Retrospective Review

# Real-World Insights into Dual Calcitonin Gene-Related Peptide (CGRP) Therapies for Chronic Migraine: A Retrospective Review

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**Background:** Patients on regimens of a single calcitonin gene-related peptide (CGRP) may show a delayed response to migraine symptoms. Individuals on such regimens may not even exhibit a reduction of migraine symptoms within a reasonable time frame. Some clinicians have elected to combine small-molecule antagonists (SMAs) and ligand monoclonal antibodies (L-mAbs) to target CGRP molecules and receptors for the purpose of potentially providing increased synergistic relief.

**Objectives:** This study aimed to compare the safety and effectiveness of dual-CGRP therapy for patients receiving combined synergistic SMA and L-mAb to the safety and effectiveness of mono-CGRP treatment.

**Study Design:** A retrospective matched cohort study.

**Setting:** This study was conducted at a single neurological center in the United States.

**Methods:** A retrospective matched cohort study at a neurological care center analyzed 90 chronic migraine patients who were aged ≥ 18 years and treated with CGRP inhibitors (L-mAbs: fremanezumab, galcanezumab, eptinezumab; SMAs: ubrogepant, rimegepant, atogepant; or a combination) between May 2018 and February 2024. The study compared 27 patients receiving dual L-mAb and SMA CGRP treatments with 63 patients receiving mono-L-mAb or mono-SMA CGRP treatments, matched by age and gender. Variables included current age, age at diagnosis, gender, onabotulinumtoxinA use, headache frequency, duration, severity, and associated symptoms before the treatment and 3 months after it. Adverse events were recorded for both treatment groups. All hypothesis tests were two-tailed and considered significant at a $P$-value < 0.05.

**Results:** Dual-CGRP therapy reduced headache severity by 20%, in contrast to the 10% reduction seen with mono-CGRP therapy ($P = 0.039$). Patients receiving dual-CGRP therapy also experienced an average reduction of 4 headache days, with some patients experiencing up to 14 fewer days, while mono-CGRP patients showed no change; however, this finding was not statistically significant ($P = 0.112$). No significant differences in other migraine-associated symptoms were found between the groups. Adverse events in the mono- and dual-CGRP groups were mild, with no serious adverse events or discontinuations reported.

**Limitations:** Limitations of our study include a relatively small sample size, the study's retrospective design, the absence of newer CGRP agents, an inability to control confounders, and the predominant use of a few CGRP inhibitors among patients.

**Conclusion:** Dual-CGRP regimens may enhance migraine symptom control by reducing headache severity without causing significant adverse events. However, these findings need confirmation through randomized, placebo-controlled clinical trials that use larger sample sizes.

**Key words:** Calcitonin gene-related peptide, calcitonin gene-related peptide inhibitors, headache, migraine, monoclonal antibodies, small molecule antagonist

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While single calcitonin gene-related peptide (CGRP) regimens are mostly effective for treating migraines, some patients who receive CGRP monotherapy show a delayed treatment response, taking weeks to months or even failing to see any clinically significant decrease in migraine frequency (1,2). Combining a small molecule antagonist (SMA) with a CGRP monoclonal antibody (mAb) can antagonize CGRP receptors and molecules simultaneously, potentially eliciting faster synergistic relief. The advantage of the dual CGRP blockade lies in the complementary mechanisms by which SMAs can cross the blood-brain barrier and be absorbed rapidly, making them effective for aborting acute migraine attacks. In contrast, mABs do not cross the barrier and are used for long-term preventive treatment (3). While this theoretical approach offers an alternative treatment option, more evidence is required to support the use of different combinations of CGRP inhibitors in clinical practice. Research on dual-CGRP therapy is limited, and the few existing studies are restricted by not including various SMAs or focusing primarily on safety and tolerability (4,5).

This study aims to add to the existing literature on dual-CGRP therapy by directly comparing the effectiveness of dual-CGRP treatment with ligand-targeting monoclonal antibody (L-mAb) and SMA to that of monotherapy therapy in a matched cohort. The novelty of our study lies in its systemic evaluation of the real-world effectiveness and safety of dual-CGRP therapy, specifically the combined use of an L-mAb and SMA in chronic migraine patients. The present study specifically addresses the hypothesis that dual-CGRP therapy is more effective than mono-CGRP therapy in reducing migraine symptoms, including headache frequency, severity, and associated symptoms, without increasing the incidence of significant adverse events.

