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Galcanezumab as a Treatment For The Prevention of Migraines

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Galcanezumab as a treatment for the prevention of Migraines.

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ABSTRACT

Objective: To determine the effectiveness of subcutaneous galcanezumab as a preventative treatment for chronic migraines via a systematic review. **Methods:** JAMA and PubMed databases were searched using the terms galcanezumab and migraines in order to survey resulting patient clinical trials. **Results:** The 3 studies reviewed here all showed a statistically significant decrease in migraine headache days (MHDs) per month when using galcanezumab. Stauffer, et al. showed a mean decrease in MHDs of 4.7 and 4.6 for the 120mg and 240 mg doses of galcanezumab vs. 2.8 for placebo[9] . Rosen, et al. showed a mean monthly 100% response rate on an average month in the 6-month double-blind phase was greater for galcanezumab 120mg (13.5%) and 240 mg (14.3%) groups vs. placebo (5.9%)[7]. Detke, et al. showed mean reduction in the number of monthly MHDs of 4.8 and 4.6 for the 120mg and 240mg doses of galcanezumab vs. a 2.7 reduction for placebo[8]. **Conclusion:** This systematic review did show significant evidence that supports the use of subcutaneous galcanezumab as a preventative treatment for those with chronic migraines. There was no difference between the effectiveness of the 120mg and 240mg galcanezumab doses. Although no major risks were identified, more clinical trials need to be done in order to further study galcanezumab as well as its possible long-term adverse effects.

INTRODUCTION

Migraines are a neurological disease that an estimated 12% of the population suffers from[1, 2]. They have a genetic component and can affect men, women, and children with women being three times more likely than men. Migraines are characterized by intense and often debilitating symptoms that have varying severities. Along with cranial pain, some other symptoms include visual disturbances, nausea, vomiting, dizziness, and photophobia, osmophobia and phonophobia[1]. Some individuals will only suffer one or two episodes per month but others can have chronic daily migraines. This disease is most common between the ages of 18 and 44, however anyone can be affected[1].

The specific cause of migraines is still poorly understood. There have been several ideas proposed as to the pathophysiology of migraines, one being that a primary dysfunction in the brain leads to a cascade of events intracranially and extracranially that cause a migraine. Some of these steps are believed to be activation of the trigeminovascular system, which may lead to release of substance P, calcitonin gene-related peptide and neurokinin A[2, 6]. This in turn leads to inflammation, which causes neurons to become increasingly responsive to stimuli. The overall

cause of a migraine is complex and is likely the relationship and interaction between genetic factors, external stimuli, and the physiology happening inside the body[6].

The diagnosis of migraine consists of a good thorough history and physical examination and is made clinically. There are no specific diagnostic tests for a migraine, however it must be distinguished clinically from secondary migraines due to another emergent issue such as a subdural hemorrhage or space occupying lesion. The diagnostic criteria, as stated by the International Classification of Headache Disorders, is as follows: at least five attacks that last 4-72 hours, 2 of either a unilateral location, pulsating quality, moderate to severe pain, aggravation by physical activity, 1 of ether nausea, vomiting, photophobia or phonophobia, and lastly, not accounted by another cause[2].

Due to the incomplete understanding of the disease process, there is no curative treatment for migraines. The current treatment regimens are broad and are categorized as either preventative or acute. Acute treatment is aimed at treating symptoms of the migraines abruptly, whereas preventative measures are focused on reducing the frequency, duration, and severity of migraines[3, 4]. There are many indications for preventative treatment including frequent or long lasting migraines, ineffectiveness of acute treatments, and risk of medication overuse headaches. Examples of FDA approved migraine prevention medications include Metoprolol (Beta Blockers), Amitriptyline (Antidepressants), and Valproate (Anticonvulsants)[4]. Acute treatments are given in accordance to the severity of symptoms. Patients may receive NSAIDs or Tylenol for their pain. If this is not effective, triptans, antiemetics, or dihydroergotamine may be used. These acute treatments are usually more effective if given early in the course of the migraine and in one large dose[3].

