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ARTICLE

CALCITONIN GENE-RELATED PEPTIDE (CGRP) INHIBITORS IN EPISODIC AND CHRONIC MIGRAINES A MULTIPLE TREATMENT COMPARISON (MTC) META-ANALYSIS

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ABSTRACT

Approximately 15% of adults worldwide suffer from migraines, a neurological disease that causes pulsing headaches. Regular treatments are often insufficient and can cause pharmaceutical overuse headaches. CGRP inhibitors target migraine pathogenesis and are prospective migraine preventative therapies. This meta-analysis examines the efficacy and safety of CGRP inhibitors in lowering episodic and chronic migraine monthly migraine days (MMD). A comprehensive search of ScienceDirect, PubMed, CENTRAL, and Wiley was conducted through January 29, 2023. CGRP inhibitor RCTs with MMD as the primary endpoint were included. To address clinical heterogeneity, Review Manager 5.4 used random-effects models to integrate 32 quantitative studies and 42 qualitative investigations. The analysis comprised 22,295 patients from 2013–2022 trials. CGRP inhibitors reduced MMD more than placebo (Mean Difference -2.12; 95% CI -2.41 to -1.84; p=0.02). Erenumab had the smallest effect, whereas galcanezumab had the largest. Good research quality and little bias were found in most investigations. Similar safety to placebo. MMD is greatly reduced by safe and effective CGRP medications for migraine prophylaxis. The findings support their inclusion in migraine management guidelines. Further study is needed to assess efficacy variations among varied populations.

Keywords: *CGRP inhibitor; Migraine; Preventive treatment*

АБСТРАКТ

Примерно 15 % взрослых во всем мире страдают от мигрени, неврологического заболевания, вызывающего пульсирующие головные боли. Регулярное лечение часто бывает недостаточным и может приводить к головным болям, вызванным чрезмерным употреблением лекарственных средств. Ингибиторы CGRP воздействуют на патогенез мигрени и являются перспективными средствами профилактики мигрени. В данном метаанализе изучается эффективность и безопасность ингибиторов CGRP в снижении числа эпизодических и хронических мигреней в месяц (MMD). Был проведен всесторонний поиск в базах данных ScienceDirect, PubMed, CENTRAL и Wiley по состоянию на 29 января 2023 года. Были включены РКИ с ингибиторами CGRP, в которых MMD был основной конечной точкой. Для устранения клинической гетерогенности в Review Manager 5.4 были использованы модели со случайными эффектами для интеграции 32 количественных исследований и 42 качественных исследований. Анализ охватил 22 295 пациентов из испытаний, проведенных в 2013–2022 годах. Ингибиторы CGRP снижали MMD в большей степени, чем плацебо (средняя разница -2,12; 95% ДИ -2,41 до -1,84; p=0,02). Эренумаб имел наименьший эффект, а галканезумаб — наибольший. В большинстве исследований было отмечено хорошее качество исследований и небольшая предвзятость. Безопасность аналогична плацебо. MMD значительно снижается благодаря безопасным и эффективным препаратам CGRP для профилактики мигрени. Результаты подтверждают их включение в рекомендации по лечению мигрени. Необходимы дальнейшие исследования для оценки различий в эффективности среди различных групп населения.

Ключевые слова: *ингибитор CGRP; мигрень; профилактическое лечение.*

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INTRODUCTION

Migraine constitutes a multifaceted neurological disorder characterized by recurrent episodes of throbbing headache pain. As of 2021, this condition has contributed to disability in at least 15% of the global adult population, with potential under-reporting likely increasing this estimate[1,2]. Migraine disproportionately affects women relative to men, exhibiting a prevalence ratio of approximately 3:1. The magnitude of its impact is determined by the severity and frequency of attacks, which can result in functional impairment and reduced quality of life, especially in instances of daily or near-daily occurrences[4]. Societal consequences are exacerbated, as migraine prevalence reaches its zenith during the second, third, and fourth decades of life, coinciding with periods of peak productivity[5]. Burdens extend across both ictal (during attacks) and interictal (between attacks) phases, with acute pain predominating in the former and anticipatory anxiety or scheduling difficulties prevailing in the latter[6].

