Original article

Cephalalgia Reports

Cephalalgia Reports
Volume 9: 1–9

DOI: 10.1177/25158163261418597
journals.sagepub.com/home/rep

Sage

Galcanezumab for the preventive treatment of episodic and chronic migraine in real life: A prospective multicenter study in Colombia and Mexico, including effects on anxiety and depression—on behalf of ASOLAC

Joe Muñoz-Cerón[1,2], Karina Vélez-Jiménez[3], Stephanía Bohórquez-Valderrama[4], Ildefonso Rodríguez-Leyva[5], Natalia Hernández[6], Loren Gallo-Eugenio[2], Claudia Moreno-Rodríguez[1], Juan Jiménez-Jaramillo[7], Carolina Guerra-Posada[8], Marta Ramos-Romero[9], Rafael Bernal-Cobo[7], Yessica Rojas-Villegas[10], Paula Cavanzo-Henao[11], Reydmar López-González[12], Daniela Gómez-Barrera[2] and ASOLAC: Asociación Latinoamericana de Cefaleas

Abstract

Background: Galcanezumab is a therapeutic option for individuals with high-frequency episodic and chronic migraine. To date, there is no information regarding treatment results for Colombia and Mexico. The aim of this study was to determine the effectiveness and tolerability of galcanezumab in real-life patients from Colombia and Mexico.

Materials and methods: This was a prospective, independent, multicenter, real-life study. Ninety-eight patients ≥18 years of age with a diagnosis of episodic and chronic migraine, who received galcanezumab 240 mg as a loading dose followed by galcanezumab 120 mg monthly following the available guidelines, were included. At baseline, 3 months, and 6 months, comparative analyses of migraine days/month, the headache impact test-6 (HIT-6), generalized anxiety disorder-7 (GAD-7), patient health questionnaire-9 (PHQ-9) scales, analgesic days/month, global self-perception, and incidence of collateral effects were performed.

Results: Ninety-eight patients were included [mean age, 43.6 (standard deviation (SD) = 12.91); age range, 18–82 years; women, 85.7%]. At baseline, 72.4% and 27.6% of patients had chronic migraine and episodic migraine, respectively. In the episodic migraine group, there was a decrease in migraine days from baseline [6.3 (interquartile range (IQR) = 3.5–9] to 6 months [3.6 (IQR = 1.7–5)] of follow-up ($p = 0.01$ baseline vs 6 months). Patients with chronic migraine changed from [24.2 (IQR = 22.9–24.9)] at baseline to [12.4 (IQR = 10.9–13.2)] at month 3 and to [10 (IQR = 8.7–11.6)] at the end of follow-up ($p < 0.01$). HIT-6, GAD-7, and PHQ-9 scores were significantly lower at months 3 and 6 than at baseline. De novo constipation occurred in 8% of participants.

Conclusion: This study offers evidence of the effectiveness of galcanezumab in real life, including an impact on psychiatric variables.

[1]Clínica Universitaria Colombia—Keralty, Bogotá, Colombia
[2]Hospital Universitario Mayor MEDERI, Universidad del Rosario, Bogotá, Colombia
[3]Hospital Ángeles Lomas Ciudad de México, Mexico
[4]Hospital Kennedy, Bogotá, Colombia
[5]Hospital Central "Dr Ignacio Morones Prieto", Universidad Autónoma de San Luis Potosí México, Mexico
[6]Neuromédica-EPS SURA, Medellín, Colombia
[7]Clínica Confamiliar, Pereira, Colombia
[8]Clínica SOMA, Medellín, Colombia
[9]Hospital La Misericordia, Bogotá, Colombia
[10]Clínica Ospedale, Manizales, Colombia
[11]Compensar EPS, Bogotá, Colombia
[12]Hospital San Vicente Fundación Rio Negro, Medellín, Colombia

Corresponding author:
Joe Muñoz-Cerón, Clínica Universitaria Colombia—Keralty, Bogotá, Colombia.
Email: joemunoz@keralty.co

Keywords
headache, real-world evidence, antibodies, monoclonal, calcitonin gene-related peptide (CGRP), depression, anxiety

Received: 26 August 2025; accepted: 17 December 2025

Introduction

Although migraine is a condition related to multiple pathophysiological factors,[1] calcitonin gene-related peptide (CGRP), which is present in the central and peripheral nervous systems, has been considered a key molecule in the pathogenesis of this disease.[2,3] Therefore, this molecule has been studied as a therapeutic target, with treatments developed that modify its function.[4] Galcanezumab is a humanized monoclonal antibody against the CGRP ligand, recently approved in our region for the preventive treatment of episodic and chronic migraine. Although the EVOLVE 1–2,[5,6] REGAIN,[7] and REALITY[8] studies showed a significant decrease in migraine days per month and a reduction in the consumption of analgesics without high-impact side effects, these studies did not include patients from Colombia and Mexico. In consideration of this argument, based on real-world data, we sought to determine the effectiveness and safety of galcanezumab in patients from these countries. Additionally, due to the importance of psychiatric comorbidities and the risk of migraine progression,[9] variations in levels of anxiety and depression were considered within the objectives of this study.

