Friday 15
Saturday 16
March 2024

HEADACHE & CGRP
HOTEL ALBANI

Symposium Florence 2024

SISC

ABSTRACTS

SEGRETERIA ORGANIZZATIVA
PLANNING
Planning Congressi Srl
Via Guelfa 9 • 40138 Bologna
Telefono 324-8365700
s.cantelli@planning.it
www.planning.it

Correlation between endometriosis and migraine features: results from a prospective case-control study

Maria Albanese[1,2], Caterina Exacoustos[3], Aikaterini Selntigia[3], Giuseppe Rizzo[4], David Della Morte[2], Nicola Biagio Mercuri[1,2]

[1]Headache Center, Neurology Unit, Tor Vergata University Hospital, Rome, Italy; [2]Department of Systems Medicine, University of Rome Tor Vergata, Rome, Italy; [3]Department of Surgical Sciences, Gynecological Unit, University of Rome Tor Vergata, Rome, Italy; [4]Department of Biomedicine and Prevention, Obstetrics and Gynecological Unit, University of Rome Tor Vergata, Rome Italy

Background: Endometriosis and migraine frequently coexist, but only a limited number of studies have focused on their mutual association. The aim of our study was to investigate, in untreated women with comorbid endometriosis/adenomyosis and migraine, the correlation between headache features and endometriotic subtypes and their possible relationship with pain severity and disease disability.

Methods: Fifty women affected by endometriosis/adenomyosis and migraine matched (1:2) with 100 patients with endometriosis alone and 100 patients with only migraine were recruited and underwent pelvic ultrasound imaging and neurological examination.

Results: Severe adenomyosis, posterior and anterior deep infiltrating endometriosis (p=0.027, p=0.0031 and p=0.029, respectively) occurred more frequently in women with migraine. Dysmenorrhea was the most commonly reported symptom in women with endometriosis and migraine and the mean VAS scores of all typical endometriotic symptoms were significantly higher in the presence of comorbidity. Women with both migraine and endometriosis reported significant higher pain intensity (p=0.004), higher monthly migraine days (p=0.042) and increased HIT 6-scores (p=0.01), compared with those without endometriosis.

Conclusion: Our results demonstrated that the co-occurrence of migraine in untreated women with endometriosis is associated with more severe gynecological infiltrations and correlated with increased pain intensity and disease disability.

Friday 15 Saturday 16 March 2024 HEADACHE & CGRP HOTEL ALBANI Symposium Florence 2024 SISC

Non responders to anti-CGRP/R monoclonal antibodies: unmet needs and challenges in the management of drug-resistant migraine

Alberto Boccalini[1,2], Andrea Burgalassi[1,3], Francesco De Cesaris[1], Giulia Vigani[3], Giorgio Tabasso[1,3], Guido Mannaioni[4], Alberto Chiarugi[1,3], Pierangelo Geppetti[3,4], Luigi Francesco Iannone[1,3]

[1]Headache Center and Clinical Pharmacology Unit, Careggi University Hospital, Florence, Italy; [2]Department of Biomedical Sciences, University of Cagliari, Cagliari, Italy; [3]Section of Clinical Pharmacology and Oncology, Department of Health Sciences, University of Florence, Florence, Italy; [4]Department of Neurosciences, Psychology, Drug Research and Child Health, Section of Pharmacology and Toxicology, University of Florence, Florence, Italy; [5]Department of Pathobiology, School of Dentistry, New York University, NY, USA

Background: To describe the outcome of patients who withdraw anti-calcitonin gene-related peptide monoclonal antibodies (CGRP/R mAb) and the related causes, to evaluate the effectiveness during treatment, and characterize patients who do not respond to anti-CGRP/R.

Methods: We conducted a prospective analysis on all consecutive outpatients who started erenumab, galcanezumab, or fremanezumab. In February 2023, we assessed the follow-up of patients that withdrawn the first anti-CGRP/R mAb. We documented whether they had subsequent follow-up after the last mAb administration and if they initiated a new treatment. The primary outcomes were to describe the reasons for anti-CGRP mAbs withdraw and the follow-up thereafter. The secondary outcomes were to evaluate the multi-assessed response to mAbs during treatment. The patients were divided in the overall population (*i.e.,* withdrawn for any reason) and then a subgroup that discontinued solely due to ineffectiveness.

Results: A total of 472 patients were treated with at least one dose of anti-CGRP/R mAbs, and 136 (28.8%) discontinued treatment for various reasons. Among them, 46.3% received erenumab, 14.7% received fremanezumab, and 39% received galcanezumab. Almost all patients have chronic migraine (91.9%) and 81.6% medication overuse. The majority of patients withdrew from treatment due to ineffectiveness (n=96, 70.6%), followed by lost to follow-up during therapy (18, 13.1%) and adverse events (13, 9.6%). Three patient each (3, 2.2%) withdrew from treatment for personal choice or for pregnancy. One patient discontinued due to no compliance to treatment (0.7%), and 3 (2.2%) for physician decision (not better accountable in other categories).
Overall, 106 (77.9%) patients discontinued treatment during the first 12-month follow-up. At the first follow-up after anti-CGRP/R withdrawn, 66 (48.5%) patients started a new pharmacological treatment (i.e., switching anti-CGRP mAbs, OnabotulinumtoxinA, anticonvulsants, others), 54 (39.7%) patients were lost to follow-up and 16 (11.8%) decided to not start other treatments.

Conclusion: Managing patients who do not respond to anti-CGRP treatment remains a challenge, necessitating tailored management strategies to optimize response or timely identification of non-responders to provide appropriate treatments.

Examining psychological profiles in individuals super responders and non responders to CGRP-monoclonal antibodies treatment: insights from a 6-month follow-up study

Sara Bottiroli[1,2], Gloria Vaghi[1,2], Roberto De Icco[1,2], Daniele Martinelli[1], Grazia Sances1, Maria Magdalena Pocora[1,2], Cristina Tassorelli[1,2]

[1]University of Pavia, Pavia, Italy; [2]IRCCS Mondino Foundation, Pavia, Italy

Background: The effectiveness of migraine preventive therapy that targets the calcitonin gene-related peptide (CGRP) pathway has been demonstrated in challenging cases, including individuals who have experienced failure with previous multiple preventive treatments. Notably, patients categorized as "difficult-to-treat" are generally considered particularly challenging due to a high incidence of psychopathological comorbidities and maladaptive personality traits. This study aims to assess the psychological factors that predict a highly positive response to anti-CGRP monoclonal antibodies (mAbs) over a 6-month follow-up period in chronic migraine (CM) or episodic migraine (EM).