Management of migraine encompasses acute abortive therapies and prophylactic preventive strategies. Conventional approaches frequently prove inadequate in achieving sufficient pain relief, may precipitate adverse effects, and pose risks of medication-overuse headache[7]. Ergot alkaloids and their derivatives address migraine etiology but demonstrate suboptimal tolerability, whereas simple analgesics provide symptomatic alleviation with enhanced tolerance yet fail to target underlying mechanisms. These shortcomings have catalyzed the advancement of calcitonin gene-related peptide (CGRP) inhibitors, a targeted therapeutic class[8].

Identified more than three decades ago, CGRP serves as a neuropeptide within the central and peripheral nervous systems, modulating pain transmission. Investigations in animal models and human subjects have established that CGRP is liberated during migraine attacks, and its exogenous administration can elicit migraine-like symptoms[9]. Present in α and β isoforms, CGRP induces cerebral artery dilation, mast cell degranulation in the trigeminovascular system, and nociception[9]. Inhibition through monoclonal antibodies (mAbs) directed at CGRP (eptinezumab, galcanezumab, fremanezumab) or its receptor (erenumab), alongside small-molecule gepants (atogepant, rimegepant for prevention), has yielded promising results in both episodic and chronic migraine[11,12,13].

Recent evidence, including systematic reviews and network meta-analyses as of 2025, underscores the efficacy of CGRP inhibitors in reducing monthly migraine days (MMDs) for episodic (<15 headache days per month) and chronic (≥15 days) migraine, with reductions ranging from 1.2 to 4.4 days compared to placebo. Among mAbs, higher doses (e.g., erenumab 140 mg, eptinezumab 300 mg) exhibit superior outcomes in achieving ≥50% MMD reductions and medication-overuse headache remission, particularly in chronic cases, with odds ratios of 2.43 and 1.97, respectively[6]. Gepants demonstrate comparable efficacy, with atogepant and rimegepant reducing MMDs by 3.6 to 4.4 days, often surpassing traditional prophylactics such as beta-blockers or antiseizure medications in consistency and magnitude[8]. Safety profiles are favorable, with lower discontinuation rates than older agents; common adverse events include injection-site reactions (15-30% for mAbs), constipation (up to 3% for erenumab), and nausea (2-4% for gepants), without elevated risks of serious events in low-risk populations. However, long-term cardiovascular monitoring is advised in patients with comorbidities due to theoretical vasodilation concerns[9].

Considerations for diverse patient populations reveal limitations in evidence. In adolescents, emerging data indicate efficacy akin to adults, though not yet approved for those under 18 years. Elderly patients exhibit

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similar profiles, with gepants preferred for injection aversion. Pregnancy and lactation warrant avoidance owing to insufficient safety data and potential fetal risks. Ethnic diversity in trials remains underrepresented, yet efficacy appears consistent across groups. Awareness of CGRP inhibitors among patients is notably low, at approximately one-third, compounded by access barriers and costs[14].

Guidelines that have been updated, such as those from the American College of Physicians and the Canadian Headache Society, suggest that CGRP inhibitors should be considered as a first- or second-line preventative therapy for individuals who have three or more migraines per day (MMDs) or who have unsatisfactory responses to traditional choices. Additionally, it is possible to combine these medications for patients who are resistant. Direct comparisons between CGRP inhibitors are rare, and network meta-analyses imply that there are no significant differences in the prevention of episodic migraines. This is despite the fact that major breakthroughs have been made. With the purpose of providing comparative evaluations of efficacy, safety, and applicability across a wide range of groups in order to facilitate clinical decision-making, the purpose of this multiple treatment comparison (MTC) meta-analysis is to consolidate information on CGRP inhibitors for episodic and chronic migraine.

MATERIAL AND METHODS

Search strategy

This meta-analysis was conducted following the PRISMA 2020 guidelines. A systematic literature search was performed to identify randomized controlled trials (RCTs) that evaluated the efficacy and safety of calcitonin gene-related peptide (CGRP) inhibitors in patients with episodic and chronic migraine. The electronic databases PubMed, ScienceDirect, Cochrane Central Register of Controlled Trials (CENTRAL), and Wiley Online Library were searched up to January 29, 2023. The search terms used were: ("Calcitonin Gene-Related Peptide" OR "CGRP" OR "CGRP inhibitor" OR "CGRP antagonist" OR "Anti-CGRP") AND ("migraine" OR "episodic migraine" OR "chronic migraine") AND ("randomized controlled trial" OR "clinical trial"). In addition, reference lists of relevant studies and review articles were screened to identify any additional eligible trials.

