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PERSISTENCE TO ANTI-CGRP MONOCLONAL ANTIBODIES AND ONABOTULINUMTOXINA AMONG PATIENTS WITH MIGRAINE: A RETROSPECTIVE COHORT STUDY[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.[1]

CONTEXT[1]

To the best of the authors knowledge (at the time of the publication), real-world comparative studies on persistence among all anti-CGRP mAb treatments and onabotulinumtoxinA for migraine had not previously been conducted.[1] This is a summary of a retrospective cohort study to compare treatment persistence among patients with migraine on anti-CGRP mAbs or onabotulinumtoxinA.[1] Refer to the full publication for more details.

KEY QUESTION[1]

How does persistence to anti-CGRP mAbs (subcutaneous [SC]-delivered erenumab, fremanezumab, and galcanezumab; and intravenous [IV]-delivered eptinezumab), or intramuscular (IM)-delivered onabotulinumtoxinA compare among patients with migraine?

METHODOLOGY[1]

- Observational, retrospective cohort study of US claims data from the IQVIA PharmMetrics Plus database
- Two analyses were performed using the same methodology: 1) A 'most recent treatment episode' analysis (base case analysis), and 2) A 'new user' sensitivity analysis (patients with no history of anti-CGRP mAb or onabotulinumtoxinA treatment) to support the robustness of the 'most recent treatment episode' analysis
- The overall study period was June 25, 2019–December 31, 2021, with the index date set as June 25, 2020

BASE CASE ANALYSIS

N=66,576 patients with ≥1 prescription claim for erenumab, fremanezumab, galcanezumab, eptinezumab, or onabotulinumtoxinA in the most recent treatment episode occurring after June 25, 2020.

PATIENTS WERE DIVIDED INTO FIVE GROUPS BASED ON INDEX TREATMENT:

- **Erenumab** (n=17,617)
- **Fremanezumab** (n=6,299)
- **Galcanezumab** (n=17,221)
- **Eptinezumab** (n=1,074)
- **OnabotulinumtoxinA** (n=24,365)

NEW USER SENSITIVITY ANALYSIS

N=30,507 after inclusion criteria applied and restriction to new users after June 25, 2020

- **Erenumab** (n=9,812)
- **Fremanezumab** (n=3,179)
- **Galcanezumab** (n=9,889)
- **Eptinezumab** (n=126)
- **OnabotulinumtoxinA** (n=7,501)

KEY INCLUSION CRITERIA

- Adults aged ≥18 years of age on the index date
- ≥12 months of continuous medical and pharmacy coverage
- ≥2 claims associated with a diagnosis code for migraine (ICD-10 diagnosis code beginning with G43.XX) ≥30 days apart occurring in the inpatient or outpatient setting within 12 months prior to the index date

KEY EXCLUSION CRITERIA

- Patients who didn't meet the inclusion criteria
- Missing covariate data
- Any diagnosis of cluster headache in the baseline period

INDEPENDENT VARIABLE OF INTEREST

Type of preventive migraine therapy used on the index date.

COVARIATES

Covariates were defined a priori, and included continuous, categorical, dichotomous, and discrete variables that could confound the association between treatment and discontinuation.

Patients were followed from their index date until the first occurrence of one of the following: discontinuation of the index therapy (**primary outcome of interest**), loss of medical or pharmacy insurance coverage (≥ 1-month gap), end of the follow-up period (1 year), or end of the study period.

DEFINITIONS

Index date: The date the first eptinezumab claim was made, and when all five treatments had claims available

Treatment episode: A period of treatment with the same drug without a ≥15-day gap in therapy.

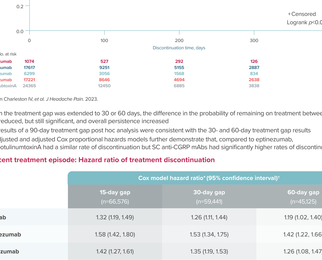
Discontinuation: A 15-day gap in therapy beginning from the date after the last day of therapy as indicated by the days' supply of the therapy.

RESULTS[1]

MOST RECENT TREATMENT EPISODE BASE CASE ANALYSIS

- The probability of remaining on treatment across time was similar between eptinezumab and onabotulinumtoxinA, and persistence for these two therapies was significantly higher compared to erenumab, fremanezumab, and galcanezumab

Most recent treatment episode: Unadjusted probability of remaining on treatment (15-day treatment gap)



No. at risk					
Eptinezumab	1074	527	292	126	0
Erenumab	17617	9251	5155	2287	0
Fremanezumab	6299	3056	1568	324	0
Galcanezumab	17221	8546	4694	2638	0
OnabotulinumtoxinA	24365	12450	6885	3838	0

Adapted from Charleston IV, *et al. J Headache Pain*. 2023.

