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QUALITY OF LIFE-RELATED TO WORK PRODUCTIVITY AND PHYSICAL FUNCTIONING IN MIGRAINE PATIENTS: A SYSTEMATIC REVIEW AND NETWORK-META ANALYSIS

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ABSTRACT: Background: Migraine is one of the major causes of disability affecting the productivity, physical, psychological and social well-being of patients. To conduct a systematic review and network meta-analysis (NMA) of randomized trials investigating the effect of anti-calcitonin gene-related peptide monoclonal antibodies (anti-CGRP mAbs) on productivity and physical functioning of adults migraineurs. **Methods:** Databases were searched from inception to May 2021. Work productivity and physical functioning were evaluated using change in patient-reported Work Productivity and Activity Impairment (WPAI) and Migraine Physical Function Impact Diary (MPFID) scores. The NMA was conducted with fixed-effects model in Bayesian framework. **Results:** Overall, 26 studies (4,393 migraineurs in five randomized trials) were included with a treatment course of at least 12 weeks. With limited treatments in network formed, subcutaneous injections of fremanezumab 675+225+225 mg QM and 225+225+225 QM were more effective in reducing loss of overall work productivity, activity impairment, and impairment experienced while at work in chronic and episodic migraine, respectively, with the higher median difference in WPAI scores from baseline compared to a low dose of fremanezumab (225 mg single dose). Similarly, the high subcutaneous dose of erenumab (140 mg QM) was more effective with an increase in daily physical activities and decreased physical impairment with a higher median difference in MPFID scores from baseline than its low dose (70 mg QM). **Conclusions:** For short-term prevention of migraine, high doses of fremanezumab and erenumab demonstrated slightly better productivity and physical functioning than other anti-CGRP mAbs in adult patients with migraine.

INTRODUCTION: Migraine is the third most prevalent neurological disorder affecting one in 10 people worldwide, more common and causing more burden in females than males, with a male to female ratio of 0.51 [1-3].

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It is characterized by unilateral localization, pulsating quality, moderate to severe pain intensity, aggravation by movement, often accompanied by nausea, vomiting, photophobia, or prodromal and postdromal symptoms [4, 5].

Treatments for migraine these days are mostly non-specific, and the existing treatments present a number of unmet needs related to inadequate treatment response [6]. Calcitonin gene-related peptide (CGRP) plays a key role in migraine's neurobiology and underlying mechanism as illustrated by abundant preclinical and human

evidence. Small molecule antagonists at the CGRP receptor were developed, and all were shown to be effective for the acute treatment of migraine. Several CGRP antagonists have been demonstrated in phase II and III to be effective for acute migraine treatment [7-12]. Monoclonal antibodies demonstrate high target specificity, thereby reducing off-target toxicity with the added advantage of undergoing metabolism through non-hepatic and non-renal pathways *via* reticuloendothelial system [13].

Migraine is one of the significant causes of disability affecting productivity, physical, psychological and social well-being of patients [14]. Productivity can be assessed using the validated, 6-item Work Productivity and Activity Impairment (WPAI) questionnaire, which measures the effect of one's general health on the extent of absenteeism (work time missed), presenteeism (impairment experienced while at work), overall work productivity loss (overall impairment estimate that is a combination of absenteeism and presenteeism), and activity impairment (impairment in regular daily activities other than work done for pay) during the previous 7 days [15]. WPAI measures the ability to work and perform regular activities. For evaluating the impact of migraine on physical functioning, the Migraine Physical Function Impact Diary (MPFID) is a novel patient-reported outcome (PRO) measure, which consists of two distinct domains: Impact on Everyday Activities and Physical Impairment. Both domain scores demonstrated evidence of excellent reliability and constructed validity in assessing the effects of migraine on physical functioning [16]. In this study, we aimed to compare the impact of different doses of anti-CGRP mAbs on productivity and physical functioning of migraineurs based on WPAI and MPFID scores, respectively, using the network meta-analysis (NMA) approach.

MATERIALS AND METHODS:

Data Sources and Study Selection: This systematic literature review (SLR) was conducted to identify relevant studies informing quality of life scores. This study is registered with the International Prospective Register of Systematic Reviews (PROSPERO), number CRD42020173667. The inclusion/exclusion criterion and database searching methods have been discussed in our previous publication [17].

In brief, randomized controlled trials (RCTs) with migraineurs aged ≥18 years taking anti-CGRP mAbs monotherapy, including erenumab, fremanezumab, galcanezumab and eptinezumab were considered for final inclusion. In terms of WPAI and MPFID scores, studies should report either direct baseline change or baseline and endpoint values to calculate the change. The searches were limited to human studies published in English from inception to May 2021. All outcomes were extracted until week 12 for all included studies. The Preferred Reporting Items reported this review for Systematic Reviews and Meta-Analyses extension for NMA (PRISMA-NMA) guidelines [18].