It has recently been hypothesized that calcitonin gene-related peptide (CGRP) is a protein implicated in the cause of migraine headaches through dilation of cerebral and dural blood vessels, release of inflammatory mediators from mast cells, and transmission of nociceptive signaling from intracranial blood vessels to the nervous system[5]. Galcanezumab is a fully humanized monoclonal antibody produced specifically to bind to CGRP in the body and block it's binding to its receptor. This prevents vasodilation activity and subsequent increased nerve sensitivity, therefore blocking the neurogenic pain pathway that causes the debilitating migraine pain. Once CGRP binds to its receptor, its effect on migraines is initiated and requires receptor antagonists for acute relief of the migraine headache. Galcanezumab binds to the CGRP protein itself, decreasing migraines.

The FDA approved Galcanezumb in 2018, and multiple studies are currently being conducted to evaluate the comparison of varying doses of Galcanezumab to placebo.

PICO

Population: Adults aged 18-65 with chronic migraines

Intervention: Subcutaneous galcanezumab

Control: Placebo

Outcome: Reduction in the number of monthly migraine headache days self reported by patients

CLINICAL QUESTION

In adults aged 18-65 with chronic migraines, does subcutaneous galcanezumab as compared to placebo reduce the number of migraine headaches.

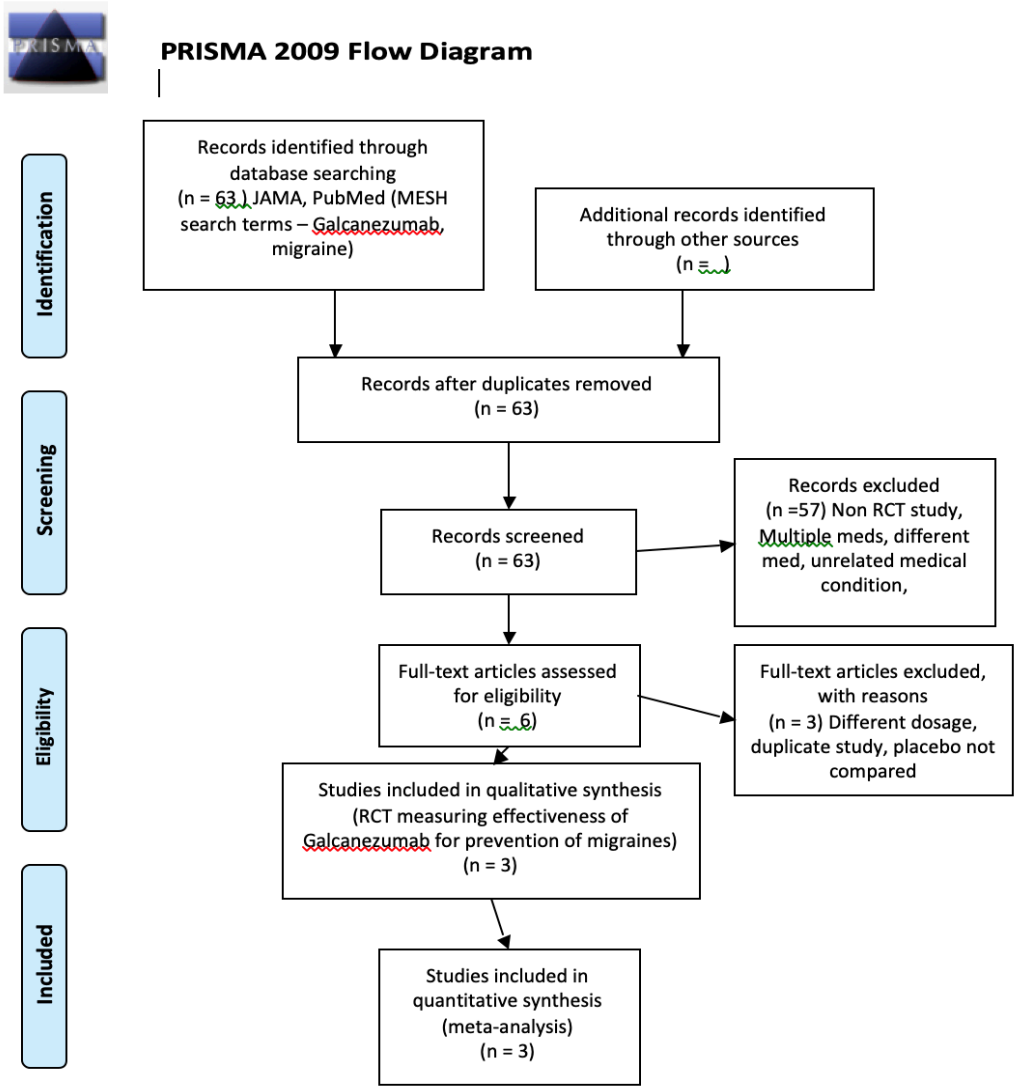

Figure 1: PRISMA flow diagram

METHODS

During September of 2019, JAMA and PubMed databases were explored using MESH terms galcanezumab and migraine. The search results yielded 63 articles. Of these 63, 57 articles were excluded for reasons such as non-randomized control trials, multiple medications being tested in the study, and not being specifically focused on migraines. The six remaining articles were reviewed and three of them were excluded due to many different dosages being studied, a duplicate study, and the placebo not being compared. This left three remaining articles that met all obligatory criteria, which included: *Evaluation of Galcanezumab for the Prevention of Episodic Migraine, The EVOLVE-1 Randomized Clinical Trial. Stauffer et al.; Galcanezumab in chronic migraine, The randomized, double-blind, placebo-controlled REGAIN study. Detke at al.; 100% Response Rate to Galcanezumab in Patients With Episodic Migraine: A Post Hoc Analysis of the Results From Phase 3, Randomized, Double-Blind, Placebo-Controlled EVOLVE-1 and EVOLVE-2 Studies. Rosen at al.* Figure 1 shows this article screening process.

RESULTS

Study 1

Evaluation of Galcanezumab for the Prevention of Episodic Migraine, The EVOLVE-1 Randomized Clinical Trial. Stauffer, et al.

Study Objective: To demonstrate that galcanezumab is superior to placebo in the prevention of episodic migraine with or without aura.