The search also specifically included Phase 3 randomized controlled trials investigating the efficacy of rimegepant in orally disintegrating tablet (ODT) formulation for the acute treatment of migraine attacks, to ensure comparability with other CGRP inhibitors such as ubrogepant, atogepant, erenumab, fremanezumab, galcanezumab, and eptinezumab. The primary efficacy outcomes extracted were pain freedom at 2 hours post-dose, freedom from the most bothersome symptom (MBS), and sustained pain relief up to 48 hours, consistent with standard endpoints used in clinical trials of acute migraine therapies.

Inclusion and exclusion criteria

The following criteria were used to determine whether or not a study was included: The following criteria must be met: (1) randomized controlled trials (RCTs) that evaluate the efficacy of CGRP inhibitor agents in patients diagnosed with episodic or chronic migraine; (2) trials that report monthly migraine days (MMD) as the primary efficacy outcome; (3) studies that involve adult participants who are at least 18 years old; and (4) a minimum treatment duration of four weeks, with clearly defined dosage regimens and administration frequency. The following were the conditions for an exclusion: (1) research that does not have full texts that can be retrieved; (2) research designs that are not randomised, such as observational studies, case reports, or reviews; (3) clinical trials that evaluate non-CGRP-based therapies or combination treatments with other migraine prophylactic drugs; (4) research that does not have

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sufficient data on primary or secondary efficacy outcomes; and (5) publications that are not in English or Bahasa Indonesia. Figure 1 depicts the procedure for selecting the studies to be participated in.

Quality and risk of bias assessment

A number of important research parameters were included in the data that was extracted from the studies that were selected. These parameters included the name of the first author, the year of publication, the patient group (episodic or chronic migraine), the sample size, the intervention type and dosage, the comparator, and the primary outcome evaluated as monthly migraine days (MMD). Consolidated Standards of Reporting Trials (CONSORT) checklist, which has a maximum score of 25 points and comprises of 25 elements, was applied in order to evaluate the quality of each trial that was included in the analysis. The checklist has a maximum score of 25 points. For the purpose of completing this evaluation, each of the reviewers worked separately, and the ultimate judgment was arrived at through conversations that were centered on reaching an agreement. The Revised Cochrane Risk-of-Bias Tool for Randomized Trials (RoB 2), which was established by Cochrane, was applied in order to analyze the risks of bias that were connected with each randomized controlled trial. This was done in order to ensure that the effectiveness of the trials was measured. This particular instrument takes into account a total of five distinct aspects of bias, which are as follows: the randomization procedure, changes from the interventions that were intended, missing outcome data, evaluation of the outcome, and selection of the result that was reported. It is possible to get an overall picture of the total risk of bias that has been found by looking at Table 1. A consistent methodological basis was provided by these evaluations for comparing the efficacy and safety profiles of CGRP inhibitors like erenumab, fremanezumab, galcanezumab, eptinezumab, atogepant, ubrogepant, and rimegepant in reducing the number of monthly migraine days experienced by patients who suffer from episodic migraine as opposed to chronic migraine. An Examination of Statistics Review Manager version 5.4 (Copenhagen: The Nordic Cochrane center. The Cochrane Collaboration) was utilized in order to carry out the meta-analysis. The unifying measure of the effect of CGRP inhibitor on the primary outcome (monthly migraine days) was chosen to be the mean difference (MD) along with their respective confidence intervals (CI) for 95%. As a result of the predicted clinical heterogeneity, effect sizes were combined through the utilization of random-effects models15. Whenever the p-value is less than 0.005, the analytical result is deemed to be significant. A statistical model known as the Higgins I-squared (I2) was utilized in order to explore heterogeneity. The results of the heterogeneity test were characterized as follows: negligible (ranging from 0 to 25 percent), low (ranging from 25 to 50 percent), moderate (ranging from 50 to 75 percent), or high (ranging from less than 75 percent).[16]