Data Extraction and Quality Assessment: A Microsoft excel based extraction form was developed to capture information, including ClinicalTrials.gov identifier (NCT number), study name, study characteristics, patient demographics, treatment details and outcomes of interest with relevant data and measure of variability. For each outcome, the mean/median estimate and associated uncertainty (*e.g.,* standard error [SE]) were extracted. Data on missing SE associated with the change in scores were obtained using the methods described in section 16.1.3.2 of the Cochrane Handbook for Systematic Reviews of Interventions [19]. To assess the risk of bias in the included studies, the Cochrane risk of bias (RoB) tool was applied to evaluate six domains *i.e.* generation of the allocation sequence, concealment of the allocation sequence, blinding, incomplete outcome data, selective outcome reporting and other biases [19]. The available data for each efficacy outcome was assessed further for the formation of connected networks.

Data Synthesis and Statistical Analyses: NMA is a technique for comparing three or more interventions simultaneously in a single analysis by combining both direct and indirect evidence across a network of studies [19]. This technique is beneficial, especially for active treatments, which cannot be compared head-to-head in a trial. NMA produces estimates of the relative effects between any pair of interventions in the network and usually yields more precise estimates than a single direct or indirect estimate.

It also allows estimation of the ranking and hierarchy of interventions [19]. NMA was conducted in a Bayesian framework combining direct and indirect comparisons and estimating posterior densities using Markov chain Monte Carlo (MCMC) simulations. The analyses were conducted using Open BUGS v3.2.3 (Open BUGS Foundation) and R 4.0.0 or higher software packages [20, 21]. The deviance information criterion (DIC) provides a measure of model fit that penalizes model complexity – lower values of the DIC suggest a more parsimonious model [22].

As the DIC differences of less than three are not considered to be significant between models [22], the data combined using a fixed-effects model were presented due to less number of studies for each outcome. The calculated point estimates were median differences (MDs) to represent a better estimate of centrality in the presence of skewed distributions. Although we don't refer to any notion of clinically meaningful results, the results were represented using two terms majorly *i.e.*, 'significant(ly)' to represent statistically significant results, when null value (zero for continuous outcomes) did not lie within the 95% CrIs ($p<0.05$) and 'numerically' to represent non-significant results with null value within the 95% CrIs ($p>0.05$).

STATA MP 13 was used to generate the overall network plot for this NMA [23]. The forest plots were generated for the comparison of each anti-CGRP mAbs dose with placebo as the reference treatment. The comparisons of all active treatment doses (including placebo) were interpreted using leagues tables, the matrices showing all pairwise comparisons with appropriate outcome measures and associated 95% CrIs. Treatment ranking probabilities for each included anti-CGRP mAbs were summarized using rankograms and Surface under the Cumulative Ranking Area (SUCRA) values (ranges 0-1). The SUCRA value closer to one suggested a higher likelihood of therapy being at the top rank. Furthermore, the Grades of Recommendation, Assessment, Development and Evaluation (GRADE) framework was used to assess the certainty of evidence contributing to network estimates as high, moderate, low, and very low [24].

RESULTS:

Included Studies: The systematic searches yielded five RCTs from 26 publications evaluating the prophylactic effects of anti-CGRP mAbs in 1,323 chronic migraineurs, 2,232 episodic migraineurs, and 838 combined populations of chronic and episodic migraineurs across a number of geographies.