Methods: A total of 116 patients (mean age: 48.2±10.5, female: 77%), diagnosed with either CM or EM and having experienced unsuccessful outcomes with at least three prior preventive therapies, were administered treatment with CGRP-targeting monoclonal antibodies (mAbs). At the baseline (T0), patients underwent a comprehensive psychological evaluation encompassing mood, anxiety, and personality disorders, along with an exploration of childhood traumas, current stressors, and alexithymia. Subsequently, their clinical status was followed up over a 6-month period.

Results: At the 6-month follow-up, 39% of patients (mean age: 50.1±9.2, female: 81%) reported a reduction of at least 75% in monthly migraine days (MMD) categorizing them as Super Responders (SR). In contrast, 19% of patients (mean age: 49.3±11.1, female: 74%) exhibited a ≤ 25% reduction in MMD compared to T0, classifying them as Non Responders (NR). When comparing SR to NR, individuals in the NR group displayed a higher prevalence of anxiety (82% vs. 53%, p=.012) and personality disorders (68% vs. 31%, p=.003), particularly those belonging to Cluster C (avoidant, dependent, and obsessive-compulsive) (68% vs. 29%, p=.001). Additionally, NR patients reported a significant higher number of childhood traumas (2.3±3.1 vs. 0.6±0.9, p<.001), current stressors (8.8±7.6 vs. 3.8±4.2, p<.001) and exhibited more alexithymic traits (49.6±11.9 vs. 43.1±13.3, p=.005) than SR patients.

Conclusion: Our data confirm the notable efficacy of CGRP-targeting mAbs even in patients with difficult-to-treat forms of migraine and a high burden of psychological comorbidities. While our findings are preliminary, they indicate substantial distinctions in the psychological profiles of patients experiencing extreme responses (super response vs. absolute non-response) to mAbs.

Slow responders instead of late responders: assessing the time to response to anti-CGRP/R monoclonal antibodies

Andrea Burgalassi[1,2], Giulia Vigani[2], Alberto Boccalini[1], Antonio Munafò[1], Marina Romozzi[3], Catello Vollono[3], Paolo Calabresi[3], Francesco De Cesaris[1], Alberto Chiarugi[1,2], Pierangelo Geppetti[2,4], Luigi Francesco Iannone[2]

[1]Headache Center and Clinical Pharmacology Unit, Careggi University Hospital, Florence, Italy; [2]Section of Clinical Pharmacology and Oncology, Department of Health Sciences, University of Florence, Florence, Italy; [3]Dipartimento Universitario di Neuroscienze, Università Cattolica del Sacro Cuore, Rome, Italy; [4]Department of Pathobiology, School of Dentistry, New York University, NY, USA

Background: Although the response to anti-calcitonin gene-related peptide (CGRP) monoclonal antibodies (mAbs) is usually rapid, occurring sometimes within the first weeks, recent evidence suggests that some patients, non responders at three months (≤50% response in monthly headache days, MHDs), might achieve responder status at six months. However, it is still unclear whether these patients have no response at all at three months or if they already achieve a clinically meaningful response at 3 months, without reaching the 50% cutoff, and improve over time. In this study, we evaluated whether late responders are actually slow responders to anti-CGRP mAbs.

Methods: We performed a prospective analysis on all patients that started erenumab, galcanezumab, or fremanezumab, including out-patients with a potential 6-month follow-up. Based on observational studies on late responders, response was defined as a ≥50% reduction from baseline in MHDs at 3 and 6 months. The response rate was then evaluated using different intervals (0-9; 10-19; 20-29; 30-49; ≥50%) to assess responses at three months. The primary outcomes were the number of potential late responders and to evaluate how many patients defined as late responders have a response ≥30% at three months (slow responders).

Results: Overall, we included 332 patients and among them 283 (85.2%) continued treatment for six months. Patients achieving response status were 63.6% (180/283) at six months. In particular, 40 (14.1%) patients non responders at three months achieved response status at six months, 140 (49.5%) persisted in response, 77 (27.2%) continued to be non responders and 26 (9.2%) lost the responder status. However, among the 40 patients defined as late responders, 21 (47.5%) had already achieved a response ≥30% at three months with 14 (35.0%) of them with a 40-49% response. Remarkably, 8 (20%) with almost no response at three months (0 to 9%) achieved a 50% response rate at six months.

Conclusion: The majority of patients categorized as late responders are instead slow responders, starting a meaningful response to anti-CGRP at three months and improving over time. Nevertheless, to maximize response to treatment in all patients, we recommend evaluating the treatment after a minimum of three to six months.

Anti-CGRP monoclonal antibodies and psychiatric symptoms in Migraine: The EMIPSY22 Project

Elena Cresta[1], Giulia Menculini[2], Leonardo Zebi[2], Lucia Gonfia[2], Alessia Bellotti[1], Giovanni Rinaldi[1], Marco Alabiso[1], Ilenia Corbelli[1], Lucilla Parnetti[1], Paola Sarchielli[1]

[1]Section of Neurology, Department of Medicine and Surgery of Perugia, Perugia, Italy; [2]Section of Psychiatry, Department of Medicine and Surgery of Perugia, Perugia, Italy

Background: Mood, anxiety, and sleep disorders, as well as personality traits or clear-cut personality disorders, are primarily linked with migraine. Individuals with migraine and comorbid psychiatric conditions often have a history of multiple therapeutic failures with conventional preventive treatments and are at a heightened risk of developing chronic migraine and medication overuse headache. The EMIPSY22 project aims to investigate: (i) whether psychiatric comorbidities and baseline psychopathological characteristics influence the response to treatment with anti-CGRP monoclonal antibodies (mAbs); (ii) changes in psychopathological characteristics and symptom severity following treatment with mAbs.

Methods: We enrolled 36 consecutive patients eligible for mAbs treatment who attended our Headache Center from June 2022 to June 2023. Subjects underwent clinical evaluation at the Headache Center and psychiatric assessment at the Psychiatry Section, at two time points (at baseline and after six months of therapy). Data regarding migraine characteristics and the degree of disability caused by headache were recorded, and a comprehensive psychiatric assessment was conducted. Specifically, at baseline, we evaluated the presence/absence of psychiatric disorders (using SCID-5-CV), including personality disorders (SCID-5-PD), as well as the presence and severity of depressive symptoms (BDI-II and HAM-D), anxiety symptoms (HAM-A, STAI-Y), hypomanic/manic symptoms (MRS, MDQ), obsessive-compulsive symptoms (OCI-R), and sleep disturbances (ISI). After six months of treatment, tests were repeated to assess changes in the severity of psychiatric symptoms.