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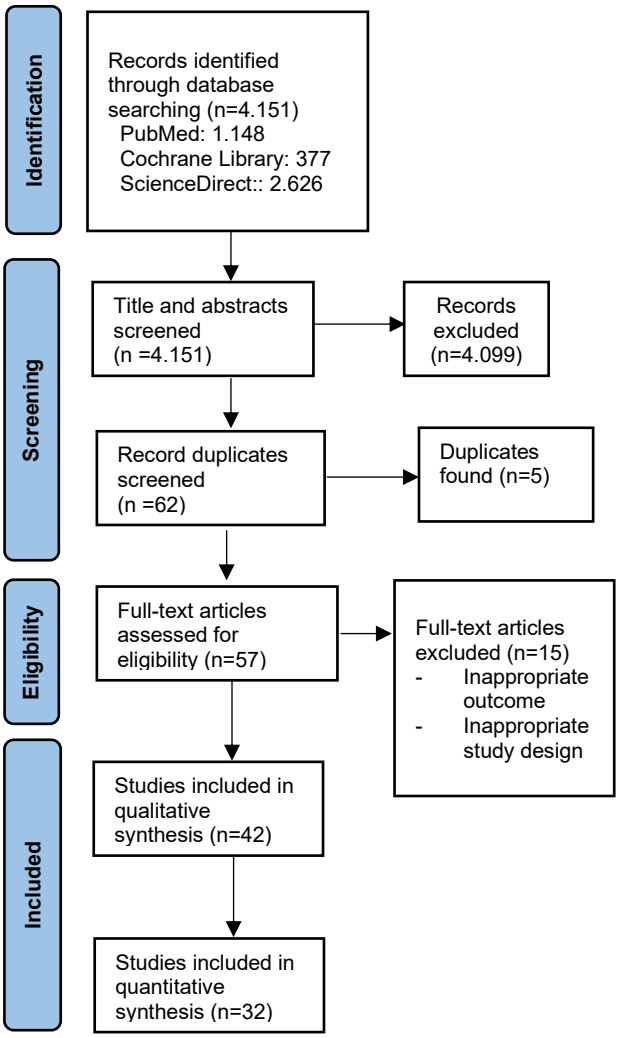

Figure 1. Diagram flow of literature search strategy for this systematic review *(56)*

RESULT

Study selection

The initial database search identified 4,151 studies. After screening titles and abstracts, 4,099 studies were excluded for irrelevance to the research question. In addition, five duplicate records were removed. A further 15 studies were excluded following full-text review because their reported outcomes were not relevant to this analysis. Finally, 42 studies met the inclusion criteria for qualitative synthesis, and 32 randomized controlled trials (RCTs) were included in the quantitative meta-analysis. The detailed selection process is presented in Figure 1.

Study characteristics, quality assessment, and risk of bias assessment

A total of 22,295 participants were included from studies published between 2013 and 2022, all of which were RCTs evaluating the efficacy of CGRP inhibitors including erenumab, fremanezumab, galcanezumab, eptinezumab, atogepant, ubrogepant, and Rimegepant in reducing monthly migraine days (MMD) among patients with episodic and chronic migraine.

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The methodological quality of the included studies was generally high. Based on the CONSORT checklist, the lowest observed score was 17.5/25 (range 17.5–20.5), indicating that more than two-thirds of the reporting standards were fulfilled in all studies. Using the Cochrane RoB 2 tool, 33 studies were rated as low risk of bias, while 11 studies showed some concerns mainly related to reporting and blinding domains. The overall summary of bias assessment is shown in Figure 2 and detailed in Table 1.