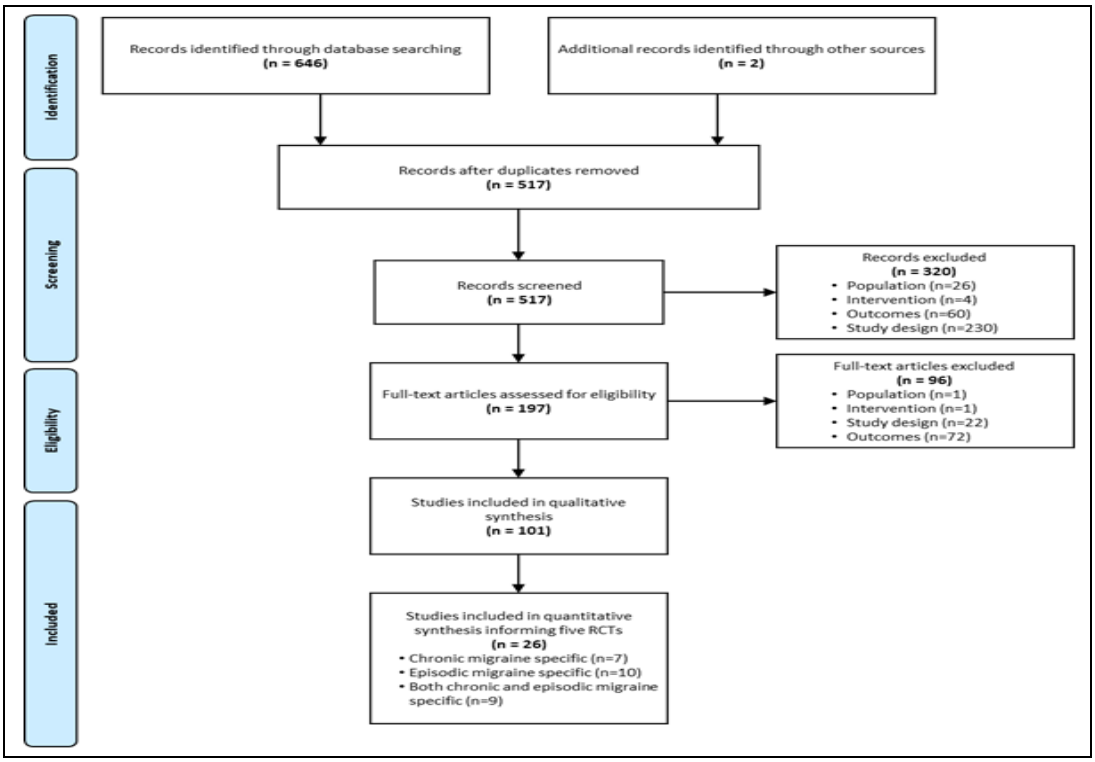

FIG. 1: STUDY SELECTION PROCESS

The included publications informed RCTs specific for chronic migraineurs (n=7), episodic migraineurs (n=10), and overall migraineurs (n=9) **Fig. 1**. Patients randomized in all trials satisfied the diagnostic criteria of migraine by the ICHD-3 beta [25]. All included studies were placebo-controlled and double-blind. The sample size for different treatment groups ranged from 96 to 376 and mean age of included patients ranged from 40.4 to 46.8 years in each treatment group which predominantly comprised of females. The treatment course was of at least 12 weeks across the included studies with a follow-up duration ranging from 12 to 28 weeks. Monthly migraine days at baseline ranged between 8.1 and 16.4 days. The characteristics of included studies are summarized in Appendix **Table 1** in the supplement. As only one study included outcomes beyond 12 weeks, the NMA was therefore limited to short-term outcomes. The risk of bias summary and graph for all included RCTs are provided in **Fig. 2**. Random sequence generation, allocation concealment and selective reporting were adequately mentioned in the studies. The included RCTs evaluated eight different dosing regimens of anti-CGRP mAbs treatments with placebo as the common comparator. The networks of eligible comparisons are displayed in **Fig. 3.**

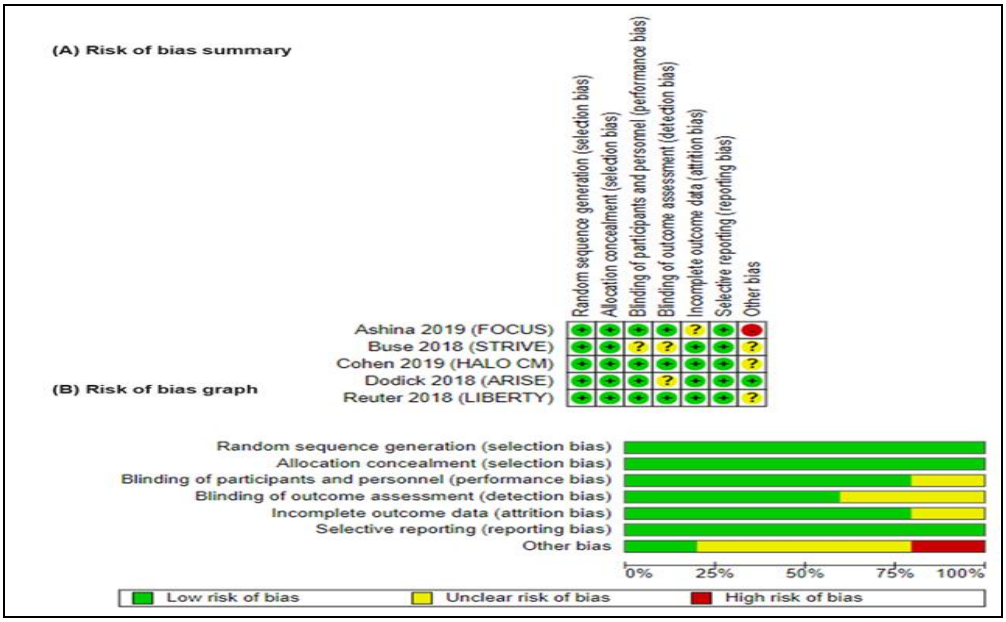

FIG. 2: RISK OF BIAS ASSESSMENT"+" denotes low risk of bias; "?" denotes unclear risk of bias; and "-" denotes high risk of bias