Materials and methods

Study design

This was an independent, multicenter, prospective real-life study conducted in 12 specialized headache centers in Colombia and Mexico. Patients who received galcanezumab 240 mg as a loading dose, followed by galcanezumab 120 mg monthly, following the available guidelines, which recommend that the drug is indicated for patients with inadequate response to two or more therapies with established efficacy,[10] were included between June and September 2022, and were followed up at 3 and 6 months. An electronic questionnaire was designed for the study that was applied face to face at each visit by neurologists, who were experts in the diagnosis and treatment of headache disorders and members of the headache chapter of the Colombian Association of Neurology or the Mexican Society of Migraine and Headache. This questionnaire was designed to collect sociodemographic information and data of monthly migraine days (MMD), monthly headache days (MHD), consumption of analgesics, Allodynia Symptom Checklist-12 (ASC-12) score, number of previous non-effective preventive medications, years with migraine, history of comorbidities, patient health questionnaire-9 (PHQ-9), generalized anxiety disorder-7 (GAD-7), headache impact test-6 (HIT-6), and global clinical self-perception.[11] Telephone contact was permitted when patients were unable to attend in-person medical appointments. Migraine days were determined only if intensity was scored 2–3 out of 3, or in the presence of typical migraine symptoms despite a pain intensity of 1 out of 3.

Ethical considerations

The study was approved by the ethics committee of Fundación Universitaria Sanitas (No. 020.23FUS), and each patient signed an informed consent form. This study was conducted in accordance with the Helsinki Declaration.

Subjects

Consecutive patients aged 18 years or older with migraine (ICHD 3 criteria) were included in this study. Individuals with conditions that impaired their ability to provide accurate information were excluded from the study. Concomitant preventive medications were permitted only if patients had been receiving stable doses for at least three months, allowing these treatments to be considered ineffective prior to the initiation of galcanezumab. In practice, all patients received galcanezumab as monotherapy.

Variables assessed in the questionnaire

Sociodemographic data were requested, such as sex, age, marital status, education level, and socioeconomic stratum; history of comorbidities; clinical characteristics, such as the presence of an aura, signs of peripheral sensitization with the ASC-12 score, and the existence of cranial autonomic symptoms. We measured MMD, MHD, time in years with migraine, and time since worsening, defined as the time since an increase in monthly days frequency, with the aim of excluding possible status migrainosus patients.

Questions about treatment regimen were asked, regarding analgesic consumption per day, preventive drugs failed, number of preventives failed, and causes of therapeutic failure (no tolerability, no efficacy, or both). Finally, PHQ-9, GAD-7, HIT-6, and global clinical self-perception were completed.

Outcomes

The change in MHD was chosen as the primary outcome for patients with chronic migraine; in those with episodic migraine, the outcome chosen corresponded to the variation in MMD.

Changes in the number of days with migraine in chronic migraine; consumption of analgesics; proportion of patients with 30% to 49% (sub-responders), ≥50%, and ≥75% improvement; changes in HIT-6, PHQ-9, and GAD-7 scores; global self-perception scores; percentage of regression to episodic migraine and the incidence of constipation, were defined as secondary endpoints.

One day of migraine headache was defined as the presence of continuous pain, with signs and symptoms lasting 4 to 24 h or less, in case of pain resolution after taking a drug with evidence in the treatment of migraine. Safety and tolerability were determined by recording the occurrence of predetermined adverse effects on a list generated referencing a pivotal clinical trial. Constipation was classified as emerging, already present, with worsening; already present, without changes; and already present, with improvement.

Statistical analysis

Categorical variables were presented as absolute and relative frequencies. Continuous variables were presented as means and standard deviations (SDs) (normal distribution) or medians and interquartile ranges (IQRs; non-normal distribution). The Shapiro–Wilk test was used to determine the normality of the data. To test for differences in the days of headache and migraine, days of analgesic use, and migraine days at the different follow-up times, the non-parametric Kruskal–Wallis test was used. Additionally, multiple comparisons were made by applying the Holm correction to the p value. Logistic regression was performed for factors related to ≥50% improvement at month 6 of follow-up.

The data were analyzed using INVESTIGA 2022 (rights reserved, Neurophysiology and Sleep Service, Neurology Department) and IBM SPSS version 25 (IBM Corporation, Armonk, NY, USA).

Results

A total of 98 consecutive patients, 58 in Colombia and 40 in Mexico, were included in this study.

Females represented 74.1% and 90.1% of the patients with episodic and chronic migraine, respectively. The average age of patients was not significantly different in the chronic migraine group than in the episodic migraine group (45 ± 19 vs. 40 ± 16, $p = 0.23$). The average number of years with migraine and the duration of worsening until the initiation of galcanezumab were greater in the chronic migraine group than in the episodic migraine group. Similarly, patients with chronic migraine had higher depression, anxiety, and headache impact scores at baseline. Before starting galcanezumab, lack of effectiveness for at least 3 months was the most frequent reason for therapeutic failure in both migraine groups, with amitriptyline and topiramate being the drugs most frequently tried before considering galcanezumab (Table 1). At month 6, 29 withdrawals occurred: $n = 1$ due to non-effectiveness, $n = 3$ due to side effects, $n = 4$ for other reasons, and $n = 21$ due to loss to follow-up.

Effectiveness outcomes

Of the 71 patients with chronic migraine at baseline, 44 (62.0%) and 50 (70.4%) converted to episodic migraine at months 3 and 6, respectively.