Comparative Effectiveness of CGRP Inhibitors

Among all included CGRP inhibitors, galcanezumab demonstrated the greatest reduction in monthly migraine days, while erenumab showed the smallest effect. Several factors may explain these differences. First, galcanezumab and fremanezumab bind directly to the CGRP ligand, thereby preventing both α- and β-CGRP isoforms from interacting with their receptors, while erenumab selectively targets the CGRP receptor, which may limit its overall inhibitory range. Second, variability in patient populations could contribute to outcome differences; galcanezumab trials tended to include a higher proportion of patients with episodic migraine, who generally respond more favorably to CGRP blockade than those with chronic migraine. Third, differences in study design, dosing frequency, and treatment duration may also influence results galcanezumab trials typically applied consistent monthly dosing regimens, whereas some erenumab studies used flexible dosing intervals or shorter follow-up durations. Collectively, these factors likely contributed to the observed variation in treatment efficacy across CGRP inhibitors.

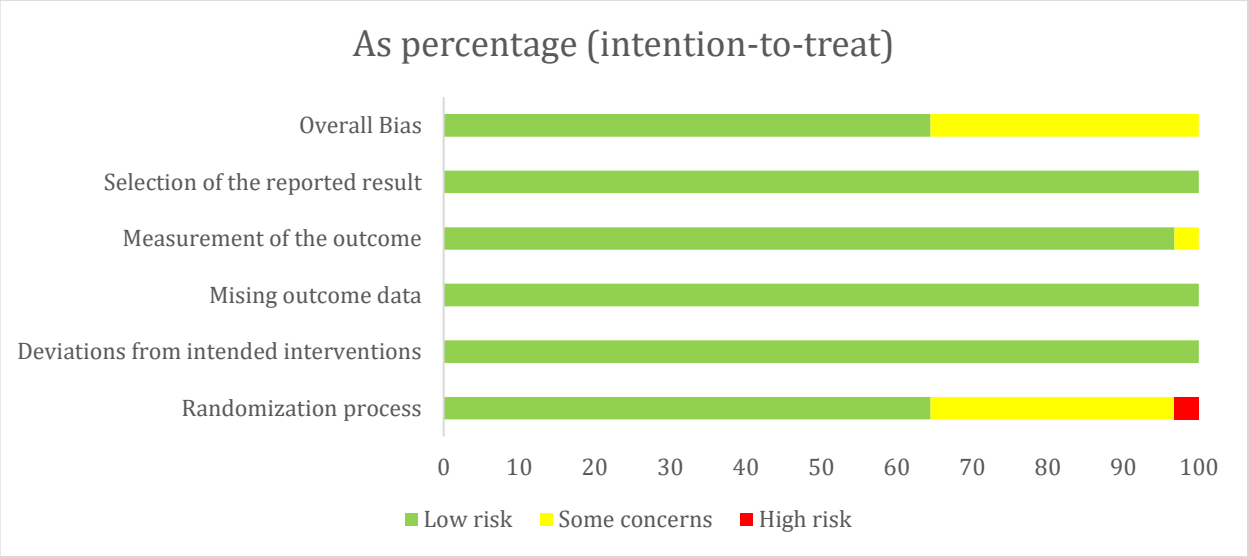

Figure 2. Summary of risk of bias assessment using RoB-2 tool from Cochrane

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Table 1. Risk of bias assessment result using RoB-2 tool from Cochrane

Study ID	Experimental	Comparator	Outcome	D1	D2	D3	D4	D5	Overall
Dodick, 2014	Eptinezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Ashina, 2019	Eptinezumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Dodick, 2019	Eptinezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Diener, 2020	Eptinezumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Lipton, 2020	Eptinezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Silberstein, 2020	Eptinezumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Goadsby, 2017	Erenumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Tepper, 2017	Erenumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Dodick, 2018	Erenumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Ashina, 2020	Erenumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Hirata, 2021a	Erenumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Wang, 2021	Erenumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Yu, 2022	Erenumab	Placebo	Monthly migraine days	-	+	+	+	+	!
Silberstein, 2017	Fremanezumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Dodick, 2018b	Fremanzumab	Placebo	Monthly migraine days	+	+	+	+	+	+

+	Low risk
!	Some concerns
-	High risk
D1	Randomisation process
D2	Deviations from the intended interventions
D3	Missing outcome data
D4	Measurement of the outcome
D5	Selection of the reported result