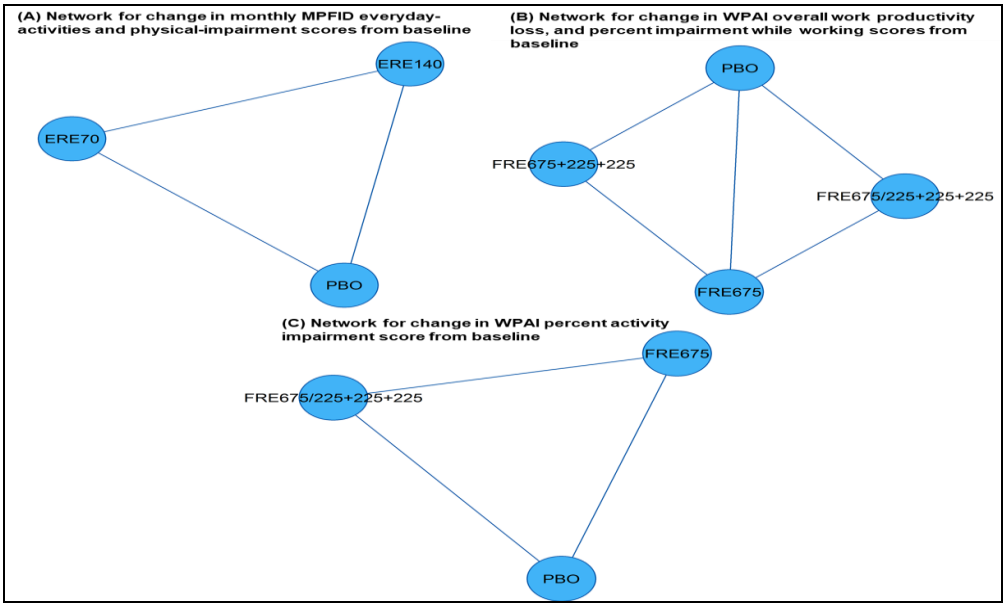

FIG. 3: NETWORK OF ELIGIBLE COMPARISONS OF DIFFERENT DOSES OF ANTI-CGRP MABS

Physical Functioning: The network for change from baseline in monthly MPFID scores of everyday activities and physical impairment included two subcutaneous doses of erenumab (70 mg QM; 140 mg QM), is presented in **Fig. 3.**

Both included erenumab doses exhibited significantly better control in everyday physical activities as well as for physical impairment due to migraine compared to placebo in terms of change from baseline in MPFID scores **Fig. 4A** and **Fig. 4B**.

Among active treatment comparisons, the analysis numerically favored high dose erenumab (140 mg QM) in terms of change in both everyday activities score (MD: -0.48, 95% CrIs: -1.49, 0.54) and physical impairment score (MD: -0.61, 95% CrIs: -1.65, 0.43) from baseline with lower MDs compared to low dose erenumab (70 mg QM) **Table 1.**

Work Productivity: In terms of WPAI overall work productivity and impairment while working, three doses of fremanezumab (675 mg single dose; initial administration of 675 mg followed by two injections of 225 mg QM *i.e.*, 675+225+225 mg QM; initial administration of 675 mg for chronic migraine or 225 mg for episodic migraine, followed by two injections of 225 mg QM *i.e.*, 675/225+225+225 mg QM) were involved in the network as active treatments along with placebo **Fig. 3**.

For WPAI percent activity impairment score, only two doses of fremanezumab (675 mg single dose; initial administration of 675 mg for chronic migraine or 225 mg for episodic migraine, followed by two injections of 225 mg QM *i.e.*, 675/225+225+225 mg QM) were involved in the network as active treatments along with placebo **Fig. 3**.

All fremanezumab doses were significantly better than placebo in reducing overall work productivity loss score, percent activity impairment score and percent impairment while working score from baseline **Fig. 4C, Fig. 4D** and **Fig. 4E**.