Study Design: This study was a double-blind, randomized, placebo-controlled trial comparing galcanezumab (120 mg and 240 mg) vs. placebo. Patients received treatments once monthly for 6 months (subcutaneous injection via prefilled syringe) and were followed up for 5 months after their last injection. It was a multicenter, clinic-based study involving 90 sites in North America. Participants in the study were adults (aged 18 to 65) with at least 1-year history of migraine, 4 to 14 migraine headache days (MHDs) per month and a mean of at least 2 migraine attacks per month within the past 3 months, and were diagnosed prior to age 50 years. During the study, no other preventive medications were allowed. A total of 1671 patients were assessed; 809 did not meet study entry or baseline criteria, and 858 were included in the intent-to-treat population. The

primary goal was to assess whether at least 1 dose of galcanezumab was superior to placebo in overall mean change from baseline of monthly MHD's.

Table 1: Inclusion and Exclusion Criteria for Study Participation *(Stauffer, et al.)*

Inclusion Criteria	Exclusion Criteria
1. Adults age 18-65 2. Migraine for at least 1 year 3. Migraine onset before age 50 4. 4-14 Migraine Headache Days/month 5. At least 2 migraine attacks/month	1. Failure to respond to 3 or more classes of migraine preventative treatments 2. Enrollment in another clinical trial in the last 30 days 3. Having taken a therapeutic antibody within the past 12 months 4. Currently receiving preventative migraine medication within 30 days of baseline period 5. Medical condition such as pregnancy, suicidal ideation within the past month, history of substance abuse or dependence in the past year, recent history of acute cardiovascular events and/or serious cardiovascular risk based on history or EKG findings

Results: 1671 patients entered the study and 862 were randomized. In total, 858 randomized patients received either galcanezumab or placebo and were included in the intent-to-treat. Overall, 703 patients completed the double-blind treatment period. The most common reason given for discontinuing treatment was, "withdrawal by patient." Monthly galcanezumab doses of 120mg and 240mg resulted in statistically significantly greater least square (LS) mean change from the baseline of monthly MHDs compared with placebo. The LS mean change difference from placebo was -1.9 days for galcanezumab 120mg and -1.8 days for galcanezumab 240mg (see figure 2). Both P values for the 120mg and 240 mg dose were <.001. Monthly headache hours was also statistically significantly different for both galcanezumab 120-mg (-29.7) and 240-mg (-29.3) with both P-values being <.001. Results of both doses of galcanezumab were seen within the first month of starting treatment. There were no significant differences seen between the 120mg and 240mg doses of galcanezumab. Overall, it was extrapolated that over a year span, a chronic migraine patient would have about 8 weeks less of MHDs while taking galcanezumab.