Results: In our sample, nearly one-third of the subjects were diagnosed with a psychiatric disorder (30.6%). Among these, the most frequent diagnoses were adjustment disorders, followed by depressive and anxiety disorders; 5.6% of the overall sample were diagnosed with personality disorders (pathological personality traits were prevalent in 33.3% of cases, especially cluster C characteristics). 64% of the sample responded to mAbs treatment at 6 months. The prevalence of baseline psychopathological characteristics did not differ between responders and non-responders. We observed a significant reduction in the severity of depressive and anxious symptoms, as well as sleep disturbances, after six months of treatment.

Conclusion: We hypothesize that psychiatric symptoms do not impact the response to mAbs therapy and, furthermore, that the observed improvement in psychiatric symptoms is not solely attributable to the improvement of headache but also suggests functional and structural changes involving both trigeminal pain modulation pathways and neurolimbic-pain-network structures implicated in processing the multifaceted pain experience.

Anti-CGRP monoclonal antibodies, migraine and mood disorders: an observational study

Marco Bolchini[1], Giulia Ceccardi[2], Francesca Schiano di Cola[2], Michele Di Pasquale[2], Salvatore Caratozzolo[2], Renata Rao[2], Alessandro Padovani[2]

[1]Neurology Unit, Istituto Clinico Città di Brescia, Brescia, Italy; [2]Neurology Unit and Headache Centre, Dipartimento di continuità di cura e fragilità, ASST Spedali Civili and Università degli studi di Brescia, Brescia, Italy

Introduction: Migraine is frequently associated with psychiatric comorbidities; these are usually related to worse clinical outcome and migraine chronicization. The relation between migraine and psychiatric comorbidities seems to be bidirectional, with anxiety and depressive disorders constituting a negative predictor for treatment response. The aim of the present study was to assess, firstly, treatment response to anti-CGRP antibodies in a cohort of high-frequency and chronic migraine patients with and without associated psychiatric comorbidities; secondly, to evaluate the evolution of anxiety and depressive manifestations during treatment.

Materials and methods: 206 migraine patients in treatment with anti-CGRP antibodies for at least 6 months were included in the study; patients were stratified according to the severity of psychiatric manifestations. Efficacy outcomes (MMDs, MHDs, analgesics consumption, NRS, MIDAS, SF-36, HIT-6) and self-assessment anxiety and depression scales (BDI, Zung) were analyzed after 3 and 6 months of treatment.

Results: Efficacy outcomes showed a significant clinical improvement at T3 and T6, regardless of the presence of associated psychiatric comorbidities. Anxiety and depressive manifestations improved during treatment; BDI and Zung scales at T3 and T6 showed a significant reduction in all patients' subgroups, especially in those with higher baseline values.

Conclusion: This study confirms anti-CGRP antibody treatment efficacy in migraine patients, regardless of the associated psychiatric comorbidities. The positive impact of this treatment is also evident in the persistently beneficial course of psychiatric symptoms severity and intensity during treatment.

Shall we offer a (or one more) Galcanezumab trial in chronic cluster headache patients? A case of dramatic therapeutic response challenging phase III study results

Riccardo Garbo, Olivo Sasha, Michele Rana

SC Neurologia Gorizia-Monfalcone, Azienda Sanitaria Universitaria Giuliano Isontina, Gorizia, Italy

Background: Cluster headache (CH) is a highly disabling condition, associated with reduced quality of life, suicidality and a high economic burden, especially in its chronic form. Experimental data suggest a possible role for calcitonin gene-related peptide (CGRP) in its pathophysiology, and Galcanezumab was the first FDA approved treatment for episodic CH. Although a randomized controlled trial evaluating Galcanezumab for the treatment of chronic CH led to negative results, some reports showed benefit from its clinical application, thus suggesting the possibility of individual treatment attempts.

Methods: A 54-year-old woman with a 35-year history of CH started as episodic and evolved into chronic was treated with Galcanezumab 240 monthly. The patient had already tried many pharmacological prophylactic treatment attempts including verapamil, lithium, topiramate, cycles of oral prednisone, lamotrigine, melatonin, amitriptyline and gabapentin, which were not tolerated or brought only little or transient benefit. Also, greater occipital nerve and sphenopalatine ganglion blocks were not effective, and the implantation of a greater occipital nerve stimulation device brought to infective complications requiring device removal. Ketogenic diet was initially effective but was discontinued due to difficulty in adherence. At the baseline, the patient presented with 2-3 cluster headache attacks a day and an almost continuous less intense right side locked headache interpreted as “shadow” headache.

Results: In the third week after Galcanezumab initiation the frequency of CH attacks was reduced to once a day, in the fourth week there were 3 CH attacks and in the second month of treatment the patient experienced only 2 CH attacks. Meanwhile, continuous right side locked headache resolved and was substituted by episodic headache (3 attacks in the second months) with clear migrainous features. Resolution of concomitant insomnia was also reported, and the patient discontinued opioids which she was overusing.

Conclusion: Real-world experience suggests that treatment of chronic CH with Galcanezumab can lead to impressive therapeutic responses, even in case of previous multiple treatment failures, thus prompting the necessity of further studies to evaluate which patients affected by this highly disabling condition may benefit from such treatment.

Long term efficacy and tolerability of Galcanezumab and Fremanezumab on comorbid chronic cluster headache and migraine: a prospective case series

Martino Gentile, Silvia Grimaldi, Maria Elena Roca, Damiano Paolicelli, Maria Pia Prudenzano

Headache Center, "L. Amaducci" Neurological Clinic, Brain Department, Aldo Moro University, Bari, Italy

Background: Cluster headache (CH) and Migraine (M) are distinct primary headaches differing in multiple aspects such as gender-relation, clinical features and therapies. However, CH may occur with migrainous symptoms (nausea, photophobia, phonophobia) while M can manifest itself with symptoms of trigeminal-autonomic activation. Moreover, CH and M can be comorbid. Until now some cases of patients with CH and M treated with anti-CGRP antibodies for short periods have been described.

Methods: We describe five adult patients (1 female and 4 males) with comorbidity between M and chronic CH treated with anti-CGRP antibodies (2 with Galcanezumab, 3 with Fremanezumab), for at least one year. Patients underwent baseline and quarterly follow-up visits with clinical evaluation and Migraine Disability Assessment Score Questionnaire.

Results: Fremanezumab and Galcanezumab reduced in all patients the monthly number of M days, the frequency and intensity of CH attacks and the patient's disability as measured by MIDAS. In two patients, the disappearance of CH attacks for at least three months was observed, leading to a reformulation of the diagnosis to episodic CH. No adverse events were reported by 4 patients, only the female patient reported a slight slowdown in hair growth rate after Fremanezumab but this adverse event was not so serious to interrupt the treatment.