## Methods

A retrospective matched cohort study was conducted at a single neurological care center in Hawaii, with ethical approval obtained from the University of Hawaii Institutional Review Board. Data from the center identified adults aged ≥ 18 years who had been diagnosed with migraines and received at least one CGRP treatment between May 2018 and February 2024. Chronic migraine patients (monthly headache days > 15) with an ICD-10 diagnosis (G43.0-9) and treated with L-mAb (fremanezumab, galcanezumab, and eptinezumab) and an SMA (ubrogepant, rimegepant, and atogepant) were included. The dual L-mAb-and-SMA CGRP treatment group was compared to the mono-L-mAb or mono-SMA CGRP group. To facilitate comparison, patients in the dual-treatment group were selected to be similar in age and gender to those in the mono-therapy group at the time of clinic presentation; however, no propensity score matching or multivariable adjustment for other covariates was performed. Patients without a 3-month follow-up after CGRP treatment initiation or not concurrently taking both CGRPs in the dual group were excluded. Patients receiving combination-CGRP regimens of receptor-targeting mAb [R-mAb] and L-mAb, dual L-mAb, SMA and R-mAb, or dual SMAs were excluded due to insufficient sample size. Rimegepant was primarily taken as needed by dual-CGRP patients.

Variables recorded included patient socio-demographics (age, age at diagnosis, and gender), onabotulinumtoxinA use, and migraine symptoms. Baseline data on headache frequency, severity, and associated symptoms for both mono- and dual-CGRP groups were collected when a new CGRP inhibitor was prescribed, and those data were compared at the 3-month follow-up (6-9). Monthly headache data and commonly associated symptoms (photophobia, phonophobia, aura, and nausea) were collected from patient recall. Headache severity was self-reported on a scale of 0 to 10 for average and maximum monthly severity (10). Adverse events in the mono- and dual-CGRP groups were recorded at the three-month follow-up visit. No data were missing in the final sampled patient group.

The normality of continuous variables was assessed using the Shapiro–Wilk normality test. Normally distributed variables were presented as means and standard deviations and evaluated using Welch's t-test. Variables not normally distributed were presented as medians and interquartiles (Q1 and Q3) evaluated using the Wilcoxon rank-sum test. Categorical variables were presented as contingency tables with percentages, and associations were assessed using Pearson's chi-squared test or Fisher's exact test when expected cell counts were 5 or fewer. Statistical significance was set at 0.05. All calculations were performed in R version 4.4.1 (11).

## Results

Sixty-seven chronic migraine patients on various dual-CGRP regimens were identified. Thirty patients were excluded due to CGRP combinations beyond the study's scope and small sample size: 2 receptor mAb (R-mAb) and L-mAb, 2 dual-L-mAbs, 10 SMA and R-mAbs, and 16 dual-SMAs. Another 10 patients were excluded

for lacking a 3-month follow-up. Thus, 27 patients on synergistic L-mAb and SMA treatment were included. They have been on their initial CGRP inhibitor for an average of 12 months, with a range of one to 34 months. Table 1 shows the dual L-mAb and SMA treatment combinations and the sequence of CGRP inhibitors prescribed. Among the 27 patients, 13 (48%) were on both fremanezumab and ubrogepant, 7 (26%) were on both fremanezumab and rimegepant, 3 (11%) were on both galcanezumab and ubrogepant, and 4 (15%) were on both galcanezumab and rimegepant.

Seventy-two mono-L-mAb or mono-SMA treatments were identified. Nine were excluded due to insurance denial or the lack of a 3-month follow-up. Among the remaining 63 patients, 7 (11%) used fremanezumab, 3 (5%) used galcanezumab, one (2%) used eptinezumab, 32 (51%) used ubrogepant, 16 (25%) used rimegepant, and 4 (6%) used atogepant.

Table 2 summarizes the demographics and pretreatment characteristics for the mono- and dual-CGRP groups. The mono-CGRP group had 46 female patients (73%), whereas the dual-CGRP group had 17 (63%). The median age at diagnosis was 29 overall, with 28 in the mono-CGRP group and 31 in the dual-CGRP ($P$ = 0.867). The mean patient age was 46 overall. Patients in the dual-CGRP group had a median age of 43, slightly younger than the 47 in the mono-CGRP group ($P$ = 0.262). OnabotulinumtoxinA was concurrently used by 44 patients overall (49%), 30 (48%) in the mono-CGRP group and 14 (52%) in the dual-CGRP group, showing no statistically significant difference ($P$ = 0.713). At baseline, the dual-CGRP group had greater headache severity, with a median severity of 7 ($P$ < 0.001). While the headache episodes in this group had shorter durations ($P$ = 0.006), the mono-CGRP group had a higher proportion of aura ($P$ < 0.002).