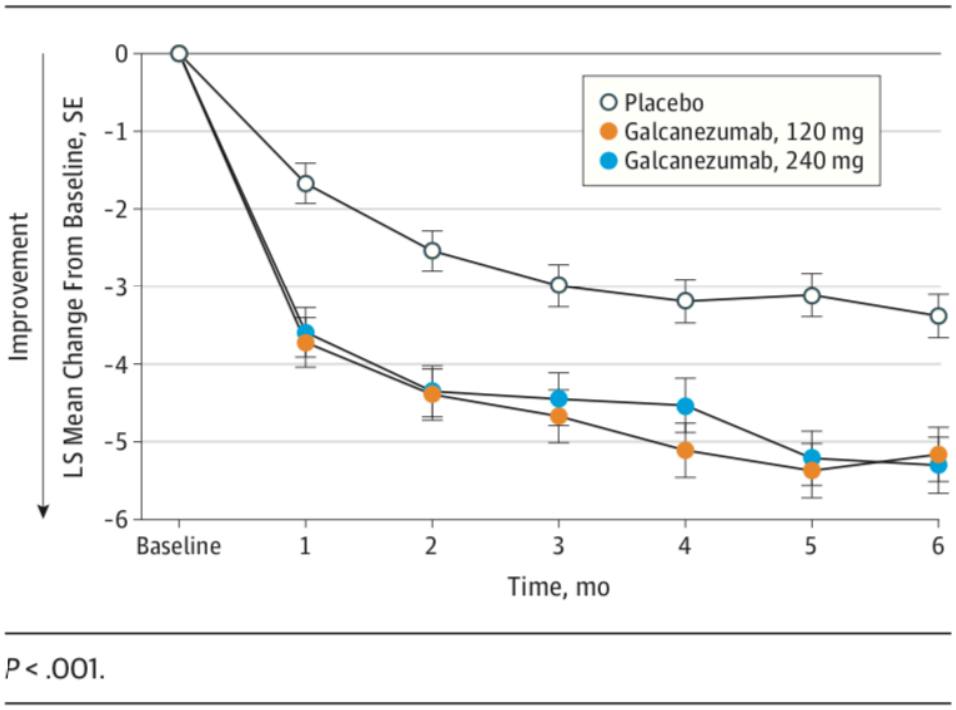

Figure 2: Results from study 1 showing reduction in MHDs over 6 month treatment period *(Stauffer, et al.)*

Critique: A few strengths of this study include that it was a randomized control study, utilized double-blind technique, and included an open age and gender requirement. These features help to reduce any chance of bias on either the patient or researcher end. Another benefit is that since the age range was wide, the results can be extrapolated to a greater range of patients. Also, this study had a large sample size and a high rate of completion (81.9%; n = 703 of 858), which provides more definitive conclusions as to the efficacy of the treatment. This study also spanned for 6 months which allowed for an appropriate assessment of patient response to the medication. Some limitations of this study were that patients were not tested in order to see if galcanezumab could be used effectively as an adjunctive treatment. Another example is that this study was conducted strictly in North America, which inhibits the generalizability of these findings in other regions of the world. No pregnant women were included in the trials, which makes it unclear as to the efficacy and safety of galcanezumab when given to pregnant women. Another limitation of this study is that the lead authors are full-time employees of the Eli Lilly and Company, the company that funded this study.

Study 2

100% Response Rate to Galcanezumab in Patients With Episodic Migraine: A Post Hoc Analysis of the Results From Phase 3, Randomized, Double-Blind, Placebo-Controlled EVOLVE-1 and EVOLVE-2 Studies. Rosen, et al.

Study Objective: To characterize adult patients with episodic migraine who achieved 100% response to galcanezumab treatment from two other studies.

Study Design: This post hoc analysis was calculated for each month from pooled data of 2 double-blind, 6 month galcanezumab studies in patients with episodic migraine. In both trials, adult patients with episodic migraine were to have a history of migraine of at least 1 year prior to study screening and onset of migraine prior to age 50. Episodic migraine was defined as having between 4 and 14 migraine headache days (MHD) and at least 2 migraine attacks per month. The patients were randomized (1:1:2) to monthly subcutaneous galcanezumab, 120 mg (after 240 mg initial loading dose) or 240 mg, or placebo. The patients recorded headache symptoms, duration, and severity with an electronic diary. Data for the 2 trials were pooled and were the basis of the post hoc analysis. The analysis consisted of 1739 adult patients with episodic migraine and a baseline and month 1 MHD. Response rates for each month and response rates across all months were calculated using a generalized linear mixed model with effects for baseline MHD, treatment, month, and treatment-by-month interaction.

