1–84)[3,4]
- In the current analysis, the timing of treatment onset was determined by finding the first day from which a treatment effect was nominally significant and sustained without interruption through the end of the first dosing interval (Week 12)[1]

RESULTS[1]

MIGRAINE FREQUENCY (PRIMARY ENDPOINT)[3]

In both studies, eptinezumab 100 mg demonstrated statistically significantly greater improvement in the frequency of migraine days from Weeks 1–12 (Days 1–84) vs placebo.

PERCENTAGE OF PATIENTS REPORTING MIGRAINE ON DAY 1 AFTER INFUSION (SECONDARY ENDPOINT)[1,3,4]

- In both studies, eptinezumab 100 mg demonstrated a reduction in the likelihood of experiencing migraine from Day 1

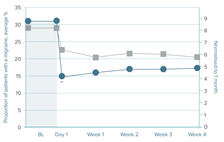
Percentage of patients reporting migraine on Day 1 after infusion	Eptinezumab 100 mg	Placebo
PROMISE-1 (EM)	(n=221)	(n=222)
Average % of patients experiencing migraine on any given day, during 28-day baseline period	31.0%	29.8%
% of patients with migraine on day 1 after dosing	14.8%	22.5%
***p*-value vs placebo**	0.031 Not statistically significant after adjustment for multiplicity	
Reduction from baseline	52.3%	24.5%
PROMISE-2 (CM)	(n=356)	(n=366)
Average % of patients experiencing migraine on any given day, during 28-day baseline period	57.5%	58.0%
% of patients with migraine on day 1 after dosing	28.6%	42.3%
***p*-value vs placebo**	<0.001 Statistically significant after adjustment for multiplicity	
Reduction from baseline	50.3%	27.1%

Adapted from Dodick DW, *et al. Headache.* 2020.

CLOSED TESTING FROM DAY 84 TO DAY 1 (POST HOC ANALYSIS)[1,3,4]

- All tests for eptinezumab 100 mg from Days 1–84 through Day 1 alone in both studies achieved nominal significance, indicating that eptinezumab 100 mg was effective beginning on Day 1 and throughout the entire dosing interval

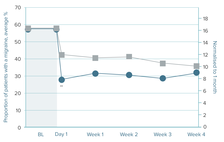
Average daily percentage of patients with EM experiencing migraine (PROMISE-1)



Day 1 reduction in proportion of patients experiencing migraine compared with baseline

***Unadjusted p<0.031 vs placebo. Not statistically significant after adjusting for multiplicity.
Adapted from Dodick DW, *et al. Headache.* 2020.

Average daily percentage of patients with CM experiencing migraine (PROMISE-2)



Day 1 reduction in proportion of patients experiencing migraine compared with baseline

***p<0.001 vs placebo.
Adapted from Dodick DW, *et al. Headache.* 2020.

Values for Weeks 1 through 4 calculated as the average daily percentage of patients with a migraine during that week. Normalisation to average monthly days was achieved by multiplying the daily percent by 28 days (baseline period).

SAFETY & TOLERABILITY[1,3,4]

- Safety data have been reported in the primary publications[3,4] and were not the subject of analysis in this post hoc closed testing analysis[1]
- In PROMISE-1, a total of 84 patients (12.6%) who received eptinezumab and 19 patients (8.6%) patients who received placebo had at least one study drug-related TEAE, as determined by the investigator. The most frequently reported study drug-related TEAEs were nausea (n=14 [1.6%]) and fatigue (n=12 [1.4%]); the remaining study-drug-related TEAEs were reported in <1% of patients[3]
- In PROMISE-2, a total of 93 patients (13.2%) who received eptinezumab and 29 patients (7.9%) who received placebo had at least one study drug-related TEAE, as determined by the investigator. The most frequently reported study drug-related TEAEs were fatigue (eptinezumab n=13 [1.8%], placebo n=3 [<1%]) and nausea (eptinezumab n=11 [1.6%], placebo n=1 [<1%]). The remaining study drug-related TEAEs occurred in <1% of patients[3]
- Please refer to the primary publications for full safety data

LIMITATIONS[1]

- The alpha-controlled day 1 endpoint to assess efficacy onset in both phase 3 PROMISE trials was the only prespecified endpoint evaluating the time of efficacy onset as the day after initial treatment in migraine prevention trials
- The closed testing procedure used to support this endpoint was defined post hoc; therefore, the results must be considered preliminary due to the limitations inherent in post hoc analyses
- Like all migraine preventive trials, the sustained response over 12 weeks is based on the population response. Future analyses evaluating individual patient-level responses over time are necessary to determine the clinical relevance of these findings for an individual patient

CONCLUSIONS[1]

In patients with EM or CM receiving eptinezumab there was fast onset of migraine preventive effect, with preventive efficacy observed as early as Day 1 after dosing, and sustained with a similar magnitude of efficacy observed across the treatment period of 84 days.

REFERENCES & ABBREVIATIONS

1. Dodick DW, *et al. Headache.* 2020;60(10):2220–31.
2. Lundbeck. VYEPTI. Summary of Product Characteristics.
3. Lipton RB, *et al. Neurology.* 2020;94(13):e1365–77.
4. Ashina M, *et al. Cephalalgia.* 2020;40(3):241–54.

BL, baseline; **CM**, chronic migraine; **EM**, episodic migraine; **TEAE**, treatment-emergent adverse event.

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