Engineering and Scientific International Journal (ESIJ)
Volume 13, Issue 3, July – September 2026
ISSN 2394-7187(Online)
ISSN 2394 - 7179 (Print)

CGRP-Targeted Monoclonal Antibodies for Migraine Prevention: A Real-World Twelve Month Cohort: Effectiveness, Tolerability and Predictors of Response

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Abstract — Monoclonal antibodies targeting calcitonin gene-related peptide (CGRP) or its receptor have transformed migraine prevention, with multiple pivotal trials demonstrating substantial reductions in monthly migraine days for both chronic and high-frequency episodic migraine. Real-world data from South Asian populations remain limited. We prospectively followed 276 patients initiated on CGRP monoclonal antibodies at a tertiary headache clinic over 12 months: 92 on erenumab, 98 on galcanezumab, and 86 on fremanezumab. Mean monthly migraine days fell from 15.8 to 6.2 with erenumab, from 16.2 to 6.4 with galcanezumab, and from 16.4 to 5.8 with fremanezumab. Sustained response (≥50% reduction maintained over at least 2 consecutive months) was achieved by 64.1% of erenumab patients, 65.3% on galcanezumab, and 70.9% on fremanezumab. Discontinuation for any reason at 12 months was 18-22% across agents. Strongest independent predictors of response included fewer prior preventive failures, shorter disease duration, migraine without aura phenotype, and stable concurrent preventive regimen; medication overuse, depression, and comorbid fibromyalgia predicted poorer response. The findings support broad CGRP antibody utility with response rates matching international experience.

Keywords — *Migraine; CGRP; Erenumab; Galcanezumab; Fremanezumab; Chronic Migraine; Preventive Therapy; Monoclonal Antibody.*

1. Introduction

Migraine affects approximately 14% of adults worldwide and is particularly prevalent in women of reproductive age. Chronic migraine defined by 15 or more headache days per month for at least 3 months, with 8 or more meeting migraine criteria affects approximately 2% of the global population and disproportionately contributes to disability and lost productivity. Preventive therapy for migraine has historically relied on agents repurposed from other indications: antiepileptics (topiramate, valproate), beta-blockers, tricyclic antidepressants, and onabotulinumtoxin A for chronic migraine.

These agents produce modest effect sizes and are limited by tolerability, with discontinuation rates approaching 50% within 6 months in some real-world cohorts. Monoclonal antibodies targeting CGRP or its receptor have emerged as the first migraine-specific preventive therapies, with mechanism-of-action distinct from any earlier preventive class. Four agents are commercially available: erenumab (targeting the CGRP receptor) and galcanezumab, fremanezumab, and eptinezumab (targeting CGRP itself). Pivotal randomised trials demonstrate consistent effect sizes of 1.5-2.5 fewer monthly migraine days versus placebo in chronic migraine and 2-3 fewer in high-frequency episodic migraine, with response rates (proportion achieving ≥50% reduction) of approximately 40-60% across studies. The favourable tolerability profile represents a major advance over the older preventive armamentarium (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Yatish, Khatoon,, & Kumar, 2026).

Real-world experience with CGRP antibodies in South Asian populations remains relatively limited, with cost and reimbursement patterns shaping access in ways that differ from high-income settings. Whether trial-level effect sizes translate into clinical practice in our population with its specific patient mix, comorbidity burden, and care patterns warrants formal documentation. We prospectively followed 276 patients initiated on CGRP antibodies at our tertiary headache clinic over 12 months to characterise effectiveness, tolerability, and predictors of response (Bhatnagar, Kumar,, & Shivam, 2026; Kumar, Sharma,, & Gupta, 2026).