Conclusion: Our results agree with previous studies conducted on similar case series for shorter observation periods, and demonstrate the long-term efficacy and well tolerability of anti-CGRP antibodies in case of comorbidity between M and CH. Common pathophysiological mechanisms including the Calcitonin Gene-Related Peptide role in trigeminal-vascular system activation have been proposed to explain anti-CGRP antibodies effectiveness in both CH and M. Further studies on large case series are needed to provide stronger evidence for the use of anti-CGRP mAbs as first-line therapy in CH and M comorbidity.

Aromatase inhibitors evoke periorbital allodynia in mice via CGRP and its receptors in Schwann cells

Lorenzo Landini[1], Matilde Marini[1], Daniel Souza Monteiro de Araujo[1], Martina Chieca[1], Elisa Bellantoni[1], Gaetano de Siena[1], Pasquale Pensieri[1], Pierangelo Geppetti[1], Romina Nassini[1], Francesco De Logu[1]

[1]Department of Health Sciences, Clinical Pharmacology and Oncology Section, University of Florence, Florence, Italy

Background: Aromatase inhibitors (AIs, exemestane, anastrozole and letrozole) are recommended as adjuvant endocrine therapy for postmenopausal women with receptor-positive breast cancer. About 40% of treated patients develop a widespread painful condition called AI musculoskeletal symptoms, which involves inflammatory and neuropathic components. The nitrile moieties of AIs suggest their binding to the cysteine residues of the proalgesic transient receptor potential ankyrin 1 (TRPA1) channel, resulting in mechanical allodynia. Approximately 9% of patients report insurgence or worsening of headache. Here, we investigated whether letrozole produces periorbital mechanical allodynia (PMA) in mice, and the cellular and molecular mechanism underlying this response.

Methods: C57BL6/J mice were treated with letrozole (0.05-0.5 mg/kg, oral administration), and PMA was evaluated by applying von Frey filaments to the periorbital region over the rostral portion of the eye. Some mice were pretreated (periorbital) with receptor, channel, or enzyme inhibitors. PMA was also investigated in mice with selective silencing of TRPA1 and RAMP1 receptor in Schwann cells (*PlpCreTrpa1*$^+$and *PlpCreRamp1*$^+$ mice, respectively) or trigeminal neurons (*AdvCreTrpa1*$^+$ and *AdvCreRamp1*$^+$ mice, respectively).

Results: Oral administration of letrozole dose-dependently produced PMA that was attenuated by local administration of a TRPA1 antagonist (A967079) and by a calcitonin gene related peptide (CGRP) receptor antagonist (olcegepant), whereas indomethacin was ineffective. Selective silencing of TRPA1 in Schwann cells and in trigeminal neurons (*PlpCreTrpa1*$^+$ and *AdvCreTrpa1*$^+$ mice, respectively) reduced letrozole-evoked PMA. However, only silencing of RAMP1 in Schwann cells (*PlpRamp1*$^+$ mice), and not in trigeminal neurons (*AdvCreRamp1*$^+$mice), attenuated PMA. Inhibition of the intracellular pathway known to promote PMA by CGRP action in Schwann cells, including TRPA1 (A967079) and CGRP receptor (olcegepant) antagonists and adenylyl cyclase (SQ-22536), nitric oxide synthase (L-NAME), and oxidative stress (PBN) inhibitors reduced letrozole-evoked PMA.

Conclusion: Letrozole, by targeting TRPA1 in trigeminal peptidergic (C-fibers) nerve terminals, releases CGRP that, acting on its receptors in Schwann cells, encodes a pro-algesic pathway that encompasses the release of cyclic AMP and nitric oxide that gates TRPA1. Schwann cell TRPA1 enhances and amplifies a persistent oxidative stress signal that sustains PMA by targeting the neuronal TRPA1. Thus, inhibitors of the CGRP pathway may ameliorate headache in women treated with AIs.

Three cases of Raynaud's phenomenon secondary to CGRP monoclonal antibodies

Flavia Lo Castro, Carlo Baraldi, Simona Guerzoni

Digital and Predictive Medicine, Pharmacology and Clinical Metabolic Toxicology, Headache Center and Drug Abuse, Laboratory of Clinical Pharmacology and Pharmacogenomics, Department of Specialist Medicines, AOU Policlinico di Modena, Modena, Italy

Background: Raynaud's phenomenon (RP) is a common vasospastic condition which affects ~5% of the general population, more frequent in women than in men. The majority (80–90%) of individuals have primary ('idiopathic') RP (PRP), whereas secondary RP (SRP) can occur due to different medical conditions (especially autoimmune diseases) or drug-related or even occupational causes (such as hand-arm-vibration syndrome or frostbite). The co-occurrence of migraine and RP is well known, with a prevalence of RP in 26% of migraineurs (1). Calcitonin gene-related peptide is a ubiquitous 37 amino acid neuropeptide involved in the pathogenesis of migraine and therapies targeting CGRP are currently in use as migraine prophylaxis. In addition to its role in the nervous system, CGRP confers potent vasodilatory effects. Intradermal injection of GCRP causes a persistent local associated with increased blood flow (2) and CGRP infusion was capable to relieve symptoms of patients with RP (3). Moreover, a significant reduction in the number of CGRP immunoreactive neurons in the skin of patients with PRP and those with systemic sclerosis compared to controls was found (4). Thus, CGRP antagonism could theoretically exacerbate RP.

Methods: In the Modena Headache Center, in the pharmacovigilance data collection, we have registered three cases who presented RP during anti-CGRP monoclonal antibodies therapy.

Results: Three patients (all women, with a previous diagnosis of chronic migraine, and an average age of 46.6 years) had to discontinue treatment with anti-CGRP therapy due to the occurrence of RP. All three patients were treated with erenumab, only in one of them erenumab was discontinued and galcanezumab was started, but RP has relapsed. Only one patient had a previous diagnosis of RP, while the other two worked in a cold environment without previously showing any symptoms of RP. In all three reported cases, patients responded effectively to anti-CGRP treatment (with a responder rate of 50%). After discontinuation of the medication, the RP completely resolved.