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Brandes, 2019	Fremanezumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Ferrari, 2019	Fremanezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Ashina, 2021	Fremanezumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Nahas, 2021	Fremanezumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Sakai, 2021	Fremanezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Dodick, 2014b	Galcanezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Camporeale, 2018	Galcanezumab	Placebo	Monthly migraine days	!	+	+	+	+	!
Detke, 2018	Galcanezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Reuter, 2018	Galcanezumab	Placebo	Monthly migraine days	!	+	+	!	+	!
Skljarevski, 2018	Galcanezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Mulleners, 2020	Galcanezumab	Placebo	Monthly migraine days	+	+	+	+	+	+
Hu, 2022	Galcanezumab	Placebo	Monthly migraine days	+	+	+	+	+	+

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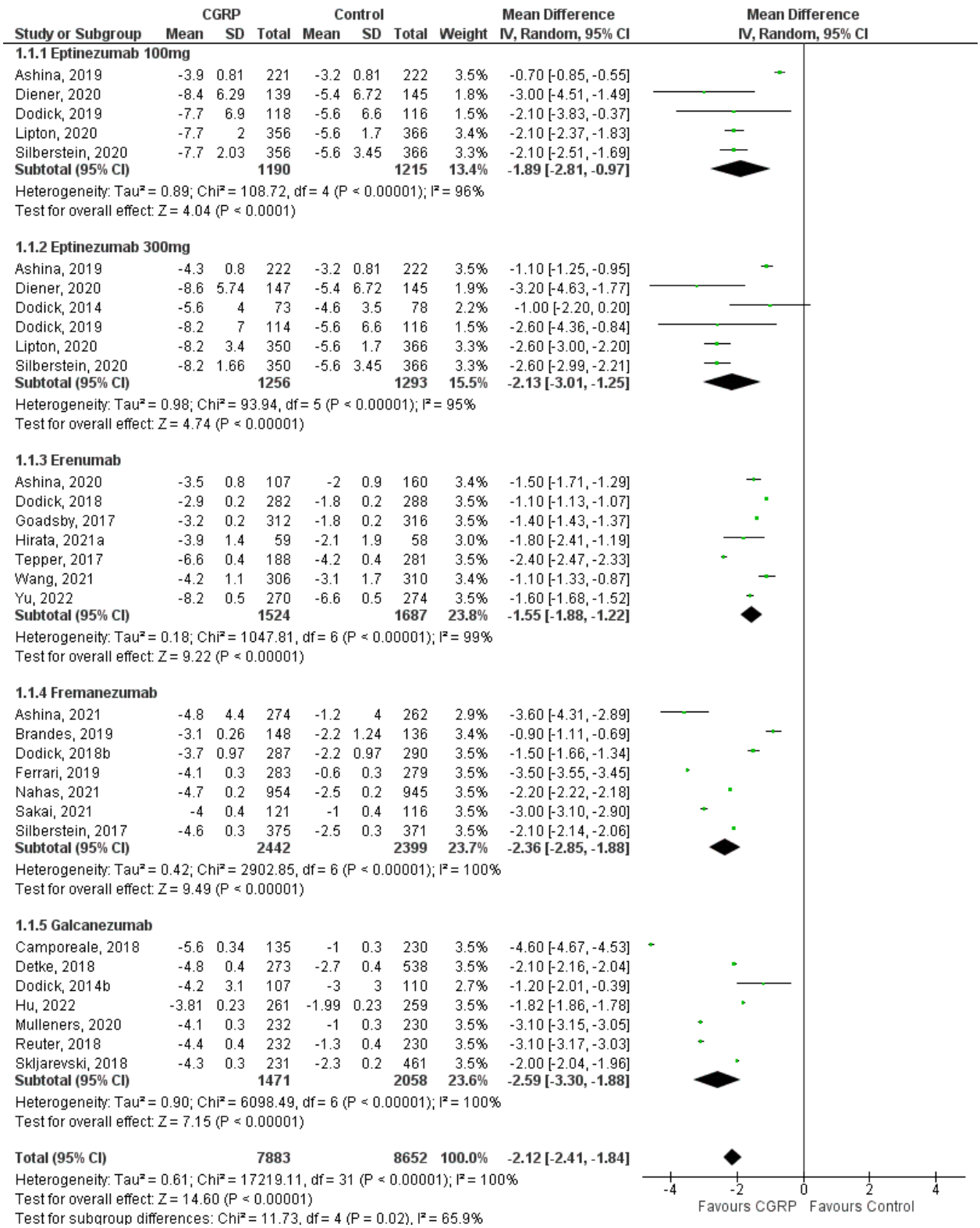

