NO "WEARING OFF" EFFECT OBSERVED WITH EPTINEZUMAB IN THE PREVENTIVE TREATMENT OF MIGRAINE[1]

Roger Cady, Divya Asher, Seema Soni-Brahmbhatt, Joe Hirman, David W Dodick

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[1,3–5]

The **PROMISE-1** and **PROMISE-2** trials have previously demonstrated the efficacy and safety of eptinezumab in patients with episodic migraine (EM) and chronic migraine (CM), respectively.[3,4] These trials reported benefits from Day 1,[3] but the question remained as to whether the benefits are sustained for the full length of the dosing interval, or whether the initial positive response to treatment had a shorter duration than expected. This is a summary of a post hoc analysis that investigated whether a "wearing off" effect was observed with eptinezumab.[1] Refer to the poster for further details.

KEY QUESTION[1]

Is there a "wearing off" effect with eptinezumab in preventive migraine treatment?

METHODOLOGY[1,3,4]

- 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[4]

PATIENT DISPOSITION[1,3,4]

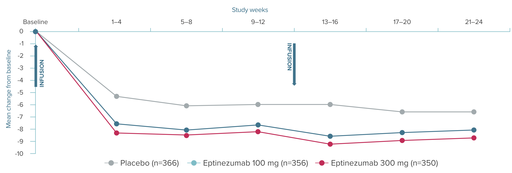
VYEPTI 30 mg is not licensed in the UK. VYEPTI 300 mg is not available in the UK.

- The primary efficacy endpoint in both PROMISE-1 and PROMISE-2 was the mean change from baseline in monthly migraine days (MMDs) over Weeks 1–12 (Days 1–84)[3,4]
- In the current analysis, consistency of effect was determined by analysing the percentage of patients experiencing a migraine attack at intervals reduced by a single day, beginning with the primary endpoint interval (Weeks 1–12, or Days 1–84) and ending with the day following treatment (Day 1)[1]

RESULTS[1]

- Eptinezumab demonstrated greater reductions in MMDs compared with placebo over 4-week intervals that were sustained across the respective treatment periods

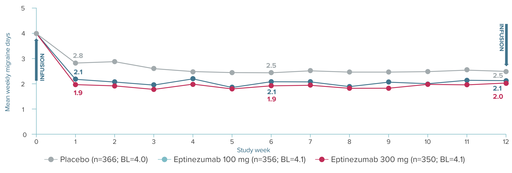
Mean change from baseline in MMDs across 4-week intervals from Weeks 1–24 in patients with chronic migraine (analysis from PROMISE-2)



Adapted from Cady R, *et al.* Poster P13.009. AAN. 2023.
Descriptive statistics. Formal statistical testing not performed.

- The weekly frequency of migraine days in PROMISE-2 was lower with eptinezumab at all time points, and with a similar magnitude, over the first dosing interval

Mean weekly migraine days over the first dosing interval in patients with chronic migraine (analysis from PROMISE-2)



Adapted from Cady R, *et al.* Poster P13.009. AAN. 2023.
Descriptive statistics. Formal statistical testing not performed.

- Closed testing analysis from Days 1–84 through Day 1 alone in PROMISE-1 and PROMISE-2 indicated that eptinezumab was effective from Day 1 and sustained throughout the entire 12-week dosing interval

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[4]
- Please refer to the primary publications for full safety data

LIMITATIONS

- There weren't any limitations included in the poster presentation[1]
- 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[5]

CONCLUSIONS[1]

As the interval between infusions of eptinezumab is 12 weeks, or approximately 3 months, at a population level no "wearing off effect" was observed at the end of the dosing interval. Therefore, in both pivotal trials for eptinezumab (PROMISE-1 and PROMISE-2), there was no significant "wearing off" of eptinezumab's preventive benefit observed through Week 12 (or Day 84).

REFERENCES & ABBREVIATIONS

1. Cady R, *et al.* Poster P13.009. American Academy of Neurology. 2023. Boston, MA & virtual.
2. Lundbeck. VYEPTI. Summary of Product Characteristics.
3. Ashina M, *et al. Cephalalgia.* 2020;40(3):241–54.
4. Lipton RB, *et al. Neurology.* 2020;94(13):e1365–77.
5. Dodick DW, *et al. Headache.* 2020;60(10):2220–31.

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

PRESCRIBING INFORMATION

PRESCRIBING INFORMATION IS AVAILABLE HERE.

Adverse events should be reported. Reporting forms and information can be found at **www.mhra.gov.uk/yellowcard**. Adverse events should also be reported to Lundbeck Limited, Medical Information, on: 01908 638972 or Email: **SafetyLuUnitedKingdom@lundbeck.com**