In the episodic migraine group, there was a decrease in MMD from baseline [6.3 (IQR = 5.6–6.9)] to 3 months [5.5 (IQR = 3.7–7.3)] and 6 months [3.6 (IQR = 1.7–5)] of follow-up ($p = 0.01$ baseline vs. 6 months).

In this group, the days of consumption of analgesics decreased from baseline [9.04 (IQR = 7.5–10.5) to 3 months [5.2 (IQR = 3.8–7.2) and 6 months [4.2 (IQR = 2.6–5.9)] of follow-up (Figure 1). In this group, the most commonly used analgesics were nonsteroidal anti-inflammatory drugs (NSAIDs) (55.6%), triptans (51.9%), combined analgesics (18.5%), and opioids (3.7%).

In the chronic migraine group, there was a decrease in MHD from baseline [24.2 (IQR = 22.9–24.9)] to 3 months [12.4 (IQR = 10.9–13.2)] and 6 months [10 (IQR = 8.7–11.6)] of follow-up ($p < 0.01$). MMD decreased from baseline [18 (IQR = 12–22.50)] to 3 months [5 (IQR = 7.6–12)] and 6 months [5 (IQR = 3–11.5)] of follow-up ($p < 0.01$). Regarding the consumption of analgesics, there was a decrease from baseline [18.6 (IQR = 17.6–19.6)] to 3 months [10 (IQR = 11.2–8.7)] and 6 months [8.2 (IQR = 7.6–9.8)] of follow-up ($p < 0.01$). For patients suffering from chronic migraine, the most frequently used analgesics were NSAIDs (73.2%), triptans (59.2%), combined analgesics (46.5%), opioids (14.1%), and barbiturates (5.6%).

The response ≥50% at 3 months was determined in 65.4% and 61.6% ($p = 0.001$) of patients with episodic and chronic migraine, respectively, and most of them remained stable at the sixth month. (Figure 2)

Other results: Regarding global self-perception, at 3 months and 6 months, there was a predominance of patients who responded "much better" in the episodic migraine group and "better" in the chronic migraine group. A significantly higher proportion of patients with episodic migraine reported clinical improvement compared with those who showed no change or worsening at months 3 and 6 ($p = 0.018$). This phenomenon was also observed among patients with chronic migraine ($p = 0.045$). (Figure 3)

HIT-6, depression (PHQ-9), and anxiety (GAD-7) scores were significantly different between baseline and 3 and 6 months of follow-up in both the chronic and episodic migraine groups.

In the total cohort, the perception of response to analgesics at baseline was reported as optimal by 26.5% of respondents, suboptimal by 57.1% of respondents and no response by 16.3% of respondents; at month 3, the percentages were 77.8%, 20.0%, and 2.2%, respectively, and at month 6, they

Table 1. Clinical and sociodemographic characteristics.

		Episodic 27 (27.6%)	Chronic 71 (72.4%)	*P* value
Variable		Mean (SD)	Mean (SD)	
Age (years)		40 ± 16	45 ± 19	0.231
Variable		*n* (%)	*n* (%)	
Sex	Female	20 (74.1)	64 (90.1)	0.048
	Male	7 (25.9)	7 (9.9)	0.048
Marital status	Single	12 (44.4)	22 (31.0)	0.232
	Married	10 (37.0)	29 (40.8)	0.801
	Other	5 (18.5)	20 (28.2)	0.321
Education level	Low	1 (3.7)	7 (9.9)	0.031
	Medium	3 (11.1)	13 (18.3)	0.051
	High	23 (85.2)	51 (71.8)	0.067
Socioeconomic stratum	Low	5 (18.5)	10 (14.1)	0.073
	Medium	20 (74.1)	44 (62.0)	0.09
	High	2 (7.4)	17 (23.9)	0.037
Presence of an aura	0 out of 10 attacks	16 (59.3)	34 (47.9)	0.041
	1 to 3 attacks	5 (18.5)	17 (23.9)	0.282
	4 to 7 attacks	1 (3.7)	12 (16.9)	0.032
	8 to 10 attacks	5 (18.5)	8 (11.3)	0.172
Allodynia	Without allodynia	9 (33.3)	11 (15.5)	0.046
	Mild allodynia	9 (33.3)	20 (28.2)	0.291
	Moderate allodynia	3 (11.1)	14 (19.7)	0.044
	Severe allodynia	6 (22.2)	26 (36.6)	0.022
Presence of trigeminal autonomic symptoms		6 (22.2)	28 (39.4)	0.017
Headache days/month—IQR		6.7 (3.2–9)	26 (20–30)	<0.000001
Days/month migraine—IQR		6.7 (3.2–9)	18 (12–22.5)	<0.000001
Days of analgesic consumption—IQR		9.04 (3–12)	20.5 (10–30)	0.005
Time in years with migraine—SD		16.2 ± 6.1	22.2 ± 8.1	0.001
Preventive drugs failed	Amitriptyline	18 (66.7)	33 (46.5)	0.001
	Topiramate	13 (48.1)	45 (63.4)	0.004
	Antagonist calcium	7 (25.9)	17 (23.9)	0.881
	Valproic acid	6 (22)	25 (35.2)	0.033
	Botulinum toxin	0 (0)	43 (61.0)	—
	Pericranial blocks	4 (14.8)	26 (36.6)	0.056
	Beta-blockers	5 (18.5)	20 (28.2)	0.044
	ARA II inhibitors	0 (0.0)	5 (7.0)	—
Therapeutic failure	No efficacy	13 (48.1)	36 (50.7)	0.84
	No safety tolerability	5 (18.5)	7 (9.9)	0.072
	Combination of the above	6 (22.2)	27 (38.0)	0.014
	Naive patients	3 (11.1)	1 (1.4)	0.031
Number of preventives failed	≤1	5 (18.5)	9 (12.6)	0.634
	2	10 (45.5)	12 (54.5)	0.026
	≥3	12 (44.4)	50 (70.4)	0.071
Comorbidities	Respiratory	11 (40.7)	9 (12.7)	0.001
	Cardiovascular	4 (14.0)	16 (22.5)	0.042
	Other types of pain	11 (40.7)	30 (42.3)	0.679
	Psychiatric	13 (48.1)	33 (46.5)	0.754
	Sleep	12 (44.4)	48 (67.6)	0.005
	Rheumatologic	1 (3.7)	5 (7.0)	1.000
	Gastrointestinal	16 (59.3)	45 (63.4)	0.162
	Allergies	8 (29.6)	23 (32.4)	0.607
PHQ-9		6 ± 4	10 ± 6	0.009
GAD-7		6 ± 2	7 ± 5	0.000
HIT-6		61 ± 10	66 ± 9	0.073