Figure 3. Meta-analysis result of CGRP inhibitor for the prevention of migraine

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DISCUSSION

The cornerstone of migraine management, be it chronic migraine (CM) or episodic migrane (EM) is to reduce the frequency and severity of headaches. Monthly migraine days (MMD) was chosen to be the main outcome to represent the efficacy of CGRP inhibitor because it's reduction are the key measures of the efficacy of migraine prophylaxis and prevention based on the diagnosis criteria of EM and CM.[17,18]

Our meta-analysis (**figure 3**) showed that patients receiving CGRP inhibitor was able to decrease the monthly migraine days (MMD) by 2.12 days more than patients who received placebo after 12 weeks (Mean Difference -2.12; 95% CI -2.41 - -1.84; p-value= 0,02). This result indicates a significant beneficial effect showed by CGRP inhibitor in preventing migraine attacks both in episodic and chronic migraine. This results means that patients receiving CGRP inhibitor showed a significant reduction in MMD by as low as 32,1% (highest placebo group MMD result by Yu, 2022 in erenumab study: -6.6)[19]. until as much as 352% (lowest placebo group MMD result by Ferrari, 2019 in Fremanezumab study: -0.6)[20]. based on the results showed by the placebo group of our included studies.

Among all of the CGRP inhibitor agents, the best result was observed in the galcanezumab studies with a mean difference of -2.59 (95%CI -3.30 - -1.88; p<0,05) while the worst was observed in erenumab studes with a mean difference of -1.55 (95%CI -1.88 - -1.22; p<0,05). After further analysis, we hypothesize that this difference could be merely caused by the differenst potency between both drugs. However, there is one possible confounding factor that could potentially influence this difference which was a different composition in terms of study population. In the galcanezumab studies, the study population was mainly European and Russian while erenumab studies introduced the Asian population to the pool. Several studies have demonstrated that Hispanic population showed a higher risk of migraine than Asian population by as much as double[21,22,23]. These data indicates a possibility in terms of our meta-analysis result which was the pooled result from galcanezumab studies could be an underestimated result in comparison to pooled result from erenumab studies, or vice versa (result from erenumab studies was overestimated). Furthermore, it also highlighted the possibility of different potency based on the race of the patient indicating the need for a further race-based comparison studies for each drugs.

This meta-analysis presents strong evidence for the effectiveness of CGRP inhibitors in decreasing the frequency of monthly migraine days (MMD) in individuals with episodic and chronic migraines. The notable decrease in MMD by 2.12 days vs to placebo highlights the promise of CGRP inhibitors as a preventive therapeutic approach. This discovery is especially pertinent to contemporary migraine treatments, which frequently fail to target the underlying pathophysiology of migraines and are linked to unpleasant effects and the potential for medication overuse headaches. The capacity of CGRP inhibitors to address the underlying etiology of headaches, rather than simply mitigating symptoms, signifies a substantial progression in migraine treatment.

CGRP inhibitors operate by inhibiting the calcitonin gene-related peptide, a neuropeptide integral to the pathophysiology of migraines. CGRP is recognized for its ability to widen cerebral arteries and stimulate the trigeminal vascular system, hence exacerbating the pain associated with migraine attacks. By blocking CGRP or its receptor, these medications may effectively obstruct the sequence of events that precipitate migraine attacks. This method of action differentiates CGRP inhibitors from conventional migraine therapies, which primarily emphasize symptomatic relief rather than targeting the underlying cause. The capacity to intervene at this foundational level

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provides optimism for more efficient and enduring migraine prevention.

The analysis demonstrated variety in the effectiveness of several CGRP inhibitors, with galcanezumab exhibiting the greatest significant impact and erenumab the least. This discrepancy may be ascribed to disparities in medication potency and the character of study cohorts. The galcanezumab investigations primarily encompassed European and Russian people, but the erenumab research featured a substantial representation of Asian participants. This demographic disparity may affect the observed efficacy, indicating a possible necessity for race-specific studies to enhance comprehension of the varying impacts of these medications. Comprehending these subtleties is essential for enhancing treatment procedures and guaranteeing that all patient demographics can reap the benefits of these improvements.