Table 3 summarizes changes in headache frequency, severity, and duration for mono- and dual-CGRP treatment patients before and after their procedures. The dual-CGRP group had an average reduction of 4 headache days, with some experiencing up to 14 fewer days. The difference in headache frequency between the 2 groups was not statistically significant ($P$ = 0.112). However, the dual-CGRP therapy was associated with a 20% reduction in headache severity, a greater decrease than the 10% reduction associated with the mono-CGRP therapy ($P$ = 0.039). Maximum headache severity decreased in both groups, though the difference was not statistically significant ($P$ = 0.305). There was no significant change in headache duration for either group, and the difference between them was not significant ($P$ = 0.423).

Table 4 presents changes in photophobia, phonophobia, aura, and nausea. One mono-CGRP patient (2%) ceased experiencing photophobia after treatment. Regarding phonophobia, 2 mono-CGRP patients (3%) developed the condition, while one dual-CGRP patient (3%) stopped experiencing it. One dual-CGRP patient (4%) developed nausea, while another dual-CGRP patient and one mono-CGRP patient (2%) no longer experienced it. Nevertheless, there were no significant differences between the 2 groups in the prevalence of new-onset photophobia, phonophobia, or nausea or the resolution of any of those conditions.

A post hoc analysis also showed that dual-CGRP patients had a higher proportion of a continued absence of auras, with auras being absent from 13 patients in the dual-CGRP group (48%) as opposed to 12 patients (19%) in the mono-CGRP group ($P$ = 0.027). Mono-CGRP therapy showed an association with a higher proportion of the continued presence of auras, which persisted in 49 patients in that group (78%) and only 12 patients (44%) in the dual-CGRP group ($P$ = 0.012). Two mono-CGRP patients (3%) and one dual-CGRP patient (4%) stopped experiencing auras post-treatment, while one dual-CGRP patient (4%) developed new-onset

Table 1. *Dual-CGRP sequence.*

| | | Secondary CGRP | | | | | |
|---|---|---|---|---|---|---|---|
| | | **Fremanezumab (n = 10)** | **Galcanezumab (n = 3)** | **Epitenezumab (n = 0)** | **Ubrogepant (n = 6)** | **Rimegepant (n = 8)** | **Atogepant (n = 0)** |
| **Initial CGRP** | Fremanezumab (n = 11) | 0 | 0 | 0 | 5 | 6 | 0 |
| | Galcanezumab (n = 3) | 0 | 0 | 0 | 1 | 2 | 0 |
| | Epitenezumab (n = 0) | 0 | 0 | 0 | 0 | 0 | 0 |
| | Ubrogepant (n = 11) | 9 | 2 | 0 | 0 | 0 | 0 |
| | Rimegepant (n = 2) | 1 | 1 | 0 | 0 | 0 | 0 |
| | Atogepant (n = 0) | 0 | 0 | 0 | 0 | 0 | 0 |

Table 2. *Patient characteristics*.

| Characteristics | Overall n = 90 | Dual-CGRP Patients n = 27 | Mono-CGRP n = 63 | *P*-value |
|---|---|---|---|---|
| Age at Diagnosis (1) | 29 (18, 41) | 31 (16, 39) | 28 (18, 42) | 0.867 |
| Current Age (2) | 46 (13) | 43 (13) | 47 (13) | 0.262 |
| Gender | | | | |
| Male (3) | 27 (30%) | 10 (37%) | 17 (27%) | 0.340 |
| Female (3) | 63 (70%) | 17 (63%) | 46 (73%) | |
| OnabotulinumtoxinA Use | | | | |
| Yes (3) | 44 (49%) | 14 (52%) | 30 (48%) | 0.713 |
| Pretreatment Characteristics | | | | |
| Migraine Frequency (days) (1) | 18 (10, 30) | 30 (15, 30) | 15 (10, 30) | 0.083 |
| Headache Severity (0-10 Scale) (1) | 6.0 (5.0, 8.0) | 7.0 (5.0, 9.0) | 5.0 (4.0, 6.0) | < 0.001 |
| Max Severity (0-10 Scale) (1) | 8.5 (7.0, 10.0) | 9.0 (8.0, 10.0) | 8.0 (7.0, 10.0) | 0.456 |
| Episode Duration (hours) (1) | 1.0 (1.0, 3.0) | 1.0 (0.3, 1.0) | 2.0 (1.0, 3.0) | 0.006 |
| Photophobia (1) | 66 (73%) | 22 (81%) | 44 (70%) | 0.252 |
| Phonophobia (1) | 51 (57%) | 19 (70%) | 32 (51%) | 0.086 |
| Aura (1) | 64 (71%) | 13 (48%) | 51 (81%) | 0.002 |
| Nausea (1) | 62 (69%) | 18 (67%) | 44 (70%) | 0.766 |