SD: standard deviation; IQR: interquartile range; PHQ-9: patient health questionnaire-9; GAD-7: generalized anxiety disorder-7; HIT-6: headache impact test-6.

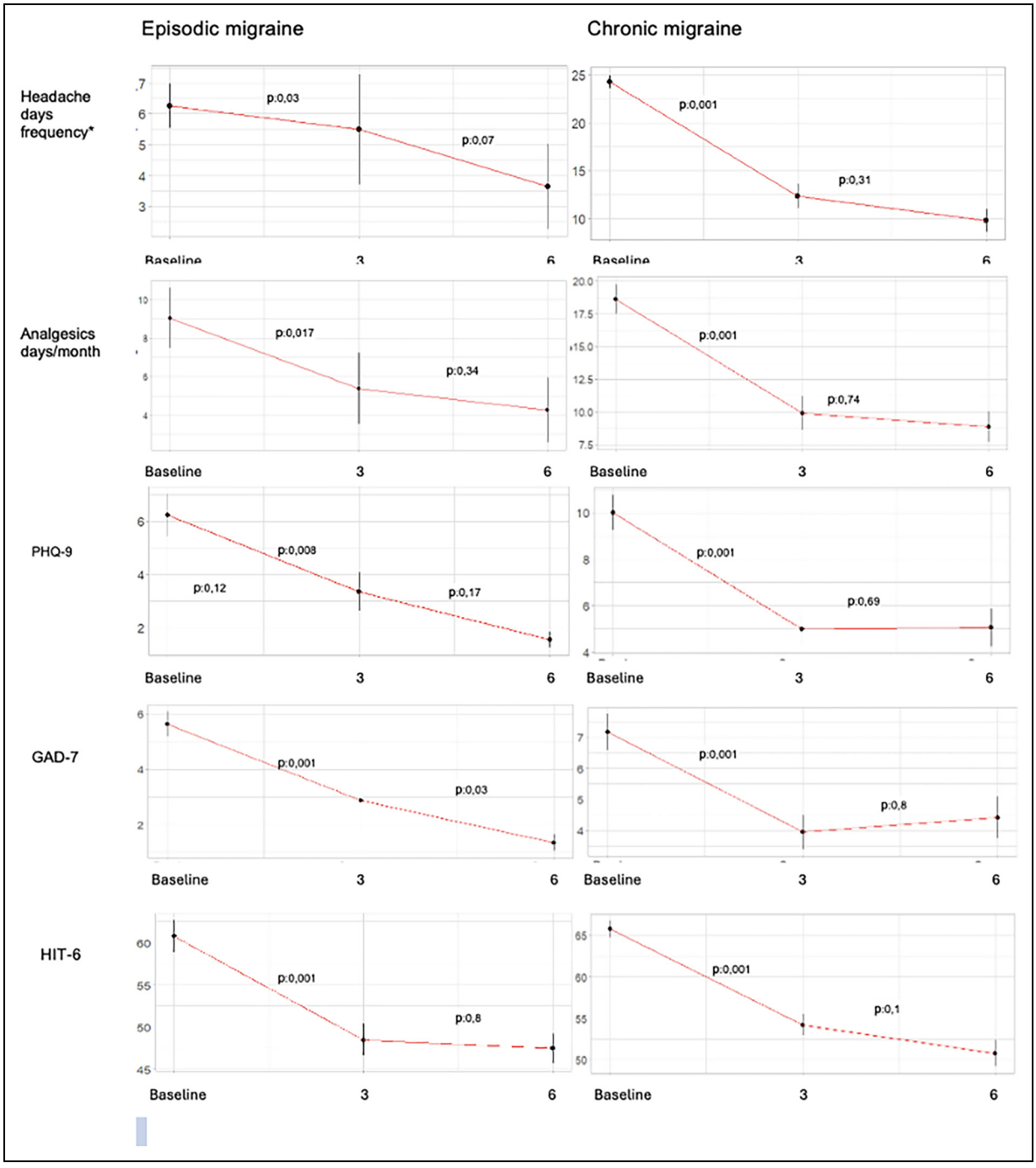

Figure 1. Comparative changes in headache days and depression, anxiety, and headache impact scores before and after treatment. *For episodic migraine, measured in monthly migraine days; for chronic migraine, measured in monthly headache days. All the data fulfilled the criteria for normal distribution (Shapiro–Wilk test $p < 0.05$) for all the cases.

were 80.5%, 18.2%, and 1.3%, respectively ($p < 0.05$ for all comparisons of proportions).