Table 2: Inclusion and Exclusion Criteria *(Rosen, et al.)*

Inclusion Criteria	Exclusion Criteria
1. Age 18-65 with a history of migraine for at least 1 year prior to study screening 2. Onset of migraine prior to age 50 3. Between 4 and 14 MHD and at least 2 migraine attacks per month	1. Any current or previous exposure to a CGRP or nerve growth factor antibody 2. History of hemiplegic, opthalmoplegic, or basilar-type migraine 3. Failure to respond to more than 2 effective migraine preventative treatments defined by the American Academy of Neurology 4. Use of botulinum toxin A and B administered in head or neck area discontinued at least 4 months prior to trial start. 5. Enrollment in another clinical trial within the last 30 days

	6. Medical condition such as pregnancy, suicidal ideation within the past month, history of substance abuse or dependence in the past year, recent history of acute cardiovascular events and/or serious cardiovascular risk based on history or EKG findings

Results: Treatment with galcanezumab 120 mg or 240 mg showed a greater effective in achieving 100% response in reduction of MHD from baseline MHD compared with placebo in the 6 month double blind phase. At month 6, 17% (+/-2%) of the 120 mg galcanzumab treatment group and 21% (+/-2%) of the 240 mg galcanezumab treatment group had a 100% response, as compared to 10% (+/-1%) of the placebo treatment group. Approximately 40% of the patients with migraine headaches achieved 100% response with galcanezumab for at least one month. The percentages of patients with 100% response increased each month during the six month study period, but only 0.7-1.4% of patients achieved 100% response for all six months of the study. More patients achieved at least one month of 100% response in the last three months of treatment than in the first three month which suggests that the longer the patient remains on medication, the more likely the patient is to have at least 1 month of 100% migraine relief.

Critique: This post hoc analysis allows for greater exploration into the nature of the success rate of the EVOLVE-1 and EVOLVE-2 studies which both showed a large percentage more of patients with 100% success rate to the galcanezumab injections as compared to placebo. It is a strength that this analysis was able to pool together such a large population group, from studies that were randomized, double-blinded, and placebo-controlled. The findings of the study allows clinicians to set appropriate expectations regarding the efficacy of galcanezumab when utilizing it in practice. The 6-month study periods were an advantage over the 3-month study period of sister studies. A limitation of the study includes the 100% response was captured in the months between injections, therefore if a 100% response occurred in a 30 day period overlapping injections, that was not considered. Also, taking those that had a 100% response to galcanezumab and grouping them into a further analysis will shed biased positive light on the drug, which is further emphasized by the fact that Eli Lilly & Company also funded this study, which is the same pharmaceutical company that marketed Emgality (brand name for galcanezumab).

Study 3

Galcanezumab in chronic migraine, The randomized, double-blind, placebo-controlled REGAIN study. Detke, et al.

Study Objective: To determine if subcutaneous injection of 120 mg and 240 mg galcanezumab is more effective in preventing total number of monthly migraine headache days (MHDs) in patients with a previous diagnosis of chronic migraines, as compared to placebo.

Study Design: In this 3-month randomized, double-blind, placebo-controlled study, 1,113 eligible patients were randomized 2:1:1 to monthly subcutaneous injections of placebo (n=558), galcanezumab 120 mg (n=278), or galcanezumab 240 mg (n=277). The study was divided into five study periods: (1) a 3- to 45-day screening period; (2) a 1-month prospective baseline period to determine patient eligibility on the basis of daily entries into an electronic patient-reported outcomes (ePRO) diary; (3) a 3-month randomized, double-blind, place-controlled treatment period; (4) a 9-month open-lab extension, and (5) a 4-month posttreatment period to observe the washout of the study drug. During study period 3, patients received monthly subcutaneous injections of placebo, galcanezumab 120 mg (with a 240 mg loading dose), or galcanzeumab 240 mg for the 3-month double-blind period. Patients in all treatment groups received two 1-mL injections at each monthly dosing visit in blinded prefilled syringes: 2 placebo injection, 1 placebo and 1 galcanezumab 120 mg injection, or 2 galcanezumab 120 mg injections. Patients in the galcanezumab 120 mg group received 240 mg at their first dosing visit, followed by 120 mg at the subsequent months.