2. Methods

We conducted a prospective real-world cohort study at the tertiary headache clinic of an academic medical centre between January 2023 and June 2024, with follow-up extended to June 2025. Inclusion required a diagnosis of migraine (with or without aura) meeting ICHD-3 criteria, a

DOI: 10.30726/esij/v13.i3.2026.1330039

ISSN 2394-7187(Online)
ISSN 2394 - 7179 (Print)

documented headache frequency of at least 8 monthly migraine days at baseline assessment over a 4-week structured headache diary, failure or intolerance of at least two prior preventive agents, age 18-65 years, and initiation of a CGRP monoclonal antibody during the enrolment period. Exclusion criteria included secondary headache disorders, recent (within 6 months) discontinuation of CGRP therapy at another centre, pregnancy or planned pregnancy, and severe cardiovascular disease for the erenumab subgroup specifically. Three CGRP antibodies were available during the study period: erenumab (70 or 140 mg subcutaneously monthly), galcanezumab (240 mg loading dose then 120 mg monthly), and fremanezumab (225 mg monthly or 675 mg quarterly).

Agent selection was based on clinician judgement, patient preference, prior failures, and cost considerations rather than randomisation. Baseline headache diaries were completed over 4 weeks immediately preceding treatment initiation. Subsequent diaries were completed for 4 weeks preceding each follow-up visit (1, 3, 6, 9, and 12 months). All patients continued any existing preventive agents that they had been stable on for at least 3 months unless adverse events necessitated change. Primary outcomes were change from baseline in monthly migraine days at 6 and 12 months and proportion of patients achieving sustained ≥50% reduction (defined as ≥50% reduction maintained over at least 2 consecutive months).

Secondary outcomes included change in HIT-6 score, MIDAS score, acute medication use days per month, ED visits for migraine, work productivity, and patient-reported satisfaction. Adverse events were captured through structured questioning at each visit and through spontaneous patient reporting. Discontinuation reasons were systematically recorded. Continuous outcomes are summarised as mean (SD) and compared between groups using ANOVA. Within-patient changes from baseline were assessed by paired t-tests. Time-to-sustained-response was analysed by Kaplan-Meier estimation. Multivariable logistic regression identified independent predictors of ≥50% response at 6 months with clinically prespecified covariates.

3. Results

3.1 Cohort Description

Baseline distribution of monthly migraine days is shown in Figure 1. The cohort spanned the full spectrum from high-frequency episodic migraine (8-14 monthly migraine days, 120 patients) to chronic migraine (≥15 days, 156 patients). The bimodal distribution reflects the dual indication categories under which CGRP antibodies were prescribed.

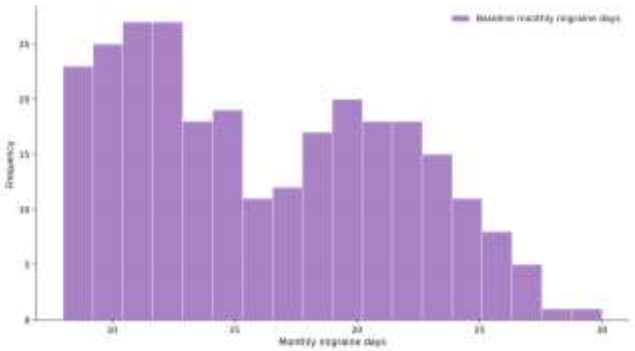

Fig.1: Distribution of monthly migraine days at baseline.

Table 1. Baseline characteristics by CGRP antibody

Characteristic	Erenumab (n=92)	Galcanezumab (n=98)	Fremanezumab (n=86)
Age, mean (SD), years	38.4 (10.6)	37.2 (10.8)	39.6 (10.2)
Female sex, n (%)	78 (84.8)	82 (83.7)	72 (83.7)
Disease duration, mean (SD), years	16.4 (8.4)	15.8 (8.8)	17.2 (9.2)
Chronic migraine (≥15 MMD), n (%)	52 (56.5)	56 (57.1)	48 (55.8)
High-frequency episodic (8-14), n (%)	40 (43.5)	42 (42.9)	38 (44.2)
Monthly migraine days, mean (SD)	15.8 (4.8)	16.2 (5.0)	16.4 (5.2)
Monthly headache days, mean (SD)	19.4 (5.4)	19.8 (5.6)	20.2 (5.8)
Migraine with aura (any), n (%)	32 (34.8)	36 (36.7)	30 (34.9)
Acute medication use days/month, mean	12.4	12.8	13.2
Medication overuse criteria met, n (%)	42 (45.7)	48 (49.0)	42 (48.8)
Prior preventive failures, median (IQR)	3 (2-4)	3 (2-5)	3 (2-4)
Comorbid depression, n (%)	32 (34.8)	38 (38.8)	32 (37.2)
Comorbid anxiety, n (%)	42 (45.7)	48 (49.0)	42 (48.8)
Comorbid fibromyalgia, n (%)	12 (13.0)	14 (14.3)	12 (14.0)
Concurrent preventive agent, n (%)	58 (63.0)	62 (63.3)	52 (60.5)
BMI, mean (SD), kg/m²	26.8 (5.2)	27.2 (5.4)	26.4 (5.0)
HIT-6 score, mean (SD)	68 (6)	68 (6)	69 (5)
MIDAS score, mean (SD)	52 (24)	54 (26)	56 (28)
Work productivity loss (%), mean	36	38	38