Safety and tolerability

No serious adverse effects were reported. The most frequent side effects were pain at the site of application (23.3%), headache (12.2%), vertigo (8.9%), and pruritus (6.7%). Due to non-tolerability, three patients withdrew from the study, with two patients withdrawing due to constipation; this symptom emerged de novo in 8% of patients and was pre-existing but worsened following treatment in 10% (Figure 4).

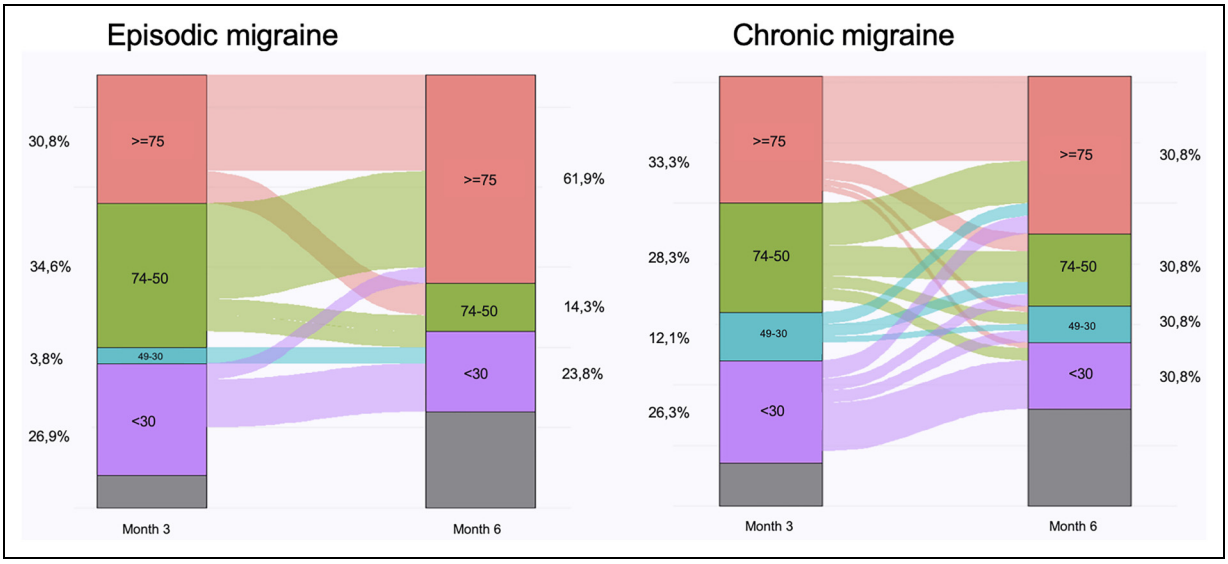

Figure 2. Alluvial plot of clinical response in percentage and migration probability from month 3 to month 6. Gray represents missing data.

Discussion

As galcanezumab is covered by the local health insurance systems in Mexico and Colombia, the findings reported herein may contribute to refining local health policy strategies for migraine treatment in these settings.

Clinical and demographic characteristics such as age, time of evolution of migraine, and worsening of the clinical course were comparable to those reported in clinical trials of galcanezumab and in similar real-life studies.[6,12]

Regarding effectiveness, the results reported herein are similar to those found in studies with similar methodologies,[12,13] with effects at 6 months of treatment being considerably better than those reported in pivotal studies of galcanezumab in episodic and chronic migraine,[6,7] phenomenon that could be explained by the placebo effect and by the opportunity offered by real-life interventions that generate higher effectiveness values.[14] This considerable decrease in headache days per month is correlated with a decrease in the proportion of patients with chronic/episodic migraine from baseline to months 3 and 6 of follow-up, an outcome recently determined as a clinical objective of interest.[15] In addition to improving the frequency of headache and migraine days, in this study, there was a lower intake of analgesics, greater effectiveness, and improvements in HIT-6 scores at month 3 and month 6, outcomes that suggest the need to include additional variables when defining effectiveness in real life, as suggested by guidelines.[10] In this study, there were also improvements in PHQ-9 (depression) scores and GAD-7 (anxiety) scores at months 3 and 6, outcomes that suggest CGRP modification improves anxiety and depression; these observations coincide with similar studies with Fremanezumab and botulinum toxin that have also shown favorable impacts on pain burden and emotional components.[16,17] Furthermore, experimental studies demonstrate that central administration of CGRPα can induce depression-like phenotypes.[19] Additional evidence also suggests that CGRP may directly or indirectly modulate the dopaminergic reward system, thereby contributing specifically to the anhedonic dimension, rather than the behavioral despair component of depression-like pathology.[20] Taken together, these data describe a potential role of CGRP signaling in the pathophysiology of mood disturbances and may provide a mechanistic link between neuropeptide dysregulation and affective symptoms.[18,21]

In relation to previous treatment failures, we identified that a substantial proportion of patients had not achieved clinical improvement despite the use of multiple preventive therapies. This observation aligns with findings from real-world evidence, such as the REALITY and GARLIT cohorts,[8,12] as well as pivotal randomized clinical trials,[22] in which galcanezumab demonstrated meaningful efficacy even among individuals with a history of multiple preventive treatment failures. Considering that our study was conducted in a Latin American population, we hypothesize that intrinsic factors such as metabolic characteristics, cultural influences, and treatment expectations could contribute to this favorable therapeutic response.