The clinical ramifications of these discoveries are substantial. CGRP inhibitors are a viable alternative for patients who exhibit inadequate responses to current therapies or suffer from side effects. The decrease in MMD can enhance quality of life and diminish functional impairment for individuals afflicted with migraines. Furthermore, the advantageous safety profile of CGRP inhibitors, exhibiting no substantial difference in adverse events relative to placebo, bolsters their application in clinical practice. The safety profile is especially crucial due to the chronic nature of migraine treatment and the necessity for long-term management techniques.

The heterogeneity shown in the study results, as denoted by the I-squared statistic, indicates variety in effect sizes among various studies. This may result from variations in study design, demographic variables, or pharmacological dosages. Subsequent study should endeavor to normalize these characteristics to yield more consistent and trustworthy outcomes. Addressing these sources of variability is essential for enhancing our comprehension of CGRP inhibitors and maximizing their application in clinical practice.

The incorporation of CGRP inhibitors into migraine care guidelines should be contemplated, owing to their proven efficacy and safety. Nonetheless, additional research is required to investigate the long-term consequences of these medications and their effectiveness across varied groups. Furthermore, research examining the ideal dosing protocols and possible dose-response correlations for various CGRP inhibitors may be beneficial. These initiatives will facilitate the effective and safe utilization of CGRP inhibitors among diverse patient populations.

This meta-analysis offers robust data endorsing the utilization of CGRP inhibitors as a prophylactic intervention for migraines. Despite certain limits, the advantages of these medications in decreasing migraine frequency and enhancing patient outcomes are evident. Subsequent study ought to further develop these findings to enhance the application of CGRP inhibitors in clinical practice. By addressing the constraints and investigating novel research pathways, we can augment our comprehension of these promising therapies and enrich the lives of individuals afflicted by migraines.

The eptinezumab studies indicates a dose-response relationship between CGRP inhibitor, in this particular case eptinezumab, and MMD which could potentially be replicated in studies involving other CGRP inhibitor drugs. In fact, several included studies already analyze this possibility such as in the fremanezumab studies, erenumab studies, and eptinezumab studies although the pooled results could not be extracted because the amount of studies analyzing it in each drugs was still lacking. Another possible treatment plan observed in our study is a quarterly dose of CGRP inhibitor as shown by fremanezumab studies[20,24,25,26,27,28,29]. These studies showed that a quarterly regiment of a higher dose of

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CGRP is equal to or even better than a monthly dose as seen in studies involving other drugs (eptinezumab, erenumab, and galcanezumab). In terms of safety, we observed that there were insignificant difference in the rate of adverse event in all of CGRP inhibitor agents in comparison to it's respective control group and also between the different treatment regiment (fremanezumab monthly vs fremanezumab quarterly).

Notwithstanding the encouraging outcomes, this investigation possesses many drawbacks that require acknowledgment. The primary outcome relied on patient-reported data, which is prone to self-report bias. This outcome was selected to conform with the majority of trials in this domain, hence ensuring consistency and comparability among studies. Furthermore, certain CGRP drugs, including atogepant and ubrogepant, were excluded due to an insufficiency of trials, thereby constraining the generalizability of the results. Subsequent research should focus on bridging these gaps and enhancing the overall comprehension of the effectiveness of all existing CGRP inhibitors

CONCLUSION

Gap on the treatment of migraine highlighted a lack of etiological treatment for migraine as current management plan only solve the symptoms of migraine while neglecting the underlying cause of migraine. Based on the current analysis, CGRP inhibitor showed a significant reduction in the frequency of migraine in the form of MMD. This promising result should justifies the consideration to include this agent in the management guideline for the prevention of migraine.

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DECLARATIONS

Dewa Ayu Sri Shita Meliani contributed to conceptualization, data collection, analysis, interpretation, and manuscript drafting. Abiyyu Didar Haq contributed to study design, methodology, critical revision, and final approval of the manuscript. All authors reviewed and approved the final manuscript.

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