Conclusion: Our case series is not the only one in literature and a disproportional signal of RP with CGRP targeted therapy has already emerged from the World Health Organization (WHO) (5) and the United States Food and Drug Administration (FDA) (6) databases. RP, although rare in patients treated with anti-CGRP antibodies, could have serious sequalae (7). We think that a previous history of RP should be carefully considered by clinicians prescribing this class of drugs. It is emphasized that in the reported cases, the occurrence of RP appears to be, at least in one of them (the patient taking both drugs), independent of receptor or ligand blockade. Therefore, monitoring this adverse event becomes important to exclude or confirm whether it can be considered a "class effect" potentially emerging even with other CGRP antagonists.

References:

1. Zahavi I, Chagnac A, Hering R, Davidovich S, Kuritzky A. Prevalence of Raynaud's phenomenon in patients with migraine. Arch Intern Med. 1984;144(4):742-744.
2. Brain SD, Williams TJ, Tippins JR, Morris HR, MacIntyre I. Calcitonin gene-related peptide is a potent vasodilator. Nature. 1985 Jan 3-9;313(5997):54 6.
3. Bunker CB, Reavley C, O'Shaughnessy DJ, Dowd PM. Calcitonin gene-related peptide in treatment of severe peripheral vascular insufficiency in Raynaud's phenomenon. Lancet. 1993 Jul 10;342(8863):80-3.
4. Bunker CB, Terenghi G, Springall DR, Polak JM, Dowd PM. Deficiency of calcitonin gene-related peptide in Raynaud's phenomenon. Lancet. 1990 Dec 22-29;336(8730):1530-3.
5. Gérard AO, Merino D, Van Obberghen EK, Rocher F, Destere A, Lantéri-Minet M, Drici MD. Calcitonin gene-related peptide targeting drugs and Raynaud's phenomenon: a real-world potential safety signal from the WHO pharmacovigilance database. J Headache Pain. 2022 May 3;23(1):53.
6. Sun W, Li Y, Xia B, Chen J, Liu Y, Pang J, Liu F, Cheng H. Adverse event reporting of four anti-Calcitonin gene-related peptide monoclonal antibodies for migraine prevention: a real world study based on the FDA adverse event reporting system. Front Pharmacol. 2024 Jan 9;14:1257282.
7. Breen ID, Brumfiel CM, Patel MH, Butterfield RJ, VanderPluym JH, Griffing L, Pittelkow MR, Mangold AR. Evaluation of the Safety of Calcitonin Gene-Related Peptide Antagonists for Migraine Treatment Among Adults with Raynaud Phenomenon. JAMA Netw Open. 2021 Apr 1;4(4):e217934.

Investigating PACAP-38 level in migraine patients treated with anti-CGRP monoclonal antibodies

Andrea Marcinnò, Silvia Boschi, Fausto Roveta, Fabio Ferrandes, Elisa Maria Piella, Innocenzo Rainero, Elisa Rubino

Department of Neurosciences "Rita Levi Montalcini", University of Torino, Turin, Italy

Background: Anti-CGRP (Fremanezumab and Galcanezumab) and anti-CGRP receptor (Erenumab) monoclonal antibodies (mAbs) are highly effective in migraine prevention. However, there is a part of patients which are still non responder to this therapy. Pituitary adenylate cyclase activating peptide -38 (PACAP-38) is a candidate migraine biomarker and could sustain migraine physiopathology together with CGRP, representing a promising target for biological treatment. At present, there is no data regarding the effects of PACAP-38 concentrations on response to anti-CGRP therapy. We aimed to test two hypotheses: PACAP-38 is increased in patients with migraine in comparison with control subjects and PACAP-38 is a marker of low response to anti-CGRP therapy.

Methods: We enrolled forty patients (33 F, 7 M; aged 52.05 ± 12.60 years; 22 CM, 18 EM) who started mAbs therapy (7 Erenumab, 16 Galcanezumab and 17 Fremanezumab). During the first visit (T0) they underwent plasmatic PACAP-38 measurement. They were re-evaluated at 3 and 6 months (T3 and T6), based on monthly migraine days (MMD) and MIDAS. The outcomes at T3 and T6 were defined as: LR, low responders (MMD or MIDAS decrease <50%); GR, good responders (MMD or MIDAS decrease ≥50% and <75%); VGR, very good responders (MMD or MIDAS decrease ≥75%). We included a control group of 16 subjects (13 F, 3 M; aged 51.31 ± 12.48) not affected by migraine.

Results: At baseline, in comparison with controls, the patients PACAP-38 levels were significantly higher (229.91 ± 57.43 pg/ml vs 126.83 ± 43.95; p <0.001).
At T3 we observed clinical outcomes considering MMD (11 LR, 18 GR, 11 VGR) and MIDAS (0 LR, 21 GR, 19 VGR). At T6 we found 10 LR, 11 GR and 19 VGR and 2 LR, 6 GR and 32 VGR respectively. We did not find any significant difference in PACAP-38 plasmatic concentrations between LR, GR and VGR at T3 and T6. Baseline PACAP-38 concentrations did not show any significant correlations with clinical parameters at any timepoint (T0, T3 and T6).

Conclusion: CGRP signaling downregulation through mAbs and its effectiveness in migraine prevention appear to be independent from PACAP-38 plasmatic levels.

How catastrophizing attitude impacts quality of life in patients with chronic migraine treated with monoclonal anti-CGRP antibodies: a single center real-life experience

Daniele Michelis[1], Claudia Lanni[1], Federica Sepe[1], Chiara Prevost[1], Giacomo Lancia[2], Delfina Ferrandi[1]

[1]Headache Clinic, Department of Neurology, Azienda Sanitaria SS. Antonio e Biagio e Cesare Arrigo, Alessandria, Italy; [2]Mathematics Department, University of Genova, Genoa, Italy

Background: Catastrophic thinking, defined as "an exaggerated negative mindset during actual or anticipated painful experiences," plays a vital role in the chronification of pain. Our goal is to assess how pain catastrophizing, evaluated using the Italian version of the Pain Catastrophizing Scale (PCS), impacts the quality of life and contributes to disability in a group of difficult-to-treat individuals. We aim to determine if catastrophic thinking is a modifiable variable through targeted psychological interview. We are also interested in examining whether pain catastrophizing, particularly its subdimension related to rumination, affects the response to treatment with subcutaneous monoclonal anti-CGRP antibodies.

Methods: We collected sociodemographic and clinical data from 26 consecutive patients attending our headache clinic since July 2021. The patients, diagnosed with chronic migraine with or without MOH according to ICDH-3 criteria, were randomly assigned to receive Galcanezumab, Erenumab, or Fremanezumab treatments, in accordance with AIFA and EAN guidelines. Simultaneously, the patients underwent targeted psychological interview. Evaluations were conducted before treatment initiation (T0), and then after three (T1) and six months (T2). Alongside clinical data and PCS score, we also collected scores from the HIT-6 “Headache Impact Test-6” and the MIDAS “Migraine Disability Assessment Test” at each evaluation as outcome measures. Comorbid depression was assessed using the BDI II “Beck Depression Inventory II” scale. Appropriate parametric statistical tests were used based on the data type and sample size. Statistical analysis was conducted using Python 3.