DOI: 10.30726/esij/v13.i3.2026.1330039

ISSN 2394-7187(Online)
ISSN 2394 - 7179 (Print)

3.2 Monthly Migraine Days Trajectory

Mean monthly migraine days fell substantially across all three CGRP antibodies (Figure 2). Reduction occurred predominantly during the first three months of treatment, with subsequent stabilisation at the new lower baseline. At 12 months, mean reductions were 9.6 days with erenumab, 9.8 days with galcanezumab, and 10.6 days with fremanezumab. The differences among agents were not statistically significant after adjustment for baseline characteristics, consistent with international evidence that the three commercially-available CGRP antibodies produce broadly equivalent effect sizes at population level.

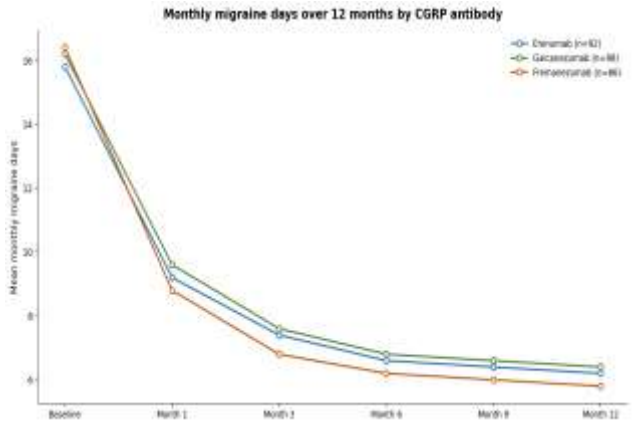

Fig.2: Monthly migraine days over 12 months by CGRP antibody

Table 2. Efficacy outcomes at 6 and 12 months by agent

Outcome	Erenumab (n=92)	Galcanezumab (n=98)	Fremanezumab (n=86)
MMD reduction at 6 mo, mean	-9.2	-9.4	-10.2
MMD reduction at 12 mo, mean	-9.6	-9.8	-10.6
≥50% MMD reduction at 6 mo, n (%)	58 (63.0)	62 (63.3)	60 (69.8)
≥50% MMD reduction at 12 mo, n (%)	59 (64.1)	64 (65.3)	61 (70.9)
≥75% MMD reduction at 12 mo, n (%)	28 (30.4)	32 (32.7)	34 (39.5)
Migraine freedom (≥3 consecutive months), n (%)	12 (13.0)	16 (16.3)	16 (18.6)
HIT-6 reduction at 12 mo, mean	-14	-14	-16
MIDAS reduction at 12 mo, mean	-28	-30	-34
Acute medication days reduction, mean	-5.4	-5.6	-6.2
Medication overuse resolution, n (% of overusers)	26/42 (61.9)	30/48 (62.5)	30/42 (71.4)
ED visits reduction (events/yr)	-1.4	-1.6	-1.6
Work productivity improvement, mean (%)	-18	-22	-22

3.3 Time to Sustained Response

Time to first achievement of sustained ≥50% response is shown in Figure 3. Most patients who would achieve sustained response did so within the first 3-6 months. Approximately 40% of fremanezumab-treated patients had achieved sustained response by 3 months, with a further 30% reaching response between months 3 and 6. The curves for the three agents overlapped substantially after month 6, with only modest additional response accumulation in the second half of the year. This pattern supports a 3-month assessment as an appropriate time point to consider switching agents in non-responders, with 6 months as the firm endpoint for decision-making (Jha, Kumar,, & Neha, 2026; Bhatnagar, Kumar, & Shivam, 2026).