(1) median (Q1, Q3); Wilcoxon rank-sum test
(2) mean (SD); Welch 2-sample t-test
(3) n (%); Pearson's chi-squared test

Table 3. *Changes in migraine frequency, severity, and duration*.

| Characteristic | Patient Group | | | |
|---|---|---|---|---|
| | Overall n = 90 | Dual-CGRP n = 27 | Mono-CGRP n = 63 | *P*-value |
| Change in Migraine Frequency (days) (1) | 0.0 (-6.0, 0.0) | -4.0 (-15.0, 0.0) | 0.0 (-5.0, 0.0) | 0.112 |
| Change in Headache Severity (0-10 scale) (1) | -1.0 (-2.0, 0.0) | -2.0 (-3.0, 0.0) | -1.0 (-2.0, 0.0) | 0.039 |
| Change in Max Severity (0-10 scale) (1) | -2.0 (-2.0, 0.0) | -2.0 (-2.0, 0.0) | -2.0 (-2.0, 0.0) | 0.305 |
| Change in Duration (hours) (1) | 0.0 (0.0, 0.0) | 0.0 (0.0, 0.0) | 0.0 (0.0, 0.0) | 0.423 |

(1) median (Q1, Q3); Wilcoxon rank-sum test

auras. The 2 mono-CGRP patients no longer experiencing auras post-treatment were on atogepant, a CGRP inhibitor not used by the dual-CGRP patients. However, the prevalence of new-onset or resolved aura between the 2 groups was not statistically significant.

Since 5 mono-CGRP patients were on epitenezumab and atogepant, which were CGRP inhibitors not included in the dual-CGRP group, a sensitivity analysis was conducted without these patients. No changes to this study's findings ensued.

The reported adverse events in the mono- and dual-CGRP groups were generally mild. In the mono-CGRP group, 4 patients reported fatigue, dizziness, and sleepiness. Two patients reported mild bruising at the injection site. In the dual-CGRP group, 3 patients reported experiencing fatigue, drowsiness, and mild constipation. No patients from either group discontinued their treatment, and no serious adverse events were reported.

## Discussion

Since the introduction of CGRP inhibitors, including mAbs as well as SMAs, these agents have revolutionized the clinical approach to migraine treatment due to their superior efficacy and tolerability profile. While CGRP inhibitors were initially not considered first-line treatments and the administration of these amino acid chains required the prior failure of other therapies, there is now a growing push to position CGRP therapy as a first-line option, since it is specifically designed for migraine treatment, unlike other abortive or preventative therapies originally developed for different indications (12). Despite the promise of this type of therapy, some migraine patients who receive it do not experience improvements in their symptoms within 3 months. A multicenter, prospective, observational study found that approximately 40% of patients did not achieve a clinically significant response rate within 12 weeks, although the majority eventually responded to treatment by 48 weeks (1). Additionally, some patients experienced a loss of efficacy or failed to respond even after switching to a different monoclonal antibody (2). Adding a second CGRP agent to achieve faster and more reliable improvement in patients is, therefore, a reasonable possibility worth investigating.