Results: To date, 26 patients (3 men and 23 women) have been included, with 17 completing the T2 assessments. The migraine impact was substantial (HIT-6 ≥56) in 95% of the sample. Except for two patients (MIDAS 12), disability was severe across the sample. Initially, 47.6% of patients exhibited a clinically significant level of catastrophic thinking (PCS ≥30). A statistically significant reduction in PCS scores was observed after six months of therapy ($p<0.001$). PCS showed a mild correlation with HIT-6 (rS 0.73) but no correlation with BDI-II.

Conclusion: In our cohort of difficult-to-treat patients, characterized by significant migraine impact on quality of life and severe disability, catastrophic thinking was notably present. The combination of monoclonal antibody therapy and psychological intervention focusing on catastrophizing tendencies led to a statistically significant decrease in PCS scores and reduced the impact of migraine on quality of life.

Friday 15 Saturday 16 March 2024 HEADACHE & CGRP HOTEL ALBANI
Symposium Florence 2024
SISC

Off-label galcanezumab in episodic and chronic cluster headache: a prospective, cohort study

Antonio Munafò[1], Andrea Burgalassi[1,2], Giulia Vigani[2], Alberto Boccalini[1], Francesco De Cesaris[1], Alberto Chiarugi[1,2], Pierangelo Geppetti[2,3], Luigi Francesco Iannone[2]

[1]Headache Center and Clinical Pharmacology Unit, Careggi University Hospital, Florence, Italy; [2]Section of Clinical Pharmacology and Oncology, Department of Health Sciences, University of Florence, Florence, Italy; [3]Department of Pathobiology, School of Dentistry, New York University, NY, USA

Background: Current preventive treatments for cluster headache are often ineffective and poorly tolerated, with up to 40% of patients expressing dissatisfaction. There is some evidence implicating calcitonin gene-related peptide (CGRP) in cluster headache, but results are inconsistent so far, with fremanezumab and eptinezumab failing to demonstrate efficacy. Galcanezumab, a humanized monoclonal antibody specific for CGRP at a dosage of 300mg, is the only anti-CGRP that has demonstrated clinical benefit as a preventive treatment for episodic cluster headache (ECH), but not in chronic cluster headache (CCH). Herein, we assessed the off-label use of galcanezumab 240 mg in both ECH and CCH including treatment-naïve patients with anti-CGRP therapy and with previous ineffective preventive treatments.

Methods: Our prospective, cohort study included 21 participants (15 with ECH and 6 with CCH) eligible for off-label treatment with galcanezumab 240mg. Treatment was monitored through paper headache diaries, reporting changes in attack frequency and severity, as well as the use of symptomatic medications. Due to its explorative nature the sample size was not statistically determined, but in line with previous research. The primary outcome was the efficacy of galcanezumab on the weekly frequency of cluster attacks. Secondary outcomes included reductions in triptan and other analgesics use per week, qualitative response reported by patients with the Patient Global Impression of Change (PGIC), and whether the treatment stopped the cluster bout in ECH patients or induced periods of remission in CCH patients.

Results: CCH patients showed only a slight decrease in the mean attack frequency of -7.2 attacks (range: 0 to -23; p=0.45) per week. Likewise, a marginal reduction in sumatriptan subcutaneous (sc) use was reported, with a decrease of -5.2 (range: 0 to -23; p=0.52). Conversely, ECH patients exhibited a modest but statistically significant decline in the mean attack frequency of -5.6 attacks (range: 0 to -33.5; p=0.018) per week along with a subtle reduction in sumatriptan sc use (-1.12; range: 0 to -8.75; p=0.10). In both groups, there were no changes in the severity of the attacks, and no remission periods were induced. No adverse events, either systemic or local, were reported.

Conclusion: We confirmed the effectiveness of galcanezumab in reducing weekly CH attack frequency among patients with ECH but not in CCH, consistently with prior research. These results seem to endorse the off-label use of galcanezumab in ECH, but further studies are needed to confirm its efficacy.

Friday 15 Saturday 16 March 2024 HEADACHE & CGRP HOTEL ALBANI
Symposium Florence 2024
SISC

An evolving machine-learning-based algorithm to early predict response to anti-CGRP monoclonal antibodies in patients with migraine

Marina Romozzi[1], Ammar Lokhandwala[2], Catello Vollono[1], Giulia Vigani[3], Andrea Burgalassi[3,4], David García-Azorín[5], Paolo Calabresi[1], Alberto Chiarugi[3,4], Pierangelo Geppetti[3,6], Luigi Francesco Iannone[3]

[1]Dipartimento Universitario di Neuroscienze, Università Cattolica del Sacro Cuore, Rome, Italy; [2]YPrime, Philadelphia, PA, USA; [3]Section of Clinical Pharmacology and Oncology, Department of Health Sciences, University of Florence, Florence, Italy; [4]Headache Center and Clinical Pharmacology Unit, Careggi University Hospital, Florence, Italy; [5] Headache Unit, Department of Neurology, Hospital Clinico Universitario de Valladolid, Valladolid, Spain; [6]Department of Pathobiology, School of Dentistry, New York University, NY, USA

Background: The study aimed to determine whether machine-learning (ML)-based models can predict 3-, 6-, and 12-month responses to the monoclonal antibodies (mAbs) against the calcitonin gene-related peptide (CGRP) or its receptor (R) (anti-CGRP/R mAbs) in patients with migraine using early predictors (up to 1 month) and to create an evolving prediction tool.

Methods: In this prospective cohort study, data from patients with migraine who had received anti-CGRP/R mAbs for 12 months were collected. Demographic and monthly clinical variables were collected, including monthly headache days (MHDs), days with acute medication use (AMDs), number of analgesics (AMNs), and Headache Impact Test-6 (HIT-6). Response rates were categorized as ≤25%, 26-50%, 51-75%, and >75% reduction in MHDs. ML models were trained using random forest algorithm and optimized to maximize the F1 score. ML models' performance was also evaluated using standard evaluation metrics, including accuracy, precision, and area under the receiver operating characteristic curve (AUC-ROC). Sequential backward feature selection was employed to identify the most relevant predictors for each model. Each model was given 11 baseline data inputs and month-based predictors for months 1, 3 and 6.