Among active treatment comparisons for WPAI overall work productivity loss score, the point estimates in the analysis numerically favored fremanezumab 675/225+225+225 mg QM compared to fremanezumab 675 mg single dose (MD: -2.02, 95% CrIs: -8.60, 4.59) and fremanezumab 675+225+225 mg QM (MD: -2.79, 95% CrIs: -10.68, 5.12). Similarly, the analysis numerically favored fremanezumab 675/225+225+225 mg QM versus both fremanezumab 675 mg single dose (MD: -1.66, 95% CrIs: -7.52, 4.22) and fremanezumab 675+225+225 mg QM (MD: -2.70, 95% CrIs: -9.74, 4.37) for WPAI percent impairment while working score, and versus fremanezumab 675 mg single dose (MD: -3.59, 95% CrIs: -8.46, 1.29) only for WPAI percent activity impairment score **Table 1.**

SUCRA Values and GRADE Assessments: The results for GRADE assessments and SUCRA rankings are provided in appendix **Table 1** respectively.

As per GRADE assessments, the results for outcome MPFID everyday activities score and MPFID physical impairment mostly corresponded to high quality and the evidence for WPAI overall work productivity loss score, WPAI percent activity impairment score and WPAI percent impairment while working score were mostly of moderate to low quality.

Further, the SUCRA values confirmed that subcutaneous erenumab 140 mg has the highest probability of being at top rank for showing improvements in physical function and fremanezumab 675/225+225+225 mg has the highest probability of being at top rank for showing improvement in work productivity scores.

TABLE 1: HEAD-TO-HEAD COMPARISONS OF DIFFERENT DOSES OF ANTI-CGRP MABS FOR PHYSICAL FUNCTIONING AND WORK PRODUCTIVITY IN MIGRAINE

Change from baseline in the Monthly MPFID everyday activities score			
	PBO	**ERE70**	**ERE140**
PBO		1.94 (1.21, 2.67)	2.42 (1.41, 3.44)
ERE70	-1.94 (-2.67,-1.21)		0.48 (-0.54, 1.49)
ERE140	-2.42 (-3.44,-1.41)	-0.48 (-1.49, 0.54)	

Change from baseline in the Monthly MPFID physicalimpairment score			
	PBO	**ERE70**	**ERE140**
PBO		1.78 (1.04, 2.52)	2.39 (1.36, 3.43)
ERE70	-1.78 (-2.53,-1.04)		0.61 (-0.43, 1.65)
ERE140	-2.39 (-3.43,-1.36)	-0.61 (-1.65, 0.43)	

Change from baseline in the WPAI overall work productivity loss score				
	PBO	**FRE675**	**FRE675+225+225**	**FRE675/225+225+225**
PBO		7.64 (3.14,12.15)	6.88 (1.56,12.18)	9.67 (3.06,16.28)
FRE675	-7.64 (-12.15,-3.14)		-0.76 (-6.22, 4.62)	2.02 (-4.59, 8.60)
FRE675+225+225	-6.88 (-12.18,-1.56)	0.76 (-4.62, 6.22)		2.79 (-5.12,10.68)
FRE675/225+225+225	-9.67 (-16.28,-3.06)	-2.02 (-8.60, 4.59)	-2.79 (-10.68, 5.12)	

Change from baseline in the WPAI percent activity impairment score			
	PBO	**FRE675**	**FRE675/225+225+225**
PBO		6.02 (2.51, 9.55)	9.60 (4.73,14.49)
FRE675	-6.02 (-9.55,-2.51)		3.59 (-1.29, 8.46)
FRE675/225+225+225	-9.60 (-14.49,-4.73)	-3.59 (-8.46, 1.29)	

Change from baseline in the WPAI percent impairment while working score				
	PBO	**FRE675**	**FRE675+225+225**	**FRE675/225+225+225**
PBO		**6.16 (2.12,10.19)**	**5.13 (0.34, 9.90)**	**7.83 (1.94,13.71)**
FRE675	**-6.16 (-10.19,-2.12)**		-1.03 (-5.94, 3.82)	1.66 (-4.22, 7.52)
FRE675+225+225	**-5.13 (-9.90,-0.34)**	1.03 (-3.82, 5.94)		2.70 (-4.37, 9.74)
FRE675/225+225+225	**-7.83 (-13.71,-1.94)**	-1.66 (-7.52, 4.22)	-2.70 (-9.74, 4.37)	

Data are MDs (95% CrIs) and comparisons should be read horizontally i.e. row-defining the treatment compared with the column-defining the treatment. MDs lower than 0 indicate favored results for the treatment on that row versus the treatment on that column. Significant results are in bold.