Our findings provide preliminary evidence for the

Table 4. *Changes in photophobia, phonophobia, aura, and nausea.*

| | Overall n = 90 | Dual CGRP n = 27 | Mono-CGRP n = 63 | *P*-value |
|---|---|---|---|---|
| Change in Photophobia (1) | | | | |
| Remained non-photophobic | 24 (27%) | 5 (19%) | 19 (30%) | 0.512 |
| Became photophobic | 0 (0%) | 0 (0%) | 0 (0%) | |
| Stopped being photophobic | 1 (1%) | 0 (0%) | 1 (2%) | |
| Remained photophobic | 65 (72%) | 22 (81%) | 43 (68%) | |
| Change in Phonophobia (1) | | | | |
| Remained non-phonophobic | 37 (41%) | 8 (30%) | 29 (46%) | 0.147 |
| Became phonophobic | 2 (2%) | 0 (0%) | 2 (3%) | |
| Stopped being phonophobic | 1 (1%) | 1 (4%) | 0 (0%) | |
| Remained phonophobic | 50 (56%) | 18 (67%) | 32 (51%) | |
| Change in Aura (1) | | | | |
| Remained without an aura | 25 (28%) | 13 (48%) | 12 (19%) | 0.004 |
| Developed an aura | 1 (1%) | 1 (4%) | 0 (0%) | |
| Stopped having an aura | 3 (3%) | 1 (4%) | 2 (3%) | |
| Retained an aura | 61 (68%) | 12 (44%) | 49 (78%) | |
| Change in Nausea (1) | | | | |
| Remained non-nauseated | 27 (30%) | 8 (30%) | 19 (30%) | 0.386 |
| Became nauseated | 1 (1%) | 1 (4%) | 0 (0%) | |
| Stopped being nauseated | 2 (2%) | 1 (4%) | 1 (2%) | |
| Remained nauseated | 60 (67%) | 17 (62%) | 43 (68%) | |

(1) n (%); Fisher's exact test

potential benefits and tolerability of dual-CGRP regimens for treating chronic migraines. Combinations, such as that of ubrogepant and CGRP mAbs, have shown promise in significantly reducing pain severity and the time before the patient resumes normal functioning (4). Case reports have highlighted the benefits of combining erenumab and rimegepant for patients resistant to multiple medications (13). A retrospective study supports the safety and tolerability of dual-CGRP treatment that combines mAbs with either ubrogepant or rimegepant (14).

Our study found that dual-CGRP therapy reduced headache severity, potentially alleviating disability and improving the quality of life for migraine patients ($P = 0.039$). While baseline and changes in monthly migraine frequency did not differ significantly between groups, the dual-CGRP group had a median of 30 headache days as opposed to 15 days in the mono-CGRP group ($P = 0.083$). This finding suggests a worse initial presentation in the dual-CGRP group, further supported by their higher baseline headache severity ($P < 0.001$). Despite the lack of statistical significance, dual-CGRP patients experienced an average reduction of 4 headache days, whereas the mono-CGRP group showed no change. While it may not be clinically significant, this reduction may decrease the economic burden of migraines, since 60,000 to 68,600 workdays are lost annually due to absenteeism and presenteeism, resulting in indirect costs 6.2 to 8.5 times higher than annual direct costs (15,16). In this study, the observed changes in migraine frequency may have been influenced by the composition of the mono-CGRP group. Many patients in this group were on a preventive regimen that included mAbs and atogepant and was aimed at reducing migraine days, while other patients were receiving acute treatment with ubrogepant or rimegepant. It is not entirely clear whether patients used rimegepant solely for abortive or preventative purposes, which might have impacted the outcome of monthly migraine days. A 2-point reduction in headache severity in the dual-CGRP group compared to a one-point reduction in the mono-CGRP group is considered moderately clinically meaningful. This difference suggests a potential benefit of up to a 30% reduction in headache severity for patients who have not responded to traditional acute and preventative migraine therapies other than CGRP inhibitors (15-17). Additionally, since dual-CGRP patients presented with a worse clinical profile, characterized by higher headache severity and likely prior mono-CGRP therapy failure, dual-CGRP therapy may still provide meaningful reductions in headache severity and significant improvements in quality of life for patients refractory to mono-CGRP therapy. Neither mono- nor dual-CGRP treatments alter headache duration significantly, indicating the possible need for additional acute medications.

Regarding associated symptoms, the mono-CGRP group had a higher proportion of patients with auras at baseline. After treatment, however, there was no difference between the 2 groups in the prevalence of patients who stopped experiencing auras or who de-

veloped auras, suggesting that CGRP therapies had a minimal impact on aura symptoms. The development of auras and nausea among dual-CGRP patients may be outliers. One patient developed an aura, while another ceased having an aura following dual-CGRP treatment. A similar finding was observed regarding nausea. The contrasting changes in aura and nausea suggest multifactorial influences beyond dual-CGRP treatment alone. As was the case with auras, the prevalence of new-onset or resolved nausea symptoms between the 2 groups was not statistically significant, and the number of reported cases was too small to draw meaningful conclusions. Larger studies are needed to assess the effects of CGRP therapy on symptoms like auras, photophobia, phonophobia, and nausea.