The primary objective endpoint tested the hypothesis that at least 1 dose of galcanezumab (either 120 mg or 240 mg) was superior to placebo in the prevention of migraine in patients looking at the overall mean change from baseline in the number of monthly MDHs during the 3-month double-blind treatment period . Throughout the study patients reported all headache information in the ePRO diary, including duration, severity, and features, as well as drug name and dose of acute headache medications taken that calendar day. Patients completed self-report scales at each monthly office visit including, Migraine-Specific Quality of Life Questionnaire (MSQ), Patient Global Impression of Severity of Illness (PGI-S), and Migraine Disability Assessment (MIDAS). Secondary objectives were also looked at, which compared galcanezumab with placebo on response rates, mean change in function, mean change in PGI-S at month 3, and additional headache parameters (i.e. monthly headache days, headache hours, and migraine headache hours). Safety assessments including adverse events, vital signs, weight, laboratory measures, ECGs, suicidality and treatment-emergent anti-drug antibodies (ADA).

Table 3. Inclusion and Exclusion Criteria for Study Participation *(Detke, et al.)*

Inclusion Criteria	Exclusion Criteria
1. Men and women 18 to 65 years of age at screening 2. Previous diagnosis of chronic migraine (CM) as defined by the International Classification of Headache Disorders 3. Migraine onset before 50 years of age 4. At least 15 headache days per month, of which at least 8 were migraine, for >3 months before screening 5. At least 1 headache-free day per month within 3 months before screening and during baseline 6. At least 80% compliant with ePRO daily diary entries 7. Blinded to diary eligibility criteria	1. Persistent daily headache, cluster headache, head or neck trauma within the past 6 months 2. Possible posttraumatic headache, or primary headache other than CM 3. Could not have previously failed to respond to adequate trials of migraine preventives from >3 different medication classes 4. Could not take therapeutic antibodies during or within 1 year before the study 5. Could not have serious or unstable medical or psychiatric conditions, history of stroke, or history of substance abused or dependence in the past year 6. Be at risk for acute cardiovascular events based on history or ECG findings

Results: Of the initial 1,903 patients that were screened for the study, 1,037 patients completed the treatment period, with more than 90% of the patients in each treatment group. On the primary endpoint, both 120 mg and 240 mg doses of galcanezumab were superior to placebo in the overall mean reduction in the number of monthly MHDs from baseline (*p* value <0.001). Monthly reductions in MHDs were statistically different from placebo for both galcanezumab doses starting with month 1 (see Figure 3).

The mean percentages of patients with ≥50% and ≥75% reduction from baseline in MHDs were higher for both galcanezumab doses than for placebo (≥50% response rate: both doses $p < 0.001$; ≥75% response rate: 120 mg $p < 0.05$, 240 mg $p < 0.001$). Galcanezumab 240 mg had statistical improvement vs placebo on the primary and all key secondary endpoints except for 100%

response rate, while galcanezumab 120 mg had statistical improvement vs placebo on the primary endpoint and the ≥50% response rate.

Overall, the study showed a statistically significant monthly decrease of MHDs with the injection of galcanzemab as compared to placebo, which represents a clinically meaningful positive change. There were no statistical differences between the 120 mg and 240 mg doses of galcanezumab on any of the efficacy measures.