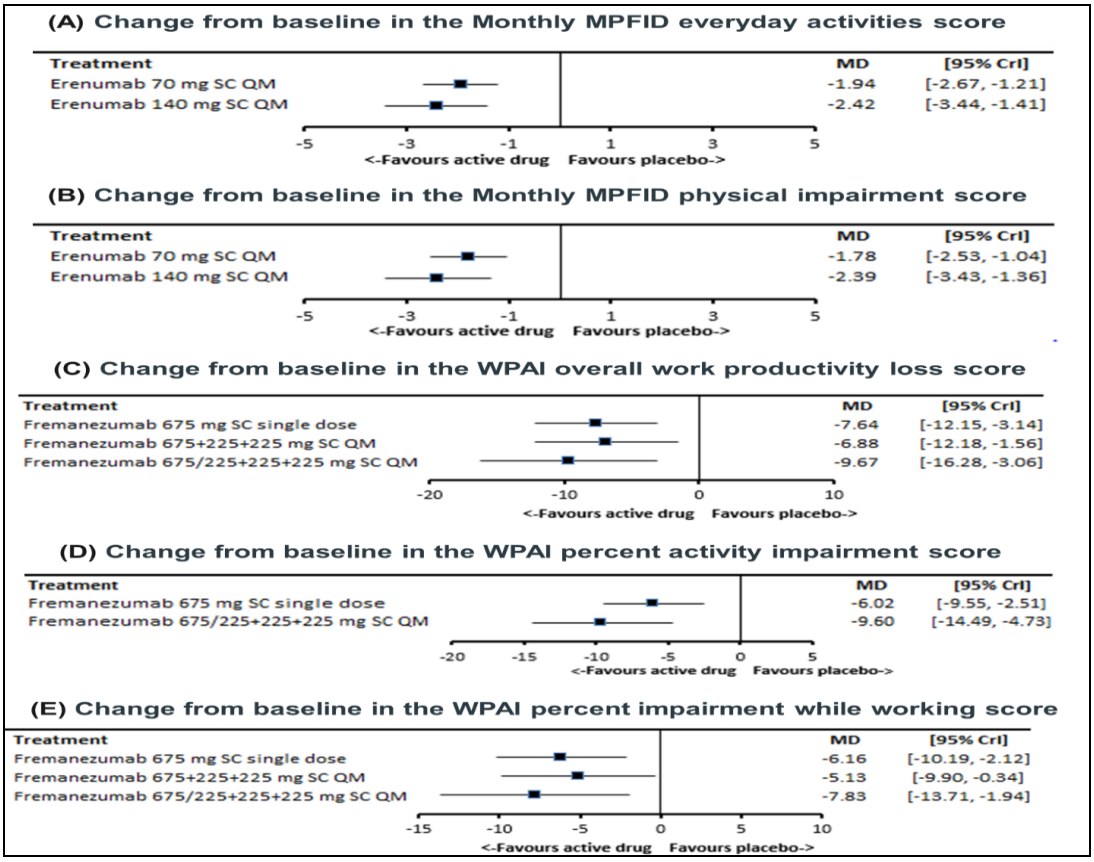

FIG. 4: FOREST PLOT OF NETWORK META-ANALYSIS RESULTS FOR PHYSICAL FUNCTIONING AND WORK PRODUCTIVITY OUTCOMES. MDs lower than 0 indicate favored results for the treatment.

DISCUSSION: In this analysis of five RCTs involving 4,393 migraineurs, we found that the effects of anti-CGRP mAbs were beneficial in maintaining physical functioning and work productivity in adult patients with migraine. The impact of migraine on physical functioning and work productivity were deemed to be the most appropriate outcome to evaluate the immediate benefits of interventions that prevented migraines.

The systematic review was conducted to inform the NMA, using prespecified inclusion/exclusion criteria. Bayesian NMA in fixed effects model using OpenBUGS (via R scripts) was conducted to synthesize relevant data for each outcome of interest. All subcutaneous doses of fremanezumab and erenumab were superior for physical functioning and work productivity, respectively, compared with effect of placebo.

In terms of comparisons among active treatments, all doses of fremanezumab and erenumab were comparable for physical functioning and work productivity, respectively, based on well-reported credible intervals with no significant difference. Hence, the numerical values of effect estimate were used to conclude the treatment superiority over each other.

In line with expectations, the high subcutaneous dose of erenumab was more effective with an increase in daily physical activities and decreased physical impairment compared to its low dose.

Similarly, high dose of subcutaneous fremanezumab with divided dosages injected across three months was more effective in reducing loss of overall work productivity, activity impairment and impairment experienced while at work based on patient-reported WPAI scores compared to other low doses of fremanezumab in both episodic and chronic migraine patients.

