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A 24-WEEK PROSPECTIVE, MULTICENTER, REAL-WORLD STUDY ON EPTINEZUMAB'S EFFECTIVENESS AND SAFETY IN MIGRAINE PREVENTION (EMBRACE II)[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 12-week EMBRACE study, conducted in 26 patients with high-frequency episodic migraine (HFEM) or chronic migraine (CM), demonstrated that eptinezumab is highly effective and well-tolerated, even in hard-to-treat populations with multiple prior preventive treatment failures, including those involving anti-CGRP mAbs.[1,3]

This is a summary of EMBRACE II, which builds on the findings from EMBRACE to evaluate the effectiveness, tolerability and safety of eptinezumab for HFEM and CM in a real-world setting.[1] Refer to the full publication for more details.

KEY QUESTION[1]

What is the impact of eptinezumab during the first treatment week in patients with prior anti-CGRP mAb failures, and the effects of dose escalation to 300 mg in those requiring enhanced migraine control?

VYEPTI 300 mg is not available in the UK. Lundbeck does not recommend use of any products outside of their licensed indication.

METHODOLOGY[1]

- EMBRACE (EptinezuMAb in RoAl-world evidenCE) II is a multicentre, prospective, real-world investigation including all consecutive outpatients with HFEM or CM treated at 22 headache centres across eight regions representing northern, central and southern Italy (Lombardy, Liguria, Emilia-Romagna, Marche, Latium, Abruzzo, Campania and Sicily)[1]

PATIENTS[1]

N=215 patients received ≥1 dose of eptinezumab 100 mg and/or 300 mg (HFEM N=52; CM N=163).

KEY INCLUSION CRITERIA

- Diagnosis of HFEM or CM according to IHCD-3 criteria
- ≥3 prior failures of preventive migraine treatments (beta-blockers, tricyclic antidepressants, antiepileptics, or onabotulinumtoxinA) in accordance with Italian Medicine Agency (AIFA) guidelines*

KEY EXCLUSION CRITERIA

- Presence of cardio-cerebrovascular disorders (e.g., myocardial infarction, angina, uncontrolled hypertension, peripheral arterial disease, stroke, or transient ischemic attack) or other conditions deemed clinically significant by the investigator
- Prior treatment with onabotulinumtoxinA within 3 months before enrolment

ASSESSMENTS[1]

- Paper-and-pencil headache diary throughout the 28-day baseline period and entire study duration to record monthly migraine days (MMDs) for HFEM patients, monthly headache days (MHDs) for CM patients, monthly analgesic intake (MAI), and pain severity using the Numerical Rating Scale
- Migraine-related disability was assessed with the HIT-6 and MIDAS, and the burden of migraine during headache-free periods measured with the MIBS-4
- Patient-reported satisfaction was evaluated using the PGIC questionnaire
- Data were collected during patient visits every 12 weeks

*Treatment failure was defined as the absence of a clinically meaningful improvement after 3 months, poor tolerability, or the presence of contraindications.[1]

PRIMARY ENDPOINT[1]

The primary endpoint was the change in the average number of headache days (of any type) from baseline to Weeks 21–24 in the overall migraine population.[1]

SECONDARY ENDPOINTS[1]

Secondary endpoints included the proportion of patients achieving reductions of ≥50%, ≥75%, and 100% in MMDs or MHDs, as well as changes in MAI, NRS, HIT-6, MIDAS and MIBS-4 scores at the same time points in the overall migraine population, patients with HFEM only, and patients with CM only.

RESULTS[1]

- 74 patients (HFEM n=12; CM n=62) completed ≥24 weeks of follow-up (≥3 doses of eptinezumab) and were included in the effectiveness analysis
- 32.4% of patients (n=24) had prior treatment failure with anti-CGRP mAbs, and 96.5% (n=55) had previously failed onabotulinumtoxinA
- The initial eptinezumab dose was 100 mg for 73 patients and 300 mg for one
- At Week 12, 25 patients (33.8%) escalated their eptinezumab dose from 100 mg to 300 mg

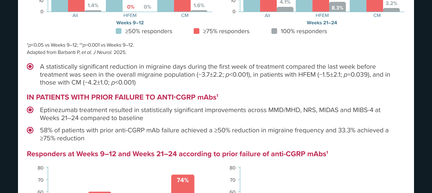
PRIMARY ENDPOINT[1]

- From baseline to Weeks 21–24, eptinezumab resulted in a statistically significant reduction in MMDs/MHDs (–15.6;t10.4) across the total population (p<0.001)

SECONDARY ENDPOINTS[1]

- Significant improvements were also observed in all secondary endpoints in the total population (all *p*<0.001), including MAI (–15.6;t25.4), NRS (–2.2;t2.3), HIT-6 (–9.9;t11.6), MIDAS (–48.7;t42.9), and MIBS-4 (–4.3;t3.7)
  - In patients with CM, statistically significant reductions were achieved in all secondary endpoints (all *p*<0.001), whereas reductions in MAI, HIT-6, MMD and MIBS-4 did not reach statistical significance in HFEM patients
- At Weeks 21–24, the proportions of patients achieving ≥50%, ≥75%, and 100% response rates compared to baseline were 69%, 39.2%, and 4.1%, respectively (HFEM: 50%, 17%, and 8.3%; CM: 73%, 43.5%, and 3.2%)