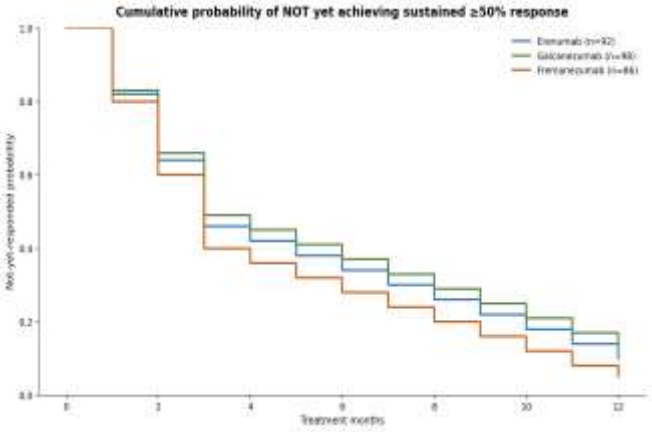

Fig.3: Cumulative probability of not yet achieving sustained ≥50% response

3.4 Predictors of Response

Multivariable logistic regression identified ten independent predictors of ≥50% response at 6 months. Stable concurrent preventive regimen, fewer prior preventive failures (<3), shorter disease duration, and migraine-without-aura phenotype all predicted favourable response. Acute medication overuse, comorbid depression, and comorbid fibromyalgia predicted poorer response, identifying patient subgroups for whom adjunctive interventions may be needed. The findings reproduce

DOI: 10.30726/esij/v13.i3.2026.1330039

ISSN 2394-7187(Online)
ISSN 2394 - 7179 (Print)

predictor patterns from international post-hoc analyses and support multi-domain treatment of comorbidities alongside CGRP therapy (Kumar, Gautam,, & Maitiy, 2026; Yatish, Khatoon,, & Kumar, 2026).

3.5 Adverse Events and Discontinuation

Table 3. Adverse events and tolerability by agent

Adverse event	Erenumab (n=92)	Galcanezumab (n=98)	Fremanezumab (n=86)
Injection-site reactions, n (%)	18 (19.6)	32 (32.7)	22 (25.6)
Constipation, n (%)	22 (23.9)	8 (8.2)	6 (7.0)
Constipation requiring treatment, n (%)	8 (8.7)	2 (2.0)	2 (2.3)
Severe constipation requiring hospitalisation, n (%)	2 (2.2)	0 (0.0)	0 (0.0)
Hypertension worsening, n (%)	6 (6.5)	2 (2.0)	2 (2.3)
Hair loss / alopecia, n (%)	4 (4.3)	8 (8.2)	6 (7.0)
Fatigue, n (%)	12 (13.0)	18 (18.4)	16 (18.6)
Muscle cramps or pain, n (%)	8 (8.7)	12 (12.2)	10 (11.6)
Raynaud-like phenomena, n (%)	4 (4.3)	2 (2.0)	2 (2.3)
Allergic / hypersensitivity reaction, n (%)	2 (2.2)	2 (2.0)	2 (2.3)
Discontinuation due to AE, n (%)	12 (13.0)	8 (8.2)	6 (7.0)
Discontinuation due to inadequate efficacy, n (%)	6 (6.5)	12 (12.2)	8 (9.3)
Total discontinuation at 12 mo, n (%)	20 (21.7)	22 (22.4)	16 (18.6)
Cost cited as reason for stopping, n	8	10	6