Despite of previously conducted literature reviews and meta-analyses on safety and efficacy of anti-CGRP mAbs compared to placebo [26-31], the evidence related to patient reported outcomes are not available and this study provides detailed assessments of anti-CGRP mAb group including all doses of treatments in terms of productivity and physical functioning. The results of this analysis should be interpreted with caution due to its limitations. The impact of gender distribution was not explored as the studies included female patients predominantly. The outcomes reported until 12 weeks were analyzed and all trials were placebo controlled. Primary studies with head-to-head comparisons will be needed to improve the evidence base, while long-term studies with increased sample size will give more precision to our effect estimates for treatment efficacy, safety, and tolerability.

The inclusion/exclusion criterion of RCTs could also bias the final results. For instance, the FOCUS trial involved patients with documented inadequate response to 2-4 migraine preventive medication classes [32]. The GRADE assessments highlighted moderate to low quality of treatment comparisons. Finally, this study only compared anti-CGRP mAbs class of migraine treatment and future analyses are needed to compare it with other treatment classes.

CONCLUSION: In the absence of head-to-head trials comparing all combinations of anti-CGRP mAbs treatments for migraine, this study provides the comparative results of treatment doses for migraine work productivity and physical functioning which will assist physicians with individual prescribing decisions to optimize care at patient level.

In conclusion, through this NMA, we came to the interpretation that high doses of subcutaneous fremanezumab and erenumab will be the effective therapies in managing work productivity and physical functioning, respectively, in adult migraine patients.

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REFERENCES:

1. Feigin VL, Abajobir AA, Abate KH, Abd-Allah F, Abdulle AM and Abera SF: Global, regional and national burden of neurological disorders during 1990–2015: a