Responders at Weeks 9–12 and Weeks 21–24[1]



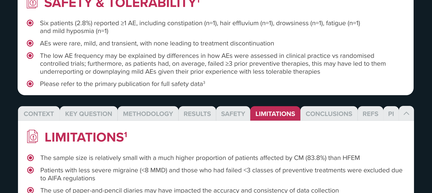
*p<0.05 vs Weeks 9–12; **p<0.001 vs Weeks 9–12
Adapted from Barbanti P, *et al*. *J Neurol*. 2025.

- A statistically significant reduction in migraine days during the first week of treatment compared the last week before treatment was seen in the overall migraine population (–3.7;t2.2; *p*<0.001), in patients with HFEM (–1.5;t2.1; p=0.039), and in those with CM (–4.2;t1.0; *p*<0.001)

IN PATIENTS WITH PRIOR FAILURE TO ANTI-CGRP mAbs[1]

- Eptinezumab treatment resulted in statistically significant improvements across MMD/MHD, NRS, MIDAS and MIBS-4 at Weeks 21–24 compared to baseline
- 58% of patients with prior anti-CGRP mAb failure achieved a ≥50% reduction in migraine frequency and 33.3% achieved a ≥75% reduction

Responders at Weeks 9–12 and Weeks 21–24 according to prior failure of anti-CGRP mAbs[1]

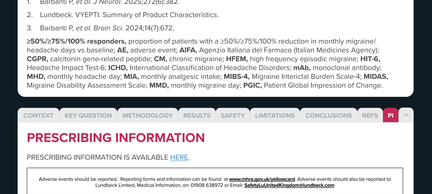


Adapted from Barbanti P, *et al*. *J Neurol*. 2025.

PATIENT-REPORTED SATISFACTION[1]

- Half of the patients in the overall migraine population reported being "very much improved" (32.4%) or "much improved" (17.6%), while 35.1% described themselves as "minimally improved" and only 14.9% reported no change
  - Among patients with prior failure to anti-CGRP mAbs, 8.3% reported being "very much improved" and 45.8% reported "much improved"

PGIC at Weeks 21–24[1]



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SAFETY & TOLERABILITY[1]

- Six patients (2.8%) reported ≥1 AE, including constipation (n=1), hair effluvium (n=1), drowsiness (n=1), fatigue (n=1) and mild hyposmia (n=1)
- AEs were rare, mild, and transient, with none leading to treatment discontinuation
- The low AE frequency may be explained by differences in how AEs were assessed in clinical practice vs randomised controlled trials; furthermore, as patients had, on average, failed ≥3 prior preventive therapies, this may have led to them underreporting or downplaying mild AEs given their prior experience with less tolerable therapies
- Please refer to the primary publication for full safety data[1]

LIMITATIONS[1]

- The sample size is relatively small with a much higher proportion of patients affected by CM (83.8%) than HFEM
- Patients with less severe migraine (<8 MMD) and those who had failed <3 classes of preventive treatments were excluded due to AIFA regulations
- The use of paper-and-pencil diaries may have impacted the accuracy and consistency of data collection
- An inherent limitation of real-world studies is the potential confounding influence of migraine's natural history, placebo effect, and patient-driven lifestyle changes

CONCLUSIONS[1]

The results demonstrate that, in a real-world setting, eptinezumab significantly improved migraine outcomes after 24 weeks of treatment by reducing frequency, analgesic use, pain severity, and both ictal and interictal disability in individuals with migraine who have experienced multiple therapeutic failures, most of whom (66.1%) presented with medication overuse, while maintaining a favourable tolerability profile.[1]

Further studies are warranted to validate and extend these findings in larger, more diverse populations, including individuals with lower migraine frequency.[1]

REFERENCES & ABBREVIATIONS

1. Barbanti P, *et al*. *J Neurol*. 2025;272(6):382.
2. Lundbeck. VYEPTI. Summary of Product Characteristics.
3. Barbanti P, *et al*. *Brain Sci*. 2024;14(7):672.

≥50%/75%/100% responders, proportion of patients with a ≥50%/≥75%/100% reduction in monthly migraine/headache days vs baseline; **AE**, adverse event; **AIFA**, Agenzia Italiana del Farmaco (Italian Medicines Agency); **CGRP**, calcitonin gene-related peptide; **CM**, chronic migraine; **HFEM**, high frequency episodic migraine; **HIT-6**, Headache Impact Test-6; **ICHD**, International Classification of Headache Disorders; **mAb**, monoclonal antibody; **MHD**, monthly headache day; **MIA**, monthly analgesic intake; **MIBS-4**, Migraine Interictal Burden Scale-4; **MIDAS**, Migraine Disability Assessment Scale; **MMD**, monthly migraine day; **PGIC**, Patient Global Impression of Change.

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