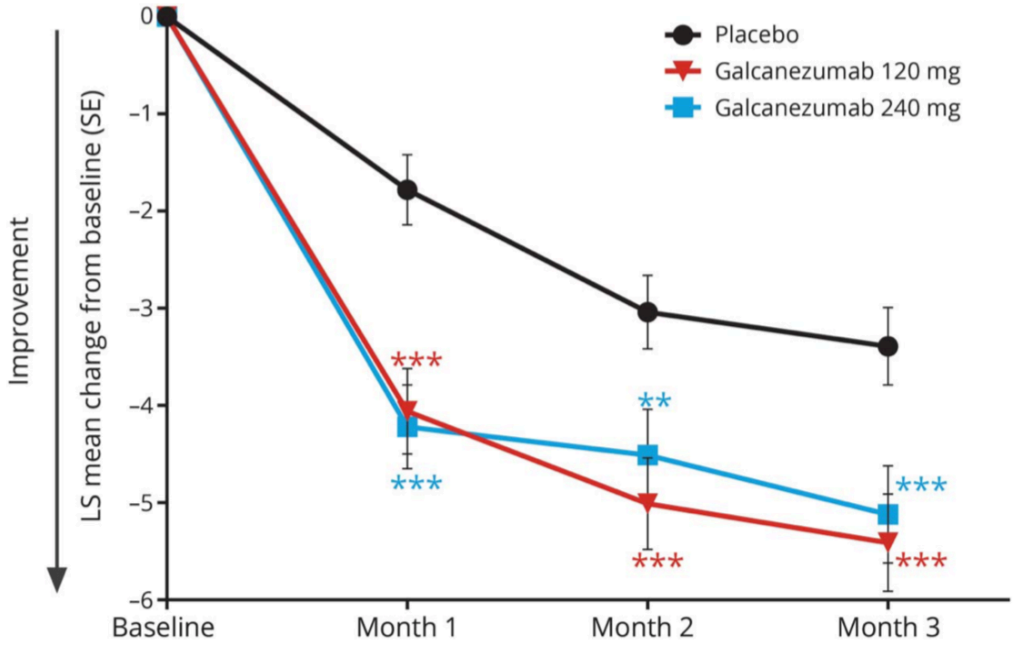

Figure 3: Results form study 3 showing reduction in MHDs over 3 month treatment period *(Detke, et al.)*

Critique: Strengths of this study include that is was a randomized, double-blind, placebo controlled study. These features helped minimize artificial causality and bias and allowed for the results to be best utilized in evidence based practice. The study looked at a large population pool, with over a thousand participants. The study included 116 headache and clinical research centers in 12 countries, including the United States, which allows the results to be applied on a global scale. Another strength is that the authors included comparison of multiple secondary endpoints, which further looked at clinically relevant information. The authors mentioned the exclusion of patients who had demonstrated significant treatment-resistance to multiple previous migraine preventive medications as a weakness, but we argue that this is actually a strength. Those patients

that are not able to respond to more than 3 preventative migraine treatments of the same mechanism of action, will waste time and money with this drug. A few limitations of the study should be mentioned. The study was funded by Eli Lilly and Company, which is the pharmaceutical company that marketed the drug Emgality (brand name for galcanezumab). Unfortunately due to the recent marketing of this drug, most if not all studies are funded by Eli Lilly and Company. Another notable limitation is the restrictions in the inclusion criteria may limit the generalizability of the results. Patients with serious medical conditions were excluded, which is a large portion of the population that suffers from chronic migraine headaches. Lastly, the 3-month duration of the study seems limited although the authors added a 9-month open-label extension to the study, which helped alleviate this issue.

DISCUSSION

This systematic review focused on the significance of galcanezumab as a preventative medical treatment for chronic migraines. The 3 studies demonstrate that galcanezumab is an effective preventative treatment for migraine headaches[7,8,9]. Table 4 summarizes the results of the studies reviewed.

Table 4: Summary of studies reviewed

	Study 1 **Stauffer, et al.**	**Study 2** **Rosen, et al.**	**Study 3** **Detke, et al.**
Objective	To demonstrate that galcanezumab is superior to placebo in the prevention of episodic migraine with or without aura.	To characterize adult patients with episodic migraine who achieved 100% response to galcanezumab treatment from two other studies.	To determine if subcutaneous injection of 120 mg and 140 mg galcanezumab is more effective in preventing total number of monthly migraine headache days (MHDs) in patients with a previous diagnosis of chronic migraines, as compared to placebo.
Study Type	Double Blind RCT	Post Hoc Analysis	Double Blind RCT

Sample Size	n = 858 (120mg - 213 240mg - 212 placebo - 433)	n = 1739 (120mg – 436 240mg – 428 placebo – 875)	n = 1113 120mg – 278 240mg – 277 placebo – 558)
Study Treatments	Galcanezumab (120mg and 240 mg)	Galcanezumab (120mg and 240mg)	Galcanezumab (120mg and 240mg)
Follow Up Period	6 months	6 months	3 months
Conclusion	Galcanezumab 120mg and 240mg both achieved a statistically significant overall mean reduction in the number of monthly MHDs during treatment (4.7 and 4.6 days, respectively) when compared with placebo (2.8 days)	Treatment with galcanezumab 120 mg or 240 mg showed a greater effectiveness in achieving 100% response in reduction of MHD from baseline compared with placebo in the 6 month double blind phase.	Both Galcanezumab 120 mg and 240 mg doses demonstrated statistically significant superior effectiveness compared to placebo in the overall mean reduction in number of monthly MHDs from baseline (p value <0.001).