systematic analysis for the Global Burden of Disease Study 2015 2017; 16(11): 877-897.
2. Vos T, Abajobir AA, Abate KH, Abbafati C, Abbas KM and Abd-Allah F: Global, regional and national incidence, prevalence, and years lived with disability for 328 diseases and injuries for 195 countries, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. 2017; 390(10100): 1211-1259.
3. Woldeamanuel YW, Cowan and Robert P: Migraine affects 1 in 10 people worldwide featuring recent rise: a systematic review and meta-analysis of community-based studies involving 6 million participants. Journal of the Neurological Sciences 2017; 372: 307-315.
4. Russo AF: Calcitonin gene-related peptide (CGRP): a new target for migraine. Annual Review of Pharmacology and Toxicology 2015; 55: 533-552.
5. Goadsby PJ, Holland PR, Martins-Oliveira M, Hoffmann J, Schankin C and Akerman S: Pathophysiology of migraine: a disorder of sensory processing. Physiological Reviews 2017;
6. Lipton RB, Munjal S, Buse DC, Alam A, Fanning KM and Reed ML: Unmet acute treatment needs from the 2017 migraine in America symptoms and treatment study. Headache: The Journal of Head and Face Pain 2019; 59(8): 1310-1323.
7. Hewitt DJ, Aurora SK, Dodick DW, Goadsby PJ, Ge Y and Bachman R: Randomized controlled trial of the CGRP receptor antagonist MK-3207 in the acute treatment of migraine. Cephalalgia 2011; 31(6): 712-722.
8. Marcus R, Goadsby PJ, Dodick D, Stock D, Manos G and Fischer TZ: BMS-927711 for the acute treatment of migraine: a double-blind, randomized, placebo controlled, dose-ranging trial. Cephalalgia 2014; 34(2): 114-125.
9. Olesen J, Diener H-C, Husstedt IW, Goadsby PJ, Hall D and Meier U: Calcitonin gene–related peptide receptor antagonist BIBN 4096 BS for the acute treatment of migraine. New England Journal of Medicine 2004; 350(11): 1104-1110.
10. Voss T, Lipton RB, Dodick DW, Dupre N, Ge JY and Bachman R: A phase IIb randomized, double-blind, placebo-controlled trial of ubrogepant for the acute treatment of migraine. Cephalalgia 2016; 36(9): 887-898.
11. Croop R, Goadsby PJ, Stock DA, Conway CM, Forshaw M and Stock EG: Efficacy, safety, and tolerability of rimegepant orally disintegrating tablet for the acute treatment of migraine: a randomised, phase 3, double-blind, placebo-controlled trial. The Lancet. 2019; 394(10200): 737-745.
12. Lipton RB, Dodick DW, Ailani J, Lu K, Finnegan M and Szegedi A: Effect of ubrogepant *vs* placebo on pain and the most bothersome associated symptom in the acute treatment of migraine: the ACHIEVE II randomized clinical trial. Jama 2019; 322(19): 1887-1898.
13. Bigal ME, Walter S and Rapoport AM: Therapeutic antibodies against CGRP or its receptor. British Journal of Clinical Pharmacology 2015; 79(6): 886-895.
14. Renjith V, Pai MS, Castelino F, Pai A and George A: Clinical profile and functional disability of patients with migraine. Journal of Neurosciences in Rural Practice. 2016; 7(2): 250.
15. Lipton RB, Lee L, Saikali NP, Bell J and Cohen JM: Effect of Headache-Free Days on Disability, Productivity, Quality of Life and Costs Among Individuals with Migraine 2020; 26(10): 1344-1352.
16. Kawata AK, Hsieh R, Bender R, Shaffer S, Revicki DA and Bayliss M: Psychometric evaluation of a novel instrument assessing the impact of migraine on physical functioning. The Migraine Physical Function Impact Diary 2017; 57(9): 1385-1398.
17. Soni P and Chawla E: Efficacy and safety of anti-calcitonin gene-related peptide monoclonal antibodies for treatment of chronic migraine: A systematic review and network meta-analysis. Clinical Neurology and Neurosurgery 2021; 106893.
18. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH and Cameron C: The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Annals of Internal Medicine 2015; 162(11): 777-784.
19. Higgins JP, Thomas J, Chandler J, Cumpston M, Li T and Page MJ: Cochrane handbook for systematic reviews of interventions. John Wiley & Sons 2019.
20. R-4.0.0 for Windows (32/64 bit). https://cran.r-project.org/bin/windows/base/
21. MRC Biostatistics Unit. OpenBUGS. https://www.mrc-bsu.cam.ac.uk/software/bugs/openbugs/
22. Dias S, Sutton AJ, Ades A and Welton NJ: Evidence synthesis for decision making 2: a generalized linear modeling framework for pairwise and network meta-analysis of randomized controlled trials. Medical Decision Making 2013; 33(5): 607-617.
23. Chaimani A, Higgins JP, Mavridis D, Spyridonos P and Salanti G: Graphical tools for network meta-analysis in STATA. PloS one 2013; 8(10): 76654.
24. Puhan MA, Schünemann HJ, Murad MH, Li T, Brignardello-Petersen R and Singh JA: A GRADE Working Group approach for rating the quality of treatment effect estimates from network meta-analysis. BMJ 2014; 349: 5630.
25. Olesen J, Bes A, Kunkel R, Lance JW, Nappi G and Pfaffenrath V: The international classification of headache disorders, (beta version). Cephalalgia 2013; 33(9): 629-808.
26. Han L, Liu Y, Xiong H and Hong P: CGRP monoclonal antibody for preventive treatment of chronic migraine: An update of meta-analysis. Brain and Behavior 2019; 9(2): 01215.
27. Hou M, Xing H, Cai Y, Li B and Wang X, Li P: The effect and safety of monoclonal antibodies to calcitonin gene-related peptide and its receptor on migraine: a systematic review and meta-analysis. The Journal of Headache and Pain 2017; 18(1): 42.
28. Huang I, Wu PC, Lin EY, Chen CY and Kang YN: Effects of Anti-Calcitonin Gene-Related Peptide for Migraines: A Systematic Review with Meta-Analysis of Randomized Clinical Trials. International Journal of Molecular Sciences 2019; 20(14): 3527.
29. Xu D, Chen D, Zhu LN, Tan G, Wang HJ and Zhang Y: Safety and tolerability of calcitonin-gene-related peptide binding monoclonal antibodies for the prevention of episodic migraine–a meta-analysis of randomized controlled trials. Cephalalgia 2019; 39(9): 1164-1179.
30. Zhu Y, Liu Y, Zhao J, Han Q, Liu L and Shen X: The efficacy and safety of calcitonin gene-related peptide monoclonal antibody for episodic migraine: a meta-analysis. Neurological Sciences 2018; 39(12): 2097-2106.
31. Deng H, Li GG, Nie H, Feng YY, Guo GY and Guo WL: Efficacy and safety of calcitonin-gene-related peptide binding monoclonal antibodies for the preventive treatment of episodic migraine–an updated systematic review and meta-analysis. BMC Neurology 2020; 20(1): 1-12.

32. Ferrari MD, Diener HC, Ning X, Galic M, Cohen JM, Yang R, Mueller M, Ahn AH, Schwartz YC, Grozinski-Wolff M, Janka L and Ashina M: Fremanezumab versus placebo for migraine prevention in patients with documented failure to up to four migraine preventive medication classes (FOCUS): a randomised, double-blind, placebo-controlled, phase 3b trial. The Lancet 2019; 394(10203): 1030-1040. doi:http://dx.doi.org/10.1016/S0140-6736%2819%2931946-4.

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