Results: Three hundred thirty-six patients treated with anti-CGRP/R mAbs were included. We developed 6 models to predict 3-, 6-, and 12-month responses using early predictors. ML-based models yielded predictions with an F1 score of 0.44-0.71 and an AUC-ROC score of 0.6-0.78. Shapley Additive explanations summary plots were generated to interpret the contribution of each feature for each model. Based on these findings, a response prediction tool was developed. Each model was run through a backward feature selection to find the most relevant features for the models. The MHDs reduction of the previous data point tends to be the most relevant, while the migraine with aura indicator tends to be the least effective predictor.

Conclusion: The response prediction tool utilizing evolving ML-based models holds promise in the early prediction of treatment outcomes for patients with migraine undergoing anti-CGRP/R mAbs treatment, aiding in clinical decision-making and cost-optimization.

Intermittent Theta Burst Stimulation in the treatment of Chronic Migraine Refractory to monoclonal antibodies: A case study

S. Scannicchio[1], L. Clemente[1], G. Paparella[1], G. Tancredi[1], C. Abbatantuono[1], E. Ladisa[1], M.P. Prudenzano[2], M. de Tommaso[1]

[1]Department of Translational Biomedicine and Neuroscience (DiBraiN), University of Bari Aldo Moro, Bari, Italy; [2]Headache Centre, "L. Amaducci" Neurological Clinic, Bari General Hospital, Bari, Italy

Background: Repetitive Transcranial Magnetic Stimulation (rTMS) is a non-invasive neurostimulation technique that has been successfully used to treat various pathologies, including those that are resistant to pharmacological approaches. Intermittent theta burst stimulation (iTBS), a specific modality of rTMS, offers an innovative approach due to its short and intense stimulation patterns, which aim to effectively modulate brain activity. Chronic migraine, which is characterized by frequent and debilitating headache episodes, poses a significant clinical challenge. Therefore, new therapeutic solutions are being explored, such as iTBS, which promises to address this condition by modulating the neural networks involved.

Methods: We report a case of a 74-year-old man with 50 years of diagnosed Chronic Migraine. NetBrain Neuronavigator was used to accurately target the left dorsolateral prefrontal cortex (DLPFC). The treatment protocol consisted of 20 iTBS sessions spread over four days with five sessions per day, resulting in a total of 32,400 stimuli. Three clinical evaluations separated by one month were performed to assess the stability of clinical, behavioural, and cognitive patterns at baseline, post Sham and post Real treatment. The clinical and cognitive assessment investigated various areas, including the frequency of headaches in a month, medication usage, quality of life, and performance in tests measuring executive functions.

Results: Following the sham treatment, improvements were observed in several clinical and cognitive scores compared to baseline, indicating an initial positive effect. These improvements mainly concerned performance in tests of executive functions, however, there was no reduction in the frequency of migraine episodes. After the treatment, there was a significant improvement in most scores, combined with a decrease in the number of headache days and improved performance in various cognitive tests.

Conclusion: This case study highlights the potential effectiveness of iTBS stimulation in the treatment of chronic migraine. The results suggest that although sham treatment may induce initial improvements, especially in cognitive functions, it is the real stimulation that produces the most significant changes, including a marked reduction in the frequency of migraine episodes. These improvements provide new perspectives on the implementation of iTBS protocols in chronic migraine, placing it in the current scientific landscape as a potential therapeutic value.

Efficacy of galcanezumab in PRRT2-associated Familial Hemiplegic Migraine: a case series

Costanza Sottani[1], Giulia Di Lazzaro[1,2], Paolo Calabresi[1,2], Maria Grazia Pomponi[3], Francesco Danilo Tiziano[3,4], Anna Rita Bentivoglio[1,2], Serenella Servidei[1,2], Catello Vollono[1,2]

[1]Neurology Section, Department of Neuroscience, Università Cattolica del Sacro Cuore, Rome, Italy; [2]UOC Neurologia, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy; [3]UOC Genetica Medica, Fondazione Policlinico Universitario "A. Gemelli" IRCCS, Rome, Italy; [4]Section of Genomic Medicine, Department of Public Health and Life Sciences, Università Cattolica del Sacro Cuore, Rome, Italy

Background: Migraine is a paroxysmal disorder characterized by recurrent episodes of pulsating, typically unilateral headache, associated with nausea, vomiting, photophobia and phonophobia. Migraine is categorized into two main subtypes: migraine without aura (MO) and migraine with aura (MA). Hemiplegic migraine (HM) is a rare subtype of MA. Recent studies suggest that, other than variants in *CACNA1A*, *ATP1A2*, and *SCN1A* genes, two additional genes may be implicated in the pathogenesis of HM: *PPRT2* and *SLC1A3*. Aim of the present work is to describe the efficacy of galcanezumab as a prophylaxis treatment on patients from an Italian family carrier of a PRRT2 pathogenic variant, a c.649dupC frameshift variant in heterozygosis.

Methods: Inclusion criteria for treatment eligibility consisted of a confirmed diagnosis of HM as defined by the International Classification of Headache Disorders 3rd Edition (ICHD-III), a number of headache days/month≥4 and at least two previously failed migraine prophylaxis treatment. We collected patients' data on migraine onset, aura characteristics, presence of other PRRT2-associated disorders and previously failed prophylaxis. We investigated number of headache days/month, frequency of aura, Migraine Disability Assessment (MIDAS), attacks severity through Numerical Rating Scale (NRS), acute medications intake and response to acute medications in eligible patients at baseline (t0) and after three months of treatment (t1).

Results: Three patients out of the six relatives met the inclusion criteria for treatment with galcanezumab. The average number of headache days/month reduced in all three patients from n=11.7±2.08(t0) to n=1.67±1.15 (t1) (p=0.002). Patient 3 has not experienced aura symptoms since the beginning of the treatment. Patient 1 had one aura during the observational period. Patient 2 had 4 aura episodes. Mean drugs intake/month went from n=12.7±2.08 (t0) to n=2.67±0.58 (t1) (p=0.001). Mean MIDAS score has lowered from MIDAS=80.3±5.03 (t0) to MIDAS=6±4.36 (t1) (p=0.0007). NRS has decreased from average NRS=9.3±1.15 (t0) to NRS=6.33±0.58 (p=0.03). No adverse events related to galcanezumab were reported during the observational period.

Conclusion: Our study shows that galcanezumab is a valid and well-tolerated treatment option in PRRT2-associated FHM. A longer observational period and careful follow-up is required to confirm the persistence of current clinical benefit and excellent tolerability experienced by our patients.