Overall, these three studies were very similar in their design with only a few differences between them. All three of the studies compared the same subcutaneous doses of galcanezumab (120mg and 240mg) against placebo as a preventative treatment for chronic migraine patients. No other forms of treatment were included in the design of each study which lowers the chance of variable factors affecting results. In addition, these studies all used migraine headache days (MHDs) per month as the primary measure for efficacy of treatment with galcanezumab. This helps to create continuity across these studies and further strengthen resulting measures of efficacy. A difference between these 3 articles is that studies 1 and 3 are RCT trials while study 2 is a post hoc analysis of two RCT trials using galcanezumab. The use of this post hoc analysis allows the author to take specific information from studies and pool the results to achieve a desired statistical outcome.

Each of these studies had notable strengths and weaknesses, both individually and collectively. A common strength they shared is they are all three randomized control trials,

double blinded, and placebo controlled. These features help minimize artificial causality and bias and allowed for the results to be best utilized in evidence-based practice. They also all looked at the same population parameters which included 18-65 year old patients with chronic migraines. This wide age range is a strength, since it allows the results to be extrapolated to a greater range of patients in practice. All studies had a large sample size, with Study 2 pooling together populations from two previous studies[7,8,9]. The large population size yields more accurate mean values and provides a smaller margin of error. Study 1 and 2 were conducted with patients solely from North America, whereas Study 3 included 116 headache and clinical research centers in 12 countries, including the United States, which allows the results to be applied on a global scale[7,8,9]. Study 1 and 2 were conducted over a period of 6 months, while Study 3 was conducted over a 3 month period[7,8,9]. The 6 month period is a notable strength compared to 3 month period, since Study 2 found that the greatest proportion of patients that demonstrated success from the treatment (100% success rate) occurs during the last 3 months of the treatment period[7]. This shows that the longer the patient is taking galcanezumab, the greatest response they will have to it.

The most notable weakness of all 3 studies is that they were all funded by Eli Lilly and Company, which is the pharmaceutical company that produced and marketed this drug (brand name of galcanezumab is Emgality). The lead authors of all three studies are full-time employees of Eli Lilly and Company[7,8,9]. Since the drug was recently approved by the FDA, Eli Lilly and Company has patent rights over the drug, which creates a short term monopoly. Studies 1 and 3 also looked at secondary endpoints such as safety and adverse effects, which actually composed the majority of both papers[8,9]. This sheds concern over potential alternative motives perhaps to distract the reader from noticing the lack of specific data from the study such as proportion of experimental and placebo groups that showed a decrease in MHDs. Although these studies have bias and weakness, it is clear that galcanezumab shows success and promise for patients that suffer from chronic migraine headaches.

CONCLUSION

This systematic review shows that galcanezumab is an effective medication that demonstrated a clinically meaningful and positive change. Despite the multiple weaknesses, the studies did show an average of 50% decrease in MHDs as compared to placebo[7,8,9]. Chronic migraines are a debilitating disease, with patients desperate for prophylactic treatment. A statistical significant benefit of galcanezumab was demonstrated in all studies, as compared to placebo. Although Study 3 found that galcanezumab 120 mg dose showed a greater response, it was not statistically significant compared to 240 mg dose, therefore further studies need to be

conducted to find the best dose for patients[8]. The high rates of study completion (95%) and low rates of discontinuation due to adverse effects (1%) in all studies for the galcanezumab-treated patients suggest that galcanezumab is well tolerated. Since this is a relatively newly approved drug, further studies need to be conducted specifically on adverse effects. CGRP plays an important role in resisting the onset of hypertension since it acts as an effective vasodilator as well as cardioprotective properties specifically on the myocardium, so blocking this protein might have cardiovascular consequences long term[10]. The most common adverse effect was found to be injection-site pain which is an acute effect, but adverse effects might be found with chronic use and is something that should be cognizant of as the drug is used long term In conclusion, galcanezumab is an effective treatment of migraine prophylaxis and should be used in evidence based practice.

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