With respect to chronic migraine, in this study, a considerable proportion of patients had previously failed treatment with onabotulinumtoxinA, a finding comparable with the REALITY study, in which 47.3% of participants had been exposed to this therapy.[8] To date, no randomized head-to-head trial comparing galcanezumab and onabotulinumtoxinA has demonstrated clear superiority of one agent over the other. Nevertheless, evidence from real-world observational studies

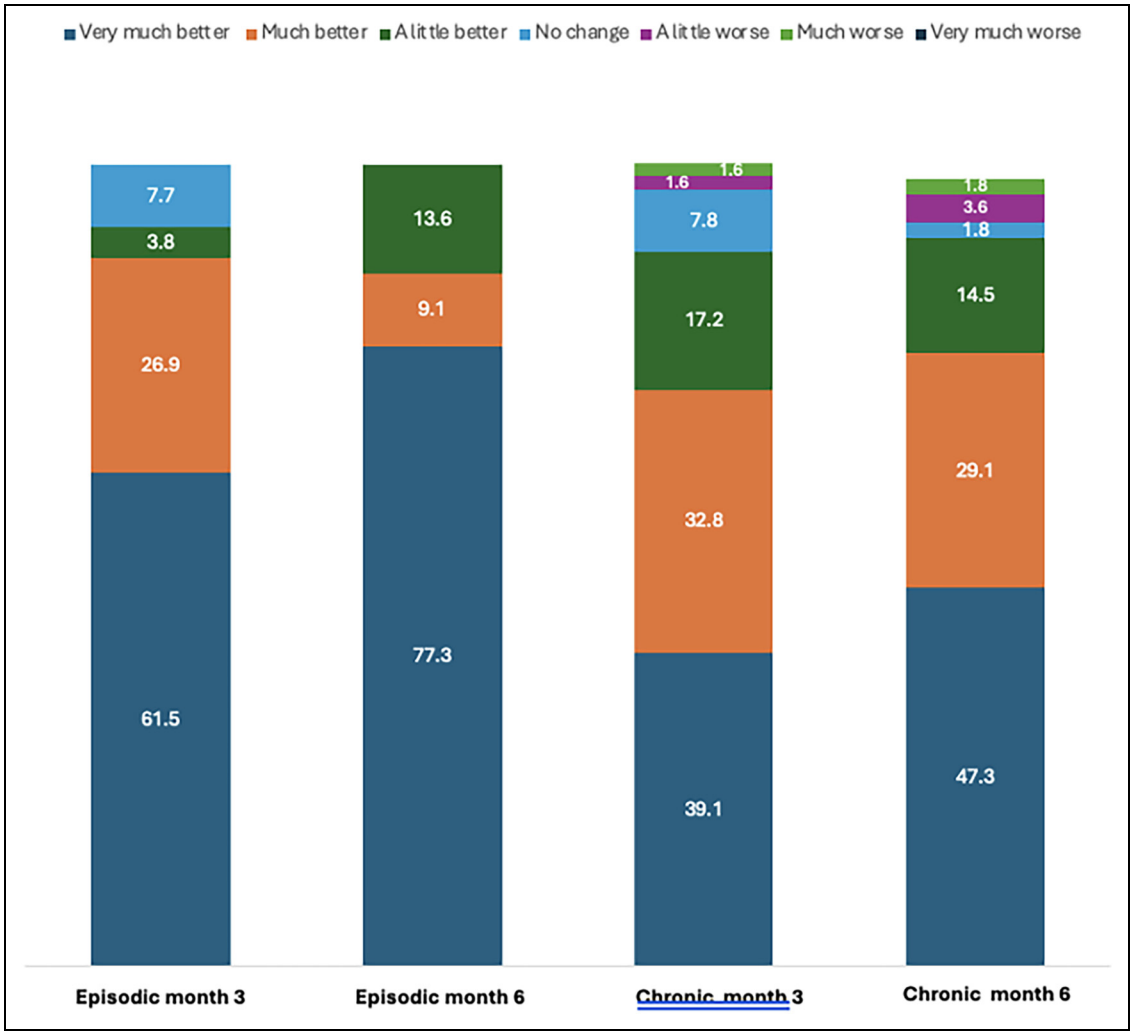

Figure 3. Global self-perception analysis at month 3 and month 6.