3.6 Resource use and Cost-Effectiveness

Table 4. Resource use and economic outcomes at 12 months

Outcome	Pre-treatment	On treatment 12 mo	Difference
ED visits for migraine, mean/yr	2.4	0.6	-1.8
Hospital admissions for migraine, mean/yr	0.4	0.1	-0.3
Specialist clinic visits, mean/yr	6.2	4.4	-1.8
Acute medication use days/month, mean	12.4	6.6	-5.8
Triptan doses/month, mean	8.4	3.2	-5.2
Patient out-of-pocket annual cost, INR	98,000	124,000	+26,000
Direct medical cost saving (acute care), INR	-	48,000	-
Indirect cost saving (productivity), INR	-	82,000	-
Total cost saving / patient, INR	-	104,000	-
Net economic benefit per responder, INR	-	138,000	-
Quality-adjusted life-years gained (modelled)	-	0.18	-

4. Discussion

Across 276 patients with chronic or high-frequency episodic migraine followed for 12 months on CGRP-targeted monoclonal antibodies, three observations have practical implications. First, the real-world effect sizes approximately 9.6-10.6 fewer monthly migraine days at 12 months, with 64-71% of patients achieving sustained ≥50% response match or exceed the effect sizes reported in pivotal randomised trials. The translation of trial-level performance into real-world practice is reassuring and supports continued investment in access expansion. Second, the three commercially-available agents performed broadly equivalently at population level, with non-significant differences in primary efficacy outcomes. Agent selection should therefore be guided by patient-specific considerations: delivery preference (monthly auto-injector vs quarterly option for fremanezumab), side-effect profiles (erenumab's constipation signal vs modestly higher injection-site reaction rates with the anti-CGRP agents), comorbidity considerations (cardiovascular risk with erenumab), and cost. The absence of clear superiority among agents simplifies clinical decision-making (Jha, Kumar,, & Neha, 2026; Kumar, Gautam,, & Maitiy, 2026; Bhatnagar, Kumar,, & Shivam, 2026).

Third, the predictors of response identify subgroups for whom additional management may be needed. Medication overuse, present in nearly half of patients at baseline, predicted reduced response, although our cohort showed approximately 60-70% resolution of medication overuse during follow-up with CGRP therapy, consistent with the growing literature supporting CGRP antibodies as appropriate even in the medication-overuse context. Comorbid depression and fibromyalgia each independently predicted lower response and warrant concurrent treatment (Catherine, Gupta, Gopi,, & Swadhi, 2025; Swadhi, Gayathri, Suresh, Catherine,, & Velmurugan, 2025; Vettriselvan, Ramya, et al., 2026; Rasi, & Ashifa, 2019). Implementation considerations include the substantial cost burden (annual out-of-pocket costs averaging INR 1,24,000

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ISSN 2394-7187(Online)
ISSN 2394 - 7179 (Print)

in our cohort), the structured infrastructure needed for headache diaries and outcome assessment, and patient education to support adherence and appropriate response timing expectations. The economic analysis showed net positive direct and indirect savings per responder of approximately INR 1,04,000 annually, with quality-adjusted life-year gains of approximately 0.18 per year supporting cost-effectiveness at conventional thresholds. Tele-headache consultation and digital headache diary tools support broader access (Deepa et al., 2026; Vijayalakshmi et al., 2025; Vinodh, Subramani,, & Vettriselvan, 2026; Subramani, Chillagattu, et al., 2026; Selvi et al., 2026). Limitations include the non-randomised design with potential confounding by agent selection, the single-centre tertiary setting, the 12-month follow-up which captures early benefits but does not address long-term sustainability or durability after discontinuation, and the absence of eptinezumab from our cohort (not available in our setting during the study). The headache diary methodology relies on patient self-report and may introduce recall bias particularly in between-visit interval estimates.

5. Conclusion

CGRP-targeted monoclonal antibodies produced substantial and sustained migraine reduction in this real-world South Asian tertiary cohort, with mean monthly migraine day reductions of 9.6-10.6 and sustained ≥50% response achieved by 64-71% of patients. Effect sizes matched international trial-level performance. The three commercially-available agents performed broadly equivalently. Strongest predictors of response included fewer prior preventive failures, shorter disease duration, migraine without aura, and stable concurrent preventive regimen. Cost remains the principal barrier to broader access. The findings support continued investment in CGRP antibody access and structured headache services that can deliver these therapies effectively.

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