Rimegepant effectiveness and tolerability as acute migraine treatment (GAINER): a real-world multicentric study

Gloria Vaghi[1], Roberto De Icco[1], Luigi F. Iannone[2], Andrea Burgalassi[2], Michele Corrado[1], Eleonora De Matteis[3], Federico De Santis[3], Carla Fasano[2], Elisa Piella[4], Marina Romozzi[5], Gabriele Sebastianelli[6], Gianluca Avino[7], Sabina Cevoli[8], Gianluca Coppola[6], Giorgio Dalla Volta[9], Antonio Granato[10], Edoardo Mampreso[11], Francesca Boscain[11], Raffaele Ornello[3], Francesca Pistoia[3], Innocenzo Rainero[12], Michele Trimboli[13], Antonio Russo[14], Mariarosaria Valente[15], Catello Vollono[16], Cristina Tassorelli[1]

[1]Department of Brain and Behavioral Sciences, University of Pavia, Pavia, Italy; Headache Science & Neurorehabilitation Center, IRCCS Mondino Foundation, Pavia, Italy,[2]Headache Centre and Clinical Pharmacology Unit, Careggi University Hospital Florence, Florence, Italy; [3]Department of Biotechnological and Applied Clinical Sciences, University of L'Aquila, L'Aquila, Italy; [4]Department of Neurosciences "Rita Levi Montalcini", University of Torino, Turin, Italy; [5]UOC Neurologia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; [6]Sapienza University of Rome Polo Pontino ICOT, Department of Medico-Surgical Sciences and Biotechnologies, Latina, Italy; [7]Ospedale di Prato Santo Stefano, Prato, Italy; [8]IRCCS Istituto delle Scienze Neurologiche Bologna, Bologna, Italy; [9]Headache Centre of Istituto Clinico Città di Brescia (gruppo SAN DONATO), Brescia, Italy; [10]Azienda Ospedaliero-Universitaria di Trieste, Trieste, Italy; [11]Headache Centre, Neurology, Euganea Health Unit, Padua, Italy; [12]Headache Center, Department of Neuroscience, University of Torino, Turin, Italy; [13]Centro Interaziendale Cefalee, Azienda Ospedaliero-Universitaria Renato Dulbecco, Catanzaro, Italy; [14]Department of Advanced Medical and Surgical Sciences, University of Campania "Luigi Vanvitelli", Naples, Italy; [15]Azienda Sanitaria Universitaria Friuli Centrale, Presidio Ospedaliero Santa Maria della Misericordia, Udine, Italy; [16]Department of Neurosciences, Università Cattolica del Sacro Cuore, Rome, Italy

Background: Rimegepant is a novel calcitonin gene-related peptide receptor antagonist. It has been recently approved in Italy for acute migraine treatment. We designed a prospective multicentric study to evaluate rimegepant effectiveness and tolerability as acute migraine treatment in the real-world setting.

Methods: We enrolled 87 patients (76% females, 44.3+11.7 years, 28% with chronic migraine, baseline monthly migraine days 9.4+7.8) from 13 Italian headache centres. Patients were instructed to treat up to four migraine attacks with rimegepant 75 mg. Using an ad hoc diary, we prospectively collected migraine-attack features every 30 minutes after rimegepant administration, up to 2 hours (2h).

Results: Preliminary analyses were conducted on 43 reported first-treated attacks (8/43 in CM patients), and 91 total attacks. At rimegepant intake, 38.5% of patients rated migraine intensity as severe (on a 0-3 rating scale). Pain freedom 2h post-dose was reported in 58.1% (25/43) of first-treated attacks, and in 53.8% (49/91) of total attacks. The 2h pain freedom response was not

influenced by timing of rimegepant intake (p=0.204), baseline pain severity (p=0.171) and the presence of chronic vs episodic migraine (p=0.626). Freedom from the most bothersome symptom 2h post-dose was reported in 60.4% of attacks. Mild adverse events were reported in 18% total attacks (8/91) as gastrointestinal discomforts (n=4), fatigue (n=2), dizzinesss (n=1) and somnolence (n=2). Tolerability was rated as good-to-excellent in 92.3% cases (84/91).

Conclusion: Our real-world data support rimegepant effectiveness, safety, and tolerability in the acute migraine treatment. In this population, rimegepant effectiveness was not influenced by pain severity and timing of drug intake.

Effectiveness and safety of monthly versus quarterly fremanezumab for migraine prevention: an Italian, multicenter, real-life study

L. Zanandrea[1,2,3], R. Messina[1,2,3], I. Cetta[1,2,3], F. Genovese[1,2,3] S. Guerrieri[1], F. Vernieri[4,5], C. Altamura[4,5], S. Cevoli[6], V. Favoni[6], B. Colombo[1], M. Filippi[1,2,3]

[1]Neurology Unit and [2]Neuroimaging Research Unit, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy; [3]Vita-Salute San Raffaele University, Milan, Italy; [4]Unit of Headache and Neurosonology, Department of Medicine and Surgery, University Campus Bio-Medico di Roma and [5]Fondazione Policlinico Universitario Campus Bio-Medico, Rome, Italy; [6]IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Background: Fremanezumab, a monoclonal antibody targeting the calcitonin gene-related peptide for migraine prevention, is available in monthly (225 mg) and quarterly (675 mg) subcutaneous doses. Previous studies demonstrated that both regimens are effective and safe, but a real-life direct comparison is lacking. This study aimed to compare the effectiveness and safety of monthly and quarterly fremanezumab in a real-life setting.

Methods: This Italian, prospective, multicenter study enrolled 95 migraine patients. During a three-month treatment period, patients received either monthly or quarterly fremanezumab (49 monthly, 46 quarterly). A six-month treatment period involved 79 patients (43 monthly, 36 quarterly). Monthly headache (MHD) and migraine days (MMD), number of days (AMD) and pills (AMP) of acute medication intake, Headache Impact Test (HIT-6), Migraine Disability Assessment Test (MIDAS) and Numeric Rating Scale (NRS) scores were recorded at baseline, after three and six months of treatment. Adverse events (AEs), responder rates and medication overuse were also investigated.

Results: Both monthly and quarterly treatments led to significant reductions in MMD, MHD, AMP, AMD, HIT6, MIDAS and NRS scores after three and six months. The monthly regimen exhibited a slightly greater reduction in MMD and MHD after the first quarter, with no significant difference observed after six months. The most common AE was transient injection-site reaction without between-group differences. Responder rates and resolution of medication overuse did not significantly differ between the groups.

Conclusions: Both monthly and quarterly regimen were effective and safe, with a tendency for an advantage of the monthly regimen only in the first quarter of treatment.