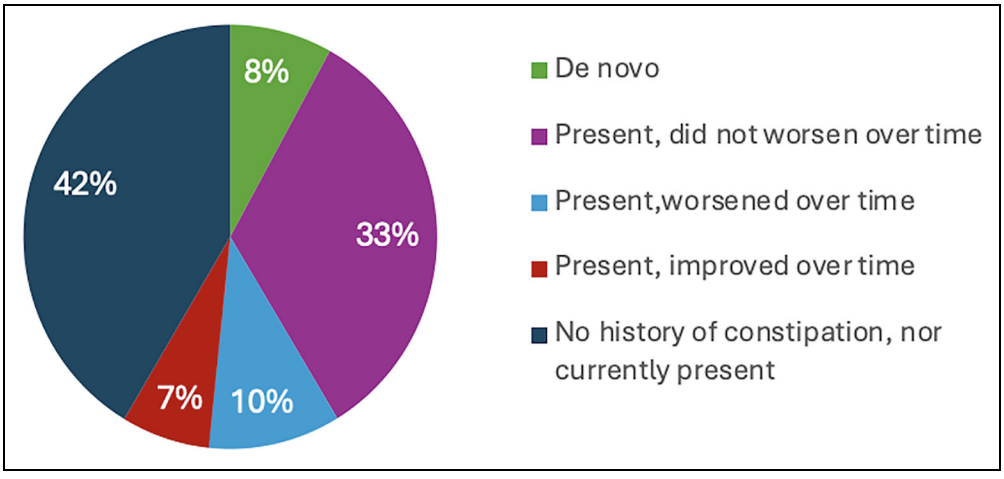

Figure 4. Safety and tolerability, constipation.

suggests that galcanezumab may provide greater efficacy, as reflected by a more pronounced reduction in MMD, compared with onabotulinumtoxinA (−13.0 vs. −8.7 days/month, $p < 0.001$).[23] This observation highlights the potential clinical relevance of CGRP monoclonal antibodies as an alternative therapeutic strategy in patients suffering from chronic migraine who do not achieve adequate benefit with onabotulinumtoxinA.

Regarding safety and tolerability, the results presented herein differ from those in pivotal studies, which did not demonstrate a considerable incidence of constipation, a frequent side effect in real-life studies.[12,24] In addition, this study provides detailed insights into the clinical course of this symptom, thereby assisting clinicians in distinguishing between new-onset constipation and the worsening of pre-existing cases.

With regard to the incidence of vertigo and headache, the study design did not permit differentiation between migraine-associated symptoms and the potential adverse effects of galcanezumab.

The main strengths of this study are the prospective methodological design, which included additional outcomes related to depression, anxiety, and self-perception, as well as the precise determination of constipation as the most relevant side effect.

In addition, the results reported here close the knowledge gap with respect to the clinical utility of these drugs in Latin America and provide useful information for local health systems to justify including new therapeutic options in guidelines for the treatment of migraine. Despite the genetic diversity across Latin American populations, shared cultural and demographic characteristics suggest that these findings may be applicable to this region.

The main limitations of this study included the relatively small sample size, which precluded the development of a reliable model for response predictors, the absence of a systematic follow-up for adverse events, and the considerable loss to follow-up observed during the study period, which may have influenced the precision, statistical power, and generalizability of the findings presented herein.

Conclusion

The data presented herein suggest that the use of galcanezumab is effective and safe for the treatment of patients with episodic and chronic migraine in real-life clinical practice in Colombia and Mexico.

Article highlights

- The effectiveness of galcanezumab supports its use as a therapeutic option for individuals with migraine in Latin America.
- In addition to its effects on migraine headache days, analgesic intake, and HIT-6 scores, this study suggests that galcanezumab improves comorbid depression and anxiety, further supporting its role in enhancing overall quality of life among patients with migraine.
- Data derived from real-world studies contribute to a more comprehensive understanding of the clinical effectiveness of galcanezumab in routine practice.

Acknowledgments

This work was made possible through the collaboration of *Neurofisiología y Sueño—Neurology unit—Hospital Méderi* and the academic commitment of the authors toward a shared goal. We also extend our gratitude to the patients for their willingness to contribute valuable information that enriched this project.

ORCID iDs

Ildefonso Rodríguez-Leyva https://orcid.org/0000-0002-3316-1471
Daniela Gómez-Barrera https://orcid.org/0009-0007-7858-2935

Ethical considerations

The study was approved by the ethics committee of Fundación Universitaria Sanitas (No. 020.23FUS). This study was conducted in accordance with the Helsinki Declaration.

Consent to participate

Each patient signed a written informed consent form.

Consent for publishing

Yes, all authors have read and authorize final approval of the article.

Author contributions

JFMC: Formulation and planning of the study, collection of information, interpretation of results, and writing of the manuscript. JSR: Information collection and manuscript construction. LMGE: Planning of the study, collection of information, analysis of data and results, and writing of the manuscript. KVJ, SBV, IRL, CMR, JJJ, CGP, MRR, RBC, YRV, PCH, and RLG: Information collection. NH: Writing of the manuscript and information collection. DGB: Information collection and manuscript adjustment.

Funding

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: This research was funded by the Center of Research CIMED-Hospital Méderi (editing style, statistical calculations, and open access fee), Neurofisiología y sueño unit (design and construction of the software for data collection).

Declaration of conflicting interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Open practices

Not applicable.

