Real-world effectiveness of fremanezumab in patients with migraine switching from another mAb targeting the CGRP pathway

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A – research concept and design; B – collection and/or assembly of data; C – data analysis and interpretation;
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Dental and Medical Problems, ISSN 1644-387X (print), ISSN 2300-9020 (online) *Dent Med Probl*. 2024;61(1):9–11

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Funding sources
None declared

Conflict of interest
None declared

Acknowledgements
None declared

Received on October 24, 2023
Reviewed on October 26, 2023
Accepted on October 31, 2023

Published online on January 26, 2024

Keywords: migraine, monoclonal antibodies, calcitonin gene-related peptide

This is a summary of the research article entitled "Real-world effectiveness of fremanezumab in patients with migraine switching from another mAb targeting the CGRP pathway: A subgroup analysis of the Finesse Study".

The discovery of calcitonin gene-related peptide (CGRP) as a therapeutic target in migraine has been one of the greatest achievements in neurology in recent years. Specific antibodies against CGRP bind to it either via a receptor (erenumab) or ligand (fremanezumab, galcanezumab, eptinezumab). Monoclonal antibodies (mAbs) are effective, safe and well-tolerated drugs that have been approved for prophylactic treatment if there are at least 4 days with migraine per month. However, in clinical practice, the failure of treatment with mAbs has been observed, and thus the question arises whether it is worthwhile to include treatment using an antibody with a different mechanism of action.

The Finesse Study was designed to evaluate the efficacy of fremanezumab in patients with a history of prior treatment failure with other mAbs against the CGRP pathway. Among the 153 patients with priorly failed mAbs, switching to fremanezumab led to a ≥50% reduction in the number of days with migraine per month in 42.8% of patients. The conclusion emphasizes that switching to another antibody should be considered in patients with prior therapy failure.

Cite as
Waliszewska-Prosół M, Martelletti P. Real-world effectiveness of fremanezumab in patients with migraine switching from another mAb targeting the CGRP pathway. *Dent Med Probl.* 2024;61(1):9–11. doi:10.17219/dmp/174706

DOI
10.17219/dmp/174706

Introduction

This article summarizes an observational, prospective, two-country study of fremanezumab treatment outcomes entitled "Real-world effectiveness of fremanezumab in patients with migraine switching from another mAb targeting the CGRP pathway: A subgroup analysis of the Finesse Study".[1] That research paper evaluates the efficacy of fremanezumab – one of 4 anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs) – in migraine patients with prior anti-CGRP pathway mAb treatment.

Study design and results

The study recruited 1,071 patients, but eventually included 867, as the remaining patients did not have complete data. All patients were treated with fremanezumab monthly (225 mg) or quarterly (675 mg).

Of these, 153 patients (episodic migraine (EM) – 52.3%, chronic migraine (CM) – 47.7%) had been previously treated with erenumab and/or galcanezumab:
– erenumab 70 mg (60.8%);
– erenumab 140 mg (71.9%);
– any erenumab (94.8%);
– galcanezumab (10.5%).

Primary endpoints – proportion of patients with a ≥50% reduction in monthly migraine days (MMDs).

Secondary endpoints – effectiveness of fremanezumab in terms of:
– changes in MMDs;
– impact on disease-induced disability (Migraine Disability Assessment (MIDAS), Headache Impact Test (HIT-6));
– use of acute medications.

Results after 3 months of treatment with fremanezumab

1. Reduction in MMDs and responder rates:
– a ≥50% reduction in MMDs → 42.8% of patients (a response rate of 48.0% in EM patients and 36.5% in CM patients);
– a ≥30% reduction in MMDs → 58.7%;
– MMDs decreased from 13.6 ±6.5 to 7.2 ±5.5 (a greater reduction in CM patients).

2. Migraine disability:
– the MIDAS scores decreased from 73.3 ±56.8 to 50.3 ±52.9;
– the HIT-6 scores decreased from 65.9 ±5.0 to 60.9 ±7.2.

3. Acute medication use:
– in all patients, it decreased from 9.7 ±5.0 to 4.9 ±3.7 days per month;
– in EM patients, it decreased to 3.8 ±3.1 days;
– in CM patients, it decreased to 6.3 ±3.9 days.

What was the discussion of the key results of the study?

– Erenumab was approved by the European Medicines Agency (EMA) earlier than ligand-acting mAbs; therefore, most of the included patients had previously undergone therapy with this mAb.
– Studies evaluating the switching of antibodies from different groups are few, and limited to single cases or retrospective studies.
– Differences in the efficacy of mAbs are attributed to their mechanisms of action, including effects on the blood–brain barrier (BBB).
– Functional magnetic resonance imaging (MRI) studies showed different responses of the central nervous system (CNS) to the ligand and receptor antibodies. Galcanezumab reduced activity in the left thalamus, hypothalamus and bridge areas, while erenumab specifically reduced activation in the insula, thalamus, cerebellum, and operculum.
– It seems that a large number of patients and broad inclusion criteria for patients with comorbidities better reflect real situations than phase 3 clinical trials.

What are the key practice points for clinicians?

– Different mechanisms of action of mAbs may affect their efficacy, safety and/or tolerability in patients with migraine.
– Patients who have not responded to one class of mAbs may benefit from switching to another class.
– It seems that a switch to mAb with a different mechanism of action would be most beneficial.

What are the perspectives for further research?

– The determinants of a response to a particular class of antibodies are still under investigation. There are more and more real-life studies suggesting that certain personal characteristics, migraine features, and comorbidities determine better responses to treatment, but long-term observations based on large groups of patients are needed.[2–4]
– An important issue in the coming years will be the development of guidelines for the duration of prophylactic treatment, including the determination of the time point after which anti-CGRP drugs can be considered ineffective.[5,6]

– Future studies should also answer the question of whether combining prophylactic therapies in a single patient can improve treatment efficacy and which combinations would be most beneficial.[7]
– Research is currently underway to identify new targets for migraine treatment.[8,9]

Prior presentation

This is a summary of a peer-reviewed article published previously in the Journal of Headache and Pain (https://doi.org/10.1186/s10194-023-01593-2).

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