- When the treatment gap was extended to 30 or 60 days, the difference in the probability of remaining on treatment between groups was reduced, but still significant, and overall persistence increased
- The results of a 90-day treatment gap post hoc analysis were consistent with the 30- and 60-day treatment gap results
- Unadjusted and adjusted Cox proportional hazards models further demonstrate that, compared to eptinezumab, onabotulinumtoxinA had a similar rate of discontinuation but SC anti-CGRP mAbs had significantly higher rates of discontinuation

Most recent treatment episode: Hazard ratio of treatment discontinuation

	Cox model hazard ratio[a] (95% confidence interval)[b]		
	15-day gap (n=66,576)	30-day gap (n=59,441)	60-day gap (n=45,212)
Erenumab	1.32 (1.19, 1.49)	1.26 (1.11, 1.44)	1.19 (1.02, 1.40)
Fremanezumab	1.58 (1.42, 1.80)	1.53 (1.34, 1.75)	1.42 (1.22, 1.66)
Galcanezumab	1.42 (1.27, 1.61)	1.35 (1.19, 1.53)	1.26 (1.08, 1.47)
OnabotulinumtoxinA	0.98 (0.87, 1.10)	0.98 (0.87, 1.12)	1.02 (0.87, 1.18)
Eptinezumab	Reference	Reference	Reference

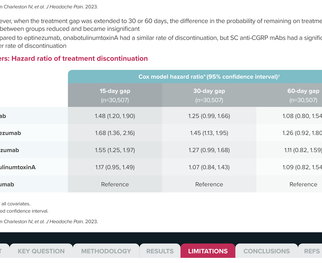
[a]Adjusted for all covariates.
[b]Bootstrapped confidence interval. Note: sample size is reduced since extending the gap period changes the definition of an episode (for example, distinct episodes with the same drug based on a 15-day gap may become a single episode and is excluded if the episode begins before June 25, 2020).

Adapted from Charleston IV, *et al. J Headache Pain*. 2023.

NEW USER SENSITIVITY ANALYSIS

- In support of the base case analysis, the probability of remaining on treatment across time was similar between eptinezumab and onabotulinumtoxinA, and both were significantly higher compared to erenumab, fremanezumab, and galcanezumab
- <5% of patients discontinued and switched from their index therapy, with only two patients discontinuing and switching from eptinezumab to galcanezumab (n=1) and onabotulinumtoxinA (n=1)

New users: Unadjusted probability of remaining on treatment (15-day treatment gap)



No. at risk					
Eptinezumab	126	64	35	15	0
Erenumab	9812	4909	2580	1353	0
Fremanezumab	3179	1464	722	382	0
Galcanezumab	9889	4681	2447	1291	0
OnabotulinumtoxinA	7501	3716	1875	949	0

Adapted from Charleston IV, *et al. J Headache Pain*. 2023.

- However, when the treatment gap was extended to 30 or 60 days, the difference in the probability of remaining on treatment over time between groups reduced and became insignificant
- Compared to eptinezumab, onabotulinumtoxinA had a similar rate of discontinuation, but SC anti-CGRP mAbs had a significantly higher rate of discontinuation

New users: Hazard ratio of treatment discontinuation

	Cox model hazard ratio[a] (95% confidence interval)[b]		
	15-day gap (n=30,507)	30-day gap (n=30,507)	60-day gap (n=30,507)
Erenumab	1.48 (1.20, 1.90)	1.25 (0.99, 1.66)	1.08 (0.80, 1.54)
Fremanezumab	1.68 (1.36, 2.16)	1.45 (1.13, 1.95)	1.26 (0.92, 1.80)
Galcanezumab	1.55 (1.25, 1.97)	1.27 (0.99, 1.68)	1.11 (0.82, 1.59)
OnabotulinumtoxinA	1.17 (0.95, 1.49)	1.07 (0.84, 1.43)	1.09 (0.82, 1.54)
Eptinezumab	Reference	Reference	Reference

[a]Adjusted for all covariates.
[b]Bootstrapped confidence interval.

Adapted from Charleston IV, *et al. J Headache Pain*. 2023.

LIMITATIONS[1]

- Only patients with commercial insurance were included, and therefore the results should not be generalised to migraine patients with other insurance cover types
- The diagnosis of migraine was based on inpatient and outpatient claims, which is subject to misclassification
- The reasons for discontinuing or switching therapy are unknown as claims data do not provide this information
- OnabotulinumtoxinA and oral preventive medications are indicated for other conditions, and their use may not be for migraine despite the patient having a migraine diagnosis
- Persistence was based on claims data and may not reflect actual treatment-taking behaviour
- Unobserved confounders such as migraine frequency and severity may confound the association between treatment and persistence to treatment

CONCLUSIONS[1]

Based on a 15-day treatment gap, persistence to eptinezumab was similar to onabotulinumtoxinA, and persistence to either therapy was superior to SC anti-CGRP mAbs among patients with a history of anti-CGRP mAb or onabotulinumtoxinA use. The authors suggest that, based on the results, eptinezumab and onabotulinumtoxinA may have superior efficacy and tolerability in patients with CM.

REFERENCES & ABBREVIATIONS

1. Charleston IV, *et al. J Headache Pain*. 2023;24(1):101 (incl. Supplemental Material).
2. Lundbeck. VYEPTI. Summary of Product Characteristics.

CGRP, calcitonin gene-related peptide; **CM,** chronic migraine; **HCP,** healthcare professional; **mAb,** monoclonal antibody; **SC,** subcutaneous.

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