References

1. Aurora SK and Brin MF. Chronic migraine: an update on physiology, imaging, and the mechanism of action of two available pharmacologic therapies. *Headache* 2017; 57: 109–125.
2. Edvinsson L, Haanes KA, Warfvinge K, et al. CGRP as the target of new migraine therapies – successful translation from bench to clinic. *Nat Rev Neurol* 2018; 14: 338–350.
3. Deen M, Correnti E, Kamm K, et al. Blocking CGRP in migraine patients – a review of pros and cons. *J Headache Pain* 2017; 18: 96.
4. Edvinsson L. Calcitonin gene-related peptide (CGRP) and the pathophysiology of headache: therapeutic implications. *CNS Drugs* 2001; 15: 745–753.
5. Stauffer VL, Dodick DW, Zhang Q, et al. Evaluation of galcanezumab for the prevention of episodic migraine. *JAMA Neurol* 2018; 75: 1080–1088.
6. Skljarevski V, Matharu M, Millen BA, et al. Efficacy and safety of galcanezumab for the prevention of episodic migraine: results of the EVOLVE-2 phase 3 randomized controlled clinical trial. *Cephalalgia,* 2018; 38: 1442–1454.
7. Detke HC, Goadsby PJ, Wang S, et al. Galcanezumab in chronic migraine: the randomized, double-blind, placebo-controlled REGAIN study. *Neurology* 2018; 91: e2211.
8. Vernieri F, Iannone LF, Guerzoni S, et al. Long-term effectiveness of galcanezumab in the prevention of migraine: an Italian retrospective analysis (REALITY). *Neurol Ther* 2024; 13: 415–435.
9. Bigal ME, Serrano D, Buse D, et al. Acute migraine medications and evolution from episodic to chronic migraine: a longitudinal population-based study. *Headache* 2008; 48: 1157–1168.
10. Muñoz-Cerón JF, Sánchez MR, Pradilla-Vesga OE, et al. Guideline on the preventive treatment of chronic migraine, chronic tension type headache, hemicrania continua and new daily persistent headache on behalf of the Colombian Association of Neurology. *Acta Neurol Colomb* 2020; 36: 150–167.
11. ECDEU assessment manual for psychopharmacology: Guy, William: Free Download, Borrow, and Streaming : Internet Archive [Internet]. [cited 2025 Sep 30]. https://archive.org/details/ecdeuassessmentm1933guyw
12. Vernieri F, Altamura C, Brunelli N, et al. Galcanezumab for the prevention of high frequency episodic and chronic migraine in real life in Italy: a multicenter prospective cohort study (the GARLIT study). *J Headach Pain* 2021; 22: 1–10.
13. Torres-Ferrus M, Alpuente A and Pozo-Rosich P. How much do calcitonin gene-related peptide monoclonal antibodies improve the quality of life in migraine? A patient's perspective. *Curr Opin Neurol* 2019; 32: 395–404.
14. Evans K, Romero H, Spierings ELH, et al. The relation between the placebo response, observed treatment effect, and failure to meet primary endpoint: a systematic review of clinical trials of preventative pharmacological migraine treatments. *Cephalalgia* 2021; 41: 247–255.
15. Altamura C, Brunelli N, Marcosano M, et al. Conversion from chronic to episodic migraine in patients treated with galcanezumab in real life in Italy: the 12-month observational, longitudinal, cohort multicenter GARLIT experience. *J Neurol* 2022; 269: 5848–5857.
16. Affatato O, Moulin TC, Pisanu C, et al. High efficacy of onabotulinumtoxinA treatment in patients with comorbid migraine and depression: a meta-analysis. *J Transl Med* 2021; 19: 1–11.
17. Lipton RB, Cohen JM, Galic M, et al. Effects of fremanezumab in patients with chronic migraine and comorbid depression: subgroup analysis of the randomized HALO CM study. *Headache* 2021; 61: 662–672.
18. Shao B, Zhou YL, Wang H, et al. The role of calcitonin gene-related peptide in post-stroke depression in chronic mild stress-treated ischemic rats. *Physiol Behav* 2015; 139: 224–230.
19. Jiao J, Opal MD and Dulawa SC. Gestational environment programs adult depression-like behavior through methylation of the calcitonin gene-related peptide gene. *Mol Psychiatry* 2013; 18: 1273–1280.
20. Hashikawa-Hobara N, Otsuka A, Okujima C, et al. CGRP Overexpression does not alter depression-like behavior in mice. *PeerJ* 2021; 9: e11720.
21. Mathé AA, Ågren H, Lindström L, et al. Increased concentration of calcitonin gene-related peptide in cerebrospinal fluid of depressed patients. A possible trait marker of major depressive disorder. *Neurosci Lett* 1994; 182: 138–142.
22. Mulleners WM, Kim BK, Láinez MJA, et al. Safety and efficacy of galcanezumab in patients for whom previous migraine preventive medication from two to four categories had failed (CONQUER): a multicentre, randomised, double-blind, placebo-controlled, phase 3b trial. *Lancet Neurol* 2020; 19: 814–825.
23. Wang YF, Yang FC, Chen LA, et al. Comparative effectiveness and tolerability of calcitonin gene-related peptide (CGRP) monoclonal antibodies and onabotulinumtoxinA in chronic migraine: a multicenter, real-world study in Taiwan. *Eur J Neurol* 2024; 31: e16372.
24. Holzer P and Holzer-Petsche U. Constipation caused by anti-calcitonin gene-related peptide migraine therapeutics explained by antagonism of calcitonin gene-related peptide's motor-stimulating and prosecretory function in the intestine. *Front Physiol* 2022; 12: 820006.