Health care providers have been hesitant to initiate dual-CGRP therapy due to limited clinical evidence and concerns about adverse events, despite these inhibitors being generally associated with mild side effects. Cardiovascular and inflammatory complications are possible, given CGRP's role in the pathogenesis of migraines via vasodilation of intracranial vessels and local neuro-inflammatory cascades (18-22). A case series highlighted 8 patients who developed inflammatory complications, such as polyarthralgia or worsening of underlying psoriatic arthritis, after starting a single CGRP mAb therapy (erenumab, fremanezumab, or galcanezumab), with no other attributable causes (22). Another study noted the exacerbation of hypertension in veteran migraine patients treated with topiramate, CGRP-mAbs, or SMAs (23). Despite potential cardiac and inflammatory complications, our study showed mild and expected side effects (fatigue, drowsiness, or constipation) in both CGRP groups, with no serious adverse events or treatment discontinuations (24-26).

## Limitations

This study has a few limitations. The retrospective cohort design precludes causal inference and is subject to potential selection and recall biases. Additionally, our sample size, particularly in the dual therapy group (n = 27), was relatively small, which limited statistical power and ability to detect significant differences between groups. Third, although we attempted to minimize confounding by matching patients on age and gender, we did not perform propensity score matching or multivariable adjustment. Consequently, the groups remained imbalanced on major clinical variables such as baseline headache frequency and severity. The dual-therapy group had a worse initial presentation, which may have influenced observed treatment effects and limited comparability. Fourth, the study was conducted at a single center with a predominance of certain CGRP inhibitor combinations, and newer CGRP agents such as zavzpret were underrepresented, which might have also limited the generalizability of our findings. In addition, 5 mono-CGRP patients, receiving either eptinezumab or atogepant, agents not used by dual-CGRP patients, were included. Including these mono-CGRP patients may have positively skewed treatment outcomes in the mono-CGRP group, since both eptinezumab and atogepant are considered superior in efficacy to other agents (27,28). However, a sensitivity analysis that excluded those 5 patients showed no statistically significant difference in outcomes. Patient distribution across treatment regimens could have also influenced our results. Most patients in both groups were on rimegepant or ubrogepant, or were receiving an mAb in addition to one of these gepants. This preference may have contributed to a potential bias in treatment outcomes. Fifth, outcomes were assessed at 3 months, which may not have captured delayed or long-term responses to therapy. Studies suggest that some patients may have a delayed response to treatment or experience a loss of efficacy over time (1,2). Including additional follow-up data at 6 months, 9 months, or one year could provide a more comprehensive understanding of long-term patient responses and tolerability. Sixth, there was variability in the timing of the initial CGRP inhibitor prescription among dual-CGRP patients. A longer duration of initial monotherapy in the dual-CGRP group may have resulted in a greater cumulative anti-migraine effect than the 3-month follow-up period for monotherapy. Finally, grouping all mono-therapy patients may have obscured the difference between L-mAb and SMA monotherapy. These limitations highlight the need for larger, prospective, multicenter studies with more comprehensive matching or adjustment for baseline characteristics and longer follow-up periods, to confirm the effectiveness and safety of dual-CGRP therapy.

While dual-CGRP therapies may not offer substantial improvement in symptoms compared to monotherapy, such management methods remain a tolerable option for patients who are refractory to multiple migraine treatments, including mono-CGRP therapy, given the significant reduction in headache severity and the potential benefit of reducing the frequency of monthly migraines. Combining SMAs with L-mAbs presents a promising approach for enhancing therapeutic outcomes and improving patients' quality of life.

## Conclusion

Our findings suggest that dual-CGRP regimens may enhance migraine symptom control by reducing headache severity significantly, with no significant adverse events observed. These findings, however, require corroboration with prospective studies.

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### Authors' Contributions

All authors read and approved the final manuscript. Responsibilities broke down as follows:

HL: conceptualization, methodology, formal analysis, investigation, data curation, original draft, reviewing and editing, project administration

AJC: methodology, formal analysis, investigation, data curation, original draft, reviewing and editing, project administration

AYL: investigation, reviewing and editing, project administration

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